Chapter 15: Survival of Incident Patients

Summary

- From the first RRT, the one year survival of all patients is 78%. From the 90th day of RRT, the one year survival is 87%.
- The 5 year survival is 43% overall, 64% in those under 65 and 14% in those over 65 at start of RRT.
- Poor reporting by renal units of patient co-morbidity and ethnicity renders interpretation of differences in patient survival between centres difficult.
- Using Z-score analysis, no significant difference in patient survival between centres was found.
- UK renal units achieve the standards set for incident patient survival in the Renal Association Standards document.
- Patient survival in the UK, adjusted for age, is improving year by year.

Introduction

The Renal Registry database enables an analysis of the influence of different factors on patient survival. These factors are related to patient case mix (e.g. age, gender, ethnicity, underlying diagnosis and other co-morbidity) or are dependent on treatment quality (e.g. haemoglobin achieved, mode of dialysis and serum phosphate level). For individual renal units, such analysis allows a comparison with performance in previous years and with other centres. In contrast with DOPPS, the UK Registry includes the outcomes from the 33% of dialysis population that are on peritoneal dialysis and the 3% of the ERF population who receive a pre-emptive transplant.

Survival rates can either be analysed in relation to:

- an *incident cohort*, in which patients who started renal replacement therapy (RRT) in a particular year are included;

  or

- a *prevalent cohort*, in which all (or a defined group of) patients undergoing RRT at a particular time are included.

The analyses presented in this chapter examine the survival from start of RRT, including transplantation of incident patients. Patients are censored when moving to a centre that does not report to the Registry.

Death rates in different centres contributing to the UK Renal Registry are reported here. These are very crude data. An adjustment can be made between centres on the basis of age but there is need for more detailed information relating to co-morbidity and ethnic origin. With this lack of information on case mix, no significance can currently be attributed to any apparent difference in survival between centres.

Statistical methods

The 'number of days at risk' was calculated for each patient, the sum of these values for all patients divided by 365 representing the 'number of patient years at risk'. The mortality rate was defined as:

$$\frac{\text{Number of deaths on dialysis}}{\text{Number of patient years at risk}}$$

The unadjusted survival probabilities (with 95% confidence intervals) were calculated using the Kaplan–Meier method, in which

the probability of surviving more than a given time can be estimated for members of a cohort of patients without accounting for the characteristics of the members of that cohort. Where centres are small or the survival probabilities are greater than 90%, the confidence intervals are only approximate.

In order to estimate the difference in survival of different subgroups of patients within the cohort, a stratified proportional hazards model (Cox) was used where appropriate. The results from the Cox model are interpreted using a hazard ratio. For diabetics compared with non-diabetics, for example, the hazard ratio is the ratio of the estimated hazards for diabetics relative to non-diabetics, where the hazard is the risk of dying at time *t* given that the individual has survived until this time. The underlying assumption of a proportional hazards model is that this ratio remains constant throughout the period under consideration. The proportional hazards model was tested for validity in all cases.

Z-scores

The enquiry into the excess of paediatric cardiac deaths at the Bristol Royal Infirmary defined an outlier as lying beyond 3 standard deviations from the mean, using the statistical methodology of Shewhart's control theory. This analysis relies on the centre sizes, and hence their standard deviation, being very similar. Renal units in the UK vary greatly in size, catchment populations varying from 300,000 to over 2 million. There is a consequent variation in the total patient number on RRT so the figure for the standard deviation will vary greatly between centres. The standard deviation for the total RRT population is not an appropriate number as this will be very small. Therefore, the Shewhart methodology cannot be applied. The Registry has used the accepted statistical technique of Z-scores to identify any outliers.

Definition

Z-scores are sometimes called "standard scores". It is a measure of the distance in standard deviations of a sample from the mean.

The Z-score transformation is especially useful when seeking to compare the relative standings of items from distributions with different means and/or different standard deviations. The Z-score for an item indicates how far and in what direction, that item deviates from its distribution's mean, expressed in units of its distribution's standard deviation.

Mathematically: the survival Z-score =

$$\frac{\text{Survival for centre X} - \text{survival for all centres}}{\text{Standard error for centre X}}$$

The Z-score is therefore an adjustment for the size of the centre and when comparing the different Z-scores for all the centres, they should be normally distributed. The observed Z value compared with the expected Z value (see explanation below) should be on a straight line.

Calculation of the expected Z value

Suppose there is a normally distributed population from which we repeatedly draw random samples of some specific size, say 10. These 10 values from each such random sample are sorted into increasing order, smallest value to largest value. When the sample data is sorted in this way, the individual numbers are called **order statistics**. The smallest value will vary somewhat from one such sample to another, but over the long run, the smallest values should tend to cluster around some average smallest value and produce a **mean** or **expected values of the order statistics**. These data have been compiled into tables so that for every specific total number of ordered samples (e.g.

38 centres with Registry survival data) there is an expected Z value for each ordered centre in that list.

Validity of the centre adjustment for proportional hazards

When the Cox model is used to adjust centre survival to a specific age (e.g. 60 years), it relies on, in addition to the assumption of proportionality within the period studied, the proportionality between centres of the slope of this relationship. If one centre had a relationship of survival with age with a slope of the graph that was different from those of the other centres, the adjustment would not be valid. Testing showed the slopes to be similar for all centres.

