Chapter 9: Management of Biochemical Variables

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Summary

- The biochemical data analysed in this chapter were: calcium, phosphate, calcium*-phosphate product, parathyroid hormone, aluminium, bicarbonate and total cholesterol for patients in England, Wales and Northern Ireland for 2006.
- A serum phosphate of <1.8 mmol/L was achieved by 67% of dialysis patients (65% of HD patients, 73% of PD patients).
- An adjusted serum calcium concentration between ⩾2.2–⩽2.6 mmol/L was achieved by 75% of dialysis patients (74% of HD patients, 79% of PD patients).
- A serum calcium*phosphate product within the KDOQI guidelines (<4.4 $mmol^2/L^2$) was achieved by 71% of dialysis patients (70% of HD patients, 75% of PD patients).
- A serum PTH <32 pmol/L was achieved by 61% of dialysis patients (61% of HD patients, 60% of PD patients).
- Serum bicarbonate of ⩾20–⩽26 mmol/L was achieved by 70% of HD patients. Serum bicarbonate of ⩾25–⩽29 mmol/L was achieved by 53% of PD patients.
- A total serum cholesterol concentration of <5 mmol/L was achieved by 83% of dialysis patients (85% of HD patients and 71% of PD patients). A total serum cholesterol <5 mmol/L was achieved by 67% of transplant patients.
- There remained inter-centre variability in achievement of Renal Association biochemical standards. The use of funnel plot analysis enabled identification of statistically outlying centres.
- Longitudinal analysis continued to show year-on-year improvement in achievement of Renal Association biochemical standards.
- With recent revision of Renal Association standards (4th edition still in draft), there may be heterogeneity in application of clinical practice guidelines between UK centres. Achievement of 'new' Renal Association standards where possible are therefore reported as a baseline analysis to allow comparison to be made in subsequent years.

Introduction

The UK Renal Registry (UKRR) collected routine biochemical data on a quarterly basis from patients in centres in England, Wales and Northern Ireland. This chapter is primarily a series of cross-sectional analyses of centre performance using Renal Association clinical practice guidelines or other surrogate guidelines as audit standards.

In addition to the indices reported in the chapter, the Registry collected additional biochemical data eg albumin which may be used in original epidemiological research studies but were not included in this report. There is ongoing work to expand the laboratory dataset collected by the Registry in order to provide innovative analyses.

The Renal Association is in the process of revising guidelines[1] to incorporate new evidence and the 4th edition is currently in draft format[2].

It is assumed that UK centres internally audit performance against Renal Association standards (as opposed to other guidelines) and so where possible the Registry does the same. However, it may be that individual centres have developed centre based guidelines that take account of local differences in policy and practice. A number of changes have also been made during revision of the Renal Association guidelines, and although these are still in draft, this may also have created heterogeneity between

centre guideline usages. For this reason, and to provide a baseline for subsequent analysis, achievement of standards this year (for 2006 data) were audited against both the 3rd and 4th edition of the Renal Association standards[1,2]. There are also a number of clinical practice guidelines internationally and these can be compared at www.kdigo.org[3].

It is widely recognised that performance data is open to misinterpretation[4]. To facilitate interpretation of performance data reported by the Registry, funnel plots were introduced for the analysis of biochemical data in 2006[5]. These enabled detection of 'outlying centres' where there were statistically significant differences between centres in achievement of Renal Association standards. The publication of these data should encourage centres to explore the differences in clinical processes of care which may underlie the statistical differences.

To complement this further, new exploratory analyses were undertaken this year to test the confidence of the rankings attributed to centres and the Registry welcomes feedback from centres on the usefulness of these data[6].

Methods

This chapter analysed the prevalent RRT cohort for England, Wales and Northern Ireland for 2006. The cohort definition for biochemical analyses has been previously described and can be found at www.renalreg.com[7].

The Registry extracted quarterly data electronically from centres. Quarterly values were extracted for the last two quarters for calcium, phosphate and bicarbonate, the last three quarters for PTH and the entire year for cholesterol and aluminium. Patients who did not have these data were excluded from the relevant analyses. Patients were analysed both as a complete cohort and also divided by RRT modality into groups. Some analyses were also performed on a combined dialysis group. The completeness of data were analysed at centre and country level. All patients were included in analyses but centres with less than 50% completeness were excluded from the figures showing centre performance. Data were also excluded from plots when there were less than 20 patients with data both at centre and country level. The number preceding the centre name in each figure indicates the percentage of missing data for that centre.

Summary statistics

These data were analysed to calculate summary statistics (maximum, minimum, mean and median values in addition to standard deviation and quartile ranges) and are represented as caterpillar plots showing median values and quartile ranges. Where applicable, the percentage achieving Renal Association or other surrogate standard was also calculated and represented as caterpillar plots with 95% confidence intervals. For 2006, data was also audited against the 'new' Renal Association standards (taken from the draft 4th edition).

Funnel plot analysis

Funnel plot analysis has been used to identify 'outlying centres'. The percentage achieving each standard was plotted against centre size along with the upper and lower 95% and 99.9% confidence intervals. The methodology for funnel plot analysis and further guidance on interpretation of the data was more extensively described in the 2006 report.

Longitudinal analysis

Longitudinal analysis has also been performed for some data to calculate overall changes in achievement of standards annually from 1998 to 2006.

Methodology for testing confidence in centre rankings

A new analysis to test the statistical certainty of centre ranking has been performed using phosphate data for HD patients. The rank of each centre has a degree of statistical uncertainty as denoted by the surrounding confidence intervals. The distribution of the proportion of patients achieving the phosphate standard can be modelled as a normal distribution for each centre. For each centre, a random proportion was sampled from this normal distribution and the centres were then ranked. This random sampling and ranking was repeated 10,000 times. From these sampled ranks it was possible

to identify the median rank and its 95% confidence interval for each centre i.e. a measure of the statistical certainty of that rank.

Results

Phosphate

The 3rd edition of the Renal Association standards document states:

> ***Serum phosphate (measured before a dialysis session in HD patients) should be below 1.8 mmol/L (1).***

The draft 4th edition of the Renal Association standards clinical practice guidelines states:

> ***Serum phosphate in dialysis patients (measured before a 'short gap' dialysis session in HD patients) should be maintained between 1.1 and 1.8 mmol/L (2).***

Results

Data quality

The completeness of data by modality is shown in Table 9.1. A technical problem with the Registry extraction of phosphate data for haemodialysis patients from four centres was identified. The data have been corrected for Bristol and Exeter but Hull and Coventry were excluded this year from the figures until the problem can be rectified. Retrospective data for all four centres are also being re-extracted.

Table 9.1: Percentage data completeness by centre for serum phosphate by modality

	HD	PD	Transplants		HD	PD	Transplants
Antrim	100	100	83	Leic	99	98	90
B Heart	95	95	79	Liv Ain	96	n/a	n/a
B QEH	96	94	86	Liv RI	98	98	92
Bangor	97	100	n/a	ManWst	82	90	89
Basldn	99	100	89	Middlbr	99	96	93
Belfast	96	95	95	Newc	100	98	96
Bradfd	100	100	85	Newry	99	86	83
Brightn	97	99	83	Norwch	96	98	95
Bristol	100	100	96	Nottm	99	100	76
Camb	64	100	91	Oxford	98	100	96
Cardff	97	99	97	Plymth	98	100	93
Carlis	95	100	91	Ports	99	90	79
Carsh	82	97	89	Prestn	100	100	77
Chelms	100	100	87	Redng	100	99	94
Chestr	100	n/a	n/a	Sheff	99	100	97
Clwyd	92	88	86	Shrew	99	100	100
Covnt	98	100	77	Stevng	94	98	70
Derby	99	91	0	Sthend	99	94	91
Derry	100	n/a	67	Sund	96	100	98
Dorset	100	98	68	Swanse	99	97	96
Dudley	84	98	99	Truro	99	100	94
Exeter	98	100	91	Tyrone	96	86	90
Glouc	100	100	97	Ulster	100	100	100
Hull	100	91	91	Wirral	95	55	n/a
Ipswi	100	96	94	Wolve	99	98	95
L Barts	100	89	82	Wrexm	3	0	67
L Guys	87	99	92	York	99	91	96
L Kings	100	100	94	**England**	**96**	**96**	**89**
L Rfree	86	94	82	**N Ireland**	**98**	**94**	**93**
L West	100	97	96	**Wales**	**88**	**87**	**97**
Leeds	99	98	94	**E, W & NI**	**95**	**95**	**89**

n/a = no patients treated for that modality in centre.

The UKRR has also identified several centres which reported serum phosphate to only one decimal place (compared to two decimal places for most centres). This has introduced a digit bias into measuring performance against the RA phosphate standard for these centres. For example, when analysing the percentage of patients achieving a phosphate <1.8 mmol/L in centres reporting data to one decimal place the audit standard was actually 1.75 mmol/L due to rounding. The effect of this was to artificially lower the percentage of patients achieving the standard in these centres. The Registry has contacted the centres affected in order to rectify the problem.

Summary statistics

The summary statistics are shown in Figures 9.1 to 9.8. 65% of HD and 73% of PD patients achieved a serum phosphate <1.8 mmol/L (Figures 9.4 and 9.7). This represented a further small improvement compared to 2005 against this audit standard (Figure 9.1).

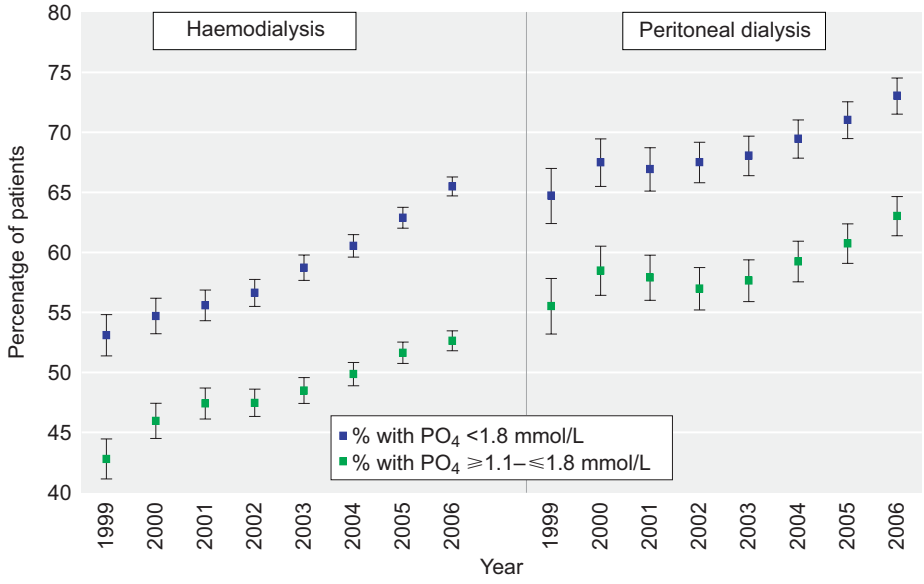

Figure 9.1: Annual change in percentage of dialysis patients with serum phosphate <1.8 mmol/L and with serum phosphate ⩾1.1–⩽1.8 mmol/L between 1999–2006

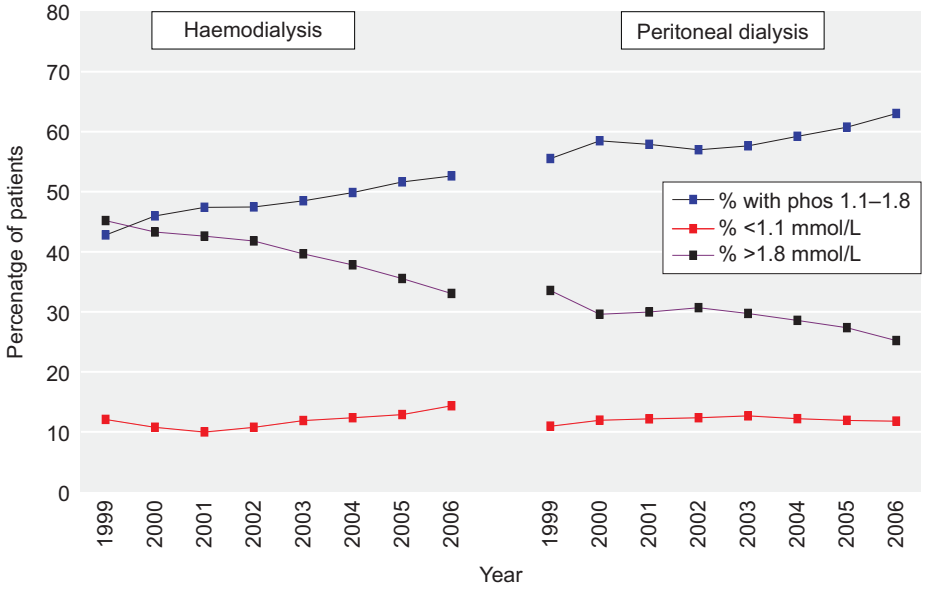

Figure 9.2: Annual change in percentage with serum phosphate ⩾1.1–⩽1.8 mmol/L, >1.8 mmol/L and <1.1 mmol/L between 1999–2006

