Chapter 11: Factors which may Influence Cardiovascular Disease – Blood Pressure and Serum Cholesterol

Summary

- Many units still fail to return blood pressure data to the Renal Registry.
- In England & Wales, 40% of haemodialysis (HD) patients achieve the Renal Association combined pre-dialysis blood pressure standard (inter unit range 12–60%) and 44% of patients achieve the post-dialysis standard (range 31–59%). 29% of peritoneal dialysis (PD) patients (range 0–50%) and 22% of renal transplant (Tx) patients (range 11–51%) achieve the standard.
- During the last 7 years there has been no significant improvement in systolic or diastolic blood pressure control.
- In England & Wales, the cholesterol standard was achieved in 81% of patients on haemodialysis (inter unit range 65–95%), 65% of peritoneal dialysis patients (range 26–83%) and 57% of transplant patients (range 36–77%).
- Cholesterol levels have fallen progressively over the last 7 years and remain consistently lower in patients treated with HD than PD or renal transplant.

Introduction

It is now well recognised that the excessive cardiovascular mortality in patients on renal replacement therapy (RRT) is due to processes distinct from atherosclerosis. Heart failure, arrhythmia and 'sudden death' are more frequent causes of death than myocardial infarction. The condition has been referred to as uraemic cardiomyopathy and arteriopathy but this is a poor descriptor as clinical studies have shown that the process starts at an early stage of chronic kidney disease (CKD)[1]. The heart disease is characterised by left ventricular hypertrophy (LVH), resulting from combined pressure and volume overload, myocardial fibrosis and calcification of coronary arteries and heart valves[2]. In conduit arteries there is hypertrophy of both intimal and medial layers with medial calcification leading to arterial stiffness, an independent risk factor for death[3]. Vascular smooth muscle cells in affected vessels dedifferentiate into osteoblast-like cells capable of producing bone matrix proteins that regulate mineralisation[4]. Arterial calcification increases rapidly with time on dialysis, even in paediatric cases[5] and hyperphosphataemia has been shown to be a major contributory factor.

Recent guidelines recommend a lower blood pressure target for patients with CKD (less than 130/80 mmHg) to reduce progression to renal failure and reduce cardiovascular complications[6,7]. So far clinical trials have been designed to evaluate the effect of lower blood pressure on progression of kidney disease. Cardiovascular outcomes have only been documented as secondary endpoints thus demanding caution when interpreting the data. Trials in non-diabetics include 'Modification of Diet in Renal Disease' (MDRD)[8], 'African–American Study of Kidney Disease and Hypertension' (AASK)[9] and 'Ramipril Efficacy in Nephropathy 2' (REIN-2)[10]. MDRD claims a benefit of 2 years from lower blood pressure on the composite end points of kidney failure and all cause mortality before kidney failure. Achieved blood pressure in the lower and usual blood pressure groups were 126/77 and 134/81 mmHg 4 months after the start of the study. Outcomes were reported to 2000 but no blood pressure data were available after 1993. Both AASK and REIN-2 reported no benefit from lower blood pressure. Achieved blood pressure in the lower and usual blood pressure groups averaged 128/78 versus 141/85 mmHg and 130/80 versus 134/82 mmHg in these respective studies.

Several trials in Type 2 diabetics with established nephropathy assess cardiovascular outcomes as secondary endpoints. The 'Reduction of endpoints in NIDDM with the Angiotensin II Antagonist Losartan Study' (RENAAL)[11] achieved an average blood pressure of 140/74 in the losartan group and 142/74 mmHg in the placebo group by the end of the study. Post hoc analysis indicated losartan significantly reduced

new onset heart failure at all stages of CKD while the incidence of heart failure increased with severity of CKD in the placebo group[12]. Baseline systolic blood pressure proved a strong predictor of outcome with a SBP in the range 140 to 159 mmHg increasing the risk of ESRD or death by 38% when compared with a systolic blood pressure (SBP) below 130 mmHg. In a multivariate model, every 10 mmHg rise in baseline SBP increased the risk for ESRD or death by 6.7%. The 'Irbesartan Diabetic Nephropathy Trial' (IDNT)[13] achieved a mean blood pressure of 140/77 mmHg for the irbesartan group, 141/77 for the amlodipine group and 144/80 mmHg for the placebo group. There was no difference in cardiovascular outcomes between treatment groups. The 'Appropriate Blood Pressure Control in Diabetes Trial' (ABCD) investigated the effect of intensive and moderate blood pressure lowering in Type 2 diabetes with varying degrees of albuminuria. In hypertensive subjects the achieved blood pressure was 132/78 and 138/86 mmHg in the different groups by the end of the study. There was a reduction in all-cause mortality in the intensively treated group[14]. In normotensive subjects the achieved blood pressure was 128/75 and 137/81 mmHg respectively with a significantly lower incidence of cerebrovascular accidents in the intensively treated group[15].

Properly designed randomised controlled trials (RCTs) are needed to assess whether blood pressure control will significantly reduce cardiovascular death in dialysis and renal transplant patients. While uncertainty remains the blood pressure audit for haemodialysis, peritoneal dialysis and renal transplant populations remains important.

In all figures where data are shown by the individual centre, the number adjacent to the name of the renal unit indicates the percentage of missing data at that time point.

Blood Pressure Control

The Renal Association standards for control of hypertension were revised in August 2002. The current standards are:

Pre-haemodialysis blood pressure <140/90 mmHg.

Table 11.1: Percentage of patients with complete returns of blood pressure values by modality

	% completed data			
	Pre HD	**Post HD**	**PD**	**Tx**
Bangor	100	98	96	n/a
Barts	0	0	0	0
Basildon	95	95	100	0
Bradford	11	8	94	92
Brighton	7	28	0	0
Bristol	100	99	100	78
Cambridge	7	0	87	4
Carlisle	93	93	6	0
Carshalton	0	0	0	0
Chelmsford	97	94	100	40
Clwyd	13	0	83	100
Coventry	99	98	78	66
Cardiff	14	0	6	95
Derby	88	88	19	33
Dorset	97	95	64	3
Dudley	81	81	84	80
Exeter	93	79	99	19
Gloucester	97	1	3	0
Guys	66	65	6	1
H&CX	0	0	0	0
Heartlands	91	91	4	1
Hull	78	77	87	1
Ipswich	96	96	1	0
Kings	0	0	0	0
Leeds	97	94	95	69
Leicester	96	93	94	73
Liverpool	16	0	38	66
ManWst	0	0	0	0
Middlesbrough	94	90	100	52
Newcastle	0	0	0	1
Norwich	97	97	13	0
Nottingham	97	96	96	91
Oxford	91	87	71	11
Plymouth	1	1	0	1
Portsmouth	0	0	0	0
Preston	0	0	0	0
QEH	0	0	0	1
Reading	94	0	99	97
Sheffield	100	97	98	98
Shrewsbury	98	98	11	3
Stevenage	95	92	7	4
Southend	98	0	0	0
Sunderland	96	96	0	1
Swansea	69	67	22	8
Truro	99	98	64	81
Wirral	2	0	8	n/a
Wolverhampton	90	90	8	1
Wrexham	0	0	0	4
York	92	92	96	96
England	56	51	42	29
Wales	34	26	18	76
England & Wales	54	49	40	32

Post-haemodialysis, peritoneal dialysis and renal transplant blood pressure <130/80 mmHg.

Separate standards have not been specified for diabetics although diabetic guidelines recommend a lower target if proteinuria is present (BP <125/75 mmHg) to reduce cardiovascular risk.

Data Returns

Units with data for less than 35% of patients in any treatment modality were excluded from the blood pressure analyses. Insufficient returns were obtained from 18 centres for pre-HD blood pressure data, 21 centres for post-HD data, 27 centres for PD blood pressure data and 33 centres for Tx blood pressure data (Table 11.1). This implies units are still having problems transferring data from clinical areas to their renal IT systems. For some units the Renal Registry may not be extracting available data in which case they should contact the Registry.

Distribution of blood pressure by modality

Figure 11.1 shows systolic, diastolic and pulse pressure distributions for each treatment modality (post-HD data are shown). The systolic/diastolic standard deviations for post-HD, PD and Tx were 26/14, 24/13 and 19/11 respectively, with the widest spread for post-HD. The values have not changed substantially over the last few years and should be compared to 18/10 for a hypertensive population without renal disease. As predicted, the mean blood pressure for each modality is approaching the specified blood pressure target of 130/80 mmHg. The significantly lower diastolic blood pressure for HD contributes to the wider pulse pressure in this group.

Achievement of combined systolic and diastolic Standard

Figures 11.2–11.5 show a wide variation between units achieving the combined blood pressure standard for each modality. In England & Wales, 40% of HD patients achieve the standard pre-dialysis (inter unit range 12–60%) and 44% post-dialysis (range 31–59%). 29% of PD patients (range 0–50%) and 22% of Tx patients (range 11–51%) achieve the standard. Chi squared testing indicates the variation between centres for each treatment modality is significant ($p < 0.0001$).

Systolic pressure alone

Figures 11.6–11.13 show wide variation between units in their achievement of the systolic blood pressure standard. In England & Wales, 42% of HD patients achieve the standard pre-dialysis (inter unit range 12–60%) and 48% post-dialysis (range 37–61%). 37% of PD patients (range 19–56%) and 31% of Tx patients (range 14–55%) achieve the standard. Chi squared testing indicates the variation between centres