Survival of new patients on RRT

The revised Renal Standards document concluded that:

> ***It is hard to set survival standards at present because these should be age, gender and co-morbidity adjusted and this is not yet possible from Registry data. The last Standards document recommended at least 90% one year survival for patients aged 18-55 years with standard primary renal disease. This may have been too low as the rate in participating centres in the Registry was 97%, though numbers were small.***

Standard Primary Renal Disease is a definition using the EDTA diagnosis codes (including only codes 0 – 49) which excludes patients with renal disease due to diabetes and other systemic diseases. It is more widespread practice to simply exclude diabetics, so these figures have also been quoted to allow comparison with reports from other registries. There are apparent differences from last year, as previously an incorrect definition of Standard Primary Renal Disease was applied to the cohort at a programming level. The results are in Table 15.1.

All the one and two year survival figures quoted in this chapter are from the first day of dialysis unless stated otherwise, not from day 90 as quoted from the USA. The data for Scotland were taken from the Scottish Renal Registry Report 2000/2001.

The key findings to note are: the high death rate in the first 90 days, the steep age related decline in survival, the greater survival on PD compared with HD after age adjustment (probably reflecting selection differences), and the similarity of survival in England and Wales. The 5 year survival is only 14% in those over 65, 64% in those under 65 and 43% overall.

Table 15.2 contains 90 day and 1 year after 90-day adjusted patient survival for England and for Wales, showing the high initial death rate.

Table 15.1. One-year patient survival – patients aged 18–55, 2001 cohort

First treatment	Standard primary renal disease	All diseases except diabetes
Recommended standard	**>90%**	
All	96.3	93.3
95% CI	95.0-97.5	91.9-94.7
HD	93.6	89.7
95% CI	91.1-96.0	86.8-92.5
PD	98.9	98.3
95% CI	97.7-100	96.8-99.8

Table 15.2. Patient survival across England and Wales, 2001 cohort

	Eng	W	E & W
Adjusted (age 60) 90 days	92.8	93.5	92.9
95%CI	91.7-93.9	91.2-96.0	91.8-93.9
Adjusted (age 60) 1 year after 90 days	86.6	85.7	86.5
95%CI	85.1-88.0	81.8-89.7	85.1-87.9

The survival by first established treatment modality is shown in Table 15.3.

Tables 15.4 – 15.9 show survival patterns, split around age 65, for up to five years after the first renal replacement therapy.

Survival of new patients by age

The incident cohort included in this analysis is all those patients starting RRT in 2001. Patients who recovered function within 90 days (i.e. patients with acute rather than chronic renal failure) have been excluded.

In Figure 15.1, the unadjusted survival has been shown for the first 90 days, the first year from day 0 of RRT, and the first year after day 90. The last figure allows comparison with many other Registries, including the US Registry, which record data only from day 90 onwards.

The UK Registry has been collecting data on incident patients since its inception in 1997. The Kaplan Meier survival curves are only able to show data for the first 6 years from starting renal replacement therapy (Figure 15.2). Because of this factor it has only been possible to calculate the 50% patient survival for those patients starting renal replacement therapy aged over 75 (21 months ±2.1m 95%CI), aged 65 – 74 (33 months ± 1.8m 95%CI) and 55 – 64 (66 months ±2.8m 95%CI). Patients with diabetes have been included in these survival figures. These data include the first 90-day period and so patients may appear to show a lower survival than data from other international Registries which exclude this period.

The hazard ratios confirm data previously shown by the Registry that the greatest hazard of death occurs in the first 120 days; thereafter the hazard ratio remains stable (Figure 15.3).

Table 15.3. One-year survival by first established treatment modality

	HD	PD
Adjusted 1 year after 90 days 95% CI	84.4 83.0-85.8	90.3 88.9-91.8

Table 15.4. Unadjusted 90 day survival of new patients, 2001 cohort by age

Age	KM[1] survival analysis (%)	KM 95% CI	No.
18–64	95.5	94.5-96.6	1524
≥65	84.7	82.9-86.5	1540
All E&W	90.1	89.0-91.2	3064

[1]KM = Kaplan–Meier.

Table 15.5. Unadjusted 1 year survival of new patients, 2001 cohort by age

Age	KM survival analysis (%)	KM 95% CI	No.
18–64	**88.0**	86.4-89.7	1524
≥65	**68.9**	66.5-71.2	1540
All E&W	**78.4**	76.9-79.9	3064

Table 15.6. Unadjusted 2 year survival of new patients, 2000 cohort by age

Age	KM survival analysis (%)		KM 95% CI	No.
	1 year	2 year	2 year survival	
<65	89.7	**82.4**	80.3-84.6	1211
≥65	68.4	**55.0**	52.1-57.9	1156
All E&W	79.3	**68.9**	67.1-70.8	2367

Table 15.7. Unadjusted 3 year survival of new patients, 1999 cohort, by age

Age	KM survival analysis (%)			KM 95% CI	No.
	1 year	2 year	3 year	3 year survival	
<65	88.1	82.3	**75.6**	72.9-78.3	1028
≥65	67.8	52.6	**39.9**	36.7-43.1	910
All	78.5	68.2	**58.7**	56.5-60.9	1938

Table 15.8. Unadjusted 4 year survival of new patients, 1998 cohort by age

Age	KM survival analysis (%)				KM 95% CI	
	1 year	2 year	3 year	4 year	4 year survival	No.
<65	86.9	80.4	73.9	**68.4**	65.3-71.5	872
≥ 65	64.8	49.7	39.7	**30.3**	27.0-33.6	767
All E&W	76.6	66.1	57.9	**50.6**	48.2-53.1	1639