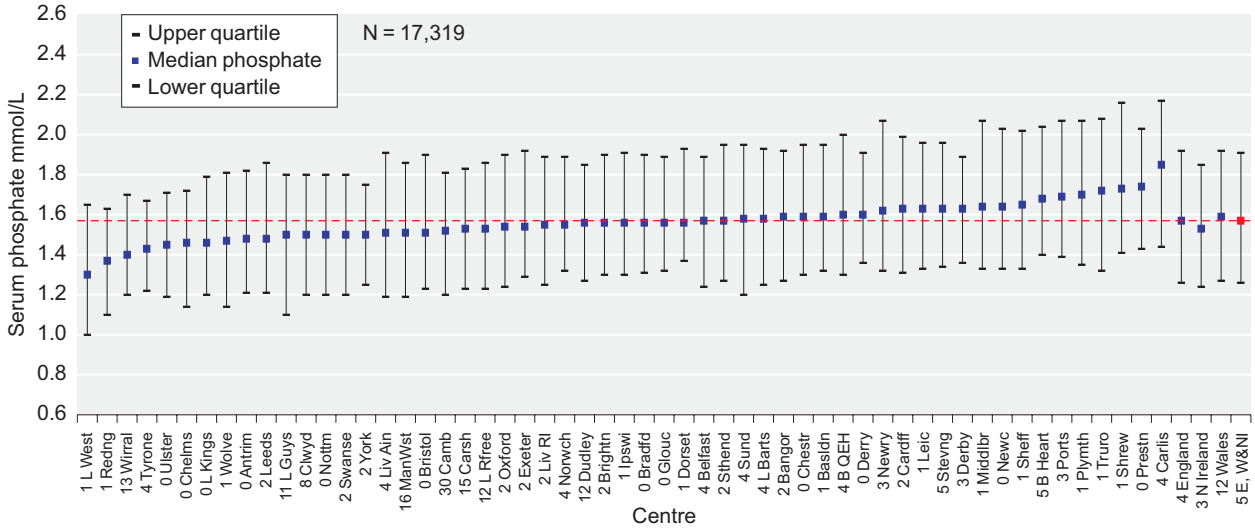

Figure 9.3: Median phosphate in dialysis patients by centre

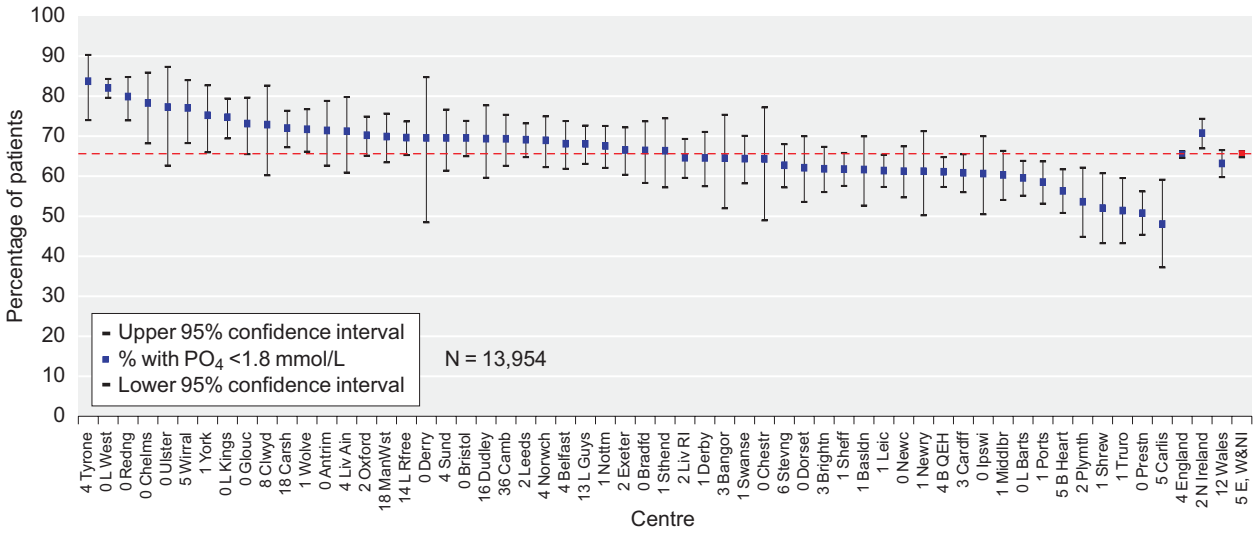

Figure 9.4: Percentage of HD patients with serum phosphate <1.8 mmol/L by centre

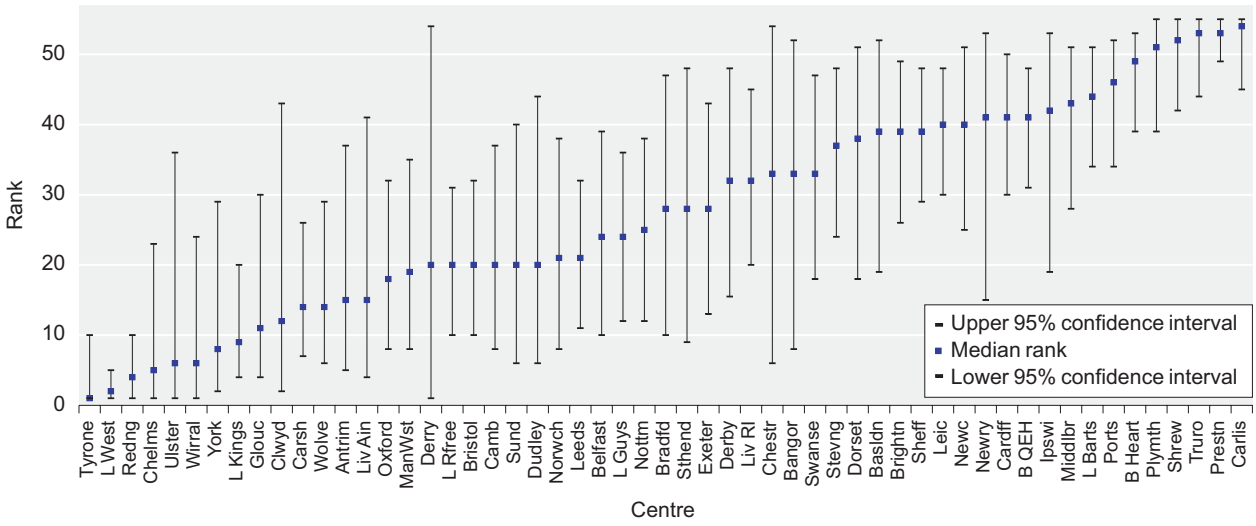

Figure 9.5: Confidence in centre ranking for percentage of HD patients with serum phosphate <1.8 mmol/L
Median rank from repeated sampling (10,000 iterations) with 95% confidence intervals

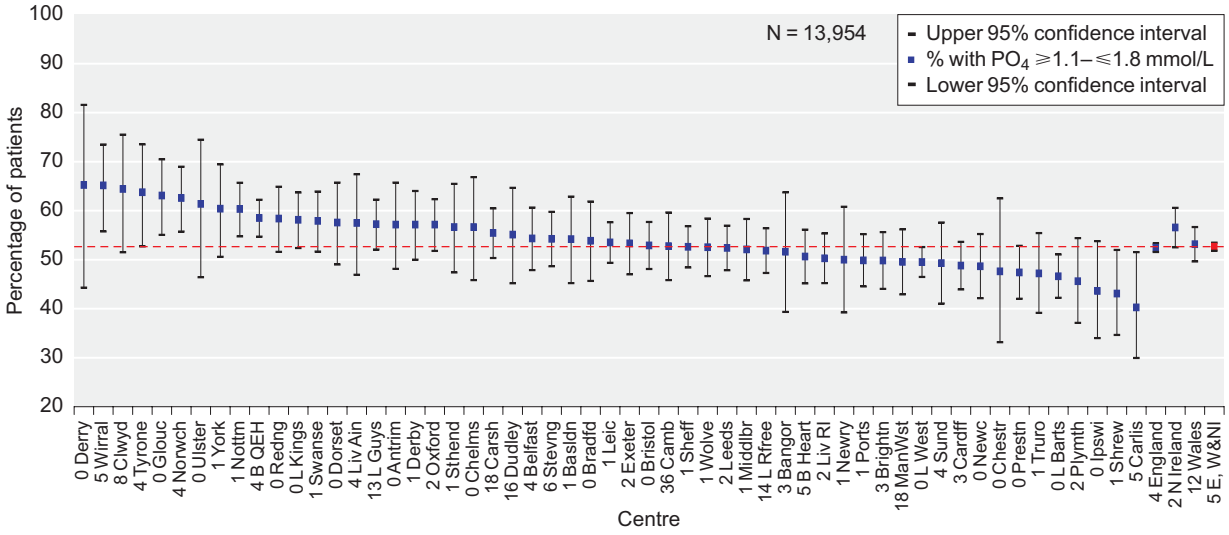

Figure 9.6: Percentage of HD patients with serum phosphate ⩾1.1–⩽1.8 mmol/L by centre

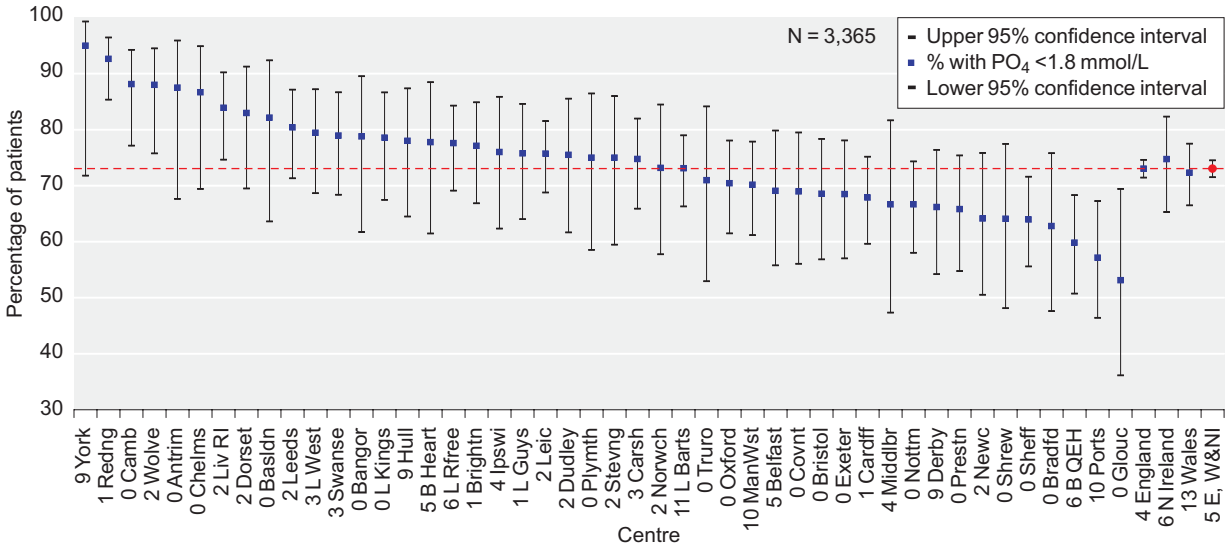

Figure 9.7: Percentage of PD patients with serum phosphate <1.8 mmol/L by centre

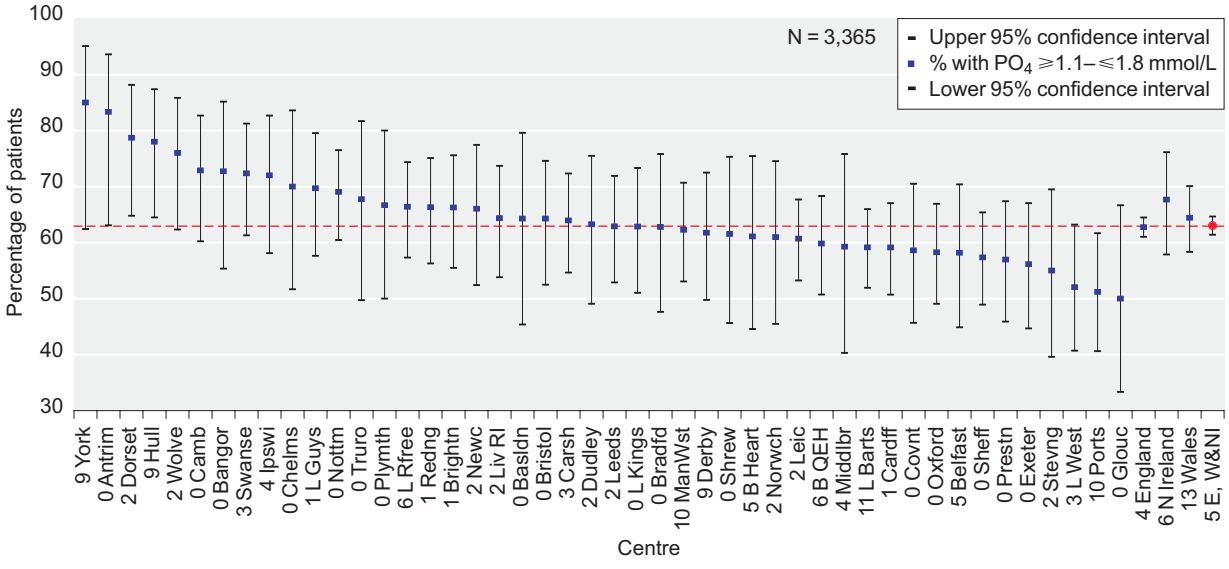

Figure 9.8: Percentage of PD patients with serum phosphate ⩾1.1–⩽1.8 mmol/L by centre

Analysing performance against the new RA guidelines, 53% of HD and 63% of PD patients achieved a serum phosphate $\geqslant 1.1 - \leqslant 1.8$ mmol/L (Figures 9.6 and 9.8). Thus applying the new RA standards, 12% of HD and 10% of PD of patients previously thought to have good phosphate control were relatively hypophosphataemic. The distribution of serum phosphate by dialysis modality is shown in Figure 9.9.

Testing the confidence in centre rankings

Figure 9.5 shows the measure of statistical uncertainty around the rankings plotted in Figure 9.4. The widely overlapping confidence intervals show that other than centres at the extremes of the plot it is difficult to be certain of centre rank.

Funnel plot analysis

There was unexplained variability between centres in achievement of the serum phosphate standard. Funnel plots identify where these differences are statistically significant.

