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

Summary

- In England and Wales, the combined blood pressure standard was achieved in 39% of patients pre-haemodialysis (inter unit range 14–64%), 48% of patients post-haemodialysis (range 32–67%), 32% of peritoneal dialysis patients (range 15–55%) and 27% of transplant patients (range 12–47%).

- The wide scatter of recorded blood pressure, especially in haemodialysis patients, implies that the ease of achievement of standards is dependent on the modality of renal replacement. Achievement of blood pressure standards in transplant cohorts appears to be easier than in haemodialysis. The framing of standards in terms of percentage compliance deserves examination.

- Widening pulse pressure increases risk of death within the first year of haemodialysis for patients with systolic blood pressure <119 mmHg, i.e. patients with cardiac failure.

- Over 4 years there has been no significant change in systolic or diastolic blood pressure achievement in England and Wales for patients on HD or PD.

- Blood pressure returns to the Renal Registry continue to be poor from some centres.

- Analysis of digit bias in the BP data returns suggests non-automated, 'rounded' values in some haemodialysis settings, and even more marked distortion in peritoneal and transplant clinics.

- Serum cholesterol levels continue to fall for renal replacement therapy patients on HD or PD or transplanted.

- Cholesterol levels are consistently lower in haemodialysis patients than in PD or transplant patients. Cholesterol levels fell significantly by 0.58 mmol/L when patients transfer from peritoneal dialysis to haemodialysis and rise by 0.59 mmol/L when dialysis patients are transplanted.

- Serum cholesterol shows a J shaped curve with (short term 1 year) survival. The curves are different for HD and PD.

- Ways by which renal units record post-haemodialysis blood pressure and episodes of symptomatic hypotension during haemodialysis, beta blocker and statin usage need to be explored so that the Registry can collect these data.

Introduction

Hypertension and hypercholesterolaemia are major risk factors for cardiac disease in the general population. Evidence from numerous randomised controlled trials indicates the lower the blood pressure or cholesterol level achieved, the lower the risk of future cardiovascular events, particularly for diabetics. The situation has not been clarified for patients with renal disease, even though cardiovascular disease is the main cause of premature death among dialysis patients. The purpose of this audit is to establish whether aggressive lowering of blood pressure and cholesterol will benefit all patients on renal replacement therapy or only certain subsets of patients. To date the Renal Registry has had insufficient data to address this important issue.

Hypertension plays a direct role in the development of LVH, LV dilatation, *de novo* ischaemic heart disease and cardiac failure in the dialysis population (discussed in detail in the last report). There is a U-shape rela-

tionship between hypertension and mortality in the dialysis population.[1] Widening pulse pressure (systolic minus diastolic blood pressure) is the strongest risk factor for increased cardiac mortality. In a retrospective analysis of 37,069 haemodialysis patients, widening pulse pressure was associated with age, diabetes, white race, female sex and number of years receiving dialysis.[2] For any given systolic or diastolic blood pressure, the wider the pulse pressure the higher the risk of death. An isolated high systolic blood pressure or low diastolic blood pressure is also associated with cardiovascular death.[3,4] More recently, post-dialysis blood pressure has been shown to correlate more closely with outcome than pre-dialysis blood pressure for the haemodialysis population.[1,2]

Co-morbidity adjustments markedly affect associations and are essential for survival analyses. Only 19% of patients logged with the Renal Registry have completed co-morbidity data returns and this must clearly improve. One omission from the co-morbidity list was cardiac failure because of difficulties in deciding whether it was primarily related to fluid overload or ischaemic heart disease. This has now been added as a co-morbidity item at the start of renal replacement therapy, due to either course. For units with poor access to echocardiography, pulmonary oedema on CXR will be sufficient to make the diagnosis. Over recent years there has been compelling evidence that beta blockers improve patient survival in cardiac failure, renal impairment and end-stage renal failure.[5,6] The Registry needs to explore with users an easy way to log these data on local IT systems so that it can be collected and analysed by the Registry.

Blood pressure control

The Renal Association standards for control of hypertension were revised in August 2002.[7] The current standards are:

Pre-haemodialysis systolic blood pressure < 140 mmHg.
Pre-haemodialysis diastolic blood pressure < 90 mmHg.
Post-haemodialysis, peritoneal dialysis and renal transplant recipient systolic blood pressure < 130 mmHg.
Post-haemodialysis, peritoneal dialysis and renal transplant recipient diastolic blood pressure < 80 mmHg.

The Renal Association does not specify separate standards for diabetics. Diabetic guidelines suggest a lower target (BP < 125/75 mmHg) to reduce cardiovascular risk.

For audit purposes the Renal Registry needs to liaise with renal units to discuss ways of collecting additional data sets which may be useful in identifying factors which impact on survival:

BP every 3 months for dialysis and 6 months for transplant patients.
Post-haemodialysis blood pressure.
Episodes of symptomatic hypotension during haemodialysis (see 3rd standards document)**.**
Beta blocker use.

Data returns

A large number of units returned incomplete blood pressure data. Lack of returns implies that blood pressure results have not been transferred to renal IT systems, rather than not recorded. This is particularly a problem for off-site clinics and satellite haemodialysis units where there may not be links in place to the renal unit main IT system. The renal NSF Information Strategy document (see Appendix E) highlights the importance of a renal unit's IT infrastructure and linkage with external sites.

Units with more than 50% missing data were excluded from the analyses. These include Bradford, Cambridge, Clwyd, Hull, Kings, Liverpool and Reading for haemodialysis (HD), Kings for peritoneal dialysis

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

Centre	Pre HD	Post HD	PD	Transp
Bangr	98	98	92	N/A
Bradf	8	8	100	97
Bristl	100	99	100	54
Camb	12	0	97	79
Carls	93	0	17	6
Carsh	0	0	0	0
Clwyd	18	0	67	96
Covnt	98	94	94	82
Crdff	30	0	8	93
Extr	94	91	100	20
Glouc	99	99	8	2
Guys	68	66	9	3
H&C	0	0	0	0
Heart	91	91	8	2
Hull	1	1	0	0
Ipswich	97	96	0	0
Kings	10	1	43	73
Leic	97	92	94	80
LGI	91	90	5	4
Livrpl	11	0	6	78
Middlbr	93	92	100	52
Newc	0	0	0	0
Notts	93	93	97	95
Oxfrd	98	86	85	24
Plym	0	0	0	0
Ports	0	0	1	0
Prstn	0	0	0	0
Redng	89	1	95	14
Sheff	100	76	99	97
Stevn	86	76	10	8
Sthend	97	0	6	3
StJms	89	99	99	90
Sund	98	97	19	2
Swnse	0	0	0	0
Truro	77	76	92	45
Wirrl	54	0	N/A	N/A
Wolve	98	91	14	5
Words	91	91	98	84
Wrex	0	0	0	0
York	92	92	90	94

(PD) and Truro for transplant. The new Renal Association blood pressure standards were used in this year's report.

Distribution of blood pressure by modality

Figures 11.1–11.6 indicate systolic and diastolic blood pressure distributions for each treatment modality. The distributions have standard deviations approaching twice the values found in hypertensive populations without ERF, with the widest spread for haemodialysis. The data have not changed materially over the past two years where systolic/diastolic standard deviations for pre HD, PD, transplant were 27/15, 25/12.5, 20/11 respectively for 2001 data and 26.9/15, (27/13.9 post-HD), 24.5/13.4 and 19.3/10.9 for 2002 data. These values should be compared to 18/10 for non-renal replacement therapy hypertensive population. (Note: this analysis used only data from units offering more than 50 values for analysis, with minor digit bias.) Where an upper limit of desired blood pressure is specified (e.g. 140 systolic for HD patients), typically this only becomes the achieved mean blood pressure of the group.

Figure 11.7 shows a plot of a centre's median systolic blood pressure for pre HD and transplant respectively, revealing the different regression of achieved outcome on the median values. The flatter the slope the greater the dispersion of data (standard deviation). The greater blood pressure dispersion of the haemodialysis population implies a lower median blood pressure is required to achieve any given standard compared with more typical hypertensive groups. A median systolic blood pressure of 115 mmHg is required for 85% of HD patients to achieve a systolic blood pressure <140 mmHg, for example.[8] If a centre achieves a median systolic pressure of 125 mmHg then 90% of transplant patients, but only 70% of HD patients (pre-HD values), will be under 140 systolic. These data relate to single readings, rather than the mean of several separate measurements, which would narrow these distributions.

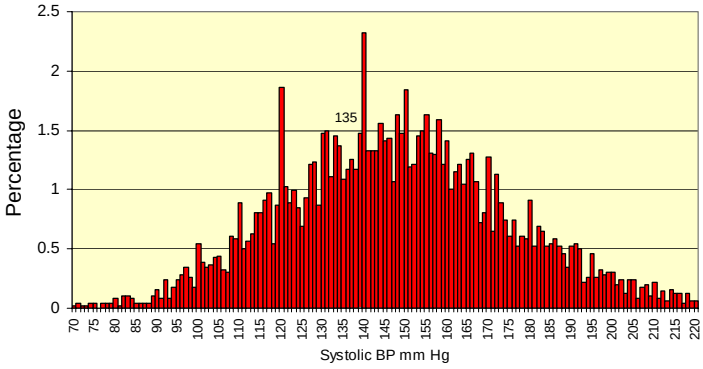

Figure 11.1. Systolic BP: pre-haemodialysis

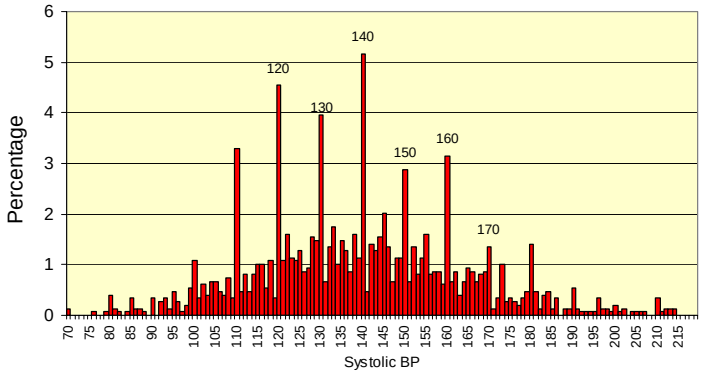

Figure 11.2. Systolic BP: peritoneal dialysis

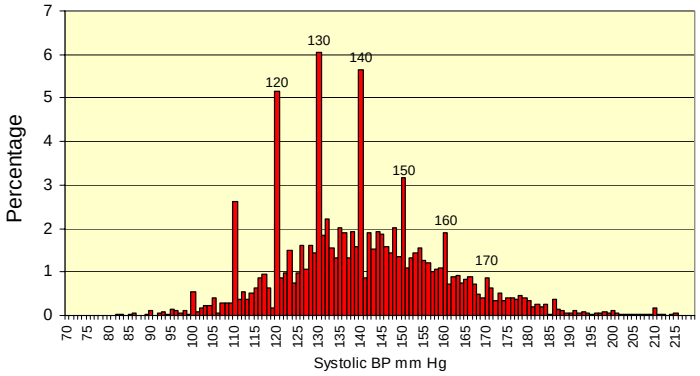

Figure 11.3. Systolic BP: transplant

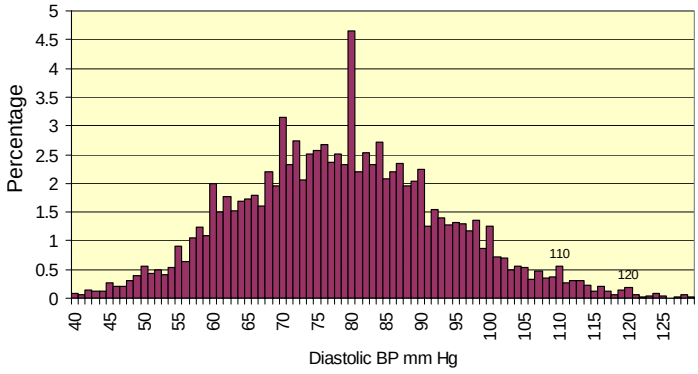

Figure 11.4. Diastolic BP: pre-haemodialysis

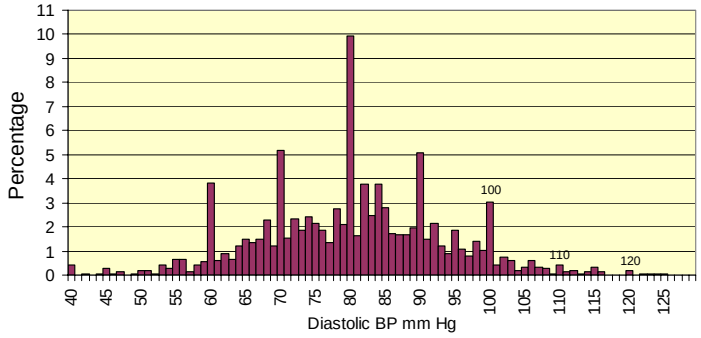

Figure 11.5. Diastolic BP: peritoneal dialysis

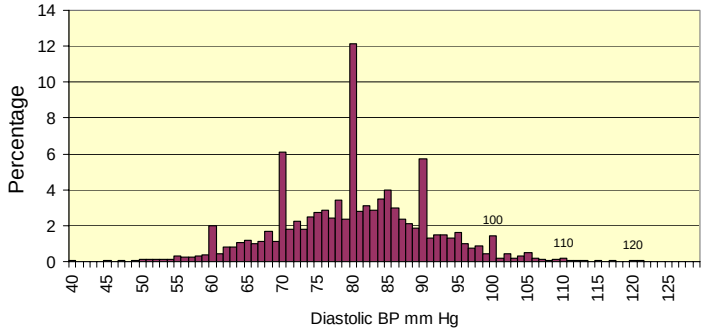

Figure 11.6. Diastolic BP: transplant

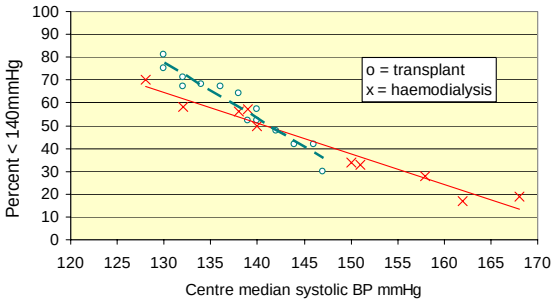

Figure 11.7. Centre median systolic BP and percentage achieving <140 mmHg

These analyses provide material for discussion on the recommended Standards and the means by which outcomes should be presented. Since ideal blood pressure standards are only partially achievable (e.g. all patients should have a systolic BP < 140), consideration should be given to reframing Standards in terms of percent compliance with the desirable maximum BP (e.g. 50% should have a systolic < 140). An auditable item defined in this fashion as a performance measure, would be a practical intermediate step between Standard declarations and clinical practice in the guidance of patient management.