Table 15.9. Unadjusted 5 year survival of new patients, 1997 cohort by age

Age	KM survival analysis (%)					KM 95% CI	
	1 year	2 year	3 year	4 year	5 year	5 year survival	No.
<65	87.4	80.4	74.4	68.3	**64.0**	59.6-68.5	454
≥ 65	65.8	45.2	33.6	23.9	**14.5**	10.7-18.2	345
All E&W	78.1	65.2	56.8	49.1	**42.6**	39.2-46.1	799

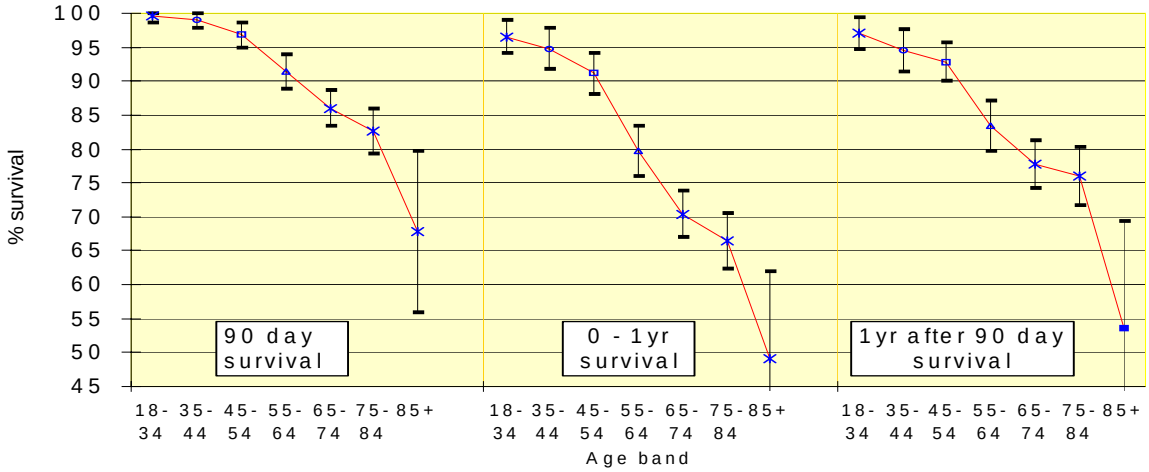

Figure 15.1. Unadjusted survival of all incident patients, by age band

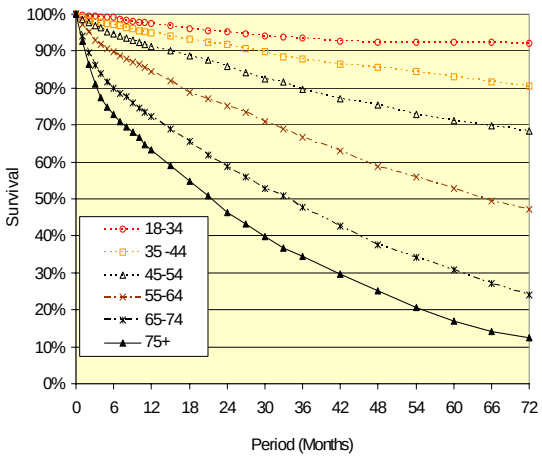

Figure 15.2. Kaplan-Meier 6-year survival

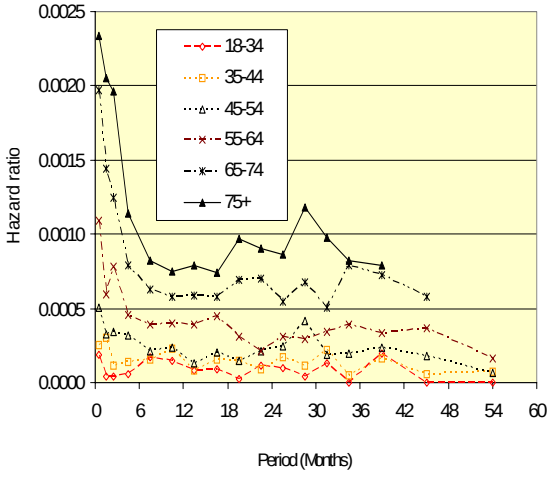

Figure 15.3. Five-year hazard of death ratios, by age band

The results beyond 36 months for the older age group are not reliable as the numbers were very small.

Age adjustment of survival in the first 90 days and thereafter

Analysing all the patients starting RRT between 1997 and 2000, the proportional hazards for each 1-year increase in age of the patients for the two time intervals of the first 90 days and the subsequent 365 days are shown in Table 15.10.

These data show that there is, in the first 90 days, a greater risk of death for every 1 year increase in patient age than there is in the subsequent 1-year period. This confirms, as stated in the Registry's previous reports, that it is incorrect to apply a single proportional hazards model for the first 365 days of starting RRT.

For every 10 year increase in patient age, there was an increase in the hazard of death of 58% (95% CI 50–65%) in the first 90 days, compared with 41% (95% CI 35–47%) in the subsequent 365 days.

Changes in incident patient survival, 1997–2001

In Figure 15.4, the right-hand figures show the one-year after 90-day survival for all incident patients on the Registry in the years 1997–2001. There is an apparent improvement in one-year after 90-day survival, but this could be an artefact as many more centres have joined the Registry since 1997 and these centres may have had a better survival. The left-hand figures show the same analysis just for those centres which joined in 1997. This shows the same overall improvement in survival, from 84.0 to 86.9%, which is an 18% reduction in one-year after 90-day mortality. This linear trend was significant ($p<0.01$). These data also demonstrate that the survival profile of the 1997 centres is similar to that of the newer centres.

