

CHAPTER 9

MANAGEMENT OF RENAL BONE DISEASE IN DIALYSIS PATIENTS

Rozina Bt Ghazalli
Fan Kin Sing
Shahnaz Shah Firdaus Khan

9.1: TREATMENT OF RENAL BONE DISEASE

In 2005 no major changes were found in the treatment of renal bone disease. The majority of dialysis patients on both HD (91%) and CAPD (84%) received calcium carbonate as a phosphate binder. The usage of aluminium phosphate binders continued to be low since its sharp fall from 1997 onwards. Vitamin D was used in an increasing number of patients in the HD group (tables 9.1.1 & 9.1.2).

Table 9.1.1: Treatment for Renal Bone Disease, HD patients 1997-2005

Year	No. of subjects	No. of subjects on CaCO ₃	% on CaCO ₃	No. of subjects on Al(OH) ₃	% on Al (OH) ₃	No. of subjects on Vitamin D	% on Vitamin D
1997	1695	1543	91	417	25	694	41
1998	2141	1956	91	343	16	652	30
1999	2996	2693	90	244	8	770	26
2000	4392	3977	91	239	5	1084	25
2001	5194	4810	93	145	3	1145	22
2002	6108	5536	91	171	3	1375	23
2003	7043	6430	91	118	2	1692	24
2004	8243	7408	90	106	1	2029	25
2005	9255	8392	91	92	1	2445	26

Table 9.1.2: Treatment for Renal Bone Disease, CAPD patients 1997-2005

Year	No. of subjects	No. of subjects on CaCO ₃	% on CaCO ₃	No. of subjects on Al(OH) ₃	% on Al (OH) ₃	No. of subjects on Vitamin D	% on Vitamin D
1997	476	393	83	57	12	114	24
1998	541	425	79	46	9	110	20
1999	610	450	74	36	6	75	12
2000	662	522	79	15	2	96	15
2001	781	588	75	5	1	84	11
2002	891	713	80	6	1	130	15
2003	1237	1040	84	10	1	238	19
2004	1341	1125	84	18	1	304	23
2005	1403	1185	84	13	1	314	22

9.2: SERUM CALCIUM AND PHOSPHATE CONTROL

The median corrected serum calcium level remained at 2.3 mmol/L in HD patients (table 9.2.1 & fig 9.2.1) and 2.4 mmol/L amongst CAPD patients (table 9.2.2 & fig 9.2.2). In 2005, 59% of patients in HD and 68% of CAPD patients have achieved the target serum calcium of 2.2 to 2.6 mmol/L as required in the MOH renal replacement therapy guidelines. The percentage of patients achieving this range increased in the CAPD population but dropped slightly in the HD patients.

Table 9.2.1: Distribution of corrected Serum Calcium, HD patients 1997-2005

Year	No. of Subjects	Mean	SD	Median	LQ	UQ	% patients ≥ 2.2 & ≤ 2.6 mmol/L
1997	1633	2.3	.3	2.3	2.2	2.5	57
1998	2060	2.3	.3	2.3	2.2	2.5	60
1999	2732	2.3	.3	2.3	2.2	2.5	59
2000	3703	2.4	.3	2.3	2.2	2.5	61
2001	4618	2.4	.2	2.4	2.2	2.5	64
2002	5485	2.3	.3	2.3	2.2	2.5	60
2003	6471	2.3	.2	2.3	2.2	2.4	62
2004	7536	2.3	.2	2.3	2.2	2.4	62
2005	8468	2.3	.2	2.3	2.1	2.4	59

Figure 9.2.1: Cumulative distribution of corrected Serum Calcium, HD patients 1997-2005

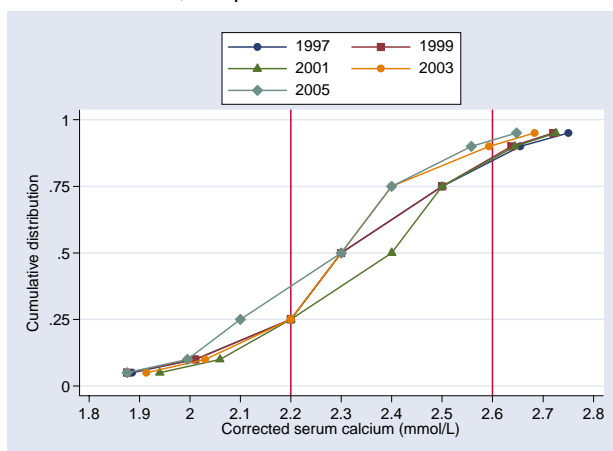


Figure 9.2.2: Cumulative distribution of corrected Serum Calcium, CAPD patients 1997-2005