Blood pressure measurement and digit bias

The information given in Figures 11.8–11.11, which indicate the accuracy with which blood pressure readings are measured and recorded, is a cause for concern. In many dialysis units and renal clinics, blood pressure is not measured according to the British Hypertension Society recommendations. Furthermore, digit bias (the tendency to round the numbers up or down) occurs when blood pressure measurements are recorded on to clinical databases.

The tendency for units to round systolic and diastolic blood pressure measurements to zero (zero should occur on average only 10% of the time) was analysed. The data shows zero digit bias is more prevalent in PD and transplant patients, presumably with measurements made in a clinic setting. It may even occur in HD patients when the blood pressure has been measured electronically and must be transcribed! There is little evidence of rounding to ‘fives’. Methods of measurement and recording must be standardised and accurate for audit purposes.

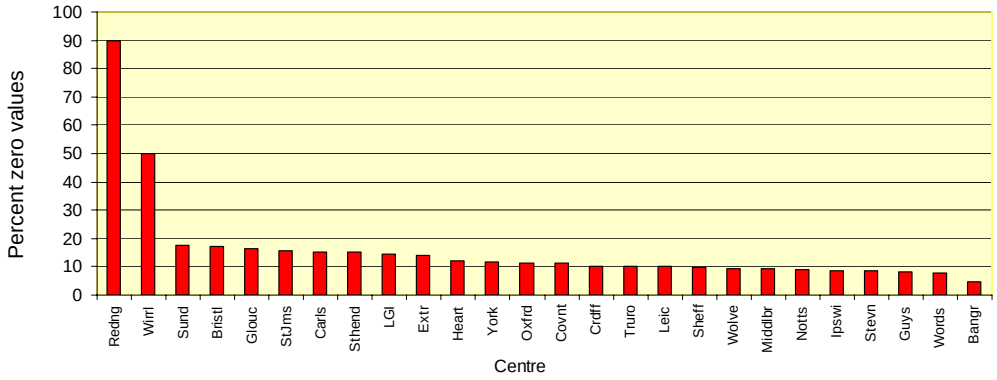

Figure 11.8. Zero digit bias pre-HD SBP 2002

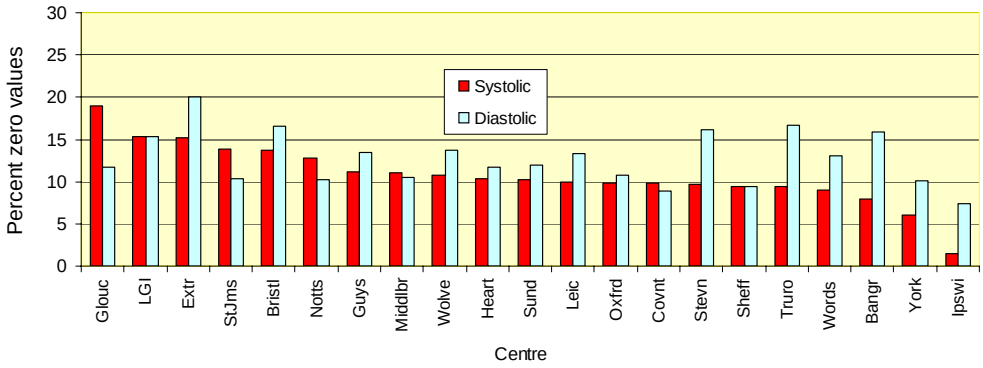

Figure 11.9. Zero digit bias of post-HD BP 2002

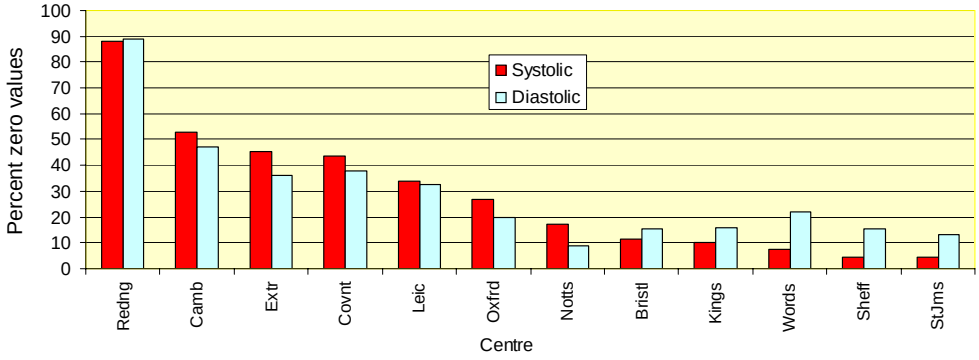

Figure 11.10. Zero digit bias of peritoneal dialysis blood pressure 2002

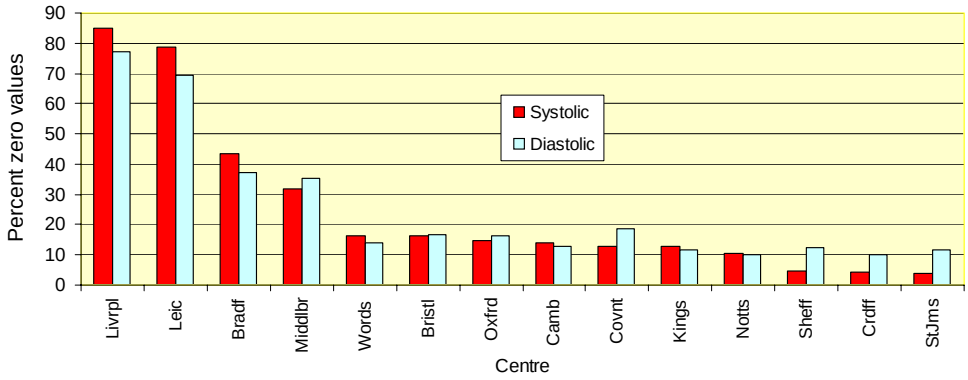

Figure 11.11. Zero digit bias of transplant blood pressure 2002

Achievement of combined systolic and diastolic Standard

Figures 11.12–11.15 show a wide variation between units achieving the combined blood pressure standard for each modality. In England and Wales, the percentage of HD patients achieving the standard pre-dialysis average 39% (range 14–64%) and post-dialysis average 48% (range 32–67%). An average of 32% of PD patients achieve the standard (range 15–55%) and 27% of transplant patients (range 12–47%). Chi squared testing indicates the variation between centres for each treatment modality is significant ($p < 0.0001$).

The median blood pressure for pre-HD, post-HD, PD and transplant is 147/78, 131/72, 139/80 and 140/80 mmHg. This equates to a pulse pressure of 69, 59, 59 and 60 mmHg respectively. The results are similar to those reported by the Finnish Registry for Kidney Diseases.[9]

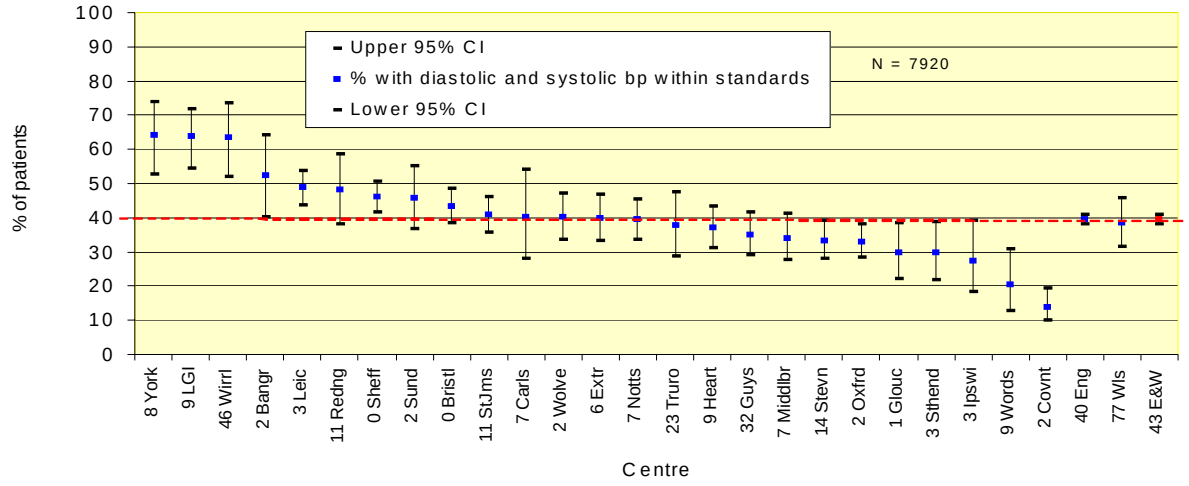

Figure 11.12. Percentage of patients with BP < 140/90 mmHg: pre-HD

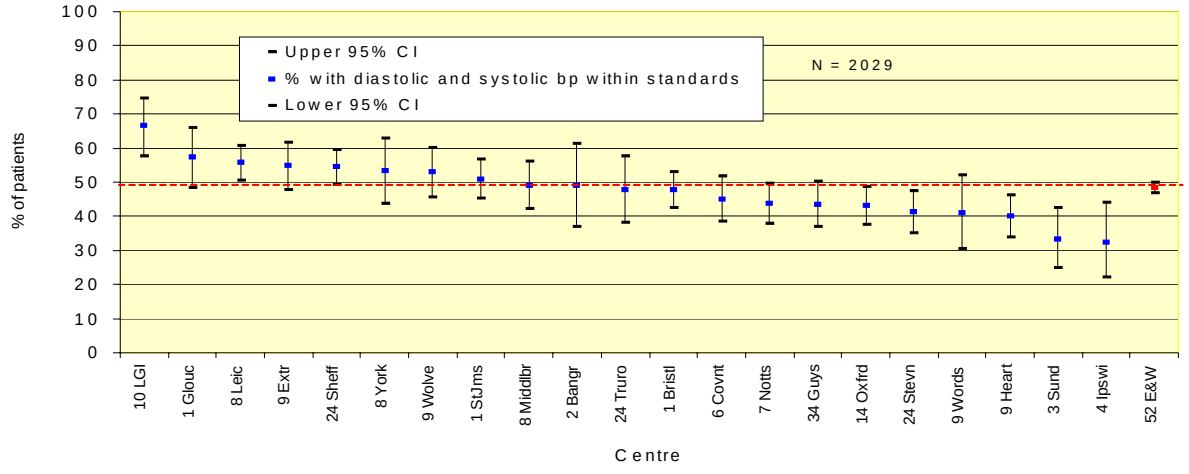

Figure 11.13. Percentage of patients with BP < 130/80 mmHg: post-HD

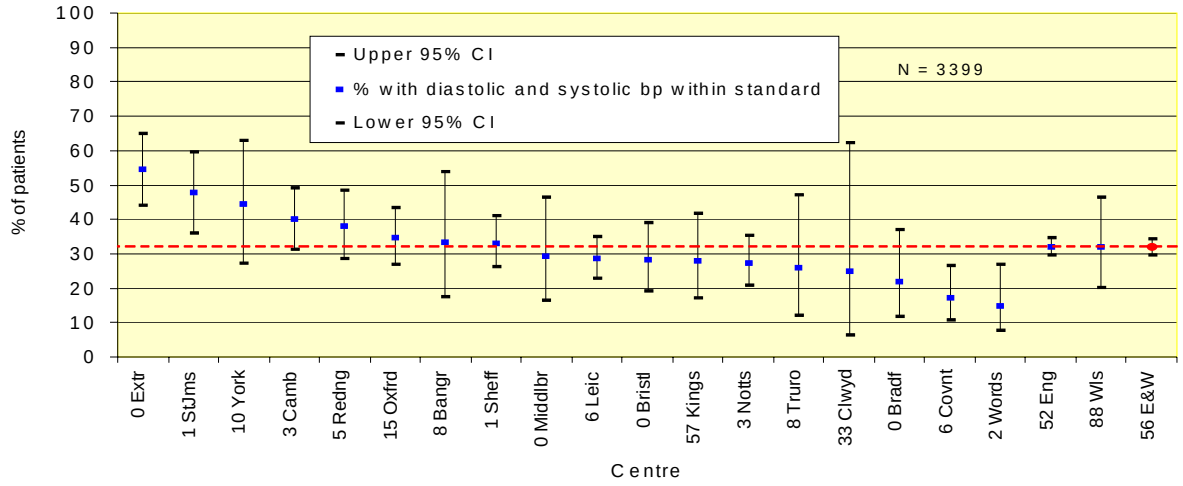

Figure 11.14. Percentage of patients with BP < 130/80 mmHg: PD

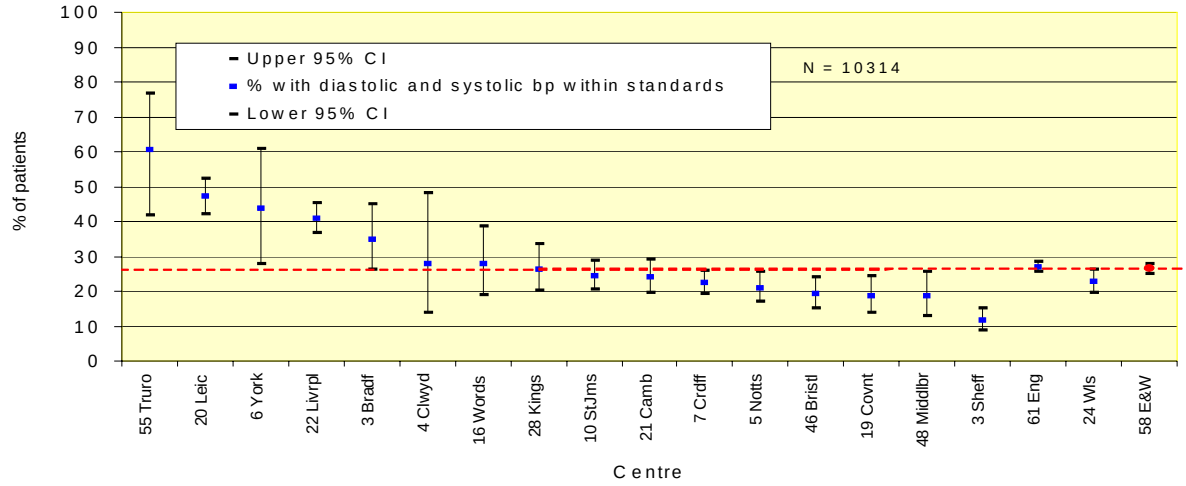

Figure 11.15. Percentage of patients with BP < 130/80 mmHg: transplant

Systolic pressure alone

Figures 11.16–11.23 show a wide variation between units achieving the systolic blood pressure standard. In England & Wales, the percentage of HD patients achieving the standard pre-dialysis average 41% (range 15–66%) and post-dialysis average 49% (range 34–66%). An average of 39% of PD patients achieve the standard (range 20–65%) and 33% of transplant patients (range 16–53%). Chi squared testing indicates the variation between centres for each treatment modality is significant ($p < 001$).