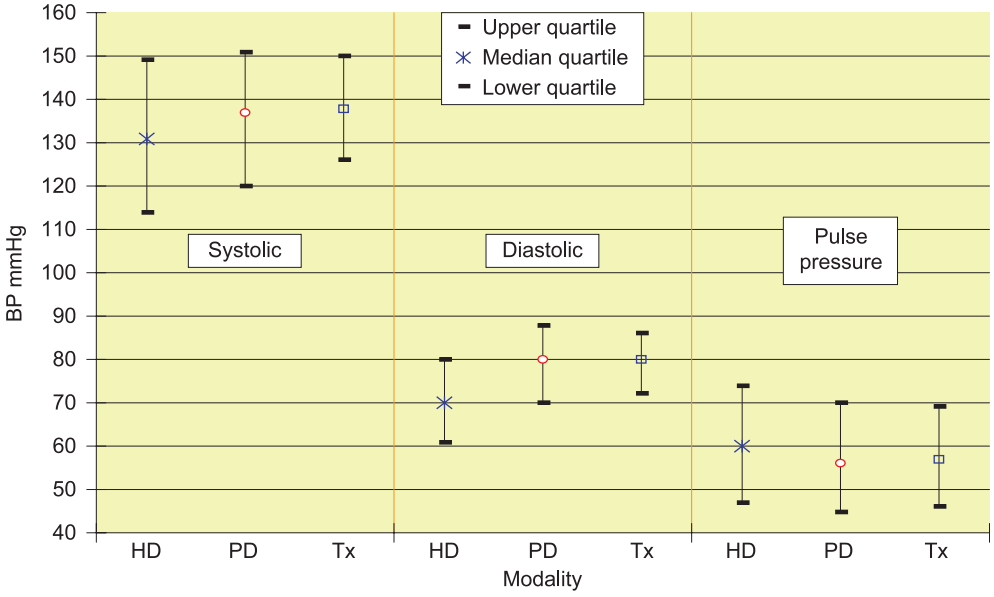

Figure 11.1: Summary of BP achievement

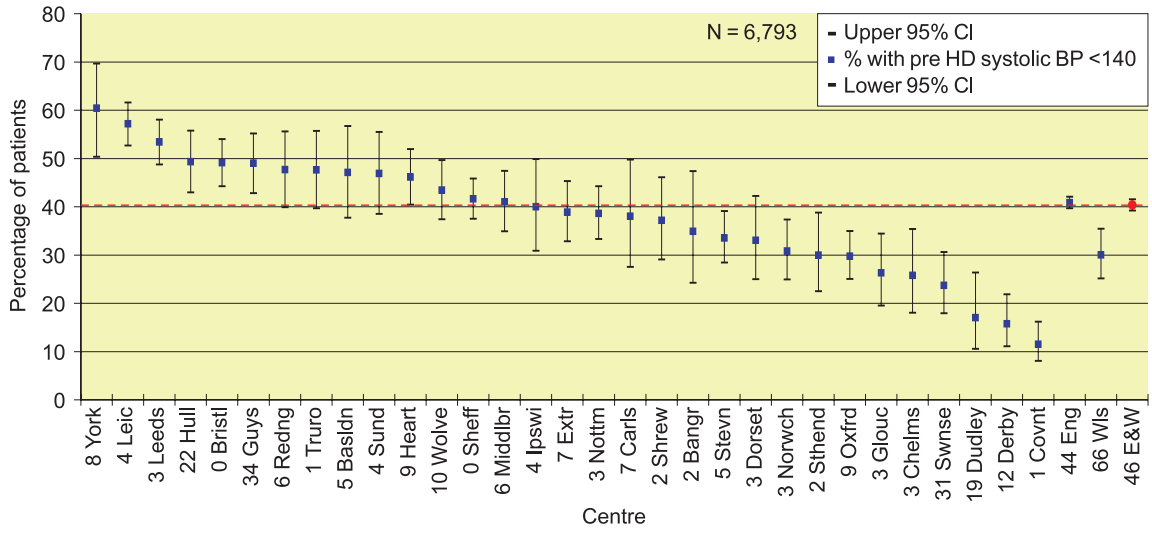

Figure 11.2: Percentage of patients with BP <140/90 mmHg: pre-HD

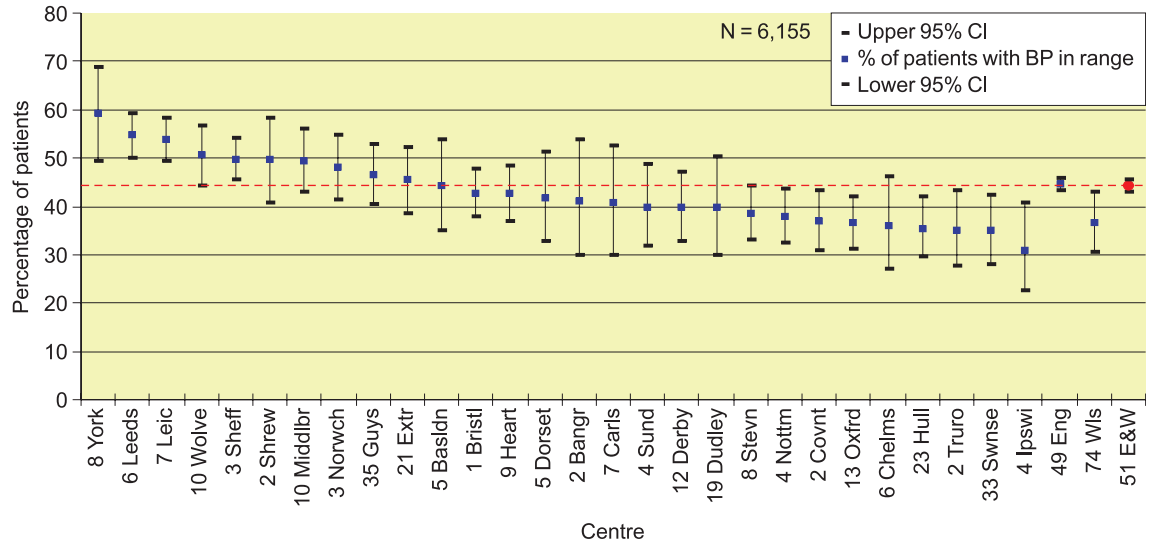

Figure 11.3: Percentage of patients with BP <130/80 mmHg: post-HD

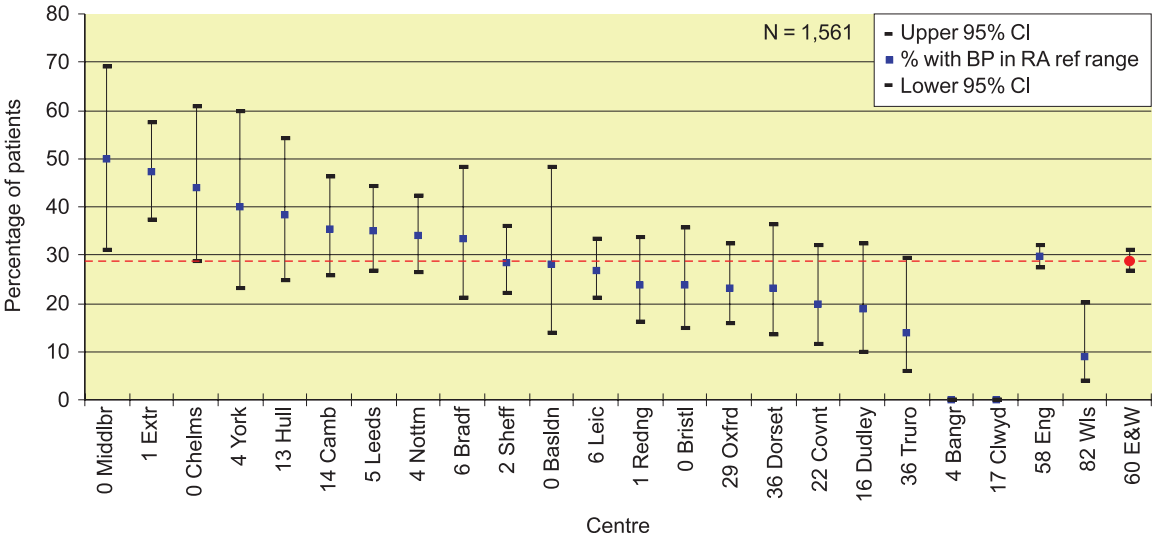

Figure 11.4: Percentage of patients with BP <130/80 mmHg: PD

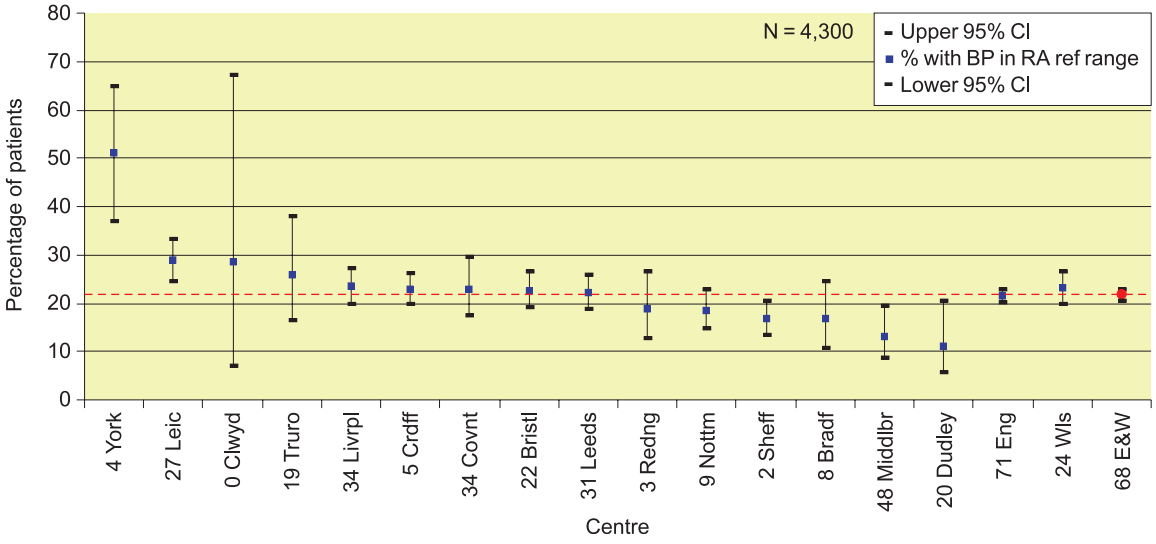

Figure 11.5: Percentage of patients with BP <130/80 mmHg: Tx

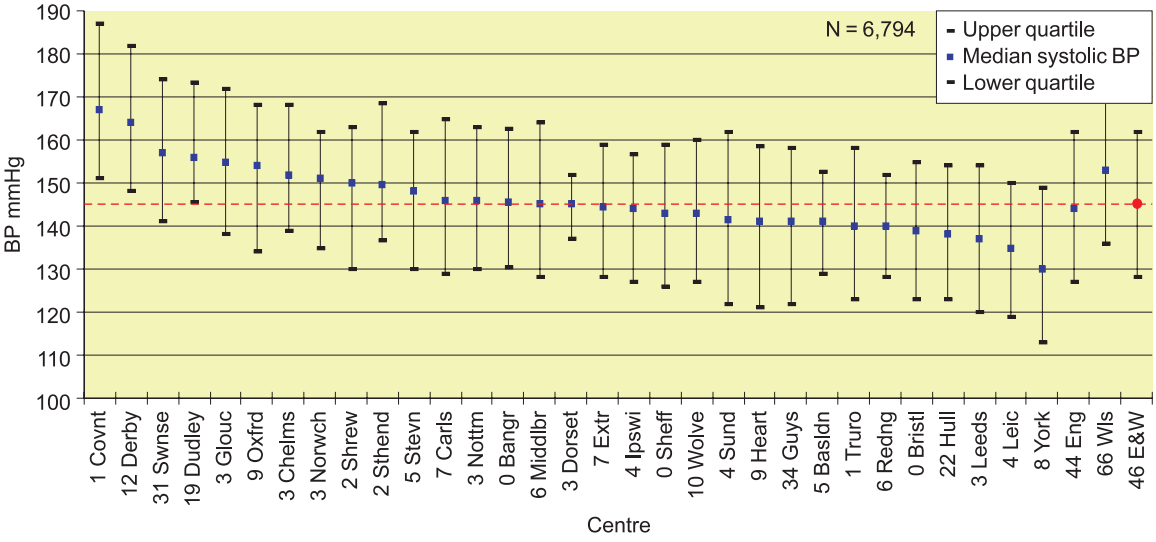

Figure 11.6: Median systolic BP: pre-HD

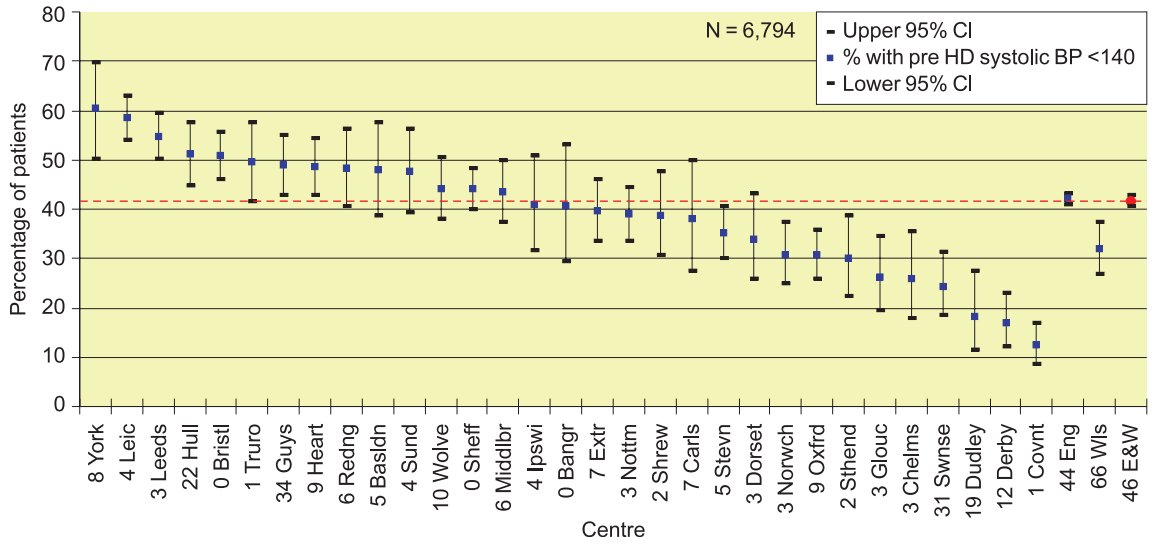

Figure 11.7: Percentage of patients with systolic BP <140 mmHg: pre-HD

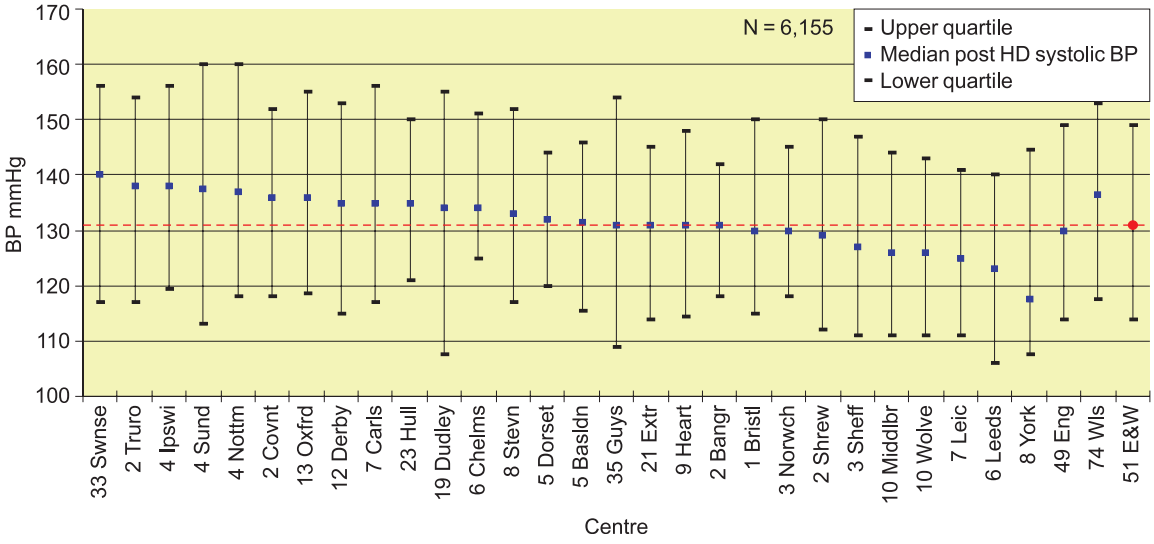

Figure 11.8: Median systolic BP: post-HD

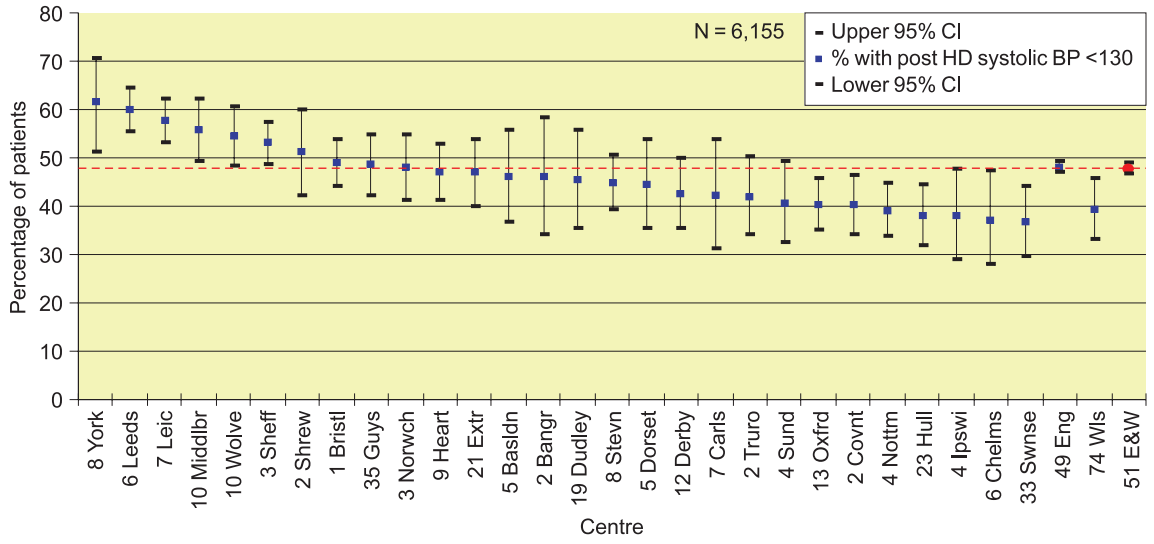

Figure 11.9: Percentage of patients with systolic BP <130 mmHg: post-HD

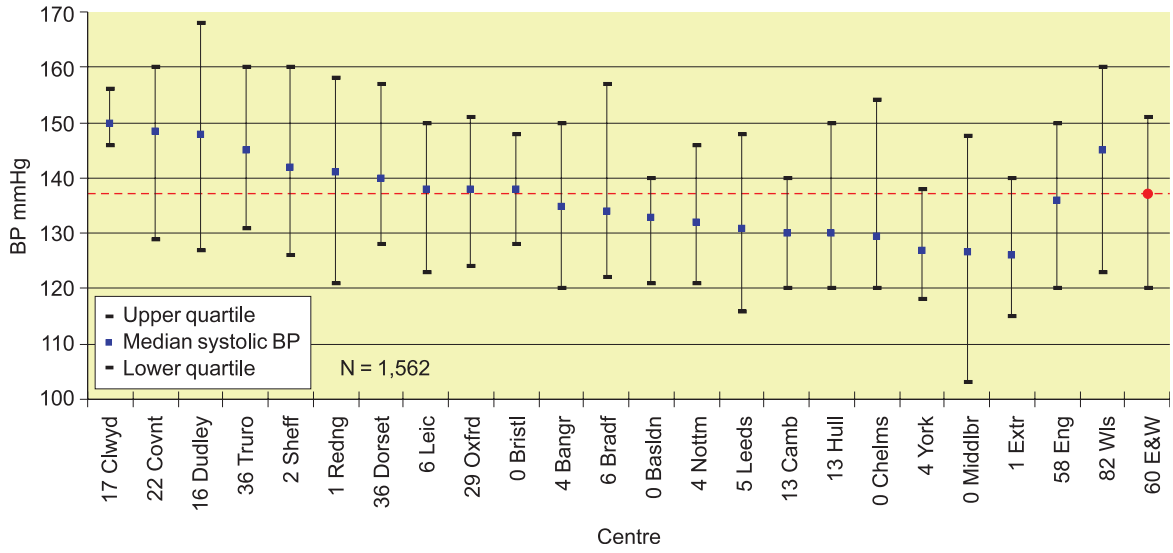

Figure 11.10: Median systolic BP: PD

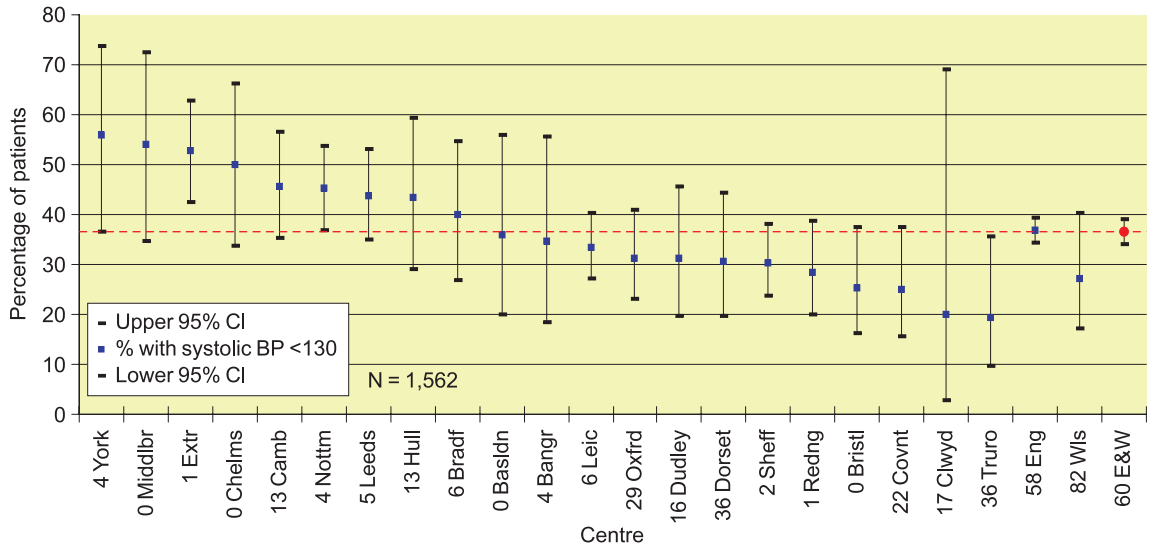

Figure 11.11: Percentage of patients with systolic BP <130 mmHg: PD

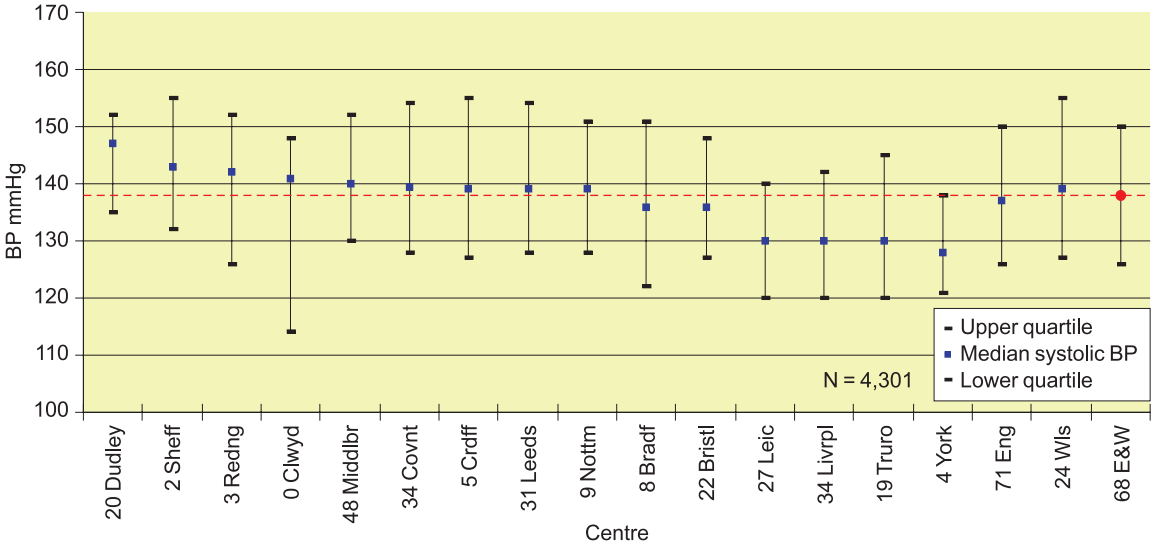

Figure 11.12: Median systolic BP: Tx

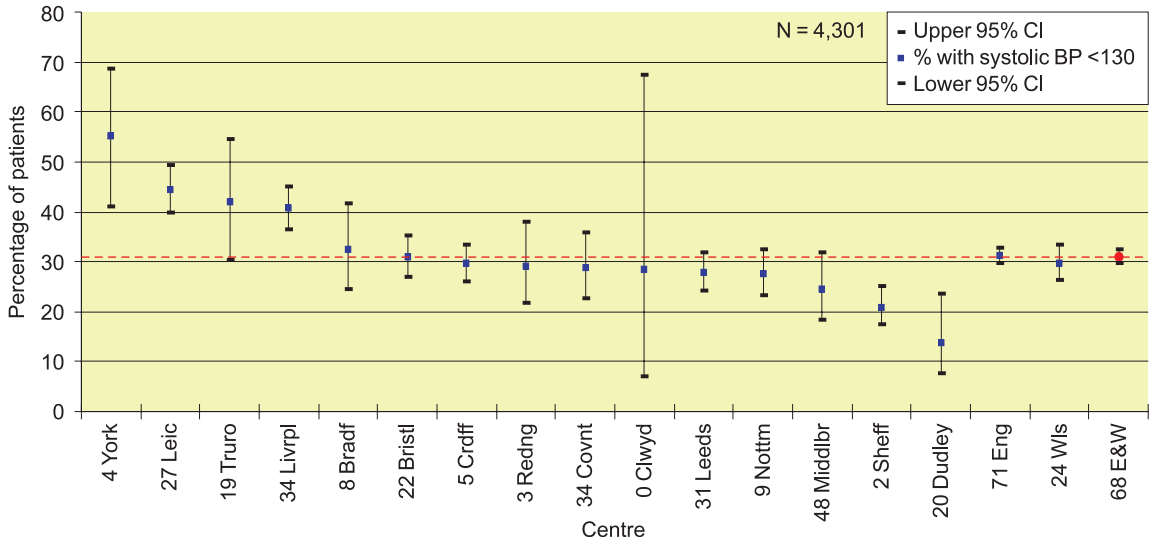

Figure 11.13: Percentage of patients with systolic BP <130 mmHg: Tx

for each treatment modality is significant ($p < 0.001$). The median SBP (England & Wales) for pre-HD, post-HD, PD and Tx is 145, 131, 137 and 138 mmHg respectively.

