Chapter 10: Bone Biochemistry: Serum Phosphate, Calcium, Parathyroid Hormone, Albumin and Aluminium

Summary

- Although serum phosphate control in dialysis patients is unsatisfactory there is a continuing year-on-year trend towards improvement. The Renal Association (RA) target (<1.8 mmol/L) was achieved in 63% of patients overall, (69% of peritoneal dialysis patients and 61% of haemodialysis patients).

- The median corrected calcium for all dialysis patients was 2.40 mmol/L with 74% of both HD and PD patients achieving a concentration within the RA target range.

- The North American Kidney Disease Outcomes Quality Improvement (KDOQI) guidelines[1] recommend the calcium × phosphate product should be less than 4.4 $mmol^2/L^2$ (=55 mg^2/dl^2). Overall 66% of dialysis patients achieved this target. Control was better in PD patients compared to HD patients (71% versus 64% achieving the standard), reflecting the better phosphate control that is achieved with PD. There was wide variation between units in both calcium and phosphate control and in achievement of the KDOQI calcium × phosphate target.

- There remains large between-centre variation in achievement of the RA target for plasma parathyroid hormone. Overall achievement was poor (median 63%, range 45–79% compliance with the standard).

- For haemodialysis patients, the median serum albumin concentration was 39 g/L (BCG) and 33 g/L (BCP). 75% (BCG) and 73% (BCP) of the patients had serum albumin above 35/30 g/L respectively.

- Peritoneal dialysis patients had lower serum albumin compared with haemodialysis patients; the median serum albumin was 35 g/L (BCG) and 29 g/L (BCP). Overall 55% (BCG) and 49% (BCP) of peritoneal dialysis patients had serum albumin concentrations above 35/30 g/L respectively.

- Most transplant patients achieve good phosphate control (99%, range 95–100%) and the percentage of patients achieving serum calcium concentrations within the target range was 84% (range 43–97%), although there was a tendency to hypercalcaemia in some renal units. Nearly all (99%) of transplant patients achieved calcium × phosphate product concentrations within the KDOQI target range. Overall median PTH was above the normal laboratory reference range (median 10, inter-quartile range 6–18 pmol/L) amongst transplant patients, although the majority (89%, range of centre means 70% to 100%) achieve the Renal Association target.

- Amongst patients who had received a renal transplant, median serum albumin was 41 g/L (range 17–56) for centres supported by laboratories using BCG methods and 37 g/L (range 14–48) for centres supported by laboratories using BCP methods. Overall, 95.4% and 95.9% of patients had serum albumin above 35 g/L for the BCG method and 30 g/L for the BCP method respectively.

- An analysis of RA target achievement against age demonstrated a strong effect of age upon phosphate control, with older patients being more likely to achieve target phosphate concentrations. Serum corrected calcium was relatively unaffected by age but better phosphate control was mirrored by better compliance with the KDOQI calcium × phosphate product standard: PTH control was also better amongst older patients.

- Strong evidence of an effect of age on achieved albumin concentration is presented. Given the many caveats to the interpretation of serum albumin data that the Registry reports have explored, it is felt that continued presentation of albumin achievement

data in the Registry annual report is of limited value: ***unless there are strong calls from the renal community with an opposing viewpoint, this data will not be published in next year's report.*** Albumin data will still be collected and used for case-mix adjustment in survival analyses in other sections of the report.

- This report has attempted an analysis of aluminium testing practices in renal units. Although there are concerns about the completeness of the data, there is some evidence to suggest that compliance with RA Standards with respect to aluminium monitoring is poor, with some renal centres possibly having abandoned routine monitoring of aluminium in dialysis patients or doing it on an annual rather than quarterly basis. It is suggested that the role of aluminium monitoring in dialysis patients needs re-evaluation.

Introduction

This Chapter contains information relating calcium, phosphate and PTH control to the RA Standards, and also presents data on the achievement of calcium × phosphate product in relation to the North American KDOQI guidelines. For calcium, phosphate and PTH no separate RA Standards are set for differing dialysis modalities. Nevertheless, differing modalities offer different challenges in achieving metabolic control. Where appropriate, data for HD and PD are shown separately in addition to/instead of the pooled dialysis data.

Data on transplant patients is included here for the first time. Although the RA has not set specific biochemical standards for calcium and phosphate concentrations in transplant patients they have suggested that PTH concentrations should be less than four times the upper limit of normal after transplantation. Calcium and phosphate have been audited here against the same standards that are applied to dialysis patients.

Last year an attempt was undertaken to assess the contribution of inter-laboratory variation to between-centre performance. Although the analysis was fairly crude, little evidence was found to suggest that laboratory variation influences Registry data for serum phosphate or calcium although there was an influence on serum albumin. The current status of analytical methodology did not allow an accurate assessment of the contribution of inter-laboratory variability to between-centre PTH differences. There is no reason to suspect that this situation has changed and so this analysis has not been repeated for this year's report.

Increasingly dialysis and transplantation are offered to older people and patients over 65 years old represent the majority of UK patients receiving renal replacement therapy. This year analyses have been undertaken to assess the effect of age upon RA Standard achievement.

Monitoring of serum aluminium concentration remains routine clinical practice amongst dialysis patients and there are RA Standards addressing this issue. Although the Registry has collected this data it has not previously been reported. This year completeness of aluminium data and its compliance with the RA Standards was surveyed.

As in previous years the number preceding the centre name in all the figures indicates the percentage of missing data for that centre.

Serum phosphate

The RA Standard states:

> ***Serum phosphate (measured before a dialysis session in HD patients) should be below 1.8 mmol/L.***

The RA sets no standard for the lower limit of serum phosphate in contrast to the KDOQI guidelines[2] which set a lower limit of 1.13 mmol/L; the KDOQI upper limit is 1.78 mmol/L, consistent with the RA Standard.

Data completeness

The completeness of data by modality is shown in Table 10.1 for each centre.

Achievement of serum phosphate

Serum phosphate control amongst dialysis patients remains poor with 63% of patients

Table 10.1: Data completeness by centre for serum phosphate

	HD	PD	Tx
Bangor	100	100	n/a
Barts	n/a	n/a	n/a
Basildon	97	100	68
Bradford	100	100	96
Brighton	74	99	75
Bristol	100	100	99
Cambridge	63	94	75
Carlisle	93	93	82
Carshalton	87	98	88
Chelmsford	99	97	60
Clwyd	91	100	100
Coventry	100	91	83
Cardiff	95	97	96
Derby	91	93	36
Dorset	100	100	64
Dudley	84	100	91
Exeter	98	100	92
Gloucester	98	92	96
Guys	92	99	88
H&CX	99	99	95
Heartlands	94	100	75
Hull	97	98	90
Ipswich	100	97	98
Kings	95	90	91
Leeds	98	98	91
Leicester	98	98	91
Liverpool	95	96	93
ManWst	68	98	71
Middlesbrough	96	100	94
Newcastle	100	98	96
Norwich	99	100	93
Nottingham	97	100	89
Oxford	99	99	93
Plymouth	91	100	89
Portsmouth	100	93	88
Preston	99	100	66
QEH	95	98	94
Reading	97	100	97
Sheffield	100	99	99
Shrewsbury	99	100	94
Stevenage	94	98	68
Southend	99	95	90
Sunderland	95	100	98
Swansea	98	99	92
Truro	100	96	95
Wirral	n/a	n/a	n/a
Wolverhampton	100	100	93
Wrexham	83	95	96
York	92	100	93
England	90	91	84
Wales	89	89	95
England & Wales	90	91	85

overall achieving the RA Standard. This should be interpreted in the light of the KDOQI guidelines, where it is reported that <30% of the dialysis population maintain serum phosphate concentrations within the target range. In general, the phosphate control is a little better on peritoneal dialysis, where 69% of patients achieved this standard, compared to haemodialysis where 61% had serum phosphate <1.8 mmol/L (Figures 10.1 and 10.2). Haemodialysis has limited efficacy in phosphate control due to the high distribution volume which leads to rapid rebound of serum phosphate after dialysis[3].

There is reasonable evidence of year-on-year improvements in phosphate control with this year's data representing a very slight improvement over the previous year, continuing the general improvement in phosphate standard achievement reported in last year's Registry report[4] (Figures 10.3 and 10.4).

The variation between units is wide (Figures 10.1 and 10.2). For both HD ($\chi^2 = 313$, $p < 0.001$) and PD ($\chi^2 = 108$, $p < 0.001$), the percentage of patients with a serum phosphate below 1.8 mmol/L differed significantly between centres. Analysis in last year's Registry report suggests that this is unrelated to differing laboratory bias[4].

For both HD ($\chi^2 = 19.1$, $p < 0.0001$, Figure 10.5) and PD ($\chi^2 = 10.9$, $p < 0.0001$, Figure 10.6) patients there was a marked increase in the percentage of patients achieving the RA target with respect to phosphate control with increasing age. This could in part reflect an effect of ageing independent of the presence of kidney disease, since lower serum phosphate concentrations have previously been reported in older healthy males (eg 50th percentile in males aged 68–71 years is 1.00 mmol/L compared to 1.09 mmol/L in males aged 25–34 years), with no change seen in females[5,6]. However, additional mechanisms must be involved, for example improved compliance with dietary or pharmacological control of serum phosphate in older patients, as the changes in median phosphate observed with ageing are far greater amongst particularly haemodialysis patients, than in the background population (Figures 10.7 and 10.8). It is also important to recognise that as there is no UK recommended lower limit for the

