

## **Chapter 11: Renal Transplantation**

### ***Summary***

Variation exists between centres with respect to access to renal transplantation for patients receiving renal replacement therapy

There appears to be a marked difference between centres in attitude towards transplanting diabetics.

The annual death rate of patients with established renal transplants is low at 2.9% for the whole UK (including patients with failed grafts returning to dialysis).

3.1% of all patients starting dialysis in the UK in 1999 were patients with failed transplants.

The quality of transplant function differs significantly between centres, as does the haemoglobin level.

Differences in modifiable risk factors for cardiovascular disease such as serum cholesterol and blood pressure also exist. Control of these factors is often poor.

In some centres up to 50% of patients did not have a blood pressure or serum cholesterol measurement returned to the Registry for 1999.

### ***Introduction***

A chapter combining data with UK Transplant is presented in Chapter 20. This chapter is written using data from the Renal Registry, with an emphasis on access to transplantation, quality of transplant function, haemoglobin and potentially modifiable cardiovascular risk factors such as blood pressure and cholesterol.

### ***Transplants performed 1999***

Once again, the intention is to provide data on transplant activity for patients on Renal Replacement Therapy in units participating in the Registry. Thus, data on patients transferring in from non-registry units specifically for transplantation are excluded, but data on patients from registry units transferring to non-registry units for transplantation are included.

During 1999, 651 patients under follow up in participating units received a renal transplant. Details are given in tables 11.1 and 11.2.

In 1999, 64.7% of newly transplanted patients in the UK were male and 35 % female (0.3% unknown). The gender distributions for both England and Wales and Scotland were similar. Table 11.2 shows the primary renal diagnosis in newly transplanted patients mirrors that in the established transplant population.

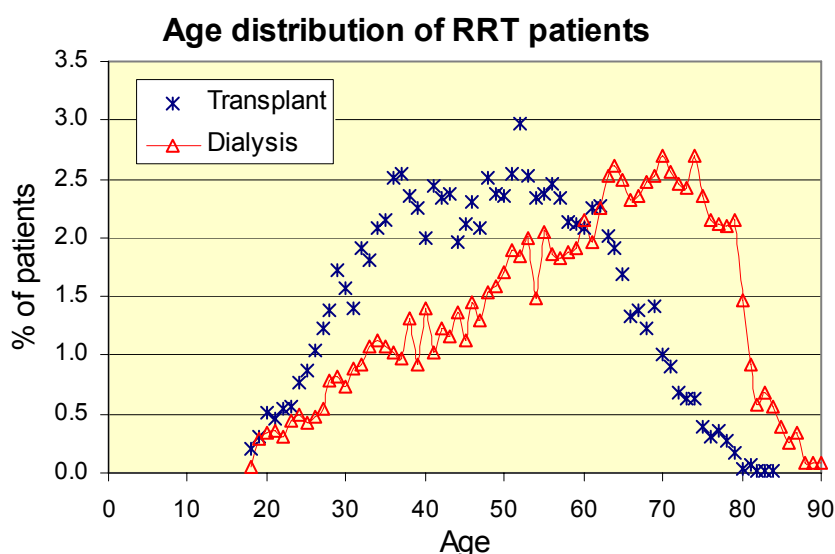
	Median age	Number
E&W (23 renal units)	43	506
Scotland (all units)	42	145
<b>Total Registry</b>	<b>43</b>	<b>651</b>

**Table 11.1 New transplants from the Registry 1999**

	New transplants in 1999		Established transplants 1/1/99	
	%	No	%	No
Aetiology unc. /Glomer. NP	20.4	133	23.0	1607
Glomerulonephritis	22.1	144	18.5	1295
Pyelonephritis	16.3	106	18.6	1302
Diabetes	7.8	51	6.2	433
Renal Vascular disease	0.9	6	1.2	85
Hypertension	3.5	23	4.9	343
Polycystic Kidney	10.9	71	11.5	803
Not sent	4.1	27	2.0	143
Other	13.8	90	14.0	975

**Table 11.2 Primary diagnosis of transplant patients in the UK**

### ***Patients with established renal transplants***



**Figure 11.1 Age histogram of dialysis and transplant patients**

The age distribution of the prevalent transplant patients for 1999 is shown in figure 11.1. The median age was 43 years compared with 61 years for the dialysis population from which they were drawn. The age distribution is consistent with the previous years report. In the UK 13% of prevalent and 5% of new transplant patients were over 65 years.

The proportion of prevalent patients aged less than 65 years receiving renal replacement therapy according to treatment modality at the end of 1999 is shown for each participating centre in figure 11.2. This age cut off is used, as most patients receiving a renal transplant for

the first time are less than 65 years old. All but 3 centres provide care for renal transplant recipients. The proportion of RRT stock composed of transplant patients for each centre varies between 14-80%. Overall for the UK, 57% of the RRT stock under the age of 65 years is made up by transplant patients. If all patients receiving RRT are included (i.e. those over 65 years old as well), this proportion falls to 47%.

For individual Registry units, the proportion of the prevalent dialysis patients under 65 years old that had ever had a renal transplant is illustrated in figure 11.3. These figures are an underestimate, as some patients had no information regarding previous transplantation when transferring in on dialysis from a non-registry unit, and are treated as unknown. In spite of this, there are wide variations (4.2-34.3%) between centres in apparent access to transplantation. Plausible explanations for these variations include a difference in the age of units. Patients in older units are likely to have had a longer exposure to possible transplantation than in newer units and older units are likely to have a larger stock of transplant patients. In addition there may be differences in the proportion of prevalent dialysis patients made up by ethnic minorities (harder to HLA match and thus transplant) as well as differences in selection criteria for accepting patients onto the waiting list. With more complete returns from participating centres, the Registry should have sufficient data in the future to test some of these hypotheses.

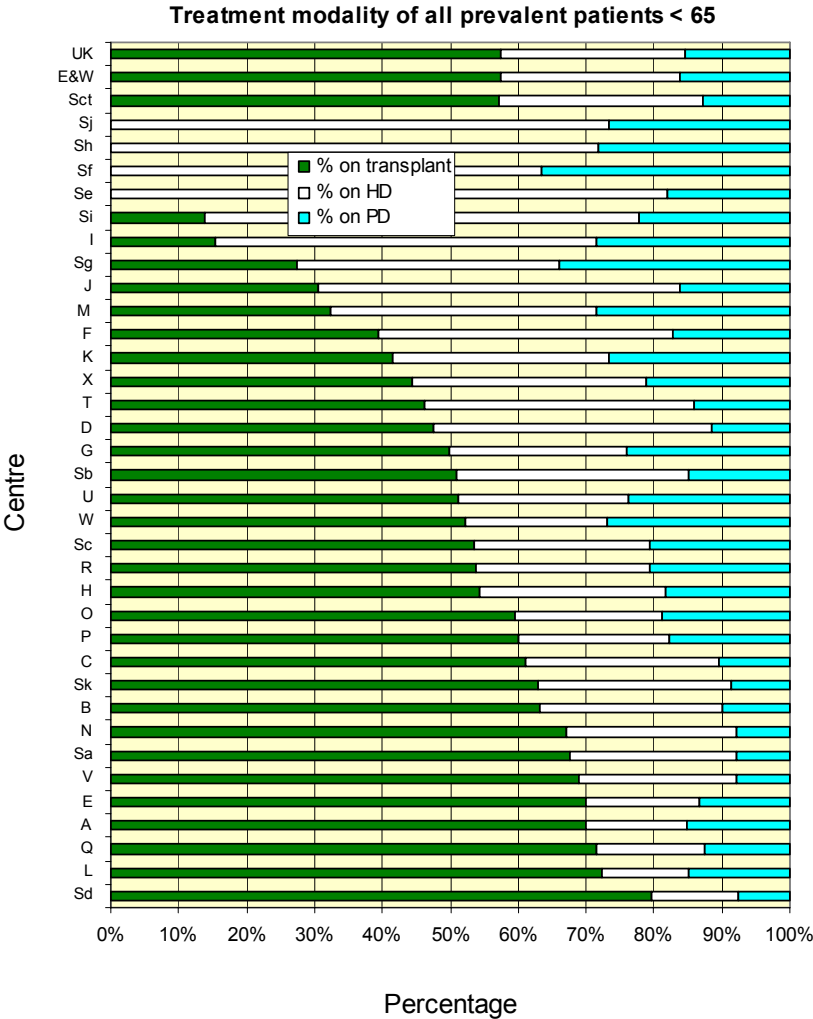
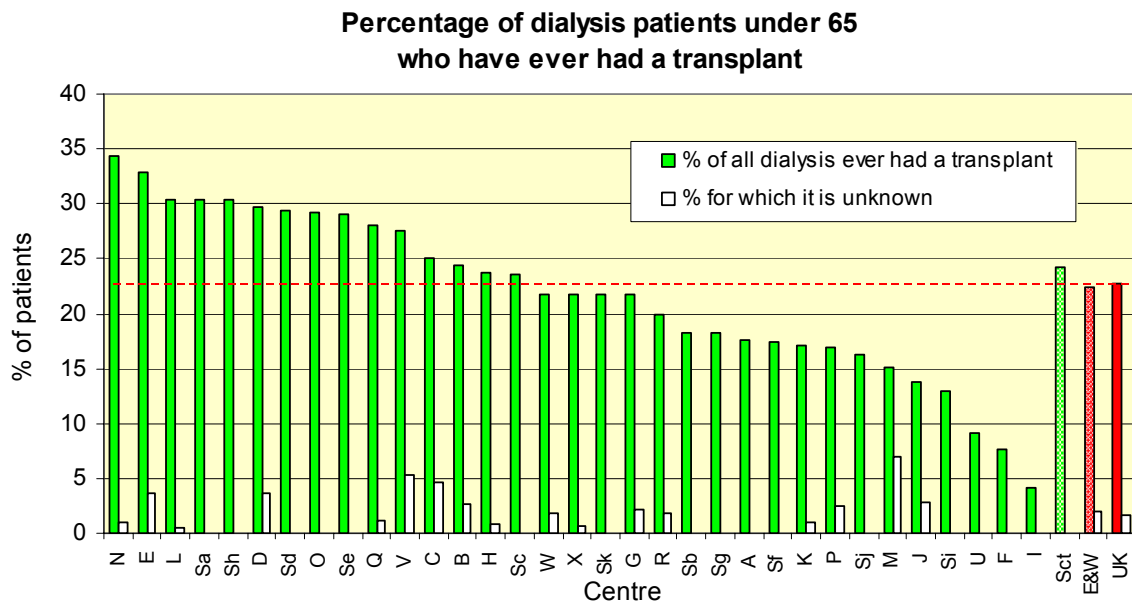