Diastolic pressure alone

Figures 11.14–11.21 show wide variation between units in their achievement of the diastolic blood pressure (DBP) standard. In England & Wales, 81% of HD patients achieve the standard pre-dialysis (inter unit range 57–95%) and 74% post-dialysis (range 56–86%). 48% of PD patients (range 20–63%) and 46% of Tx patients (range 30–74%) achieve the standard. Chi squared testing indicates the variation between centres for each treatment modality is significant ($p < 0.001$). The median DBP (England & Wales) for pre-HD, post-HD, PD and Tx is 76, 70, 80 and 80 mmHg respectively. It is not clear whether DBP is lower in the HD population because patients are older (DBP starts to fall after 60 years of age in the general population) or because HD patients have increased 'arterial stiffness'.

Mean arterial pressure

Figures 11.22–11.29 show wide variation between units in their achievement of the desired mean arterial pressure (MAP). MAP is calculated as DBP plus one third of the pulse pressure. In England & Wales, 68% of HD patients achieve the standard pre-dialysis (inter

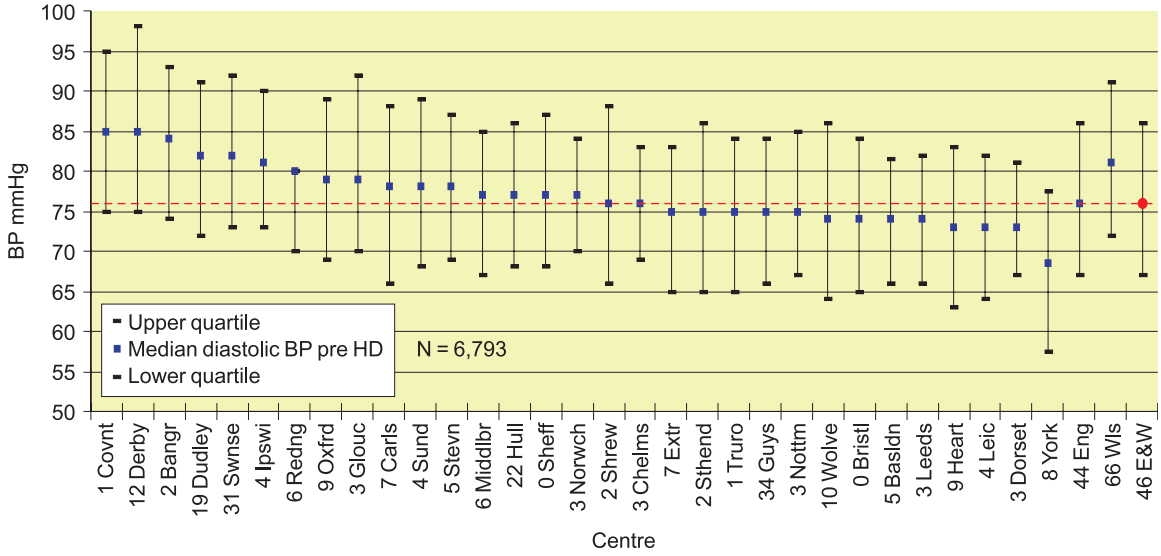

Figure 11.14: Median diastolic BP: pre-HD

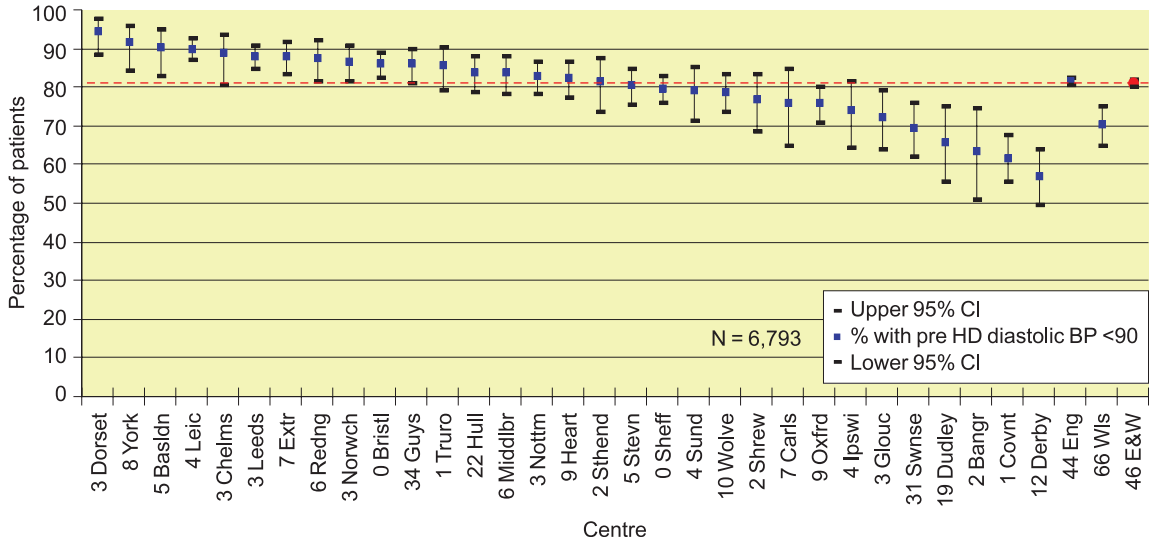

Figure 11.15: Percentage of patients with diastolic BP <90 mmHg: pre-HD

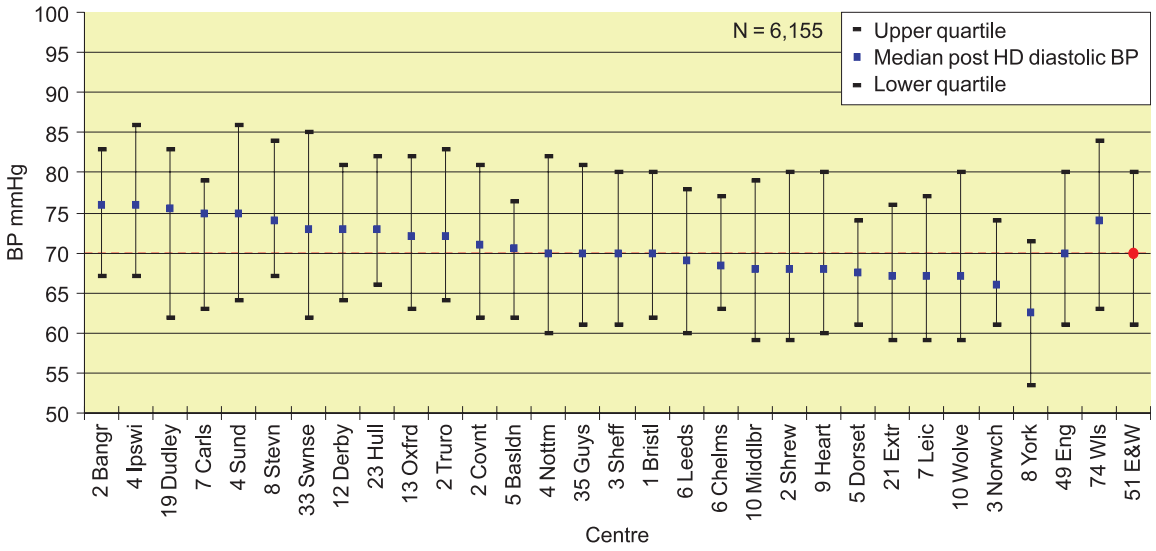

Figure 11.16: Median diastolic BP: post-HD

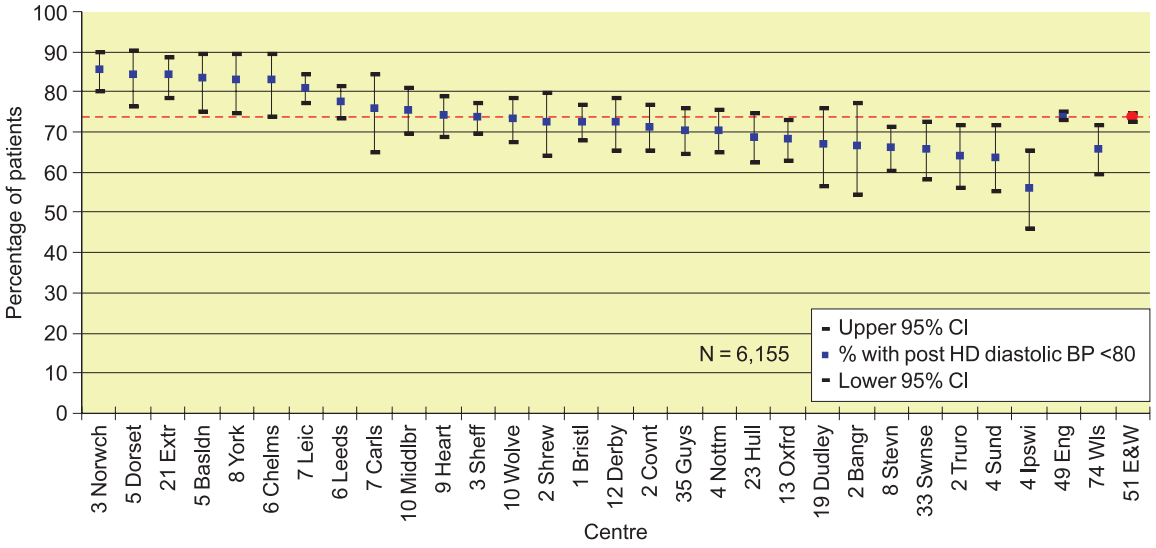

Figure 11.17: Percentage of patients with diastolic BP <80 mmHg: post-HD