The funnel plot for achievement of serum phosphate <1.8 mmol/L showed a number of centres outlying the upper and lower 95% and 99.9% confidence intervals both for HD and PD (Figure 9.10 and Table 9.2 (HD), Figure 9.12

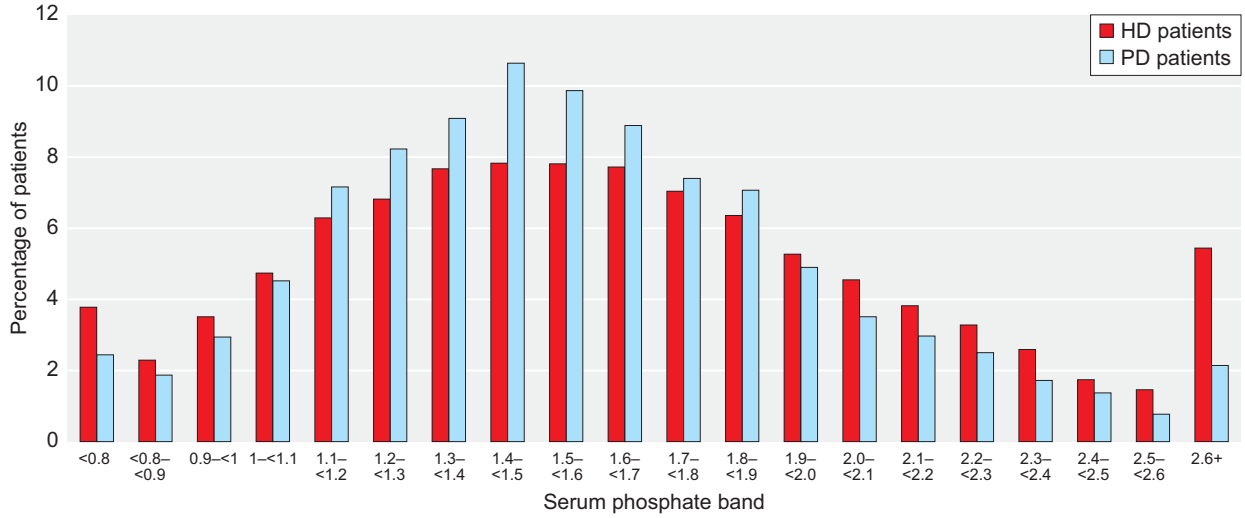

Figure 9.9: Percentage of dialysis patient split by phosphate bands and dialysis modality

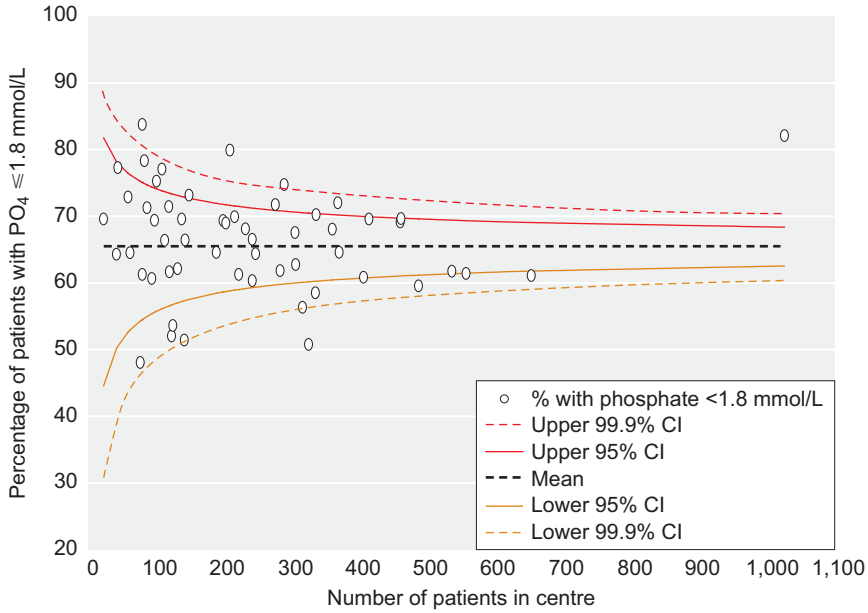

Figure 9.10: Funnel plot for the percentage of HD patients with serum phosphate <1.8 mmol/L by centre size

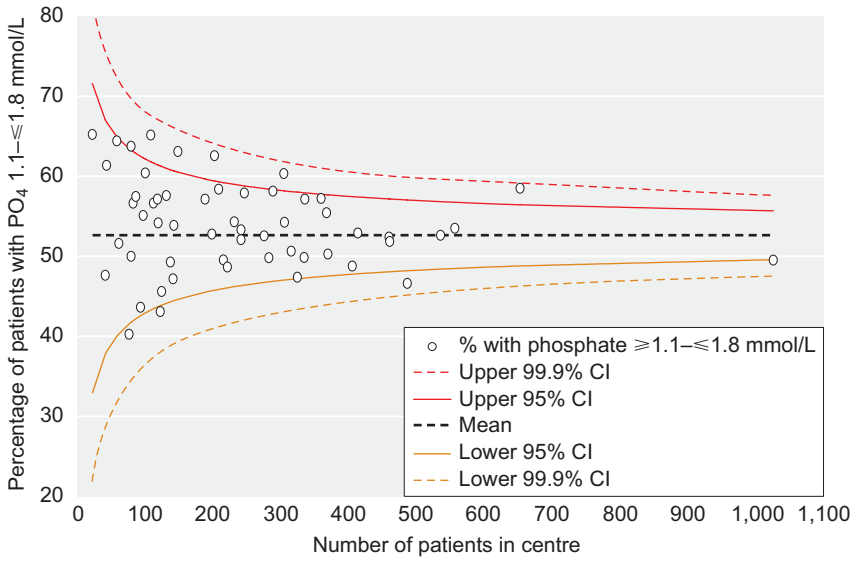

Figure 9.11: Funnel plot for the percentage of HD patients with serum phosphate ⩾1.1–⩽1.8 mmol/L by centre size

Table 9.2: Centre size and percentage of HD patients with serum phosphate <1.8 mmol/L and ⩾1.1–⩽1.8 mmol/L to enable centre identification in Figures 9.10 and 9.11

Treatment centre	Total pts	% with PO_4 <1.8 mmol/L	% with PO_4 ⩾1.1–⩽1.8 mmol/L	Treatment centre	Total pts	% with PO_4 <1.8 mmol/L	% with PO_4 ⩾1.1–⩽1.8 mmol/L
Derry	23	70	65	ManWst	216	70	50
Chestr	42	64	48	Newc	222	61	49
Ulster	44	77	61	Belfast	232	68	54
Clwyd	59	73	64	Middlbr	242	60	52
Bangor	62	65	52	Exeter	242	67	53
Carlis	77	48	40	Swanse	247	64	58
Newry	80	61	50	Wolve	276	72	53
Tyrone	80	84	64	Brightn	283	62	50
Chelms	83	78	57	L Kings	289	75	58
Liv Ain	87	71	57	Nottm	305	68	60
Ipswi	94	61	44	Stevng	306	63	54
Dudley	98	69	55	B Heart	316	56	51
York	101	75	60	Prestn	325	51	47
Wirral	109	77	65	Ports	335	59	50
Sthend	113	66	57	Oxford	336	70	57
Antrim	119	71	57	L Guys	360	68	57
Basldn	120	62	54	Carsh	368	72	55
Shrew	123	52	43	Liv RI	370	65	50
Plymth	125	54	46	Cardff	406	61	49
Dorset	132	62	58	Bristol	414	70	53
Sund	138	70	49	Leeds	460	69	52
Truro	142	51	47	L Rfree	461	70	52
Bradfd	143	66	54	L Barts	487	60	47
Glouc	149	73	63	Sheff	536	62	53
Derby	189	65	57	Leic	557	61	54
Camb	199	69	53	B QEH	653	61	59
Norwch	203	69	63	L West	1,026	82	50
Redng	209	80	58				

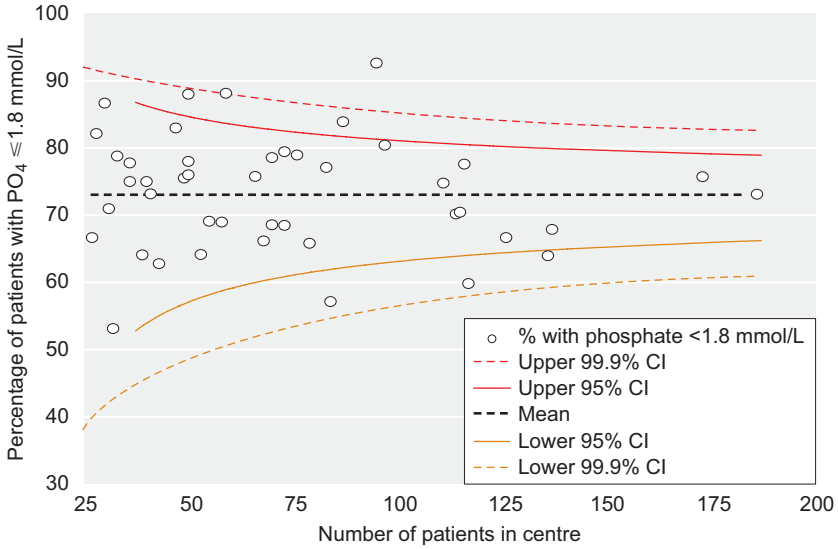

Figure 9.12: Funnel plot for the percentage of PD patients with serum phosphate <1.8 mmol/L by centre size

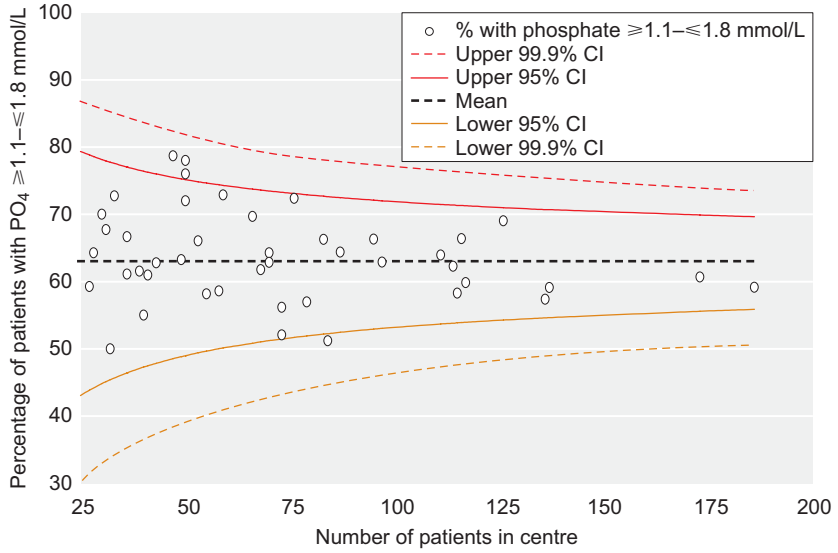

Figure 9.13: Funnel plot for the percentage of PD patients with serum phosphate ⩾1.1–⩽1.8 mmol/L by centre size

and Table 9.3 (PD)). The data for London West (which lies above the upper 99.9% confidence interval on the funnel plot) was difficult to interpret as this was amalgamated data from Hammersmith & Charing Cross and St Mary's (not previously submitting data to the UKRR). When broken down to satellite level data, the median phosphate was lower in haemodialysis patients treated at St Mary's and its satellites (median 1.18 mmol/L, quartiles 0.92–1.48 mmol/L) than in patients treated at Hammersmith & Charing Cross and satellite units (median 1.41 mmol/L, quartiles 1.09–1.82 mmol/L).

The funnel plots for achievement of phosphate ⩾1.1–⩽1.8 mmol/L (Figure 9.11 and Table 9.2 (HD), Figure 9.13 and Table 9.3 (PD)) had a notably different appearance with most centres clustered within the funnel. No centres out lie the upper or lower 99.9% confidence intervals although there were centres lying between the 95% and 99.9% confidence intervals. There was also redistribution of centres within the funnel plot when performance against 1.1–1.8 mmol/L was audited. For some centres, performance deteriorated when audited against the 'new' standard because median serum phosphate was relatively low as shown in Figure 9.3. Redistribution of centres also occurred due to centre change in achievement of standard (old vs. new) relative to the change in the UK mean achievement of standard.

Table 9.3: Centre size and percentage of PD patients with serum phosphate <1.8 mmol/L and ⩾1.1–⩽1.8 mmol/L to enable centre identification in Figures 9.12 and 9.13

Treatment centre	Total pts	% with PO_4 <1.8 mmol/L	% with PO_4 ⩾1.1–⩽1.8 mmol/L	Treatment centre	Total pts	% with PO_4 <1.8 mmol/L	% with PO_4 ⩾1.1–⩽1.8 mmol/L
York	20	95	85	L Guys	66	76	70
Antrim	24	88	83	Derby	68	66	62
Middlbr	27	67	59	Bristol	70	69	64
Basldn	28	82	64	L Kings	70	79	63
Chelms	30	87	70	Exeter	73	68	56
Truro	31	71	68	L West	73	79	52
Glouc	32	53	50	Swanse	76	79	72
Bangor	33	79	73	Prestn	79	66	57
Plymth	36	75	67	Brightn	83	77	66
B Heart	36	78	61	Ports	84	57	51
Shrew	39	64	62	Liv RI	87	84	64
Stevng	40	75	55	Redng	95	93	66
Norwch	41	73	61	Leeds	97	80	63
Bradfd	43	63	63	Carsh	111	75	64
Dorset	47	83	79	ManWst	114	70	62
Dudley	49	76	63	Oxford	115	70	58
Hull	50	78	78	L Rfree	116	78	66
Ipswi	50	76	72	B QEH	117	60	60
Wolve	50	88	76	Nottm	126	67	69
Newc	53	64	66	Sheff	136	64	57
Belfast	55	69	58	Cardff	137	68	59
Covnt	58	69	59	Leic	173	76	61
Camb	59	88	73	L Barts	186	73	59

Commentary

The new standard specifies measuring phosphate before a 'short gap' dialysis. The Registry does not currently identify whether the quarterly data extracted from centres was measured before a 'short gap' dialysis and this might introduce bias when comparing centre performance.

Some centres performed 'better than expected' when audited against a phosphate of 1.8 mmol/L and 'worse than expected' when audited against 1.1–1.8 mmol/L and vice versa. This can be explained by considering the properties of the distribution of patients in each centre. Serum phosphate was normally distributed and each centre had an individual median and standard deviation. The centre median and standard deviation were important determinants of performance against each audit measure. Centres with lower median values will perform better when audited against phosphate <1.8 mmol/L. However centres with a smaller standard deviation i.e. those with less variability will perform better when audited against a phosphate of 1.1–1.8 mmol/L. The relative contribution of each of these factors explains the observed differences in both simple rankings and on the funnel plots.

The underlying clinical explanations for these differences were unknown but may be due to differences in case mix and/or processes of care between centres. The longitudinal data might support the hypothesis that processes of care i.e. modifiable factors were important. This data shows year-on-year improvement of the percentage of patients with both serum phosphate <1.8 mmol/L and serum phosphate ⩾1.1–⩽1.8 mmol/L and the proportion of patients with a low phosphate (not previously included as an audit standard) was stable over time (Figure 9.2).

Introduction of a lower limit for the phosphate standard also has implications for interpreting these data. Although both hyper and hypophosphataemia are associated with

increased mortality in dialysis patients, both the underlying biological explanation and the magnitude of risk are probably different[8]. For this reason when the 4th edition of the standards are formalised the Registry plans to analyse hyper and hypophosphataemic patients separately.

Calcium

The 3rd edition of the Renal Association standards document 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 (1).

The draft 4th edition of the Renal Association clinical practice guidelines states:

Serum calcium, adjusted for albumin concentration, should be maintained within the normal reference range for the laboratory used (measured before a 'short gap' dialysis session in HD patients) and ideally kept below 2.5 mmol/L (2).

Results

Data quality

The completeness of data by modality is shown in Table 9.4.