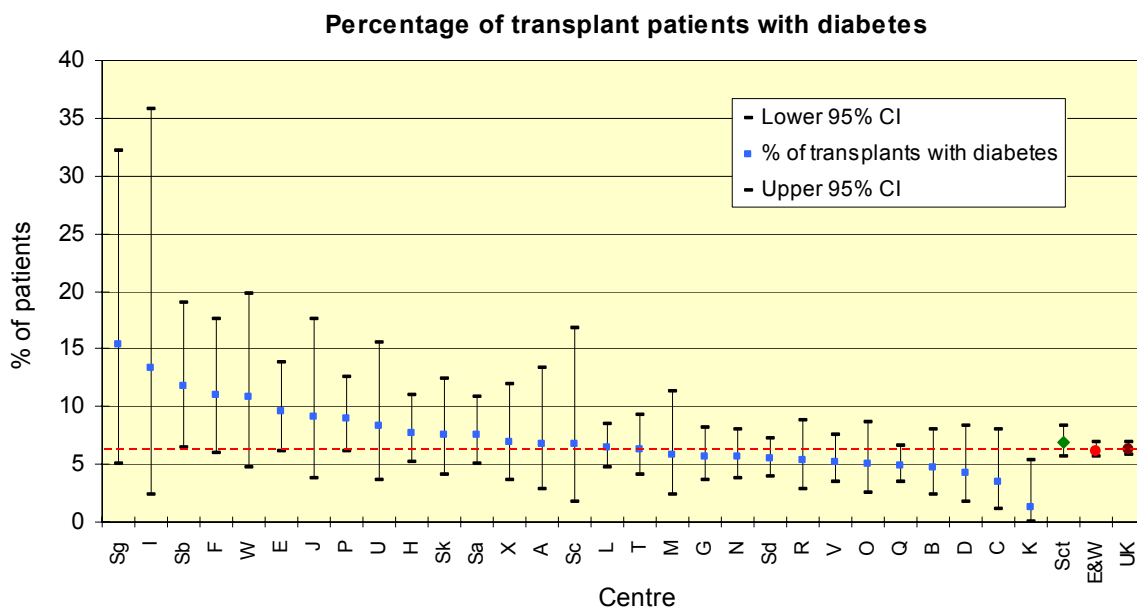
Figure 11.2 Treatment modality of all prevalent patients < 65



**Figure 11.3 Percentage of prevalent dialysis patients age <65 years who have ever received a renal transplant**

### ***Transplantation in patients with diabetes mellitus***

The recently published European Best Practice Guidelines for Renal Transplantation advise that “Kidney transplantation should be considered as the first therapeutic choice for all suitable patients with end-stage renal disease due to diabetes mellitus, because kidney transplantation is able to significantly extend survival as compared with dialysis (Evidence level B)”<sup>1</sup>. Figure 11.4 shows the proportion of all patients in each registry centre with a functioning renal transplant on 31/12/99 whose primary diagnosis was diabetes mellitus.



**Figure 11.4 Percentage of current transplant patients with diabetes mellitus, by centre**

In addition, the proportion of patients with a primary diagnosis of diabetes mellitus at each centre whose renal replacement therapy on 31/12/99 was with a functioning renal transplant is illustrated in figure 11.5.

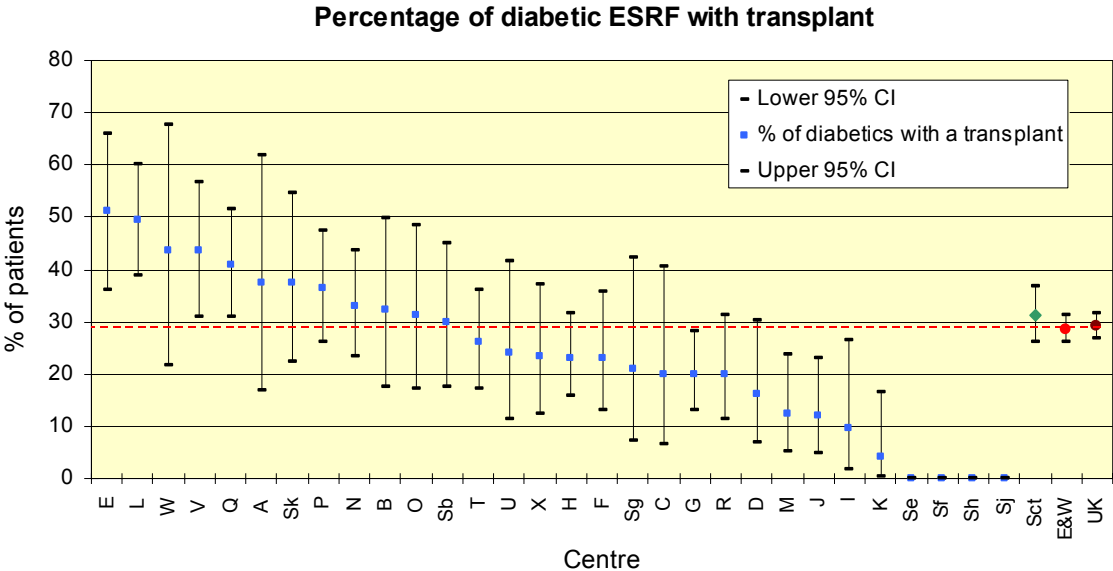


Figure 11.5 Percentage of diabetic ESRF patients with a transplant, by centre

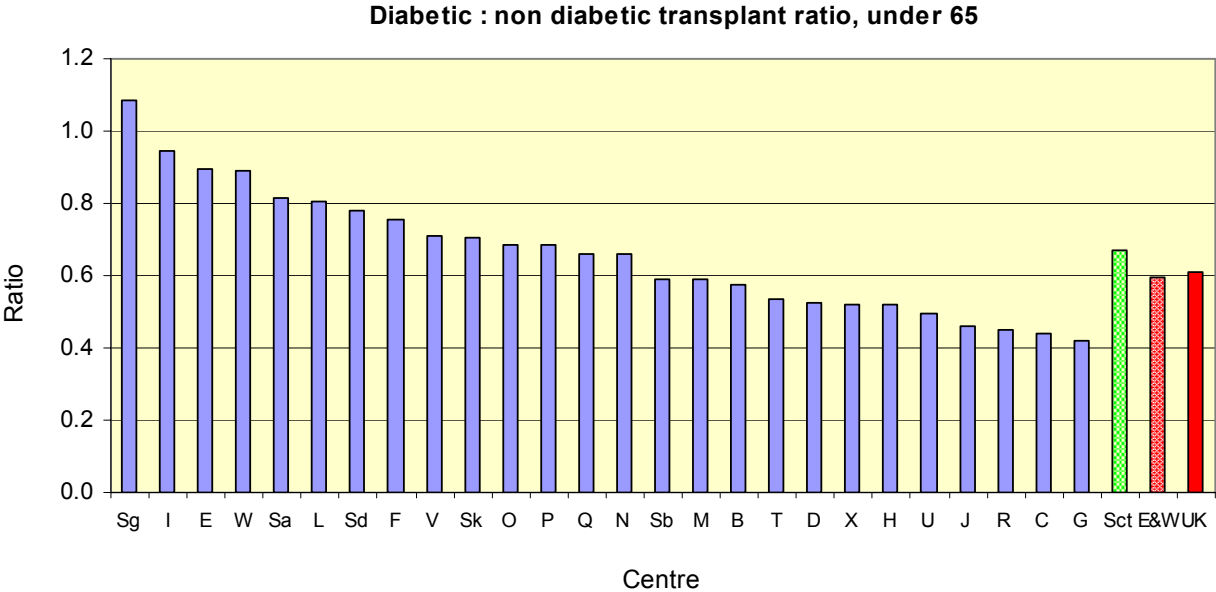


Figure 11.6 Ratio of % patients with a transplant under 65, diabetics : non-diabetics