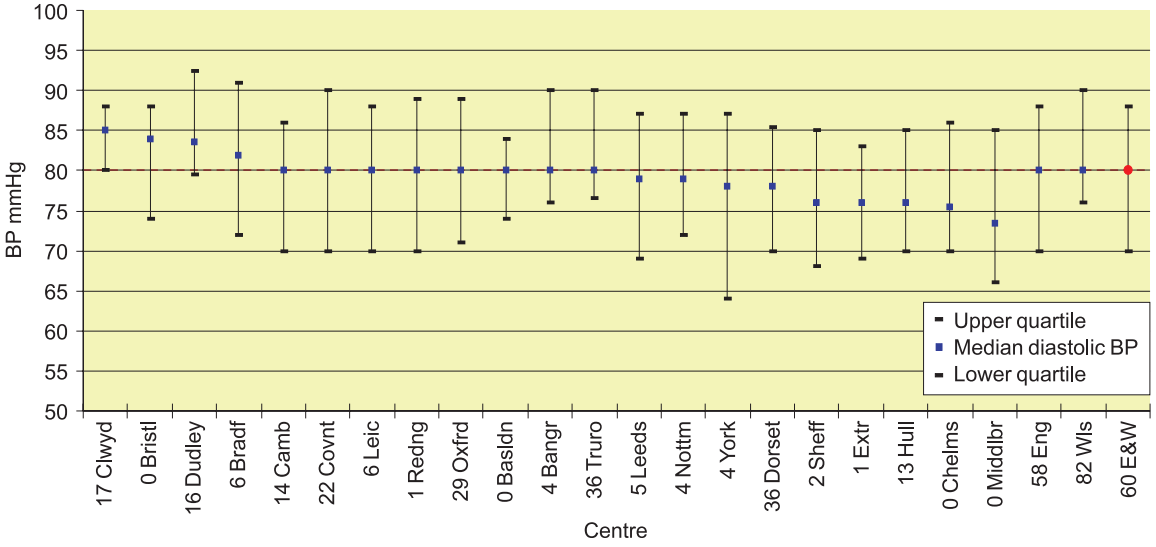

Figure 11.18: Median diastolic BP: PD

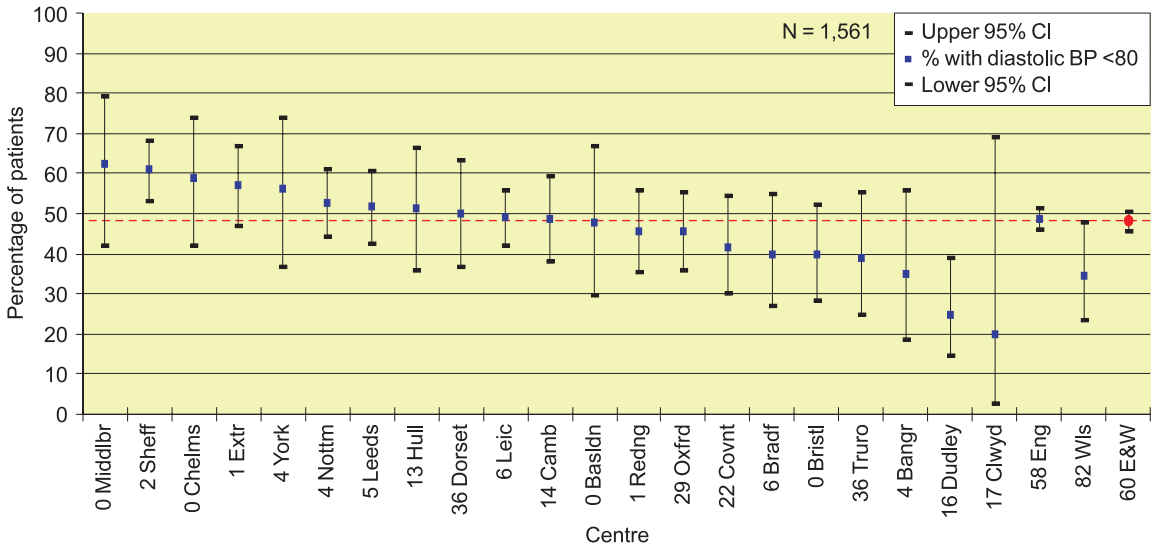

Figure 11.19: Percentage of patients with diastolic BP <80 mmHg: PD

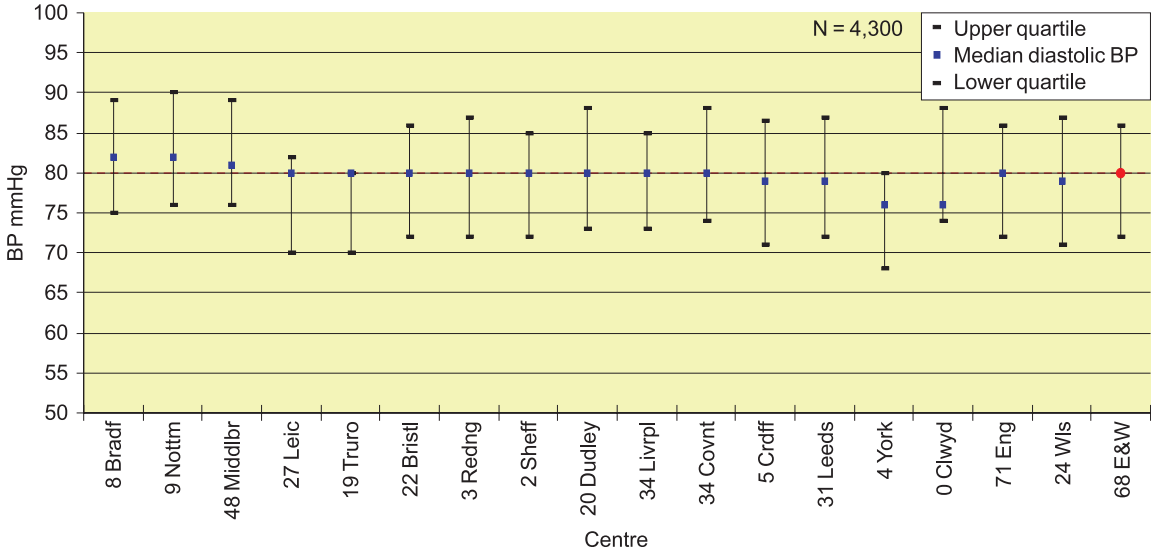

Figure 11.20: Median diastolic BP: Tx

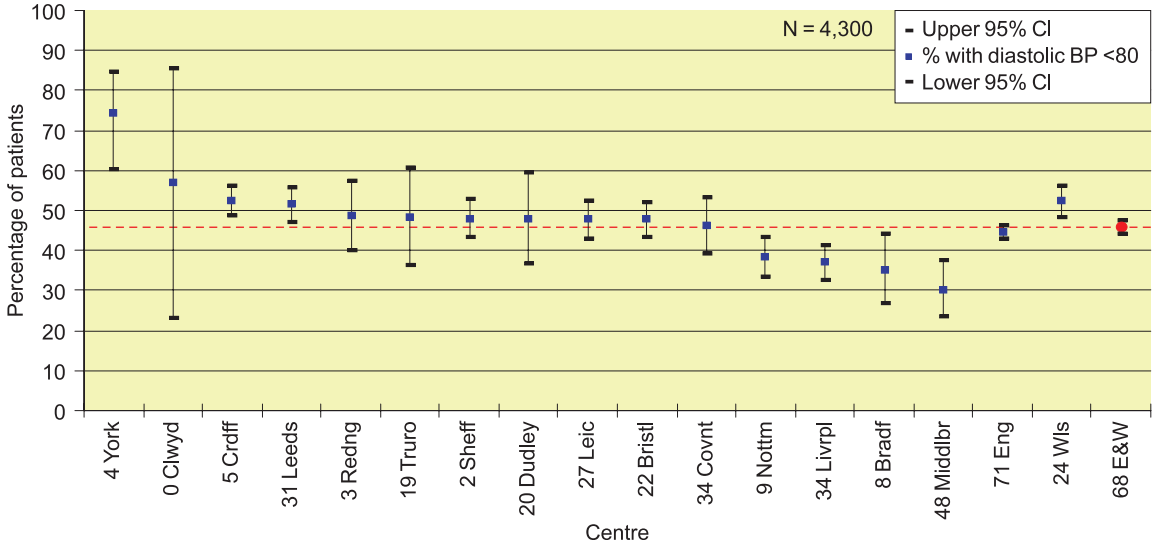

Figure 11.21: Percentage of patients with diastolic BP <80 mmHg: Tx

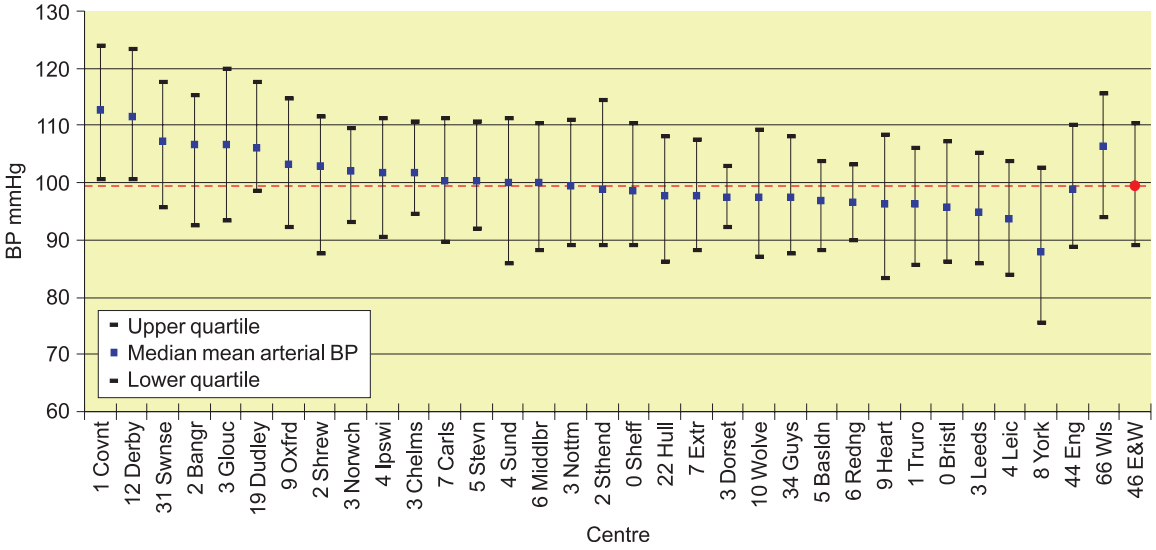

Figure 11.22: Median MAP: pre-HD

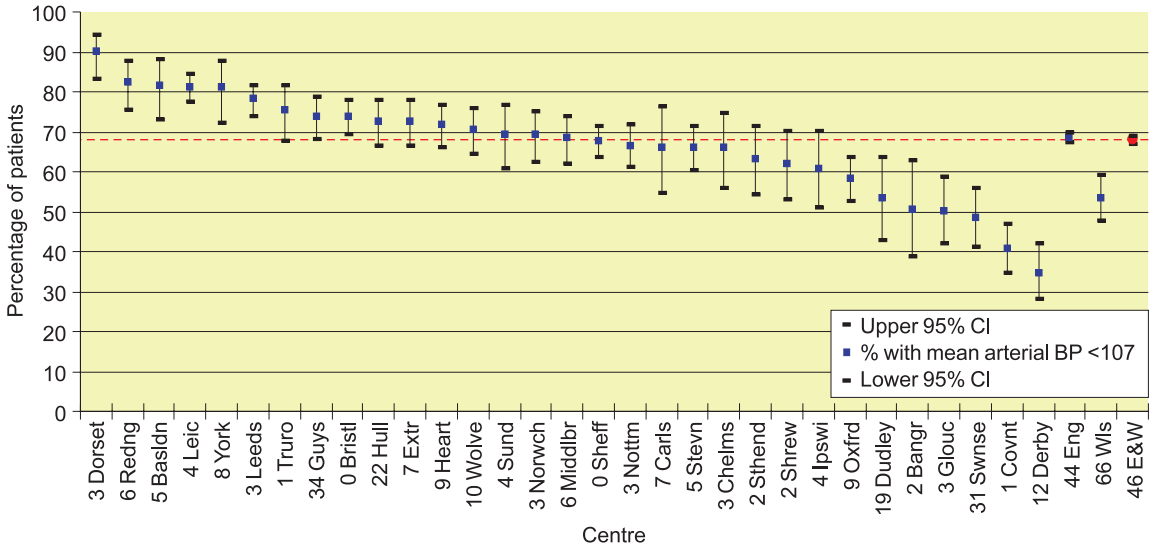

Figure 11.23: Percentage of patients with MAP <107 mmHg: pre-HD

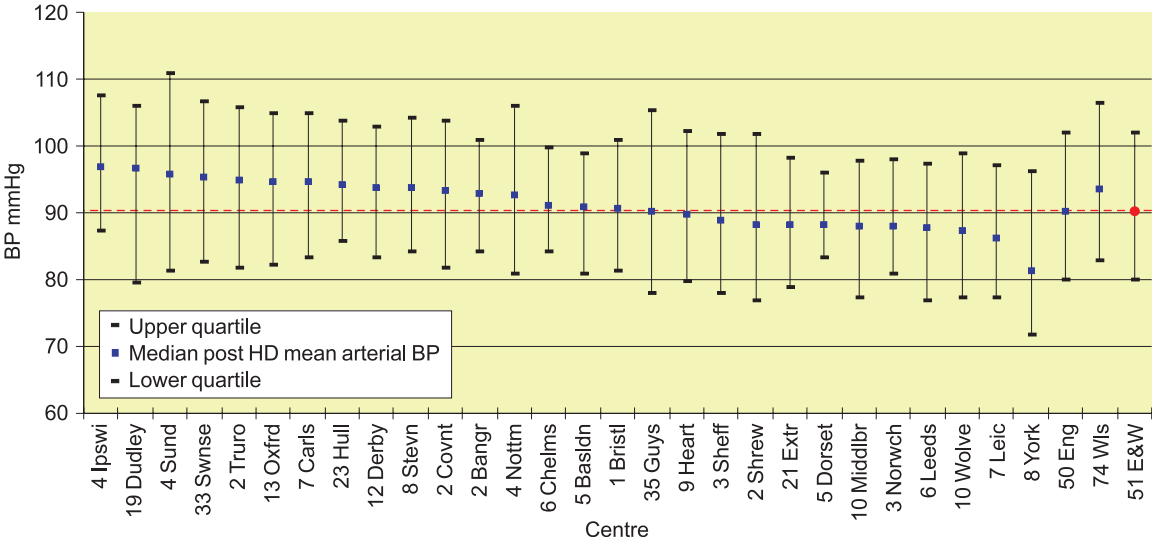

Figure 11.24: Median MAP: post-HD

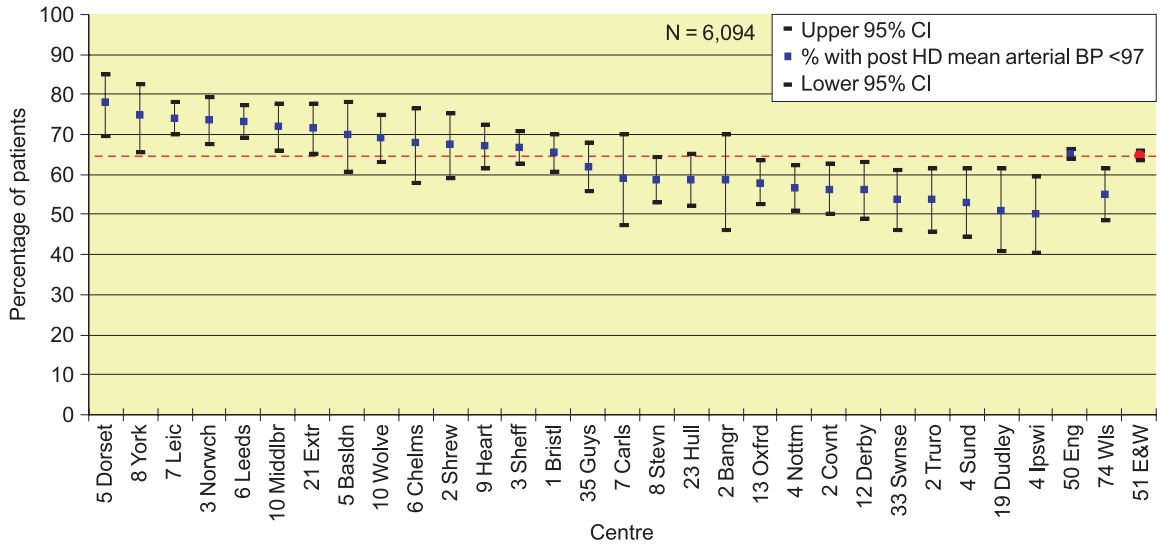

Figure 11.25: Percentage of patients with MAP <97 mmHg: post-HD

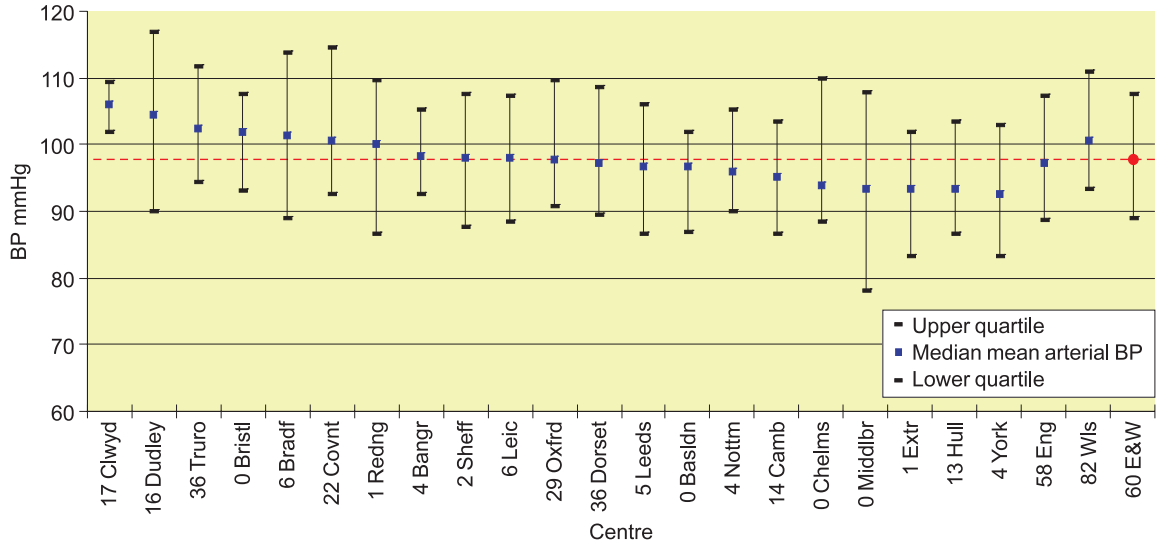

Figure 11.26: Median MAP: PD

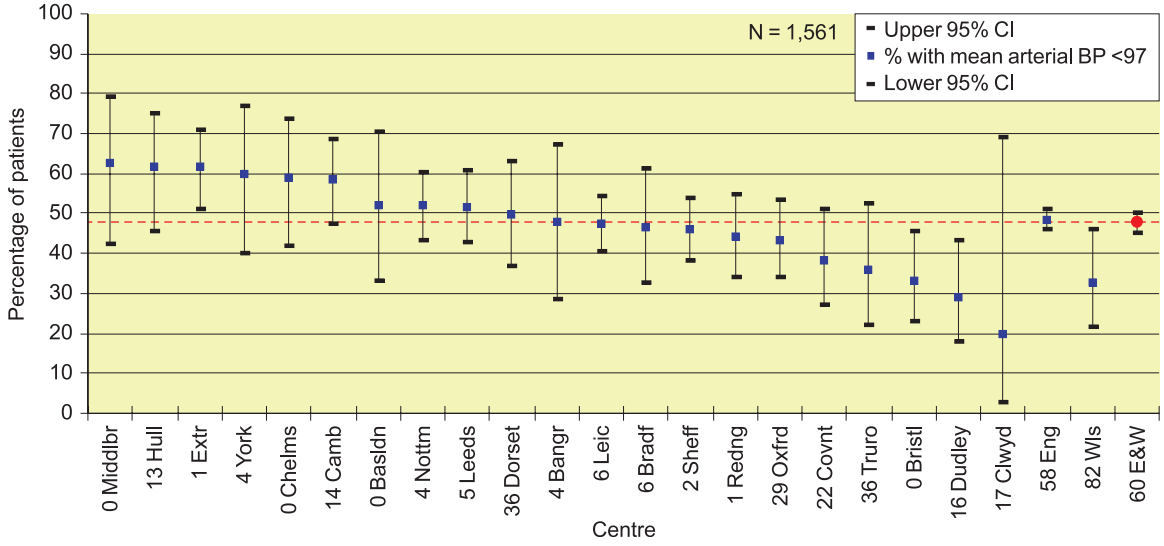

Figure 11.27: Percentage of patients with MAP <97 mmHg: PD

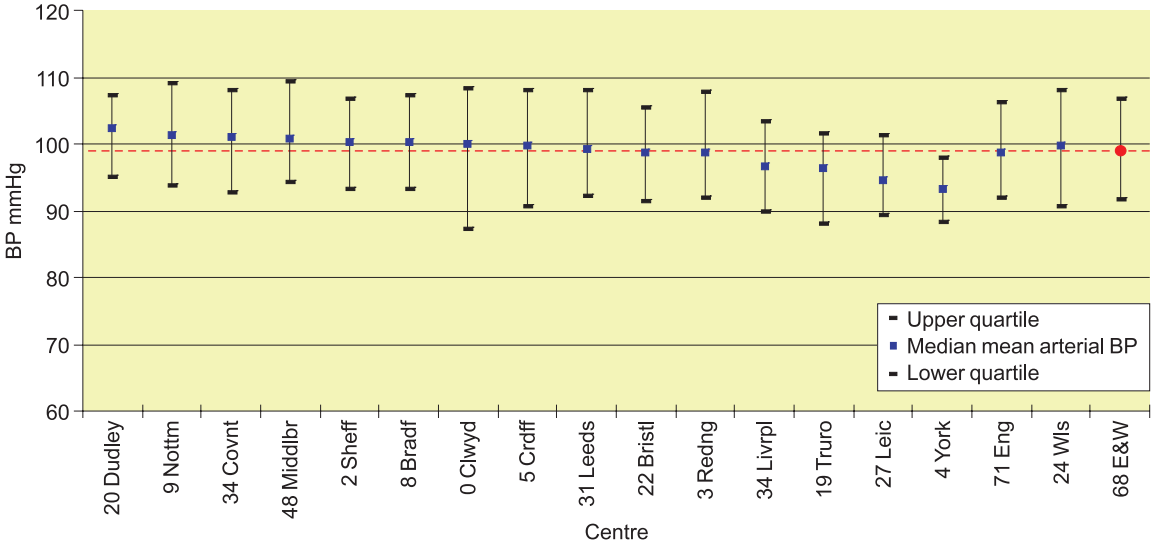

Figure 11.28: Median MAP: Tx

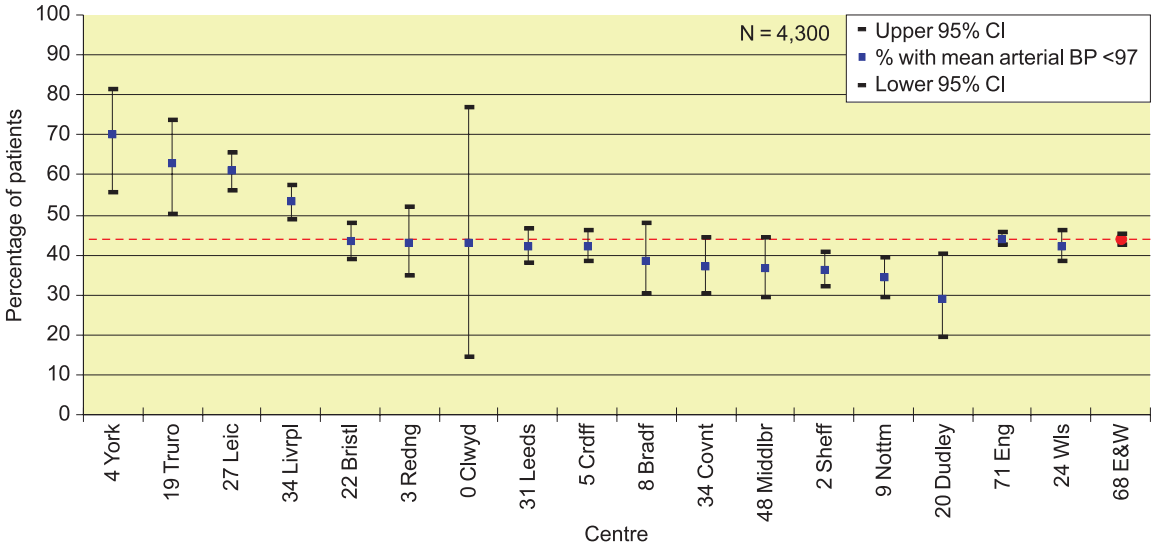

Figure 11.29: Percentage of patients with MAP <97 mmHg: Tx

unit range 35–90%) and 65% post-dialysis (range 50–78%). 48% of PD patients (range 20–63%) and 44% of Tx patients (range 29–70%) achieve the standard. Chi squared testing indicates the variation between centres for each treatment modality is significant ($p < 0.001$). The median MAP for pre-HD, post-HD, PD and Tx is 99, 90, 98 and 99 mmHg respectively.