The median systolic blood pressure for pre-HD, post-HD, PD and transplant is 147, 131, 139 and 140 mmHg respectively. Diabetics and patients with reno-vascular disease have the highest systolic blood pressures post-haemodialysis (see Chapter 19 on diabetes). This is a major cause for concern given the more stringent blood pressure targets recommended by diabetic guidelines to reduce cardiovascular risk.

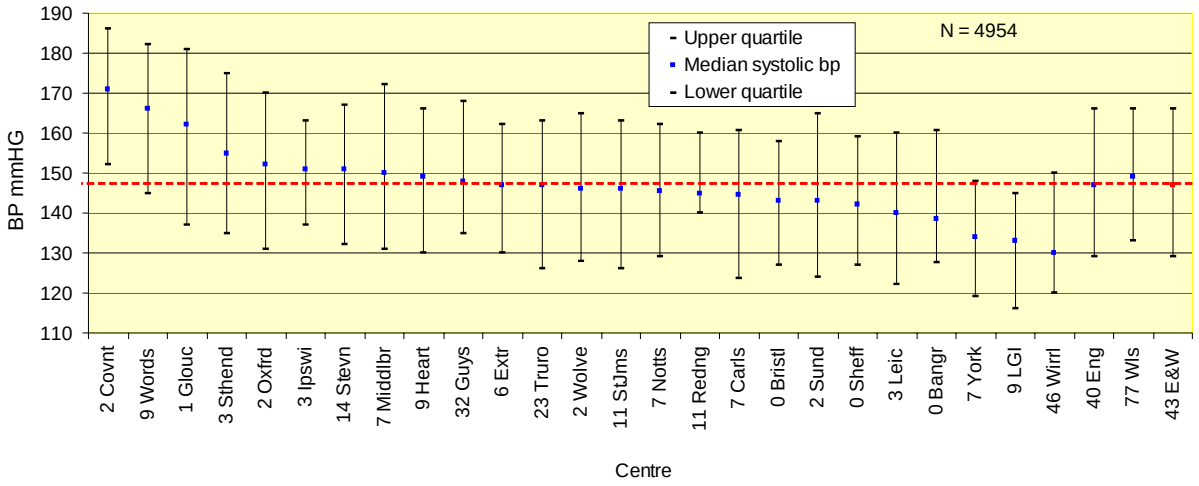

Figure 11.16. Median systolic BP; pre-HD

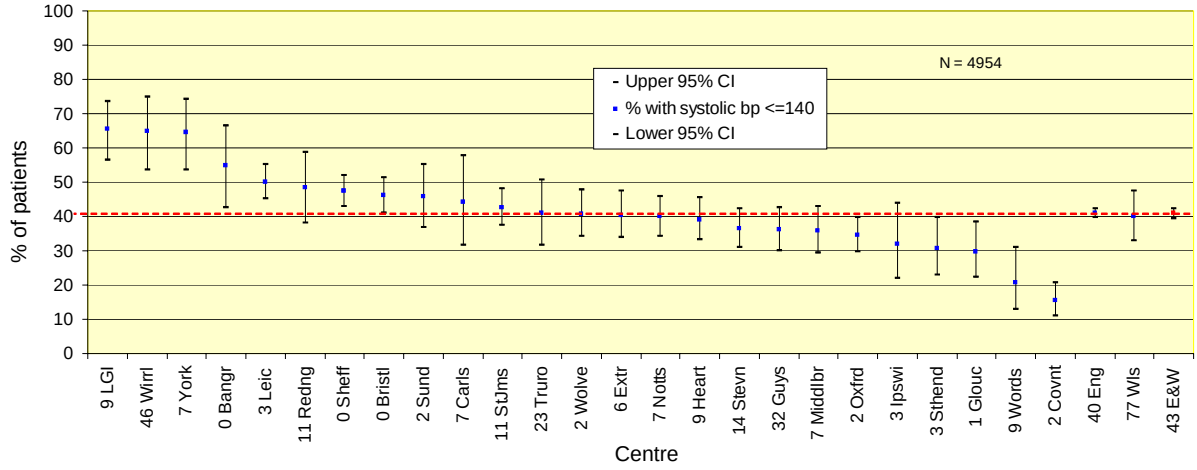

Figure 11.17. Percentage of patients with systolic BP < 140 mmHg; pre-HD

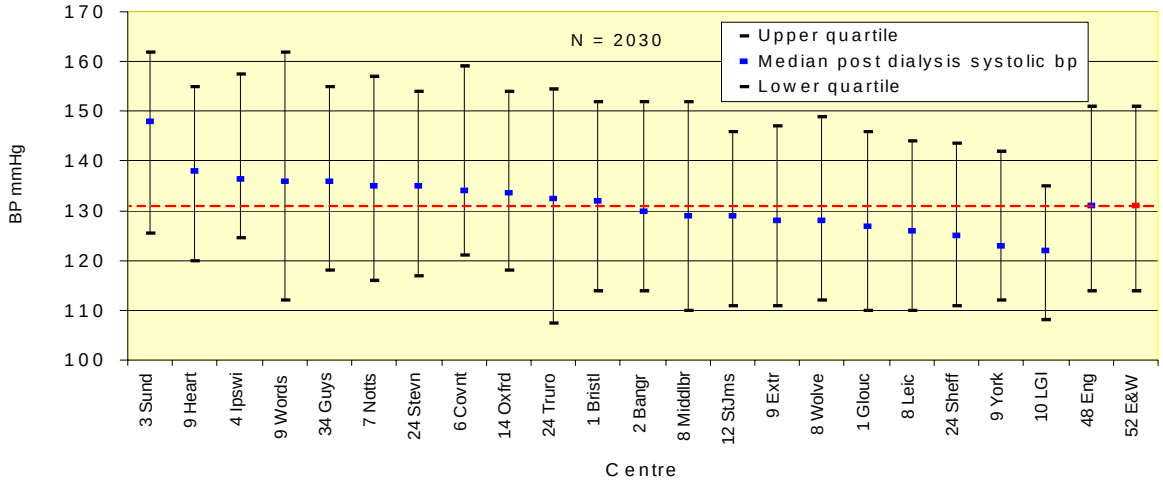

Figure 11.18. Median systolic BP; post-HD

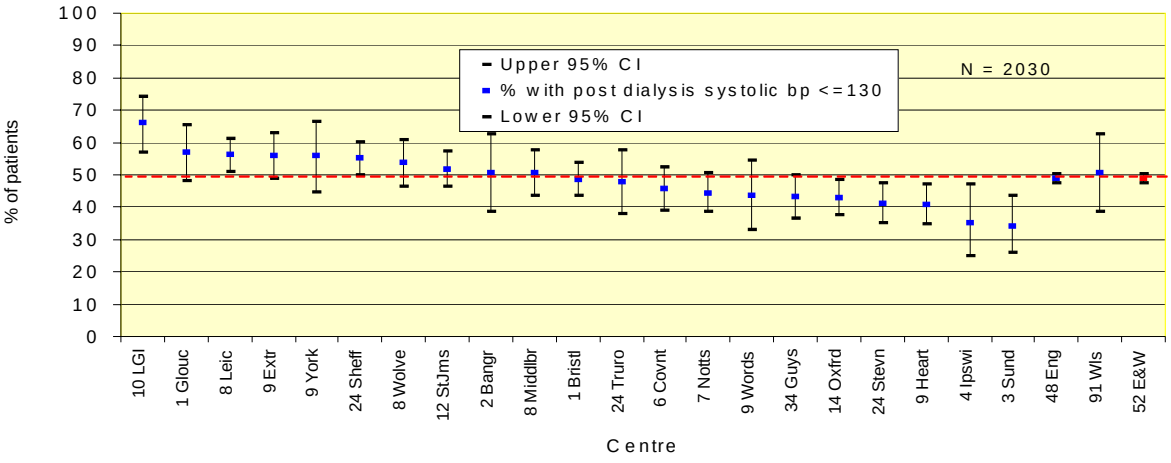

Figure 11.19. Percentage of patients with systolic BP < 130 mmHg; post-HD

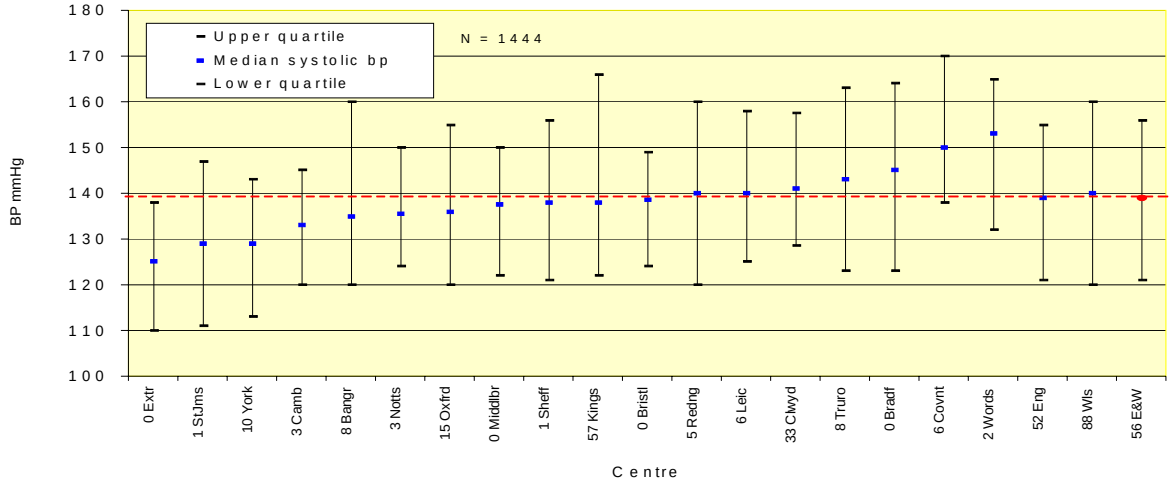

Figure 11.20. Median systolic BP; PD

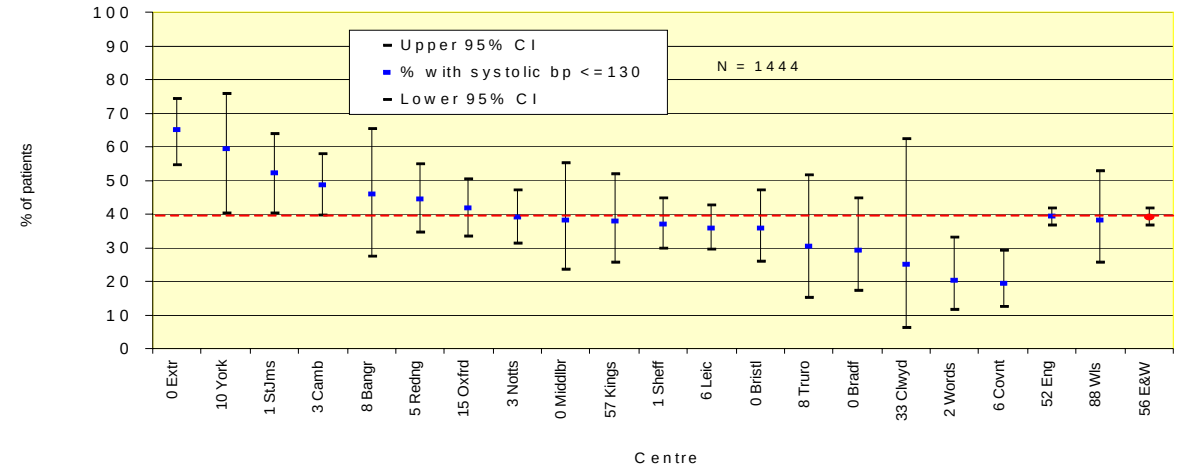

Figure 11.21. Percentage of patients with systolic BP < 130 mmHg; PD

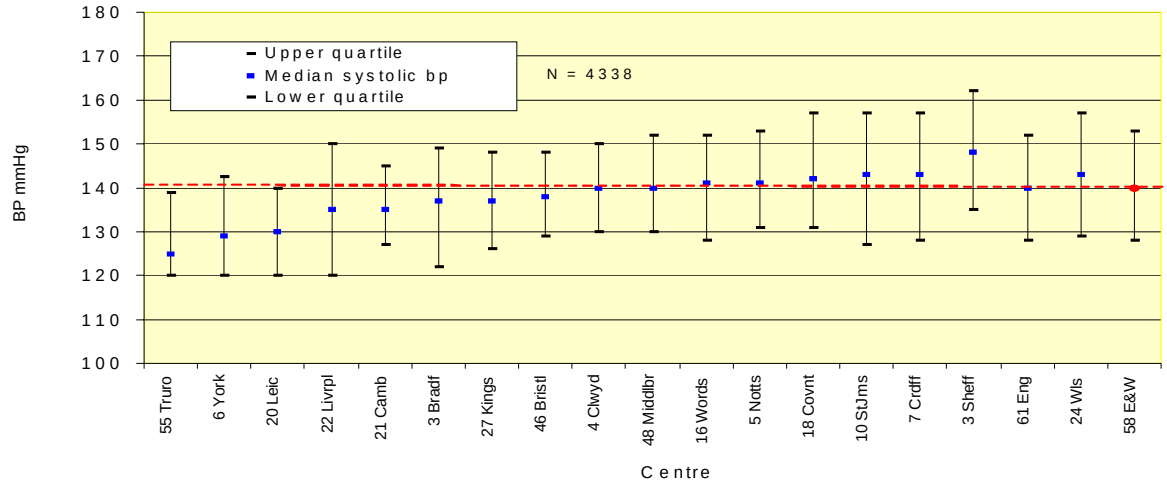

Figure 11.22. Median systolic BP; transplant

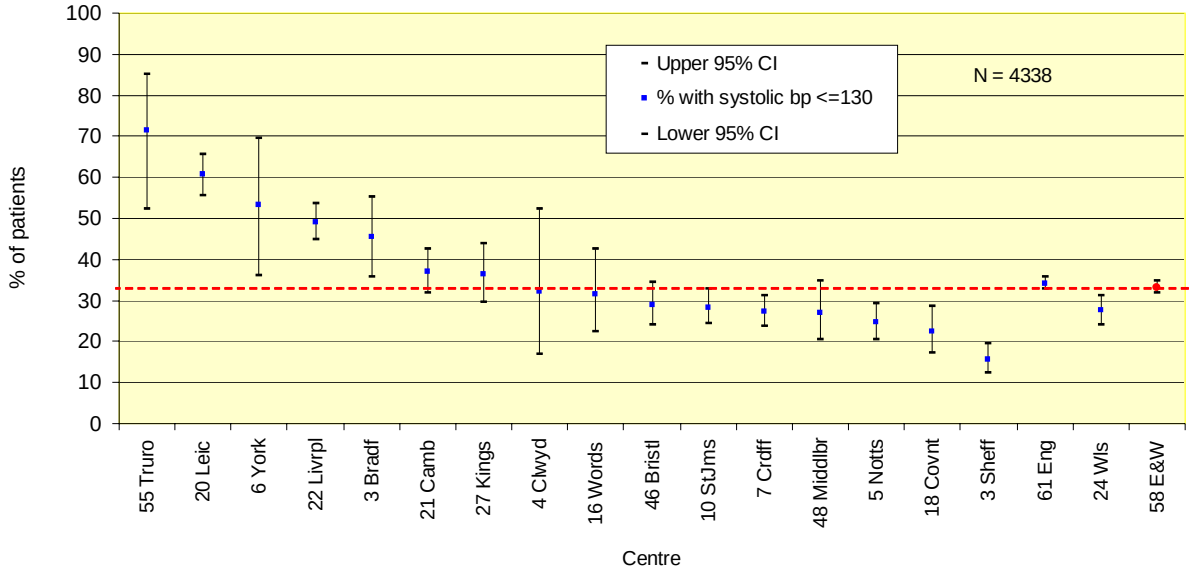

Figure 11.23. Percentage of patients with systolic BP < 130 mmHg; transplant

Diastolic pressure alone