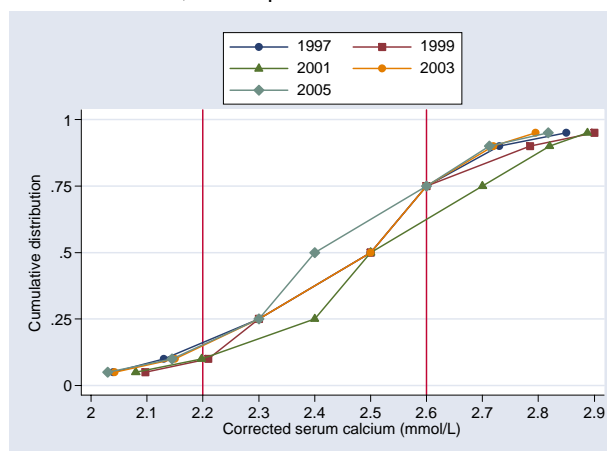


Table 9.2.2: Distribution of corrected Serum Calcium, CAPD patients 1997-2005

Year	No. of Subjects	Mean	SD	Median	LQ	UQ	% patients ≥ 2.2 & ≤ 2.6 mmol/L
1997	469	2.5	.3	2.5	2.3	2.6	57
1998	535	2.4	.3	2.4	2.3	2.6	59
1999	593	2.5	.2	2.5	2.3	2.6	63
2000	635	2.5	.2	2.5	2.3	2.6	60
2001	744	2.5	.3	2.5	2.4	2.7	56
2002	859	2.5	.2	2.5	2.3	2.6	63
2003	1169	2.4	.2	2.5	2.3	2.6	62
2004	1277	2.5	.2	2.5	2.3	2.6	66
2005	1337	2.4	.2	2.4	2.3	2.6	68

The median serum phosphate levels were higher among patients on HD (1.8mmol/L) compared to CAPD patients (1.5 mmol/L) (tables and figs 9.2.3 & 9.2.4).

Table 9.2.3: Distribution of Serum Phosphate, HD patients 1997-2005

Year	No of Subjects	Mean	SD	Median	LQ	UQ	% patients ≥ 1.6 & < 1.8 mmol/L	% patients ≥ 1.8 & < 2.2 mmol/L	% patients ≥ 2.2 & ≤ 2.6 mmol/L
1997	1649	1.9	.5	1.9	1.6	2.3	16	27	19
1998	2051	1.9	.5	1.9	1.6	2.2	16	33	17
1999	2861	1.9	.5	1.9	1.5	2.2	15	28	18
2000	4080	1.9	.6	1.8	1.5	2.2	16	29	15
2001	4765	1.9	.5	1.8	1.5	2.2	17	27	16
2002	5679	1.9	.5	1.8	1.5	2.2	17	27	17
2003	6593	1.8	.5	1.8	1.5	2.2	17	26	15
2004	7620	1.8	.5	1.8	1.5	2.2	17	25	15
2005	8657	1.8	.5	1.7	1.4	2.1	17	25	13

Figure 9.2.3: Cumulative distribution of Serum Phosphate, HD patients 1997-2005

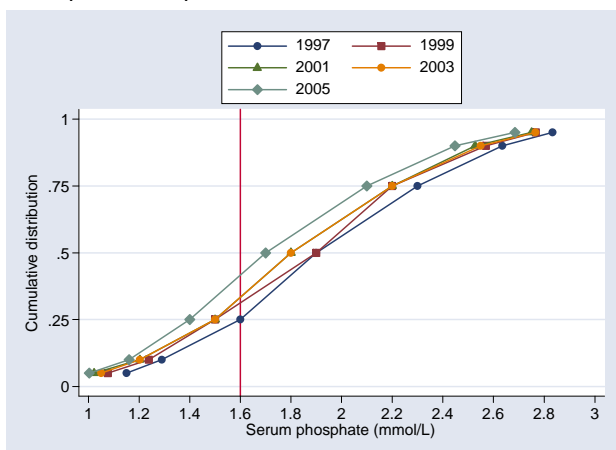


Figure 9.2.4: Cumulative distribution of Serum Phosphate, CAPD patients 1997-2005