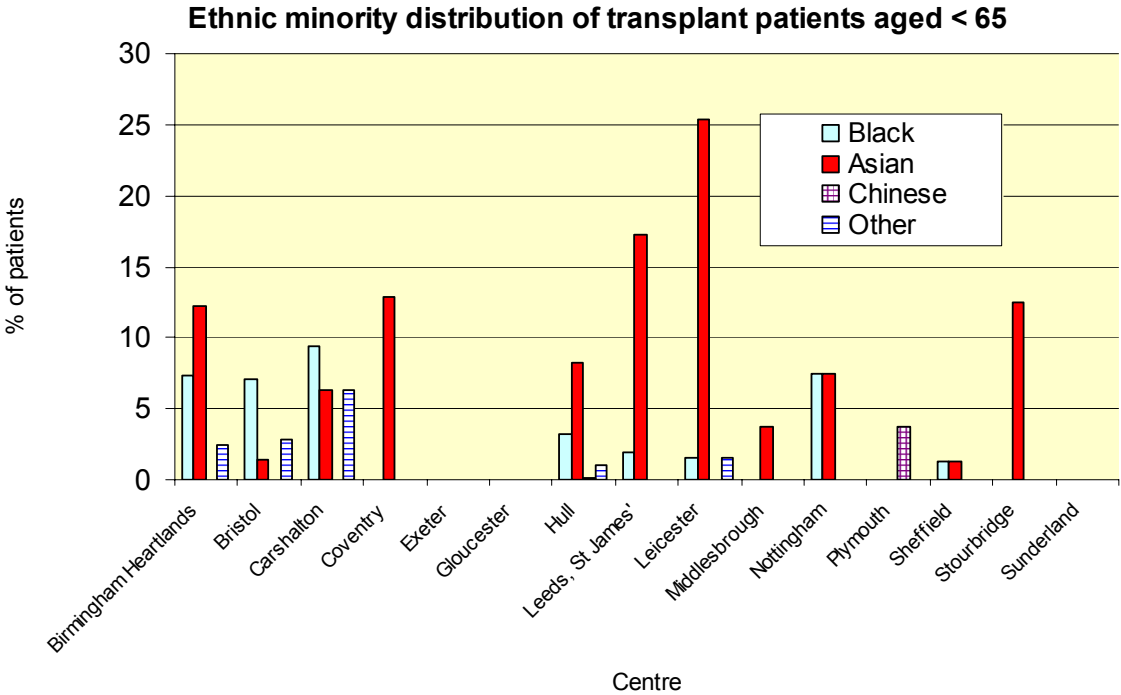
There is a wide variation (0-51.2%) between centres in the proportion of diabetic patients with end-stage renal failure that have a transplant. In order to explore a possible difference in access to transplantation for diabetic patients between centres, the proportion of transplanted diabetic patients and transplanted non-diabetic patients under 65 was expressed as a ratio for each centre (figure 11.6). This age limit was used in an effort to make the populations comparable, as most patients receiving a transplant are under 65, and diabetic patients on RRT have a lower median age than other patients. Centres with fewer than 20 diabetic patients aged under 65 have been excluded from the figure.

To identify reasons for these observed differences between centres, a number of variables would need to be examined. These include the overall percentage of live RRT patients with diabetes, the median age of this diabetic cohort, and the percentage of the cohort originating from ethnic minorities (and thus likely to experience difficulty in HLA matching). Some of the difference in the proportion of transplant patients with a primary diagnosis of diabetes mellitus observed between centres could be accounted for by differences in these variables.

Overall, RRT patients with diabetes mellitus seem less likely to receive a transplant than other patients on RRT presumably due to significant co-morbidity making them less suitable for transplantation. However, attitudes towards transplantation of diabetic patients appear to differ between units.

**Ethnicity**

Figures 11.7 and 11.8 compare the ethnic minority distribution for each centre of prevalent renal transplant patients (end of 1999) under age 65 and renal replacement therapy patients under 65 who have never received a transplant.



**Figure 11.7 Ethnic minority distribution of transplant patients < 65 by centre**

The centre names are shown to preserve anonymity so that the centres with a percentage of ethnic minorities cannot be identified from the prevalence chapter.

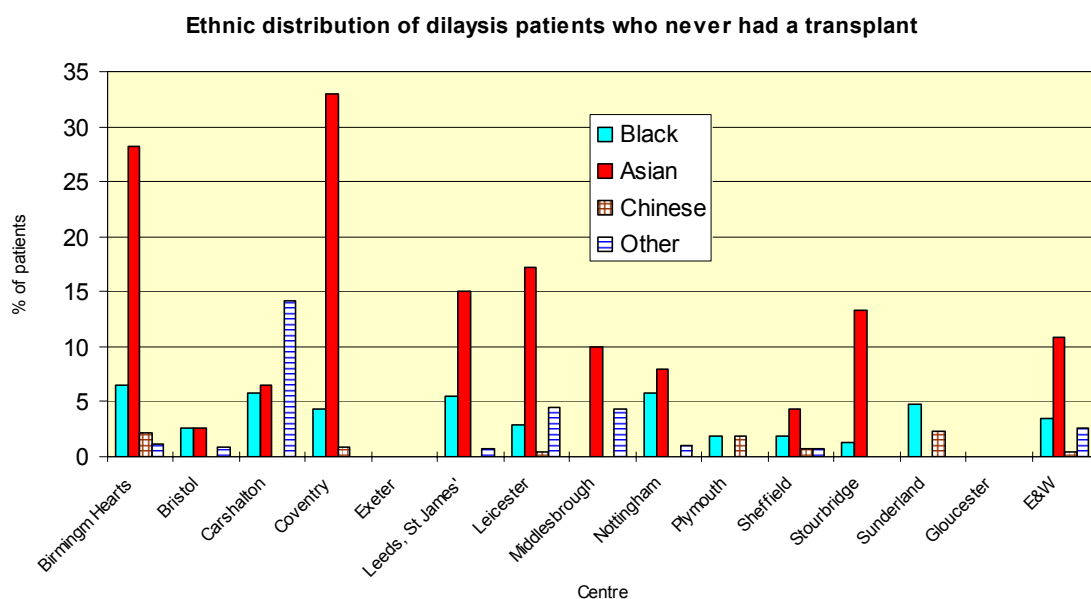


Figure 11.8 Ethnic minority distribution of dialysis patients who have never had a transplant

### Failed transplants

Within the participating centres, 3% of all patients commencing dialysis in 1999 were patients whose renal transplants had failed during the year as opposed to new patients on Renal Replacement Therapy. The percentage in Scotland was 3.4% and for the UK as a whole it was 3.1%. In last year's report it was incorrectly stated that 9% of all patients commencing dialysis in 1998 were individuals with failed transplants. The correct figures should have been 3.1% for England and Wales and 3.2% for the UK as a whole.

### Survival of patients with established renal transplants

Table 11.3 shows the one-year patient survival for established transplant patients alive on 1/1/99. Patients who had been transplanted within six months prior to this date were excluded from these figures as they were still considered to be in the post-operative high-risk period. Survival was calculated both censoring at return to dialysis and with continuing follow-up of patients after return to dialysis (Table 11.3). The overall annual death rate for the UK is 2.8% (censored at dialysis).

	Transplant censored at dialysis			Transplant including dialysis returns		
	E&W	Scot	UK	E&W	Scot	UK
<b>No. of patients</b>	5228	1259	6487	5228	1259	6487
<b>No of deaths</b>	138	35	173	149	38	187
<b>Death rate</b>	2.7	2.9	2.8	2.9	3.1	2.9
<b>(95% CI)</b>	2.3 - 3.2	2.0 - 4.0	2.4 - 3.2	2.5 - 3.4	2.2 - 4.2	2.6 - 3.3
<b>K-M 1 yr survival</b>	97.3	97.2	97.3	97.2	97.0	97.2
<b>(95% CI)</b>	96.9 - 97.8	96.3 - 98.0	96.9 - 97.8	96.7 - 97.8	96.3 - 97.7	96.7 - 97.6

Table 11.3 Survival during 1999 of established transplant patients alive 1.1.99

## Quality of transplant function

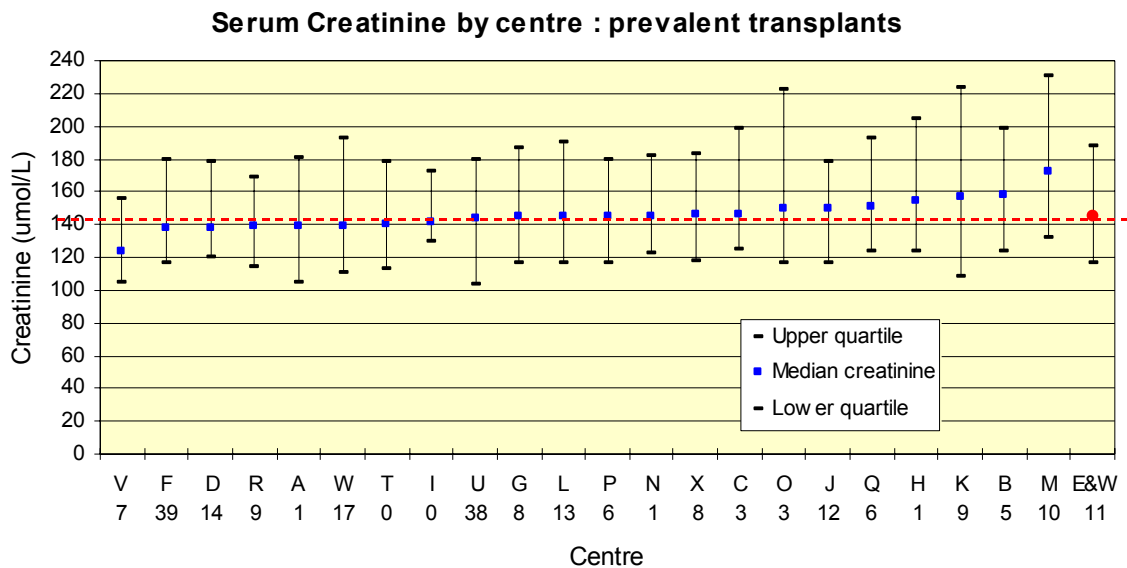
This analysis considered transplant patients on 31/12/1999 whose transplant had been functioning for at least one year. The most recent serum creatinine within 6 months was used in the analysis. The relationship between primary diagnosis and graft function is shown in Table 11.4

Diagnosis	% with creatinine < 200 (no of pts)
Aetiology uncertain*	80.3 (902)
Glomerulonephritis	75.6 (591)
Pyelonephritis	77.4 (590)
Diabetes	72.3 (192)
Renal Vascular disease	88.6 (48)
Hypertension	75.3 (182)
Polycystic Kidney	82.5 (431)
Not sent	82.1 (49)
Other	78.0 (480)

\* Includes "glomerulonephritis– not histologically proven"

**Table 11.4 Relationship between transplant function and primary renal diagnosis**

For each centre the median serum creatinine of prevalent transplant recipients was similar (Figure 11.9).