Figures 11.24–11.31 show wide variation between units achieving the diastolic blood pressure standard. In England and Wales, the percentage of HD patients achieving the standard pre-dialysis average 80% (range 59–95%) and post-dialysis average 74% (range 49–87%). An average of 53% of PD patients achieve the standard (range 25-72%) and 54% of transplant patients (range 40–75%). Chi squared testing indicates the variation between centres for each treatment modality is significant ($p < 0.001$). The median diastolic blood pressure for pre-HD, post-HD, PD and transplant is 78, 72, 80 and 80 mmHg respectively.

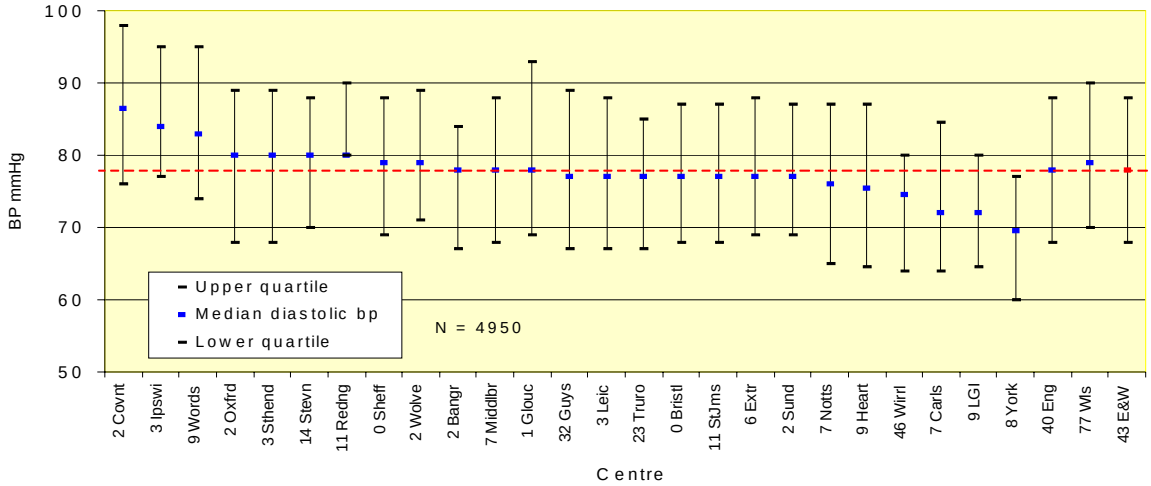

Figure 11.24. Median diastolic BP; pre-HD

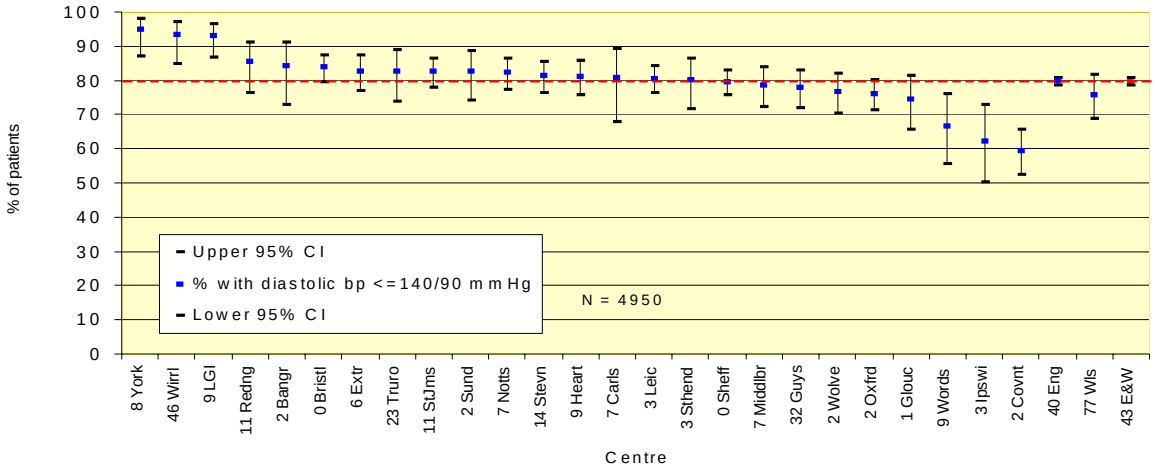

Figure 11.25. Percentage of patients with diastolic BP < 90 mmHg; HD

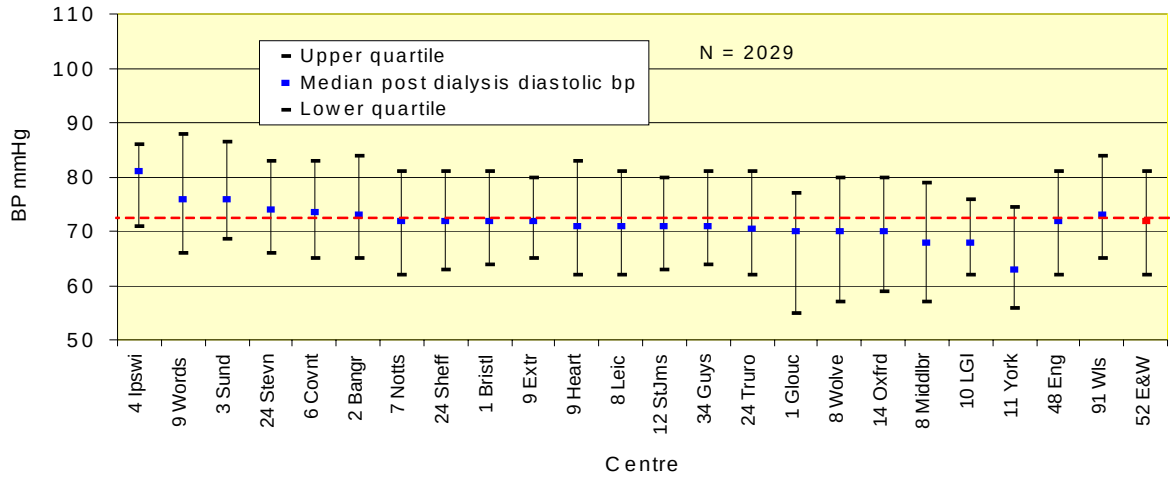

Figure 11.26. Median diastolic BP; post-HD

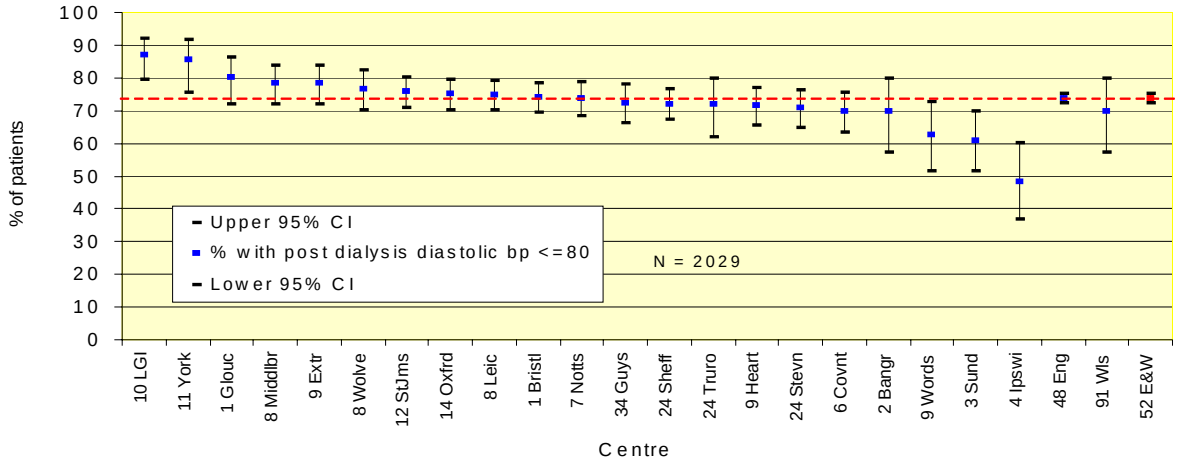

Figure 11.27. Percentage of patients with Diastolic Blood Pressure <80 mm Hg : post haemodialysis

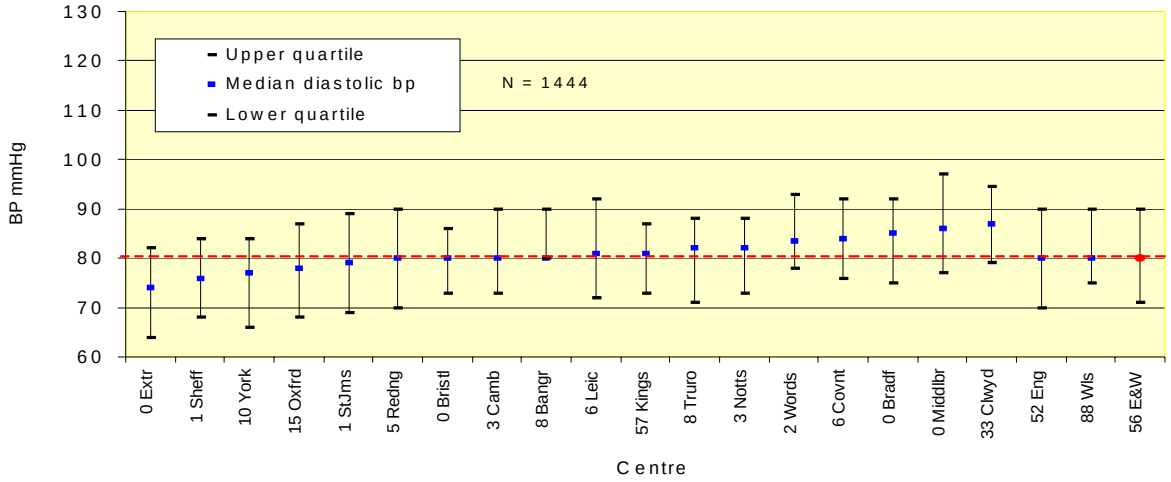

Figure 11.28. Median Diastolic Blood Pressure mm Hg : peritoneal dialysis

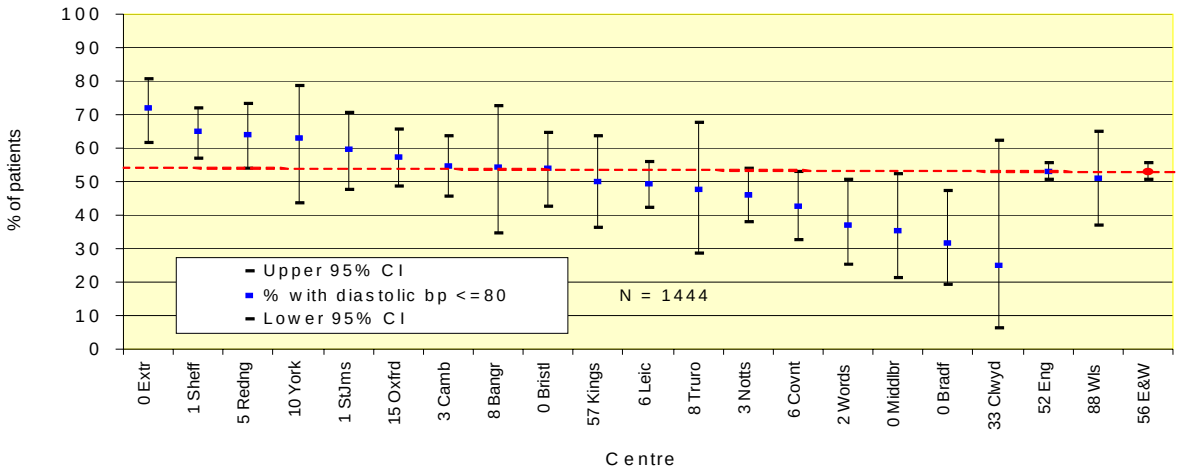

Figure 11.29. Percentage of patients with Diastolic Blood Pressure <=80 mm Hg : peritoneal dialysis