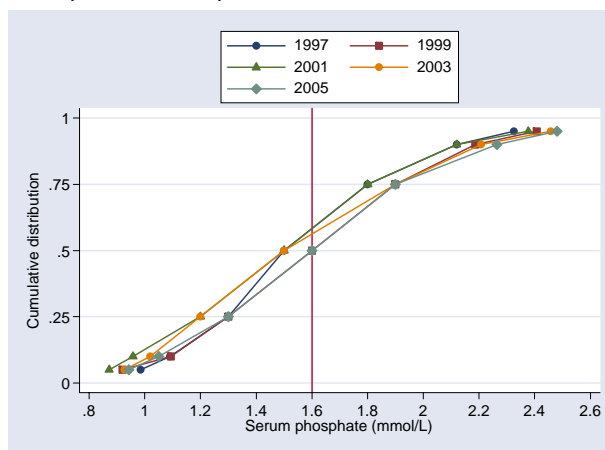


Table 9.2.4: Distribution of Serum Phosphate, CAPD patients 1997-2005

Year	No of Subjects	Mean	SD	Median	LQ	UQ	% patients ≥ 1.6 & < 1.8 mmol/L	% patients ≥ 1.8 & < 2.2 mmol/L	% patients ≥ 2.2 & ≥ 2.6 mmol/L
1997	470	1.6	.4	1.5	1.3	1.8	17	20	6
1998	537	1.6	.5	1.6	1.3	1.9	17	20	8
1999	583	1.6	.5	1.6	1.3	1.9	16	22	7
2000	633	1.5	.5	1.5	1.3	1.8	14	19	6
2001	732	1.5	.5	1.5	1.2	1.8	14	17	5
2002	862	1.5	.5	1.5	1.2	1.8	15	16	7
2003	1175	1.6	.5	1.5	1.2	1.9	14	19	8
2004	1279	1.6	.5	1.6	1.3	1.9	16	20	8
2005	1342	1.6	.5	1.6	1.3	1.9	16	20	9

The median corrected calcium phosphate product has declined from 4.1 mmol²/L² in 2004 to 3.9 in 2005 in HD but remained stable at 3.7 mmol²/L² in the CAPD patients (tables and figs 9.2.5 & 9.2.6). The percentage of patients within the 4 to 4.5 mmol²/L² range has remained unchanged in both groups.

Table 9.2.5: Distribution of corrected calcium x phosphate product, HD patients 1997-2005

Year	No of Subjects	Mean	SD	Median	LQ	UQ	% patients <3.5 mmol ² /L ²	% patients >3.5 & <4 mmol ² /L ²	% patients ≥4 & <4.5 mmol ² /L ²	% patients ≥4.5 & <5 mmol ² /L ²	% patients ≥5 & <5.5 mmol ² /L ²	% patients ≥5.5 mmol ² /L ²
1997	1615	4.5	1.3	4.5	3.6	5.3	23	14	15	17	12	20
1998	2020	4.5	1.2	4.4	3.7	5.2	21	15	18	15	13	19
1999	2698	4.4	1.3	4.3	3.4	5.2	27	14	15	14	11	18
2000	3650	4.4	1.3	4.3	3.5	5.2	25	15	16	15	10	19
2001	4555	4.3	1.3	4.2	3.4	5.2	27	16	16	13	11	18
2002	5403	4.4	1.3	4.3	3.4	5.2	27	16	15	13	10	19
2003	6388	4.2	1.3	4.1	3.3	5.1	30	16	15	13	10	16
2004	7414	4.2	1.3	4.1	3.3	5	32	16	15	12	10	15
2005	8350	4	1.3	3.9	3.2	4.8	36	17	15	11	9	12

Figure 9.2.5: Cumulative distribution of corrected Calcium x Phosphate product, HD patients 1997-2005

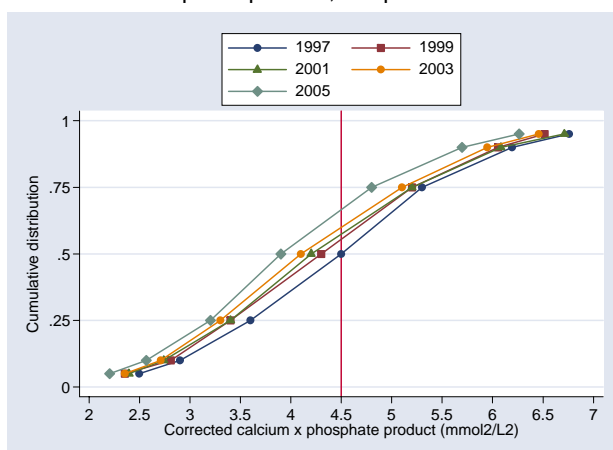


Figure 9.2.6: Cumulative distribution of corrected Calcium x Phosphate product, CAPD patients 1997-2005

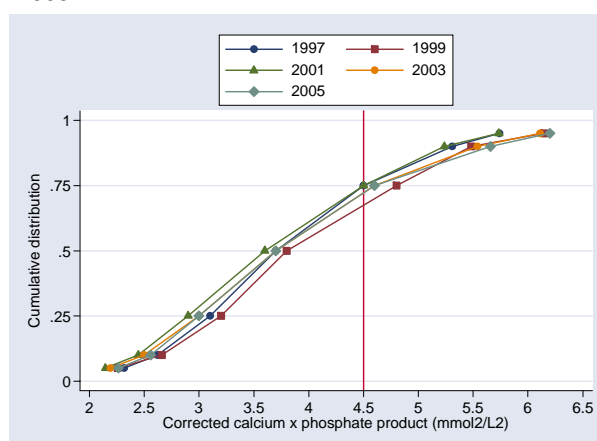


Table 9.2.6: Distribution of corrected calcium x phosphate product, CAPD patients 1997-2005