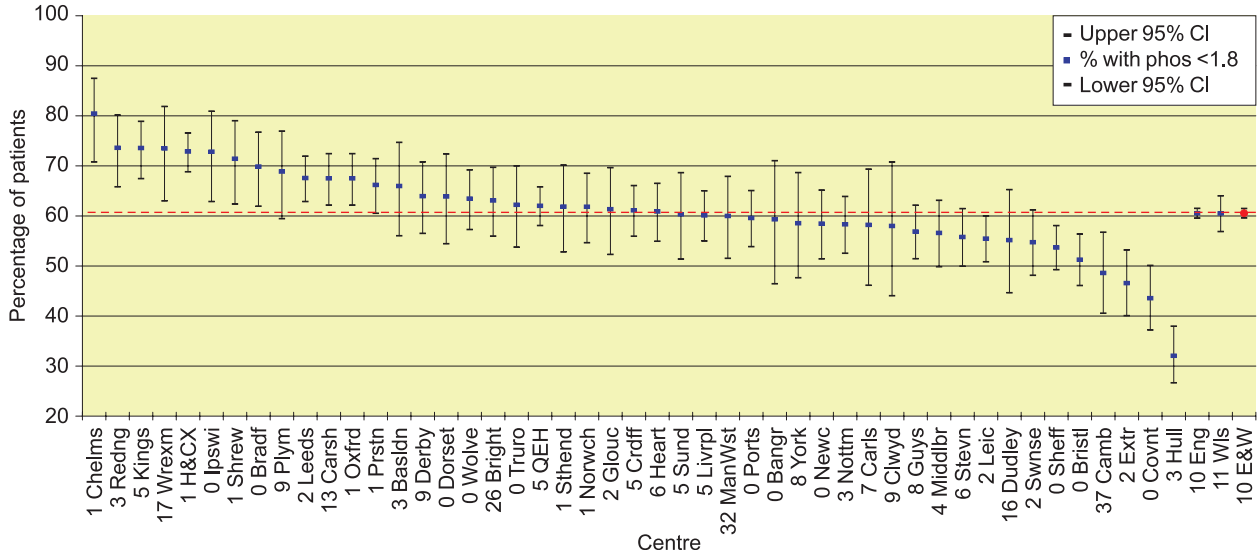

Figure 10.1: Percentage of HD patients in RA range for serum phosphate

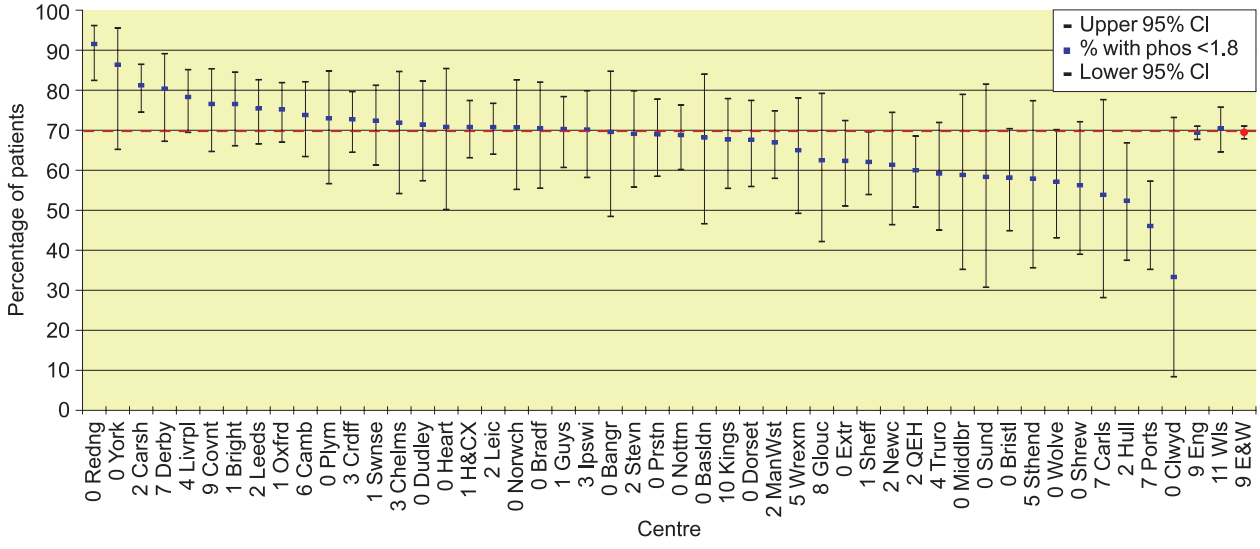

Figure 10.2: Percentage of PD patients in RA range for serum phosphate

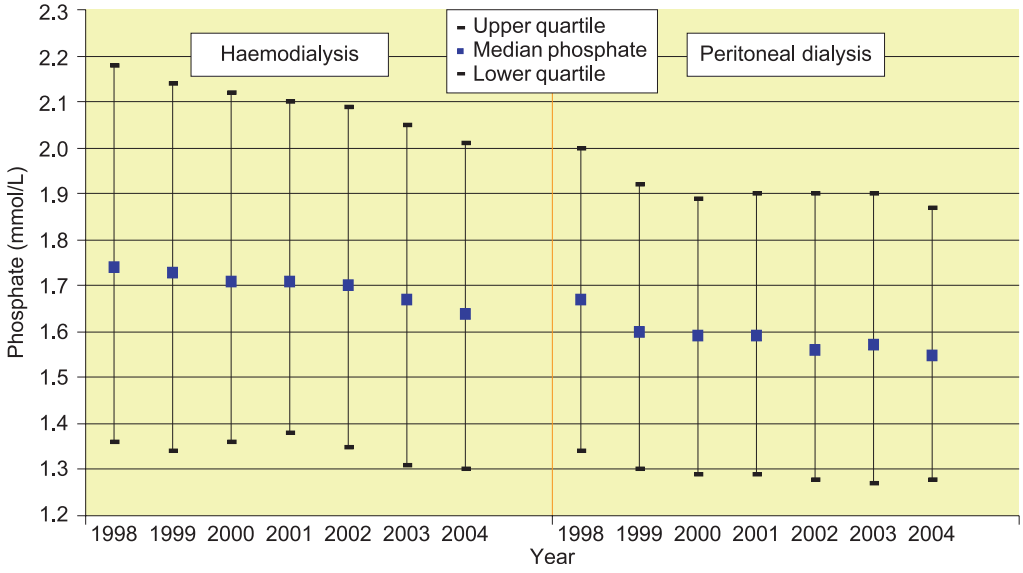

Figure 10.3: Change in median serum phosphate, 1998–2004

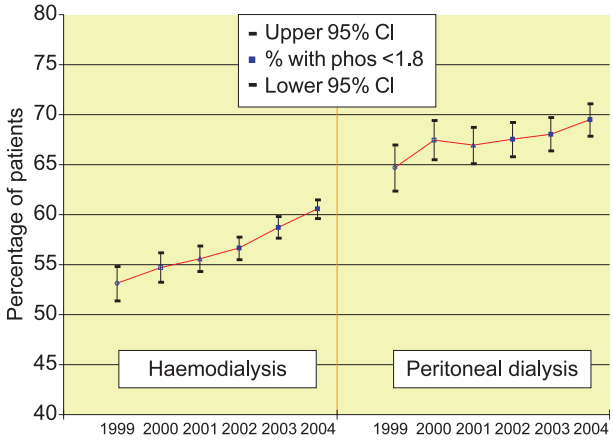

Figure 10.4: Change in percentage of patients achieving serum phosphate <1.8 mmol/L, 1999–2004

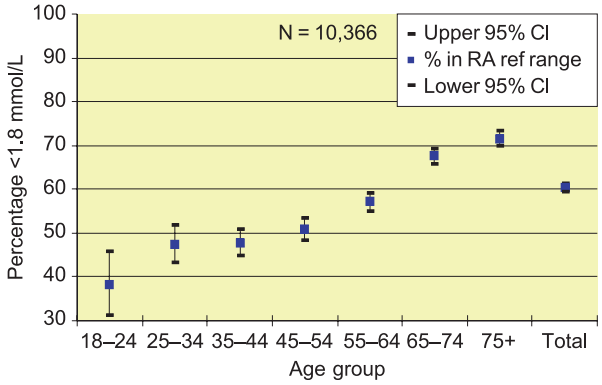

Figure 10.5: Variation in achievement of the RA phosphate standard by age group: HD

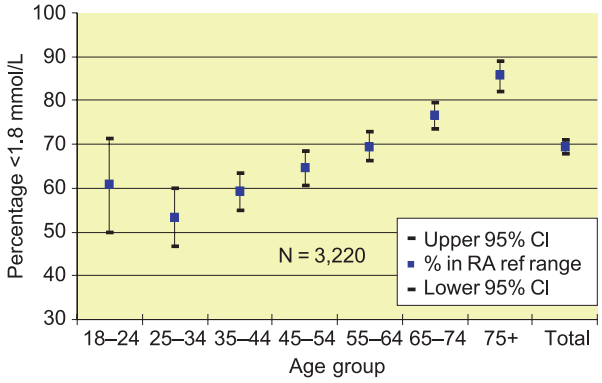

Figure 10.6: Variation in achievement of the RA phosphate standard by age group: PD

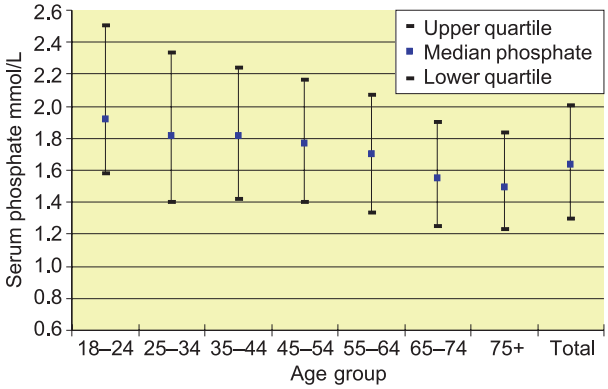

Figure 10.7: Median serum phosphate by age group: haemodialysis

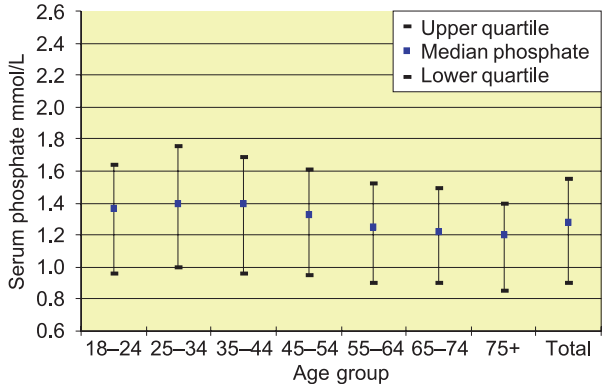

Figure 10.8: Median serum phosphate by age group: peritoneal dialysis

phosphate standard and that 'improved compliance' may reflect inadequate protein intake in the elderly. The authors are unaware of this effect having been reported before or of evidence to support an explanatory mechanism.

Amongst patients who had received a transplant, phosphate control was good (median 1.01 mmol/L, mean 5th–95th centiles 0.66–1.50 mmol/L, Figure 10.9) with 99% of patients (mean range between units 95% to 100%) achieving the target. There was no evidence of significant variation between units ($\chi^2 = 47$, $p = 0.4457$) but there was a statistically significant ($\chi^2 = 3.2$, $p < 0.005$), although minimal, influence of age (data not shown).

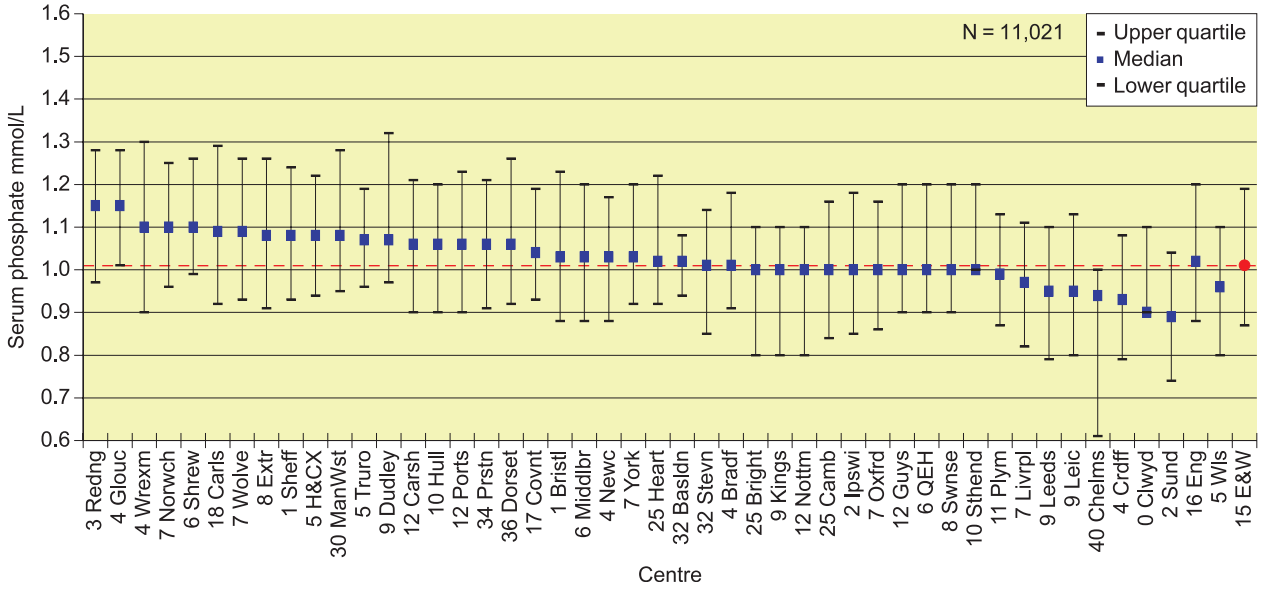

Figure 10.9: Median serum phosphate concentration by centre in transplant patients

Serum calcium

The RA Standard states:

> ***Serum calcium, adjusted for albumin concentration, should be between 2.2 and 2.6 mmol/L, in HD (pre-dialysis sample) and in PD patients.***

Comparative audit in this area remains difficult due to differences in analytical methods between units, (and even between satellite units managed by one clinical team), different mathematical methods being applied to correct serum calcium for serum albumin concentration and different methods in analysing serum albumin (see the Registry reports 1999–2003). However, as discussed in previous Registry reports, since nephrologists in each unit will be making clinical decisions based on their local corrected calcium results, these data are in some sense the most valid and this data has been chosen for illustration. Some units provide data already corrected for albumin concentration and these are analysed directly; uncorrected calcium data provided by some units is corrected using a formula in widespread use[7]:

$$\text{Corrected calcium} = \text{uncorrected calcium} + [(40 - \text{albumin}) \times 0.02]$$

Data completeness

The completeness of data by modality is shown in Table 10.2 for each centre.