The adjustment for age using the Cox proportional hazards method has been calculated for each of the above years in the two groups. There has been no change over these 5 years in the increase in hazard of death for each 1 year increase in age. This indicates that the improvement in survival occurs across all age bands.

Survival by ethnicity

This analysis has been included in Chapter 20.

Survival of incident patients in 2001 by centre

Comparability of figures for survival within the first 90 days are heavily dependent on consistency between renal units in ensuring that all early chronic renal failure deaths are included and that all acute renal failure patient deaths are excluded. This is not the case. As the 1 year survival from day 0 of starting renal replacement therapy includes this time period, the more appropriate figure for comparing renal units is the 1 year after 90 days, shown in figures 15.5 (unadjusted) and 15.6 (adjusted to age 60), with their 95% confidence intervals.

Some of the smaller centres have wide confidence intervals. An analysis using the Z-score technique (see description at the start of this chapter) for any significant differences between centres is described below.

Table 15.10. Increase in proportional hazard of death for each year increase in age, at 90 days and for 1 year thereafter

Interval	Proportional hazards	95% CI
First 90 days	1.058	1.050–1.065
1 year after first 90 days	1.041	1.035–1.047

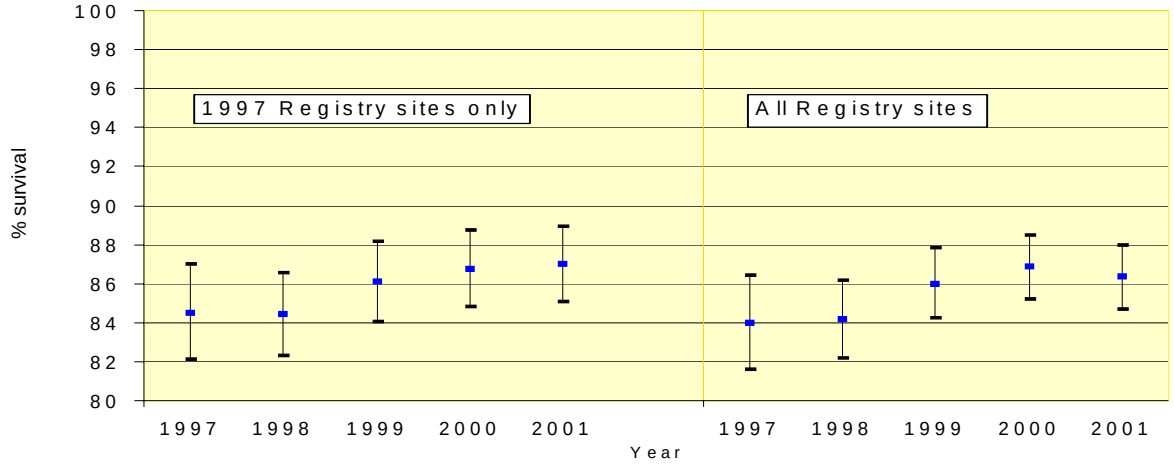

Figure 15.4. Change in one-year after 90 day adjusted (age 60) survival, 1997-2001