Year	No of Subjects	Mean	SD	Median	LQ	UQ	% patients <3.5 mmol ² /L ²	% patients ≥3.5 & <4 mmol ² /L ²	% patients ≥4 & <4.5 mmol ² /L ²	% patients ≥4.5 & <5 mmol ² /L ²	% patients ≥5 & <5.5 mmol ² /L ²	% patients ≥5.5 mmol ² /L ²
1997	468	3.9	1.1	3.7	3.1	4.5	40	20	15	10	6	7
1998	533	4	1.1	3.8	3.2	4.6	38	18	16	10	6	11
1999	580	4	1.2	3.8	3.2	4.8	36	20	13	12	9	10
2000	621	3.8	1.1	3.7	3.1	4.5	44	19	12	10	7	8
2001	723	3.8	1.1	3.6	2.9	4.5	46	18	12	10	8	7
2002	856	3.8	1.2	3.6	2.9	4.5	45	17	12	11	7	8
2003	1164	3.9	1.2	3.7	3	4.6	43	17	13	10	8	10
2004	1275	4	1.2	3.8	3	4.7	41	15	14	10	8	12
2005	1332	3.9	1.3	3.7	3	4.6	43	15	14	11	6	11

In 2005 the median corrected serum calcium level among HD patients from 212 centres ranged widely from as low as 1.8 to as high as 2.6 mmol/L in some centres. For CAPD patients all 18 centres had a median within the 2.2 to 2.6 mmol/L range (tables 9.2.7a and 9.2.8a).

Table 9.2.7: Variation in corrected serum calcium levels among HD centres, 2005
(a) Median serum calcium level among HD patients

Year	No. of centres	Min	5th Centile	LQ	Median	UQ	95th Centile	Max
1997	46	2.1	2.2	2.3	2.3	2.4	2.5	2.5
1998	50	2	2.1	2.3	2.3	2.4	2.5	2.5
1999	69	1.5	2	2.3	2.3	2.4	2.5	2.6
2000	93	2	2.1	2.3	2.3	2.4	2.6	3.2
2001	116	2	2.1	2.3	2.4	2.4	2.5	2.6
2002	138	1.9	2.1	2.2	2.3	2.4	2.5	2.6
2003	164	2	2.1	2.2	2.3	2.4	2.5	2.5
2004	190	1.9	2.1	2.2	2.3	2.3	2.4	2.5
2005	212	1.8	2	2.2	2.3	2.4	2.4	2.6

Figure 9.2.7(a): Variation in median serum calcium level among HD patients, HD centres 2005

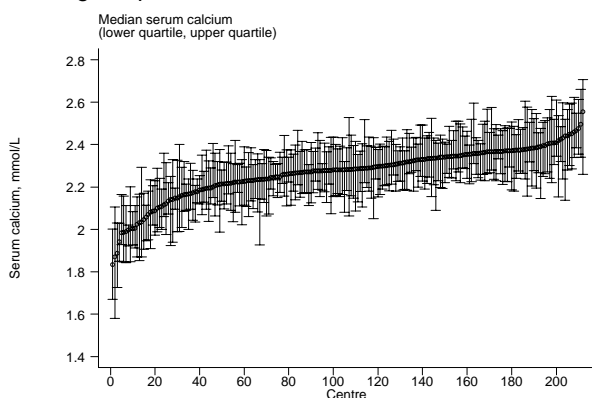
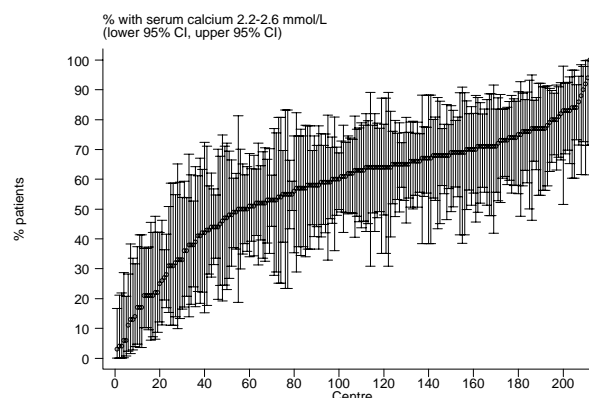


Figure 9.2.7(b): Variation in proportion of patients with serum calcium 2.2 to 2.6 mmol/L, HD centres 2005



We reviewed the proportion of patients with serum calcium range between 2.2 to 2.6 mmol/L from 1997 to 2005. The median was lower for HD centres (62.5%) (table 9.2.7b) compared to CAPD centres (64.5%) (table 9.2.8b) for the year 2005. In some HD centres less than 5% of their patients achieved a serum calcium of 2.2 to 2.6 mmol/L. The percentage of CAPD patients within a centre with serum calcium 2.2 to 2.6 mmol/L ranged from 38% to 75%.