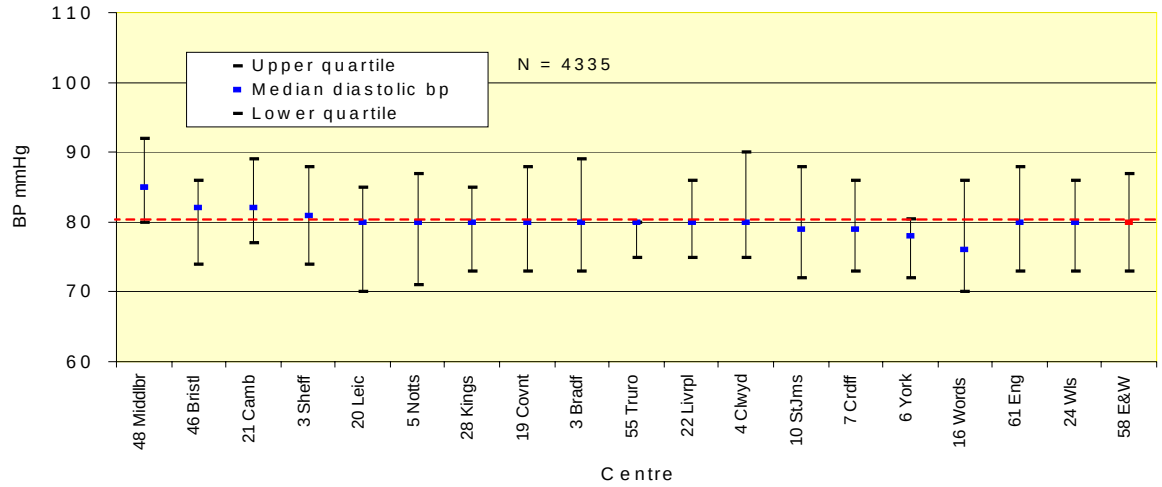

Figure 11.30. Median diastolic BP; transplant

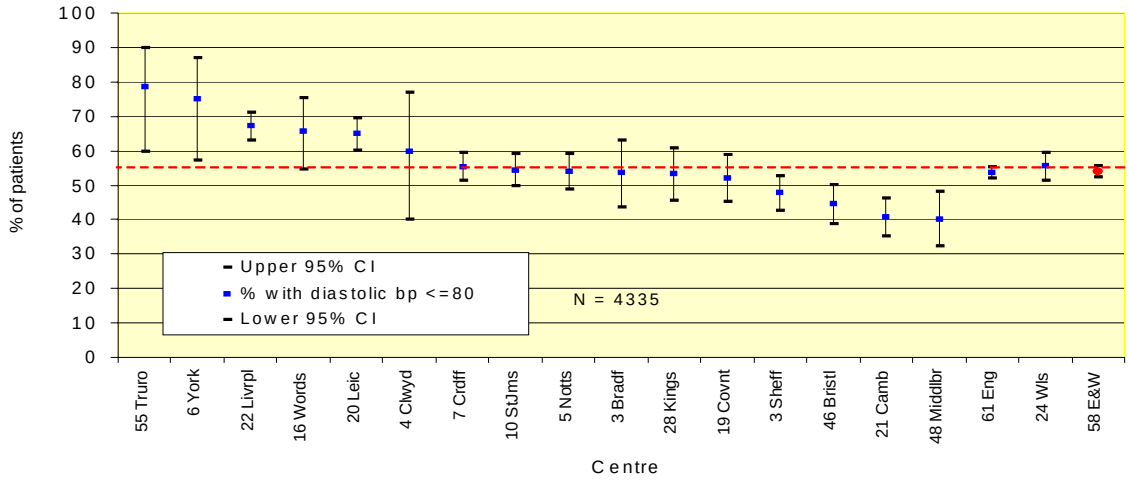

Figure 11.31. Percentage of patients with diastolic BP < 80 mmHg; transplant

Change in blood pressure achievement 1999–2002

Figure 11.32 indicates that for England and Wales as a whole there has been no change in improving systolic BP in patients. Only the Sheffield renal unit appears to have made a significant improvement in systolic BP achievement during this 4 year time period. During the same period, the Oxford renal unit is the only centre to have shown a change in improvement of diastolic blood pressure achievement (64% compliance in 1999 to 76% compliance in 2002), although this is now only in line with England and Wales average of 78% with diastolic BP ≤ 90 mmHg. It is too early to tell whether the 2002 change in Renal Association 3rd Standards will have any impact on achievement.

There were no significant changes in achievement of PD BP standards apart from the Oxford renal unit where achievement of the diastolic BP standard again improved from 41% in 1999 to 58% in 2002 (compared with E&W 54% 1999–2002).

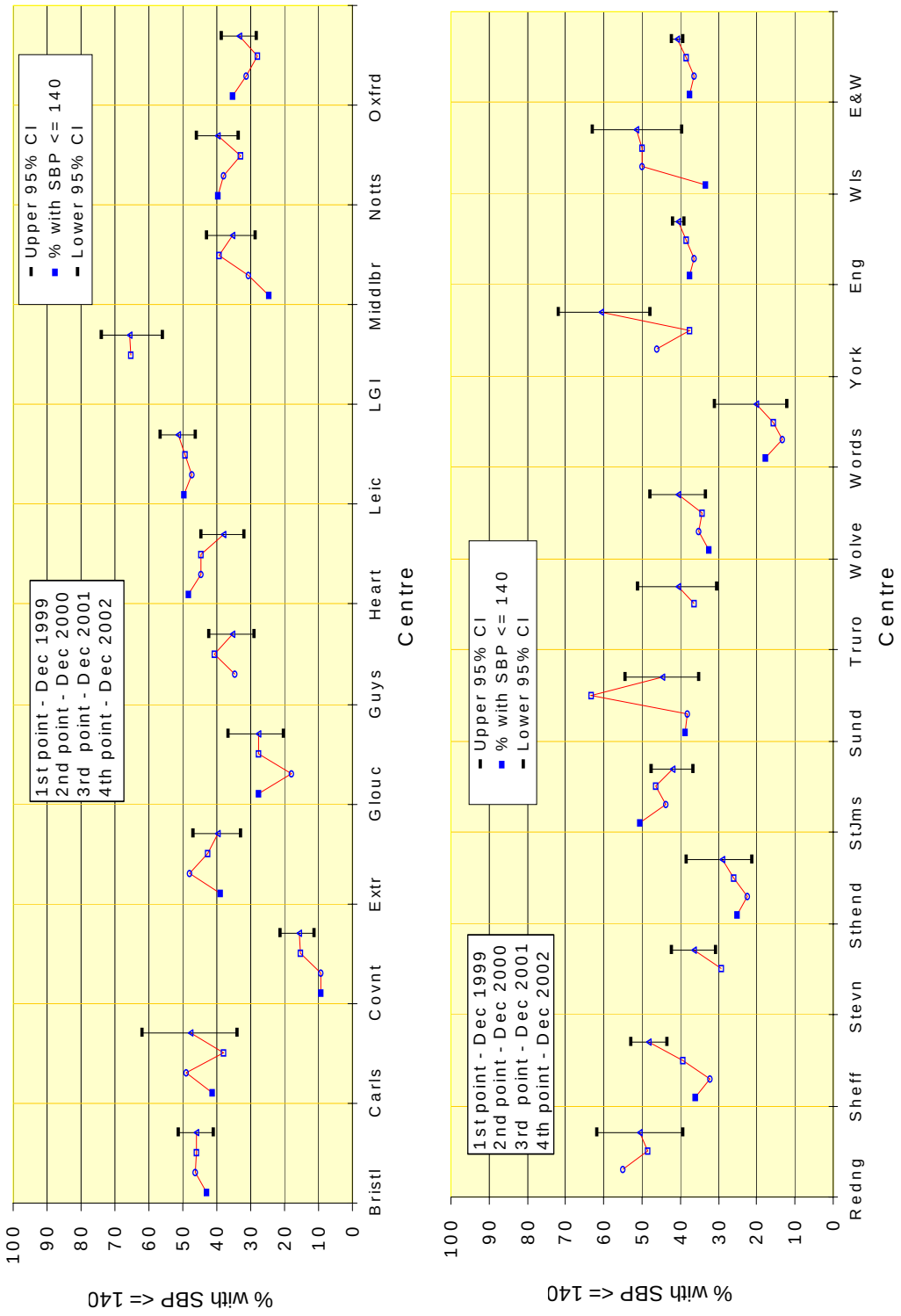

Figure 11.32. Change in achievement of systolic BP pre HD 1999–2002

Blood pressure changes during haemodialysis

This is the first time the Registry has analysed blood pressure changes that occur during haemodialysis. For patients with cardiac function normal (defined as systolic BP > 110 mmHg pre-dialysis), systolic blood pressure falls in 72% of patients and rises in 26%. The median drop in systolic blood pressure post HD is 16 mmHg, but in 10% of patients it rises and exceeds 30% of the pre-dialysis value. Diastolic blood pressure falls in 65% of patients and rises in 31% post HD. The median drop in diastolic blood pressure is 6 mmHg but in 8% of patients it rises and exceeds 30% of the pre-dialysis value. Pulse pressure changes during haemodialysis have not been analysed.

Data were available for only 267 patients with poor cardiac function (defined as systolic blood pressure <110 mmHg pre-haemodialysis). Systolic blood pressure falls in 41% of patients and rises in 55% post HD. Diastolic blood pressure falls in 47% of patients and rises in 48% post HD.

It is not clear what these blood pressure changes mean. For example, a rise in blood pressure following dialysis may reflect improved cardiac output in patients with cardiac failure or increased peripheral resistance in patients with normal cardiac function. The prognostic implications of these blood pressure changes should become clearer as these patients are observed over a longer period.

Pulse pressure and mortality in incident haemodialysis patients

As discussed at the start of this chapter, patients with end-stage renal disease (ESRD) exhibit vascular abnormalities that contribute to elevated pulse pressure, including increased arterial stiffness and pulse wave velocity. Pulse pressure has been shown as a risk factor for mortality or cardiovascular events in several dialysis cohorts. The Registry has previously analysed the effect of systolic and diastolic blood pressure on a prevalent cohort survival (Report 2000, Chapter 18).

This analysis looks at the importance of pulse pressure for predicting mortality in incident chronic haemodialysis patients in England & Wales.

Methods

Patients starting haemodialysis between January 1997 and September 2001 were included in the study and followed for 1 year (excluding the first 90 days). Pre and post dialysis blood pressure measurements were averaged over the four quarters:

- For patients who died, blood pressure readings from the quarter of their death were excluded from the analysis.
- Patients with a diagnosis of diabetes (as primary cause of renal replacement therapy or as a co-morbidity) were excluded as systolic BPs were higher than in non-diabetics, and their risk factors are different).
- Patients were censored if they changed modality or were lost to follow up.
- Patients who died within the first 90 days of starting renal replacement therapy were excluded from the analysis.

The final sample included 2181 pre-dialysis incident non-diabetic HD patients and 1642 post-dialysis incident non-diabetic HD patients.

The principal outcome in this analysis was all-cause mortality during the first year after 90 days. The effects of both systolic (SBP), diastolic (DBP) and pulse pressure (PP), pre- and post-dialysis, on total mortality were analysed using Cox proportional hazards regression with age as a linear variable. These BP measurements were categorised and the proportional hazard measured relative to a reference category.

Results

Table 11.2. Study cohort

Number included	2181
Mean Age	63 years
Percentage Male	63%
Died (%)	218 (10%)
Mean Systolic BP pre HD (s.d.)	148 (21) mm Hg
Mean Systolic BP post HD (s.d.)	138 (21) mm Hg
Mean Diastolic BP pre HD (s.d.)	79 (11) mm Hg
Mean Diastolic BP post HD (s.d.)	75 (12) mm Hg
Pulse pressure pre HD (s.d.)	68 (16) mm Hg
Pulse pressure post HD (s.d.)	63 (17) mm Hg

Figures 11.33–11.34 show the results of age adjusted Cox proportional hazard model relating systolic blood pressure to one year mortality. There is a non linear inverse relationship between pre-HD systolic blood pressure and mortality although only patients with a systolic blood pressure above 160 mm Hg had a significantly different survival (better) from patients with a BP of 140–149. There was no significant relationship between survival and post HD systolic BP.