Pulse pressure

Figures 11.30–11.33 show the variation between units for pulse pressure (PP). PP is calculated as SBP minus DBP. The median PP for pre-HD, post-HD, PD and Tx is 67, 60, 56 and 57 mmHg respectively. A significantly lower DBP contributes to the wider PP in HD patients. Future analyses should be able to determine whether this is an age related phenomenon. If this proves not to be the case, the data would support either better blood pressure control or increased 'arterial stiffness' in the HD population. Interestingly, Renal Registry data show HD patients have consistently poorer phosphate control than PD or Tx patients thus increasing the risk of arterial calcification.

Blood pressure by primary diagnosis

Figures 11.34–11.41 show the variation in blood pressure control for each treatment modality when categorised by primary diagnosis. Diabetes is the most commonly identified cause of renal failure in England & Wales. Both blood pressure and pulse pressure are higher for

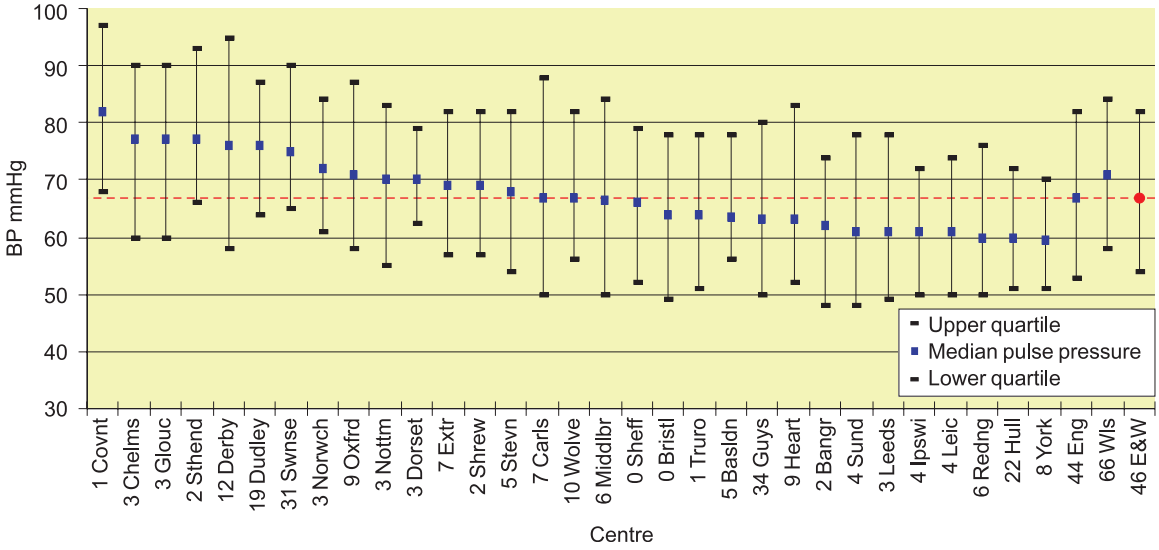

Figure 11.30: Median Pulse Pressure: pre-HD

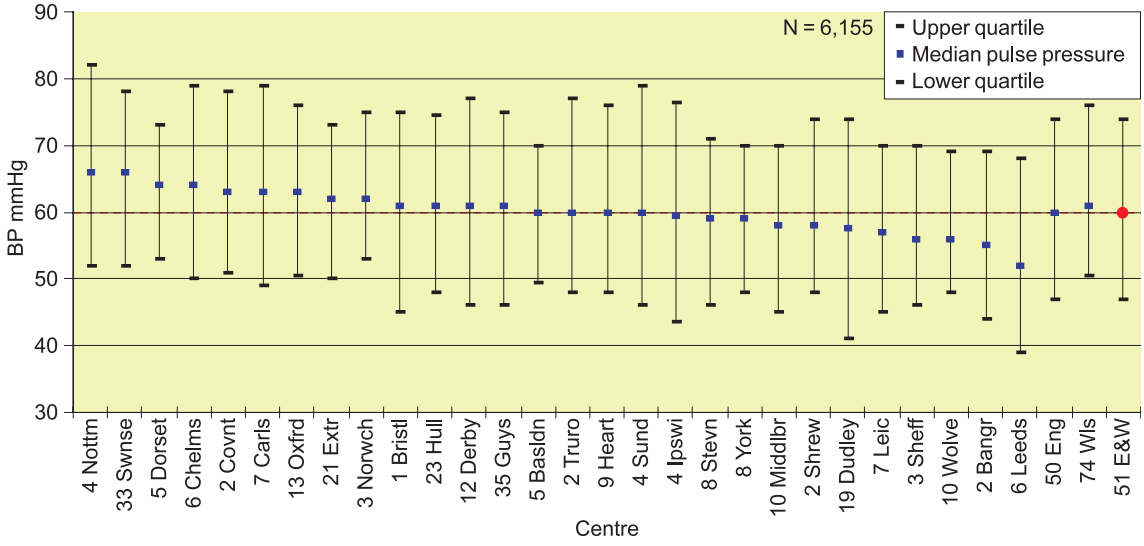

Figure 11.31: Median Pulse Pressure: post-HD

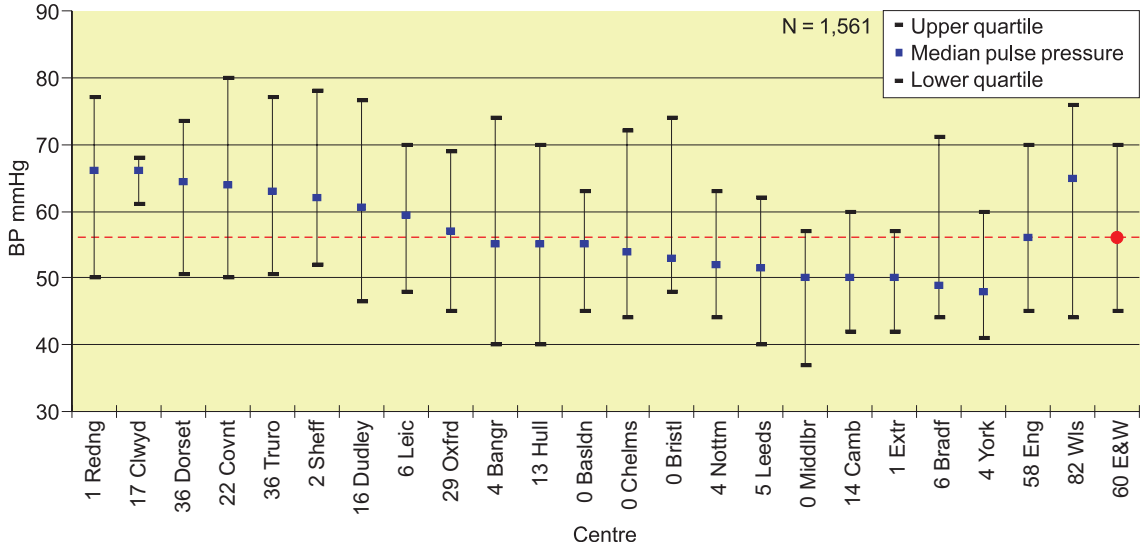

Figure 11.32: Median Pulse Pressure: PD

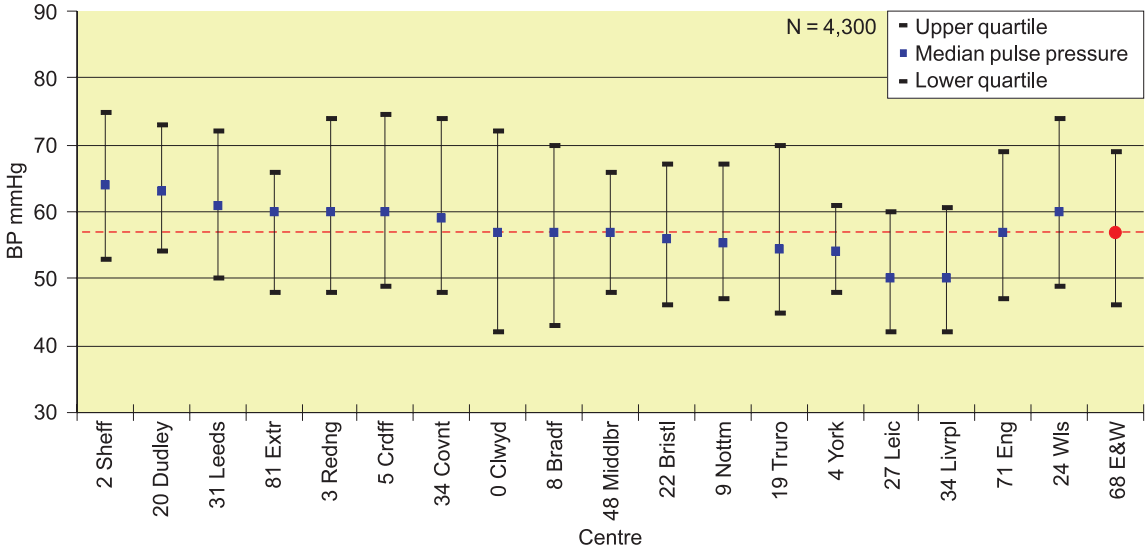

Figure 11.33: Median Pulse Pressure: Tx

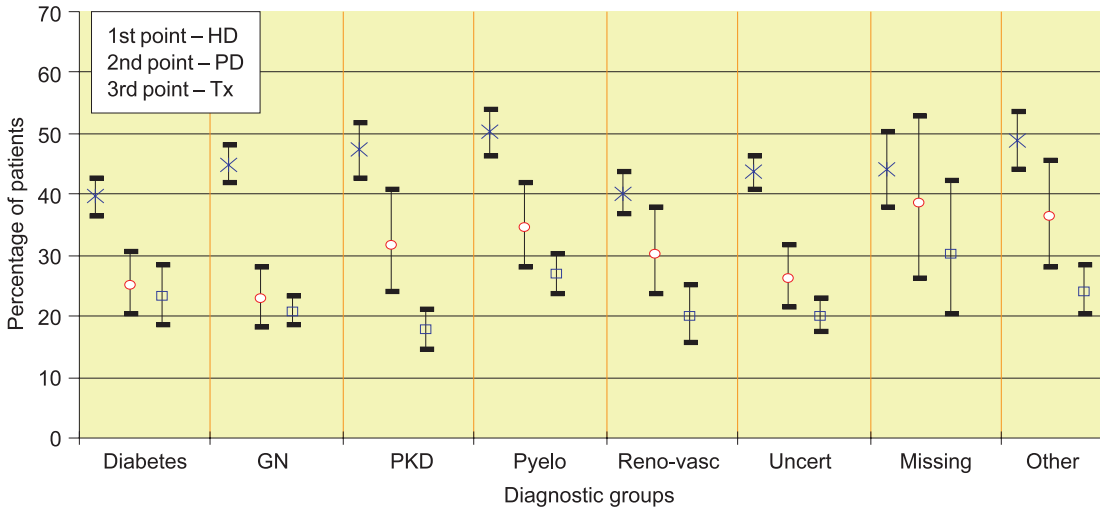

Figure 11.34: Percentage of patients by primary diagnosis achieving BP standard

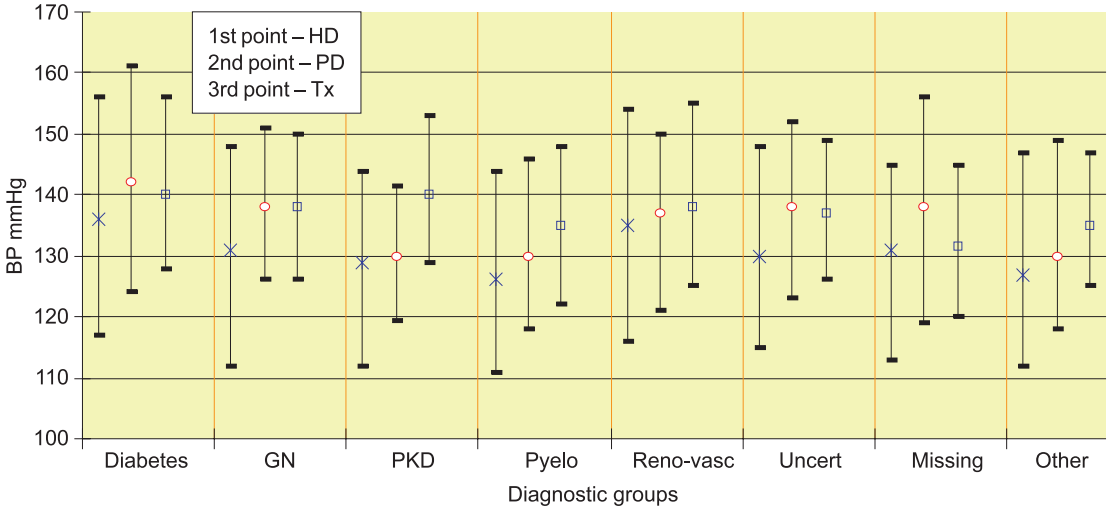

Figure 11.35: Median Systolic BP according to primary diagnosis

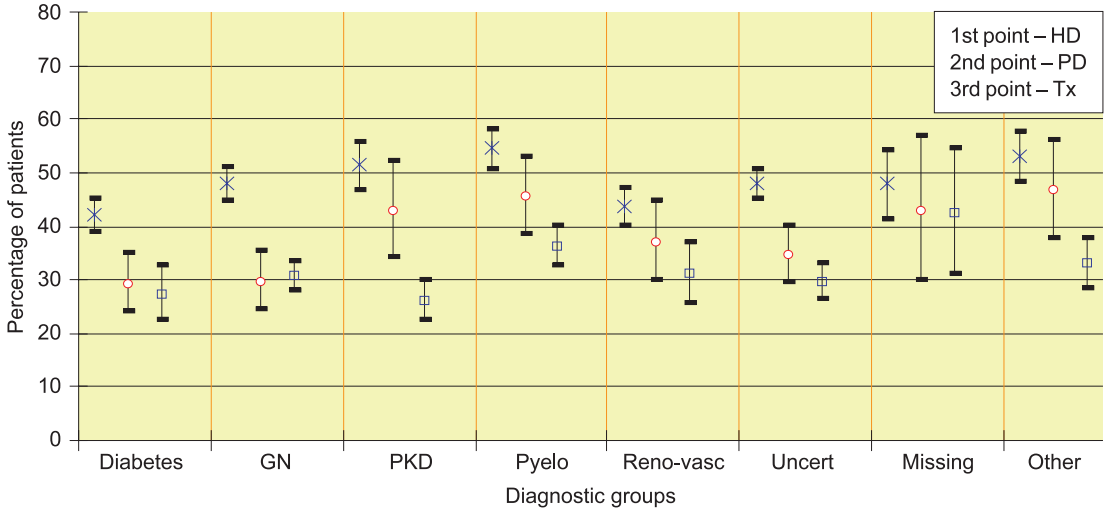

Figure 11.36: Percentage of patients by primary diagnosis achieving SBP standard

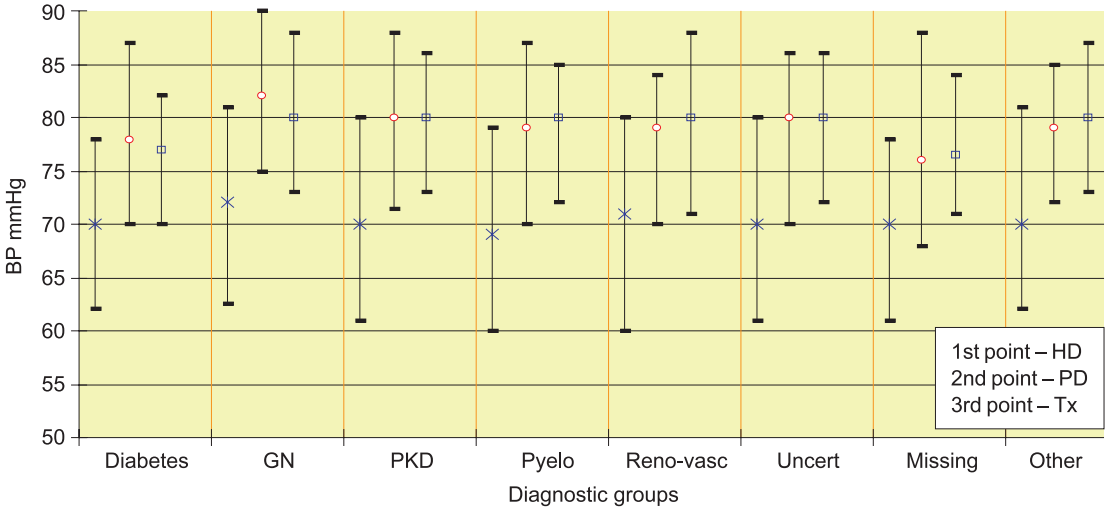

Figure 11.37: Median diastolic BP according to primary diagnosis

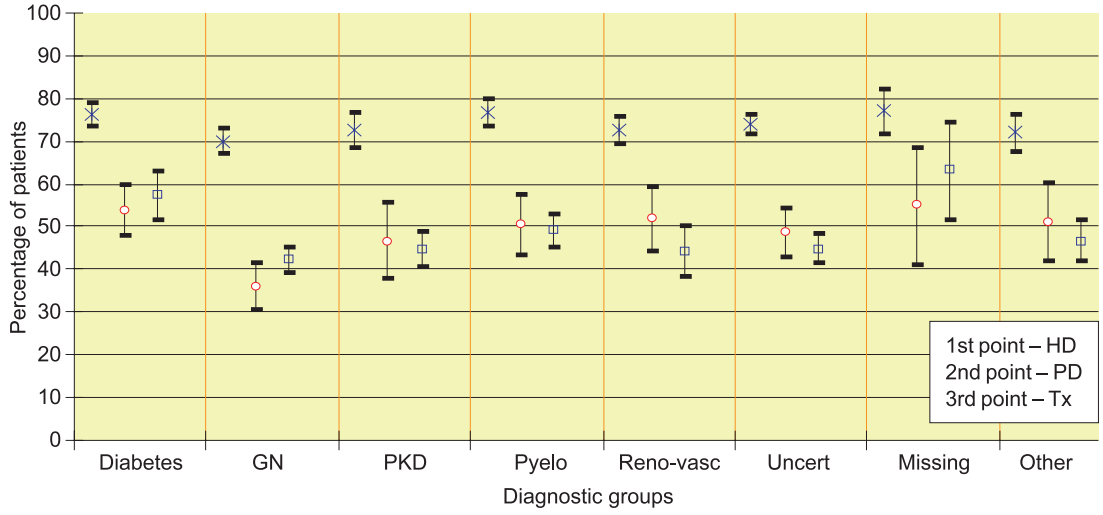

Figure 11.38: Percentage of patients by primary diagnosis achieving DBP standard

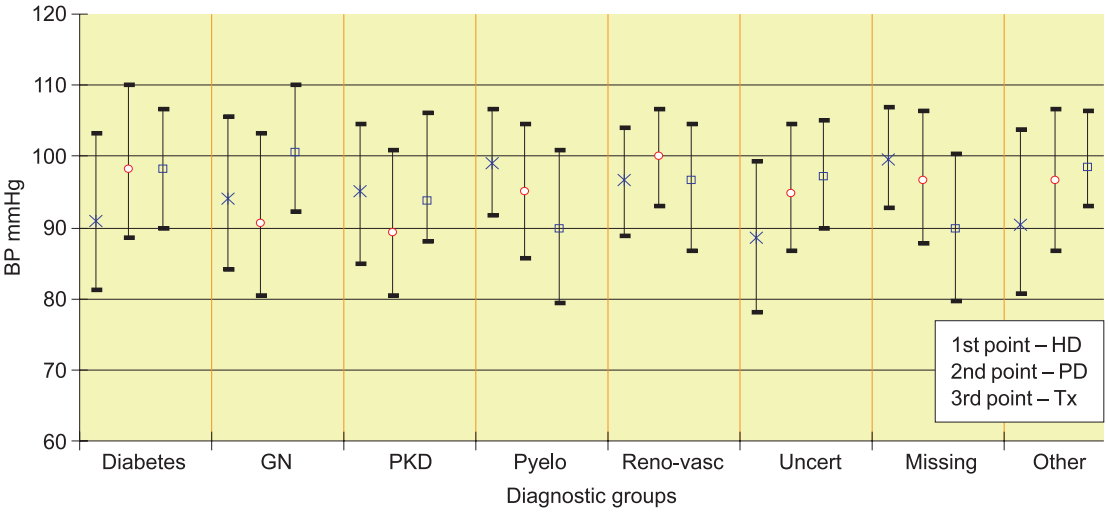

Figure 11.39: Median MAP according to primary diagnosis

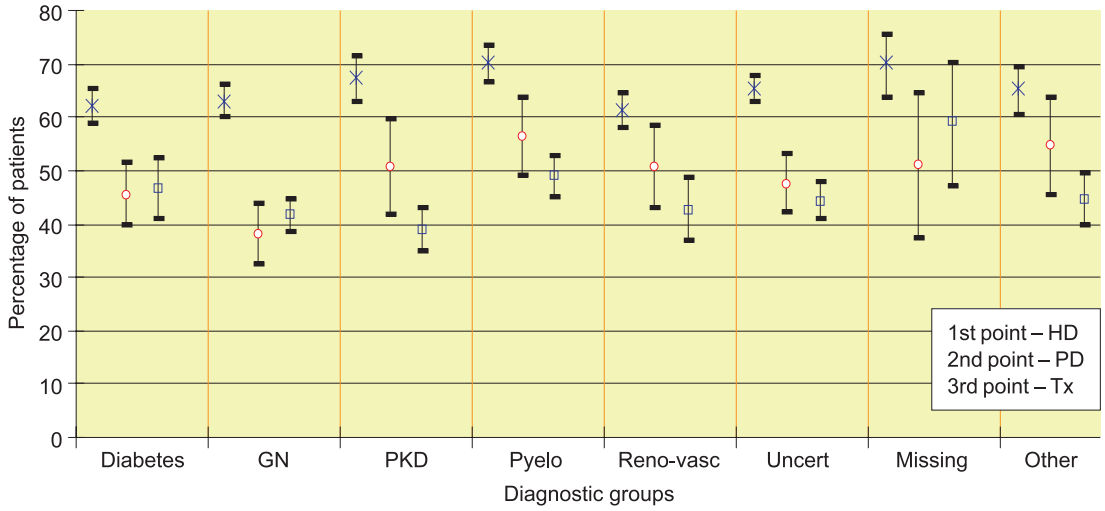

Figure 11.40: Percentage of patients by primary diagnosis achieving MAP standard

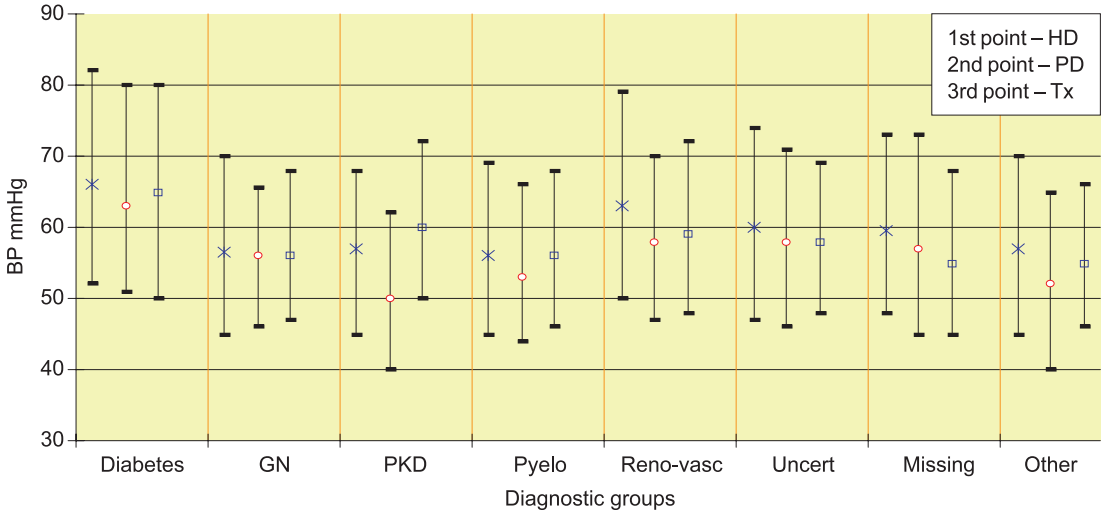

Figure 11.41: Median pulse pressure according to primary diagnosis

diabetics than non-diabetics across all treatment modalities. In non-diabetics on HD, salt intake correlates closely with water intake. Conversely, hyperglycaemia accounts for 50% of the water intake in diabetic patients on HD[16]. As the HbA1c standard was only achieved in 46% HD, 35% PD and 34% Tx patients, poor glucose control may contribute to poor blood pressure control in diabetic patients on RRT. There is a trend towards higher blood pressure readings in patients with glomerular rather than tubular disorders. As has occurred in previous years, blood pressure control is better in patients on HD compared with other treatment modalities for each of the diagnostic groups.

Blood pressure variability

Longitudinal studies in dialysis patients have identified seasonal variation in blood pressure with lower blood pressures in the warmer months, possibly related to temperature and humidity. Climate is also likely to have some effect on blood pressure variability in the UK. Each year the Renal Registry shows significant variation in achievement of the blood pressure standards by different centres suggesting that factors other than climate are responsible. This variability might either reflect differences in co-morbidity or differences in the blood pressure treatment protocols employed by individual units. On the whole, stable patients are treated in satellite units while patients with clinical problems dialyse in main units with more medical supervision. One might therefore predict greater blood pressure variability between patients and within individual patients dialysing in the main units when compared with patients dialysing in the associated satellite units.

Methods

Only main units with satellites were selected for this analysis. Patients were assigned to either a main or satellite unit on the basis of where they were dialysing 90 days after their first dialysis. Pre and post dialysis blood pressure measurements were obtained for each quarter.

- **Blood pressure variability in incident patients**. Patients starting haemodialysis during 2003 and 2004 were selected for this analysis. The first blood pressure recorded after 90 days was obtained for 1,300 patients from 30 main units and 465 patients from 67 satellite units. Blood pressure measurements were analysed for this cohort using the Mixed Model Analysis of Variance (see Appendix B). Initially, two analyses were performed to calculate the 'between centres' and 'residual' variances for main units and satellites separately. Residual variance covers factors that may account for variability that were not included in the model, eg ethnicity, primary renal diagnosis. These values were adjusted for age and the year in which the patient started RRT. The ratio of the variances for main units and satellites were calculated and their significance determined. The ratio is greater than 1.0 if variance is greater in the main units than in their satellite units.

- **Blood pressure variability in prevalent patients**. Patients were selected who started dialysis between 1998 and 2004 and had blood pressure data for at least eight consecutive quarters. Data were available for 1,615 patients in 19 main units and 544 patients in 29 associated satellites. Patients were not censored if dialysis location changed during this period. Initially, two analyses were performed to calculate 'between centres', 'between patients within centres' and 'residual' variances for main units and satellites separately. These values were adjusted for age and the year in which the patient started RRT and the ratios calculated as before.

- **Blood pressure variability by shift and day of the week**. Patients dialysing in Bristol during June and July 2005 were included in this analysis. In total, 317 patients were studied over this two month period. Analysis of variance was used to analyse blood pressure variability between inpatients dialysed on the main unit, main unit day shift patients, main unit twilight patients and satellite patients. Also analysis of variance was used to assess whether there was significant blood pressure variability by day of the week ie Monday–Tuesday vs Wednesday–Thursday vs Friday–Saturday.

Results

Table 11.2 shows blood pressure variability 90 days after starting dialysis using a single observation for patients in main and satellite units. Although there were differences noted

Table 11.2: Variance in BP of incident patients at day 90 in satellite units and their main unit

Parameter	Unit variance	Satellite variance	Ratio	p value
Pre HD				
SBP	19.1	21.4	0.89	0.625
DBP	5.9	3.8	1.54	0.074
MAP	8.3	7.0	1.17	0.288
PP	8.7	11.6	0.75	0.801
Post HD				
SBP	29.2	26.6	1.09	0.367
DBP	7.0	5.5	1.26	0.213
MAP	11.2	8.9	1.25	0.223
PP	14.3	16.2	0.88	0.633

Table 11.3: Variance in BP (over 2 years) between satellite and their main units

Parameter	Unit variance	Satellite variance	Ratio	p value
Pre HD				
SBP	16.2	27.3	0.59	0.873
DBP	3.3	3.9	0.85	0.630
MABP	5.7	9.6	0.59	0.875
PP	8.6	10.9	0.79	0.692
Post HD				
SBP	43.6	20.1	2.17	0.038
DBP	7.3	3.9	1.83	0.081
MAP	14.8	8.2	1.80	0.088
PP	21.0	6.3	3.32	0.003

between the BP variability in the satellite units and their main units none reached significance. As only one reading has been analysed per patient, it is not possible to distinguish whether the variability observed is 'between patients' or 'within patients'.

