UK Renal Registry 19th Annual Report: Chapter 7 Haemoglobin, Ferritin and Erythropoietin amongst UK Adult Dialysis Patients in 2015: National and Centre-specific Analyses

Daniel Ford^a, Julie Gilg^b, Andrew J Williams^c

^aUniversity Hospital Coventry and Warwickshire, Coventry, UK; ^bUK Renal Registry, Bristol, UK; ^cMorriston Hospital, Swansea, UK

Keywords

Anaemia · Chronic kidney disease · Dialysis · End stage renal disease · Epidemiology · Erythropoietin · Erythropoiesis stimulating agent · European Best Practice Guidelines · Ferritin · Haemodialysis · Haemoglobin · NICE · Peritoneal dialysis · Renal Association

Summary

In the UK in 2015:

- The median haemoglobin (Hb) of patients at the time of starting dialysis was 98 g/L with 47% of patients having a Hb ≥ 100 g/L.
- The median Hb in patients starting haemodialysis (HD) was 96 g/L (IQR 87–105) and in patients starting peritoneal dialysis (PD) was 107 g/L (IQR 98–116).
- At the start of dialysis 51% of patients presenting early had Hb ≥ 100 g/L compared with only 34% of patients presenting late.

- The median Hb of prevalent patients on HD was 110 g/L (IQR 101–119).
- The median Hb of prevalent patients on PD was 112 g/L (IQR 103–120).
- 79% of HD patients and 81% of PD patients had Hb ≥ 100 g/L.
- 59% of HD patients and 57% of PD patients had Hb ≥ 100 and ≤ 120 g/L.
- The median serum ferritin in HD patients was 415 $\mu\text{g/L}$ and 94% of HD patients had a ferritin ≥ 100 $\mu\text{g/L}$.
- The median serum ferritin in PD patients was 295 $\mu\text{g/L}$ and 88% of PD patients had a ferritin ≥ 100 $\mu\text{g/L}$.

In England, Wales and Northern Ireland in 2015:

- The median erythropoiesis stimulating agent (ESA) dose in HD patients was 7,500 IU/week.
- The median ESA dose in PD patients was 4,000 IU/week.

Introduction

Anaemia is a common feature of chronic kidney disease (CKD) and when untreated is strongly associated with poor outcomes resulting in increased hospitalisations and mortality. This chapter describes analyses of the management of anaemia in dialysis patients in the UK in 2015.

A number of clinical practice guidelines exist for the management of anaemia in patients with CKD. The Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Anemia in Chronic Kidney Disease was published in August 2012 [1]. Commentaries and position statements on this document were made by both the Kidney Disease Outcomes Quality Initiative (KDOQI), and the European Renal Best Practice Guidelines Group (ERBP) [2, 3]. The Renal Association Clinical Practice Guideline for Anaemia of CKD (5th edition) was published in 2010 with the 6th edition expected in 2017 [4]. The National Institute for Health

and Care Excellence (NICE) Clinical Guideline on Chronic Kidney Disease: Managing Anaemia was published in June 2015, mid-way through the data collection period [5].

This chapter reports on the analyses of data items collected by the UK Renal Registry (UKRR) measured against the audit parameters set in the Renal Association Clinical Practice Guideline (5th edition) [4]. Table 7.1 lists the audit measures recommended in these guidelines alongside those parameters measured in this chapter and reasons for exclusion.

Methods

Most of the analyses in this chapter use the incident or prevalent renal replacement therapy (RRT) cohorts for 2015. Some analyses use data from earlier years. Haemoglobin levels are given in g/L as the majority of UK laboratories have now switched to reporting using these units rather than g/dl.

Table 7.1. Summary of recommended Renal Association audit measures

RA audit measure	Included in UKRR annual report?	Reason for exclusion
1. Proportion of CKD patients with eGFR <30 ml/min by 4 variable MDRD method with an annual Hb level	No	Data not available for the period covered by this report
2. Proportion of patients starting an ESA without prior measurement of serum ferritin and/or TSAT	No	UKRR does not know when all patients start ESA treatment. UKRR does not collect TSAT data
3. Proportion of patients on renal replacement therapy with Hb level <10 who are not prescribed an ESA	Yes	
4. Each renal unit should audit the type, route and frequency of administration and weekly dose of ESA prescribed	UKRR reports the completeness of these data items	
5. The proportion of CKD stage 4–5 patients with Hb 10–12 g/dl	No	Data not available for the period covered by this report
6. The proportion of patients treated with an ESA with Hb >12 g/dl	Yes	
7. Each renal unit should monitor ESA dose adjustments	No	UKRR does not collect this data
8. Proportion of patients with serum ferritin levels <100 ng/ml at start of treatment with ESA	No	UKRR does not know when all patients start ESA treatment
9. Proportion of pre-dialysis and PD patients receiving iron therapy; type: oral vs. parenteral	No	Data not available for the period covered by this report/poor data completeness
10. Proportion of HD patients receiving IV iron	No	Poor data completeness
11. Prevalence of resistance to ESA among renal replacement therapy patients	Yes	
12. Proportion of HD patients who received a blood transfusion within the past year	No	Data held at NHS Blood and Transplant

The UKRR extracted quarterly data electronically from renal centres in England, Wales and Northern Ireland (E,W&NI) taking the latest available result from each quarter. Data from Scotland were provided by the Scottish Renal Registry (SRR).

For the analyses of Hb for incident patients, those patients commencing RRT on PD or HD were included whilst those receiving a pre-emptive transplant were excluded. Hb measurements from after starting dialysis but still within the same quarter of the year were used. Therefore, depending on when in the quarter a patient started RRT the Hb data could be from zero to 90 days later. Due to possible deficiencies with extract routines it is possible that a small number of the values extracted electronically may actually be from before the person started dialysis. This problem will not occur for Scottish data. Patients who died within the first 90 days on treatment were excluded. Results are also shown with the cohort subdivided into early and late presenters (date first seen by a nephrologist, 90 or more days and less than 90 days before starting dialysis respectively). For these analyses only centres with at least 75% completeness of presentation time data were included.

For the analyses of prevalent dialysis patients those patients receiving dialysis on 31st December 2015 were included if they had been on the same modality of dialysis in the same centre for at least three months. In order to improve completeness, the last available measurement for each patient from the last two quarters was used for Hb and from the last three quarters for ferritin.

The completeness of data items was analysed at both centre and country level. All patients were included in analyses but centres with less than 50% completeness were excluded from the caterpillar and funnel plots showing centre level results. Centres providing relevant data from less than 10 patients were also excluded from the plots. The number preceding the centre name in the caterpillar plots is the percentage of patients who have data missing.