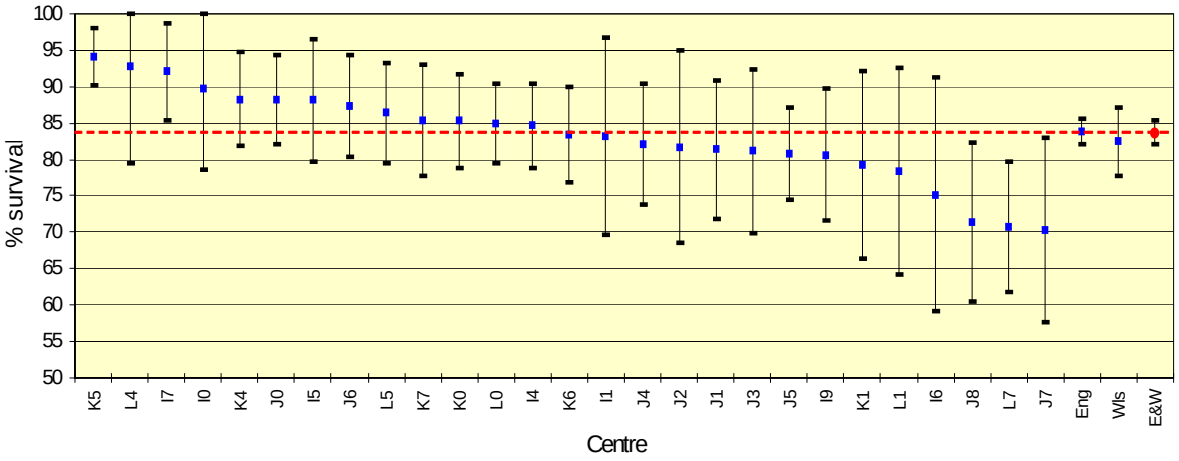

Figure 15.5. Unadjusted survival 1 year after 90 days; 2001 cohort

Showing 95% confidence intervals

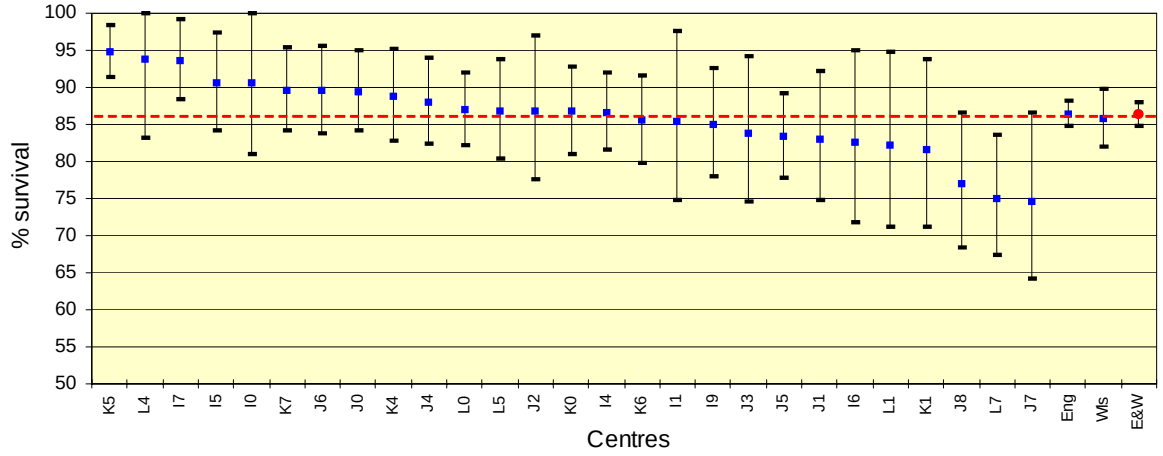

Figure 15.6. Adjusted survival 1 year after 90 days; 2001 cohort

Showing 95% confidence intervals

Analysis of centre variability in survival in 1 year after 90 days

A normal probability plot can be drawn to look at the distributions of the adjusted survival scores. This graph would have on the y-axis the observed values and on the x-axis the expected values given that this sample had come from a normal distribution. To overcome the variability in centres with small numbers, the 1999, 2000, and 2001 cohorts of patients have been combined (Figure 15.7).

If it is true that these observations are normally distributed, they should lie on a straight line. Centres above the line have a better than expected survival, whereas those below it have a worse than expected survival. Figure 15.7 has been plotted using the adjusted survival data for each centre and shows that the results are relatively close to a normal distribution. Centres above the line have a better than expected survival, whereas those below it have a worse than expected survival. The 95% confidence intervals have been plotted for these data. If centres have a significantly different survival from the mean they fall outside the confidence intervals.

In this analysis, none of the centres fall outside the 95% confidence intervals.

Analysis of centre survival within the first 90 days

The unadjusted and age-adjusted 90-day survivals of patients incident in 2001 are shown in Figures 15.8 and 15.9.

Figure 15.10 shows the age adjusted Z-scores for the 2001 cohort, and figure 15.11 for a 3-year cohort 1999-2001.

Comparison of the 90 day and 1 year after 90 day survival

Similar to previous years, Figure 15.12 demonstrates that there is no relationship between the 1 year after 90 days survival and the survival of patients within the first 90 days. This supports the view that part of this variability is related to the definition of acute renal failure patients, which makes interpretation of the first 90-day survival difficult.

Changes in survival by centre 1997 - 2001

Annual changes in survival by individual renal units are shown in Figures 15.13 and 15.14.

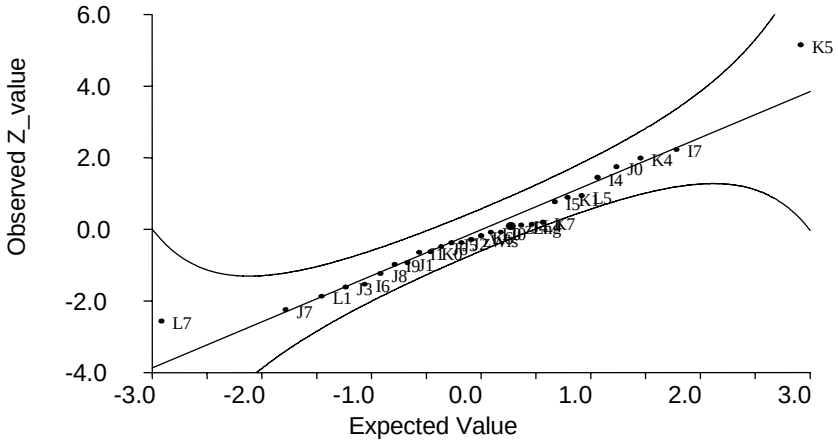

Figure 15.7. Z-score for age adjusted 1 year after 90 days survival 1999 - 2001 cohort