Figures 11.35–11.36 show the results of age adjusted Cox proportional hazard model relating pulse pressure to all cause mortality at one year. There is a non-linear relationship between pre-HD pulse pressure and mortality but no significant relationship post-HD. A low pulse pressure pre HD (<40 mmHg) is associated with a significantly greater risk of death than the reference group of 40–49 mm Hg.

The relationship between systolic blood pressure, pulse pressure and death is shown in Figure 11.37. A widening pulse pressure may be associated with greater mortality risk only when the systolic blood pressure is <119 mmHg (i.e. very low diastolic pressures and diastolic dysfunction). With high systolic pressure the combination with higher diastolic pressure was associated with the highest risk of death.

This analysis shows the risk of death within the first year of dialysis is greatest for

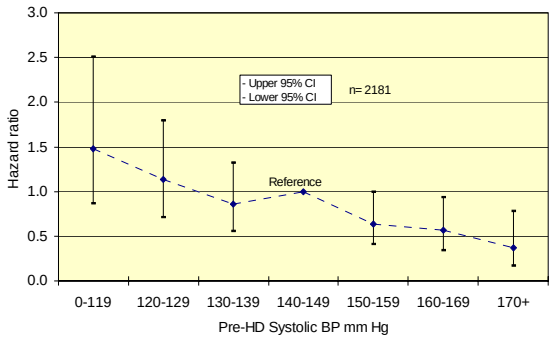

Figure 11.33. Hazard ratio for first year mortality associated with pre-HD systolic BP

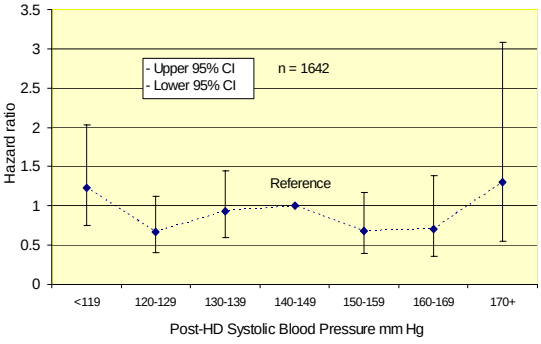

Figure 11.34. Hazard ratio for first year mortality associated with post-HD systolic BP

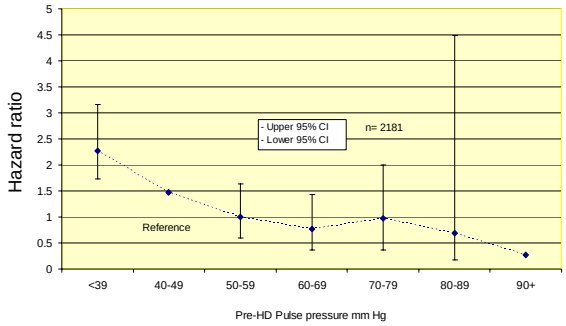

Figure 11.35. Hazard ratio for first year mortality associated with pre-HD pulse pressure

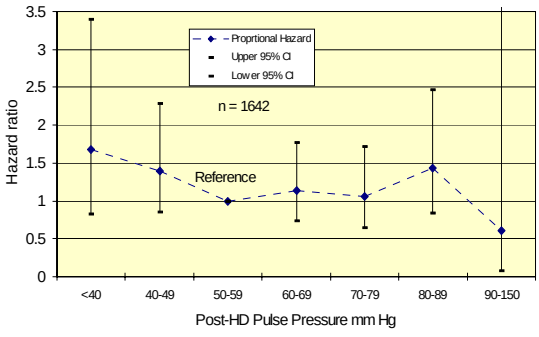

Figure 11.36. Hazard ratio for first year mortality associated with post-HD pulse pressure

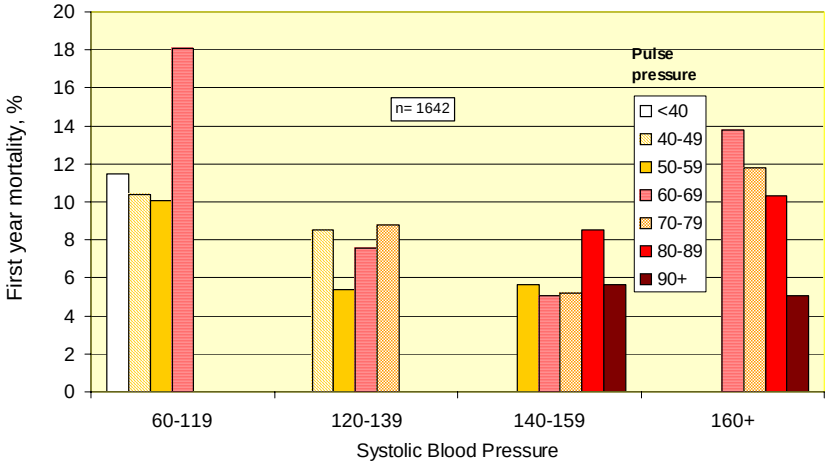

Figure 11.37. % of patients who died in 1st year by post-HD systolic BP and pulse pressure

patients with low systolic blood pressure and high pulse pressure, i.e. patients with cardiac failure. Although patients with blood pressure readings above the Renal Association standards are at low risk of dying during the first year on haemodialysis, hypertension precedes cardiac failure by many years. It will take a longer period of observation to demonstrate the true association between hypertension and mortality in this haemodialysis population.

Cholesterol and achievement of the Standard

Hyperlipidaemia is common in the dialysis population. The typical changes are raised triglycerides, low high-density lipoprotein (HDL) and variable changes in low-density lipoprotein (LDL) and total cholesterol. Less than a quarter of cardiac mortality is attributed to acute myocardial infarction, a condition potentially avoided by lowering cholesterol. More common causes of cardiac death such as cardiac arrest and arrhythmia may not be related to serum cholesterol concentration. There is a J-shaped relationship between cholesterol level and short term mortality in the dialysis population.[10,11] Last year's report indicated optimal survival for a cholesterol range between 5 and 8 mmol/L, presumably reflecting better nutrition. Malnutrition, chronic disease and chronic inflammation are all associated with low cholesterol levels and are major independent risk factors for death. Co-morbidity adjustments and statin use will help unravel these confounding associations. As discussed at the start of this chapter, the Registry needs to investigate methods to facilitate collection of this data item by renal units.

Atherosclerosis is an inflammatory process and in the general healthy population, C-reactive protein (CRP) is a stronger predictor of future cardiovascular events than LDL-cholesterol.[12] The Framingham risk score and European SCORE system do not take CRP into account. A single CRP level using a high-sensitivity assay has been shown to have prognostic value for both haemodialysis and peritoneal dialysis populations.[13,14] Generally the process of haemodialysis is considered to be pro-inflammatory. However, the Finnish Registry in 2002 showed no difference in CRP concentrations between haemodialysis and peritoneal dialysis populations.[9] The Renal Registry will now start to collect CRP as part of the data returns from centres that download this item in their laboratory link.

The Renal Association set standards for lipids for the first time in August 2002.[7] 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 <3mmol/L

Secondary prevention:

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

The Renal Association does not specify separate standards for patients with established cardiovascular disease, diabetics or renal transplant patients. Neither does it recommend how frequently lipids should be measured.

European guidelines suggest the dialysis standards should also be applied to transplant patients.[15] Patients with established cardiovascular disease and diabetics have lower targets (total cholesterol <4.5 mmol/L and LDL-cholesterol 2.5 mmol/L).[16] Lipid profiles are advised annually for transplant patients and every 6 months for dialysis patients.[15] Blood samples should be taken immediately before dialysis or at least 12 hours after, preferably with the patient in a fasting state.

Currently few UK renal units collect data on fasting samples or full lipid profiles but a number of units will collate detail of the latter as part of the SHARP trial and the Renal Registry will present this data if sufficient numbers of units participate. The current audit is based on random, non-fasting total cholesterol measurements only.

For audit purposes, the Renal Registry is seeking ways to collect the following new data sets:

- CRP every 6 months
- Statin use.

Achievement of cholesterol standard

Figures 11.38–11.44 show wide variation between units achieving the cholesterol standard. In England and Wales, the number of patients achieving the standard for HD average 75.3% (range 52–86%), 55.2% for PD (range 27–77%) and 51% for transplant (range 27–76%). Chi squared testing indicates the variation between centres for each treatment modality is significant ($p < 0.0001$).

Cholesterol levels are lower in haemodialysis patients; the median cholesterol concentration for HD, PD and transplant is 4.3, 4.9