Summary statistics including minimum, maximum, inter-quartile ranges (IQR), averages (mean and median) and standard deviations were calculated. The median values and the IQRs are shown using caterpillar plots. The percentages achieving standards were also calculated and these are displayed using caterpillar plots with the percentages meeting the targets and 95% confidence intervals (CIs) shown. Funnel plots show the distribution of the percentages meeting the targets and also whether any of the centres were significantly different from the average. Longitudinal analyses were performed to show overall changes in achievement of standards over time.

Erythropoietin data from the last quarter of 2015 were used to define which patients were receiving erythropoietin stimulating agents (ESAs). Scotland was excluded from this analysis as data about ESAs were only available for May (and average doses over the year were used here – see later). Each individual was defined as being on ESA if a drug type and/or a dose was present in the data. Centres reporting fewer than 60% of HD patients or fewer than 40% of PD patients being treated with ESAs were considered to have incomplete data and were excluded from further analysis. It is recognised that these exclusion criteria are relatively arbitrary but they are in part based upon the frequency distribution graph of centres' ESA use as it appears in the data. The percentage of patients on ESAs was calculated from these data and incomplete data returns risk seriously impacting on any conclusions drawn.

For analyses of ESA dose, values are presented as weekly erythropoietin dose. Doses of less than 150 IU/week (likely to be

darbepoietin) were harmonised with erythropoietin data by multiplying by 200. No adjustments were made with respect to route of administration. Patients who were not receiving ESAs were not included in analyses of dose (rather than being included with dose = 0). Many centres provided data on ESA dose but not on ESA frequency. The ESA dose field is defined as the weekly dose and the dose is presumed to have been converted accordingly on submission to the UKRR. This may be an incorrect assumption for a number of patients and this needs to be considered when interpreting the ESA information.

Starting with the cohort of patients receiving ESAs in the final quarter of the year and having a dose value present for that quarter, any further dose values available from the earlier three quarters of the year were used (provided the patient was on the same treatment and receiving the same drug in those quarters). The average (mean) of the available values was then used in analyses rather than the dose in the final quarter.

The ESA data were collected electronically from renal IT systems but in contrast to laboratory linked variables the ESA data required manual data entry. The reliability depended upon the data source, whether the entry was linked to the prescription or whether the prescriptions were provided by the primary care physician. In the latter case, doses may not be as reliably updated as the link between data entry and prescription is indirect.

Results

Anaemia management in incident dialysis patients

Haemoglobin in incident dialysis patients

As the UKRR does not collect comprehensive data on patients who are not yet receiving RRT Hb at the time of starting RRT is the only indication of concordance with anaemia clinical practice guidelines in the pre-dialysis (CKD not (yet) on dialysis) group. The percentage data returned and outcome Hb are listed in table 7.2. Cambridge was unable to submit any data prior to closing the database. About 33% of Sheffield's incident patients' data were entirely missing from the data extracts, including all their late presenters, so the cohort included is possibly not representative of all their incident dialysis patients. Stevenage did not submit any Hb data except for the first quarter of the year. The cause of this extraction problem has now been resolved and Stevenage are submitting Hb data for 2016.

The median Hb of patients at the time of starting dialysis in the UK in 2015 was 98 g/L. The median Hb for patients at the time of starting dialysis by renal centre is shown in figure 7.1. The percentage of patients starting dialysis with Hb ≥ 100 g/L is shown in figure 7.2. Using data from centres with adequate completeness for date of first presentation the difference in median Hb between early (100 g/L) and late (92 g/L) presenters is shown in

Table 7.2. Haemoglobin data for incident patients starting RRT on haemodialysis or peritoneal dialysis during 2015, both overall and by presentation time

Centre	All incident dialysis patients			Early presenters (≥ 90 days)		Late presenters (< 90 days)	
	% data return	Median Hb g/L	% Hb ≥ 100 g/L	Median Hb g/L	% Hb ≥ 100 g/L	Median Hb g/L	% Hb ≥ 100 g/L
England							
B Heart	100	94	34	94	34		
B QEH	100	99	48	99	49	95	43
Basldn	98	89	25	98	33		
Bradfd	91	96	37	96	38		
Brightn	100	101	51	101	51	101	53
Bristol	100	105	78	104	79	104	73
Camb	n/a						
Carlis	100	109	72	110	77		
Carsh	100	97	40				
Chelms	100	106	66	107	67		
Colchr	72	97	39				
Covnt	98	96	47	100	50	95	39
Derby	98	100	51	100	53		
Donc	100	100	53	105	62		
Dorset	97	103	54	105	67	87	8
Dudley	95	103	56	104	59		
Exeter	100	106	80	106	80	104	73
Glouc	98	103	58	103	58		
Hull	77	100	51	102	55	94	39
Ipswi	93	99	50				
Kent	99	95	37	95	38	87	27
L Barts	100	98	44				
L Guys	100	92	25	94	30	85	0
L Kings	97	96	38	97	41	91	26
L Rfree	98	100	50	100	52	96	41
L St.G	86	92	29				
L West	90	104	62	105	66	97	44
Leeds	97	94	34	95	37	85	14
Leic	99	95	38	96	39	89	32
Liv Ain	97	99	48	102	52	93	30
Liv Roy	99	98	48	100	51	93	35
M RI	97	97	44	99	48	91	29
Middlbr	99	99	49	100	53	86	33
Newc	99	99	44	99	48	92	24
Norwch	99	96	37				
Nottm	99	92	32	92	33	81	8
Oxford	100	97	44	99	48	87	20
Plymth	100	100	52	108	65		
Ports	99	100	52				
Prestn	100	99	46	99	49	97	35
Redng	99	100	53	102	63	83	8
Salford	100	96	38				
Sheff*	100	100	51	100	51		
Shrew	98	102	57				
Stevng	26						
Sthend	100	96	43	97	45		
Stoke	97	101	56	102	59	94	38
Sund	97	99	48	99	47		
Truro	100	103	59	103	64	96	47
Wirral	96	99	48				
Wolve	96	93	40	97	44	80	21
York	92	97	43	98	47	95	30