Table 11.3 shows blood pressure variability over a two year period for main units and their satellites. By comparison with main units, there was greater variability in all pre-dialysis readings in the satellite units although none of these differences reached significance. The trend in observed differences might be a result of differing criteria for patient transfer to satellite units or differences in medical supervision. In contrast, there was greater variability in post-dialysis readings in the main units than in the satellites and this difference was of significance for pulse pressure. Cardiac instability related to pre-existing co-morbidity or inter-current illness may be one possible explanation for this finding.

Table 11.4: Variance in BP (over 2 years) between patients at satellites and patients at main units

Parameter	Unit variance	Satellite variance	Ratio	p value
Pre HD				
SBP	237.0	226.7	1.04	0.272
DBP	55.2	58.8	0.93	0.810
MAP	83.5	83.3	1.01	0.496
PP	145.1	139.6	1.03	0.300
Post HD				
SBP	212.0	220.2	0.96	0.702
DBP	46.8	48.8	0.95	0.723
MAP	73.6	76.3	0.96	0.691
PP	126.5	132.7	0.95	0.746

Table 11.4 shows blood pressure variability over a 2 year period between patients in either main units or satellites. No significant differences were observed.

Tables 11.5 and 11.6, show blood pressure variability and blood pressure of 317 patients dialysing in Bristol over a two month period. Patient age and 'dialysis day within any given week' had significant impact on blood pressure variability. Blood pressure readings were

Table 11.5: BP variability by shift and days of the week

	Pre Haemodialysis				Post Haemodialysis			
Parameter	SBP	DBP	MAP	PP	SBP	DBP	MAP	PP
No of patients	317	317	317	317	317	317	317	317
No of obs used	8071	8068	8068	8068	7967	7967	7967	7967
Age (p-value)	**0.016**	**<0.001**	**0.015**	**<0.001**	**0.005**	**<0.001**	0.088	**<0.001**
Units (p-value)	0.233	0.056	0.084	0.593	0.446	0.095	0.230	0.522
Sessions (p-value)	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.029**
MT vs WT (p-value)	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.002**	**0.007**	**<0.001**	0.194
MT vs FS (p-value)	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.023**
WT vs FS (p-value)	0.336	0.705	0.636	0.924	0.464	0.806	0.560	0.643

Table 11.6: BP (mmHg) by days of the week

	Mon–Tue	Wed–Thu	Fri–Sat
Pre HD			
SBP	141.3	138.2	137.8
DBP	73.2	72.2	72.1
MAP	95.9	94.2	94.0
PP	68.0	65.8	65.7
Post HD			
SBP	132.6	131.3	130.8
DBP	69.5	68.7	68.6
MAP	90.6	89.6	89.4
PP	63.0	62.4	62.1

significantly higher after a 3-day interval (Monday–Tuesday) than they were after a 2-day interval (Wednesday–Thursday or Friday–Saturday) without dialysis. These data support the belief that fluid status has a significant effect on blood pressure in HD patients.

Discussion

In summary, greater blood pressure variability was evident between units rather than within patients within the same unit. The fact that there was not greater variability in the main units than in their satellite units contradicts the hypothesis that blood pressure variability primarily reflects patients' state of health. The Bristol data provide supportive evidence as neither inpatient status, dialysis location, nor dialysis shift had a major effect on blood pressure. There are several possible explanations for the observed trend towards an increased variability in pre-dialysis blood pressure within satellite units than their main unit. The impact of differences in case mix, treatment protocols and degree of medical supervision warrant further investigation. In addition the schedule for logging blood pressure readings into the database may itself generate some of this variability. The majority of main units will have the ability to log blood pressure readings for each dialysis session into their database. Whilst in some satellite units this is possible, in others there is not direct access to the database. In these units, blood pressure readings, which are often only a single observation for each patient per month, have to be transcribed by IT staff from paper into the database. If the date that readings are taken is not accurately recorded into the database the Registry will not be able to assign the reading to the correct day of the week or even the correct quarter for subsequent analyses. The Registry would like to ensure that blood pressure data are collected in a standardised way in units without direct IT links. If only a single observation is recorded for each patient per month the midweek blood pressure may be most informative. Further analysis needs to be performed by the Registry before making specific recommendations.

Serum Cholesterol and Achievement of the Standard

In the general population, higher cholesterol levels are associated with increased risk of cardiovascular death from atherosclerosis. Meta-analysis of 14 trials including 90,000 participants showed a clear benefit from statins for both primary and secondary prevention[17]. The 5-year event rate is typically reduced by 20% per mmol/L reduction in low-density lipoprotein (LDL) cholesterol, irrespective of the initial lipid profile. By contrast, only a weak association is shown between cholesterol reduction and incidence of heart failure, the more common manifestation of uraemic cardiomyopathy. Unfortunately too few patients with CKD were included in these trials to assess whether they also derived benefit from statins.

The typical lipid profile in renal failure includes raised triglycerides, low high-density lipoprotein (HDL) and variable changes in low-density lipoprotein and total cholesterol. It is far from clear whether a high cholesterol level has the same significance in renal patients as it does for the general population. Each year the Renal Registry reports a U-shaped and reverse association between cholesterol level and short term survival for dialysis patients. The Chronic Renal Impairment in Birmingham (CRIB) study shows no association between baseline cholesterol level and four year mortality in a cohort of 370 patients with CKD[18]. Furthermore there is no definitive evidence that statins significantly reduce cardiac death in patients on RRT. The Assessment of Lescol in Renal Transplantation (ALERT) study compared fluvastatin 40 mg vs placebo in 2,102 renal transplant patients[19]. Although LDL fell on average by 1 mmol/L the reduction in cardiac death and myocardial infarction was not significant over six years follow up. The Deutsche Diabetes Dialyse (4-D) study compared atorvastatin 20 mg vs placebo in

1,255 HD patients with Type 2 diabetes[20]. LDL fell on average by 1.2 mmol/L but the reduction in cardiac death and myocardial infarction was not significant over a 4 year period. Only a quarter of cardiac deaths were attributed to acute myocardial infarction in the ALERT and 4-D studies, heart failure, arrhythmia and sudden death being more common. These initial trials therefore support conclusions drawn from general population studies that non-infarction cardiac death is not related to cholesterol level or reduced by statin use. Statins do offer effective secondary prevention in renal patients with established atherosclerosis. The Cholesterol and Recurrent Events (CARE) study showed pravastatin 40 mg reduced further cardiac events in 1,711 patients with previous myocardial infarction and mild CKD[21].

The Renal Association set standards for lipids for the first time in August 2002. The current standards are:

Primary prevention:

Statins should be initiated in dialysis patients with a 10 year risk of coronary disease >30% to achieve:

Total cholesterol <5 mmol/L or a 30% reduction from baseline

Fasting LDL-cholesterol of <3 mmol/L

Secondary prevention:

Patients should be treated with aspirin, an ACE inhibitor, a beta-blocker and a statin unless contraindicated.