Achievement of serum calcium

The median corrected calcium was 2.39 mmol/L for HD patients and 2.42 mmol/L for PD patients with 74% of both HD and PD patients achieving a concentration within the RA target range (Figure 10.10). There has been a general trend towards improved performance over the period 1998–2004 (Figure 10.11). A sub-analysis including only those individual patients that have remained on dialysis throughout that entire period confirmed that this is a true effect and not a consequence of the inclusion of additional renal centres to the Registry database over that period (data not shown). The variation between units is wide and as discussed in last years report, seems unlikely to be related to laboratory variation[4]. For both HD ($\chi^2 = 610$, $p < 0.001$) and PD ($\chi^2 = 337$, $p < 0.001$) modalities, the percentage of patients with a serum corrected calcium within the RA target range differed significantly between centres.

The percentage of patients with serum corrected calcium of 2.2 to 2.6 mmol/L differed significantly between age groups for HD ($\chi^2 = 5.7$, $p < 0.001$, Figure 10.12) but not for PD ($\chi^2 = 0.4$, $p = 0.706$, data not shown) although even amongst HD patients the effect was slight. In the general population, marked changes with age in serum uncorrected total calcium concentrations have not generally been observed[5,8].

Table 10.2: Data completeness by centre for corrected calcium

	HD	PD	Tx		HD	PD	Tx
Bangor	87	96	n/a	Liverpool	99	98	93
Barts	n/a	n/a	n/a	ManWst	69	98	85
Basildon	97	96	92	Middlesbrough	96	100	94
Bradford	100	100	98	Newcastle	100	98	96
Brighton	74	99	76	Norwich	99	100	93
Bristol	100	100	99	Nottingham	100	100	88
Cambridge	63	96	75	Oxford	99	99	93
Carlisle	93	93	87	Plymouth	99	100	92
Carshalton	87	98	88	Ports	100	95	90
Chelmsford	99	97	80	Preston	99	100	89
Clwyd	91	100	100	QEH	96	98	93
Coventry	100	91	83	Reading	99	100	97
Cardiff	96	100	98	Sheffield	100	99	99
Derby	89	93	100	Shrewsbury	99	100	94
Dorset	99	100	92	Stevenage	95	98	68
Dudley	84	100	92	Southend	99	100	85
Exeter	98	100	92	Sunderland	95	100	98
Gloucester	98	92	97	Swansea	97	97	97
Guys	92	99	88	Truro	100	96	95
H&CX	99	99	96	Wirral	n/a	n/a	n/a
Heartlands	94	100	80	Wolverhampton	100	100	99
Hull	97	98	90	Wrexham	80	93	95
Ipswich	100	97	98	York	92	100	56
Kings	95	90	91	England	90	91	86
Leeds	98	97	90	Wales	92	98	97
Leicester	98	98	89	England & Wales	90	92	86

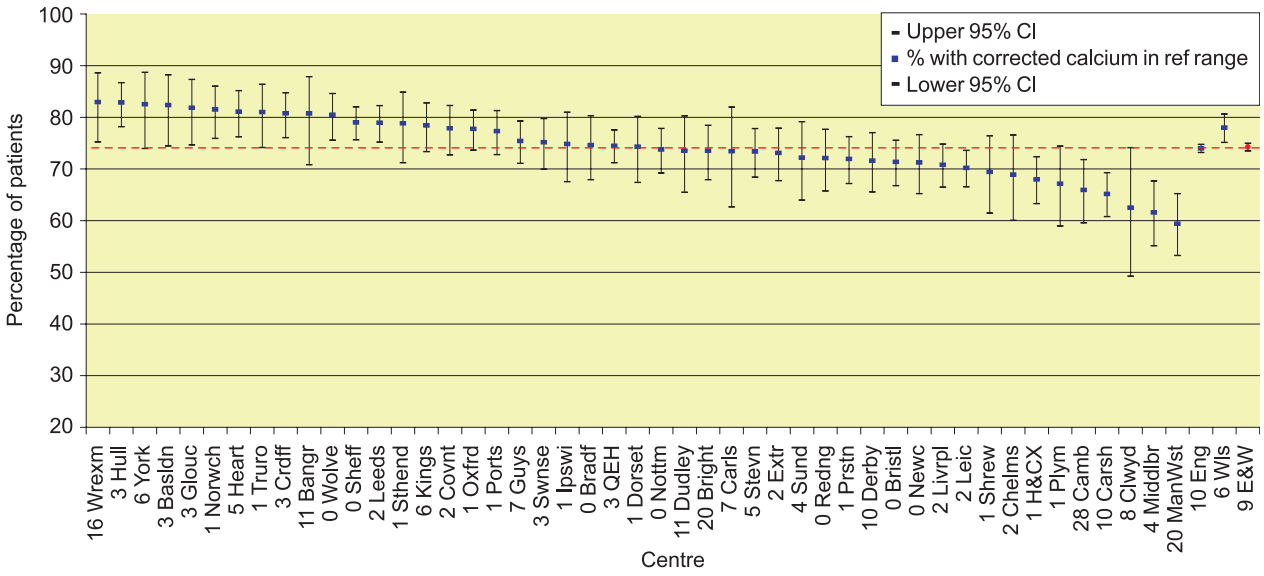

Figure 10.10: Percentage of patients with corrected calcium within 2.2 to 2.6 mmol/L: dialysis

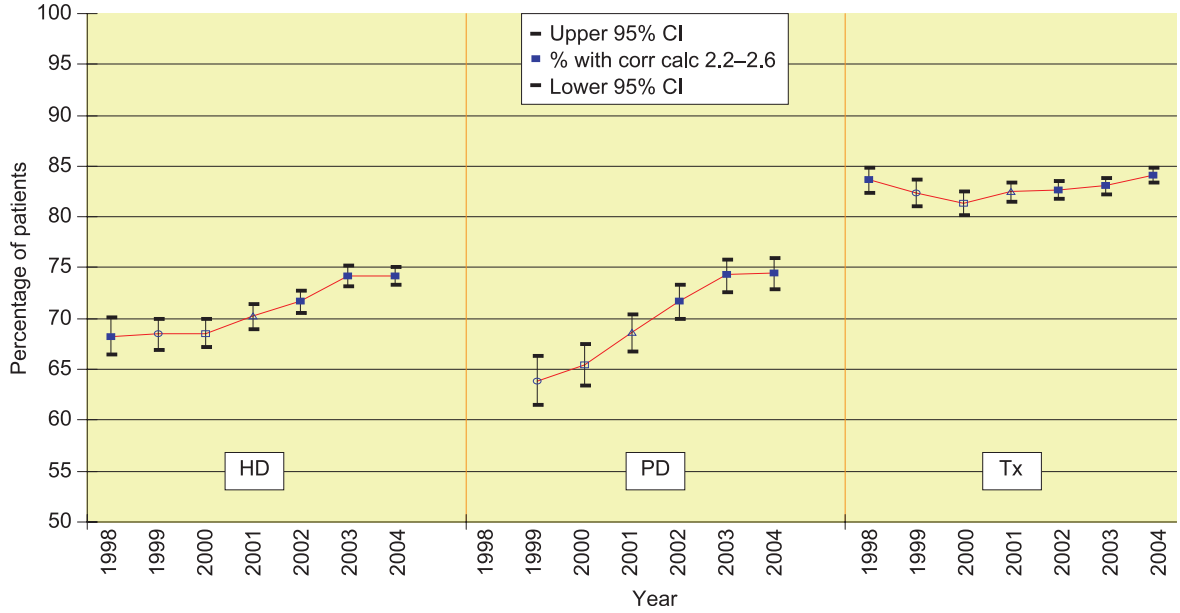

Figure 10.11: Change in percentage of patients achieving serum corrected calcium within the RA target range, 1998–2004

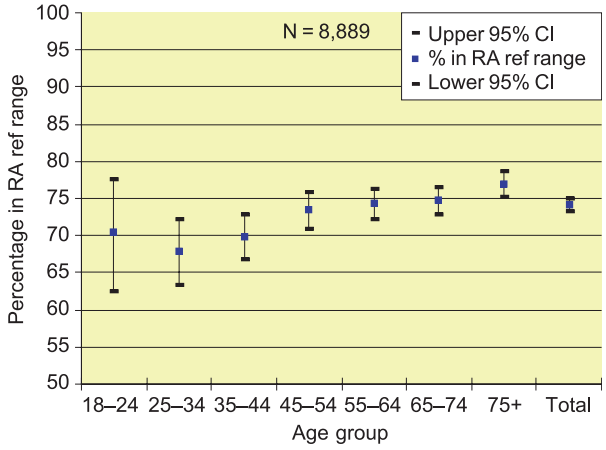

Figure 10.12: Percentage of patients achieving corrected calcium within the RA target range by age band: HD

Achievement of the calcium target amongst patients who had received a transplant was better than that amongst dialysis patients, with 84% of transplant patients achieving corrected calcium concentrations within the target range (Figure 10.13). However, there was a tendency to hypercalcaemia in some centres (Figure 10.14). The percentage of transplant patients with a serum corrected calcium within the RA target range differed significantly between centres ($\chi^2 = 1042$, $p < 0.001$).

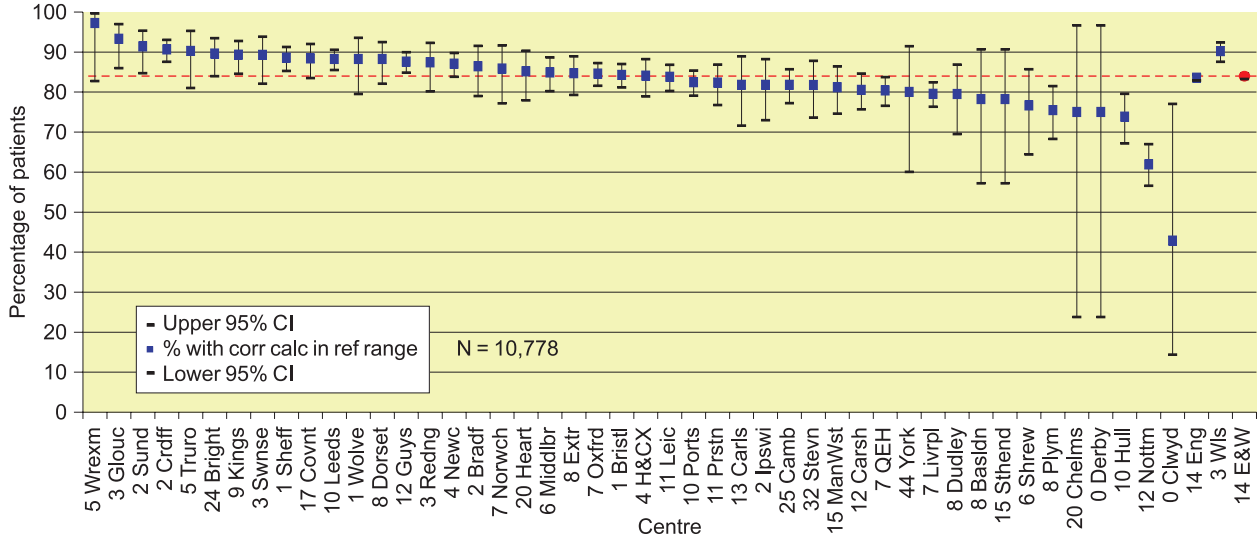

Figure 10.13: Percentage of patients with corrected calcium within 2.2 to 2.6 mmol/L: transplant