**Figure 11.9 Median serum creatinine of prevalent transplant patients, by centre**

However, figure 11.10 shows the percentage of established transplant patients with a serum creatinine greater than 250 micromoles/l for each unit. The differences between units are significant but unexplained although they may include differences in immunosuppressive protocols and attitude to use of marginal donors.



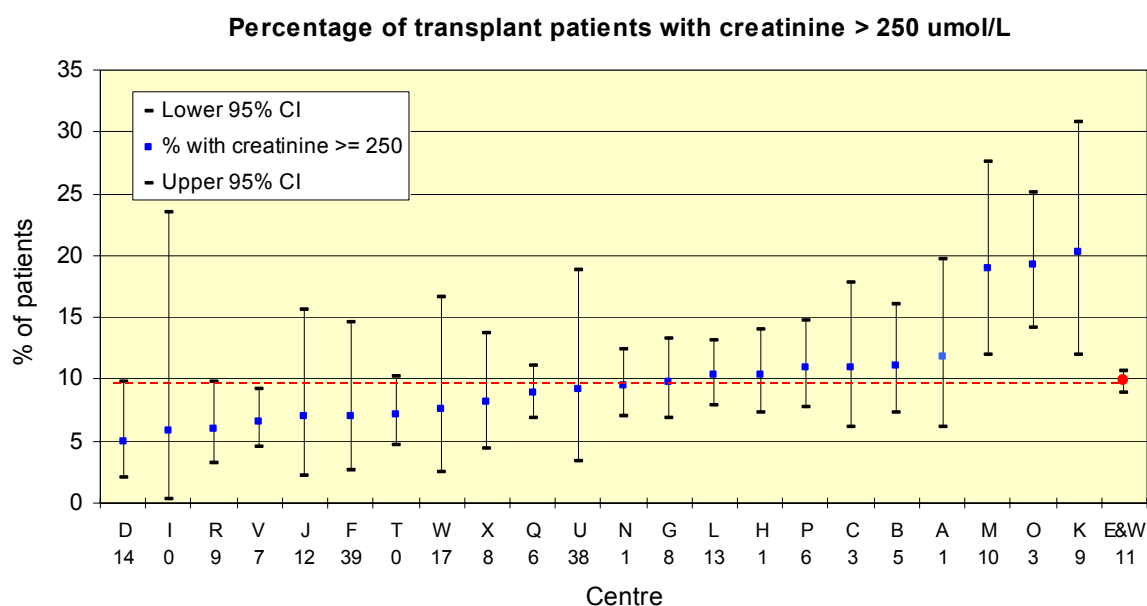


Figure 11.10 Percentage of established transplant patients with serum creatinine >250 umols/l

### Haemoglobin in transplanted patients

There are no recommended haemoglobin standards for renal transplant patients.

Haemoglobin concentrations of 5630 transplant patients in England and Wales were available for analysis. Results are shown in figures 11.11 and 11.12. Overall, 7.6% of these patients had a haemoglobin level less than 10 g/d and 2% less than 9 g/dl. These values are similar to last year's haemoglobin data when 6.1% and 2% of transplant patients had haemoglobin concentrations less than 10g/dl and 9g/dl respectively.

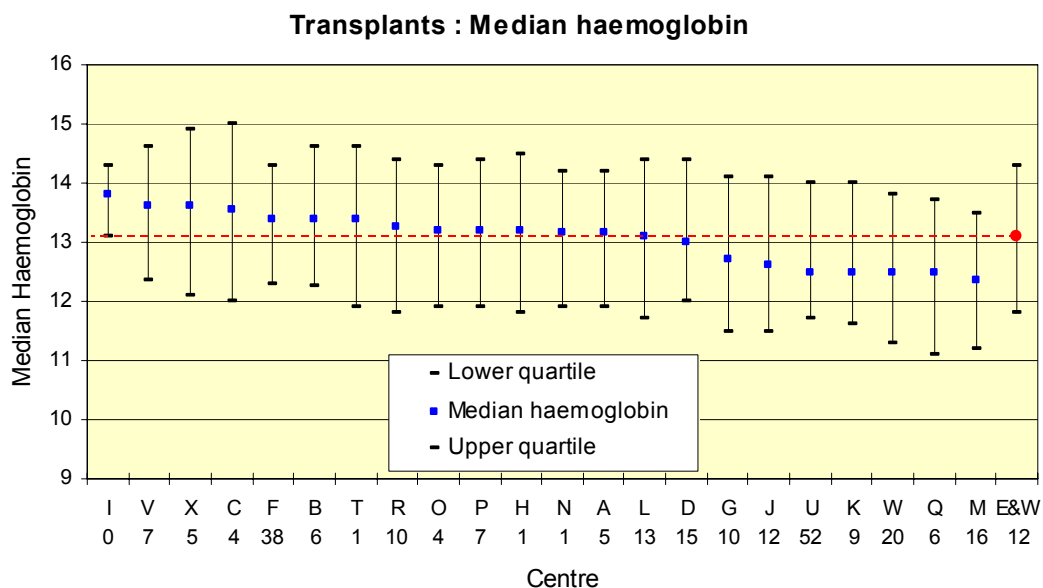
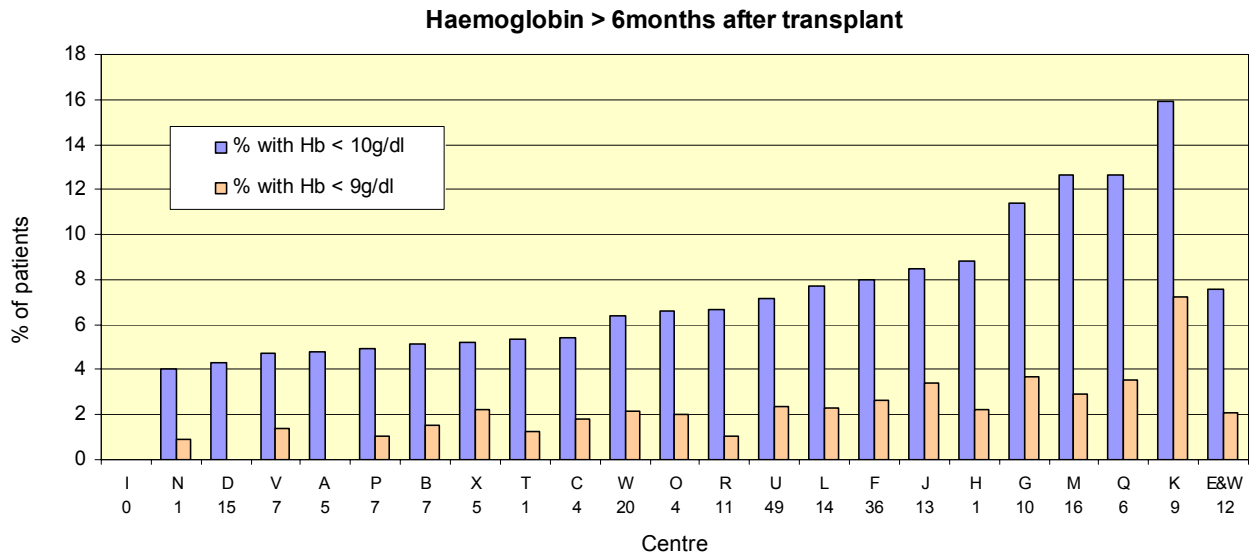


Figure 11.11 Median haemoglobin of transplant patients by centre

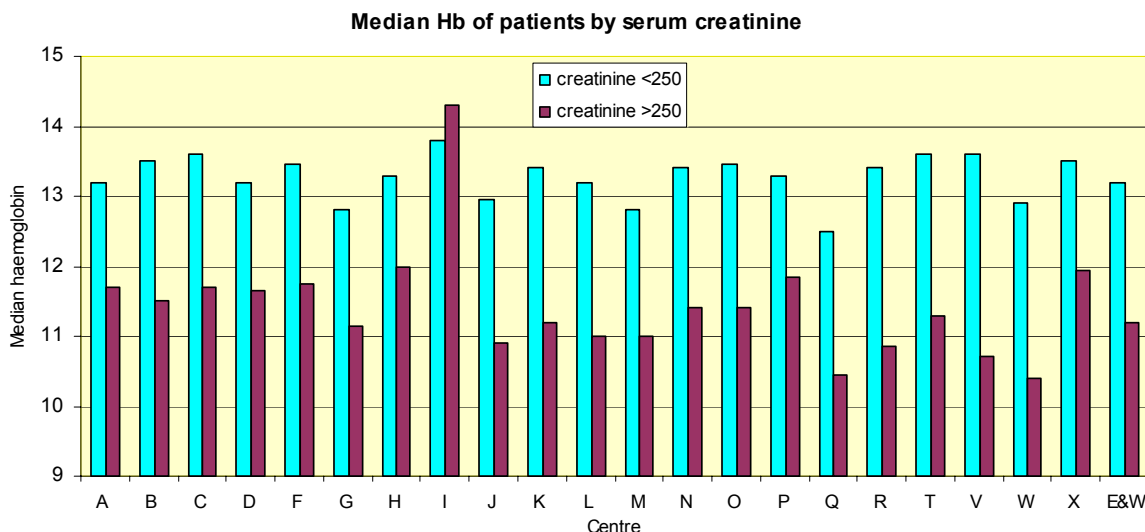
Figure 11.11 shows the median haemoglobin for prevalent transplant patients according to registry centre.

