Chapter 9: Factors Influencing Haemoglobin

Summary

- Ninety–three per cent of haemodialysis and 84% of peritoneal dialysis patients achieved a serum ferritin level above 100 mcg/L. This has shown a continuing, albeit small, annual improvement.
- Three-year changes in serum ferritin by centre show that few centres have protocols that are consistently applied across both modalities of peritoneal dialysis and haemodialysis.
- There was a wide variation in erythropoietin dosages between centres, which was not always reflected in the achievement of haemoglobin targets.
- There was a trend towards a greater prescription of erythropoietin at the extremes of age, and advancing age was not a barrier to erythropoietin provision.

Haemoglobin and serum ferritin

Introduction

The second edition of the Renal Standards document did not recommend a specific Standard, whereas, in contrast, the third edition (SDIII) recommends (evidence level B):
'A serum ferritin > 100 mcg/l and <10% hypochromic red cells (transferrin saturation > 20%) and* that *levels should not consistently exceed 800 mcg/l'.

Both the European best practice and Disease Outcomes Quality Initiative guidelines also advocate a target serum ferritin of over 100 mcg/L. Although centres use different measures of iron status, including serum ferritin, transferrin saturation and percentage red cell hypochromicity, serum ferritin is the most widely used and comprehensively recorded index and is presented in this report.

The distribution of ferritin concentration is expressed as median and 90% ranges, and is presented in Table 9.1 for haemodialysis (HD) and Table 9.2 for peritoneal dialysis (PD). The percentage of patients achieving a serum ferritin of over 100 mcg/L is presented graphically in Figures 9.1 and 9.2. The numbers by each centre name in the figures indicate the percentage of missing data.

Treatment centre	% Data return	Median ferritin mcg/L	90% Range	Quartile range	% Ferritin >100 mcg/L
Bradf	98.4	273	118–837	118–414	96.8
Bristl	99.7	229	27–837	27–411	75.9
Carls	93.3	404	222–837	222–507	97.6
Carsh	77.8	358	106–837	106–468	94.9
Covnt	99.4	327	83–837	83–579	93.8
Crdff	96.4	731	146–837	146–1037	97.5
Derby	83.5	242	27–837	27–527	76.5

Treatment centre	% Data return	Median ferritin mcg/L	90% Range	Quartile range	% Ferritin >100 mcg/L
Extr	100.0	273	88–837	88–390	93.4
Glouc	100.0	289	44–837	44–424	87.6
Guys	87.9	488	70.5–837	70.5–726	92.5
Heart	85.8	164	27–837	27–238	73.1
Hull	93.6	445	159–837	159–570	98.9
Leic	96.7	332	87.5–837	87.5–544	93.8
LGI	95.9	430	119–837	119–638	96.8
Livrpl	89.5	618	112–837	112–982	96.1
Notts	95.7	568	214–837	214–712	99.3
Oxfrd	98.1	283	65–837	65–441	90.4
Plym	94.8	484	190–837	190–643	99.1
Ports	92.6	219	51–837	51–319	87.3
Prstn	96.5	460	78–837	78–781	92.8
Redng	98.7	784	237–837	237–958.5	97.4
S Cleve	92.3	292	68–837	68–574.5	88.9
Sheff	98.5	503	101–837	101–700	94.9
Sthend	100.0	351	190.5–837	190.5–422	100.0
St Jms	100.0	485	177–837	177–621	97.9
Sund	96.5	447	162–837	162–695	98.8
Swnse	79.9	515	123–837	123–683	97.6
Truro	100.0	494	192–837	192–752	100.0
Wolve	99.4	514	216–837	216–736	98.3
Words	100.0	312	59–837	59–484	92.4
Wrex	86.6	414	201–837	201–597	98.8
York	91.3	496	268–837	268–567	98.4
Eng	88.6	395	73–837	73–599	92.4
Wls	89.4	564	146–837	146–860	97.8
E&W	88.6	405	77–837	77–619	92.9

Table 9.1: Serum ferritin concentration in HD patients

Centre	% Data return	Median ferritin mcg/L	90% Range	Quartile range	% Ferritin >100 mcg/L
Bradf	100	373	86–801	215–513	87
Bristl	98	196	39–697	85–417	72
Carls	100	441	166–1260	341.5–567.5	100
Carsh	90	293	80–973	173–442	91
Covnt	89	163	32–988	84.5–341.5	67
Crdff	95	280	55–1023	144–412	86
Derby	93	183	27–654	85–389	74
Extr	100	238	31–942	141–416	84
Glouc	97	175	5–800	78–318	72
Guys	93	180	43–683	99–364	73
Heart	92	162	32–477	101–256	77
Hull	97	269	111–784	192–423	97
Leic	98	283	112–1140	208–489	95
LGI	95	397	22–681	271–506	88
Livrpl	94	199	24–721	91–382	71
Notts	96	246	60–826	146–418	90
Oxfrd	99	178	41–716	106–365	75
Plym	100	224	58–694	142–350	85
Ports	68	273	20–1082	141–448	81
Prstn	100	222	54–789	137–338	83
Redng	100	278	89–710	211–396	95
S Cleve	100	480	91–1626	244–729	95
Sheff	96	293	78–917.5	189–457.5	90
Sthend	100	329	43–702	233–396	93

Centre	% Data return	Median ferritin mcg/L	90% Range	Quartile range	% Ferritin >100 mcg/L
St Jms	100	319	107–732	229–433	96
Sund	100	476	150–855	274–743	100
Swnse	95	172	65–644	120–318	85
Truro	100	215	40–415	122–302	76
Wolve	100	166	37–551	94.5–296.5	72
Words	80	220	40–681	120–410	82
Wrex	98	368	45–867	240–501	90
York	100	221	68–447	127–323	86
Eng	88	249	43–826	140–416	84
Wls	95	245	53–959	137–432	87
E&W	89	248	44–840	140–417	84