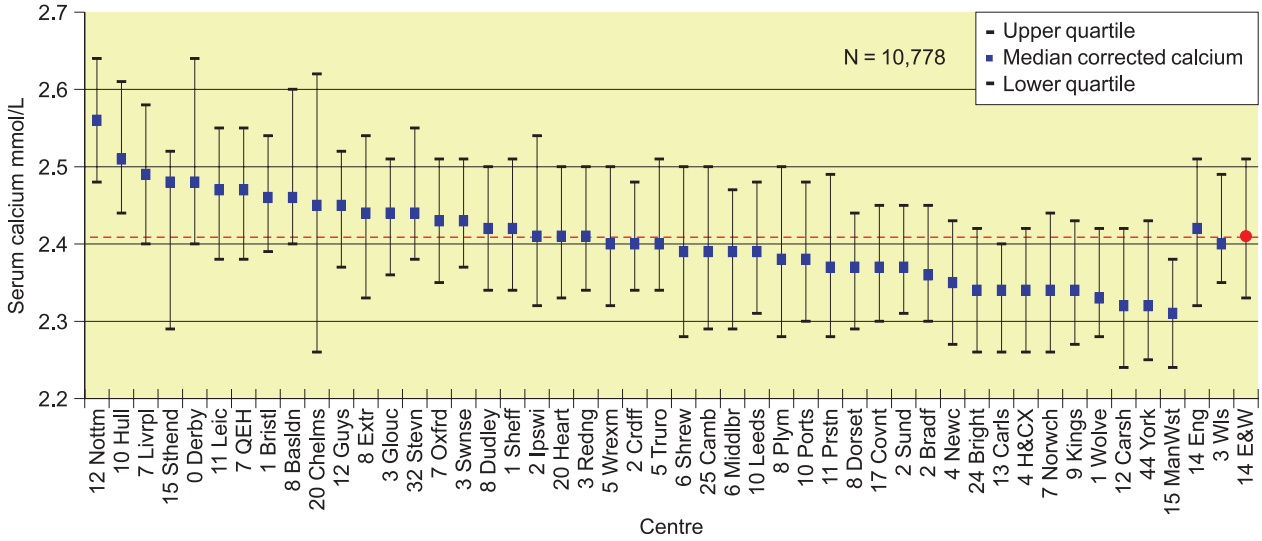

Figure 10.14: Median serum calcium concentration by centre in transplant patients

Serum calcium phosphate product

The RA has no standard for the serum calcium × phosphate product, but the KDOQI guidelines[2] recommend the product should be less than 4.4 $mmol^2/L^2$ (=55 mg^2/dl^2). More than half (66%) of patients achieve this but the range between units is wide (38–83%, Figure 10.15). This is similar to the 67% (range 44–82%) of patients that achieved this standard in the last Registry report[4]. Control was better in PD patients with 71% (range 47–89%) of patients achieving the standard, compared to 64% (range 35–85%) of patients on HD (Figures 10.16 and 10.17). The variation between units was significant for both HD ($\chi^2 = 360$, $p < 0.001$) and PD ($\chi^2 = 104$, $p < 0.001$) modalities.

Amongst patients who had received a transplant, 99% (mean range between units 95–100%) achieved the KDOQI guideline target; there was no evidence of significant variation between units ($\chi^2 = 60$, $p = 0.075$).

In keeping with the age-related changes observed in phosphate achievement, the percentage of patients achieving the KDOQI calcium × phosphate targets increased with

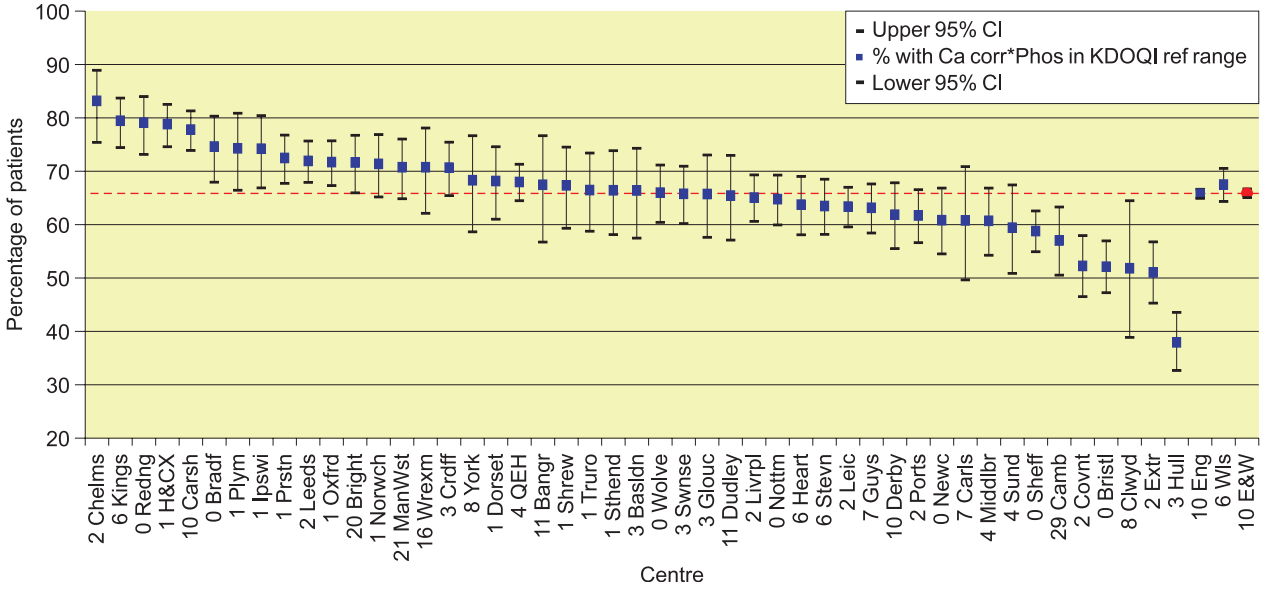

Figure 10.15: Calcium phosphate product in dialysis patients: percentage achieving KDOQI target

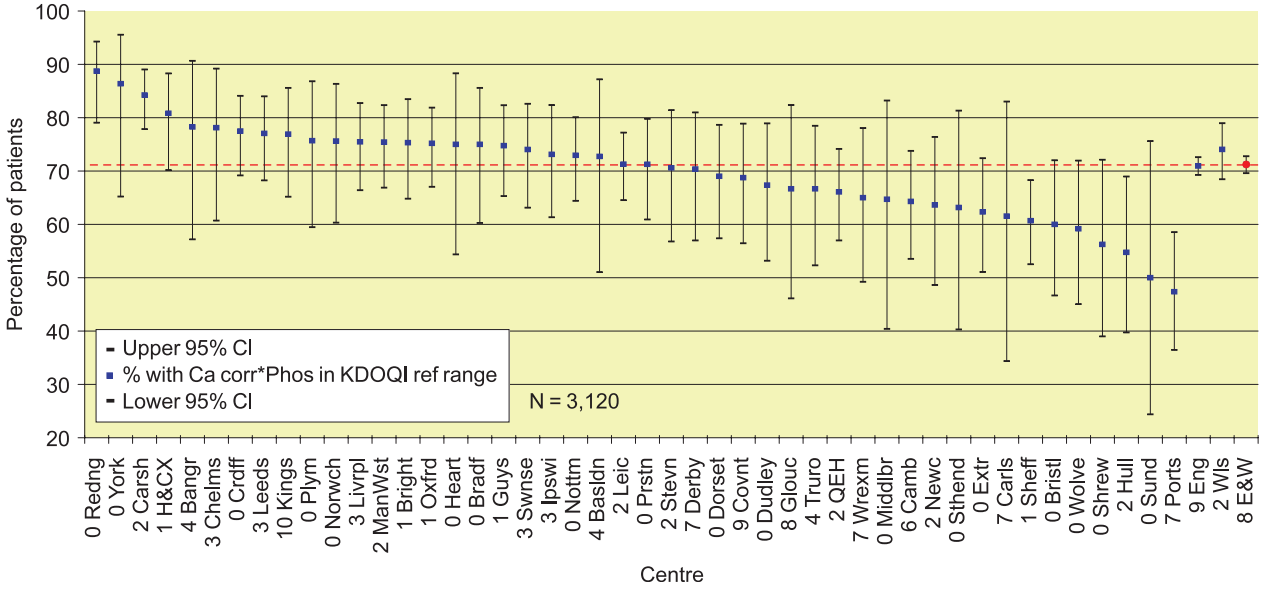

Figure 10.16: Percentage of PD patients with calcium phosphate product in the KDOQI reference range

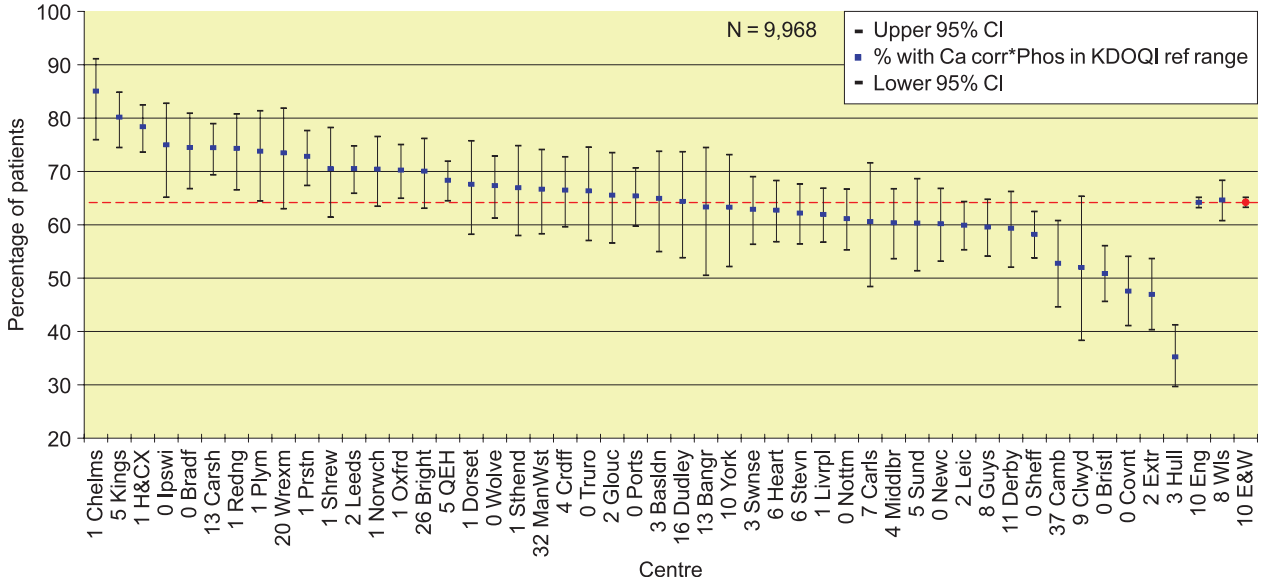

Figure 10.17: Percentage of HD patients with calcium phosphate product in the KDOQI reference range

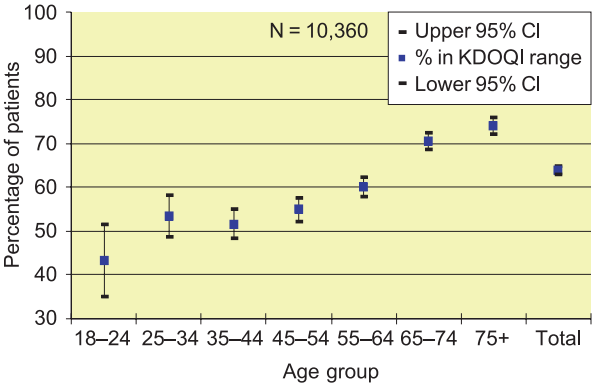

Figure 10.18: Percentage of patients achieving KDOQI calcium × phosphate product by age band: HD