Figure 11.12 shows the percentage of transplant patients in each participating Registry unit with a haemoglobin concentration less than 10g/dL and 9g/dL respectively, at least 6 months after transplantation. The variation of 0-16% between centres (3-9% in 1998) with Hb <10g/dL is unexplained. Centre I is one of the small centres on the Registry. The possible reasons include quality of graft function, type of immunosuppression (use of azathioprine and mycophenolate mofetil) and use of erythropoietin when there are failing grafts.



**Figure 11.12 Haemoglobin achieved in established transplant patients – by centre**

Figure 11.13 shows the relationship between median haemoglobin and serum creatinine in transplant recipients at each centre.



**Figure 11.13 Median Hb of patients with serum creatinine greater and less than 250 umol/l**

As expected haemoglobin was lower in women and in patients with a higher serum creatinine (Table 11.5).

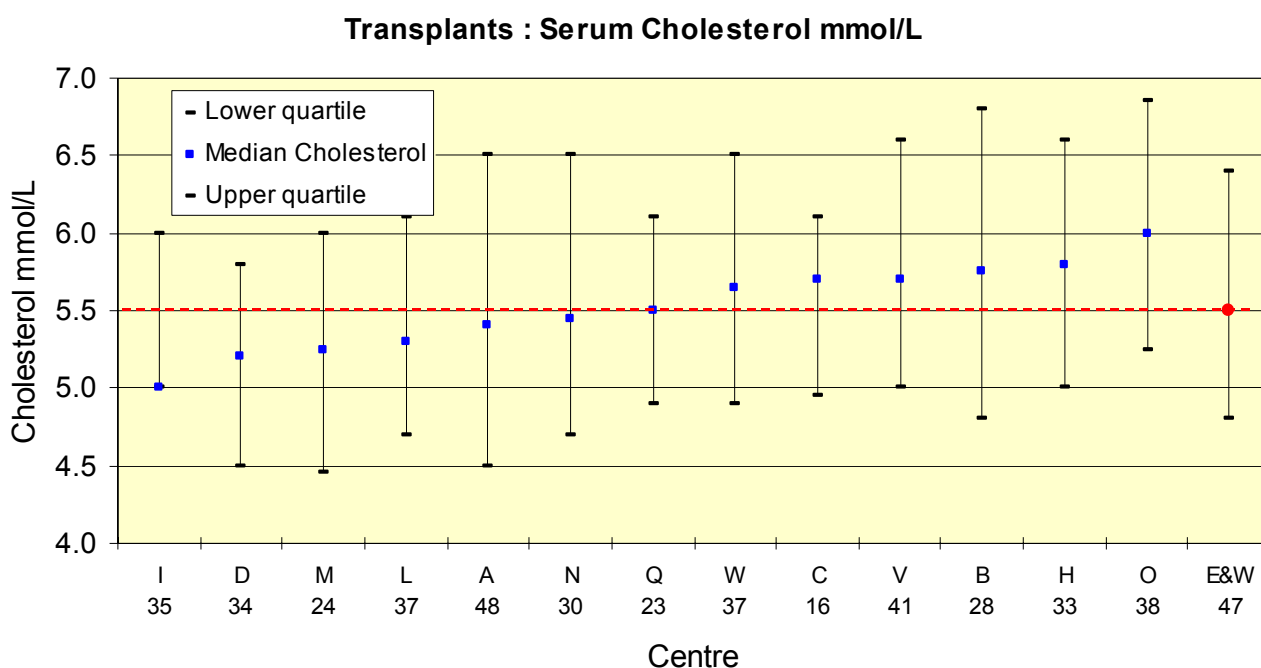
		Haemoglobin							
Gender	Creatinine	Mean Hb	Std dev	5th centile	Lower quartile	Median Hb	Upper quartile	95th centile	No. with data
Male	<250	13.6	1.7	10.7	12.5	13.7	14.8	16.2	2150
Male	250+	11.5	1.9	8.6	10.2	11.4	12.8	14.7	294
Female	<250	12.5	1.6	10.0	11.4	12.5	13.6	15.0	1417
Female	250+	10.9	1.5	8.7	9.7	10.9	11.9	13.4	124

**Table 11.5 Transplant patients: relationship between haemoglobin, creatinine and gender.**

## Serum cholesterol

This analysis considered all transplant patients on the 31/12/1999 whose grafts had been functioning for at least one year. The most recent serum cholesterol over a 12-month period was used and the cholesterol was harmonised for inter-laboratory variation. Results were available from 3060 patients. In 47% of established transplant patients serum cholesterol had not been recorded in the last year.

The distribution of serum cholesterol in prevalent transplant recipients according to centre is shown in figure 11.14



**Figure 11.14 Median Serum cholesterol for transplant patients – by centre**

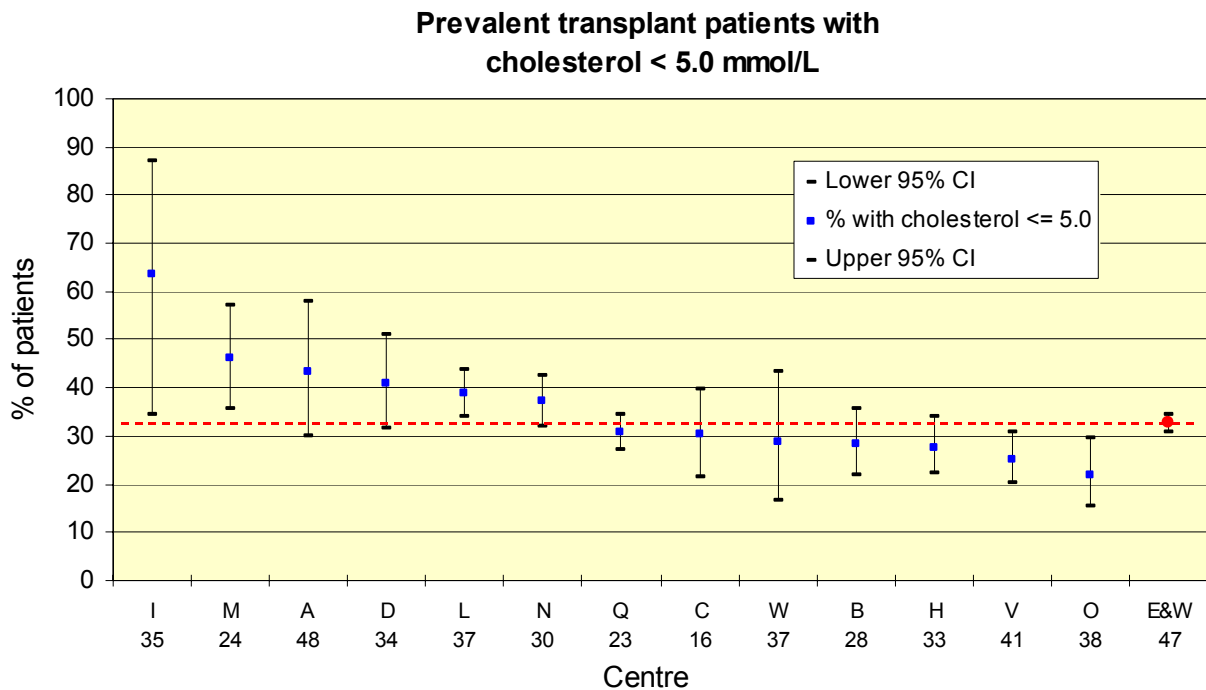
In most units the median serum cholesterol is above the recommended level for primary prevention in the high-risk non-transplant population (5.0 mmol/L)<sup>2</sup>.

Table 11.6 shows that there is no relationship between serum cholesterol and transplant function.

Serum Creatinine	Serum cholesterol					No. with data
	5th centile	Lower quartile	Median cholesterol	Upper quartile	95th centile	
<150	3.9	4.8	5.5	6.3	7.5	1630
150-250	3.9	4.8	5.6	6.4	7.7	1125
250+	3.6	4.7	5.5	6.5	8.3	305

**Table 11.6 Renal transplant patients: relationship of serum cholesterol and creatinine**

Figure 11.15 shows the percentage of prevalent transplant patients for each registry centre with a serum cholesterol level below 5.0 mmol/l.