Table 9.2: Serum ferritin concentration in PD patients

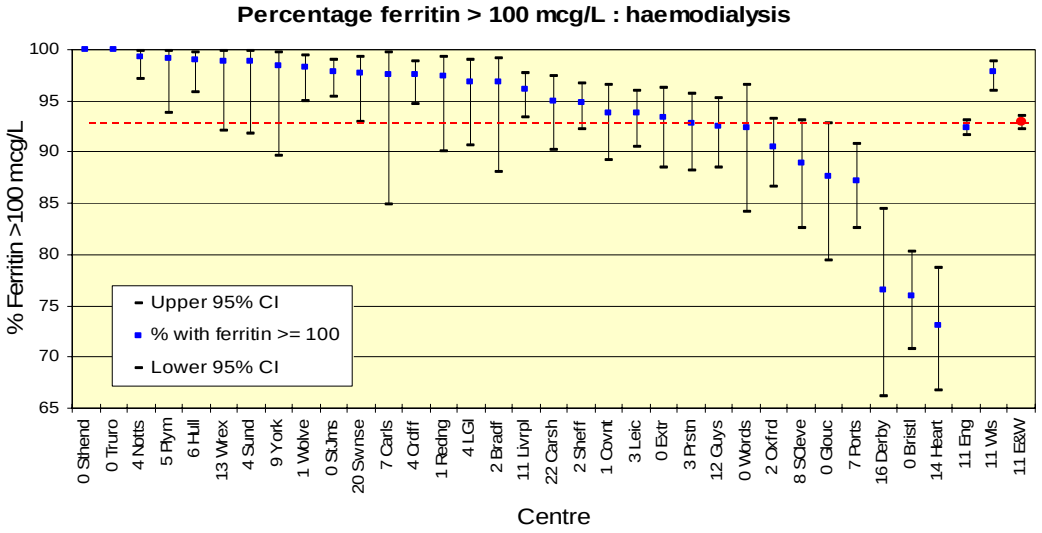

Figure 9.1: Percentage of HD patients with serum ferritin >100 mcg/L

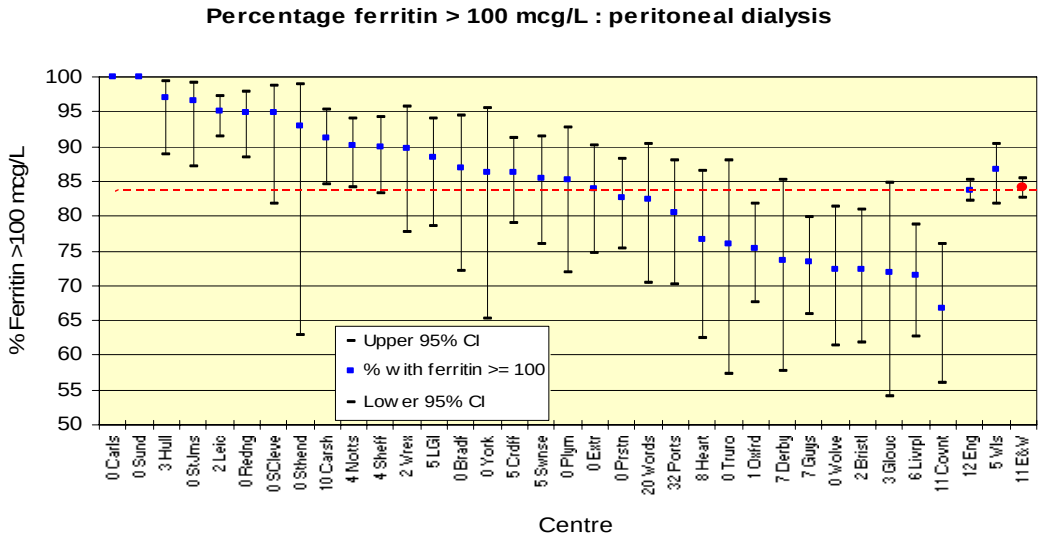

Figure 9.2: Percentage of PD patients with serum ferritin >100 mcg/L

As in previous reports, HD patients had a consistently higher serum ferritin level than PD patients. The median ferritin exceeded 100 mcg/L in all centres for both HD and PD, although a greater percentage of HD than PD patients had a serum ferritin above 100 mcg/L (93 versus 84% respectively), and the lower limit of the 90% range was under 100 mcg/L in only 13 centres for PD compared with 27 centres for HD. As can be expected, there is, with such a high achievement of the ferritin Standard by all centres, no relationship between the achievement of a haemoglobin level of over 10 g/dL and a serum ferritin of more than 100 mcg/L. Figure 9.3 shows an apparent relationship between the percentage of patients with a serum ferritin above 200 mcg./L and the achievement of the haemoglobin Standard for patients on HD. This relationship was not apparent for PD patients.

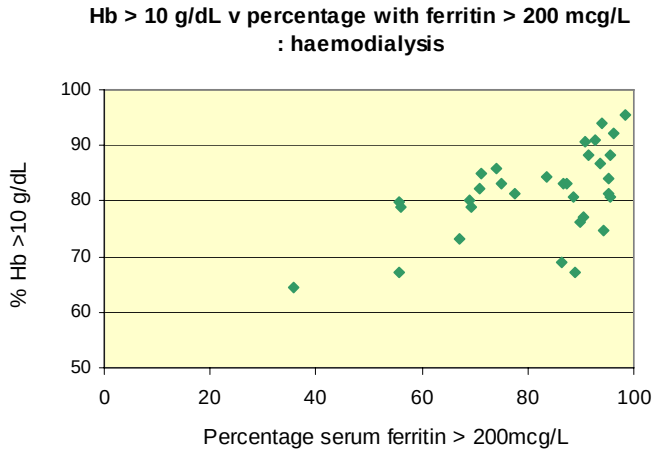

Figure 9.3: Percentage of patients with serum ferritin >200 mcg/L and Hb >10 g/dL on HD

The Southend and Hull renal units achieved a high attainment of the Standard for serum ferritin in patients on HD and PD; this contrasts with the Truro renal unit, which had an equally high achievement of the Standard for HD patients but was in the lower end of achievement for PD patients.