Table 9.4: Percentage data completeness by centre for adjusted calcium by modality

	HD	PD	Transplants		HD	PD	Transplants
Antrim	100	100	83	Leic	99	97	89
B Heart	95	95	79	Liv Ain	96	n/a	n/a
B QEH	97	95	87	Liv RI	98	98	90
Bangor	97	100	n/a	ManWst	82	89	89
Basldn	99	100	100	Middlbr	99	96	94
Belfast	96	95	95	Newc	100	98	96
Bradfd	100	100	90	Newry	99	86	83
Brightn	97	99	84	Norwch	96	98	95
Bristol	100	100	97	Nottm	99	100	77
Camb	64	100	91	Oxford	98	100	96
Cardff	97	99	97	Plymth	98	100	94
Carlis	95	100	92	Ports	99	91	85
Carsh	82	97	89	Prestn	100	100	84
Chelms	100	100	87	Redng	100	99	94
Chestr	100	n/a	n/a	Sheff	99	100	97
Clwyd	92	88	86	Shrew	99	100	100
Covnt	98	100	84	Stevng	95	98	70
Derby	99	91	n/a	Sthend	99	94	91
Derry	100	n/a	67	Sund	96	100	98
Dorset	100	98	90	Swanse	99	97	96
Dudley	84	98	99	Truro	99	100	94
Exeter	99	100	93	Tyrone	96	86	90
Glouc	100	100	98	Ulster	100	100	100
Hull	100	91	91	Wirral	95	55	n/a
Ipswi	100	96	94	Wolve	99	98	97
L Barts	100	89	82	Wrexm	3	n/a	67
L Guys	87	99	92	York	90	91	53
L Kings	100	100	95	**England**	**96**	**96**	**90**
L Rfree	86	94	82	**N Ireland**	**98**	**94**	**93**
L West	100	97	96	**Wales**	**88**	**87**	**97**
Leeds	99	98	91	**E, W & NI**	**95**	**96**	**90**

n/a = no patients treated for that modality in centre.

Summary statistics

The summary statistics are shown in Figures 9.14 to 9.17 and Table 9.5. The median adjusted calcium was 2.35 mmol/L (interquartile range 2.24–2.47 mmol/L) for HD patients and 2.38 mmol/L (interquartile range 2.28–2.5 mmol/L) for PD patients with 74% of HD (Figure 9.15) and 79% of PD patients (Figure 9.17) achieving an adjusted serum calcium between 2.2–2.6 mmol/L. The percentage of patients achieving the standard was similar to 2005. Improvement in this standard seems to have levelled off in recent years. This may be due to increasing concern about raising calcium*phosphate product.

Commentary

Comparative audit in this area remained difficult, due to differences in analytical methods between centres (and even between satellites managed by one centre), different formulae being applied to adjust 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 centre will be making clinical decisions based on their locally adjusted calcium results, these data are in some sense the most valid[9]. Some centres provided data already adjusted for albumin concentration and these were analysed directly; unadjusted

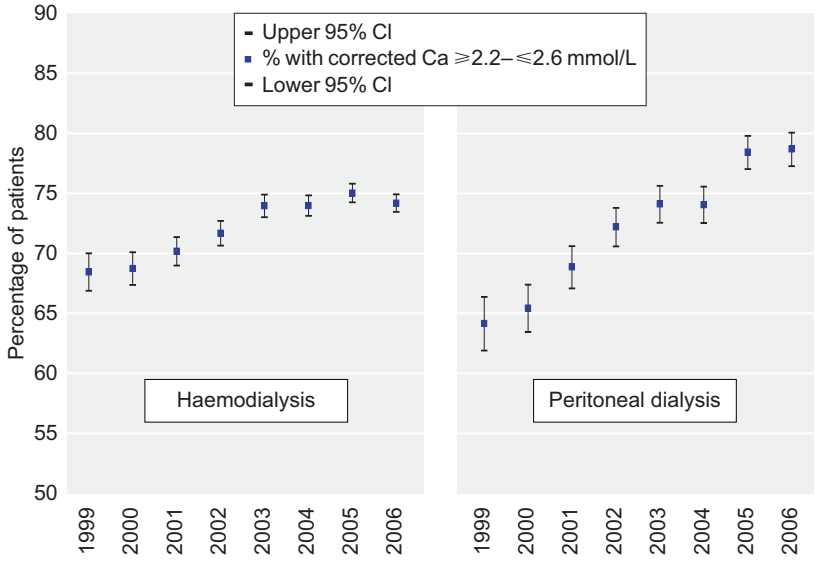

Figure 9.14: Annual change in percentage of dialysis patients with adjusted serum calcium ⩾2.2–⩽2.6 mmol/L split by modality 1999–2006

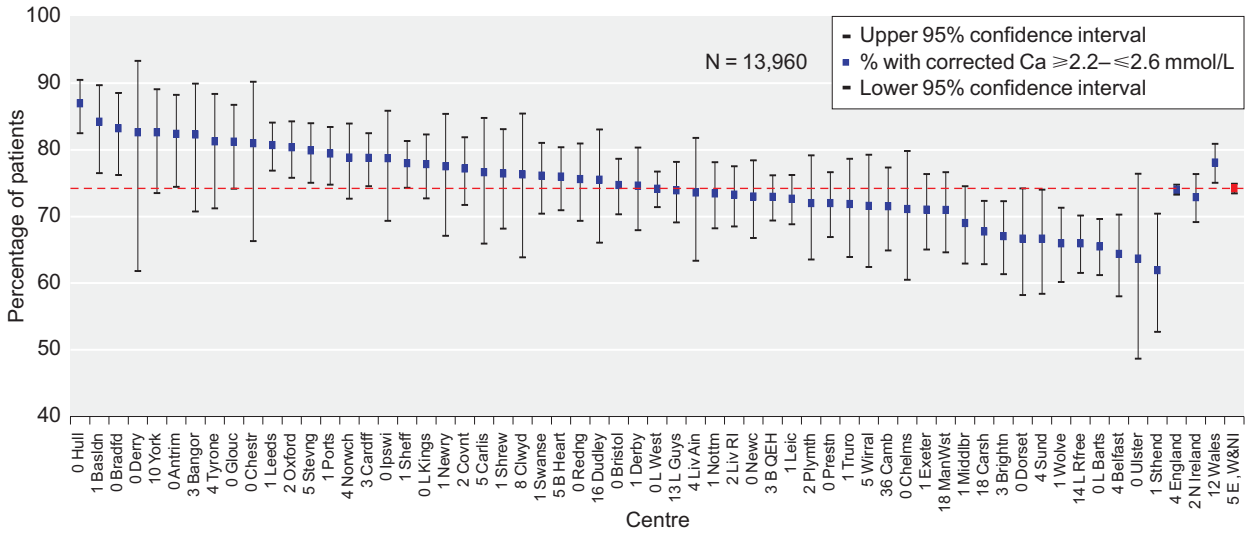

Figure 9.15: Percentage of HD patients with adjusted serum calcium ⩾2.2–⩽2.6 mmol/L by centre

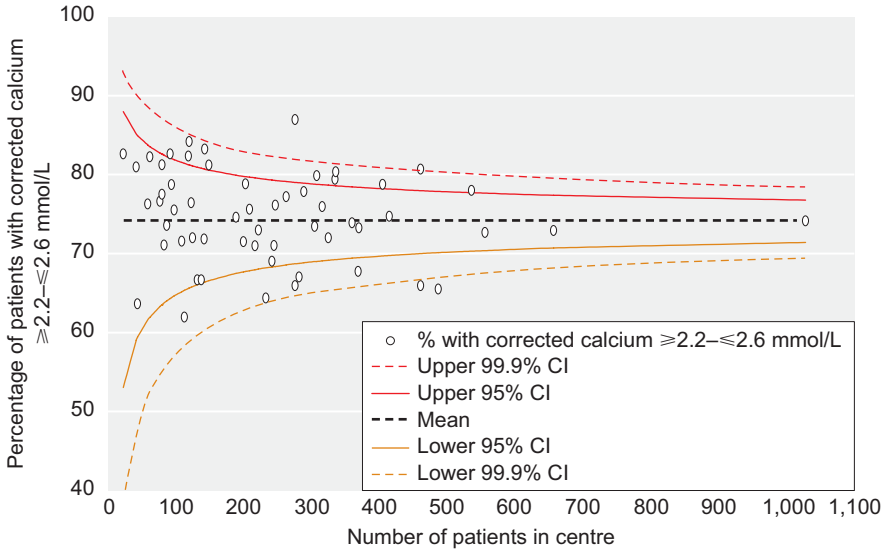

Figure 9.16: Funnel plot of percentage of HD patients with adjusted serum calcium ⩾2.2–⩽2.6 mmol/L by centre size

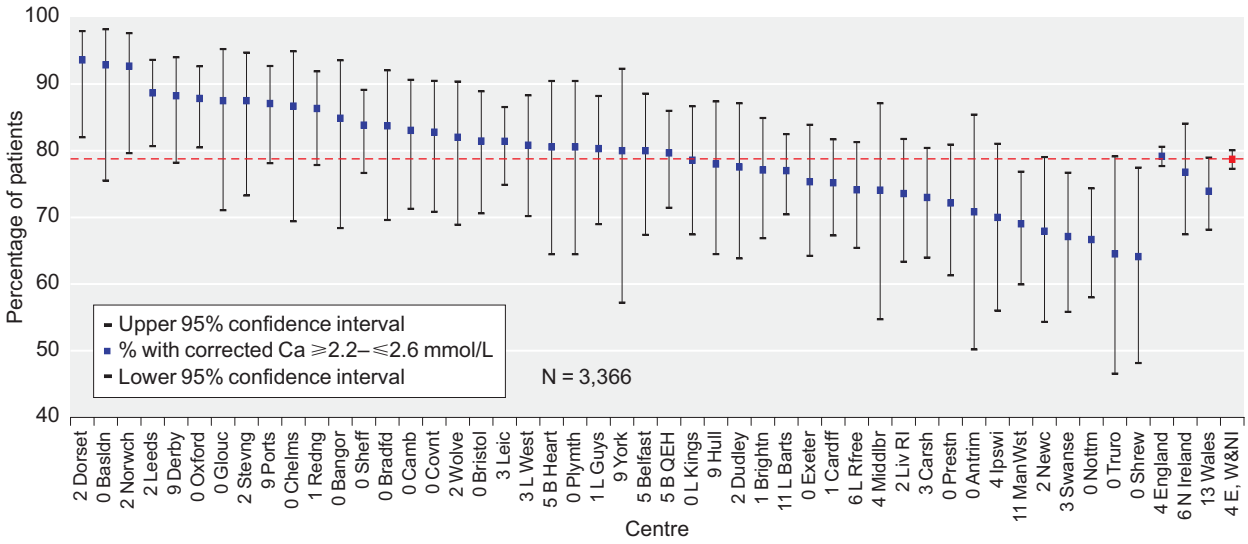

Figure 9.17: Percentage of PD patients with adjusted serum calcium 2.2–2.6 mmol/L by centre

Table 9.5: Centre size and percentage of HD patients with adjusted serum calcium ⩾2.2–⩽2.6 mmol/L and with calcium*phosphate product <4.4 mmol²/L² to enable centre identification in Figures 9.16 and 9.20

Treatment centre	Total pts	% with corrected Ca ⩾2.2–⩽2.6 mmol/L	% with Ca*PO_4 product <4.4 mmol²/L²
Derry	23	83	74
Chestr	42	81	67
Ulster	44	64	77
Clwyd	59	76	75
Bangor	62	82	71
Carlis	77	77	56
Newry	80	78	65
Tyrone	80	81	81
Chelms	83	71	76

Table 9.5: (continued)

Treatment centre	Total pts	% with Corrected Ca ⩾2.2–⩽2.6 mmol/L	% with $Ca^{*}PO_4$ product <4.4 $mmol^2/L^2$
Liv Ain	87	74	75
York	92	83	80
Ipswi	94	79	65
Dudley	98	76	71
Wirral	109	72	81
Sthend	113	62	73
Antrim	119	82	75
Basldn	120	84	60
Shrew	123	76	51
Plymth	125	72	64
Dorset	132	67	66
Sund	138	67	71
Truro	142	72	57
Bradfd	143	83	65
Glouc	149	81	75
Derby	189	75	66
Camb	200	72	74
Norwch	203	79	74
Redng	209	76	83
ManWst	217	71	72
Newc	222	73	64
Belfast	233	64	73
Middlbr	242	69	66
Exeter	245	71	70
Swanse	247	76	73
Covnt	263	77	Phosphate data unreliable
Hull	276	87	Phosphate data unreliable
Wolve	276	66	76
Brightn	282	67	69
L Kings	289	78	80
Nottm	305	73	68
Stevng	308	80	69
B Heart	316	76	62
Prestn	325	72	63
Ports	335	79	62
Oxford	336	80	71
L Guys	360	74	76
Carsh	369	68	78
Liv RI	370	73	65
Cardff	405	79	64
Bristol	415	75	69
L Rfree	461	66	74
Leeds	461	81	76
L Barts	487	66	66
Sheff	536	78	69
Leic	556	73	67
B QEH	657	73	70
L West	1,028	74	86

calcium data provided by some centres was adjusted using a formula in widespread use:

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

For this reason, 2006 data has been audited against adjusted serum calcium of 2.2–2.6 mmol/L.

The Registry will need to consider how to apply the statement of 'within the normal reference range' in the 4th edition of the RA standards to future analyses.