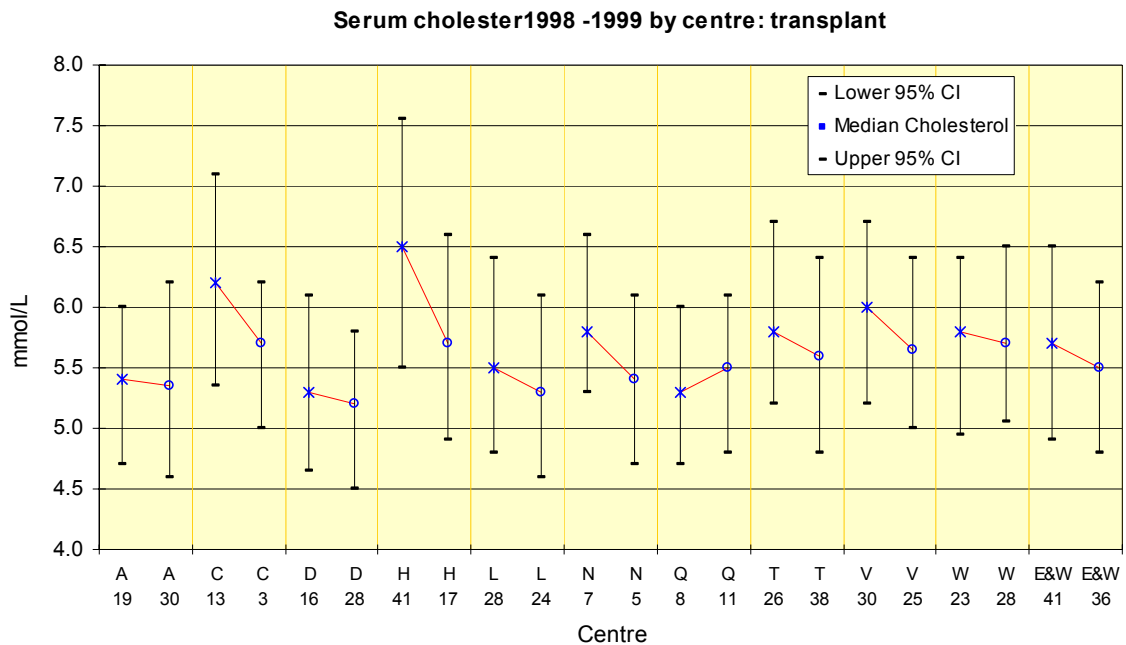
**Figure 11.15 Percentage of transplant patients with cholesterol  $\leq 5.0$  mmol/L**

Given that death from cardiovascular disease in the UK transplant population is 8-10 times more common than in the age and sex- matched general population<sup>3</sup>, this is an important modifiable risk factor that in some centres appears to be ignored. This is reinforced by the percentage of patients with no data, the number shown below each centre in figure 11.15. In many centres, no measurement has been made in a significant proportion of patients over the preceding 12 months.

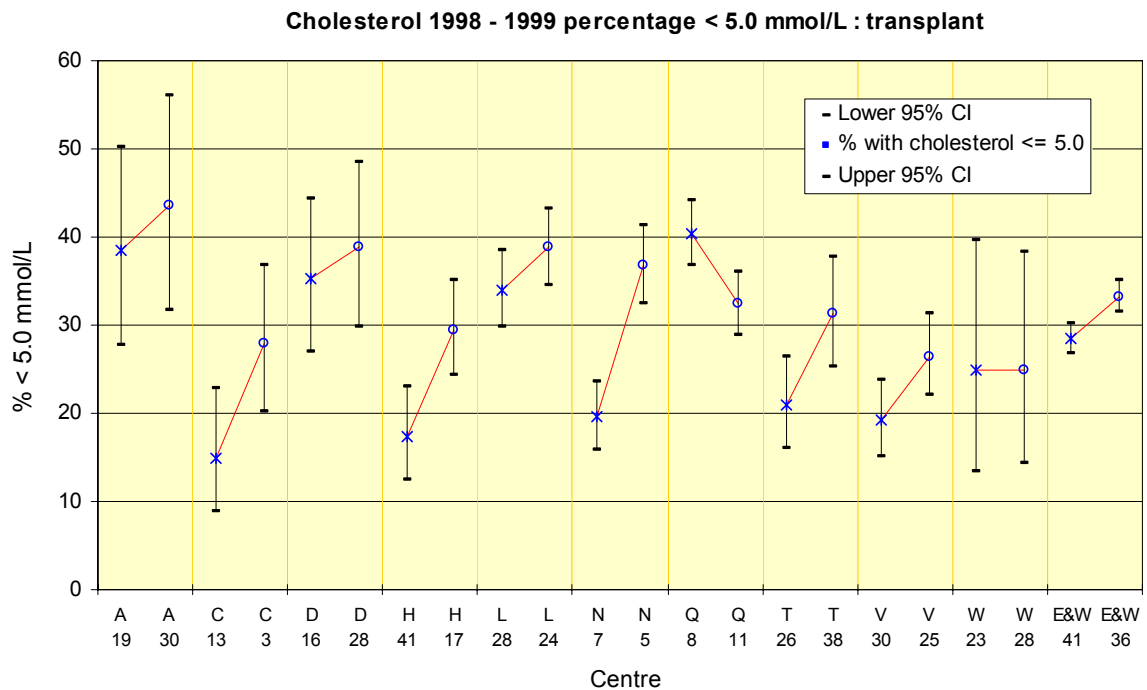
A chi-squared test was used to determine whether the percentage of patients with a serum cholesterol  $\leq 5.0$  mmol/L differed between centres. The percentage of patients with serum cholesterol  $\leq 5.0$  mmol/L was found to vary significantly between centres ( $X^2 = 45.8$ , d.f. = 12,  $p < 0.001$ ). In comparison there was no significant variation of serum cholesterol between centres in the dialysis population.

### Changes in serum cholesterol 1998-99

Compared with 1998 data, there was no overall significant change in median serum cholesterol although there was a trend towards a lower level (figure 11.16). There was a fall in median serum cholesterol in most centres. Similarly from 1998 to 1999, apart from one centre, there was an improvement within centres in the percentage of patients with serum cholesterol  $\leq 5.0$  mmol/l 99 (figure 11.17). In a few centres, the change was significant.



**Figure 11.16 Median serum cholesterol, mmol/L, in transplant patients by centre 1998-9**



**Figure 11.17 Percentage transplant patients with a serum cholesterol  $\leq 5.0$  mmol/l in 1998-9**

## Blood pressure

Neither the Renal Association nor the British Transplantation Society has recommended standards for blood pressure control in transplanted patients. In the following analysis the standards recommended for dialysis patients have been adopted (<140/90mmHg age <60 years, <160/90mmHg age  $\geq$ 60 years). The acceptance of higher blood pressure in the elderly may not be appropriate (British Hypertension Society guidelines)<sup>4</sup>.

There may be errors due to incomplete data. Table 11.7 shows the percentage of renal transplant recipients with blood pressure data. Disappointingly, the completeness of blood pressure returns has fallen somewhat compared with 1998 when data on 50% of patients aged <60 years and 47% of patients aged >60 years were available.

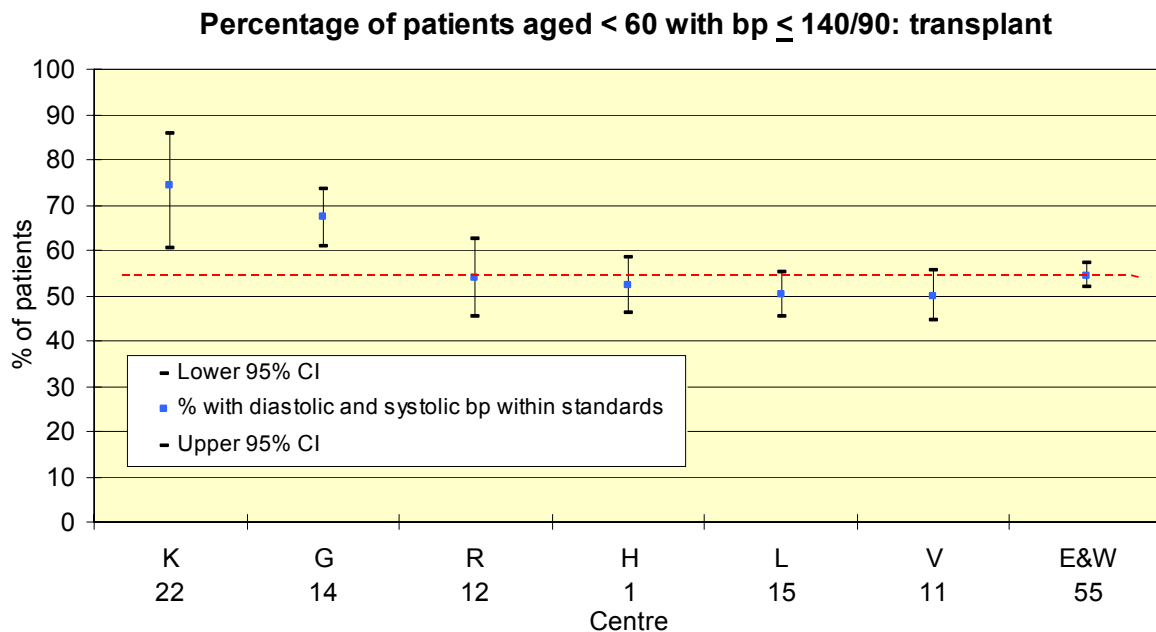
<b>% with BP return from last 6 months</b>		
<b>Centre</b>	<b>Age &lt; 60</b>	<b>Age &gt; 60</b>
A	0	0
B	42	42
C	0	0
D	2	0
E	0	0
F	0	0
G	86	84
H	99	98
I	0	0
J	0	0
K	78	81
L	85	85
M	0	0
N	56	47
O	6	2
P	0	0
Q	33	37
R	88	84
T	4	3
U	0	0
V	89	98
W	0	0
X	1	0
<b>E&amp;W</b>	<b>45</b>	<b>44</b>