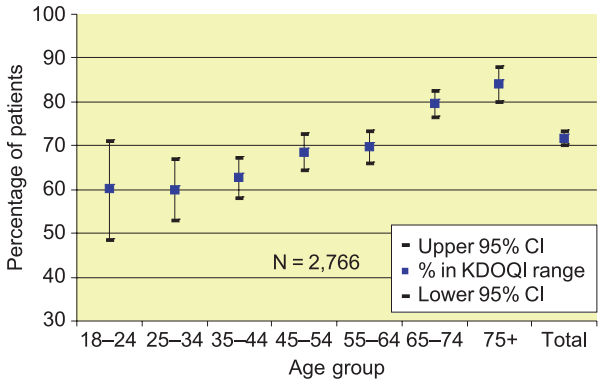

Figure 10.19: Percentage of patients achieving KDOQI calcium × phosphate product by age band: PD

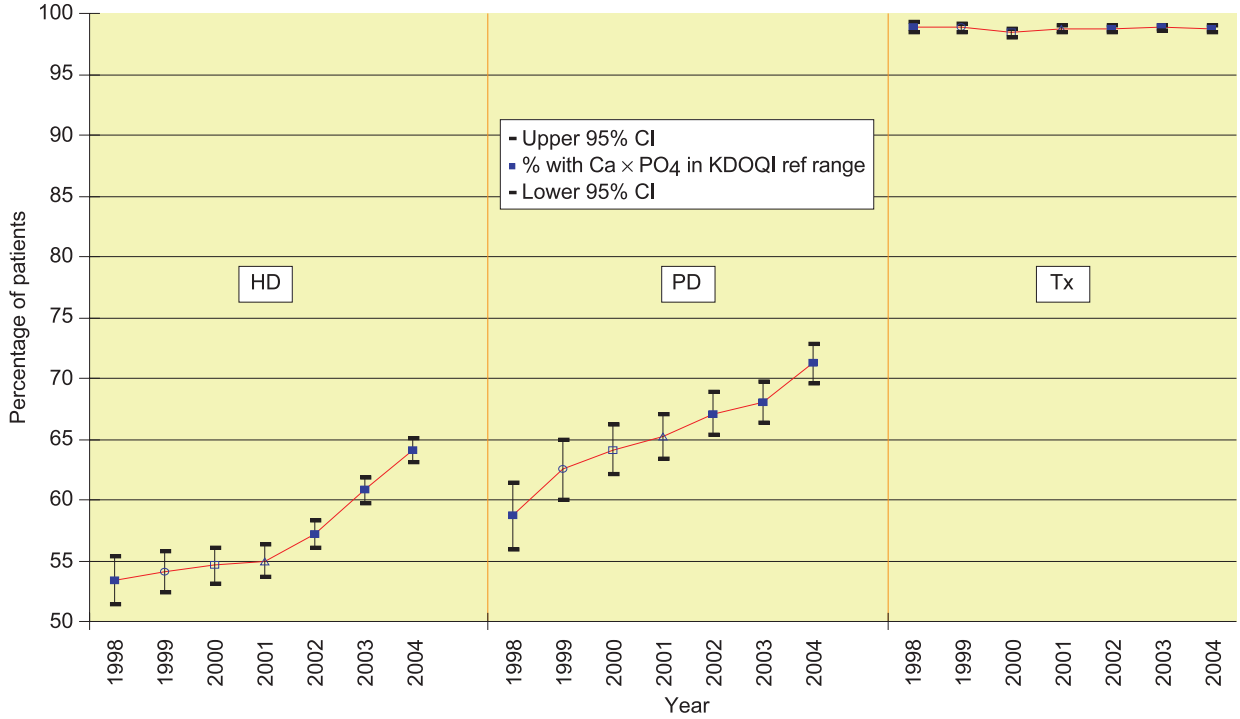

Figure 10.20: Change in percentage of patients achieving the KDOQI calcium × phosphate target, 1998–2004

increasing age in HD ($\chi^2 = 18.6$, $p < 0.0001$), PD ($\chi^2 = 9.3$, $p < 0.0001$) (Figures 10.18 and 10.19) and transplant ($\chi^2 = 3.4$, $p = 0.0006$) patients.

In both modalities, analysis of data from all prevalent dialysis patients within a particular year demonstrates a gradual improvement in achievement of the KDOQI calcium × phosphate target over the period 1998 to 2004 (Figure 10.20). As noted for corrected calcium above, a longitudinal sub-analysis including only those individual patients that have remained on dialysis throughout that entire period confirmed that this is a true effect and not a consequence of the inclusion of additional renal centres to the Registry database over that period (data not shown).

Serum parathyroid hormone

The RA Standard states:

> ***Parathyroid hormone (PTH) concentration should be less than four times the upper limit of normal of the assay used in patients being managed for chronic renal failure or after transplantation and in patients who have been on HD or PD for longer than three months.***

Comparison of serum PTH values from different units is difficult due to the variety of methods and reference ranges in use. Last years report (Chapter 9) discusses these issues in some detail, together with an attempt to assess the influences of laboratory bias and differential reactivities with the PTH 7-84 fragment known to accumulate in uraemia[4]. To enable some form of comparative audit, the Registry has expressed all results in pmol/L, and chosen an upper limit of four times the median upper lab value; this equates to 32 pmol/L.

Data completeness

The completeness of data by modality is shown in Table 10.3 for each centre.

Achievement of serum iPTH

The median PTH for all dialysis patients (22 pmol/L) lies well within the standard although the range of medians was wide (9 to 35 pmol/L, Figure 10.21). Median PTH appeared to be slightly higher overall amongst PD (23 pmol/L, inter-quartile range 11–46 pmol/L, range of medians 12 to 48 pmol/L) patients compared to HD (21 pmol/L, inter-quartile range 9–46 pmol/L, range of medians 4 to 36 pmol/L) patients. Overall, 63% of dialysis patients (62%

Table 10.3: Data completeness by centre for PTH

	HD	PD	Tx		HD	PD	Tx
Bangor	100	83	n/a	Liverpool	82	86	43
Barts	n/a	n/a	n/a	ManWst	64	92	67
Basildon	97	100	56	Middlesbrough	85	59	9
Bradford	98	95	52	Newcastle	97	98	30
Brighton	58	83	13	Norwich	94	68	11
Bristol	94	100	84	Nottingham	95	93	72
Cambridge	57	90	11	Oxford	83	86	29
Carlisle	92	86	10	Plymouth	85	78	33
Carshalton	59	72	8	Ports	93	45	7
Chelmsford	95	88	20	Preston	97	99	37
Clwyd	80	100	43	QEH	69	74	53
Coventry	83	76	21	Reading	97	96	27
Cardiff	84	96	18	Sheffield	96	87	9
Derby	8	7	36	Stevenage	93	93	37
Dorset	90	92	37	Southend	89	95	3
Dudley	n/a	n/a	n/a	Sunderland	96	100	98
Exeter	96	100	25	Swansea	55	88	37
Gloucester	97	88	27	Truro	97	94	32
Guys	76	96	18	Wirral	n/a	n/a	n/a
H&CX	51	90	35	Wolverhampton	97	100	56
Heartlands	79	79	7	Wrexham	66	81	60
Hull	78	81	17	York	91	100	22
Ipswich	92	97	30	England	77	78	32
Kings	91	86	22	Wales	75	90	24
Leeds	97	97	30	England & Wales	77	79	31
Leicester	84	85	58				

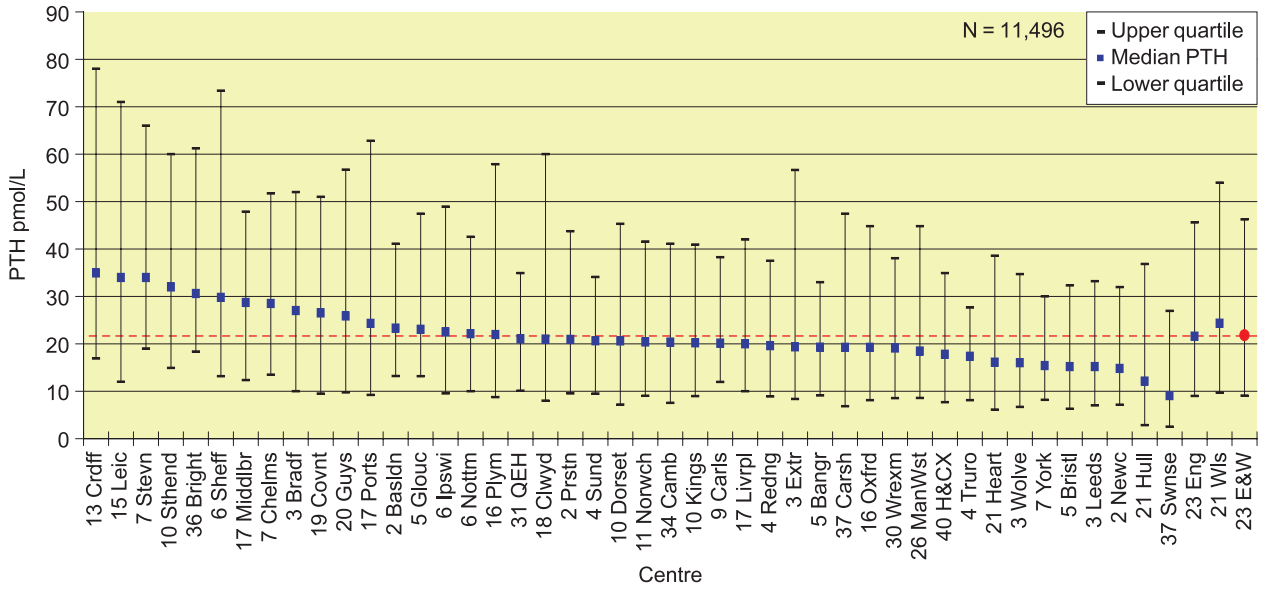

Figure 10.21: Median PTH by centre; dialysis

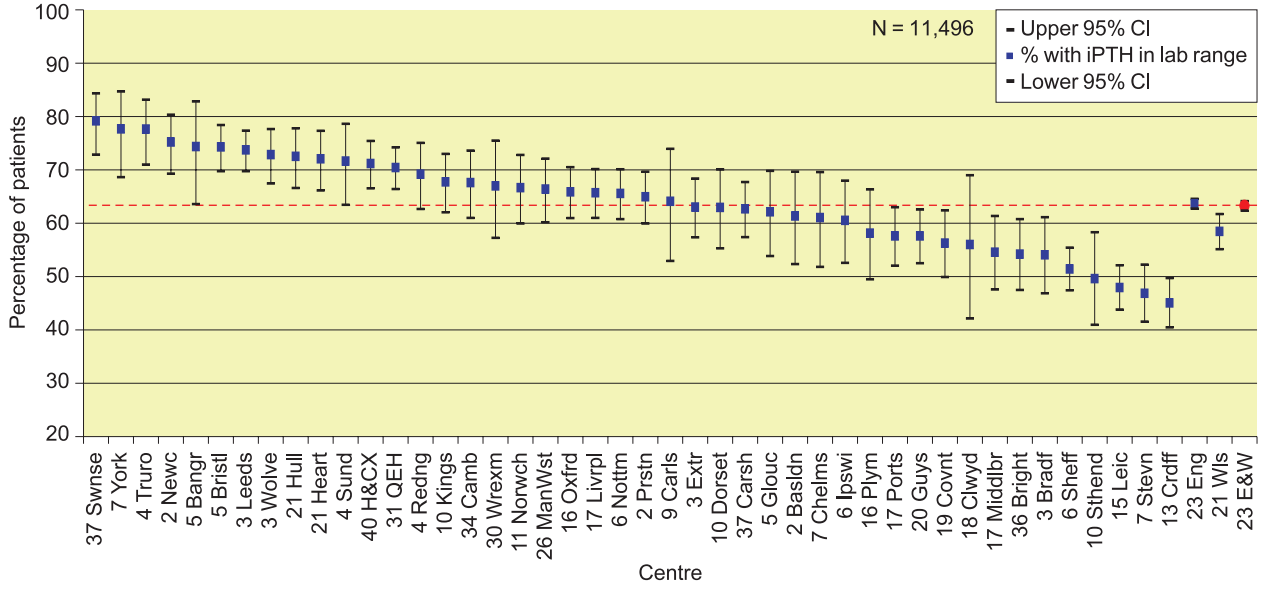

Figure 10.22: Percentage of patients with PTH <32 pmol/L; dialysis

PD; 64% HD) achieved the RA Standard, but the spread of data was remarkable, ranging from 45 to 79% compliance with the standard (Figure 10.22).