(b) Proportion of patients with serum calcium 2.2 to 2.6 mmol/L

Year	No. of centres	Min	5th Centile	LQ	Median	UQ	95th Centile	Max
1997	46	23	36	50	57.5	63	72	76
1998	50	22	30	51	63	71	82	94
1999	69	8	20	49	60	70	81	94
2000	93	0	25	52	62	69	79	100
2001	116	16	28	57	64	71	85	98
2002	138	0	25	49	62	70	81	92
2003	164	9	30	53.5	63	70.5	81	91
2004	190	5	25	50	63	73	83	91
2005	212	3	17	49	62.5	70	83	100

Table 9.2.8: Variation in corrected serum calcium levels among CAPD centres, 2005

(a) Median serum calcium level among CAPD patients

Year	No. of centres	Min	5th Centile	LQ	Median	UQ	95th Centile	Max
1997	7	2.1	2.1	2.4	2.4	2.5	2.6	2.6
1998	9	2.2	2.2	2.3	2.4	2.4	2.6	2.6
1999	10	2.4	2.4	2.4	2.5	2.6	2.6	2.6
2000	11	2.4	2.4	2.4	2.5	2.5	2.6	2.6
2001	12	2.3	2.3	2.4	2.5	2.5	2.6	2.6
2002	14	2.4	2.4	2.4	2.5	2.5	2.6	2.6
2003	18	2.3	2.3	2.4	2.4	2.5	2.6	2.6
2004	18	2.3	2.3	2.4	2.4	2.5	2.5	2.5
2005	18	2.2	2.2	2.3	2.4	2.5	2.6	2.6

Figure 9.2.8(a): Variation in median serum calcium level among CAPD patients, CAPD centres 2005

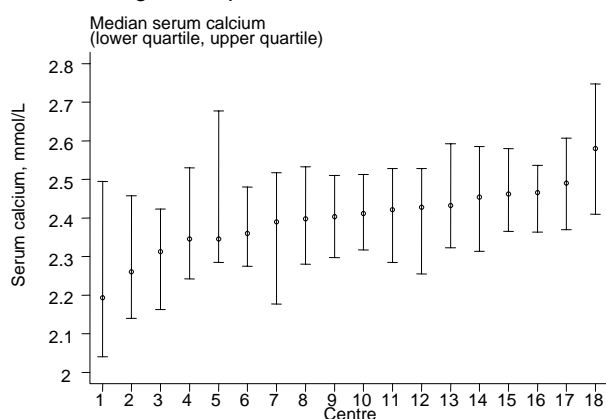
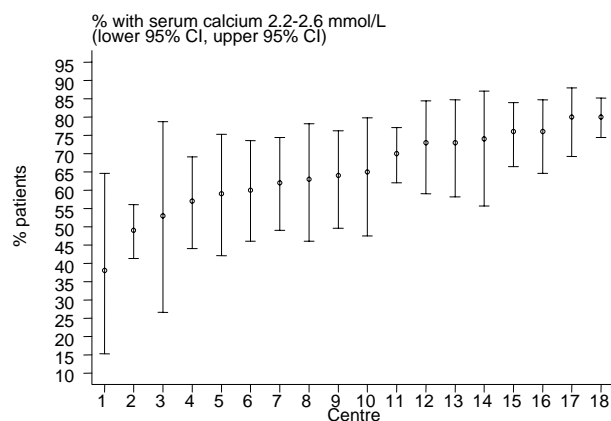


Figure 9.2.8(b): Variation in proportion of patients with serum calcium 2.2 to 2.6 mmol/L, CAPD centres 2005



(b) Proportion of patients with serum calcium 2.2 to 2.6 mmol/L

Year	No. of centres	Min	5th Centile	LQ	Median	UQ	95th Centile	Max
1997	7	34	34	35	59	67	71	71
1998	9	43	43	47	55	60	78	78
1999	10	36	36	53	58	62	82	82
2000	11	45	45	48	57	70	83	83
2001	12	45	45	54	57.5	60.5	69	69
2002	14	50	50	56	68.5	71	73	73
2003	18	41	41	57	64	69	76	76
2004	18	45	45	61	68	75	80	80
2005	18	38	38	59	64.5	74	80	80

In reviewing the proportion of patients with a serum phosphate level below 1.6 mmol/L the CAPD centres have a higher median proportion of patients with serum phosphate level below 1.6 mmol/L (52.5%) compared to HD centres (37%) (tables 9.2.9a & 9.2.9b). However since 2002 the trend shows an increasing proportion of HD patients is achieving a serum phosphate of <1.6 mmol/L.

Table 9.2.9: Variation in serum phosphate levels among HD centres, 2005
(a) Median serum phosphate level among HD patients

Year	No. of centres	Min	5th Centile	LQ	Median	UQ	95th Centile	Max
1997	46	1.3	1.5	1.8	1.9	2.1	2.3	2.8
1998	50	1.5	1.5	1.8	1.9	2.1	2.2	2.6
1999	71	1.1	1.6	1.8	1.9	2	2.1	2.1
2000	100	1.4	1.6	1.7	1.9	1.9	2.2	3.8
2001	117	1.3	1.5	1.7	1.8	1.9	2.1	2.3
2002	145	1.3	1.5	1.8	1.9	2	2.2	2.4
2003	169	.9	1.5	1.7	1.8	1.9	2.2	2.4
2004	191	1.4	1.5	1.7	1.8	1.9	2.1	2.2
2005	218	.9	1.4	1.6	1.8	1.9	2.1	2.2