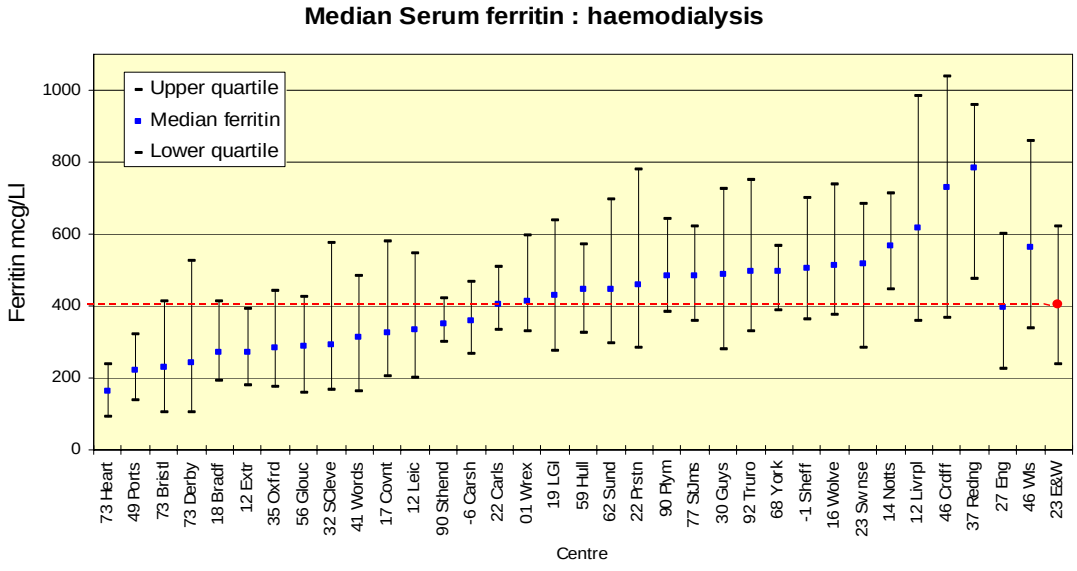

Figure 9.4: Median serum ferritin on HD

The median serum ferritin by centre is shown in Figures 9.4 and 9.5 for HD and PD respectively. Southend and Truro achieved the ferritin Standard for all patients on HD, but Southend had a median serum ferritin below average for England & Wales, and Truro was just above average, indicating that achievement of the Standard does not have to be attained at the expense of a high serum ferritin level for all patients.