Calcium*phosphate product

The 3rd edition of the Renal Association standards document has no guideline for the calcium*phosphate product. The 2003 KDOQI clinical practice guideline states:

> ***The serum calcium–phosphorus product should be maintained at $<55\ mg^2/dL^2$ ($4.4\ mmol^2/L^2$) (1).***

The 4th edition of the Renal Association clinical practice guidelines states:

> ***The serum albumin corrected calcium phosphorus product should be kept below $4.8\ mmol^2/L^2$ and ideally below $4.2\ mmol^2/L^2$ in all CKD patients (2).***

Results

Summary statistics

The summary statistics are shown in Figures 9.18, 9.19 and 9.21 to 9.23. Dialysis patients

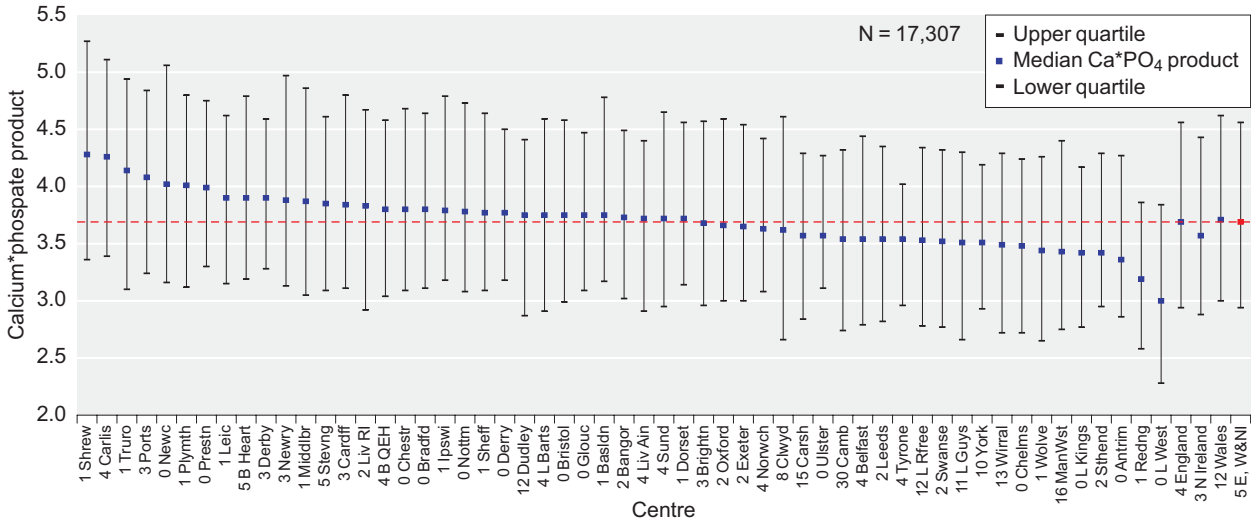

Figure 9.18: Median calcium*phosphate product for dialysis patients by centre

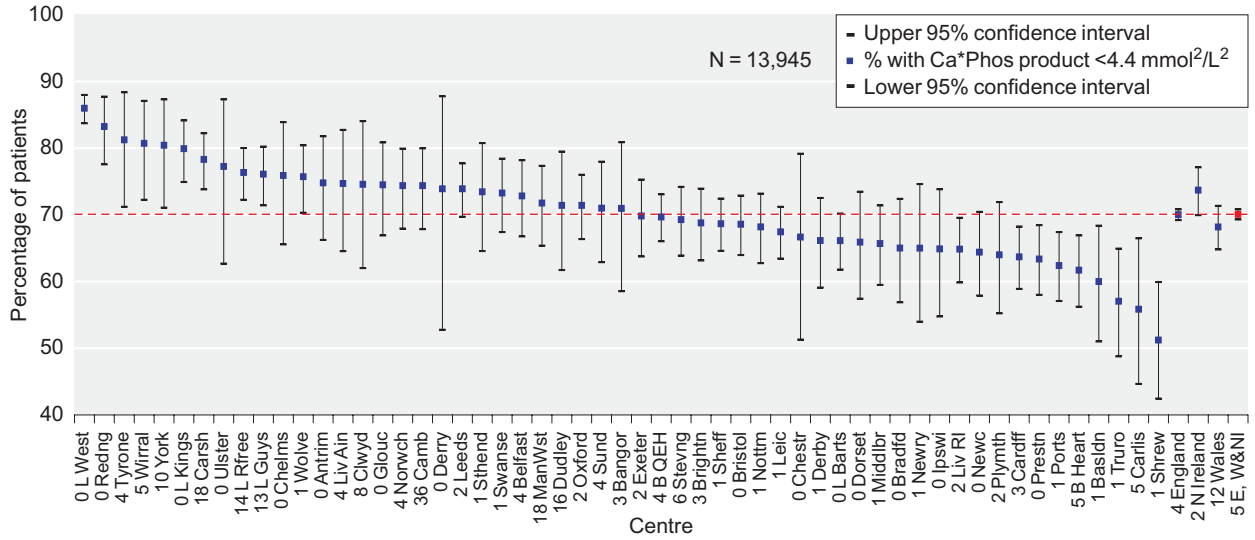

Figure 9.19: Percentage of HD patients with calcium*phosphate product $<4.4\ mmol^2/L^2$ by centre

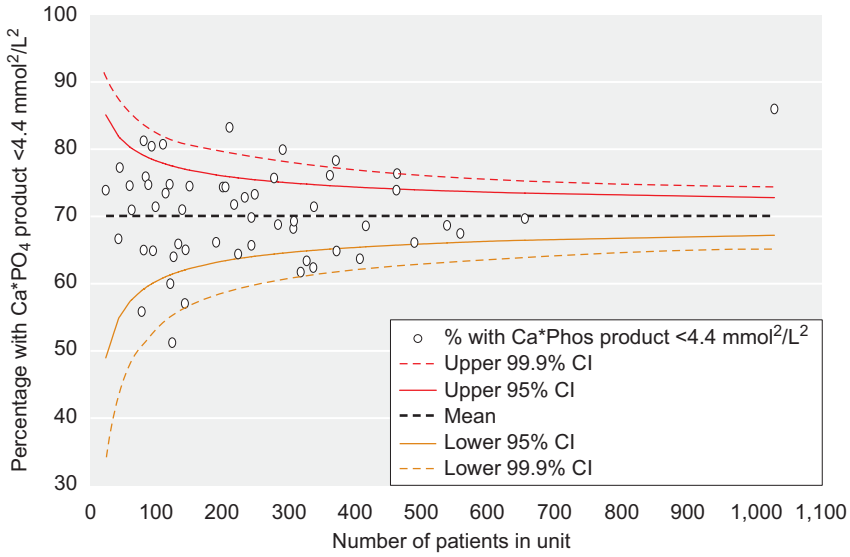

Figure 9.20: Funnel plot for percentage of HD patients with calcium*phosphate product <4.4 mmol^2/L^2 by centre

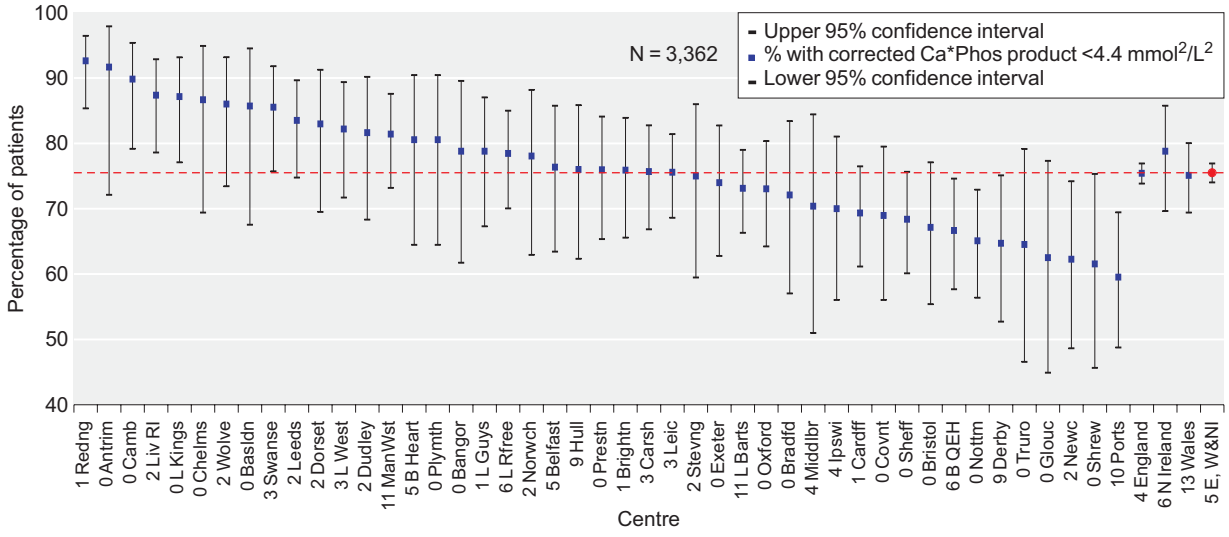

Figure 9.21: Percentage of PD patients with calcium*phosphate product <4.4 mmol^2/L^2 by centre

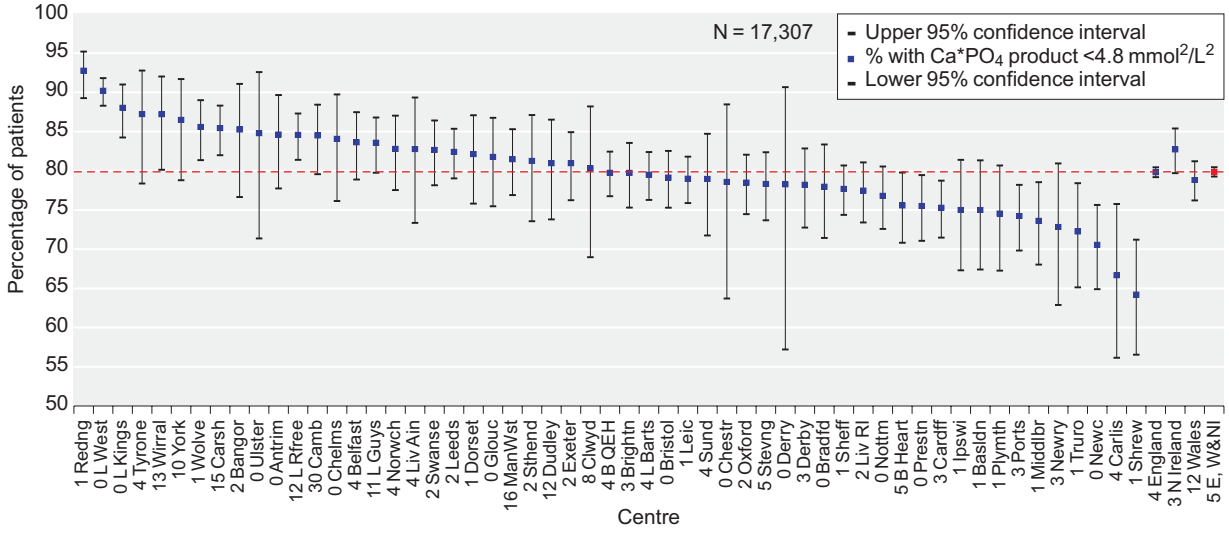

Figure 9.22: Percentage of dialysis patients with calcium*phosphate product <4.8 mmol^2/L^2

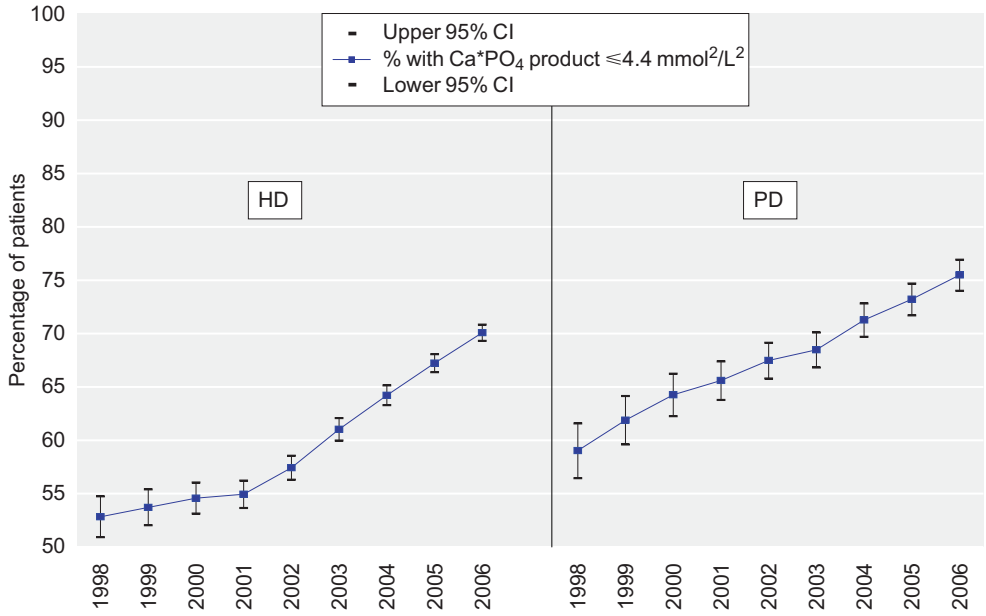

Figure 9.23: Annual change in percentage of dialysis patients with adjusted serum calcium*phosphate product $<4.4\,mmol^2/L^2$ split by modality 1998–2006

median calcium*phosphate product was $3.7\,mmol^2/L^2$ (inter quartile range 2.9–$4.6\,mmol^2/L^2$ (HD patients = $3.7\,mmol^2/L^2$ and PD patients = 3.6 $mmol^2/L^2$).

The percentage of patients who achieved a calcium*phosphate product of $<4.4\,mmol^2/L^2$ was 71% (HD = 70%, PD = 75%). When data was audited against $<4.8\,mmol^2/L^2$, 80% (HD = 79%, PD = 85%) of patients achieved a calcium*phosphate product within the draft RA upper standard.

Funnel plot analysis

The funnel plot analysis is shown for HD patients in Figure 9.20 and Table 9.5. The pattern of outlying centres resembles the funnel plot showing the percentage of patients with phosphate <1.8 mmol/L (Figure 9.10) rather than the plot showing percentage of patients with serum adjusted calcium 2.2–2.6 mmol/L (Figure 9.16).

Commentary

The figures shown have predominantly been selected to reflect the current use of the KDOQI guideline as an audit standard. Dialysis patients as a group have been audited against the new RA guideline as a preliminary analysis to allow comparison in subsequent years.

The funnel plot data emphasise that phosphate was a more powerful determinant than calcium in achievement of the standard for calcium*phosphate product because serum calcium fluctuates within a narrower range than serum phosphate.

Audited against a calcium*phosphate product of $4.4\,mmol^2/L^2$ there has been a further small improvement compared to 2005 (Figure 9.23).

Parathyroid hormone

The 3rd edition of the Renal Association standards document 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 (1).***

The 4th edition of the Renal Association clinical practice guidelines states:

> ***The target range for parathyroid hormone measured using an intact PTH assay should be between 2 and 4 times the upper limit of normal for the intact PTH assay used. The same target range should apply when using the whole molecule PTH assay (2).***

Results

Data quality

The completeness of data by modality is shown in Table 9.6.

Summary statistics

The summary statistics are shown in Figures 9.24 to 9.26. The median PTH for dialysis patients was 24 pmol/L (interquartile range 11–48 pmol/L). The median values were slightly higher for PD patients (26 pmol/L) than HD patients (24 pmol/L) with similar interquartile ranges.

Overall 61% of dialysis patients (HD = 61%, PD = 60%) have a serum PTH <32 pmol/L but only 25% (HD = 24%, PD = 28%) have a PTH between 16–32 pmol/L. The overall spread of data remained large ranging from 42% to 80% compliance with PTH <32 pmol/L.