Figure 9.2.9(a): Variation in median serum phosphate level among HD patients, HD centres 2005

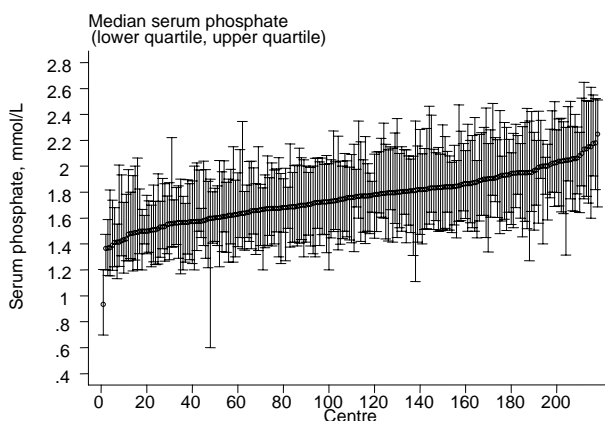
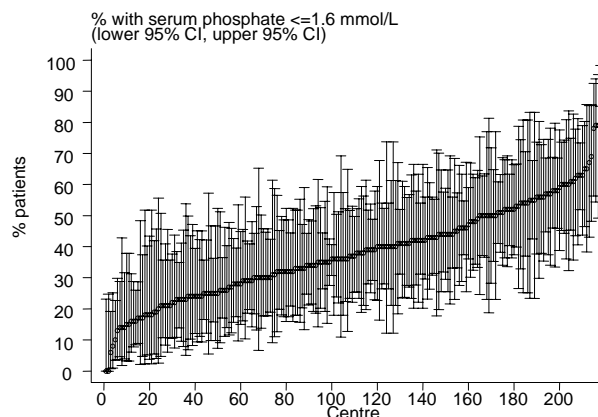


Figure 9.2.9(b): Variation in proportion of patients with serum phosphate <=1.6 mmol/L among HD patients, HD centres 2005



(b) Proportion of patients with serum phosphate ≤ 1.6 mmol/L

Year	No. of centres	Min	5th Centile	LQ	Median	UQ	95th Centile	Max
1997	46	0	10	17	25.5	38	55	71
1998	50	0	7	17	22	30	54	59
1999	71	6	10	21	29	39	55	81
2000	100	0	13	21	31	38.5	50.5	66
2001	117	0	11	23	30	38	57	77
2002	145	0	8	21	28	36	58	76
2003	169	5	13	22	31	40	56	89
2004	191	0	11	23	33	44	60	95
2005	218	0	15	27	37	49	63	94

Table 9.2.10: Variation in serum phosphate levels among CAPD centres, 2005
(a) Median serum phosphate level among CAPD patients

Year	No. of centres	Min	5th Centile	LQ	Median	UQ	95th Centile	Max
1997	7	1.4	1.4	1.5	1.5	1.6	1.7	1.7
1998	9	1.4	1.4	1.5	1.6	1.6	1.8	1.8
1999	9	1.5	1.5	1.5	1.6	1.6	1.7	1.7
2000	11	1.3	1.3	1.4	1.5	1.6	1.8	1.8
2001	12	1.3	1.3	1.4	1.5	1.6	1.9	1.9
2002	14	1.4	1.4	1.4	1.5	1.6	2.1	2.1
2003	18	1.1	1.1	1.4	1.5	1.6	1.7	1.7
2004	18	1.4	1.4	1.4	1.5	1.6	1.8	1.8
2005	18	1.4	1.4	1.5	1.5	1.6	1.9	1.9

Figure 9.2.10(a): Variation in median serum phosphate level among CAPD patients, CAPD centres 2005

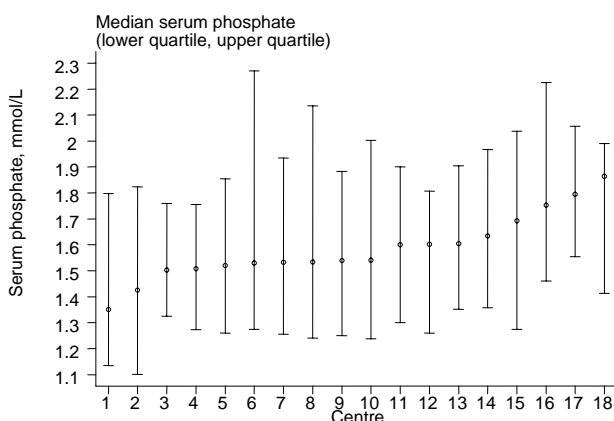
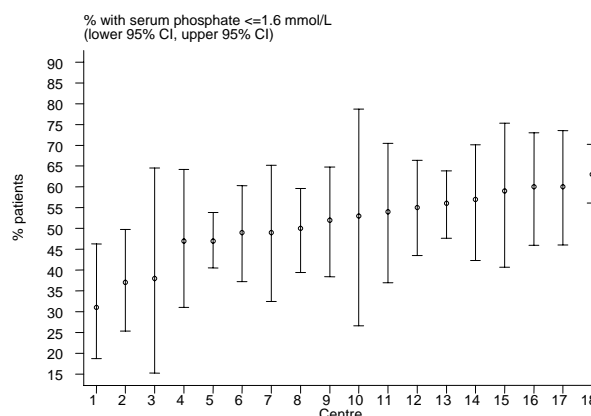