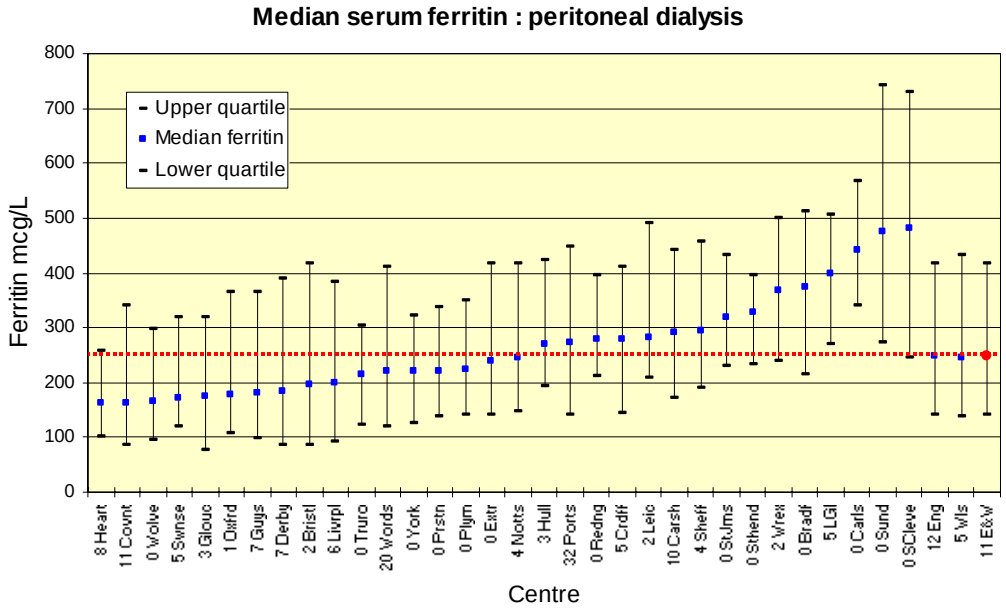

Figure 9.5: Median serum ferritin on PD

Changes in serum ferritin 1999–2001 in England & Wales

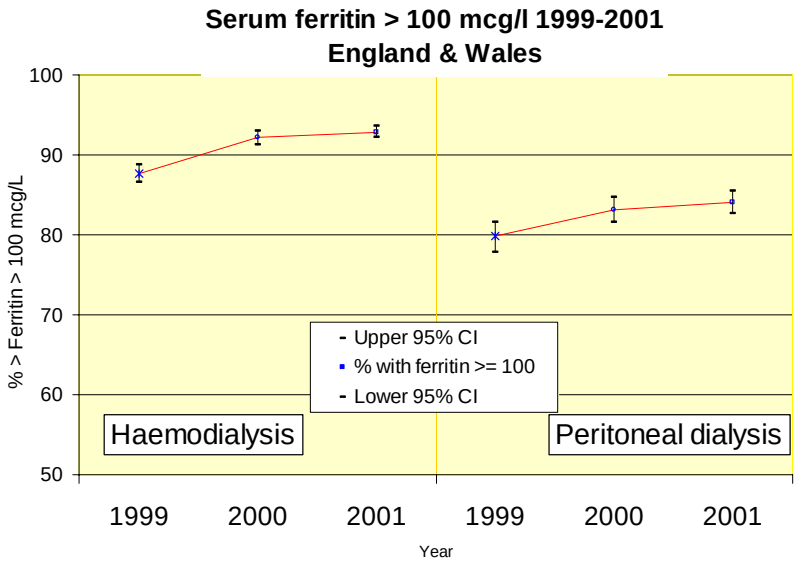

Figure 9.6: Change in achievement of a serum ferritin >100 mcg/L, 1999–2001

Figure 9.6 shows the continuing increase in median serum ferritin in England & Wales from 1999 through to 2001. In Figure 9.7, both HD and PD patients showed a trend of increasing serum ferritin during the period 1999–2001, with a reduction in the number of patients with a ferritin concentration of less than 100 mcg/L and a corresponding rise in those with a ferritin level above 300 mcg/L.

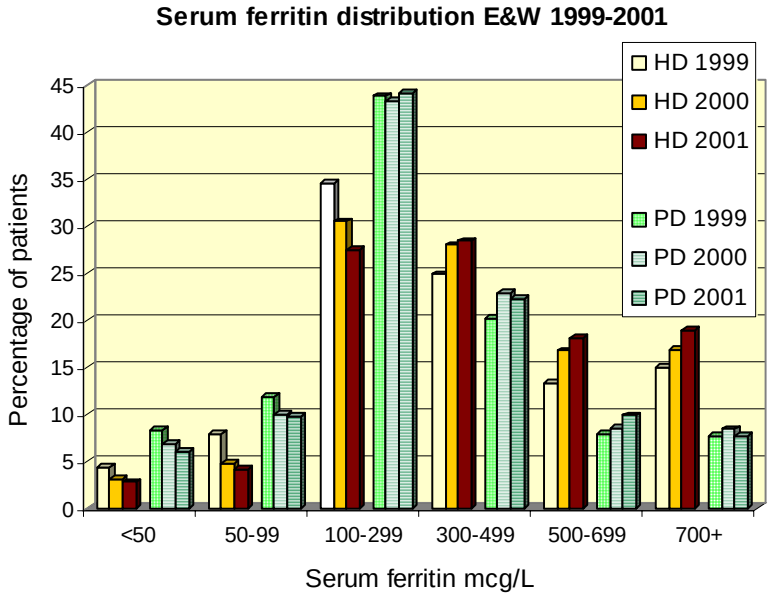

Figure 9.7: Serum ferritin distribution, 1999–2001

This trend suggests either that centres are increasingly effective in the provision of intravenous iron or that ferritin targets greater than the recommended minimum of 100 mcg/L are being adopted. HD patients show a small rise in the percentage of patients with a serum ferritin above 700 mcg/L; this will be analysed according to SDIII in the next report.