Commentary

Comparison of serum PTH values from different centres was difficult due to the variety of methods and reference ranges in use and this may explain some of the large inter-centre variability in PTH[9,10]. 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. This was also similar to the upper limit of the KDOQI guidelines (31 pmol/L). The revised guidelines have

Table 9.6: Data completeness by centre for serum PTH split by RRT modality

	HD	PD	Transplant		HD	PD	Transplant
Antrim	100	100	13	Leic	89	79	60
B Heart	83	84	14	Liv Ain	78	n/a	n/a
B QEH	66	76	51	Liv RI	94	91	62
Bangor	95	100	n/a	ManWst	74	84	78
Basldn	98	100	64	Middlbr	92	64	15
Belfast	95	91	20	Newc	99	91	45
Bradfd	100	93	36	Newry	98	86	20
Brightn	86	94	17	Norwch	92	86	27
Bristol	98	96	77	Nottm	98	97	72
Camb	58	100	77	Oxford	92	93	31
Cardff	92	96	15	Plymth	81	56	36
Carlis	94	100	9	Ports	86	52	9
Carsh	70	82	15	Prestn	98	99	43
Chelms	99	97	27	Redng	95	92	55
Chestr	7	n/a	n/a	Sheff	98	87	19
Clwyd	91	13	43	Shrew	93	95	49
Covnt	82	66	19	Stevng	97	88	32
Derby	99	97	7	Sthend	86	75	7
Derry	100	n/a	0	Sund	94	100	96
Dorset	84	85	23	Swanse	97	96	29
Dudley	71	76	43	Truro	97	81	31
Exeter	96	100	27	Tyrone	90	86	30
Glouc	96	94	29	Ulster	95	50	33
Hull	91	78	40	Wirral	93	55	n/a
Ipswi	93	96	33	Wolve	97	96	67
L Barts	79	58	13	Wrexm	1	0	33
L Guys	84	93	19	York	98	86	27
L Kings	0	0	0	**England**	**80**	**80**	**35**
L Rfree	0	0	0	**N Ireland**	**96**	**91**	**20**
L West	58	92	17	**Wales**	**85**	**83**	**17**
Leeds	97	98	24	**E, W & NI**	**81**	**80**	**34**

n/a = no patients treated for that modality in centre.

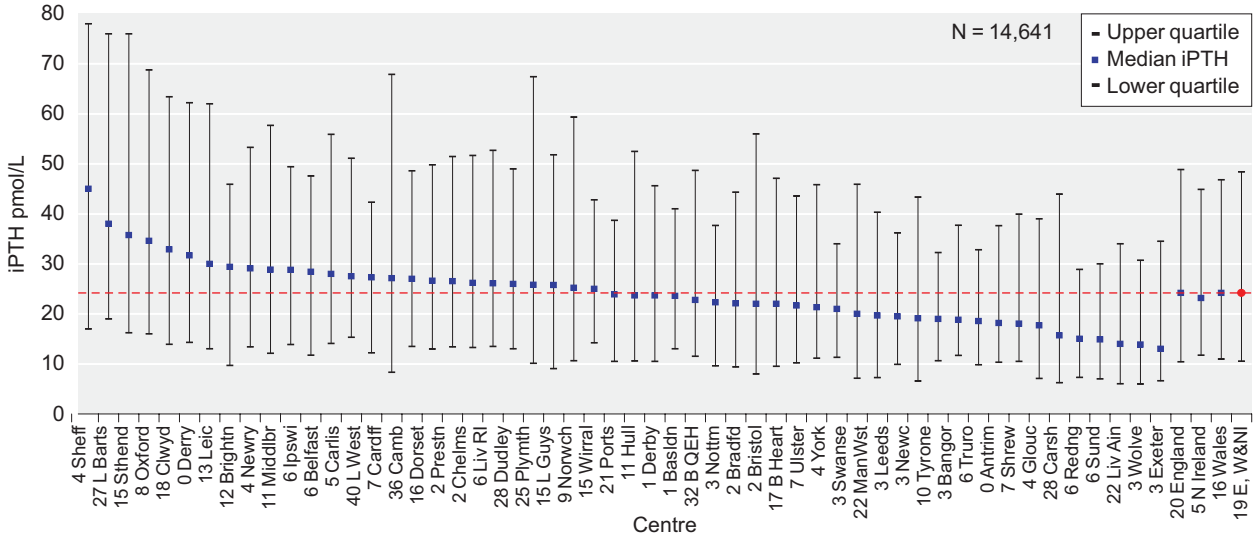

Figure 9.24: Median PTH for dialysis patients by centre

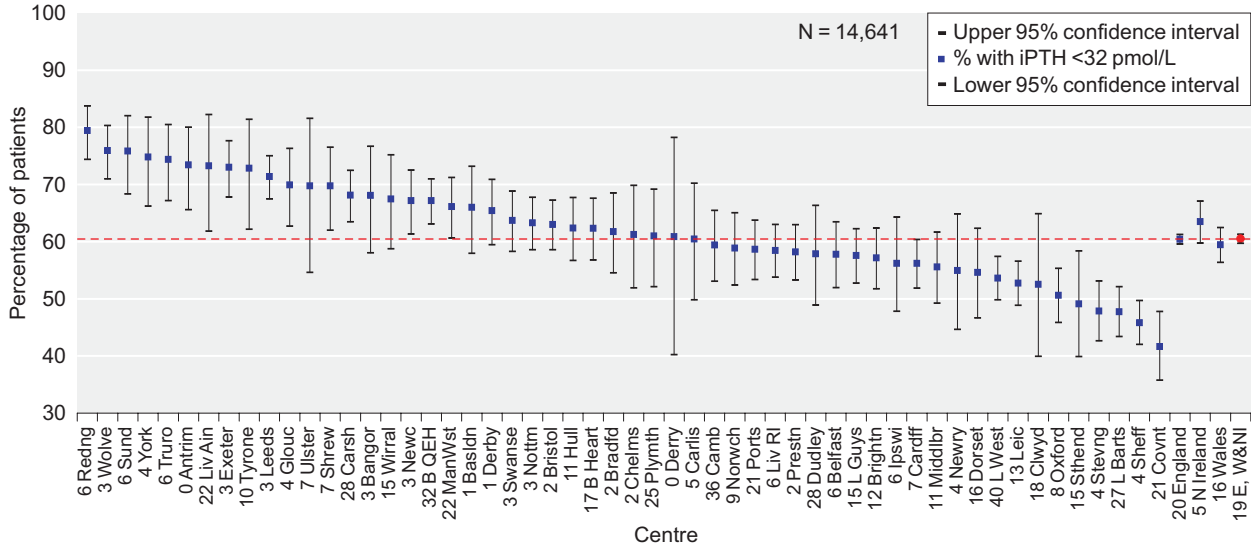

Figure 9.25: Percentage of dialysis patients with PTH <32 pmol/L by centre

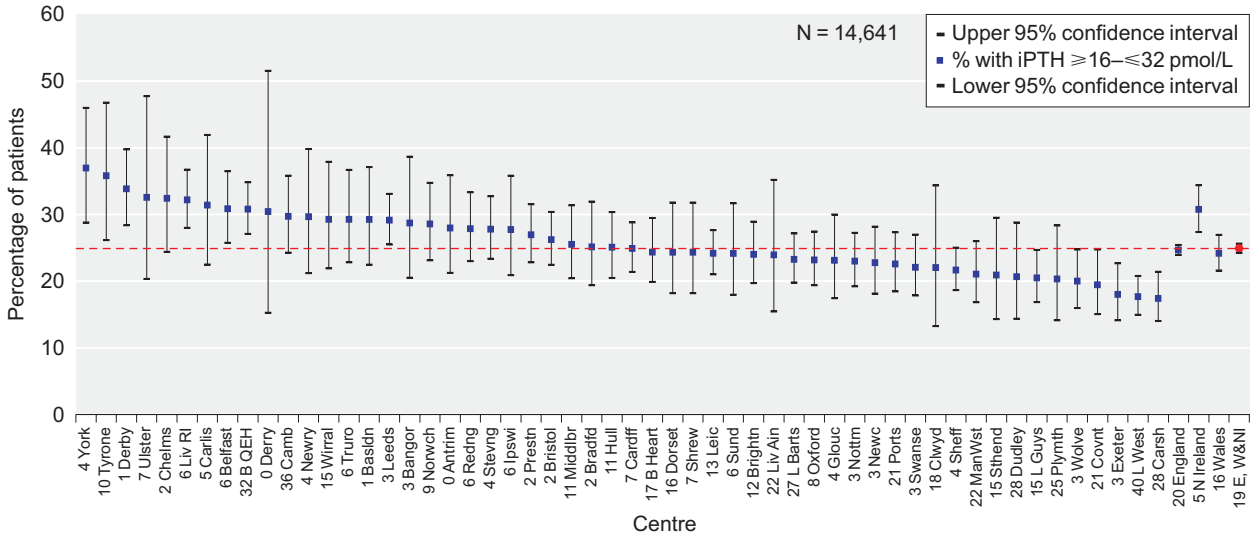

Figure 9.26: Percentage of dialysis patients with PTH ⩾16–⩽32 pmol/L

introduced a lower limit for PTH. Using the same principle to calculate the lower limit this equated to 16 pmol/L (KDOQI recommended 15 pmol/L).

When audited against PTH of 16–32 pmol/L compared to <32 pmol/L there was considerable redistribution of some centres within the caterpillar plots. This suggested that some centres had processes of care which shifted the whole distribution and reduced median PTH whereas others were able to narrow their distribution and reduce PTH variability. This also means that there was variability between centres in the proportion of patients with a PTH <16 pmol/L. This may be an important finding given the concerns about over suppression of PTH with respect to risks of adynamic bone disease and vascular calcification.

Aluminium

The 3rd edition of the Renal Association standards document states:

> ***Serum aluminium concentration should be measured every three months in all patients on HD and in all PD patients receiving oral aluminium hydroxide (1).***

The 4th edition of the Renal Association clinical practice guidelines state:

> ***Aluminum toxicity can occur in stage 4 and 5 CKD and in dialysis patients. If clinically suspected serum aluminum levels should be determined. Care needs to be taken to avoid aluminum contamination of the blood sample.***
>
> ***Serum aluminium concentration should be measured every three months in all patients receiving oral aluminium phosphate binders.***
>
> ***Serum levels should be less than 20 μg/L. A desferrioxamine test should be performed to support the diagnosis where random serum levels are indeterminate. A bone biopsy provides confirmation of aluminium bone disease (2).***

Commentary

Overall of the 14,637 HD patients and 3,524 PD patients who were included in this analysis, 5,542 (38%) of HD and 309 (9%) of PD patients had serum aluminium measured in 2006. This was similar to 2005 data where 36% of HD and 9% of PD patients had a serum aluminium measurement.

There remained large variability in centre reporting for aluminium data and it was possible that the Registry was not capturing all of the aluminium monitoring that was taking place, not least because aluminium measurement was not generally available in local laboratories and there may therefore be practical limitations in respect of data transmission back to the renal centre database. A retrospective study looking at aluminium reporting to the UKRR between 2000 and 2004 identified a reduction in the proportion of patients having routine samples taken for aluminium monitoring and a reduced proportion with high aluminium levels over time[11]. The more pragmatic approach of the 4th edition of the RA guidelines probably more accurately reflect current practice for aluminium monitoring in the UK.

Bicarbonate

The 3rd edition of the Renal Association standards document states:

> ***Serum bicarbonate, before a haemodialysis (HD) session, measured with minimal delay after venepuncture should be between 20 and 26 mmol/l.***
>
> ***For continuous ambulatory peritoneal dialysis (CAPD) patients serum bicarbonate, measured with minimal delay after venepuncture, should be between 25 and 29 mmol/l (1).***

The standards are essentially unchanged in the 4th edition of the Renal Association guidelines other than the PD guideline now states that serum bicarbonate should be maintained within the normal range.

Results

Data quality

The percentage completeness of data by modality is shown in Table 9.7.

Table 9.7: Percentage data completeness by centre for serum bicarbonate by modality

	HD	PD		HD	PD
Antrim	100	100	Leic	89	94
B Heart	93	95	Liv Ain	96	n/a
B QEH	96	90	Liv RI	98	98
Bangor	97	94	ManWst	0	1
Basldn	99	100	Middlbr	98	96
Belfast	97	95	Newc	100	98
Bradfd	99	100	Newry	99	71
Brightn	97	96	Norwch	96	98
Bristol	100	100	Nottm	78	21
Camb	60	100	Oxford	98	78
Cardff	83	97	Plymth	98	100
Carlis	95	100	Ports	99	77
Carsh	80	97	Prestn	84	85
Chelms	100	100	Redng	99	99
Chestr	100	n/a	Sheff	99	100
Clwyd	92	88	Shrew	100	100
Covnt	19	48	Stevng	95	98
Derby	99	91	Sthend	99	94
Derry	100	n/a	Sund	97	100
Dorset	100	100	Swanse	99	97
Dudley	81	96	Truro	99	90
Exeter	94	100	Tyrone	98	86
Glouc	100	100	Ulster	100	100
Hull	99	89	Wirral	95	59
Ipswi	99	96	Wolve	99	98
L Barts	100	88	Wrexm	2	0
L Guys	87	99	York	99	95
L Kings	0	0	**England**	**81**	**80**
L Rfree	0	0	**N Ireland**	**98**	**92**
L West	47	96	**Wales**	**81**	**85**
Leeds	99	98	**E, W & NI**	**82**	**81**

n/a = no patients treated for that modality in centre.

Summary statistics

The summary statistics are shown in Figures 9.27, 9.28, 9.30 and 9.31. The median serum bicarbonate was 23 mmol/L (interquartile range 21–25 mmol/L) in HD patients and 26 mmol/L (interquartile range 24–28 mmol/L) in PD patients. 70% of HD and 53% of PD patients achieved the RA standard for serum bicarbonate but there was a large spread of data between centres. For HD patients compliance in centres ranged from 39–89% and for PD patients from 24–68%.

Funnel plots

The funnel plot data is shown in Figure 9.29 and Table 9.8 (HD) and Figure 9.32 and Table 9.9 (PD). The distribution of centres for bicarbonate data was different to that for other biochemical variables. Centres that lie outwith the lower 99.9% confidence interval comprise both centres with high and low median serum bicarbonates whereas centres which lie outwith the upper 95% confidence interval lie in the middle of the plot showing median serum bicarbonate with a median value similar to the UK average.

Commentary

The Registry has previously conducted a survey into the cause of between centre variation in achievement of the bicarbonate standard and few of these causes of variation have been eliminated[12].