Figure 9.2.10(b): Variation in proportion of patients with serum phosphate ≤ 1.6 mmol/L, CAPD centres 2005



(b) Proportion of patients with serum phosphate ≤ 1.6 mmol/L

Year	No. of centres	Min	5th Centile	LQ	Median	UQ	95th Centile	Max
1997	7	24	24	53	54	63	75	75
1998	9	37	37	49	53	54	67	67
1999	9	41	41	49	53	56	57	57
2000	11	29	29	48	54	66	73	73
2001	12	30	30	48	59	65	72	72
2002	14	36	36	51	55.5	61	72	72
2003	18	33	33	49	56.5	67	75	75
2004	18	34	34	44	55.5	61	76	76
2005	18	31	31	47	52.5	57	63	63

A higher number of CAPD centres have median calcium phosphate product less than $4.5 \text{ mmol}^2/\text{L}^2$ as compared to HD centres (73.5% versus 69%). In 2005 more than half of the CAPD patients in all the 18 CAPD centres were able to achieve a calcium phosphate product of $<4.5 \text{ mmol}^2/\text{L}^2$. Nevertheless there is an increasing trend among HD centres achieving a corrected calcium phosphate product less than $4.5 \text{ mmol}^2/\text{L}^2$ (tables and figs 9.2.11 & 9.2.12). In some HD centres 90% of their patients achieved a calcium phosphate product of $<4.5 \text{ mmol}^2/\text{L}^2$.

Table 9.2.11: Variation in corrected calcium x phosphate product among HD centres, 2005

(a) Median corrected calcium x phosphate product among HD patients

Year	No. of centres	Min	5th Centile	LQ	Median	UQ	95th Centile	Max
1997	46	2.9	3.7	4.1	4.4	4.8	5.3	6.2
1998	50	3.2	3.3	4.1	4.5	4.7	5.3	5.3
1999	69	2.3	3.1	4	4.3	4.7	5.2	5.2
2000	91	3.1	3.7	4	4.3	4.6	5.2	6.2
2001	113	2.9	3.6	3.9	4.2	4.6	5	5.7
2002	138	2.9	3.5	3.9	4.3	4.6	5.2	6.2
2003	164	2.1	3.4	3.8	4.1	4.5	5	5.7
2004	189	2.9	3.3	3.8	4.1	4.3	5	5.5
2005	210	2.1	3.2	3.6	3.9	4.3	4.8	5.1

Figure 9.2.11(a): Variation in median corrected calcium x phosphate product among HD patients, HD centres

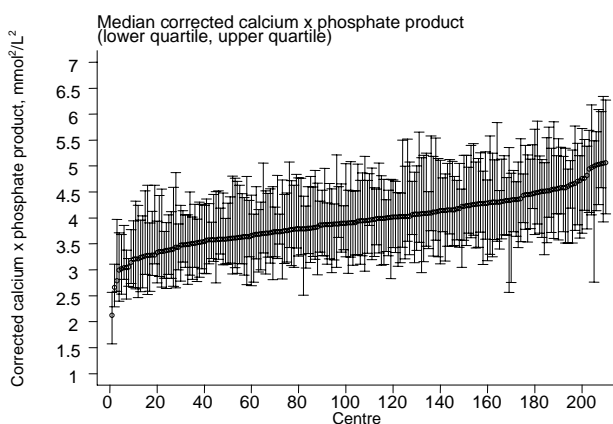
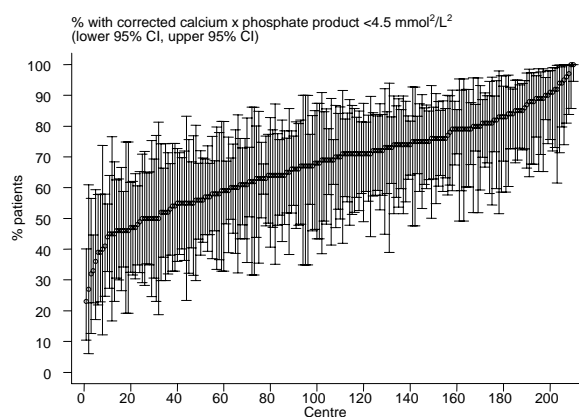


Figure 9.2.11(b): Variation in proportion of patients with corrected calcium x phosphate product $<4.5 \text{ mmol}^2/\text{L}^2$, HD centres 2005