Serum ferritin and length of time on renal replacement therapy

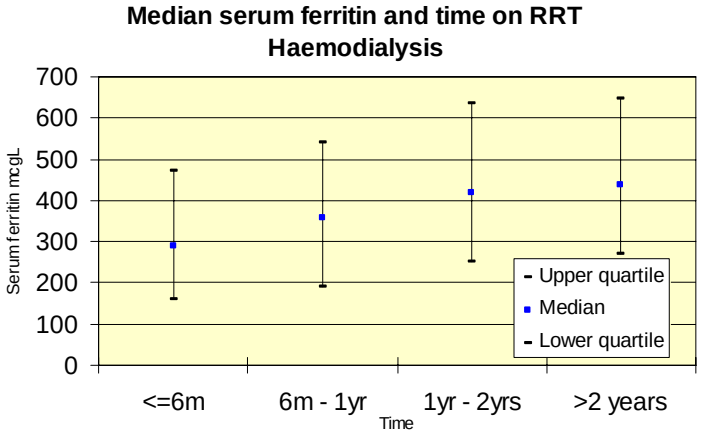

Figure 9.8: Median ferritin, by length of time on renal replacement therapy: HD

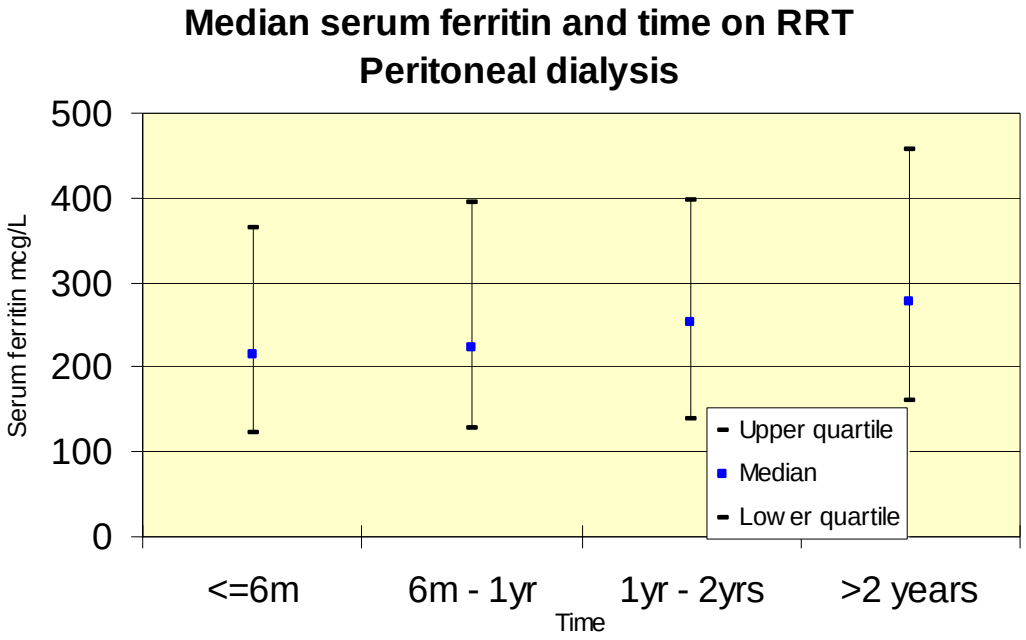

Figure 9.9: Median ferritin, by length of time on renal replacement therapy: PD

Figures 9.8 and 9.9 are a cross-sectional analysis of patients at the end of 2001 by their length of time on renal replacement therapy (RRT). These data show an increase with time for both HD and PD patients, the median serum ferritin rising from 290 to 440 mcg/L in patients on HD by the end of 2 years and from 220 to 280 mcg/L for patients on PD.

Changes in serum ferritin by centre 1999–2001

Although both HD and PD patients showed a progressive increase in serum ferritin level with increasing time on dialysis, the incremental rise was more marked in HD than PD. Assuming that ferritin levels achieved after 2 years on HD more closely approximate to individual centres' target levels, it is likely that the slower rate of rise of ferritin in the PD population results from practical difficulties in administering intravenous iron to this patient group.

Figure 9.10 and 9.11 demonstrate that Cardiff and Swansea show a marked variation in the year-on-year variability of serum ferritin in HD patients, Cardiff also showing the same variability in PD patients. Some centres, for example, Nottingham, Plymouth and Southend have made consistent improvements in median serum ferritin level for patients on HD, in contrast with centres who have not changed their practice. Carlisle has shown a big improvement in serum ferritin for patients on PD, and now patients on PD have serum ferritin levels similar to those of patients on HD.

These 3 year changes in serum ferritin show clearly which centres have changed practice in the use of intravenous iron. Several centres have similar ferritin levels for both their PD and HD patients, suggesting that there are consistent protocols that are applied across all patients on dialysis.