**Table 11.7 Completeness of BP returns for transplant patients**

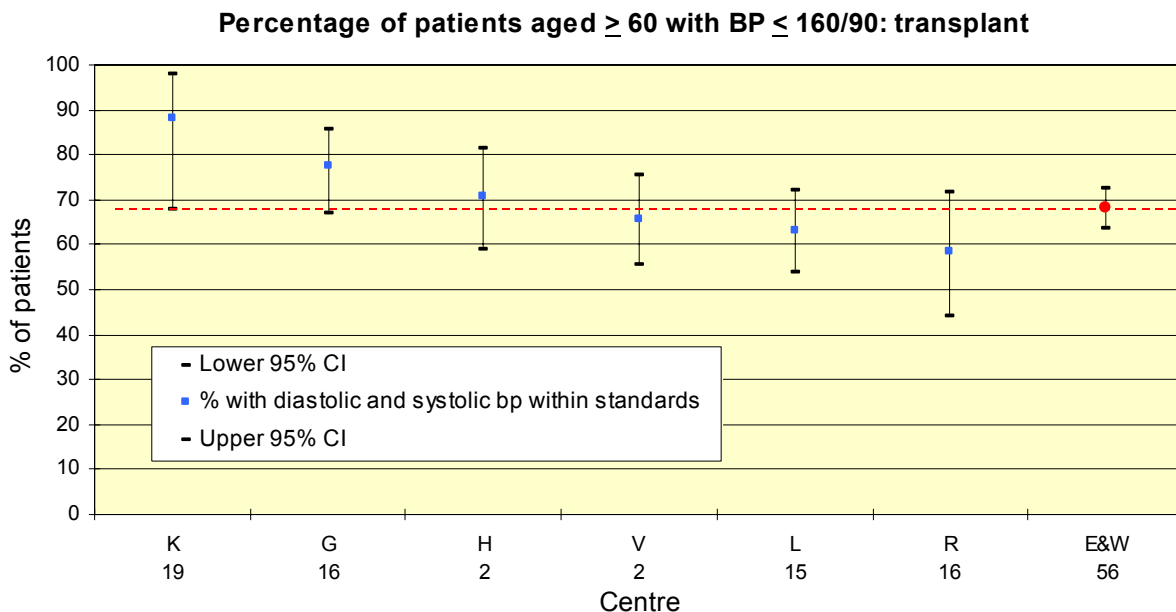
Blood pressure recordings may also be subject to a variety of biases. Fit patients with infrequent clinic attendance will have infrequent BP assessment. High BP readings may be selectively included or excluded from computer records depending on operator bias. The following data must be interpreted with this in mind.

Figures 11.18 and 11.19 show the proportion of transplant patients achieving the Renal Association standards in each centre for those aged less than 60 years and those aged 60 years or older respectively.

Because the blood pressure target for older patients is less stringent, a greater proportion of older patients achieved the blood pressure standards overall; 68.2% vs 53.3% in the older and younger age groups respectively.



**Figure 11.18 % patients under 60 with systolic and diastolic BP below 140/90 mmHg**



**Figure 11.19 % patients over 60 with systolic and diastolic BP below 160/90 mmHg**

Figures 11.20-11.27 show the systolic and diastolic blood pressure for each age range by centre together with the proportion of patients achieving the Renal Association Standards for each measure. The overall median diastolic pressure in those below and above age 60 is similar at 80 mmHg. and 81 mmHg respectively. The overall median systolic pressure is higher in those aged over 60 years at 150 mmHg compared with 138 mmHg in the younger age group.