Table 7.2. Continued

Centre	All incident dialysis patients			Early presenters (≥ 90 days)		Late presenters (< 90 days)	
	% data return	Median Hb g/L	% Hb ≥ 100 g/L	Median Hb g/L	% Hb ≥ 100 g/L	Median Hb g/L	% Hb ≥ 100 g/L
N Ireland							
Antrim	100	103	63	103	59		
Belfast	96	104	60	103	54	107	70
Newry	96	103	56	103	55		
Ulster	100	107	63	105	65		
West NI	100	100	52				
Scotland							
Abrdn	90	98	42				
Airdrie	67	94	34				
D&Gall	50						
Dundee	83	99	49				
Edinb	61	95	41				
Glasgw	72	96	39				
Inverns	97	102	59				
Klmarnk	67	97	31				
Krkcldy	74	99	50				
Wales							
Bangor	100	99	44	99	48		
Cardff	98	101	54	101	53	95	41
Clwyd	96	100	52				
Swanse	97	97	47	99	49	96	36
Wrexm	97	99	47	102	55		
England	96	98	47	100	51	92	33
N Ireland	98	103	59	103	58	108	65
Scotland	74	97	42				
Wales	98	100	50	100	52	95	33
UK	94	98	47	100	51	92	34

n/a: not available

Blank cells: centres excluded from the analysis due to poor data completeness or low patient numbers

*Sheffield: approximately 33% of their incident patients were missing from the analysis, including all late presenters so the group analysed may not be representative of their whole cohort

Fig. 7.1. Median haemoglobin for incident dialysis patients at start of dialysis treatment in 2015

Fig. 7.2. Percentage of incident dialysis patients with Hb ≥ 100 g/L at start of dialysis treatment in 2015

table 7.2. Of early presenters, 51% had a Hb ≥ 100 g/L compared with 34% of late presenters.

Again, there is a substantial difference between Hb at the time of starting dialysis by modality. Patients starting on HD had a median Hb of 96 g/L (IQR 87–105) whilst those starting on PD had a median Hb of 107 g/L (IQR 98–116). Of HD patients, 40% started dialysis with a Hb ≥ 100 g/L compared with 73% of PD patients.

Incident dialysis patients from 2014 were followed for one year and the median haemoglobin and percentage with ≥ 100 g/L in survivors on the same treatment at the same centre were calculated for each quarter. Only patients with Hb data for each of the four time points were included in this analysis. Results by modality and length of pre-dialysis care are shown in figures 7.3 and

7.4. The ‘PD-late’ group consisted of only 30 patients so care should be taken in interpreting the results.

The distribution of Hb ranges in incident dialysis patients by year of start is shown in figure 7.5. The proportion of incident dialysis patients with Hb ≥ 120 g/L has fallen from 17.2% in 2006 to 8.4% in 2015. In contrast, the proportion of patients starting dialysis with Hb < 100 g/L has increased from 40.0% in 2006 to 53.2% in 2015.

The proportion of patients receiving an ESA by length of time on dialysis for patients starting dialysis in 2014 is shown in figure 7.6. The difference in ESA use between early and late starters was reduced substantially after six months of treatment. Only 11 patients presenting late to dialysis and starting on PD had ESA data so this group has not been included in the analysis.

Fig. 7.3. Median haemoglobin, by time on dialysis and length of pre-RRT care, for incident dialysis patients in 2014

Fig. 7.4. Percentage of incident dialysis patients in 2014 with Hb ≥ 100 g/L by time on dialysis and by length of pre-RRT care

Fig. 7.5. Distribution of haemoglobin in incident dialysis patients by year of start

Anaemia management in prevalent dialysis patients

Compliance with data returns for Hb and serum ferritin are shown in table 7.3. Data completeness was generally good for Hb and ferritin. Cambridge did not

Fig. 7.6. Percentage of incident dialysis patients in 2014 on ESA, by time on dialysis and by length of pre-RRT care

submit any data prior to closing the database. Stevenage did not submit any Hb data except for the first quarter of the year. This Q1 data has been shown in tables 7.4 and 7.5 but not used in the figures. Salford did not submit any ferritin data. Percentages of patients reportedly receiving ESAs are shown in table 7.3. These are as

Table 7.3. Percentage completeness of data returns for haemoglobin and serum ferritin and percentages on ESA for prevalent HD and PD patients in 2015

Centre	HD				PD			
	N	Hb	Ferritin	% on ESA	N	Hb	Ferritin	% on ESA
England								
B Heart	397	100	99	78	40	100	90	55
B QEH	933	100	99	88	121	100	100	64
Basltn	153	99	99	92	27	100	100	89
Bradfd	217	100	100	94	14	100	93	86
Brightn	402	100	99	83	60	100	97	2
Bristol	489	100	100	93	47	100	96	74
Camb								
Carlisle	74	100	100	69	30	100	97	63
Carsh	761	100	99	13	101	95	92	0
Chelms	139	99	99	92	23	96	87	65
Colchr	111	95	94	5				
Covnt	332	100	100	84	76	99	96	61
Derby	222	100	100	0	73	100	97	0
Donc	163	100	100	89	18	100	100	67
Dorset	270	100	100	93	35	100	94	80
Dudley	155	100	100	3	52	100	94	2
Exeter	403	100	100	94	71	99	100	76
Glouc	216	100	96	90	28	100	93	61
Hull	327	100	100	62	66	98	98	47
Ipswi	129	100	100	67	27	100	100	0
Kent	397	100	100	94	54	100	98	46
L Barts	928	100	100	0	182	99	96	0
L Guys	629	100	100	0	29	100	93	0
L Kings	522	100	98	92	80	100	100	78
L Rfree	665	100	100	0	134	100	99	0
L St.G	311	97	96	0	45	98	100	0