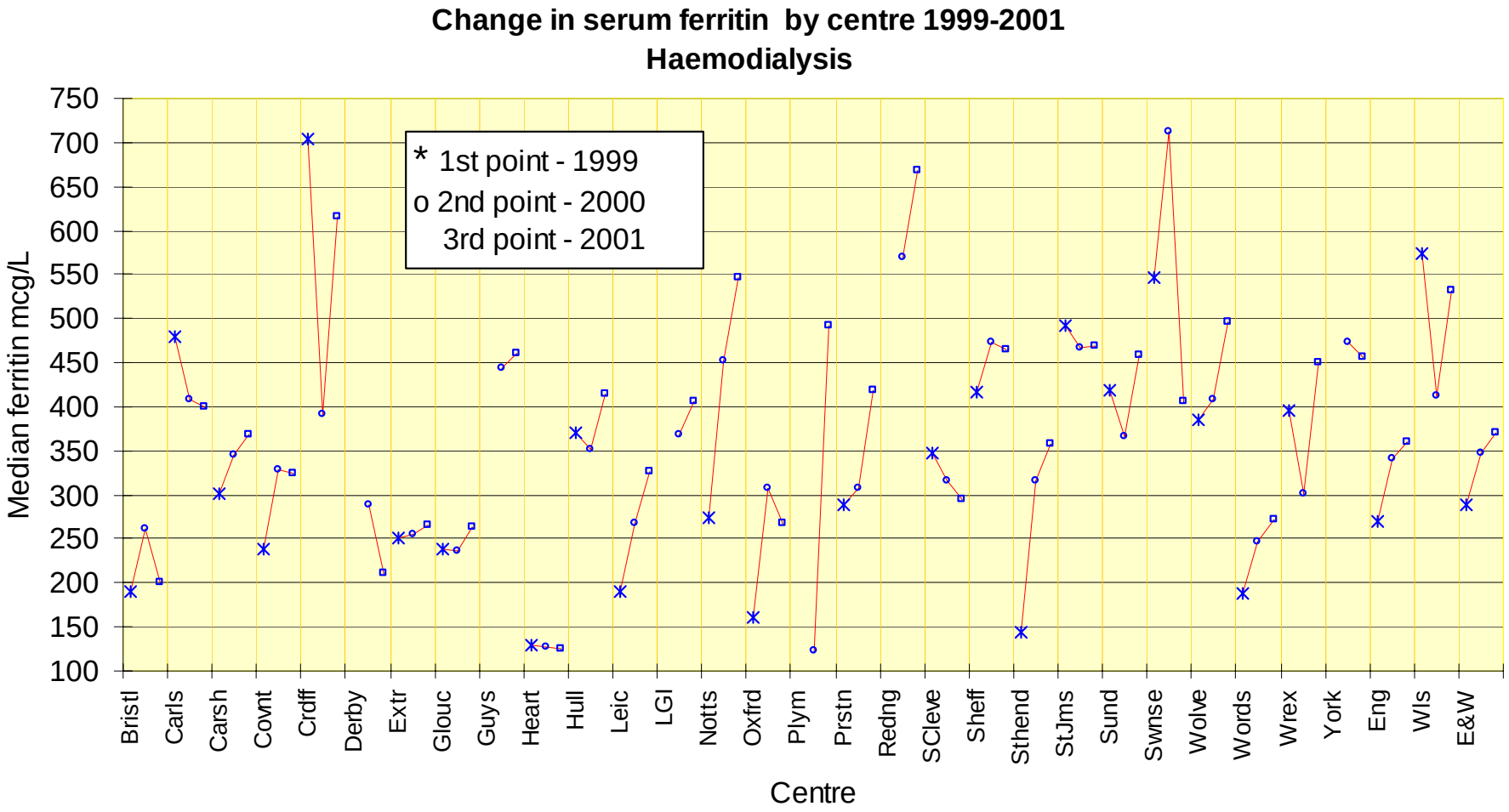

Figure 9.10: Serial ferritin concentrations in HD patients

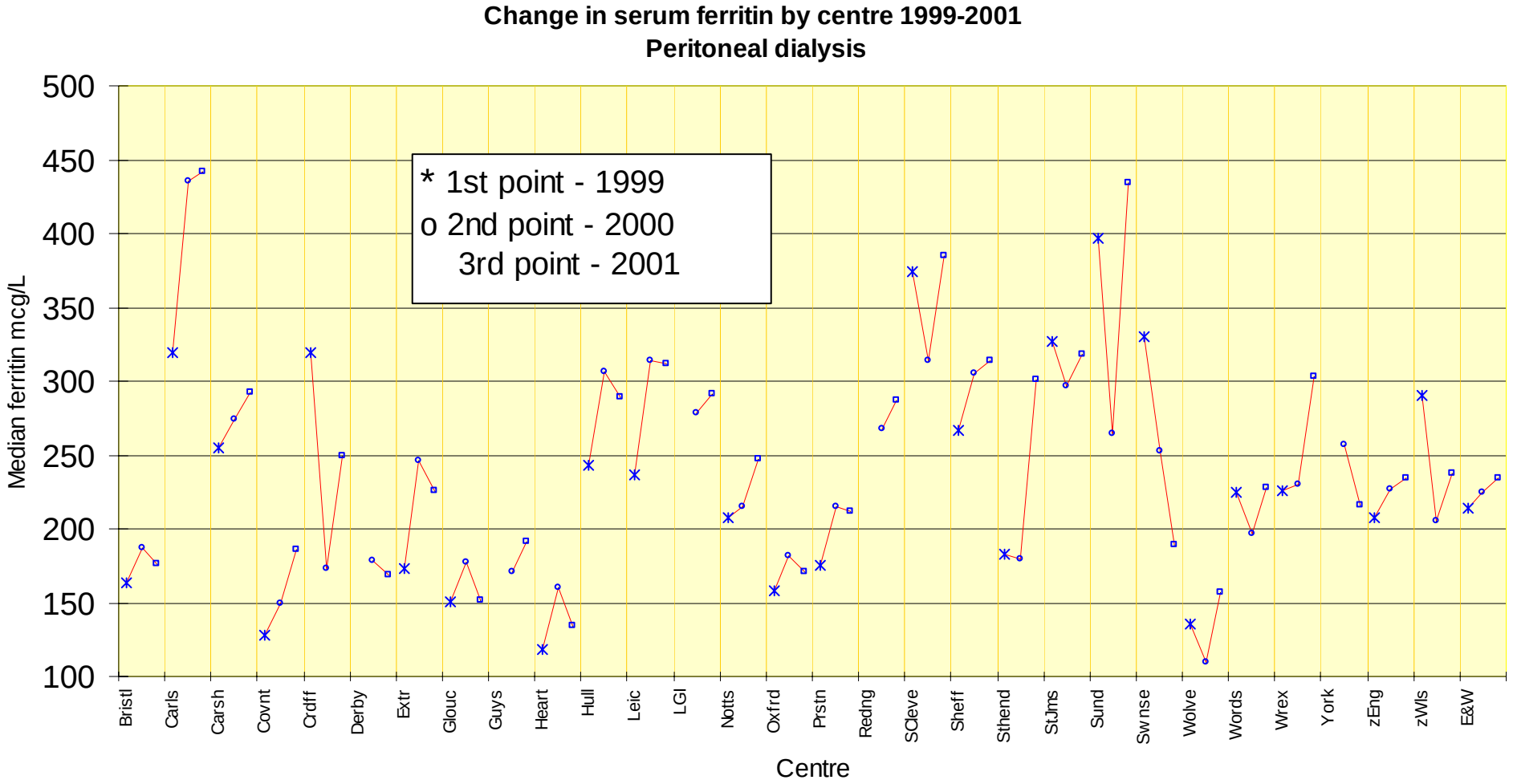

Figure 9.11: Serial ferritin concentrations in PD patients

Haemoglobin and erythropoietin

Dosage of erythropoietin

The number of centres returning data on erythropoietin provision has risen from 9 to 19 during the period 2000–02 (Tables 9.3 and 9.4). The percentage of HD patients prescribed erythropoietin ranged from 54 to 97% (mean 83%), and for PD from 28 to 93% (mean 68%). Consistent with these figures, all but three centres treated a greater percentage of HD than PD patients with erythropoietin.

For patients with a haemoglobin level of under 10g/dL, however, the median percentage treated was virtually identical for PD and HD, suggesting that centres are targeting treatment to more anaemic patients in both modalities. Behind this general picture, individual units showed a striking variation between HD and PD in the provision of erythropoietin to patients whose haemoglobin was below 10 g/dL. St James's and Bristol treated many more HD than PD patients in this category, whereas Bradford, Carlisle and Oxford treated more of the PD population. Although a better provision of erythropoietin to unit-based HD patients is an expected consequence of their easier accessibility to medical and nursing staff, it is less clear why some centres apparently treated PD patients with a haemoglobin of under 10 g/dL more effectively than did their HD peers.