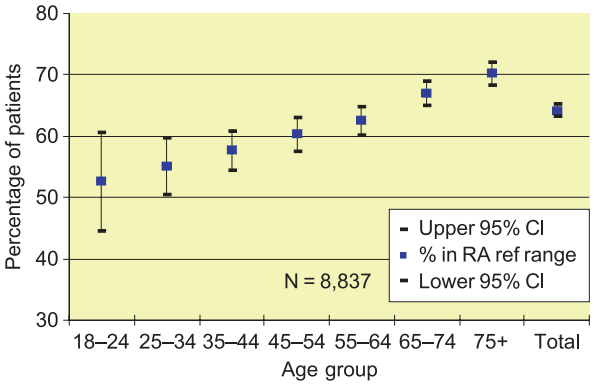

Figure 10.23: Percentage of patients achieving PTH <32 pmol/L by age band: HD

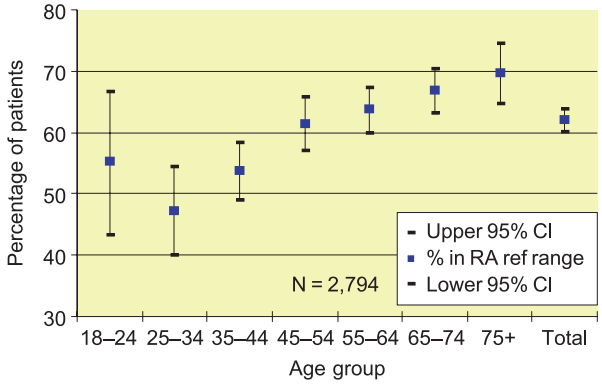

Figure 10.24: Percentage of patients achieving PTH <32 pmol/L by age band: PD

For both HD ($\chi^2 = 9.7$, $p < 0.0001$, Figure 10.23) and PD ($\chi^2 = 6.1$, $p < 0.0001$, Figure 10.24) patients the percentage achieving the RA target with respect to PTH increased with increasing age. This is unlikely to be an effect of ageing per se, since higher serum PTH concentrations have previously been reported in healthy older individuals[5]. This data could reflect improved phosphate control with increasing age as noted above.

Amongst patients who had received a transplant, median PTH is above the normal laboratory reference range (median 10 pmol/L, inter-quartile range 6–18 pmol/L), although the majority of patients (89%, range of centre means 70–100%) achieve the RA target; there was evidence of significant variation between units ($\chi^2 = 428$, $p < 0.0001$) but no evidence ($\chi^2 = 0.7$, $p = 0.47$) of an effect of age upon standard achievement.

Serum albumin

The RA has no standard for the serum albumin.

The RA Standards document[3] recognises the importance of serum albumin as a marker of outcome, but does not recommend setting an audit standard for serum albumin, predominantly due to lack of standardisation of albumin assays between laboratories. Serum albumin concentration is influenced significantly

by the dye used in the assay method; either bromocresol green (BCG) or bromocresol purple (BCP). As in previous years, for this report, centres have been separated both by methodology of albumin measurements and by dialysis modality. The difference between BCG and BCP methods in uraemic patients is widely known and has been discussed at length in previous reports.

Data completeness

The completeness of data by modality is shown in Table 10.4 for each centre.

Achievement of serum albumin

For centres supported by laboratories using BCG methods (n = 35) the median serum albumin was 39 g/L (range 36 to 41 g/L, Figure 10.25). As anticipated, centres using the BCP method (n = 12) generally had lower albumin concentrations (median 33 g/L, range 32 to 34 g/L, Figure 10.26). Overall, 75% of patients had serum albumin above 35 g/L for the BCG method (Figure 10.27) and 73% for BCP (Figure 10.28). For both BCG ($\chi^2 = 217$, $p < 0.001$) and BCP ($\chi^2 = 55$, $p < 0.001$) centres, the percentage of patients achieving serum albumin concentrations above these levels differed significantly between centres.

Serum albumin is generally lower in PD patients than in HD patients, predominantly due to peritoneal protein losses[9]. Furthermore, peritoneal albumin clearance increases with time on treatment due to increasing effective peritoneal surface area[10]. For centres supported by laboratories using BCG methods (n = 35) the median serum albumin was 35 g/L (range 30 to 39 g/L, Figure 10.29). As anticipated, centres using the BCP method (n = 12) generally had lower albumin concentrations (median 29 g/L, range 27 to 33 g/L, Figure 10.30). Overall, 55% of patients had serum albumin above 35 g/L for the BCG method (Figure 10.31) and 49% above 30 g/L for BCP (Figure 10.32), in both cases a slight fall in achievement compared to last years report. For both BCG ($\chi^2 = 240$, $p < 0.001$) and BCP ($\chi^2 = 80$, $p = 0.0015$) centres, the percentage of patients achieving serum albumin concentrations above these levels differed significantly between centres. The data indicate how difficult it is to keep serum

Table 10.4: Data completeness by centre for serum albumin

	HD	PD	Tx
Bangor	100	100	n/a
Barts	n/a	n/a	n/a
Basildon	97	100	92
Bradford	100	100	97
Brighton	75	99	78
Bristol	100	100	99
Cambridge	63	96	75
Carlisle	93	93	87
Carshalton	87	98	90
Chelmsford	99	97	80
Clwyd	89	100	100
Coventry	100	94	84
Cardiff	96	98	96
Derby	91	93	36
Dorset	100	100	93
Dudley	84	100	91
Exeter	98	100	92
Gloucester	98	92	96
Guys	91	99	84
H&CX	99	95	76
Heartlands	94	100	77
Hull	97	98	92
Ipswich	100	97	98
Kings	95	90	91
Leeds	99	98	93
Leicester	98	98	91
Liverpool	95	96	93
ManWst	69	98	71
Middlesbrough	96	100	95
Newcastle	100	98	96
Norwich	99	100	93
Nottingham	97	100	91
Oxford	99	99	93
Plymouth	91	100	93
Portsmouth	100	95	91
Preston	99	100	74
QEH	96	98	94
Reading	97	100	99
Sheffield	100	99	99
Shrewsbury	100	100	95
Stevenage	98	98	69
Southend	99	95	90
Sunderland	95	100	98
Swansea	98	99	94
Truro	100	98	99
Wirral	n/a	n/a	n/a
Wolverhampton	100	100	98
Wrexham	83	95	96
York	96	100	98

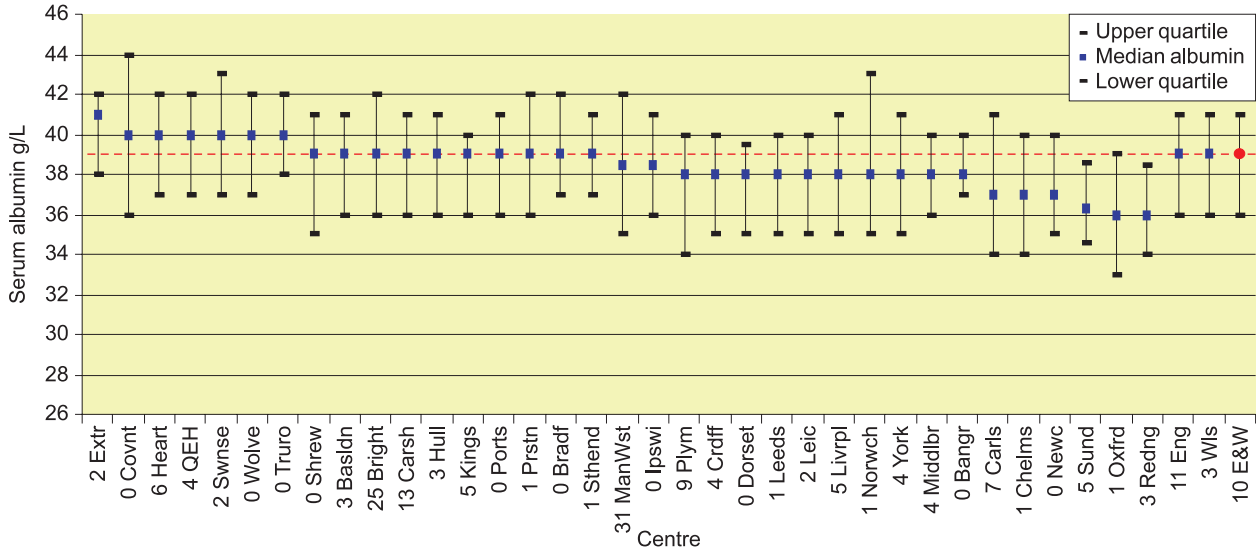

Figure 10.25: Median serum albumin in HD patients by centre: BCG method

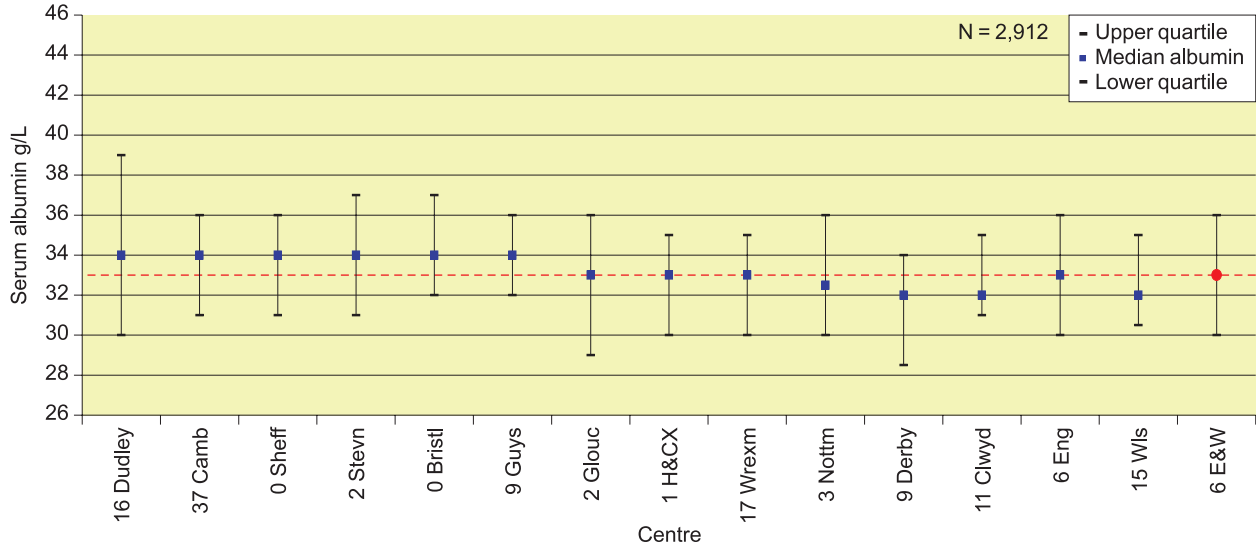

Figure 10.26: Median serum albumin in HD patients by centre: BCP method

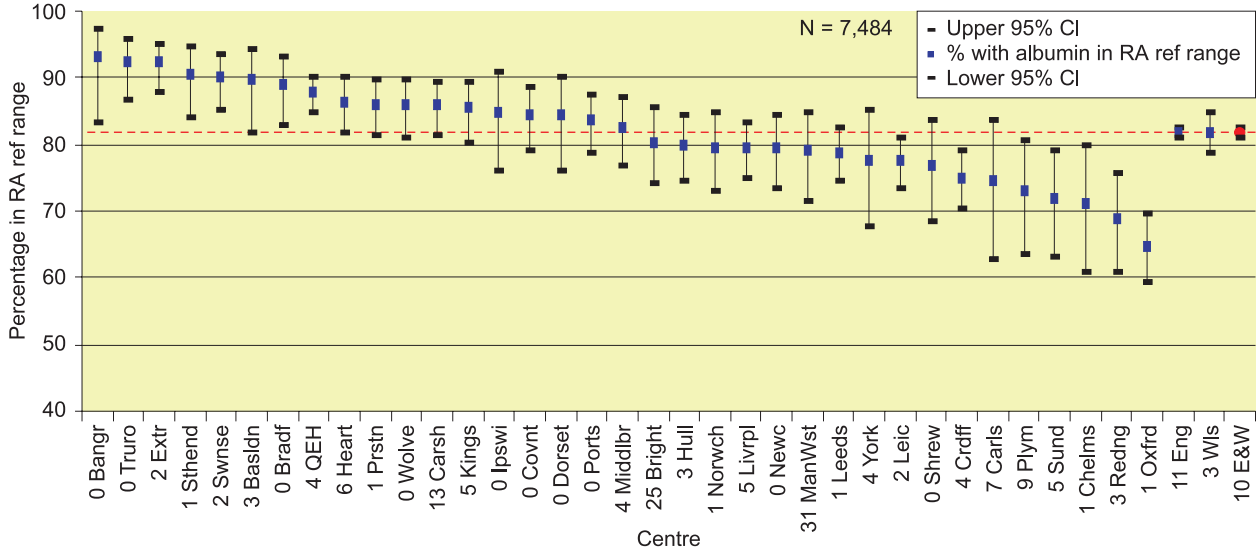

Figure 10.27: Percentage of HD patients by centre with serum albumin >35 g/L (BCG)