As discussed in last year's report, European guidelines suggest the dialysis standards should be applied to transplant patients and recommend lower targets for patients with established cardiovascular disease or diabetes (total cholesterol <4.5 mmol/L and LDL-cholesterol 2.5 mmol/L). Lipid profiles should be checked annually for transplant patients and every 6 months for dialysis patients. Blood samples should be taken immediately before dialysis or at least 12 hours after, preferably with the patient in a fasting state. The current audit is based on random, non-fasting total cholesterol measurements.

Cholesterol data returns

Units with data for less than 35% of patients in a particular treatment modality were excluded

Table 11.7: Percentage of patients with complete returns of cholesterol values by modality

	% completed data		
	HD	**PD**	**Tx**
Bangor	92	96	n/a
Barts	n/a	n/a	n/a
Basildon	97	100	92
Bradford	87	100	94
Brighton	38	77	55
Bristol	94	93	98
Cambridge	58	96	50
Carlisle	82	86	87
Carshalton	3	18	14
Chelmsford	69	76	20
Clwyd	24	17	100
Coventry	0	0	0
Cardiff	87	92	87
Derby	81	76	45
Dorset	83	93	89
Dudley	54	65	63
Exeter	96	90	86
Gloucester	91	96	77
Guys	90	96	71
H&CX	100	99	97
Heartlands	41	96	44
Hull	84	77	54
Ipswich	97	96	93
Kings	82	63	91
Leeds	86	88	94
Leicester	85	96	94
Liverpool	5	2	19
ManWst	64	88	75
Middlesbrough	97	100	84
Newcastle	92	100	97
Norwich	99	100	95
Nottingham	80	94	91
Oxford	94	87	83
Plymouth	89	81	91
Portsmouth	40	61	74
Preston	98	99	72
QEH	94	97	93
Reading	97	96	88
Sheffield	94	61	98
Shrewsbury	97	94	44
Stevenage	47	86	62
Southend	92	95	90
Sunderland	96	100	99
Swansea	85	97	93
Truro	90	94	87
Wirral	n/a	n/a	n/a
Wolverhampton	93	92	87
Wrexham	72	83	81
York	81	86	62
England	72	74	71
Wales	81	91	87
England & Wales	72	75	72

from the cholesterol analyses. Six centres had insufficient data for HD, six centres insufficient data for PD and five centres insufficient data for Tx (Table 11.7). Transfer of laboratory data to renal IT systems is now available in all main renal units but not all satellites. In the centres without data they may either not be measuring cholesterol regularly or the Renal Registry is not extracting available data, in which case they should contact the Registry.

Figures 11.42–11.48 show wide variation between units achieving the cholesterol standard. In England & Wales, the number of patients achieving the standard for HD average 81% (range 65–95%), 65% for PD (range 26–83%) and 57% for Tx (range 36–77%). Chi squared testing indicates the variation between centres for each treatment modality is significant ($p < 0.0001$).

As in previous years, cholesterol levels are significantly lower in HD patients; the median cholesterol concentration for HD, PD and transplant is 4.0, 4.5 and 4.8 mmol/L respectively. The Renal Registry does not have drug data to correlate cholesterol levels with statin use. There are reports that the lower cholesterol level found in HD patients is due to increased plasma water, however the Registry does not collect haematocrit data to test this hypothesis. Furthermore, the Registry does not have

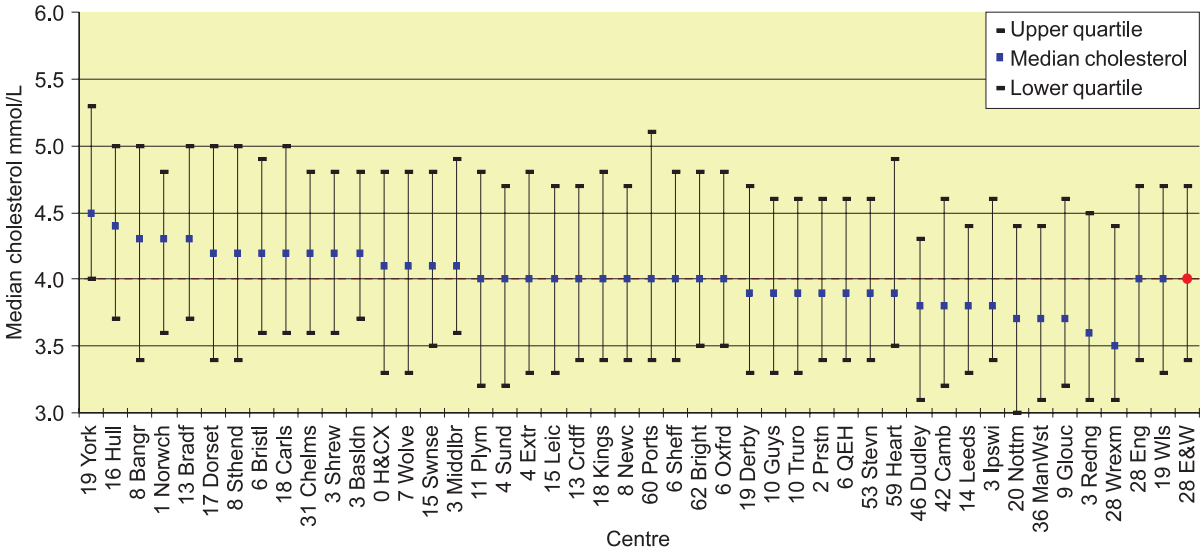

Figure 11.42: Median cholesterol: HD

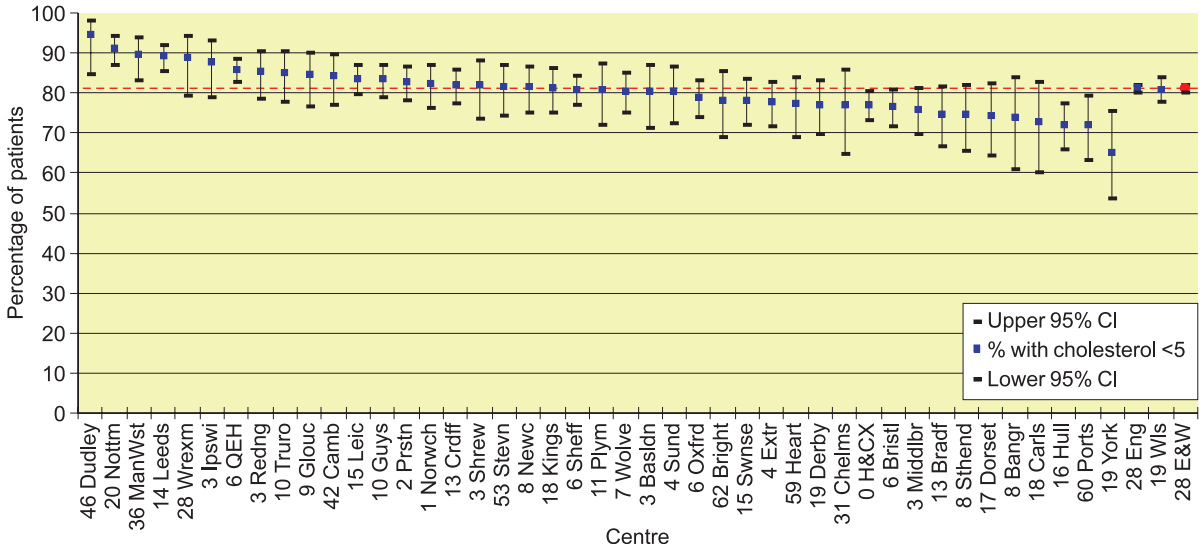

Figure 11.43: Percentage of patients with cholesterol <5 mmol/L: HD

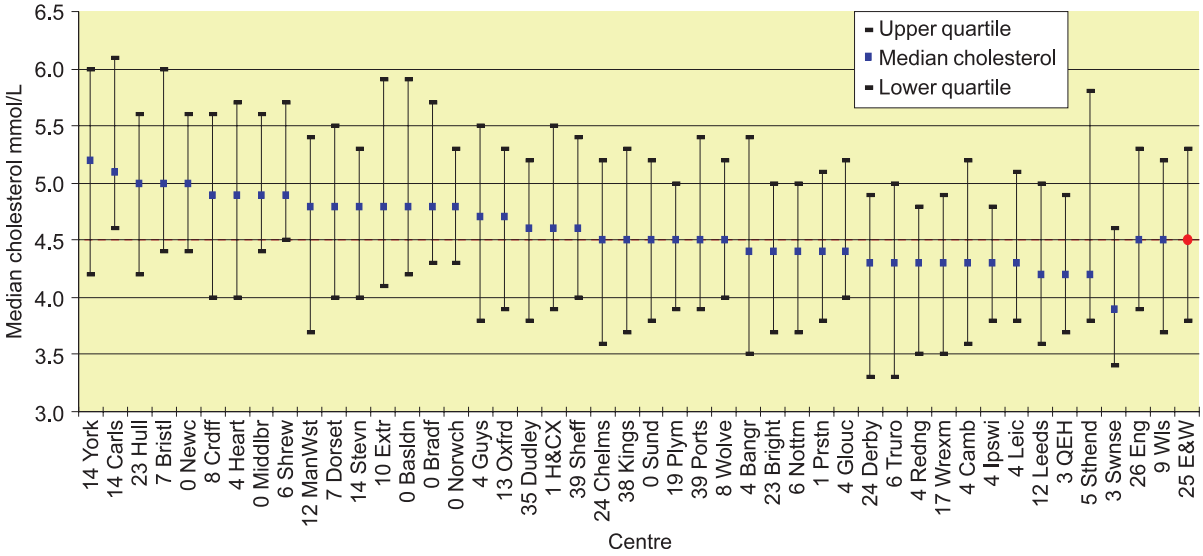

Figure 11.44: Median cholesterol: PD

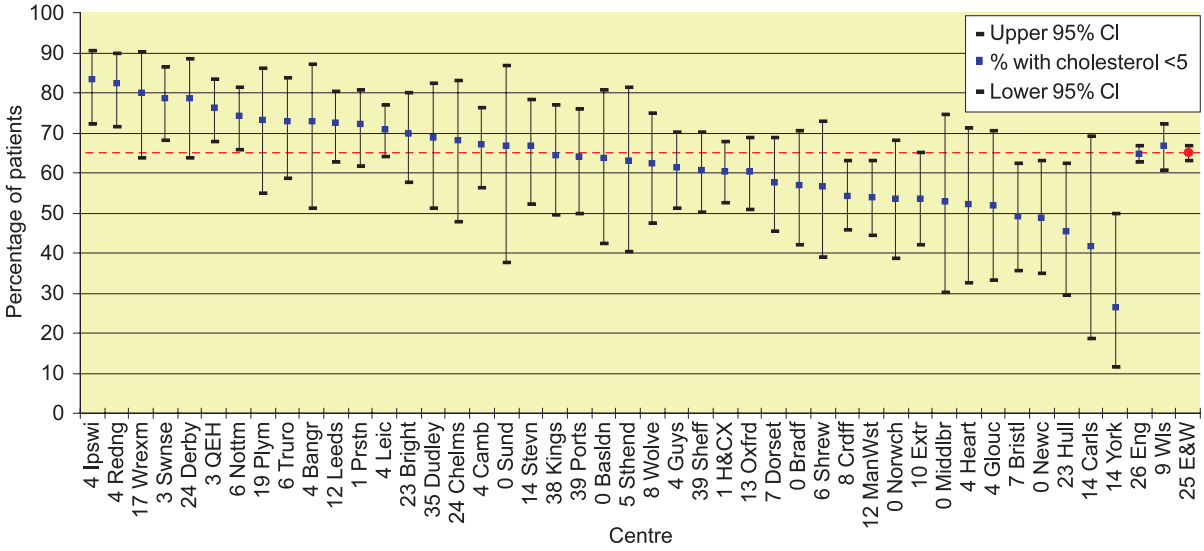

Figure 11.45: Percentage of patients with cholesterol <5 mmol/L: PD

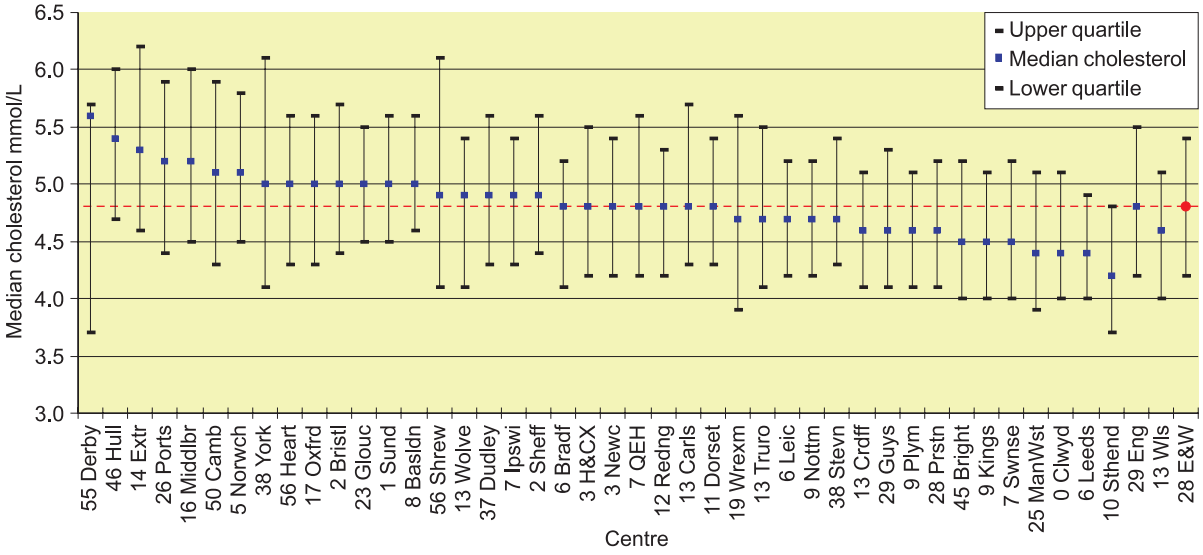

Figure 11.46: Median cholesterol: Tx

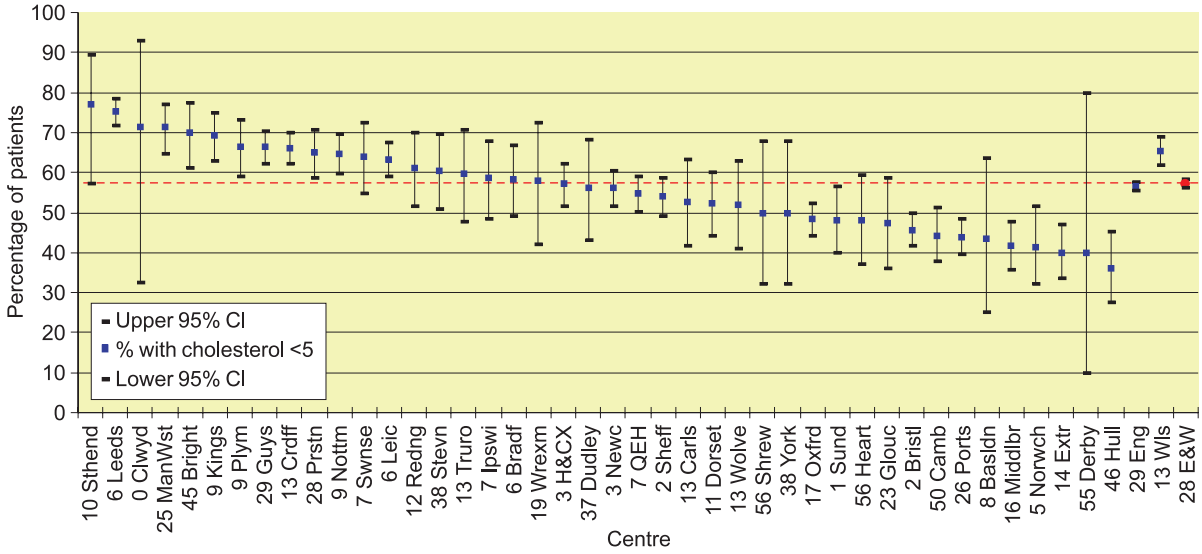

Figure 11.47: Percentage of patients with cholesterol <5 mmol/L: Tx

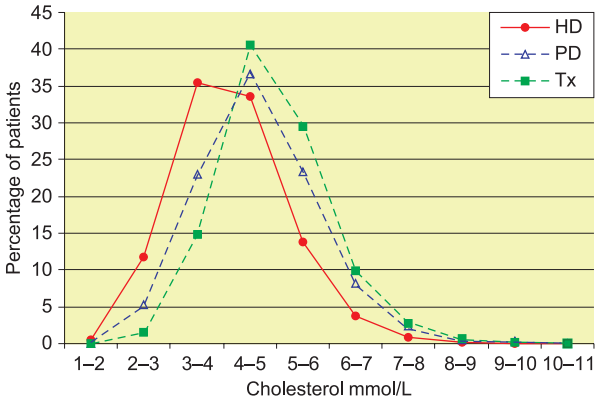

Figure 11.48: Serum cholesterol distribution by modality 31/12/2004

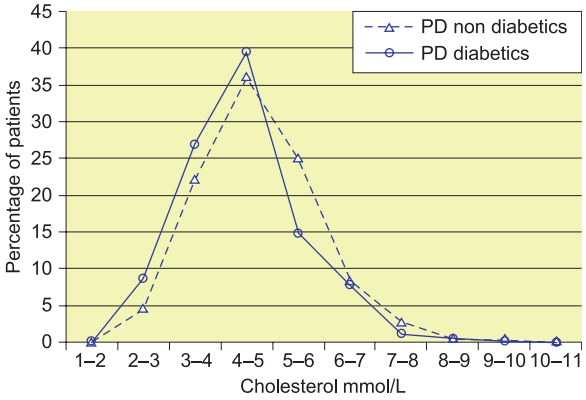

Figure 11.50: Distribution of serum cholesterol diabetics v non-diabetics: PD

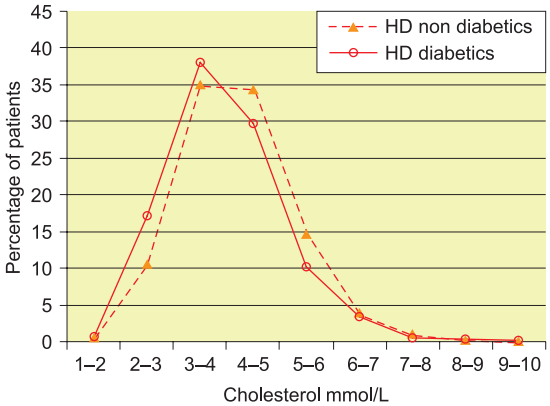

Figure 11.49: Distribution of serum cholesterol diabetics v non-diabetics: HD

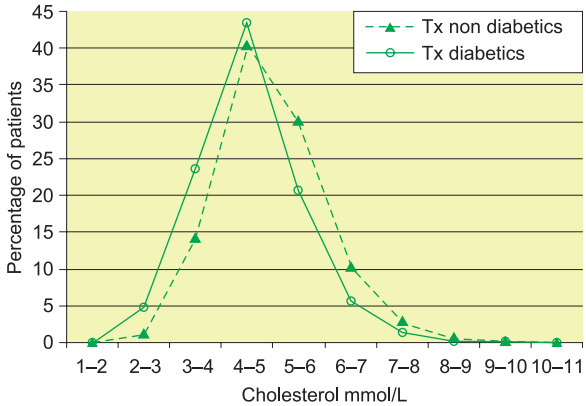

Figure 11.51: Distribution of serum cholesterol diabetics v non-diabetics: Tx

C-reactive protein (CRP) data to correlate with cholesterol levels for the different treatment modalities.