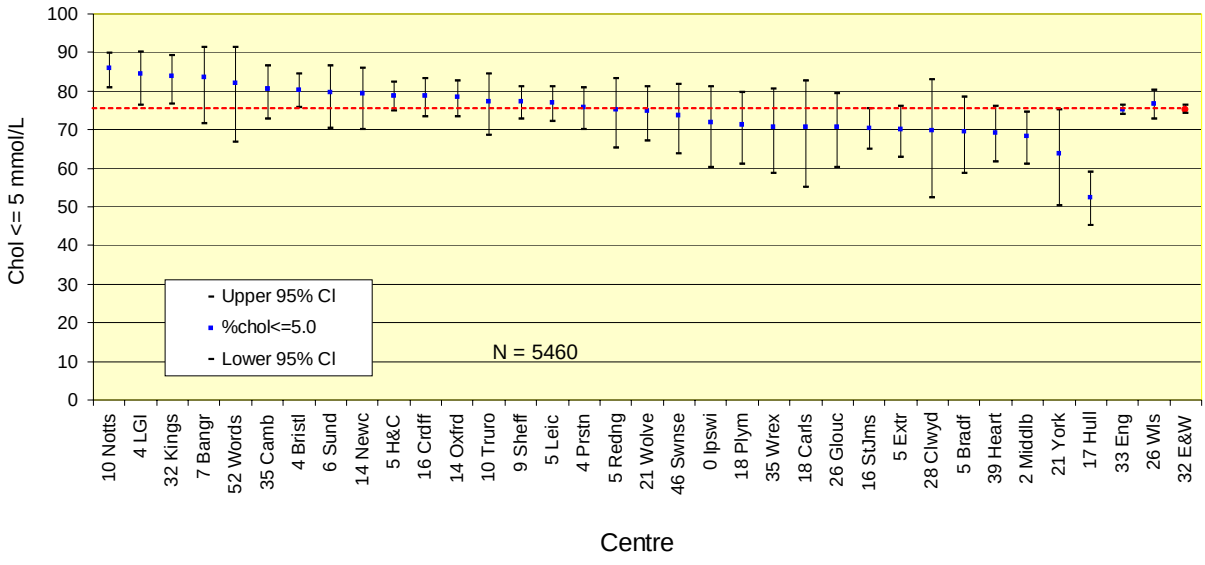

Figure 11.38. Percentage of patients with cholesterol <5 mmol/L; HD

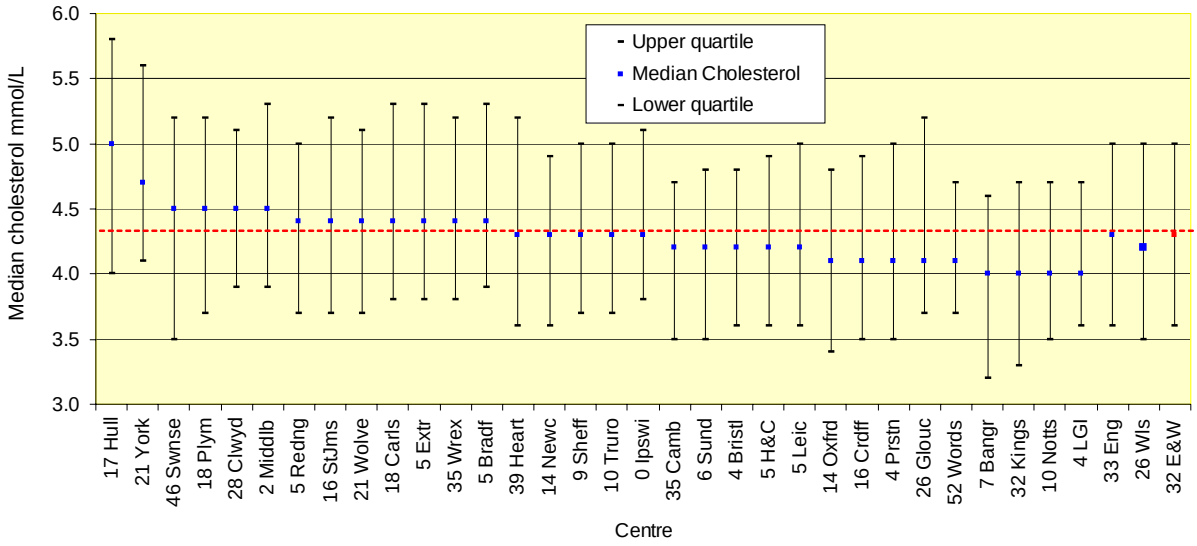

Figure 11.39. Median cholesterol; HD

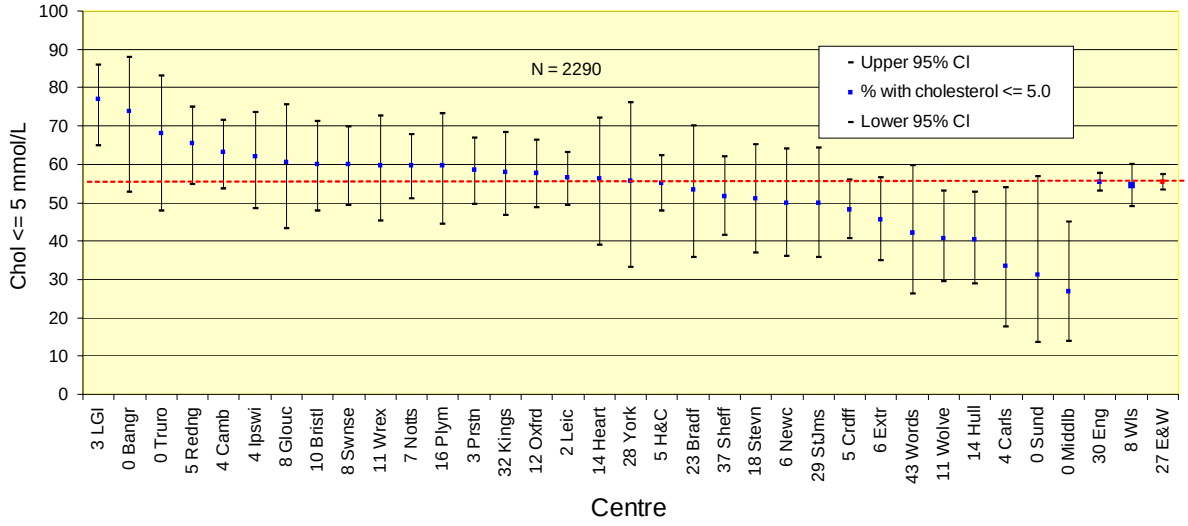

Figure 11.40. Percentage of patients with cholesterol <5 mmol/L; PD

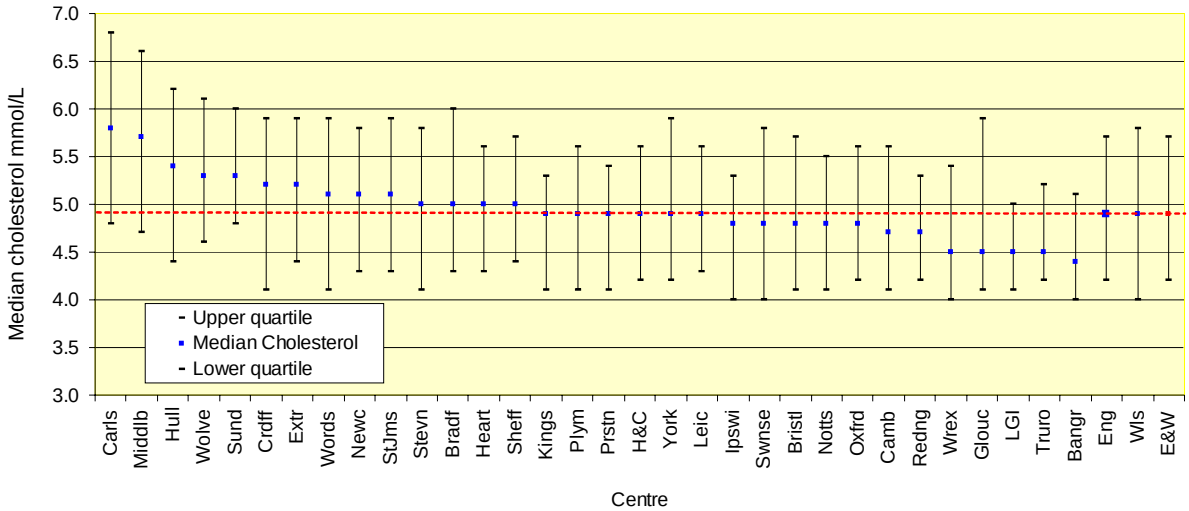

Figure 11.41. Median cholesterol; PD

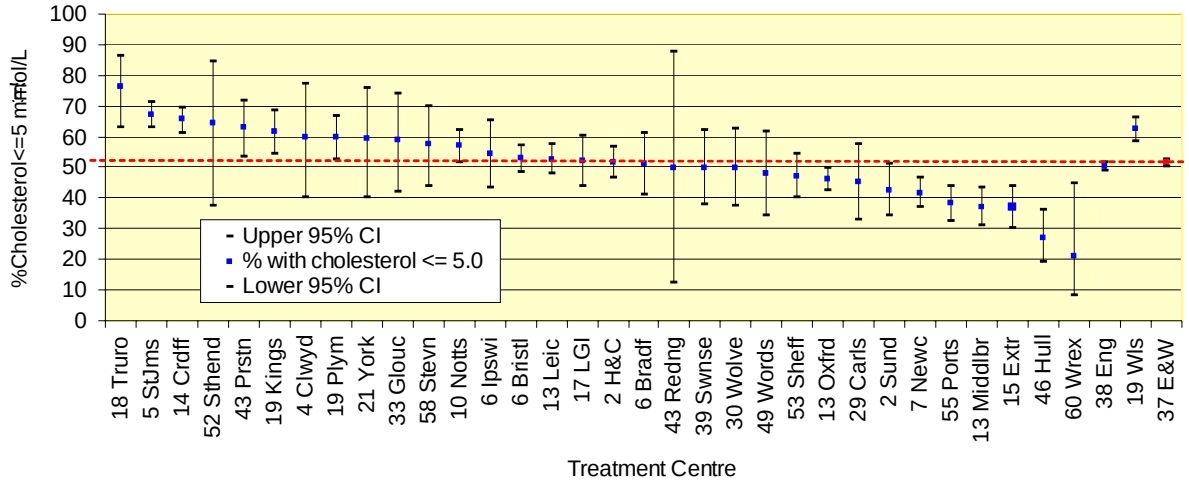

Figure 11.42. Percentage of patients with cholesterol <5 mmol/L; transplant

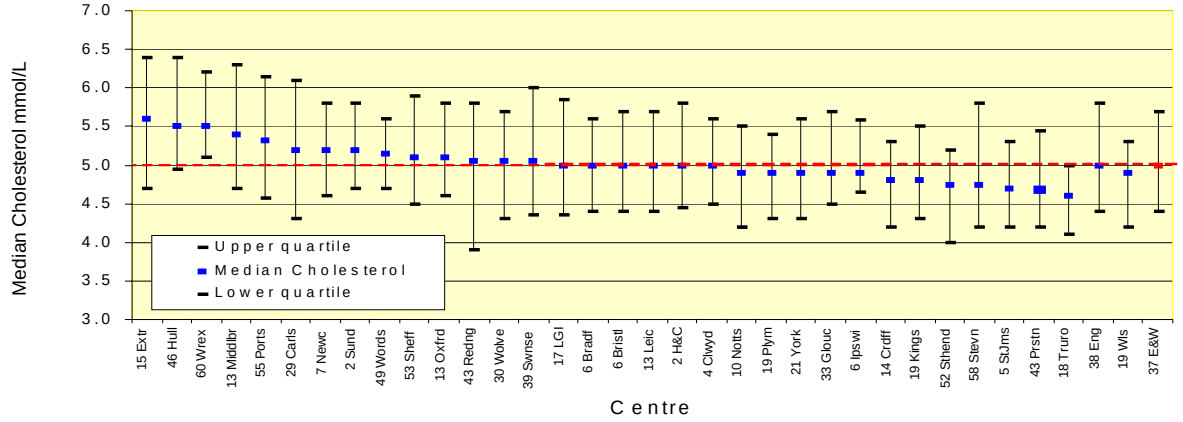

Figure 11.43. Median cholesterol; transplant

and 5.0 mmol/L respectively. Possible explanations include better targeting with statin therapy, exposure to inflammatory processes during haemodialysis and concentration of the sickest patients (malnourished with the greatest co-morbidity) on the haemodialysis programme. In addition, PD patients are in a 'nephrotic' protein loss state and may have increased cholesterol production (see cholesterol and modality change below).

Figures 11.45–11.47 show that diabetic patients have lower cholesterol concentrations compared to non-diabetics for each treatment modality. The difference is most marked for transplant patients.

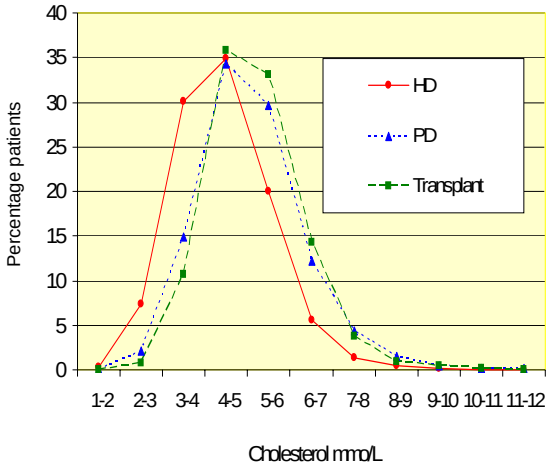

Figure 11.44. Serum cholesterol distribution by modality 31/12/2002

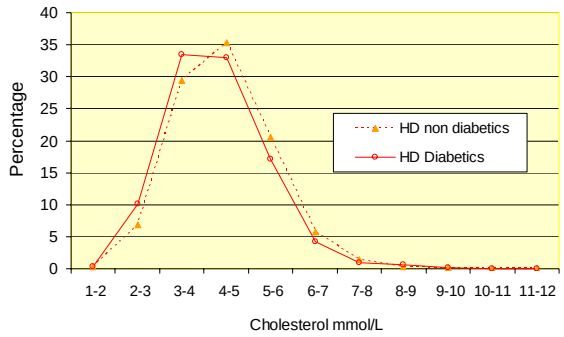

Figure 11.45. Distribution of serum cholesterol diabetics v non-diabetics; HD

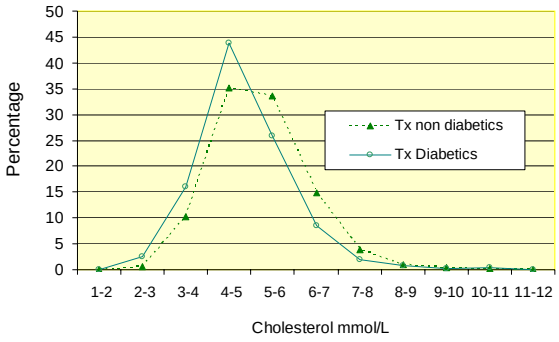

Figure 11.47. Distribution of serum cholesterol diabetics v non-diabetics; transplant

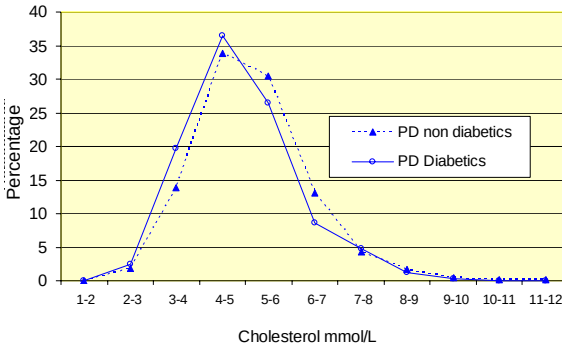

Figure 11.46. Distribution of serum cholesterol diabetics v non-diabetics; PD

Change in cholesterol achievement 1997–2002

Figure 11.48 shows the cholesterol data for all treatment modalities between 1997 and 2002 and Figures 11.49 and 11.50 show these data by each centre. Over these 5 years the concentration of total cholesterol has decreased in all treatment groups. The percentage of patients achieving the stan-

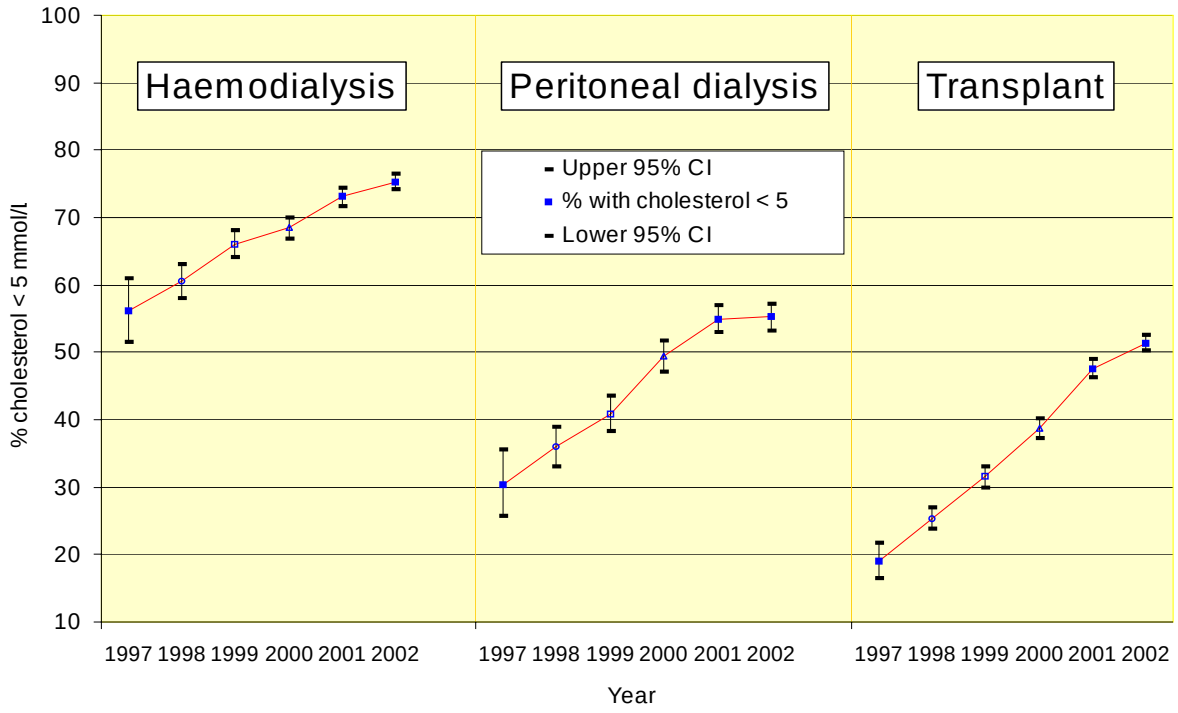

Figure 11.48. % of patients with cholesterol <5 mmol/L HD vs PD vs Tx 1997–2002

dard over this period has risen by 36%, 80% and 150% for HD, PD and transplant respectively. However, the number of PD patients achieving the cholesterol standard plateaued between 2001 and 2002. By comparison, Finnish Registry data shows cholesterol has decreased in all treatment groups between 1999 and 2002 because of a reduction in LDL-cholesterol. In Finland, triglyceride levels have remained static with higher levels in PD patients and HDL-cholesterol levels have also remained constant with higher levels in transplant patients.