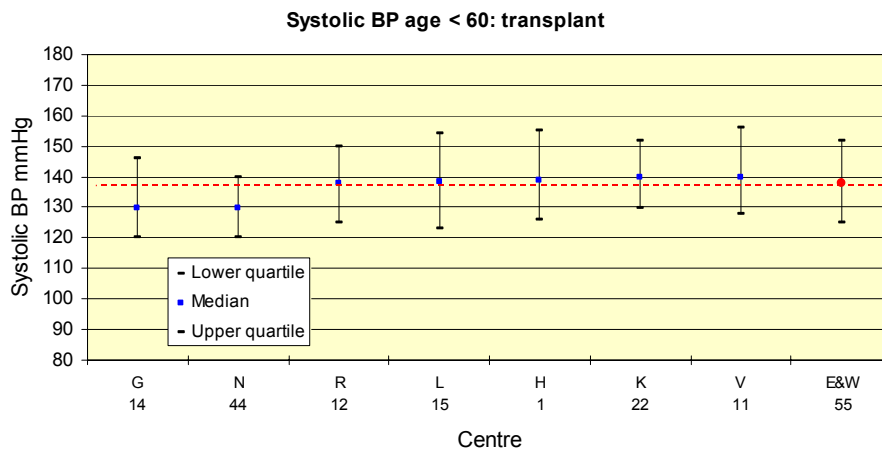


Figure 11.20 Transplant patients under 60: median systolic pressure

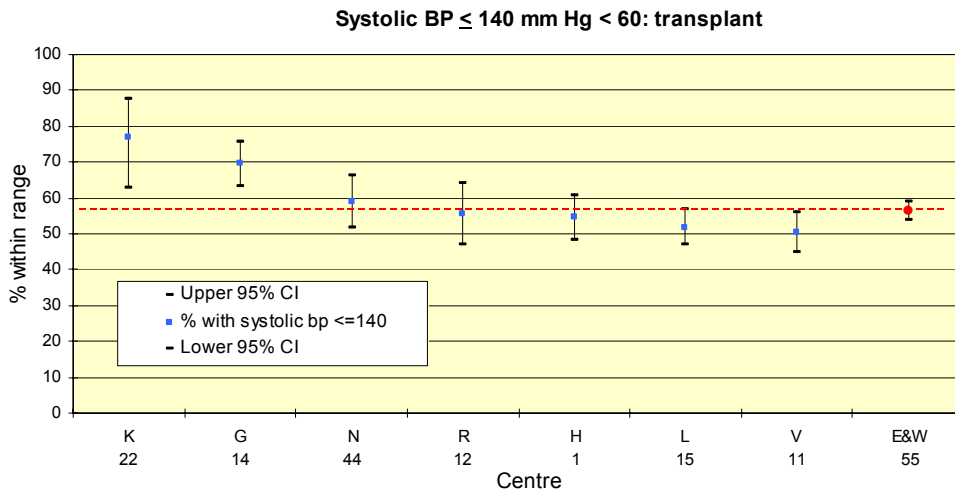


Figure 11.21 Percentage transplant patients under 60 with systolic BP <140 mmHg

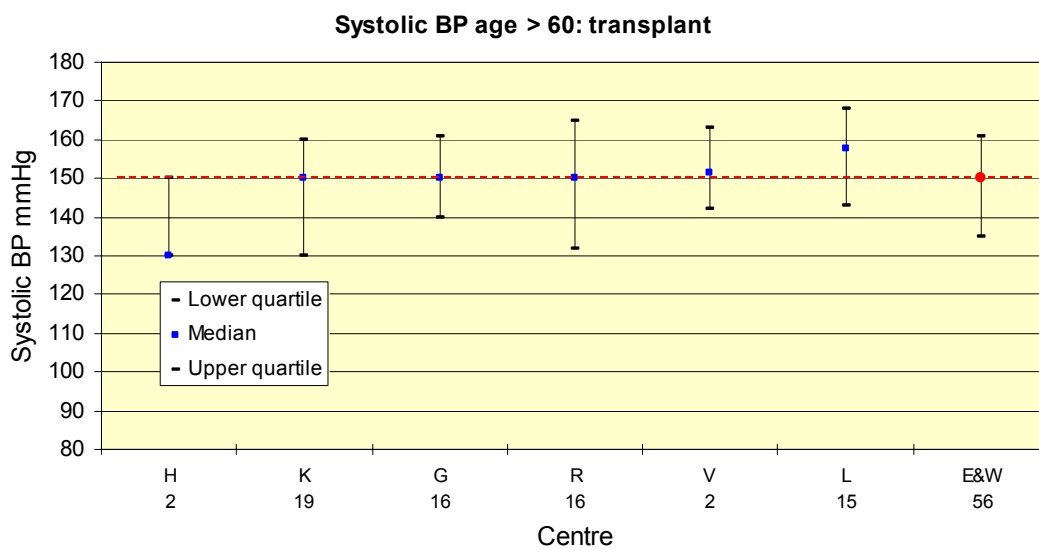


Figure 11.22 Transplant patients over 60: median systolic pressure



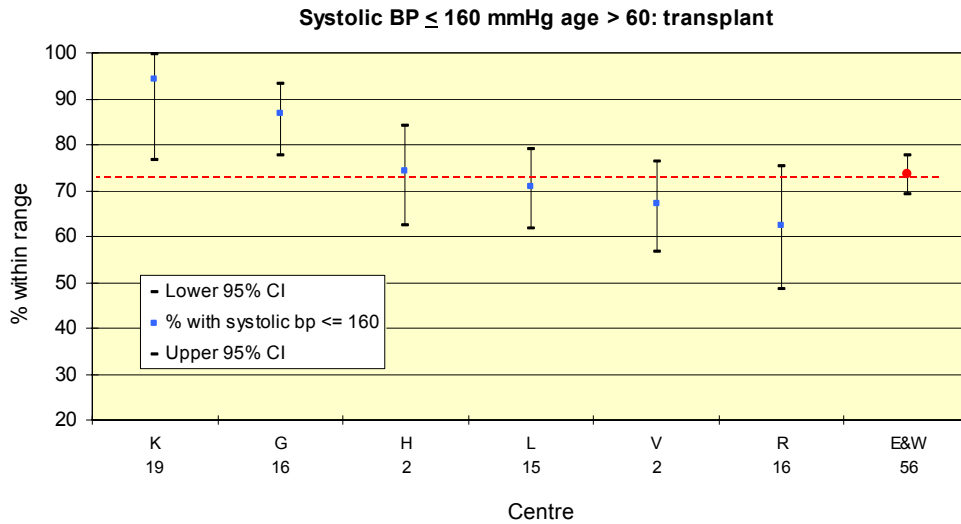


Figure 11.23 % patients over 60 with systolic BP <160 mmHg

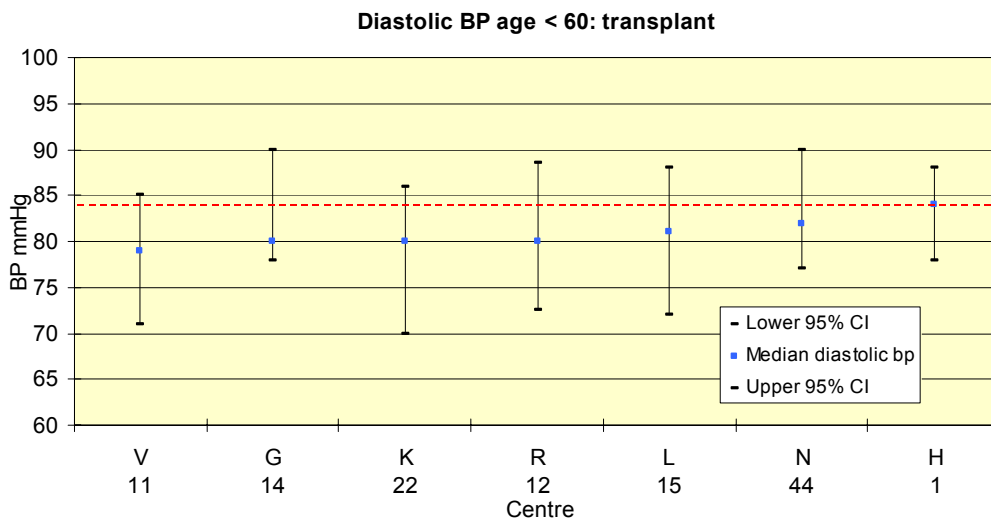


Figure 11.24 Transplant patients under 60; median diastolic pressure

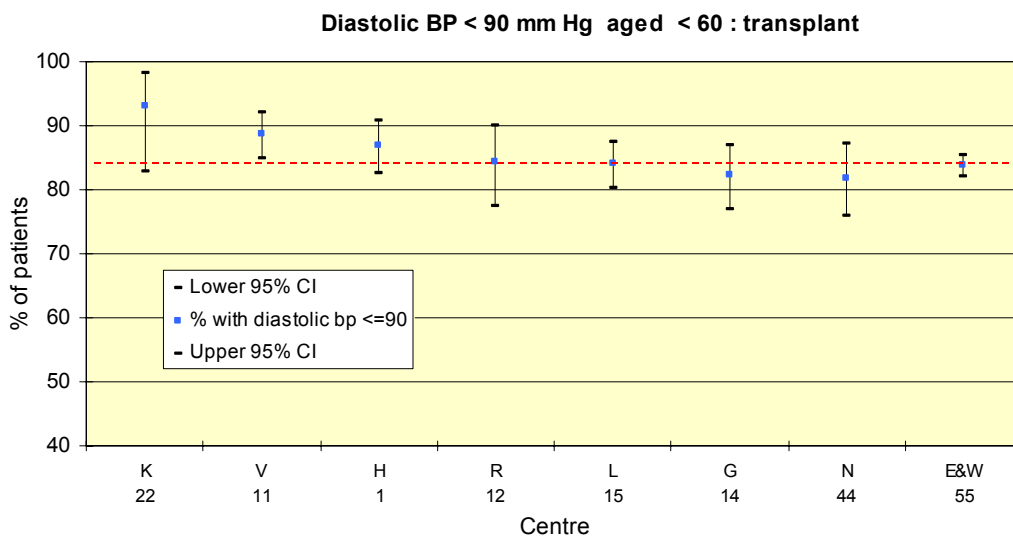
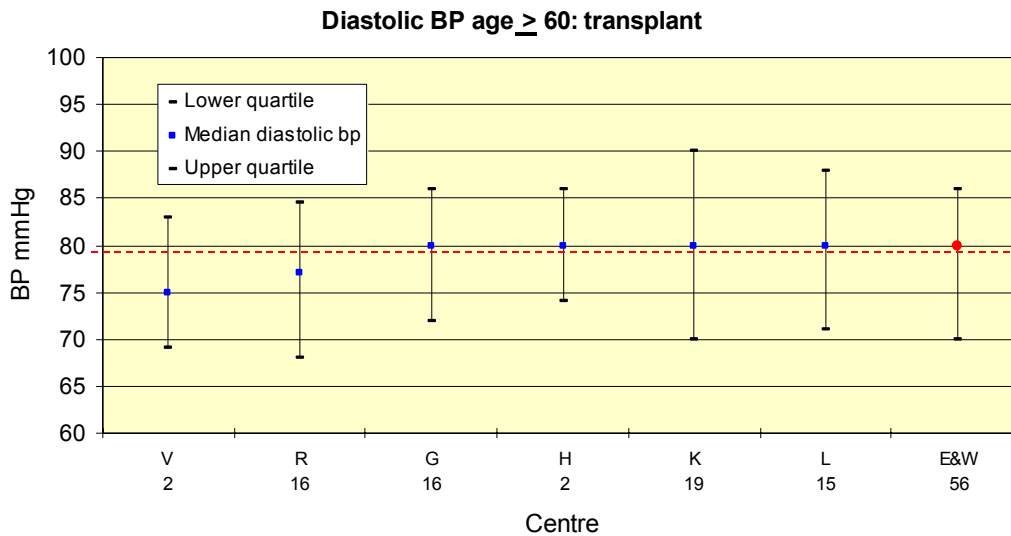
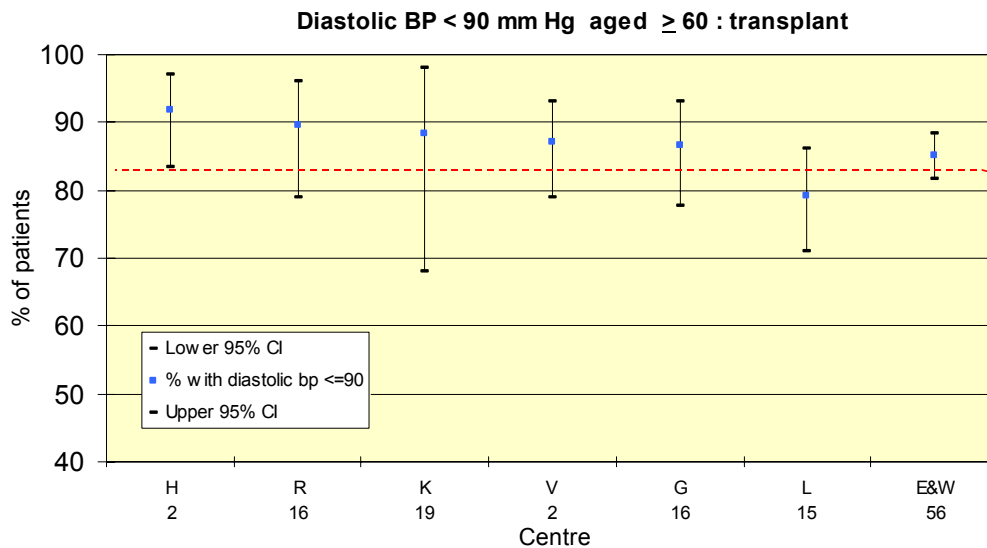


Figure 11.25 % patients under 60 with diastolic BP <90mmHg



**Figure 11.26 Transplant patients over 60: median diastolic pressure**



**Figure 11.27 % patients over 60 with diastolic BP <90mHg**

The relationship between systolic, diastolic and mean arterial blood pressure and transplant function as reflected by serum creatinine is shown in Table 11.8. It is not possible to determine whether higher blood pressure causes or results in poorer graft function. As the Registry collects further sequential data on these patients, the relationship of blood pressure both before and after transplantation to graft and patient survival will be investigated.

Serum Creatinine	Median mean arterial BP	Median Systolic BP	Median Diastolic BP
< 150 mmol/L	99.0	139.0	80.0
150-250 mmol/L	102.0	143.0	81.0
> 250 mmol/L	105.0	149.0	82.0

**Table 11.8 Relationship between BP and graft function in transplant patients in E&W.**

## **Conclusion**

Once again this report has concentrated on providing data on renal transplant patients that are not available from other sources or registries.

Variation exists between centres with respect to access to renal transplantation for both stock patients receiving renal replacement therapy as well as patients whose primary diagnosis is diabetes mellitus. In future reports it may be possible to obtain additional and more complete information (e.g. ethnicity) that could enable reasons for these differences to be examined in more detail.

The annual death rate of patients with established renal transplants is low at 2.9% for the whole UK (including patients with failed grafts returning to dialysis).

3.1% of all patients starting dialysis in the UK in 1999 were patients with failed transplants. This proportion is likely to vary substantially between units depending on the size of the stock transplant population.

The quality of transplant function differs significantly between centres, as does the haemoglobin level. Differences in modifiable risk factors for cardiovascular disease such as serum cholesterol and blood pressure also exist.

More sequential data will be available in the future and should enable individual centres to monitor the impact of new policies and protocols as well as allow comparison in outcome with other centres.

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1. European Best Practice Guidelines for Renal Transplantation (Part 1) Nephrology Dialysis and Transplantation 2000;**15**(7):3-38
2. Wood D, Durrington P, Poulter N, McInnes G, Rees A, Wray R. (1998). "Joint British recommendations on prevention of coronary heart disease in clinical practice." *Heart* 80(2): S1-S29.
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4. Ramsay LE, Williams B, Johnston DG, MacGregor GA, Poston L, Potter JF, Poulter NR, Russell G. (1999). "Guidelines for the management of hypertension: report of the third working party