Table 7.3. Continued

Centre	HD				PD			
	N	Hb	Ferritin	% on ESA	N	Hb	Ferritin	% on ESA
L West	1372	92	91	0	60	88	87	0
Leeds	470	100	100	92	50	100	100	82
Leic	839	100	100	97	95	100	98	84
Liv Ain	158	98	97	0	28	96	96	0
Liv Roy	356	100	99	0	61	100	100	0
M RI	475	94	83	0	58	98	97	0
Middlbr	323	100	99	72	15	93	93	53
Newc	285	100	100	67	38	100	95	0
Norwch	312	100	99	91	28	100	100	79
Nottm	350	99	100	87	64	100	100	73
Oxford	398	100	99	92	78	100	97	87
Plymth	129	99	97	2	28	100	100	0
Ports	617	100	99	7	60	100	97	7
Prestn	531	100	96	92	49	100	98	67
Redng	283	100	99	87	59	100	100	2
Salford	367	100	0	19	82	100	0	21
Sheff	517	100	100	88	53	100	96	42
Shrew	193	99	100	0	27	100	96	0
Stevng	468	0	99	0	13	0	85	0
Sthend	108	100	100	95	15	100	100	73
Stoke	308	98	97	1	70	100	99	0
Sund	206	100	75	90	14	93	57	71
Truro	145	100	99	0	19	100	89	0
Wirral	177	99	99	82	17	100	100	88
Wolve	286	100	99	85	68	99	99	62
York	145	100	100	91	22	95	95	73
N Ireland								
Antrim	114	100	100	94	17	100	100	76
Belfast	169	100	100	92	19	100	100	84
Newry	84	95	100	88	18	100	100	56
Ulster	97	100	100	91	6	100	100	100
West NI	113	100	100	93	9	100	100	89
Scotland								
Abrdn	205	100	97		21	100	95	
Airdrie	174	100	98		8	100	100	
D&Gall	52	96	96		10	100	100	
Dundee	173	99	98		16	100	100	
Edinb	252	100	99		19	95	95	
Glasgw	545	100	100		44	100	100	
Inverns	78	99	87		13	100	100	
Klmarnk	124	100	100		33	100	100	
Krkldy	132	100	98		16	100	88	
Wales								
Bangor	78	100	100	81	13	100	100	15
Cardff	460	100	100	43	72	100	81	15
Clwyd	76	100	100	47	13	100	85	15
Swanse	342	100	100	93	55	100	93	62
Wrexm	99	100	100	30	33	100	100	6
England	19,163	97	96		2,604	99	94	
N Ireland	577	99	100		69	100	100	
Scotland	1,735	100	98		180	99	98	
Wales	1,055	100	100		186	100	89	
UK	22,530	97	96		3,039	99	94	

Blank cells denote centres with no PD patients or because data were not available

Percentages of patients receiving ESA are shown but centres with less than 60% HD patients or 40% PD patients on ESA have been excluded (see text). Therefore, country averages are not shown – these can be found in tables 7.4 and 7.5

Table 7.4. Summary statistics for haemoglobin, serum ferritin and ESA for prevalent HD patients in 2015

Centre	N with Hb data	Median Hb g/L	% Hb ≥ 100 g/L	% Hb 100–120 g/L	Median ferritin $\mu\text{g/L}$	% ferritin ≥ 100 $\mu\text{g/L}$	% ferritin >200 and ≤ 500 $\mu\text{g/L}$	% on ESA	Median ESA dose (IU/week)	% with Hb ≥ 100 g/L and not on ESA
England										
B Heart	396	109	76	57	295	92	58	78	6,667	20
B QEH	929	109	75	61	392	95	61	88	6,000	10
Basldn	152	110	77	60	294	91	72	92	7,000	7
Bradfd	217	109	77	54	474	95	42	94	7,000	4
Brightn	402	110	79	54	478	98	46	83	5,350	15
Bristol	489	112	92	69	540	95	35	93	8,000	7
Camb										
Carlis	74	114	85	53	745	95	16	69	5,333	30
Carsh	760	109	79	65	330	93	65			
Chelms	138	113	87	60	614	97	22	92	10,625	7
Colchr	105	112	90	68	532	96	38			
Covnt	332	106	69	59	396	96	61	84	9,000	13
Derby	221	115	86	59	485	96	38			
Donc	163	108	70	56	403	94	50	89	6,000	11
Dorset	270	112	86	64	452	99	55	93	7,000	7
Dudley	155	115	85	55	325	94	61			
Exeter	403	112	95	73	296	92	60	94	6,500	6
Glouc	216	109	79	65	421	91	45	90		10
Hull	326	113	81	55	389	96	58	62	5,000	30
Ipswi	129	112	82	67	539	96	36	67	7,385	29
Kent	395	109	76	56	418	90	37	94	8,875	6
L Barts	928	111	82	64	635	96	23			
L Guys	629	109	75	61	481	93	35			
L Kings	522	107	76	64	452	94	38	92	8,000	8
L Rfree	665	109	77	61	527	95	36			
L St.G	302	107	73	60	429	94	50			
L West	1,266	113	86	65	321	94	59			
Leeds	470	108	74	61	482	95	42	92	5,250	7
Leic	839	111	77	51	338	94	62	97	6,000	2
Liv Ain	155	108	70	54	407	86	34			
Liv Roy	355	112	81	55	332	88	43			
M RI	448	111	76	54	347	94	56			
Middlbr	323	111	78	57	939	97	18	72	5,250	24
Newc	285	111	79	55	347	90	43	67	13,267	29
Norwch	312	115	80	49	484	91	34	91	9,500	9
Nottm	346	110	80	61	496	97	44	87	7,500	13
Oxford	396	108	72	56	291	89	51	92	12,000	8
Plymth	128	111	78	57	741	93	21			
Ports	616	113	81	54	394	93	51			
Prestn	531	109	76	56	594	95	29	92		8
Redng	283	114	78	49	477	98	43	87	13,154	7
Salford	366	110	77	57						
Sheff	515	111	76	51	468	95	46	88	7,500	10
Shrew	192	116	86	52	348	94	61			
Stevng ^a		108 ^a	76 ^a	61 ^a	667	98	23			
Sthend	108	108	80	71	315	95	81	95	9,250	4
Stoke	301	111	80	58	267	90	45			
Sund	205	112	77	51	344	94	40	90	9,615	9
Truro	145	106	76	66	408	99	59			
Wirral	176	109	83	68	432	95	52	82	9,000	16
Wolve	285	114	84	50	459	92	43	85	8,000	14
York	145	110	81	68	400	96	70	91	4,833	9
N Ireland										
Antrim	114	108	75	64	392	92	51	94	7,000	6
Belfast	169	110	80	56	465	92	37	92	8,000	6
Newry	80	109	76	60	384	93	49	88	5,750	13
Ulster	97	114	87	57	672	98	14	91	5,000	9
West NI	113	111	85	62	535	95	32	93	6,667	7