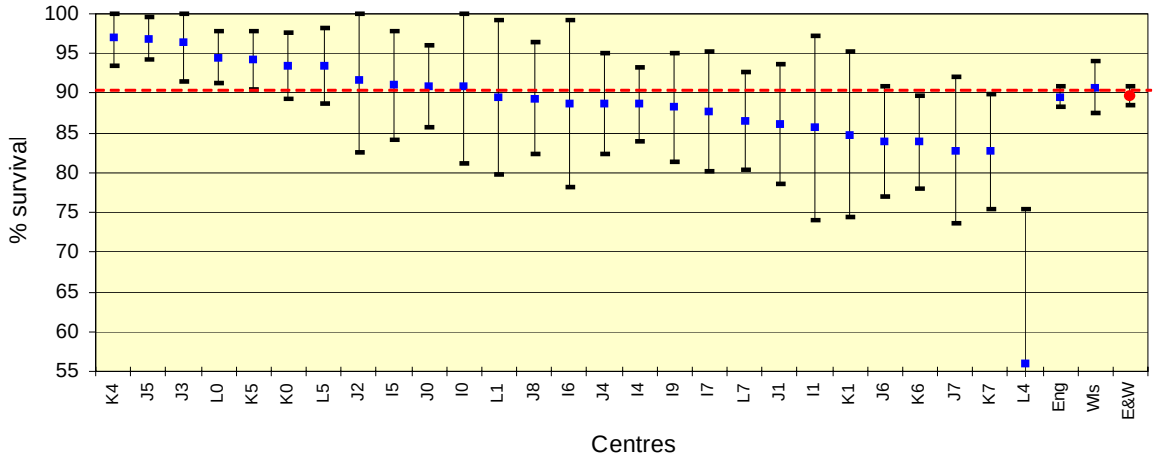

Figure 15.8. Unadjusted survival in the first 90 days; 2001 cohort

Showing 95% confidence intervals

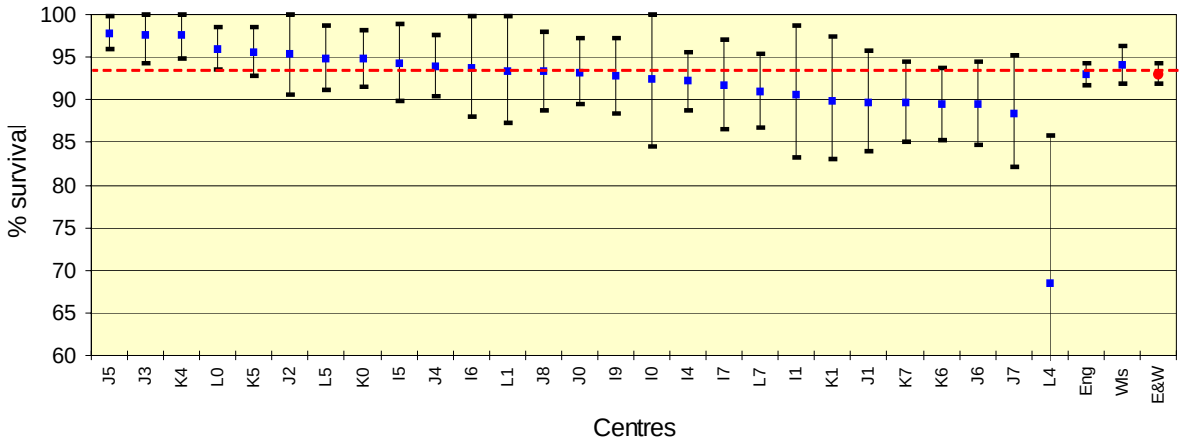

Figure 15.9. Age adjusted survival in the first 90 days; 2001 cohort

Showing 95% confidence intervals

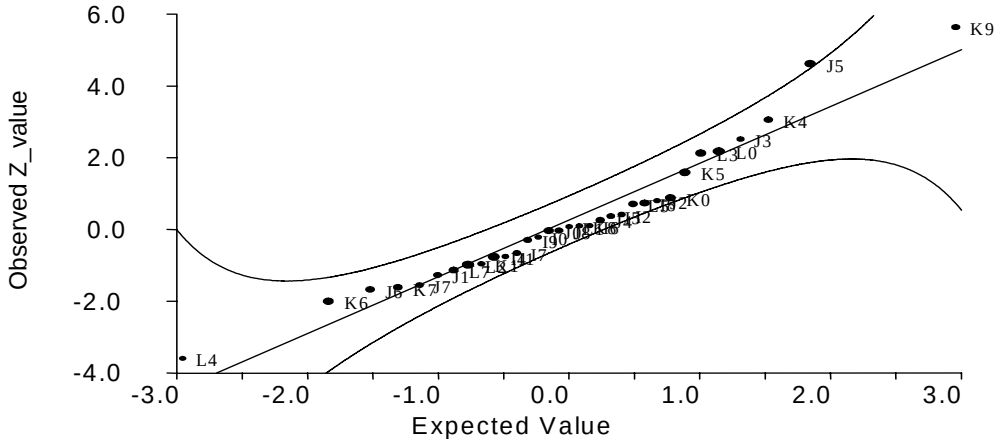

Figure 15.10. Z-score for age-adjusted survival within the first 90 days; 2001 cohort