Figures 11.49–11.51 show lower cholesterol levels in diabetics for each treatment modality. However, these differences are not significant.

Change in cholesterol achievement 1997–2004

Figure 11.52 shows the cholesterol data for all treatment modalities between 1997 and 2004. Figures 11.53–11.55 show these data by centre. Over 8 years cholesterol levels have fallen in all treatment groups and it is likely this is due to statin use. The percentage of patients currently achieving the standard for HD, PD and Tx is 81%, 65% and 57% respectively. The majority of units show an improvement in cholesterol control over this period. The units with the worst control initially show a fall in median cholesterol in excess of 1 mmol/L (data not shown). Previously, the Finnish Renal Registry has shown that a fall in total cholesterol is mainly due to a fall in LDL-cholesterol and that triglycerides are highest in PD patients and HDL-cholesterol is highest in Tx patients. Data from the SHARP trial should indicate whether lipid profiles of UK patients show similar trends.

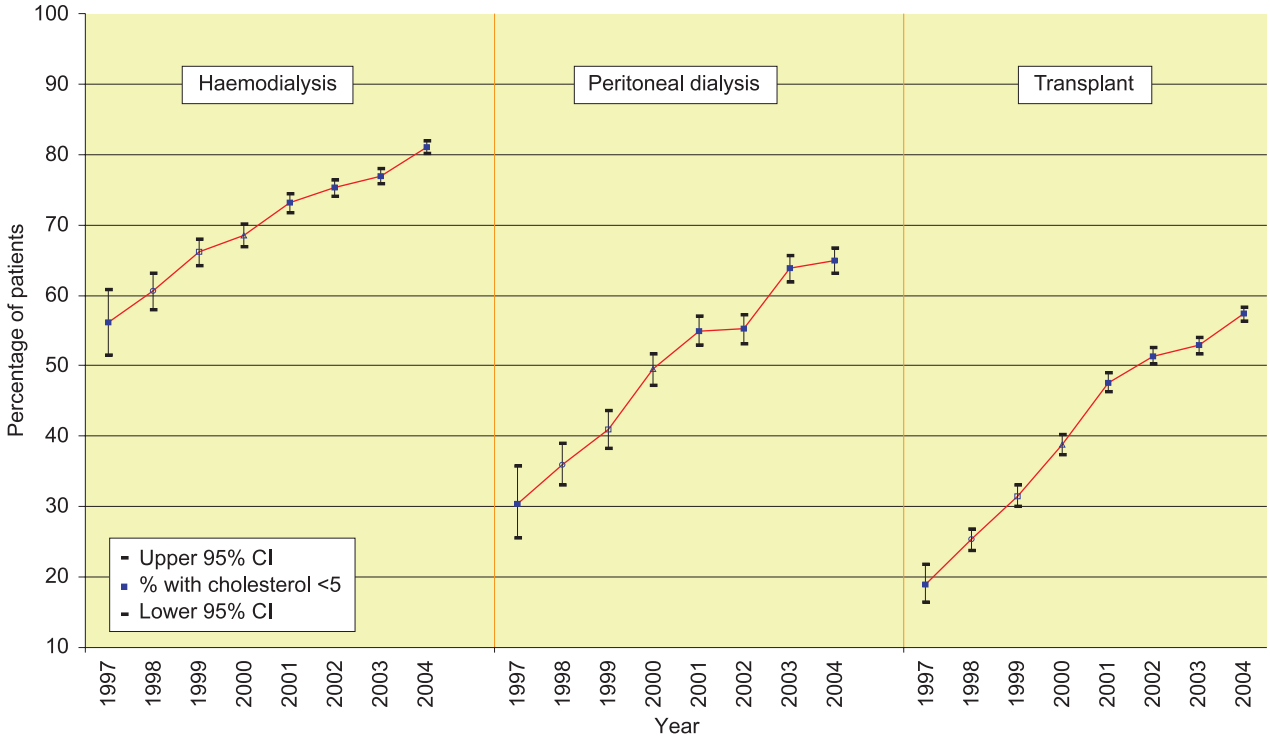

Figure 11.52: Percentage of patients with cholesterol <5 mmol/L HD vs PD vs Tx 1997–2004

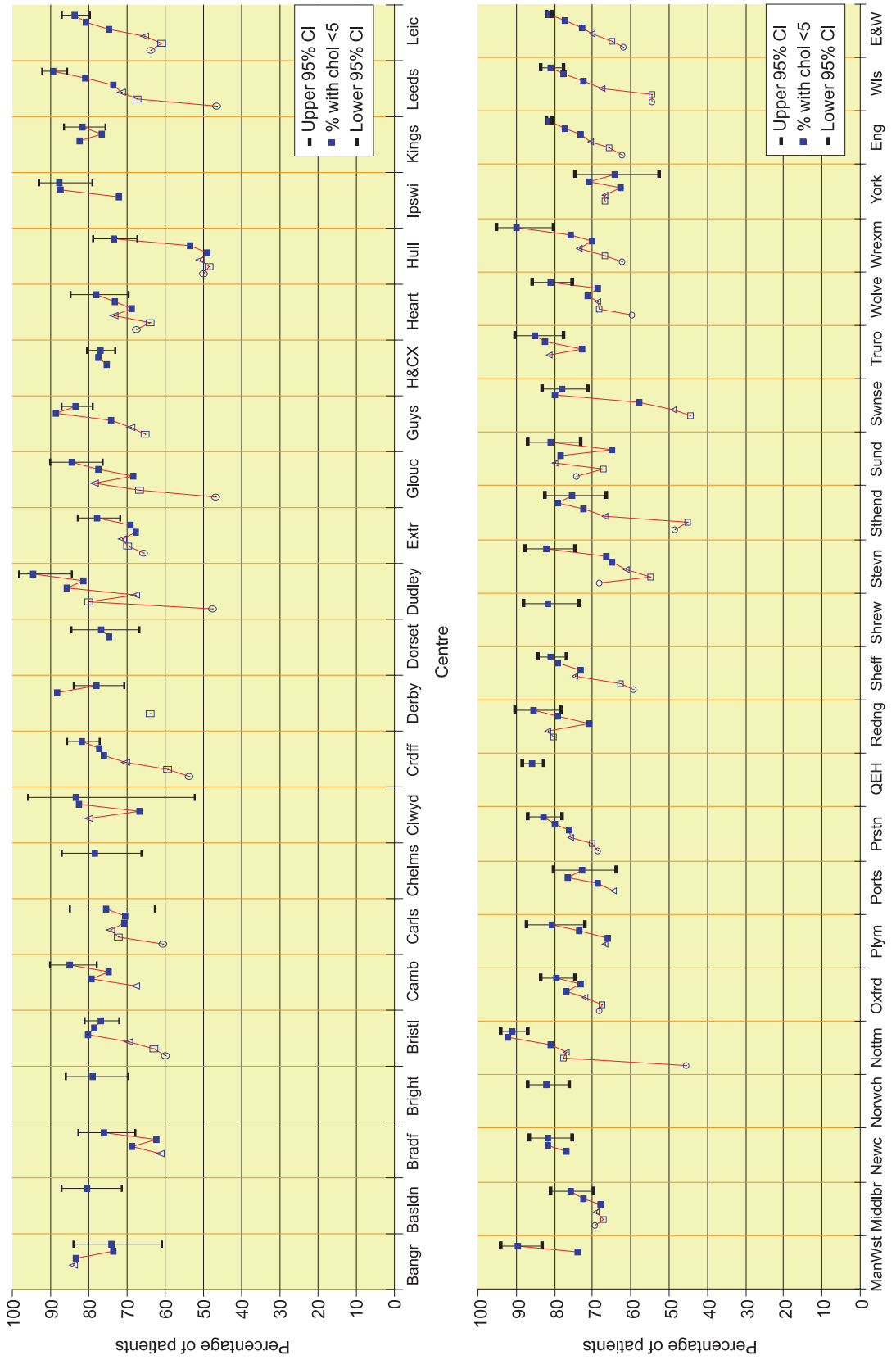

Figure 11.53: Change in % HD patients with cholesterol <5 mmol/L by centre 1998–2004

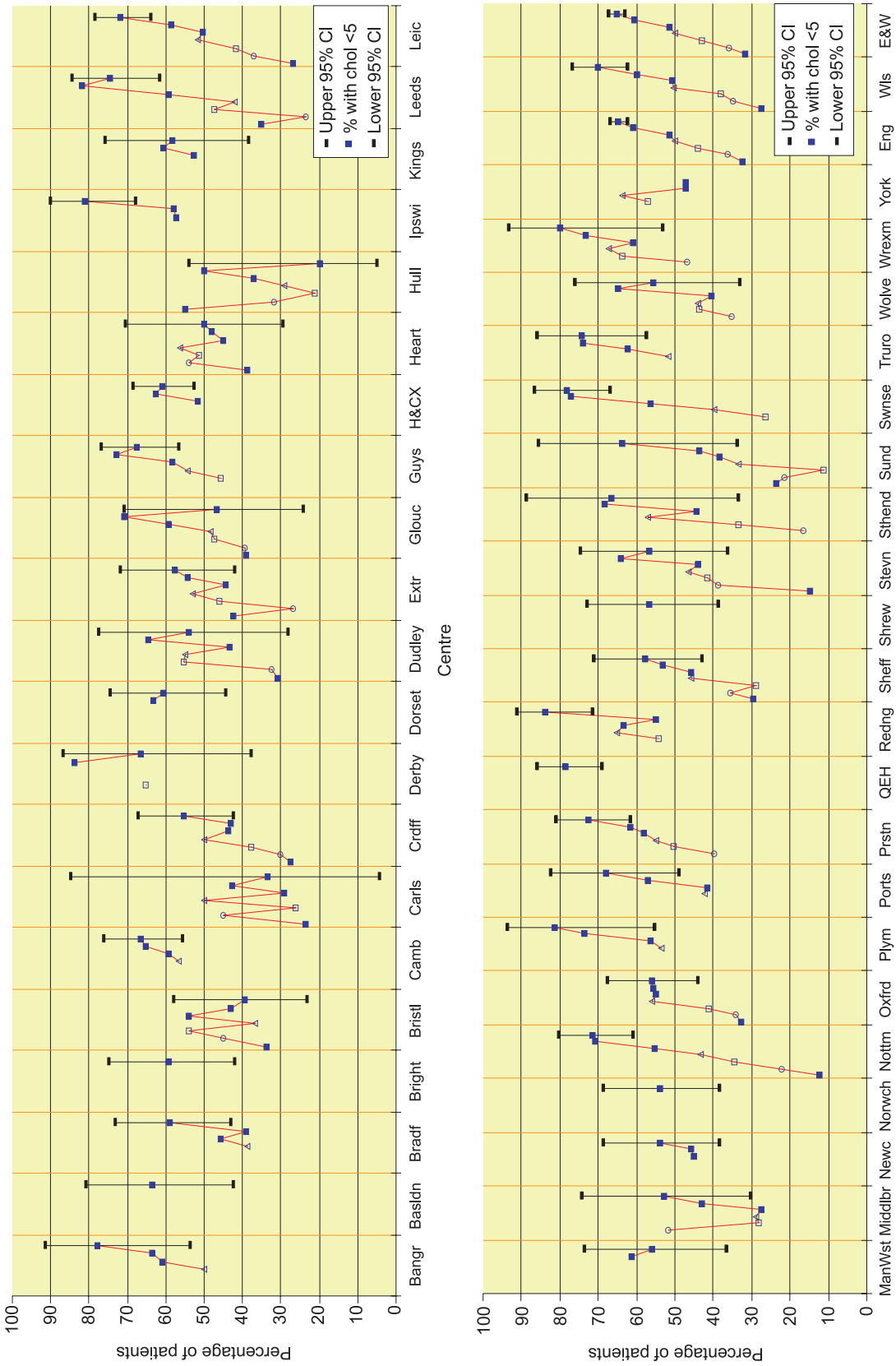

Figure 11.54: Change in % PD patients with cholesterol <5 mmol/L by centre 1998–2004

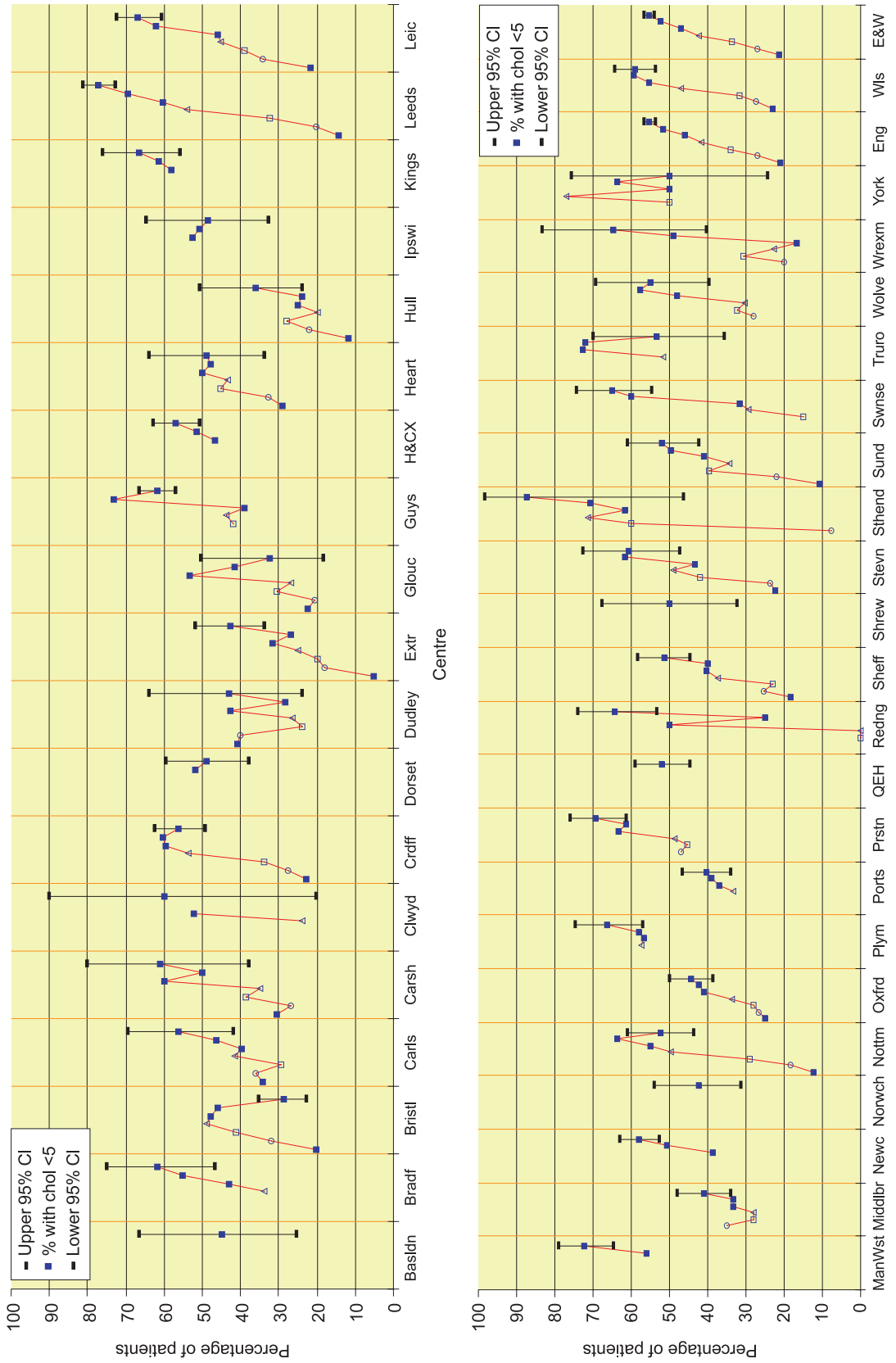

Figure 11.55: Change in % Tx patients with cholesterol <5 mmol/L by centre 1998–2004

Ongoing Trials

The AURORA study is investigating rosuvastatin 10 mg vs placebo in 2,700 HD patients and results are expected in 2008. The SHARP trial is investigating ezetimibe 10 mg/simvastatin 20 mg vs placebo in 9,000 CKD patients (3,000 on dialysis). Results are expected in 2009.

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