(b) Proportion of patients with corrected calcium x phosphate product $<4.5 \text{ mmol}^2/\text{L}^2$

Year	No. of centres	Min	5th Centile	LQ	Median	UQ	95th Centile	Max
1997	46	15	26	39	51.5	66	77	100
1998	50	20	27	40	52	64	83	91
1999	69	20	31	47	55	65	95	100
2000	91	12	33	48	58	67	80	88
2001	113	18	38	48	55	71	82	91
2002	138	14	31	48	57	69	88	100
2003	164	21	32	50	61.5	72.5	85	100
2004	189	21	36	54	64	74	89	100
2005	210	23	45	57	69	79	91	100

Table 9.2.12: Variation in corrected calcium x phosphate product among CAPD centres, 2005

(a) Median corrected calcium x phosphate product among CAPD patients

Year	No. of centres	Min	5th Centile	LQ	Median	UQ	95th Centile	Max
1997	7	3.5	3.5	3.6	3.7	3.8	3.9	3.9
1998	9	3.5	3.5	3.6	3.7	3.9	4	4
1999	9	3.6	3.6	3.7	3.9	4.1	4.2	4.2
2000	11	3.4	3.4	3.5	3.7	4	4.4	4.4
2001	12	3.1	3.1	3.4	3.7	4	4.3	4.3
2002	14	3.4	3.4	3.4	3.7	4	4.9	4.9
2003	18	2.7	2.7	3.4	3.6	3.9	4.1	4.1
2004	18	3.2	3.2	3.5	3.8	4	4.4	4.4
2005	18	3.3	3.3	3.5	3.7	3.9	4.2	4.2

Figure 9.2.12(a): Variation in median corrected calcium x phosphate product among CAPD patients, CAPD centres 2005

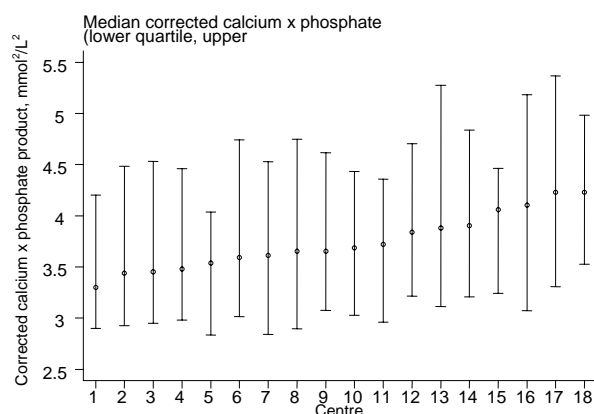
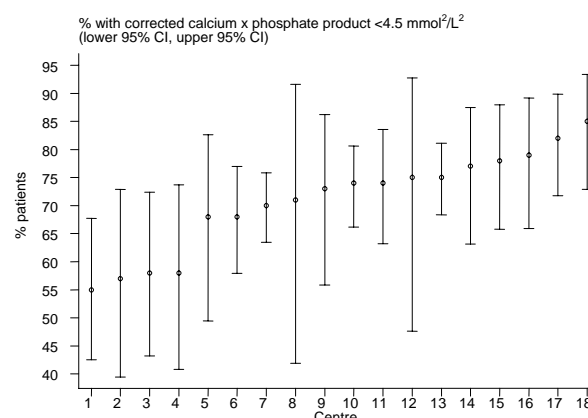


Figure 9.2.12(b): Variation in proportion of patients with corrected calcium x phosphate product < 4.5 mmol²/L², CAPD centres 2005



(b) Proportion of patients with corrected calcium x phosphate product < 4.5 mmol²/L²

Year	No. of centres	Min	5th Centile	LQ	Median	UQ	95th Centile	Max
1997	7	70	70	74	78	82	94	94
1998	9	66	66	71	73	79	91	91
1999	9	59	59	65	72	74	77	77
2000	11	59	59	70	73	81	85	85
2001	12	50	50	71.5	76	79	84	84
2002	14	43	43	65	74.5	82	88	88
2003	18	62	62	67	74	81	100	100
2004	18	56	56	66	72	78	91	91
2005	18	55	55	68	73.5	77	85	85

Conclusion

In 2005 calcium carbonate remains the major phosphate binder in both HD and CAPD patients. Phosphate control continues to be better in the CAPD group. The target of calcium phosphate product of less than $4.5 \text{ mmol}^2/\text{L}^2$ is achieved more by CAPD patients than HD although there is an increasing trend among HD centres achieving a corrected calcium phosphate product less than $4.5 \text{ mmol}^2/\text{L}^2$. Continued differences in dialysis management have resulted in variation of outcome results in serum calcium, phosphate and calcium phosphate product.

The relationship of these factors to increased cardiovascular mortality in our patients has not been determined. It is hoped that in future reports this can be studied. It is also necessary to look at intact parathyroid hormone levels (iPTH) in the context of renal bone disease and cardiovascular disease. With the use of newer phosphate binders and vitamin D compounds in the coming years better control of bone disease is to be expected.