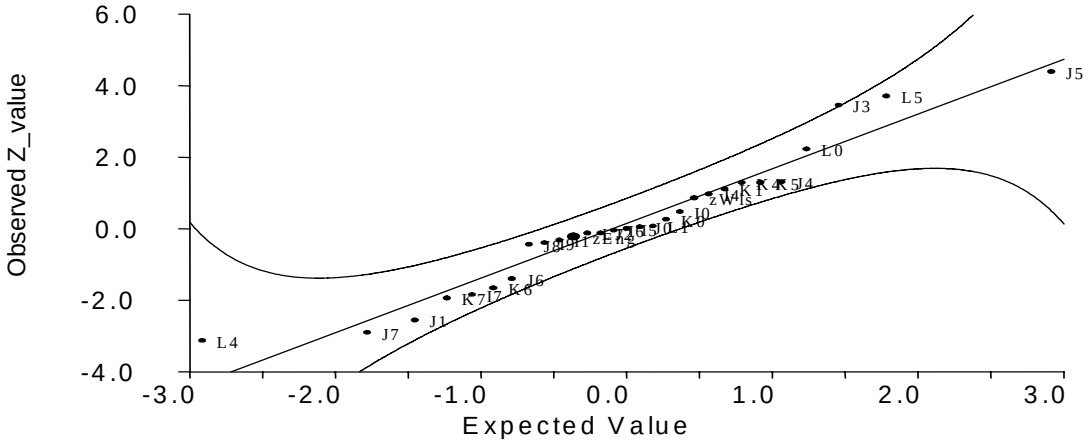

Figure 15.11. Z-score for age-adjusted survival within the first 90 days; 1999-2001 cohort

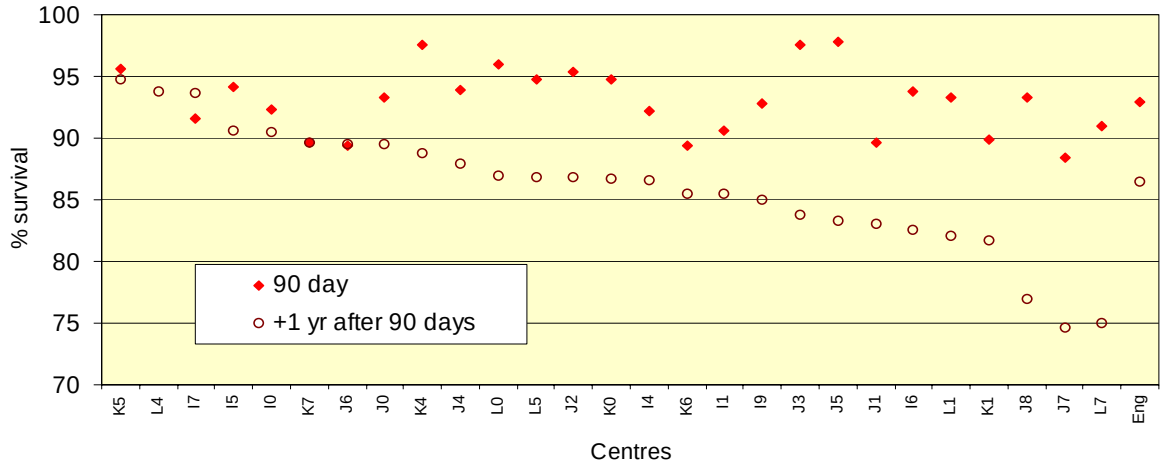

Figure 15.12. Adjusted survival of new patients, 90 day compared with 1 year after 90 days