Table 7.4. Continued

Centre	N with Hb data	Median Hb g/L	% Hb ≥ 100 g/L	% Hb 100–120 g/L	Median ferritin $\mu\text{g/L}$	% ferritin $\geq 100 \mu\text{g/L}$	% ferritin >200 and $\leq 500 \mu\text{g/L}$	% on ESA	Median ESA dose (IU/week)	% with Hb ≥ 100 g/L and not on ESA
Scotland										
Abrdn	205	111	83	67	602	99	34			
Airdrie	174	113	80	60	754	96	23			
D&Gall	50	111	76	50	583	100	34			
Dundee	171	111	86	66	306	85	44			
Edinb	251	115	88	55	421	91	37			
Glasgw	544	111	77	54	458	92	37			
Inverns	77	111	87	69	373	93	60			
Klmarnk	124	110	77	59	282	89	49			
Krkcdly	132	113	80	48	436	87	28			
Wales										
Bangor	78	113	82	62	514	95	36	81		15
Cardff	459	111	78	55	316	94	55			
Clwyd	76	112	84	57	350	99	72			
Swanse	342	108	76	66	283	85	46	93	10,000	6
Wrexms	99	110	84	63	508	98	34			
England	18,511	110	79	59	416	94	46	88	7,500	11
N Ireland	573	110	81	60	487	94	37	92	6,500	8
Scotland	1,728	112	81	58	447	92	37			
Wales	1,054	110	79	60	330	92	50	91	10,000	8
UK	21,866	110	79	59	415	94	46	88^b	7,500^b	11^b

Blank cells denote centres excluded from analyses due to poor data completeness or low patient numbers or because the data item was not available

^aData from Q1 only

^bESA summary results are for E, W & NI (not UK)

ESA data only shown for those centres where the percentage on ESA was 60% or more

Table 7.5. Summary statistics for haemoglobin, serum ferritin and ESA for prevalent PD patients in 2015

Centre	N with Hb data	Median Hb g/L	% Hb ≥ 100 g/L	% Hb 100–120 g/L	Median ferritin $\mu\text{g/L}$	% ferritin $\geq 100 \mu\text{g/L}$	% ferritin >100 and $\leq 500 \mu\text{g/L}$	% on ESA	Median ESA dose (IU/week)	% with Hb ≥ 100 g/L and not on ESA
England										
B Heart	40	107	78	65	208	81	72	55	6,000	35
B QEH	121	111	76	55	327	91	72	64	4,000	35
Basldn	27	104	78	78	185	81	70	89	4,250	11
Bradfd	14	109	79	64	237	85	46	86	8,000	14
Brightn	60	113	92	65	381	90	48			
Bristol	47	112	89	66	400	98	62	74	4,923	23
Camb										
Carlisle	30	113	87	63	291	83	62	63	3,333	37
Carsh	96	108	79	59	186	81	73			
Chelms	22	116	91	55	156	55	50	65	2,500	36
Colchr	n/a									
Covnt	75	109	72	55	238	86	66	61	8,000	32
Derby	73	112	79	55	408	97	58			
Donc	18	116	89	50	338	89	78	67	4,125	33
Dorset	35	113	74	54	322	97	73	80	4,000	20
Dudley	52	114	81	54	135	63	59			
Exeter	70	115	94	64	232	87	75	76	4,000	24
Glouc	28	111	86	54	147	62	46	61		29
Hull	65	111	88	75	332	97	77	47	4,000	49
Ipswi	27	109	67	37	346	85	48			
Kent	54	109	81	67	274	94	77	46	4,000	43
L Barts	180	110	80	56	280	87	59			
L Guys	29	102	52	41	207	89	78			
L Kings	80	109	76	56	215	90	81	78	4,000	21
L Rfree	134	109	79	56	613	94	34			

Table 7.5. Continued

Centre	N with Hb data	Median Hb g/L	% Hb ≥ 100 g/L	% Hb 100–120 g/L	Median ferritin $\mu\text{g/L}$	% ferritin ≥ 100 $\mu\text{g/L}$	% ferritin > 100 and ≤ 500 $\mu\text{g/L}$	% on ESA	Median ESA dose (IU/week)	% with Hb ≥ 100 g/L and not on ESA
L St.G	44	109	66	50	335	93	69			
L West	53	113	83	66	262	90	67			
Leeds	50	115	88	60	365	92	70	82	4,585	18
Leic	95	111	84	64	301	94	72	84	3,000	15
Liv Ain	27	116	89	44	492	89	44			
Liv Roy	61	113	75	43	243	92	75			
M RI	57	116	84	44	220	91	82			
Middlbr	14	118	100	71	388	93	64	53		43
Newc	38	111	82	58	455	92	50			
Norwch	28	119	86	39	306	82	54	79	4,000	21
Nottm	64	108	69	52	539	97	34	73	3,200	23
Oxford	78	110	85	67	256	89	76	87	6,000	13
Plymth	28	115	82	46	531	96	39			
Ports	60	113	92	63	412	98	62			
Prestn	49	117	88	57	433	96	48	67		33
Redng	59	113	80	56	385	95	63			
Salford	82	114	88	60						
Sheff	53	112	75	58	479	92	49	42	8,000	49
Shrew	27	108	70	52	182	85	69			
Stevng ^a		111 ^a	82 ^a	59 ^a	260	91	73			
Sthend	15	116	80	60	244	87	73	73		27
Stoke	70	114	80	50	266	93	77			
Sund	13	110	85	54				71	2,769	31
Truro	19	117	79	37	206	88	88			
Wirral	17	109	71	71	453	100	65	88	6,000	12
Wolve	67	110	72	46	158	61	55	62	5,550	31
York	21	109	67	52	362	90	71	73	3,750	19
N Ireland										
Antrim	17	109	76	76	325	94	71	76	3,000	18
Belfast	19	114	95	74	361	95	63	84	3,875	16
Newry	18	109	78	56	371	100	78	56	4,000	44
Ulster	6									
West NI	9									
Scotland										
Abrdn	21	116	76	43	222	90	66			
Airdrie	8						60			
D&Gall	10	116	100	70	321	100	90			
Dundee	16	117	94	50	442	94	56			
Edinb	18	113	78	33	205	83	67			
Glasgw	44	117	84	50	191	80	64			
Inverns	13	106	77	46	210	92	92			
Klmarnk	33	115	82	55	219	91	73			
Krkldy	16	117	94	63	256	71	29			
Wales										
Bangor	13	115	92	69	186	85	77			
Cardff	72	116	82	46	118	64	59			
Clwyd	13	108	85	62	417	91	55			
Swanse	55	112	84	60	318	90	65	62	4,125	36
Wrexm	33	112	82	58	303	88	70			
England	2,566	112	81	57	301	89	63	69	4,000	28
N Ireland	69	111	84	62	361	96	65	77	4,000	22
Scotland	179	115	84	51	237	86	66			
Wales	186	113	83	55	217	80	64	62	4,125	36
UK	3,000	112	81	57	295	88	64	69^b	4,000^b	28^b

Blank cells denote centres excluded from analyses due to poor data completeness or low patient numbers or because the data item was not available

^aData from Q1 only

^bESA summary results are for E, W & NI (not UK)

ESA data only shown for those centres where the percentage on ESA was 40% or more

Fig. 7.7. Median haemoglobin in patients treated with HD by centre in 2015

received by the UKRR. As stated in the methods section, centres returning unexpectedly low ESA returns were assumed to have had problems with data entry and/or data transfer. Centres were excluded from further ESA analyses if they reported ESA use in less than 60% of HD patients or less than 40% of PD patients.