Treatment centre	% on EPO	Mean weekly dose for those on EPO	Median dose for patients on EPO	Hb <10g/dL % on EPO	Hb ≥10 g/dL % not on EPO
Bradf	59	6,790	6,000	44	33
Bristl	90	10,151	8,000	91	8
Camb	54	8,283	6,000	73	29
Carls	62	8,589	8,000	60	33
Covnt	57	10,151	8,000	94	9
Exeter	92	8,198	8,000	96	8
Glouc	97	6,622	6,000	100	3
Guys	80	5,845	4,000	72	10
Lpool	83	12,667	12,000	89	12
Oxford	85	7,062	6,000	60	11
Sheff	72	7,252	6,000	83	24
St James	87	8,350	6,000	100	12
Steven	88	4,929	4,000	89	8
Sund	95	6,790	6,000	100	4
Swan	84	7,083	6,000	100	4
Wolve	94	8,283	6,000	89	6
Words	85	6,388	6,000	100	13
Wrex	67	8,700	9,000	77	17
York	91	9,723	9,000	100	5
E&W	83	7,992	6,000	85	13

Table 9.3: Erythropoietin (EPO) prescribing in HD patients

Treatment centre	% on EPO	Mean weekly dose for those on EPO	Median dose for patients on EPO	Hb <10 g/dL % on EPO	Hb ≥10g/dL % not on EPO
Bradf	66	4929	4000	100	34
Bristl	74	6593	6000	67	24
Camb	56	6058	5000	67	25
Carls	63	4200	4000	96	29
Covnt	57	6593	6000	50	33
Exeter	75	4918	4000	100	36

Treatment centre	% on EPO	Mean weekly dose for those on EPO	Median dose for patients on EPO	Hb <10 g/dL % on EPO	Hb ≥10g/dL % not on EPO
Glouc	70	4372	4000	100	26
Guys	60	4014	4000	74	70
Lpool	69	N/A	N/A	84	27
Oxford	68	5062	4000	94	27
Sheff	44	5073	6000	63	48
St.James	77	5250	4000	59	23
Steven	74	4696	4000	86	25
Sund	93	4929	4000	86	7
Swansea	64	4800	4000	91	38
Wolve	79	6058	5000	88	20
Words	77	5336	4000	87	23
Wrex	28	7125	6000	100	70
York	91	4778	4000	100	9
E&W	65	5266	4500	84	31

Table 9.4: Erythropoietin (EPO) prescribing in PD patients

There was a striking predominance of PD patients among those achieving a haemoglobin level of over 10g/dL without erythropoietin, implying that the greater susceptibility of HD patients to anaemia outweighs the advantages of their better access to intravenous iron than PD patients. Interestingly, Wrexham, which prescribed erythropoietin for the smallest proportion of its PD population of any centre and achieved a haemoglobin of over 10 g/dL without erythropoietin in 70% of PD patients, reported ferritin levels that, although just exceeding the median for England & Wales, were lower than those of many centres, with far fewer haemoglobins reaching the target without erythropoietin. This illustrates the fact that iron provision is only one of several factors that influence anaemia in patients not receiving erythropoietin.

As in previous reports, there was wide variation between centres in erythropoietin dosage, HD patients receiving higher average doses than their PD peers. Even within modalities, however, centres giving higher doses were not necessarily more successful in meeting the Renal Association haemoglobin target. As an example, Liverpool HD patients received the highest average dose of erythropoietin of any centre and achieved a target haemoglobin in 81% of cases. In Stevenage, however, which gave the lowest average dose of erythropoietin to its HD population, 86% of patients had a haemoglobin of over 10 g/dL. Some centres with GP prescribing of erythropoietin may not be logging all the prescriptions and accurate dosage of erythropoietin, which may account for their apparently lower usage.

Erythropoietin and time on RRT

In contrast with the 2000 data, the cross-sectional analysis of the 2001 returns (Table 9.5) shows was no increase in the proportion of patients treated with erythropoietin with increasing time on dialysis.

Time on treatment	<1 year	1–2 years	2–3 years	3–5 years	5–10 years	>10 years
HD %	81 (490)	87 (546)	84 (429)	83 (551)	84 (526)	80 (351)
PD %	66 (237)	61 (213)	67 (161)	66 (160)	63 (108)	69 (65)

Table 9.5: Erythropoietin use and length of time on dialysis

The percentage of HD and PD patients treated during the first year (81% and 66% respectively) was similar to the combined means for the first 10 years of treatment (80% and 68%). This suggests an increasing provision of pre-dialysis erythropoietin and an earlier commencement of erythropoietin in patients on dialysis, consistent with the earlier peaks in haemoglobin shown in Chapter 8.

Age and erythropoietin provision

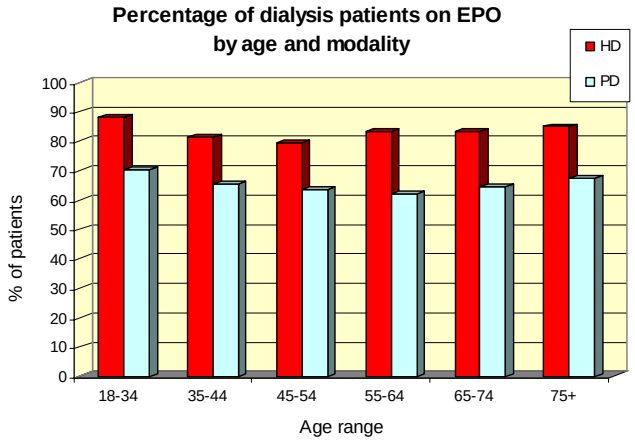

Figure 9.12: Age and the provision of erythropoietin (EPO), by modality

Although the difference between age groups in the percentage of patients prescribed erythropoietin was small, Figure 9.12 shows a trend towards a greater provision at the extremes of age. For HD, but not PD, this trend also applied to the provision of erythropoietin to patients with a haemoglobin level less than 10 g/dL. Data on erythropoietin prescription in the over-75 age group demonstrate that advancing age is not considered a barrier to erythropoietin provision (Figure 9.13).