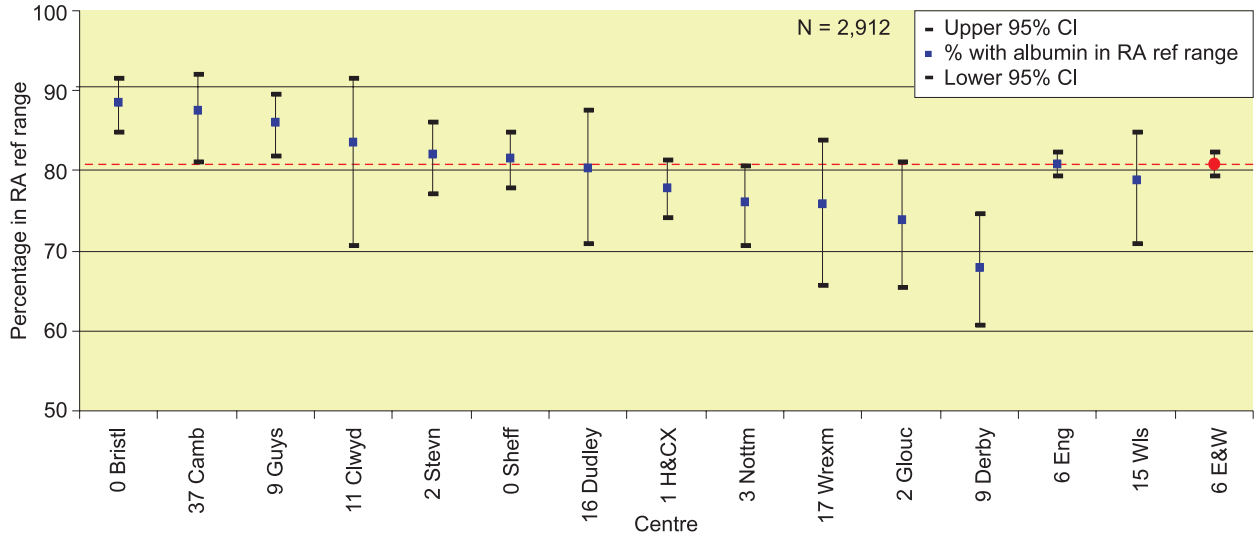

Figure 10.28: Percentage of HD patients by centre with serum albumin >30 g/L (BCP)

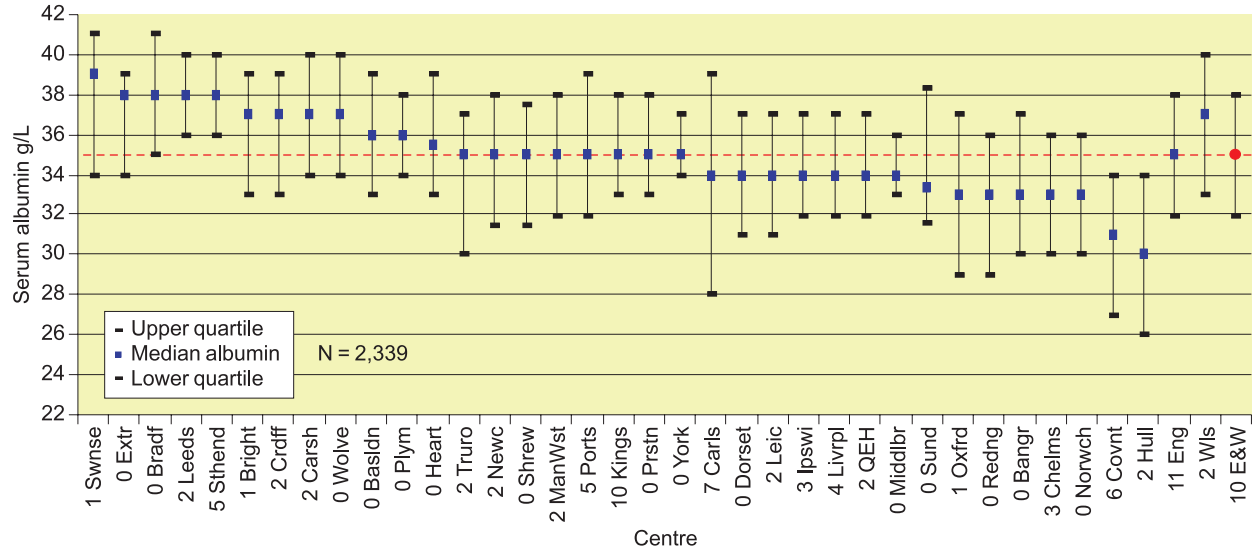

Figure 10.29: Median serum albumin in PD patients by centre: BCG method

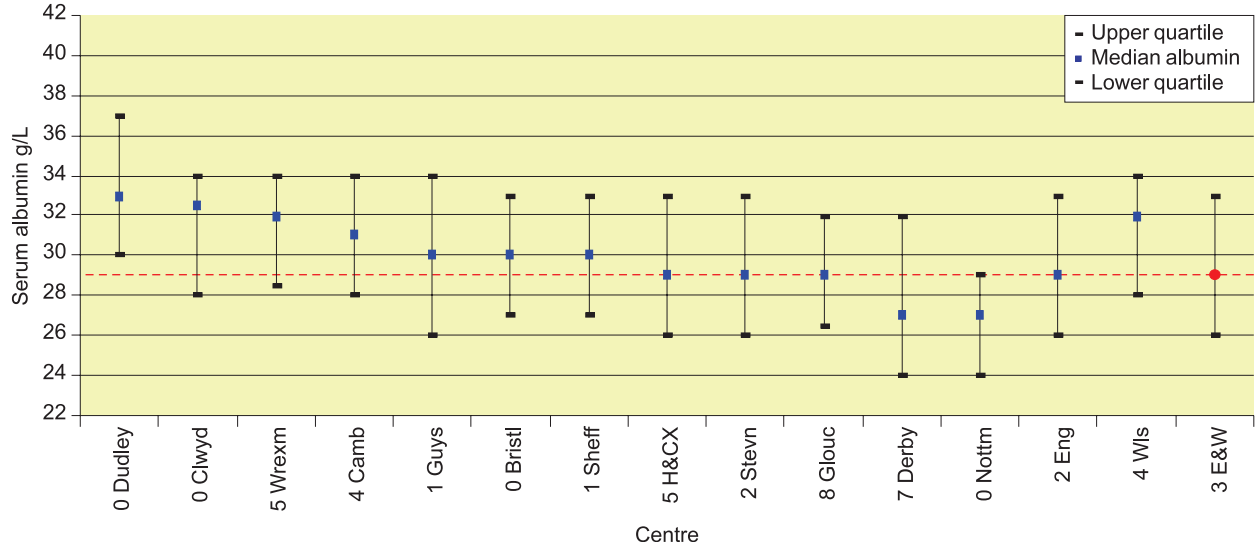

Figure 10.30: Median serum albumin in PD patients by centre: BCP method

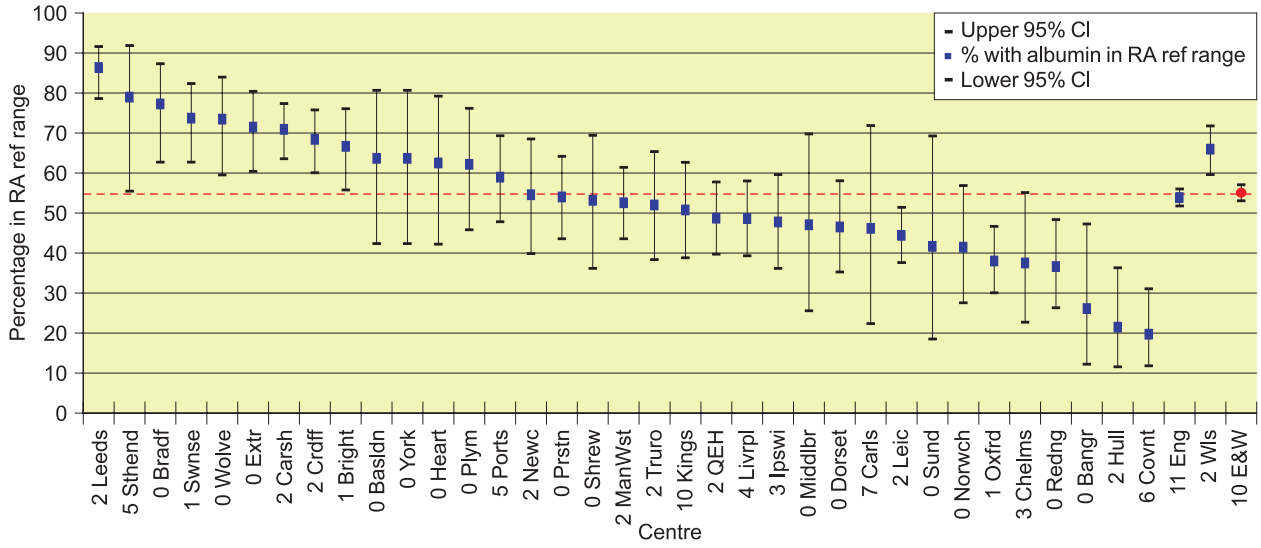

Figure 10.31: Percentage of PD patients by centre with serum albumin >35 g/L (BCG)

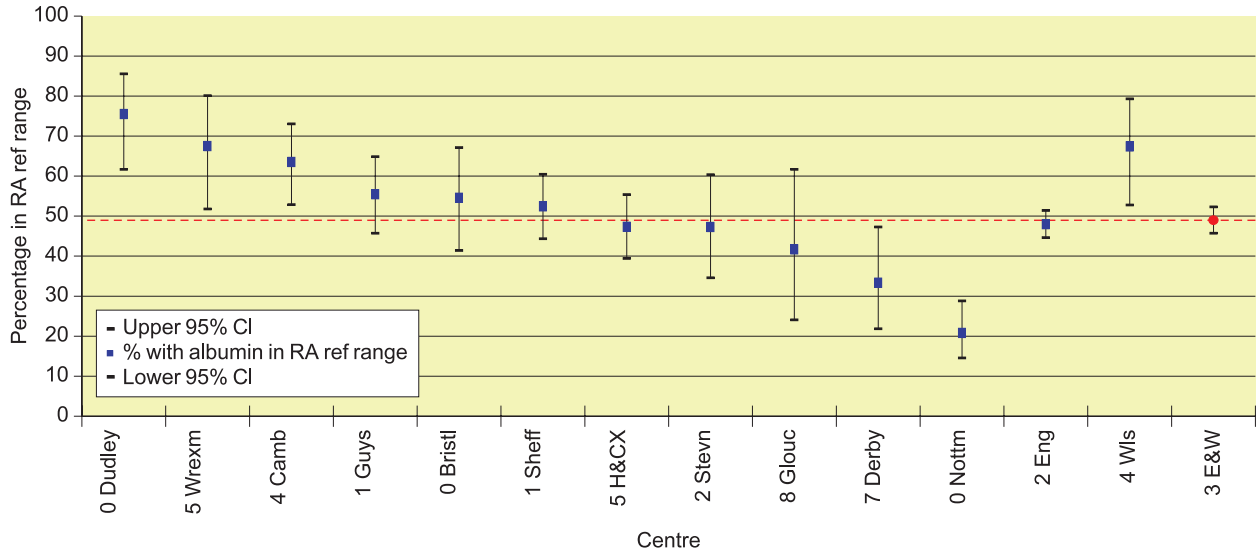

Figure 10.32: Percentage of PD patients by centre with serum albumin >30 g/L (BCP)

albumin above the recommended minimum in patients treated by peritoneal dialysis.