Summary statistics for haemoglobin, serum ferritin and ESA are shown in table 7.4 for HD and 7.5 for PD.

Haemoglobin in prevalent haemodialysis patients

The median Hb of patients on HD in the UK in 2015 was 110 g/L (IQR 101–119) and is shown in table 7.4. For HD patients 79% had a Hb ≥ 100 g/L. Figure 7.7 shows the median Hb in HD patients by renal centre. Figure 7.8 shows the proportion of patients by centre with Hb

within the Renal Association guideline range (100–120 g/L) and figure 7.9 shows the distribution of Hb within, above and below this range.

Funnel plots for the percentage of patients with Hb ≥ 100 g/L (figure 7.10) and between 100–120 (figure 7.11) are shown with 95% and 99.9% confidence limits. Table 7.4 can be used to identify centres in these funnel plots.

Haemoglobin in prevalent peritoneal dialysis patients

The median Hb of patients on PD in the UK in 2015 was 112 g/L (IQR 103–120, table 7.5). For PD patients 81% had a Hb ≥ 100 g/L. Figure 7.12 shows the median Hb in PD patients by centre. Figure 7.13 shows the proportion of patients by centre with Hb within the Renal Association guideline range (100–120 g/L) and

Fig. 7.8. Percentage of HD patients with Hb ≥ 100 g/L and ≤ 120 g/L by centre in 2015

Fig. 7.9. Distribution of haemoglobin in patients treated with HD by centre in 2015

figure 7.14 shows the distribution of Hb within, above and below this range.

Figures 7.15 and 7.16 are funnel plots showing the percentage of PD patients by centre in 2015 with $Hb \geq 100$ g/L and $Hb \geq 100$ g/L and ≤ 120 g/L respectively.

Relationship between Hb in incident and prevalent dialysis patients

The relationship between the percentage of incident and prevalent patients with $Hb \geq 100$ g/L is shown in figure 7.17. As expected, all centres had a higher

percentage of prevalent patients achieving a $Hb \geq 100$ g/L than of incident patients.

Changes in achievement of $Hb \geq 100$ g/L by year of start in both incident and prevalent patients is shown in figure 7.18. This shows a continuing fall in the proportion of patients achieving a $Hb \geq 100$ g/L over the last decade.

Ferritin in prevalent haemodialysis patients

The median and IQR for serum ferritin for patients treated with HD are shown in figure 7.19. The percentages with serum ferritin ≥ 100 μ g/L, >200 μ g/L to

Fig. 7.10. Funnel plot of percentage of HD patients with $Hb \geq 100$ g/L by centre in 2015

Fig. 7.11. Funnel plot of percentage of HD patients with $Hb \geq 100$ g/L and ≤ 120 g/L by centre in 2015

Fig. 7.12. Median haemoglobin in patients treated with PD by centre in 2015

Fig. 7.13. Percentage of PD patients with Hb ≥ 100 g/L and ≤ 120 g/L by centre in 2015

Fig. 7.14. Distribution of haemoglobin in patients treated with PD by centre in 2015

Fig. 7.15. Funnel plot of percentage of PD patients with Hb ≥ 100 g/L by centre in 2015

Fig. 7.16. Funnel plot of percentage of PD patients with Hb ≥ 100 g/L and ≤ 120 g/L by centre in 2015

Fig. 7.17. Percentage of incident and prevalent dialysis patients with Hb ≥ 100 g/L by centre in 2015

Fig. 7.18. Percentage of incident and prevalent dialysis patients (1998–2015) with Hb ≥ 100 g/L

Fig. 7.19. Median ferritin in patients treated with HD by centre in 2015

$\leq 500 \mu\text{g/L}$, and $\geq 800 \mu\text{g/L}$ are shown in figures 7.20, 7.21 and 7.22 respectively. The median serum ferritin in HD patients was $415 \mu\text{g/L}$ with 94% of HD patients achieving a serum ferritin $\geq 100 \mu\text{g/L}$.

Ferritin in prevalent peritoneal dialysis patients

The median and IQR for serum ferritin for patients treated with PD are shown in figure 7.23. The percentages with serum ferritin $\geq 100 \mu\text{g/L}$, $>100 \mu\text{g/L}$ to $\leq 500 \mu\text{g/L}$, and $\geq 800 \mu\text{g/L}$ are shown in figures 7.24, 7.25 and 7.26 respectively. The median serum ferritin in PD patients was $295 \mu\text{g/L}$ with 88% of PD patients achieving a serum ferritin $\geq 100 \mu\text{g/L}$.

Erythropoiesis stimulating agents in prevalent haemodialysis patients

The median dose of ESA for prevalent HD patients in England, Wales and Northern Ireland was 7,500 IU/week

with wide variation between centres from 4,833 IU/week (York) to 13,267 IU/week (Newcastle) (table 7.4). There was very little correlation between median ESA dose and either median Hb (figure 7.27) or compliance with Hb 100–120 g/L (figure 7.28). For these analyses only patients with both Hb and ESA data were included.

Erythropoiesis stimulating agents in prevalent peritoneal dialysis patients

The median dose of ESA for prevalent PD patients in England, Wales and Northern Ireland was 4,000 IU/week (table 7.5).

ESA prescription and association with achieved haemoglobin

Figures 7.9 and 7.14 show the distribution of Hb concordance with the RA guideline (100–120 g/L). Not all patients with Hb $>120 \text{ g/L}$ are receiving ESA. The

Fig. 7.20. Percentage of HD patients with ferritin $\geq 100 \mu\text{g/L}$ by centre in 2015

Fig. 7.21. Percentage of HD patients with ferritin >200 and ≤ 500 $\mu\text{g/L}$ by centre in 2015

Fig. 7.22. Percentage of HD patients with ferritin ≥ 800 $\mu\text{g/L}$ by centre in 2015

Fig. 7.23. Median ferritin in patients treated with PD by centre in 2015

Fig. 7.24. Percentage of PD patients with ferritin ≥ 100 $\mu\text{g/L}$ by centre in 2015

Fig. 7.25. Percentage of PD patients with ferritin > 100 and ≤ 500 $\mu\text{g/L}$ by centre in 2015

Fig. 7.26. Percentage of PD patients with ferritin ≥ 800 $\mu\text{g/L}$ by centre in 2015