Cholesterol levels following modality change

Figure 11.51 shows the change in serum cholesterol when patients switch from one treatment modality to another. The means have been adjusted for the fall in cholesterol for each modality each year. When patients transfer from PD to HD the mean serum cholesterol falls by 0.58 mmol/L. The drop in cholesterol occurs within the first quarter and is maintained over the following year. It is not clear whether systemic inflammation induced by HD or withdrawal of PD solutions are responsible for the fall in cholesterol level. By contrast when dialysis patients are transplanted their cholesterol levels rise within the first quarter by 0.59 mmol/L. These levels are sustained until the end of the first year when the mean cholesterol falls by 0.2 mmol/L. This may reflect hyperlipidaemia induced by immunosuppression as higher doses are used initially to prevent acute rejection.

Serum cholesterol and mortality

Figure 11.52 shows a J-shaped association between cholesterol level and mortality for HD and PD poppulations in England & Wales over the 1 year period in 2001. Only 1% of patients have cholesterol levels outside the range 2.5–9 mmol/L and within this range the curve is the same as last year. The Registry has not previously produced a separate analysis by dialysis modality. Short-term survival is optimal for a serum cholesterol level of 5–7.5 mmol/L for HD patients and 5–9 mmol/L for PD patients. A raised serum cholesterol in PD patients appears to have less impact on short term survival than in HD patients.

A recent prospective study of 823 HD patients shows the inverse association between cholesterol level and mortality is due to the cholesterol-lowering effect of systemic inflammation and malnutrition, not to a protective effect of high cholesterol concentration.[17] This supports treatment of raised cholesterol in the dialysis population. Following the publication of this study, the UK data has been reanalysed adjusting for the effect of albumin (Figure 11.53). As albumin methodology is split between BCG and BCP, the analysis included only sites using the BCG methodology as there were insufficient numbers for a separate BCP analysis. After adjustment for albumin, the relative risk of a raised cholesterol increases in the HD population. These data need to be analysed over a longer term.

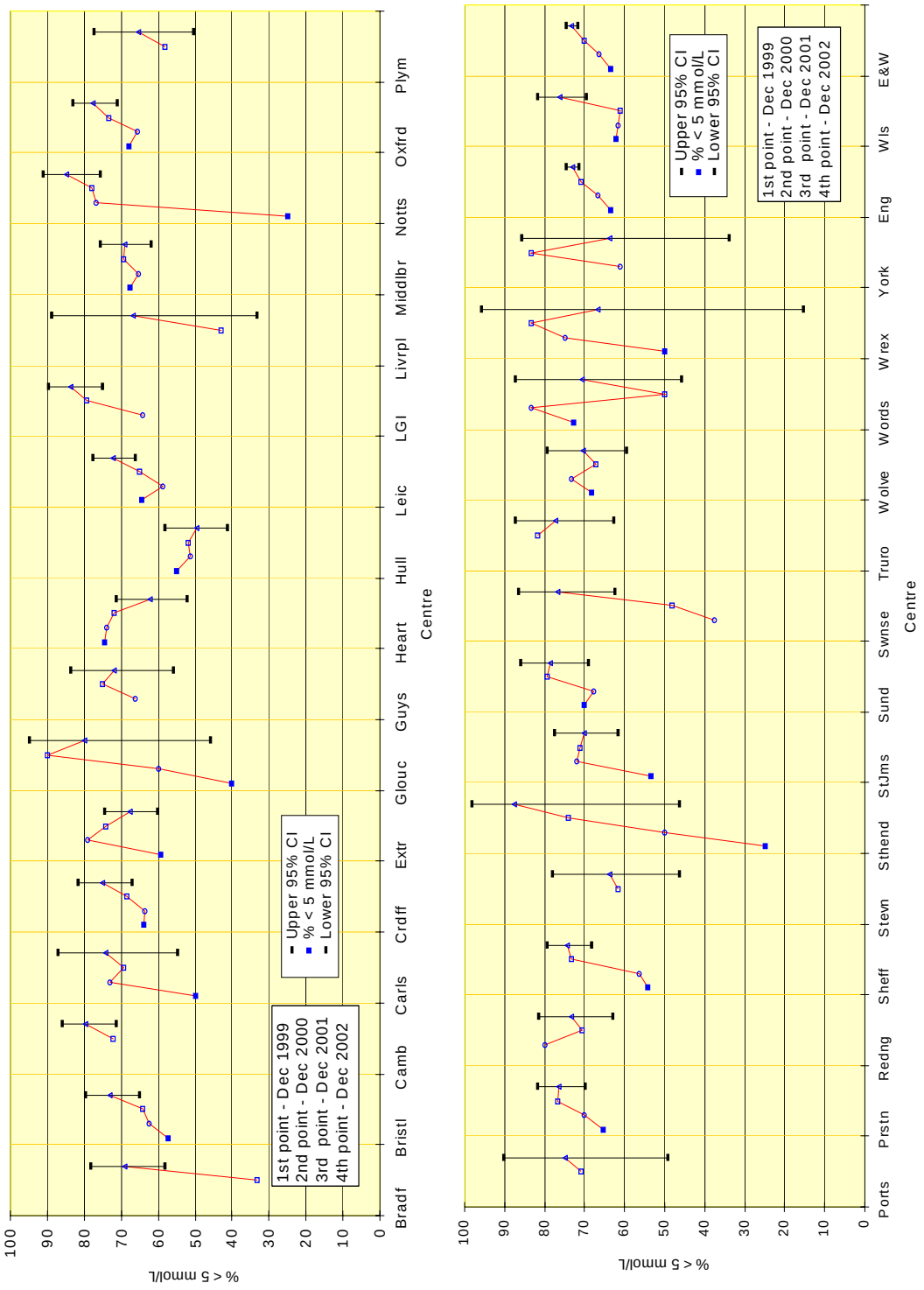

Figure 11.49. Change in % of HD patients with cholesterol <5 mmol/L by centre 1999–2002

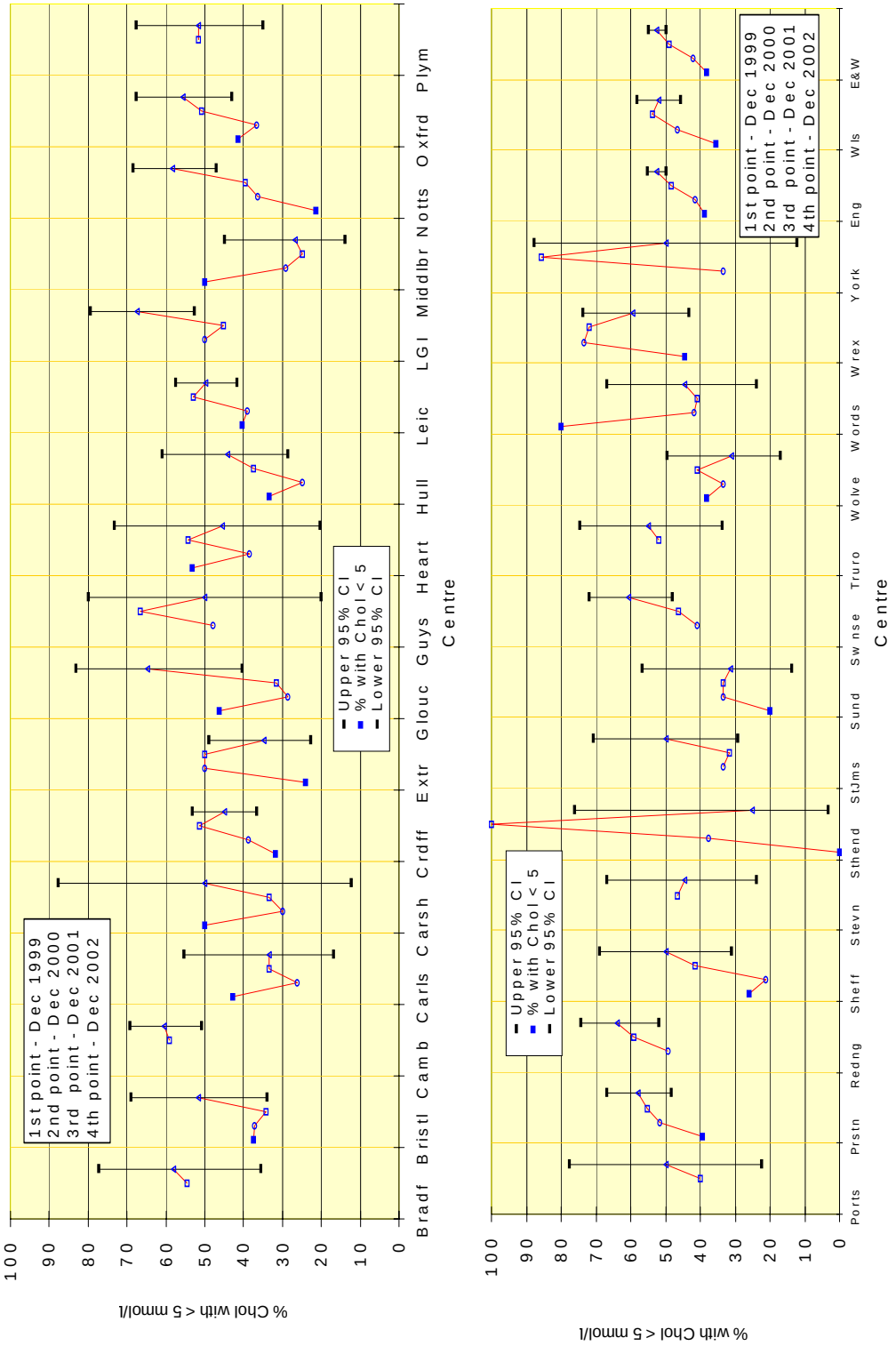

Figure 11.50 Change in % of PD patients with cholesterol <5 mmol/L by centre 1999–2002

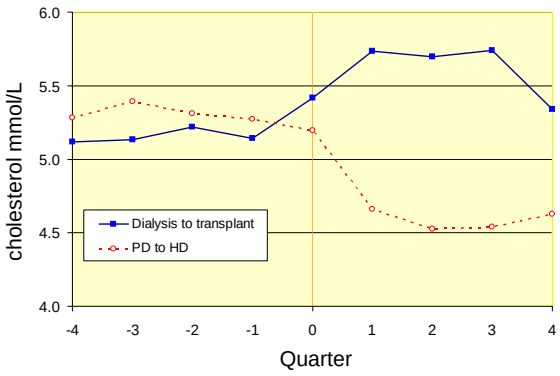

Figure 11.51. Serum cholesterol by quarter before and after modality change

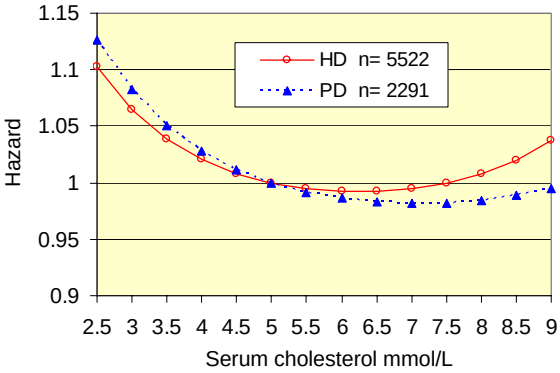

Figure 11.52. Serum cholesterol and relative hazard, by dialysis modality

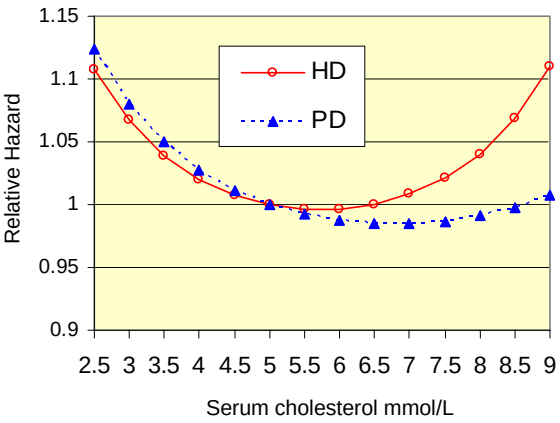

Figure 11.53. Serum cholesterol and relative hazard adjusted for albumin

In Lowrie's original report from 1990, the relative risk of death for HD patients with cholesterol <2.5 mmol/L or >9.3 mmol/L was 4.0 and 1.3 respectively.[11] The relative risk of death for these cholesterol levels in our population are very much lower, 1.1 and 1.05 for HD and 1.125 and 1.0 for PD. Age and diabetes increases risk of death at any given cholesterol level. The hazard ratios for each 1 year increase in age for HD, PD, and transplant are 1.03, 1.043, and 1.039 respectively. The hazard ratios for diabetes are 1.75, 1.84, and 1.87 respectively. This is comparable with iDOPPS data that shows risk of death on haemodialysis increases by 1.036 for each year and doubles for diabetes.

Clinical trials of cholesterol lowering in chronic renal failure

The UK Heart and Renal Protection study showed simvastatin 10mg/d reduced total cholesterol in dialysis patients by 20%, LDL by 26%, triglycerides by 13% but HDL levels remained stable.[18] SHARP, an international randomised trial (Study of Heart and Renal Protection), is designed to assess the impact of lowering cholesterol on major vascular outcomes and progression of chronic kidney failure. A combination of simvastatin and ezetimibe will be used to achieve the lowest cholesterol level possible. Recruitment is currently in progress and it is important that all UK nephrologists support enrolment into this study. The Clinical Trials Support Unit in Oxford can be contacted on 01865 404846.

The 4D study is expected to provide insight into the link between triglycerides and cardiovascular outcomes. Type 2 diabetics on haemodialysis are assigned either atorvastatin 20mg daily or placebo and the results are expected in 2004.

Acknowledgements

Dr Sarju Shrestha, Clinical Research Fellow, Southmead Hospital for the analysis on blood pressure, pulse pressure and mortality in incident haemodialysis patients.

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