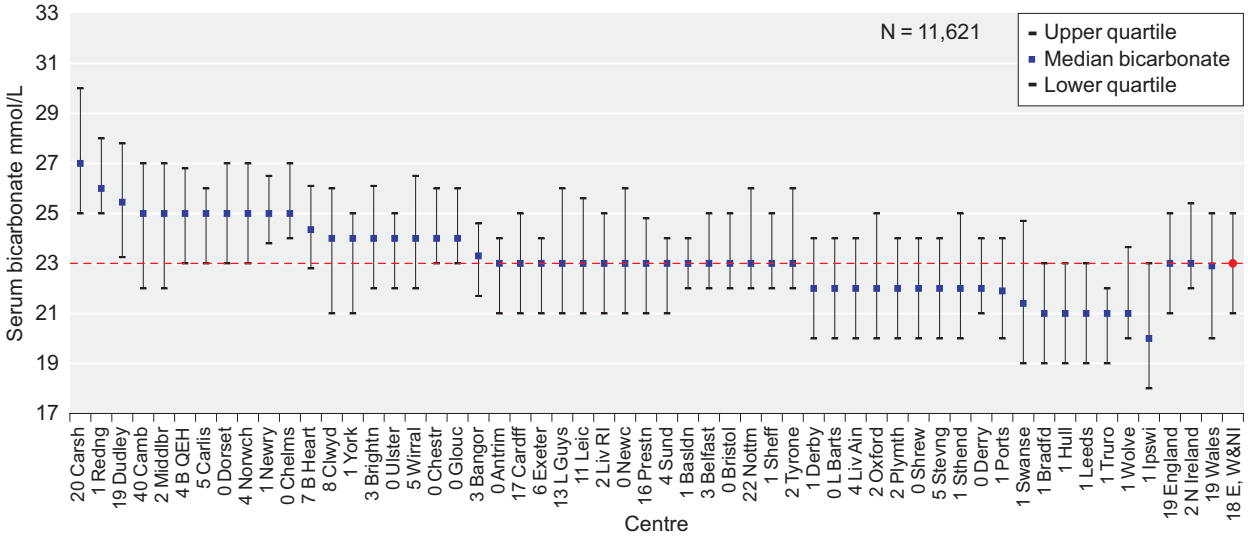

Figure 9.27: Median serum bicarbonate in HD patients by centre

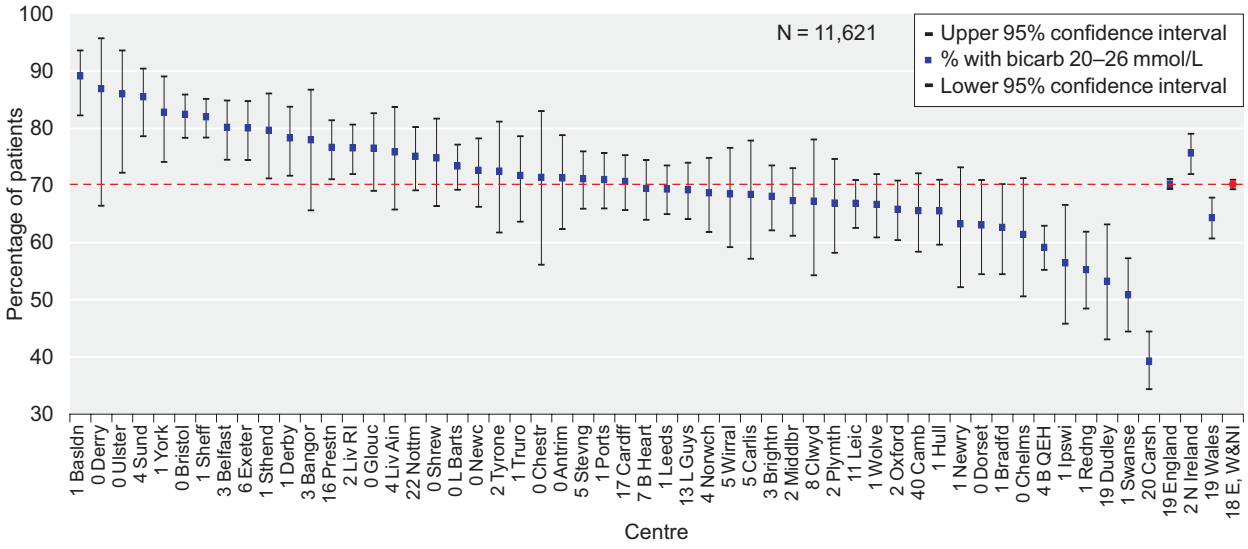

Figure 9.28: Percentage of HD patients with serum bicarbonate ⩾20–⩽26 mmol/L by centre

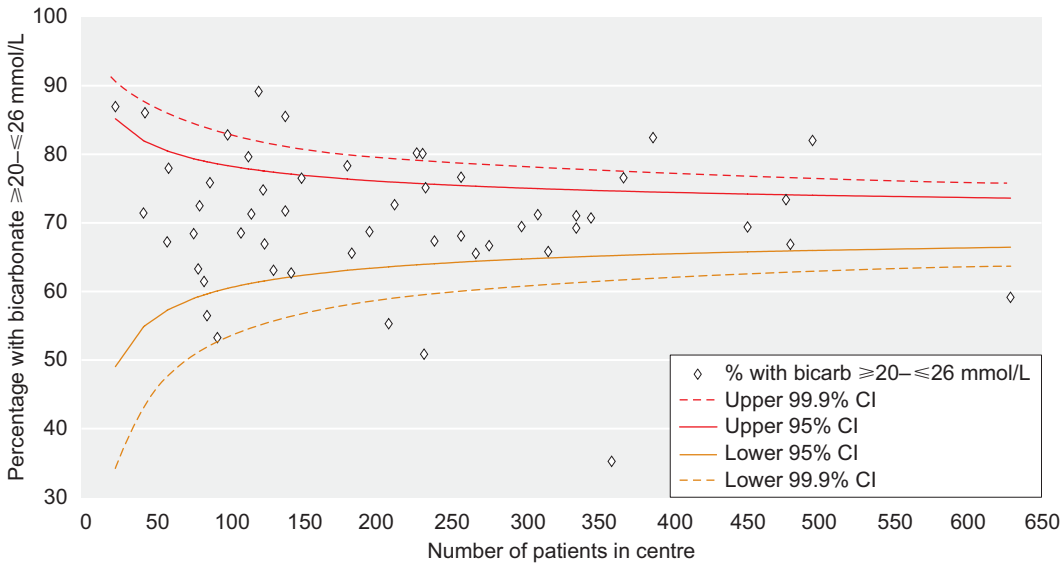

Figure 9.29: Funnel plot of percentage of HD patients with serum bicarbonate ⩾20–⩽26 mmol/L by centre size

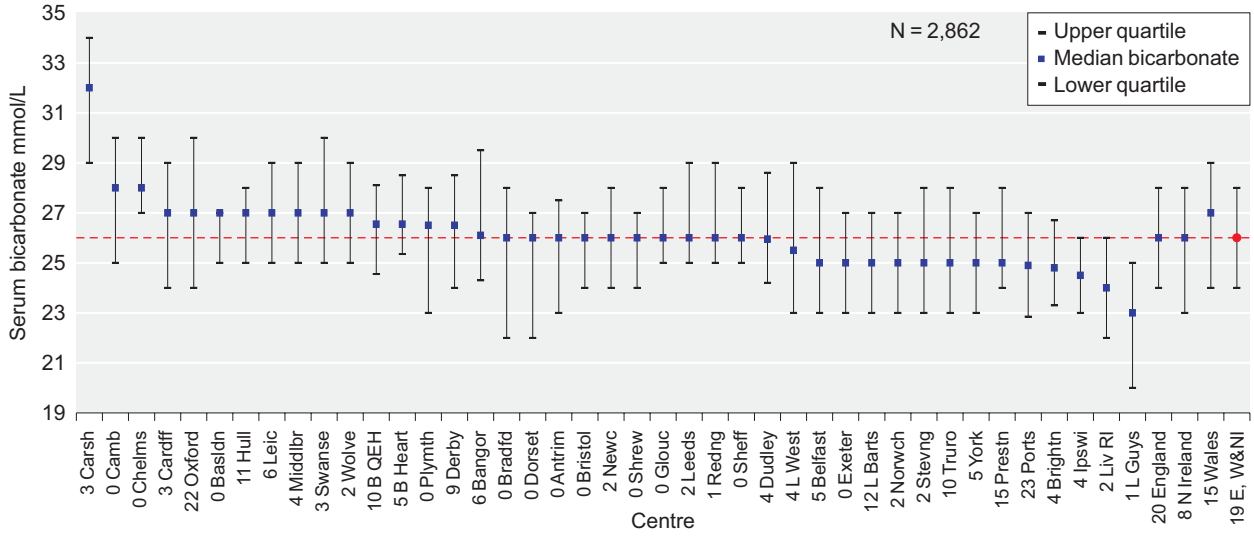

Figure 9.30: Median serum bicarbonate in PD patients by centre

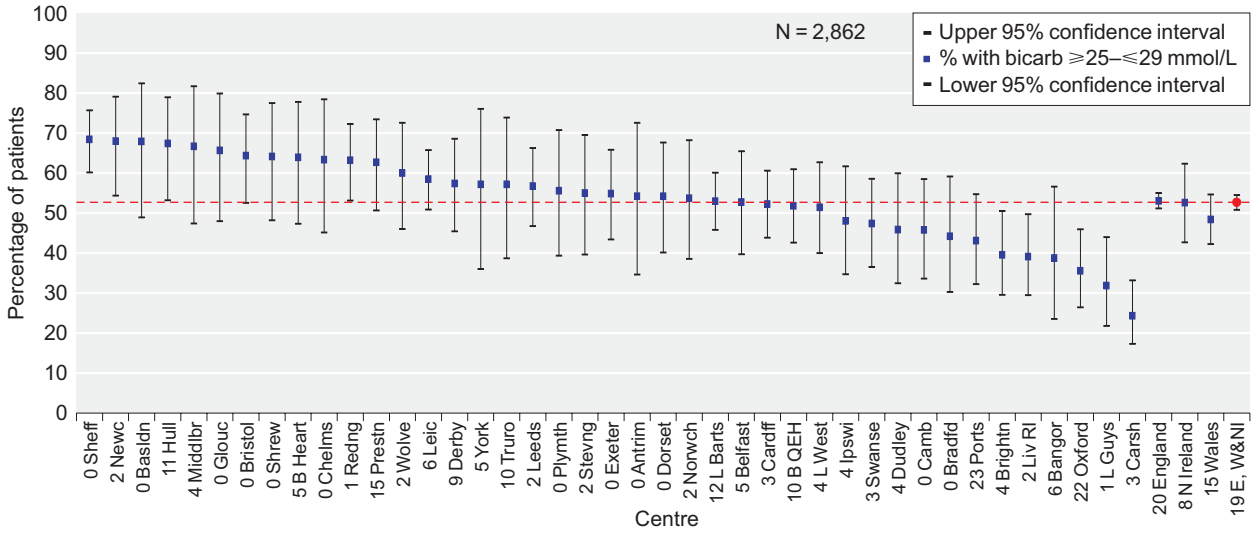

Figure 9.31: Percentage of PD patients with serum bicarbonate ⩾25–⩽29 mmol/L by centre

The funnel plot data might suggest that there were differences in centre processes but that these may not all be within direct control of clinicians altering patient management. Certain centres, in particular Carshalton which had significantly higher median serum bicarbonate in both HD and PD patients, can be identified as statistical outliers in these analyses. It is possible that differences in sample processing may explain the observed differences instead of, or in addition to, dialysis and oral bicarbonate prescription.

Total cholesterol

There has been little change for the cholesterol standard. The 4th edition of the Renal Association standards document states:

> ***3 hydroxy-3 methylglutaryl-Co-enzyme A reductase inhibitors (statins) should be considered for primary prevention in all CKD patients with a 10-year risk of coronary disease, calculated as 30% according to the Joint British Societies' chart or the coronary risk calculator, ignoring the fact that these calculations may not be accurate in patients with renal disease. A total cholesterol of <5 mmol/l or a 30% reduction from baseline, or a fasting low density lipoprotein (LDL)-cholesterol of <3 mmol/l, should be achieved, whichever is the greatest reduction in all patients (Evidence in CKD 1-3, Good Practice in CKD 4-5 and dialysis patients). Statins***

Table 9.8: Centre size and percentage of HD patients with serum bicarbonate ⩾20–⩽26 mmol/L by centre size to enable centre identification in Figure 9.29

Treatment centre	Total pts	% with bicarbonate ⩾20–⩽26 mmol/L	Treatment centre	Total pts	% with bicarbonate ⩾20–⩽26 mmol/L
Derry	23	87	Norwch	195	69
Chestr	42	71	Redng	208	55
Ulster	43	86	Newc	212	73
Clwyd	58	67	Belfast	227	80
Bangor	59	78	Exeter	231	80
Carlis	76	68	Swanse	232	51
Newry	79	63	Nottm	233	75
Tyrone	80	73	Middlbr	239	67
Chelms	83	61	Brightn	257	68
Ipswi	85	56	Prestn	257	77
Liv Ain	87	76	Hull	267	66
Dudley	92	53	Wolve	276	67
York	99	83	B Heart	298	69
Wirral	108	69	Stevng	309	71
Sthend	113	80	Oxford	316	66
Antrim	115	71	Ports	335	71
Basldn	120	89	L Guys	335	69
Shrew	123	75	Cardff	345	71
Plymth	124	67	Carsh	359	39
Dorset	130	63	Liv RI	367	77
Truro	138	72	Bristol	387	82
Sund	138	86	Leeds	451	69
Bradfd	142	63	L Barts	477	73
Glouc	149	77	Leic	480	67
Derby	180	78	Sheff	495	82
Camb	183	66	B QEH	629	59

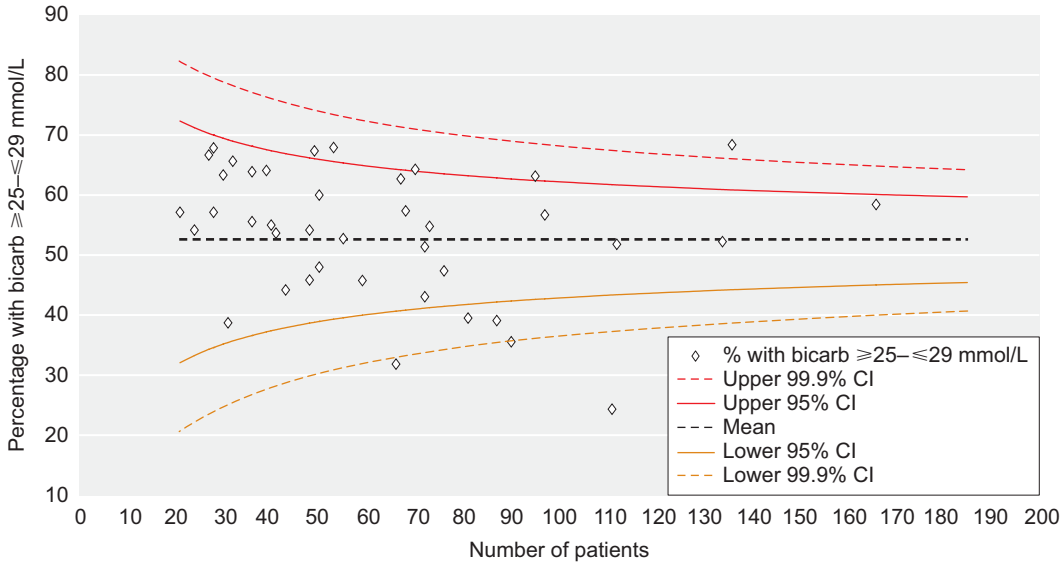

Figure 9.32: Funnel plot of percentage of PD patients with serum bicarbonate ⩾25–⩽29 mmol/L by centre size

Table 9.9: Centre size and percentage of PD patients with serum bicarbonate ⩾25–⩽29 mmol/L by centre size to enable centre identification in Figure 9.32

Treatment centre	Total pts	% with bicarbonate ⩾25–⩽29 mmol/L	Treatment centre	Total pts	% with bicarbonate ⩾25–⩽29 mmol/L
York	21	57	Camb	59	46
Antrim	24	54	L Guys	66	32
Middlbr	27	67	Prestn	67	63
Basldn	28	68	Derby	68	57
Truro	28	57	Bristol	70	64
Chelms	30	63	Ports	72	43
Bangor	31	39	L West	72	51
Glouc	32	66	Exeter	73	55
Plymth	36	56	Swanse	76	47
B Heart	36	64	Brightn	81	40
Shrew	39	64	Liv RI	87	39
Stevng	40	55	Oxford	90	36
Norwch	41	54	Redng	95	63
Bradfd	43	44	Leeds	97	57
Dorset	48	54	Carsh	111	24
Dudley	48	46	B QEH	112	52
Hull	49	67	Cardff	134	52
Ipswi	50	48	Sheff	136	68
Wolve	50	60	Leic	166	58
Newc	53	68	L Barts	185	53
Belfast	55	53			

should not be withdrawn from patients in whom they were previously indicated and should continue to be prescribed when such patients start renal replacement therapy (RRT) or change modality. (Good Practice) (2).