Fig. 7.27. Median Hb versus median ESA dose in HD patients on ESA, by centre in 2015

Fig. 7.28. Compliance with Hb 100–120 g/L versus median ESA dose in HD patients on ESA, by centre in 2015

consensus was that these patients should not be included in the group of patients not meeting this target. There are two reasons: first, the high Hb remains largely outside the control of the clinician; secondly, the trials suggesting it may be detrimental to achieve a high Hb in renal patients were based upon patients treated with ESAs [6–8]. Figures 7.29 and 7.30 therefore show the percentages of HD and PD patients in each centre whose Hb lies below, within or above the RA guideline range. For those patients with Hb >120 g/L it also differentiates between those receiving, or not, ESAs. In centres with useable ESA data, 20.0% of HD patients had a Hb >120 g/L and 4.9% had a Hb >120 g/L and were not receiving ESAs. For PD patients 21.3% had a Hb

>120 g/L and 11.8% had a Hb >120 g/L and were not receiving ESAs.

ESA prescription: age and modality associations

The proportion of patients on ESA was higher for HD (88%) than for PD (69%). This difference was maintained across all age groups (figure 7.31). The proportion of patients with Hb ≥ 100 g/L without requiring an ESA is shown (by age group and modality) in figure 7.32.

ESAs and time on renal replacement therapy

The percentage of patients on ESA by time on RRT and dialysis modality is shown in figure 7.33. This is a

Fig. 7.29. Distribution of haemoglobin in patients treated with HD and the proportion of patients with Hb >120 g/L receiving ESA by centre in 2015

Fig. 7.30. Distribution of haemoglobin in patients treated with PD and the proportion of patients with Hb >120 g/L receiving ESA by centre in 2015

cross-sectional analysis of patients at the end of 2015. Patients who had previously changed RRT modality were included in the analysis. The proportion of PD patients receiving ESA rises with duration of RRT from 65% after 3–12 months to 84% after 10 or more years.

Resistance to ESA therapy

The Renal Association guidelines define resistance to ESA therapy as ‘*failure to reach the target Hb level despite sc epoetin dose >300 IU/kg/week (450 IU/kg/week iv epoetin) or darbepoetin dose >1.5 mcg/kg/week*’ [4]. Figure 7.34 shows the frequency distribution

of weekly ESA dose adjusted for weight by treatment modality. Centres included in this analysis were restricted to those with good completeness for weight (>75%) and ESA data. Thirty three centres were included for HD data and 20 centres for PD. The prevalence of PD patients receiving over 300 IU/kg/week was 1.6% with 6.1% of HD patients receiving more than 300 IU/kg/week and 1.1% more than 450 IU/kg/week.

Success with guideline compliance

The percentage of prevalent dialysis patients achieving a Hb ≥ 100 g/L by year (1998–2015) is shown in

Fig. 7.31. Percentage of dialysis patients on ESA, by age group and treatment modality in 2015

Fig. 7.32. Percentage of whole cohort (2015) who were not on ESA and had Hb ≥ 100 g/L, by age group and treatment modality

Fig. 7.33. Percentage of patients on ESA by time on RRT in 2015

Fig. 7.34. Frequency distribution of mean weekly ESA dose corrected for weight in 2015

figure 7.35. This has shown a gradual fall in achievement of this guideline over the last decade.

Table 7.6 shows that the percentage of all patients treated with an ESA and having Hb ≥ 120 g/L ranged between 6–27% for HD and between 0–27% for PD.

Table 7.7 shows the percentage completeness for ESA type, dose, route and frequency for centres reporting ESA data. Even for this group of centres which is already restricted to those with useable ESA data, completeness of frequency and administration route average below 50%. Roughly half of the centres have very good completeness for these items and the other half did not submit at all.

Discussion

Anaemia is one of the major comorbidities associated with chronic kidney disease. This is largely caused by a reduction (absolute or relative) in erythropoietin production, though there are a number of other contributory factors including (absolute or relative) iron deficiency; inflammatory processes related to underlying kidney disease or other comorbidities; inflammatory processes related to dialysis; blood loss (CKD-associated platelet dysfunction, frequent phlebotomy, dialysis-associated

Fig. 7.35. Percentage of prevalent HD and PD patients (1998–2015) with Hb ≥ 100 g/L

Table 7.6. Percentage of patients with Hb >120 g/L and on ESA and percentage of patients with serum ferritin <100 µg/L and on ESA, by modality

Centre	HD		PD	
	% with Hb >120 g/L and on ESA	% with ferr <100µg/L and on ESA	% with Hb >120 g/L and on ESA	% with ferr <100µg/L and on ESA
England				
B Heart	10	4	5	7
B QEH	9	2	5	0
Basldn	14	7	0	19
Bradfd	20	4	14	20
Brightn	20	1		
Bristol	18	4	11	0
Carlisle	11	0	7	4
Chelms	21	2	27	35
Covnt	8	2	5	3
Donc	9	2	11	0
Dorset	17	0	14	4
Exeter	18	6	16	1
Glouc	9	4	11	15
Hull	13	2	2	0
Ipswi	8	2		
Kent	16	9	4	2
L Kings	9	6	11	8
Leeds	10	4	18	2
Leic	24	6	15	4
Middlbr	11	0	0	0
Newc	13	5		
Norwch	27	6	36	14
Nottm	12	1	5	0
Oxford	12	10	9	10
Prestn	17	3	12	0
Redng	27	1		
Sheff	19	2	0	0
Sthend	6	5	13	7
Sund	19	0	15	0
Wirral	9	1	0	0
Wolve	26	4	12	15
York	10	0	5	0
N Ireland				
Antrim	9	4	0	0
Belfast	21	6	11	6
Newry	13	7	0	0
Ulster	25	0		
West NI	20	4		
Wales				
Bangor	17	4		
Swanse	7	12	7	5
England	15	4	9	5
N Ireland	18	5	12	3
Wales	9	11	7	5
E, W & NI	15	4	9	5

Blank cells: centres excluded from analyses due to poor data completeness, small numbers with data or incomplete ESA data

Table 7.7. Percentage completeness for type, dose, route and frequency of administration of ESA