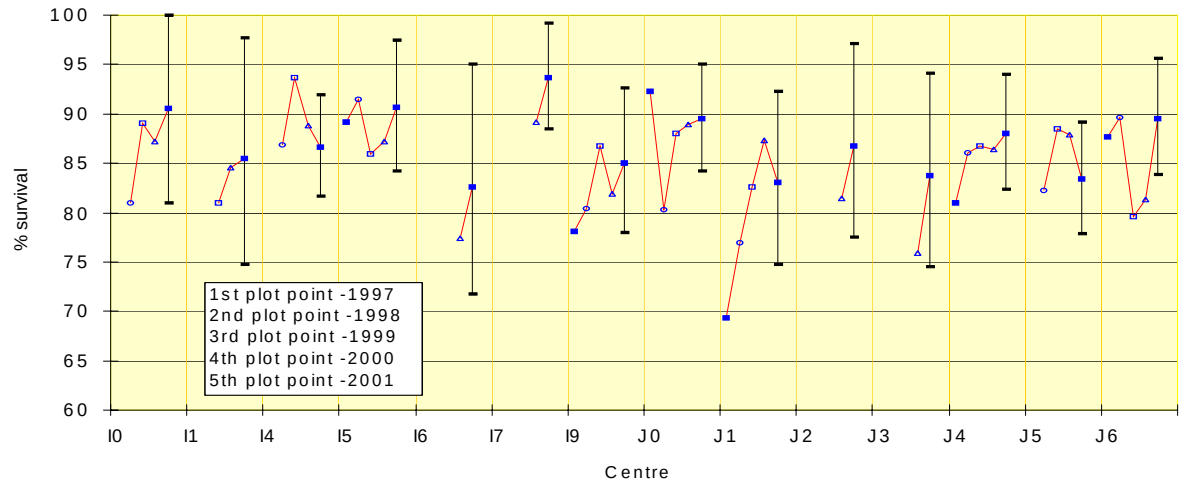

Figure 15.13a. Age adjusted survival, 1 year after 90 days; 1997–2001 cohort

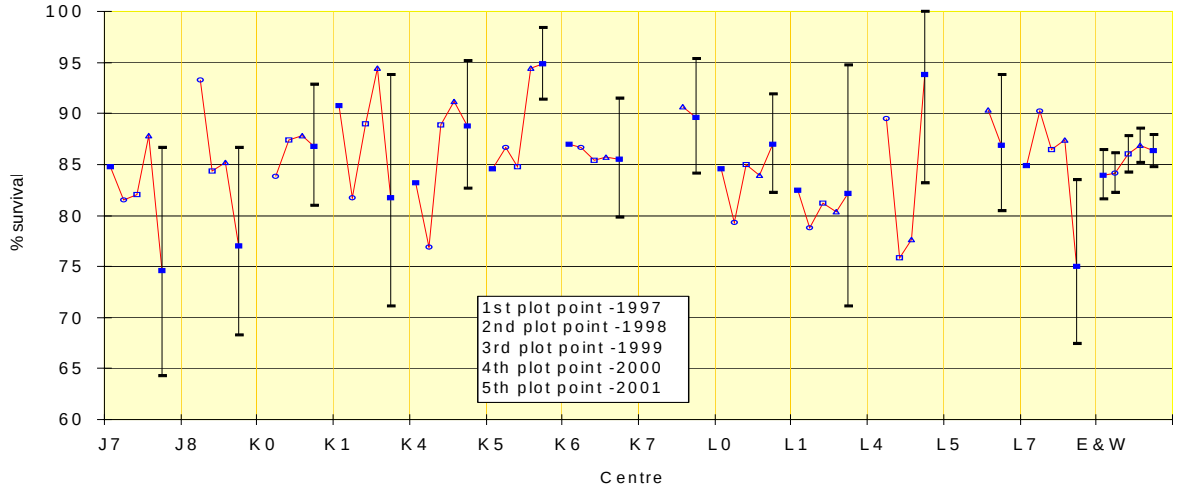

Figure 15.13b. Age adjusted survival, 1 year after 90 days; 1997–2001 cohort

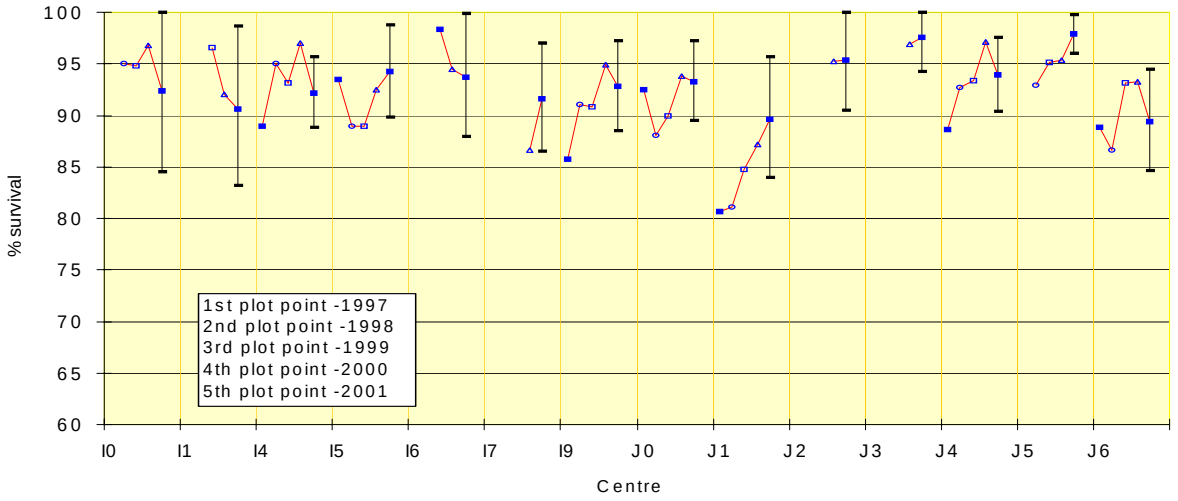

Figure 15.14a. Age adjusted survival in the first 90 days; 1997–2001 cohort

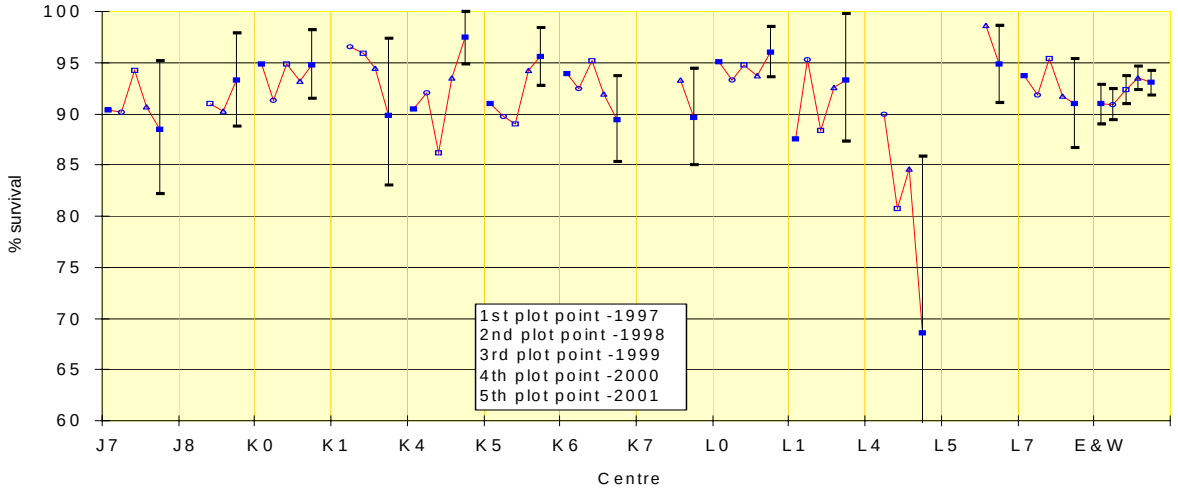

Figure 15.14b. Age adjusted survival in the first 90 days; 1997–2001 cohort