Amongst patients who had received a renal transplant, median serum albumin was 41 g/L (range 17–56) for centres supported by laboratories using BCG methods and 37 g/L (range 14–48) for centres supported by laboratories using BCP methods. Overall, 95.4% and 95.9% of patients had serum albumin above 35 g/L for the BCG method and above 30 g/L for the BCP method respectively.

Albumin concentrations in both PD and HD patients decreased with increasing age. The percentage of HD patients achieving serum albumin $\geqslant 35$ g/L (BCG, $\chi^2 = 9.8$, $p < 0.0001$) or $\geqslant 30$ g/L (BCP, $\chi^2 = 5.8$, $p < 0.0001$) decreased significantly with age. Similarly the percentage of PD patients achieving serum albumin $\geqslant 35$ g/L (BCG, $\chi^2 = 7.3$, $p < 0.0001$) or $\geqslant 30$ g/L (BCP, $\chi^2 = 4.9$, $p < 0.0001$) decreased significantly with age (Figures 10.33 and 10.34, BCG data only shown).

In part, this effect may be attributable to the known age-related decline in serum albumin concentration in the male general population (eg 50th percentile in males aged 68–71 years 45 g/L compared to 48 g/L in males aged 25–34 years)[6]. In a study of community-dwelling individuals aged 75 years and over in Australia, 30% were noted to have serum albumin concentrations below the normal laboratory reference

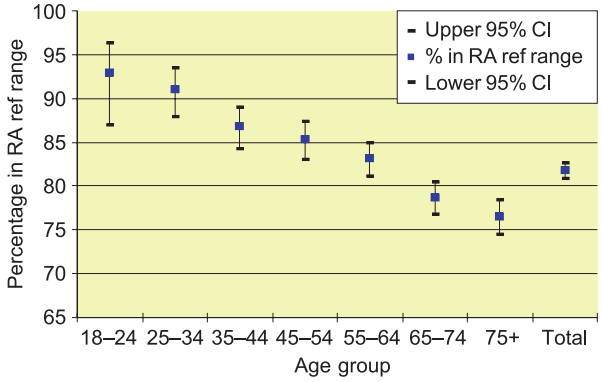

Figure 10.33: Percentage of patients achieving RA albumin standard by age band: HD

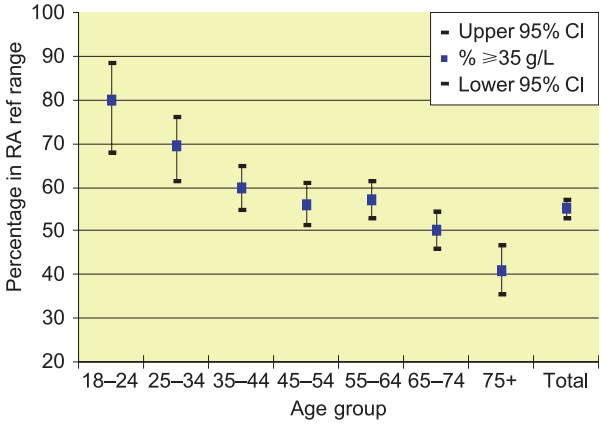

Figure 10.34: Percentage of patients achieving RA albumin standard by age band: PD

range[8]. In support of this it can be seen that the marked decrease in percentage achievement is effected by relatively small decreases in median serum albumin concentration (Figures 10.35 and 10.36; BCG data only shown). Further, achieved serum albumin concentration also

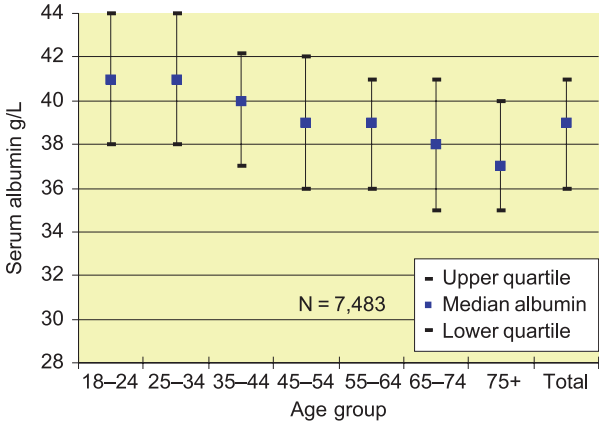

Figure 10.35: Median serum albumin by age group in haemodialysis patients. BCG data only shown

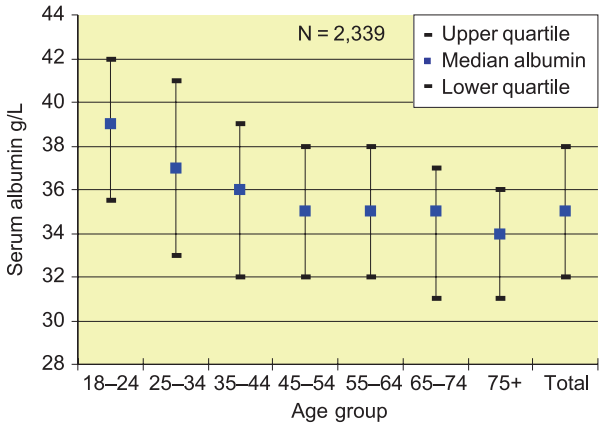

Figure 10.36: Median serum albumin by age group in peritoneal dialysis patients. BCG data only shown

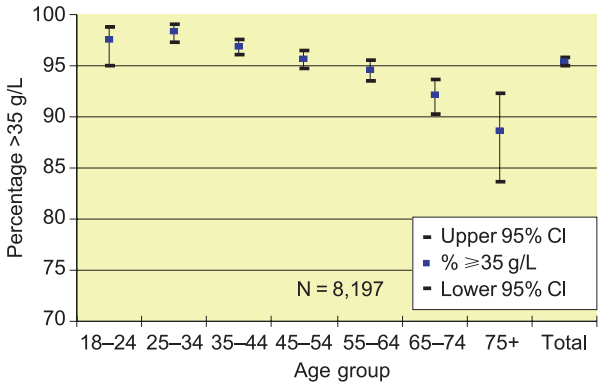

Figure 10.37: Percentage of patients achieving RA albumin standard by age band: transplant

declines with age in renal transplant recipients (BCG; $\chi^2 = 8.5$, $p < 0.0001$, Figure 10.37) although this effect did not achieve significance amongst transplant recipients having albumin measured by BCP methods ($\chi^2 = 0.8$, $p = 0.41$).

Albumin is affected by method of analysis, including a within method group effect[4]. Previous reports have described other influences on serum albumin concentration in dialysis patients including effects of time on treatment and social deprivation. The data presented above, describing the influence of age on serum albumin concentration, further illustrate the difficulties of using serum albumin as an audit standard in this setting. It is felt that continued presentation of albumin achievement data in the Registry annual report is of limited value: unless there are strong calls from the renal community with an opposing viewpoint, this data will not be published in next year's report.

Serum aluminium

The RA Standard states:

> ***Serum aluminium concentration should be measured every three months in all patients on HD and in all PD patients receiving oral aluminium hydroxide. No patient whose ferritin level is <100 μg/L should have a serum aluminium concentration of >60 μg/L (2.2 μmol/L).***

This wording may reflect a typographical error in the Standards document as there is no mention of a Standard for patients who are iron replete and have a serum ferritin above 100 μg/L.

Aluminium measurement is not available in most biochemistry laboratories, tending to be measured in a handful of regional reference centres. It is possible that the reports generated by these laboratories are not transcribed into local pathology or renal unit databases, so the following data interpretation should be regarded with some caution.

During 2004, aluminium was measured on 9,119 HD samples and 780 PD samples. Overall, 39% of HD patients (4,342 of 11,060) and 15% of PD patients (524 of 3,410) had a serum aluminium concentration checked once during the year. However, there was enormous variation in reported compliance with this standard with 14 centres reporting no aluminium data for HD patients and a further 7 reporting data in less than 10% of their patients. Amongst PD patients, 24 centres reported no aluminium data and a further 9 reported data in less than 10% of their patients. The Registry does not collect information on aluminium hydroxide prescription. An analysis of quarterly data suggests that many of those centres that are reporting data may be doing so on an annual basis in most patients rather than the three-monthly interval suggested by the RA.

Median aluminium amongst HD patients in England and Wales was 0.3 μmol/L (95% range 0.1 to 1.3 μmol/L) and amongst PD patients was 0.2 μmol/L (95% range 0.1 to 1.2 μmol/L). Serum aluminium concentration was $\geqslant$2.2 μmol/L in 80 HD patients: concurrent ferritin concentration was <100 μg/L in three of these patients (all of whom had polycystic kidney disease). Serum aluminium concentration was $\geqslant$2.2 μmol/L in 3 PD patients, all of whom had concurrent ferritin concentration <100 μg/L. The Registry has identified audit follow-up of patients with high reported aluminium concentrations as a future area of work.

The RA Standards document states that aluminium may be increased in the presence of relative iron deficiency and that serum aluminium concentration should therefore be re-investigated after iron repletion. However, this is somewhat at odds with the RA Standard recommendation that 'no patient whose ferritin level is <100 μg/L should have a serum aluminium concentration of >60 μg/L (2.2 μmol/L)'. In fact, increased aluminium concentration in the presence of ferritin >100 μg/L may be more likely to imply an underlying aluminium toxicity requiring further investigation including repeat testing.

The Registry data is consistent with a four year study from the north of England[11]. In this report, patients who had aluminium measured had it measured only once a year on average. From 5,918 aluminium determinations, 104 were $\geqslant$2.2 μmol/L. However, the vast majority of these were normal on repeat testing and only one case of true aluminium toxicity was identified. It is likely that this patient would have been identified without an aluminium screening programme: they were receiving alucaps and had erythropoietin-resistant anaemia which was attributed to aluminium toxicity and responded to desferrioxamine treatment.

It is possible that many renal centres have abandoned routine monitoring of aluminium in dialysis patients. Others appear to be deviating from the RA Standard recommendations in terms of frequency of testing whilst the yield of useful clinical information from those centres still undertaking routine monitoring is questionable, although the Registry does not collect information on aluminium hydroxide prescribing so the prevalence of this practice nationally is uncertain. The cost of a single aluminium analysis is approximately £11.25 (Keith Allen, Department of Clinical Biochemistry, Leeds Teaching Hospitals, personal communication) to which must be added sample processing costs from the referring laboratories. The added

value of this practice should probably be examined and we agree with Gault *et al*[11] that the role of aluminium monitoring in dialysis patients needs re-evaluation. The KDOQI guidelines are slightly less stringent than the RA guidelines, with the recommendation that serum aluminium should be measured at least yearly and every three months in patients receiving aluminium-containing medications. Generally it is acknowledged that aluminium-related bone disease is a diminishing problem in units where aluminium-phosphate binders are not widely used.

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