Centre	HD					PD				
	N on ESA	% with drug type	% with dose	% with frequency	% with administration route	N on ESA	% with drug type	% with dose	% with frequency	% with administration route
England										
B Heart	311	100	99	0	0	22	100	100	0	0
B QEH	822	100	100	100	0	77	100	100	100	0
Basldn	141	100	100	100	100	24	100	100	100	100
Bradfd	203	100	100	100	98	12	100	100	100	100
Brightn	333	100	100	0	0					
Bristol	454	100	100	0	0	35	100	100	0	0
Carlisle	51	100	100	0	0	19	100	100	0	0
Chelms	128	100	100	99	100	15	100	100	100	100
Covnt	279	100	98	0	0	46	100	100	0	0
Donc	145	100	100	100	100	12	100	100	100	100
Dorset	251	100	100	97	100	28	100	100	86	100
Exeter	380	100	99	0	0	54	100	100	0	0
Glouc	195	100	0	0	0	17	100	0	0	0
Hull	204	100	100	100	100	31	100	90	90	100
Ipswi	86	100	100	0	0					
Kent	372	100	100	99	100	25	100	100	96	100
L Kings	480	100	100	0	0	62	100	100	0	0
Leeds	434	100	100	100	100	41	100	100	100	98
Leic	817	100	100	0	0	80	100	100	0	0
Middlbr	231	100	100	0	0					
Newc	191	100	100	0	0					
Norwch	284	100	100	98	100	22	100	100	82	100
Nottm	304	100	100	97	100	47	100	100	100	100
Oxford	367	100	99	0	0	68	100	91	0	0
Prestn	486	100	19	0	0	33	100	0	0	0
Redng	246	100	100	0	0					
Sheff	457	100	91	0	0	22	100	100	0	0
Sthend	103	100	97	0	0	11	100	55	0	0
Sund	186	100	100	0	0	10	100	100	0	0
Wirral	146	100	100	100	100	15	100	100	93	100
Wolve	243	100	100	98	100	42	100	100	98	98
York	132	100	100	100	98	16	100	100	100	100
N Ireland										
Antrim	107	100	100	100	100	13	100	100	100	100
Belfast	155	100	100	100	100	16	100	100	100	100
Newry	74	100	100	99	100	10	100	100	100	100
Ulster	88	100	100	100	100					
West NI	105	100	100	99	100					
Wales										
Bangor	63	100	0	0	0					
Swanse	318	100	96	96	98	34	91	85	85	91
England	9,462	100	93	40	31	894	100	93	44	37
N Ireland	529	100	100	100	100	53	100	100	98	100
Wales	381	100	80	80	82	34	91	85	85	91
E, W & NI	10,372	100	93	44	37	981	100	93	48	42

Blank cells: centres with useable data for HD patients but not for PD patients

blood loss); hyperparathyroidism and dialysis inadequacy.

Since the introduction of ESAs in the 1980s the management of renal anaemia has changed markedly, from the general acceptance of severe anaemia punctuated by intermittent blood transfusions, to the maintenance of acceptable Hb concentrations for patients with CKD. The understanding of what constitutes an acceptable Hb range has evolved with the published literature and is illustrated by the historic analyses in figures 7.18 and 7.35. These figures show a steady increase in Hb until the middle of the last decade followed by a steady fall during the last ten years. This change in trend followed the publication of the CHOIR and CREATE studies in 2006 which unexpectedly showed adverse outcomes from the physiological correction of haemoglobin with ESAs [6–7]. These findings were supported by the TREAT study in 2009 [8].

Haemoglobin outcomes were similar for both HD and PD patients with proportions of prevalent patients compliant with Hb 100–120 g/L of 59% and 57% respectively. Prevalent HD patients had a higher median serum ferritin (415 µg/L vs 295 µg/L), a higher proportion of patients requiring ESAs (88% vs 69%) and a higher median ESA dose in those receiving ESAs (7,500 IU/week vs 4,000 IU/week) compared with prevalent PD patients.

As expected, a greater proportion of prevalent patients than incident patients attained a Hb ≥ 100 g/L (80% vs 47%). Only 34% of late presenters achieved a Hb ≥ 100 g/L suggesting that part of this difference is because there was less opportunity for anaemia to be treated with iron or ESAs. The fact that even in the early presenting incident group of patients only 51% achieved Hb

≥ 100 g/L suggests that opportunity is only part of the explanation for incident patients. Alternative explanations include the fact that a number of patients commence dialysis at the time of an acute illness when acute anaemia is common.

The proportion of patients achieving a serum ferritin of ≥ 100 µg/L was 94% of HD patients and 88% of PD patients.

The NICE guideline on managing anaemia was published mid-way through the data collection period [5] and there are some fundamental differences between these and the previous Renal Association guideline, especially with respect to measurements of iron status. Specifically, the new NICE guidance recommends that percentage hypochromic red blood cells or reticulocyte haemoglobin are preferable markers of iron deficiency than serum ferritin or transferrin saturation. Renal centres will need to consider the incorporation of these changes into local guidelines as well as the need to ensure electronic collection of these data items. Assuming these recommendations are incorporated into the revised RA anaemia guidance, these additional iron indices will then need to be added to the UKRR dataset.

The analysis of ESA usage was limited by incomplete data returns. From the available data, 88% of HD patients and 69% of PD patients were receiving ESAs. The attainment of Hb targets correlated poorly with median ferritin and ESA usage.

There continued to be variation in concordance with anaemia guidelines between UK renal centres.

Conflicts of interest: the authors declare no conflicts of interest

References

- 1 Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical practice guideline for anemia in chronic kidney disease. *Kidney Int Suppl.* 2012;2:S279–S335
- 2 Kilger AS, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for anemia in CKD. *Am J Kidney Dis.* 2013; 62(5):849–859
- 3 Locatelli F, et al. Kidney Disease: Improving Global Outcomes guidelines on anaemia management in chronic kidney disease: a European Renal Best Practice position statement. *Nephrol Dial Transplant* 2013; 28:1346–1359
- 4 Renal Association Clinical Practice Guidelines Committee: Anaemia of CKD, 5th Edition. 2010 <http://www.renal.org/docs/default-source/default-document-library/anaemia-in-ckd—5th-edition.pdf?sfvrsn=0>
- 5 National Institute for Health and Care Excellence (NICE). Chronic kidney disease: managing anaemia. 2015 nice.org.uk/guidance/ng8
- 6 Singh AK, et al. Correction of anemia with epoetin alfa in chronic kidney disease. *N Engl J Med.* 2006;355(20):2085–2098
- 7 Drüeke TB, et al. Normalization of hemoglobin level in patients with chronic kidney disease and anemia. *N Engl J Med.* 2006; 355(20):2071–2084
- 8 Pfeffer MA, et al. A trial of darbepoetin alfa in type 2 diabetes and chronic kidney disease. *N Engl J Med.* 2009;361(21):2019–2032