Results

Data quality

The percentage data completeness by modality is shown in Table 9.10.

Summary statistics

The summary statistics are shown in Figures 9.33 to 9.36. The median total cholesterol in HD patients was 3.8 mmol/L (inter quartile range 3.2–4.5 mmol/L) and 85% of patients had a serum total cholesterol ⩽5 mmol/L. The median total cholesterol in PD patients was 4.3 mmol/L (inter quartile range 3.6–5.0 mmol/L) and 73% of patients had a serum total cholesterol ⩽5 mmol/L. Transplanted patients had a median serum total cholesterol of 4.6 mmol/L (inter quartile range 4.0–5.2 mmol/L) and 67% of patients had a serum total cholesterol ⩽5 mmol/L.

The distribution of cholesterol split by modality is shown in Figure 9.35 which shows that dialysis patients had a total lower serum cholesterol than transplanted patients with the whole distribution shifted to the left. HD patients also had lower total cholesterol than PD patients. Figure 9.36 shows an improvement in the proportion of patients with a serum total cholesterol ⩽5 mmol/L over time.

Commentary

The cause of differences between serum cholesterol between treatment modalities is unknown but probably multifactorial. The Registry does not currently collect prescribing data to enable this to be linked to a lipid-lowering treatment effect and these data were confounded by the known associations between chronic disease, inflammation, malnutrition and hypocholesterolaemia. Likewise, higher cholesterol concentrations in transplant recipients may reflect improved appetite or the hypercholesterolaemic

Table 9.10: Percentage data completeness by centre for serum total cholesterol by modality

	HD	PD	Transplants		HD	PD	Transplants
Antrim	100	100	74	Leic	95	93	89
B Heart	60	89	60	Liv Ain	76	n/a	n/a
B QEH	96	94	89	Liv RI	10	1	22
Bangor	89	100	n/a	ManWst	74	89	91
Basldn	99	100	100	Middlbr	99	96	83
Belfast	89	97	97	Newc	93	100	97
Bradfd	89	95	92	Newry	99	86	85
Brightn	17	76	57	Norwch	95	98	97
Bristol	92	89	93	Nottm	97	96	88
Camb	58	100	89	Oxford	87	89	74
Cardff	83	99	89	Plymth	92	69	96
Carlis	95	90	92	Ports	46	42	60
Carsh	75	94	79	Prestn	100	99	90
Chelms	99	93	53	Redng	97	98	97
Chestr	83	n/a	n/a	Sheff	94	79	88
Clwyd	84	75	86	Shrew	100	97	91
Covnt	1	0	1	Stevng	51	78	68
Derby	0	0	7	Sthend	87	94	74
Derry	100	n/a	67	Sund	96	100	99
Dorset	81	92	91	Swanse	99	97	98
Dudley	49	72	84	Truro	97	94	81
Exeter	95	78	90	Tyrone	98	86	95
Glouc	91	100	69	Ulster	100	100	100
Hull	91	58	70	Wirral	94	52	n/a
Ipswi	85	94	81	Wolve	93	82	88
L Barts	99	81	82	Wrexm	27	24	33
L Guys	86	94	92	York	95	68	88
L Kings	94	94	91	**England**	**80**	**81**	**80**
L Rfree	88	95	90	**N Ireland**	**95**	**95**	**93**
L West	86	99	98	**Wales**	**83**	**89**	**90**
Leeds	94	94	95	**E, W & NI**	**81**	**83**	**81**

n/a = no patients treated for that modality in centre.

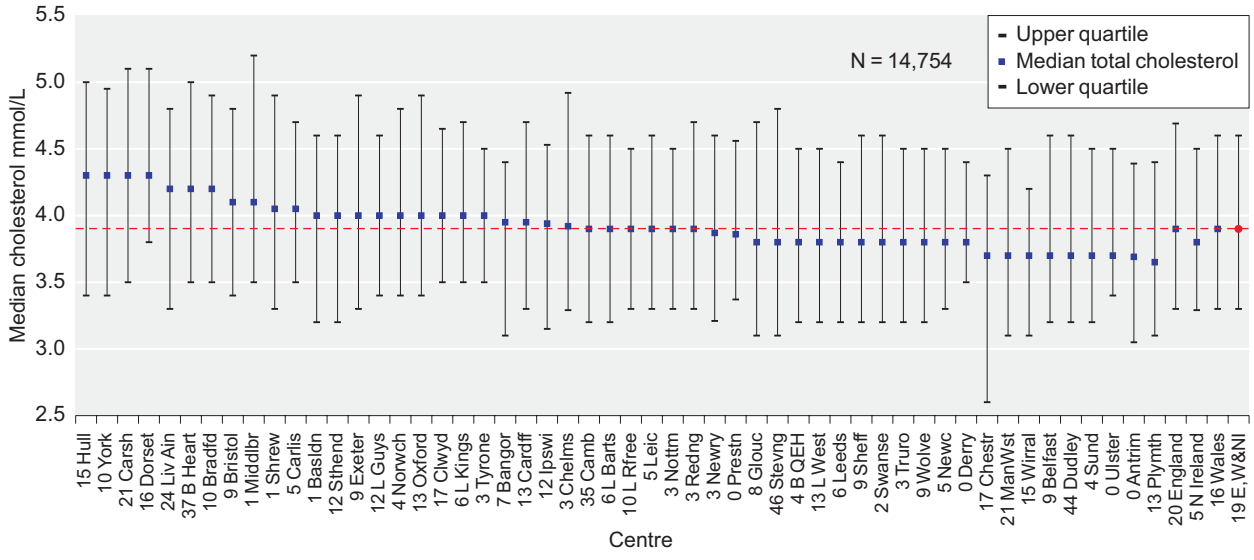

Figure 9.33: Median serum total cholesterol in dialysis patients by centre

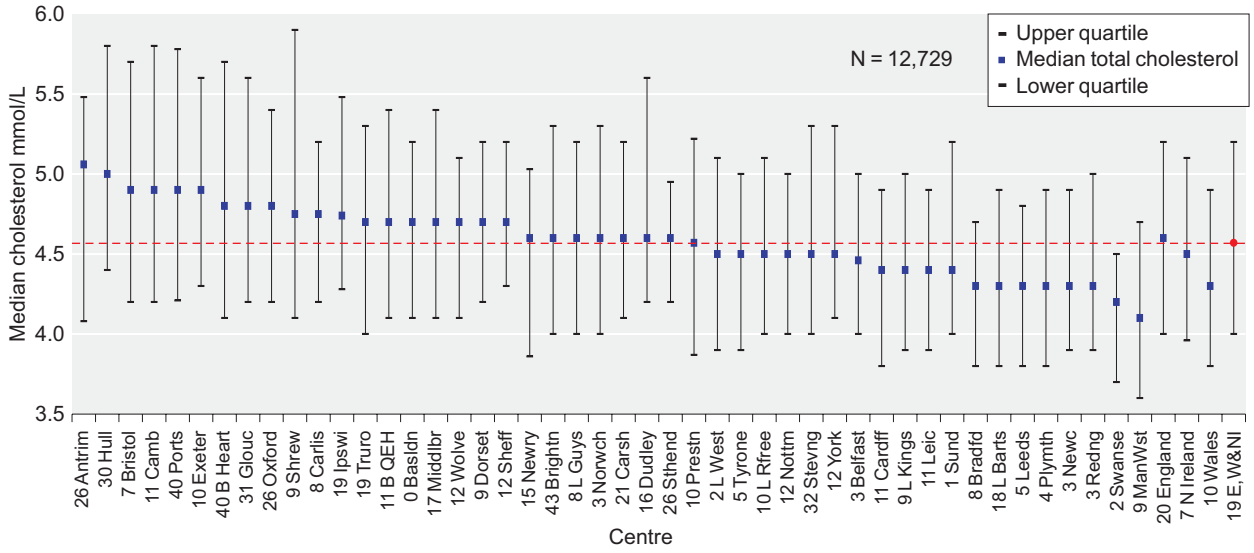

Figure 9.34: Median serum total cholesterol in transplant patients by centre

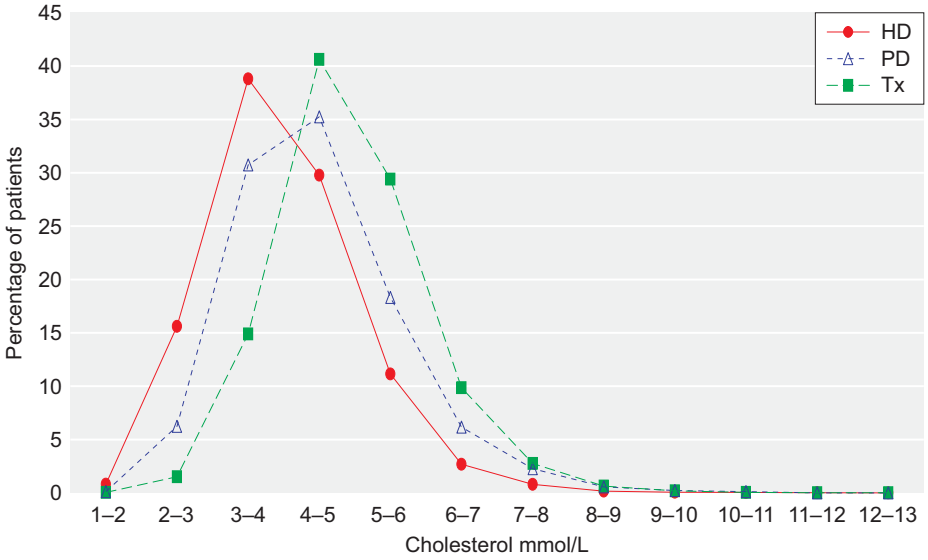

Figure 9.35: Distribution of serum total cholesterol by band, by modality

influence of steroids, calcineurin inhibitors and sirolimus.

The Registry is in the process of expanding the dataset to collect both more detailed lipid profiles and statin use to provide renal centres with a more comprehensive picture. The results of the SHARP and AURORA trials should help to clarify the benefits of statin use in CKD and dialysis populations.

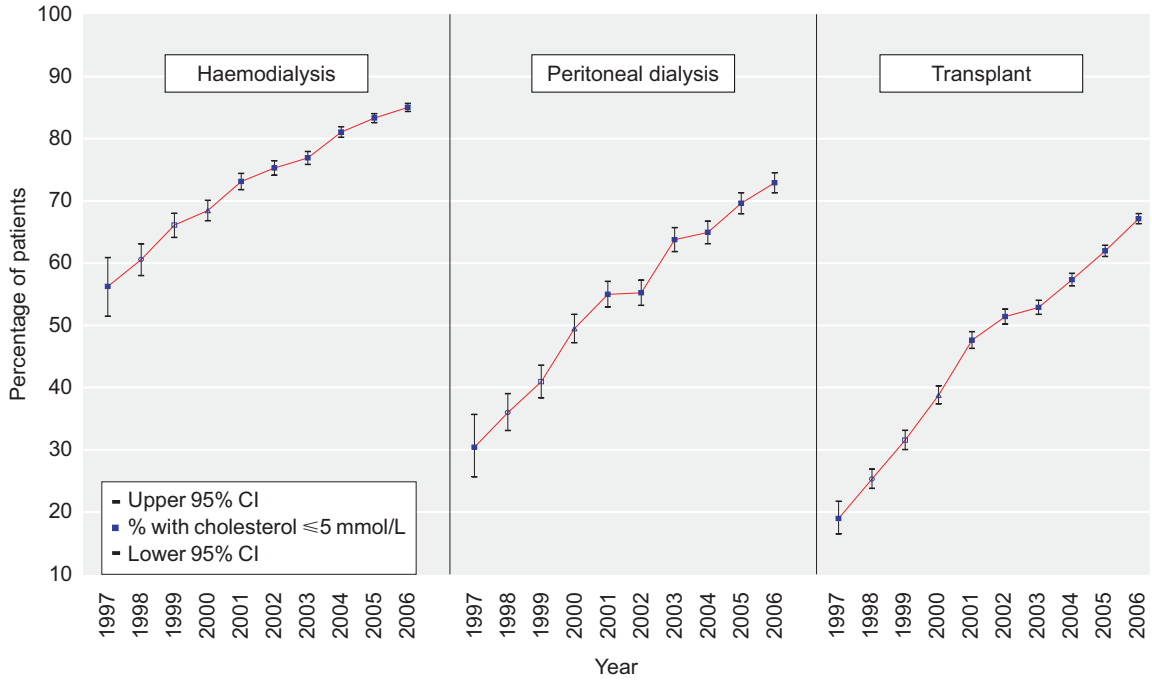

Figure 9.36: Annual change in percentage of RRT patients with serum total cholesterol ⩽5 mmol/L, 1997–2006

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