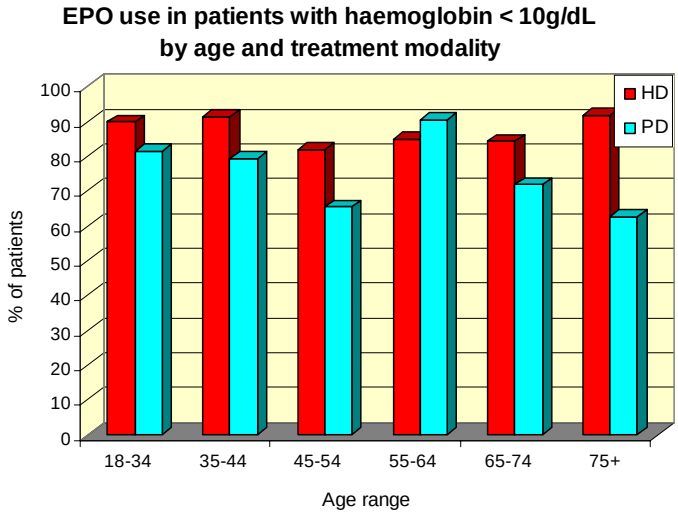

Figure 9.13: Erythropoeitin (EPO) use in patients with haemoglobin <10 g/dL, by age group

Consistent with the high erythropoietin requirements of the 18–34-year-old group shown in Figure 9.12, the proportion of patients in this category achieving a haemoglobin of 10 g/dL or more without erythropoietin was the lowest of all groups for both HD and PD patients (Tables 9.6 and 9.7). In addition, and consistent with the 2000 data, there was a trend towards a higher achievement of a haemoglobin level of 10 g/dL without erythropoietin in middle age than in the young or elderly.

Age group (years)	18–34	35–44	45–54	55–64	65–74	75+
% on EPO	88	81	79	83	83	85
%Hb >10 g/dL no EPO	8	16	15	12	12	10
%Hb <10 g/dL on EPO	90	91	82	85	84	92

Table 9.6: Percentage use of erythropoietin , by Hb achievement, for patients on HD

Age group (years)	18–34	35–44	45–54	55–64	65–74	75+
% on EPO	70	65	64	62	65	67
%Hb >10 g/dL no EPO	23	31	33	37	33	25
% Hb <10 g/dL on EPO	82	79	65	91	72	63

Table 9.7: Percentage use of erythropoietin, by Hb achievement, for patients on PD

Erythropoietin prescription and gender

Consistent with the overall year-on-year improvement in the treatment of anaemia, Tables 9.8 and 9.9 demonstrate that haemoglobin values in both males and females were higher than in the 2000 report for both dialysis modalities.

Gender	Mean Hb (g/dL)	Standard deviation	% on EPO	Hb <10 g/dL % on EPO	Hb >10 g/dL % without EPO
Male	11.4	1.66	82	86	14
Female	11.2	2.97	86	88	9

Table 9.8: Erythropoietin, by gender, on HD

Gender	Mean Hb(g/dL)	Standard deviation	% on EPO	Hb <10 g/dL % on EPO	Hb >10g/dL % without EPO
Male	11.9	1.69	62	79 (78)	36 (315)
Female	11.6	3.58	70	72 (65)	25 (143)

Table 9.9: Erythropoietin, by gender, on PD

As in all previous Registry reports, the mean haemoglobin was higher in males than females for both HD and PD, although a greater proportion of females than males received erythropoietin, demonstrating an appropriate targeting of treatment.

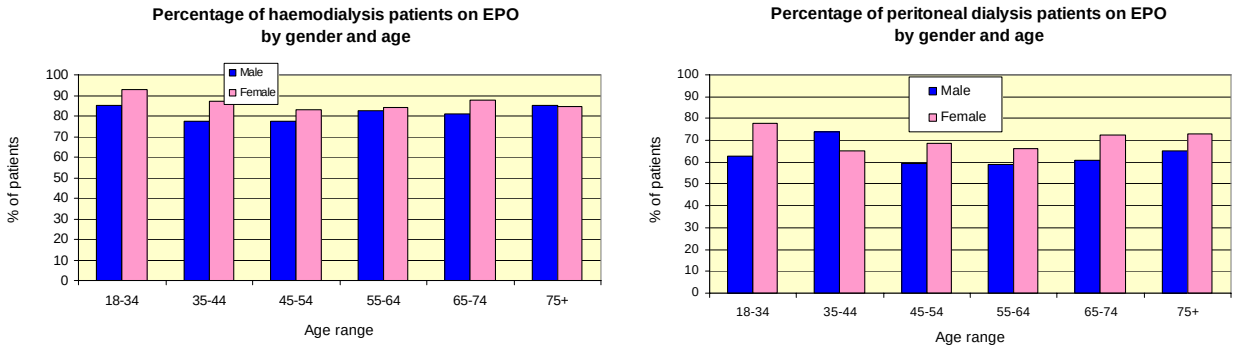

Figure 9.14: Erythropoietin (EPO) use by age, gender and dialysis modality

Figure 9.14 demonstrates that the prescription of erythropoietin for more females than males applied to all age groups and both modalities, with the exception of PD patients aged 35–44. In addition, a greater proportion of males than females achieved a haemoglobin concentration of 10 g/dL without erythropoietin.

Conclusion

An increasing proportion of HD and PD patients are achieving the target serum ferritin of 100 mcg/L.

The median serum ferritin was higher with HD than PD.

All patients showed a progressive rise in ferritin level with increasing time on dialysis, although this effect was more marked for HD than PD.

A greater proportion of HD than PD patients were treated with erythropoietin, although for patients with a haemoglobin concentration of less than 10g/dL, the percentage treated was similar for both modalities.

There was a wide variation in erythropoietin dosage between centres, which was not always reflected in the achievement of haemoglobin targets.

There was a trend towards a greater prescription of erythropoietin at the extremes of age, and advancing age was not a barrier to erythropoietin provision.

The mean haemoglobin reading was higher in males than females for both dialysis modalities, although a greater proportion of females than males were prescribed erythropoietin across all age groups for HD and in all but the 35–44-year-old group for PD.