Appendix B: Definitions, Statistical Methodology and Analysis Criteria

B:1 Definitions of analysis quarters

Quarter	Dates
1	1 January–31 March
2	1 April–30 June
3	1 July–30 September
4	1 October–31 December

The quarterly biochemistry data were extracted from renal centre systems as the last data item stored for that quarter. If the patient treatment modality was haemodialysis, the software will try to select a pre-dialysis value.

B:2 Renal Registry modality definitions

Home haemodialysis

Home haemodialysis patients cease to be classed as such if they need longer than two weeks of hospital dialysis when not an in-patient.

Satellite dialysis unit

A renal satellite unit is defined as a haemodialysis facility that is linked to a main renal centre and not autonomous for medical decisions, and that provides chronic outpatient maintenance haemodialysis but with no acute or inpatient nephrology beds on site.

Treatment modality at 90 days

This is used by the United States Renal Data System (USRDS) and is the modality that the patient is on at day 90 regardless of any changes from the start. It is a general indicator of initial dialysis but could miss failed CAPD. This would also miss patients intended for home haemodialysis who were not home yet. This modality is calculated by the Registry, which allows the definition to be changed.

Start of established renal failure

Established renal failure (also known as end-stage renal failure/end-stage renal disease) was defined as the date of the first dialysis (or of pre-emptive transplant).

If a patient started as 'acute' renal failure and did not recover, the date of start of renal replacement should have been backdated to the start of acute dialysis.

If a patient was started on dialysis and dialysis was temporarily stopped for less than 90 days for any reason (including access failure and awaiting the formation of further access) except the recovery of renal function, the date of start of renal replacement therapy (RRT) remained the date of first dialysis. If the patient had stopped for longer than 90 days, he or she was classed as 'recovered'.

Change of modality from PD to HD

Sites are requested to log in their timeline changes from PD to HD if the modality switch is for longer than 30 days.

In analyses that included PD technique survival, patients on peritoneal dialysis who changed to haemodialysis for 30 days or less before changing back to PD were classified as remaining on PD. Those remaining on haemodialysis for more than 30 days and then changing back to PD were classified as having changed to haemodialysis.

B:3 Analysis criteria

Definition of the take-on population (Incidence)

The take-on population in a year included patients who later recovered from ERF after 90 days from the start of treatment. Patients newly transferred into a centre who were already on RRT were **excluded** from the take-on population for that

centre. Patients restarting dialysis after a failed transplant were also excluded (unless they started RRT in that current year).

Since patients who restarted RRT after recovering from ERF were included in the take-on population, the following scenario can occur: a patient may start RRT in 2005, recover and then restart RRT in 2005. Such patients were counted twice in the analysis providing they had been receiving RRT for more than 90 days on each occasion.

Patients who started treatment at a centre and then transferred out soon after receiving treatment were counted at the original centre for all analyses of treatment on the 90th day.

Definition of the prevalent population

This was calculated as all patients who were alive on 31 December and included the incident cohort for that year alive on that date.

Confidence interval

The 95% confidence intervals have been calculated using the normal approximation of the Poisson.

Death rate calculation

The death rate per 100 patient years was calculated by counting the number of deaths and dividing by the person years exposed. This included all patients, including those who died within the first 3 months of therapy. The person years at risk were calculated by adding up, for each patient, the number of days at risk (until they died or transferred out) and dividing by 365.

Odds ratio

The odds of dying was the:

$$\frac{\text{(Probability of dying for someone with a phosphate of 1.71}-\text{2.10 mmol/L)}}{\text{(Probability of surviving for someone with a phosphate of 1.71}-\text{2.10 mmol/L)}}$$

The odds ratio was the:

$$\frac{\text{(Odds of dying with a phosphate of 1.71}-\text{2.10 mmol/L)}}{\text{(Odds of dying in the reference group)}}$$

Hazard function

The hazard function was the probability of dying in a short time interval considering survival to that interval.

Hazard ratio

The hazard ratio was the:

$$\frac{\text{(Probability of dying in the next interval for a phosphate of 1.71}-\text{2.10 mmol/L)}}{\text{(Probability of dying in the next interval for a phosphate in the reference range)}}$$

Relative Hazard

Following the notation of Collett, D. (2003): Modelling survival data in medical research, Chapman & Hall, p. 57:

$$h_i(t) = \exp(\beta x_i) \,.\, h_0(t)$$

The relative hazard was the $\exp(\beta x_i)$ component in the general proportional hazards model with age, the variable of interest and it's square as covariates. The plots were done for $\exp(\beta x_i)$ for different values of the variable of interest only, in other words, age was taken as a constant value of zero.

Survival analyses of prevalent cohort

These analyses excluded the current year's incident cohort. Note some Renal Registries include these patients in the prevalent survival.

Criteria for analysis by treatment modality in a quarter

The following quarterly entries were included and excluded:

- Patients on haemodialysis with a treatment centre of 'elsewhere' were **removed**. It should be noted that there were some patients on transplant with a treatment centre of 'Elsewhere'; these patients were **included**.
- Entries for which the hospital centre was not the primary treatment centre were removed from the analysis of data for that centre.
- Patients who had been on RRT for less than 90 days were removed (by definition of ERF).

There were however, a few exceptions to these rules:

1. If a patient's initial entry on the treatment timeline contained a **'transferred in'** code, the patient was assumed to have been on RRT for longer than 90 days since the patient must have started RRT earlier than this elsewhere. Therefore, patients with an initial entry on the treatment timeline with a **'transferred in'** code were included for all quarters. A patient with an initial treatment modality of **'transferred in'** on 1 March 2005 would, for example, be included for the quarter 1 2005 even though the number of days on RRT would be calculated as 30 days.

2. For patients who **recovered** renal function for a period of time and then went into ERF, the length of time on RRT was calculated from the day on which the patient restarted RRT. For example, a patient with an initial treatment start date of 1 March 2006 who recovered on the 1 June 2006 and then resumed RRT again on 1 November 2006, the number of days on RRT would be calculated from 1 November 2006. The patient would be excluded from the analysis for quarter 4/06 since on 31 December 2006, he or she would have been on RRT for only 60 days. The patient would be included in the analysis from quarter 1/07 onwards.

If recovery was for less than 90 days, the start of renal replacement therapy was calculated from the date of the first episode and the recovery period ignored. Patients who had **transferred out** or **stopped treatment without recovery of function** before the end of the quarter were excluded.

Criteria for analysis of biochemistry in a quarter

The analysis used information from the quarterly treatment table. In addition to the treatment modality criteria listed above, patients with the following quarterly entries were also excluded:

1. Patients who had **'transferred in'** to the centre in that particular quarter were excluded. If for example, a patient transferred in on 1 March 2006, the patient was excluded from that biochemistry analysis of the centre transferred to in that quarter.

2. Patients who had changed treatment modality in that particular quarter were excluded.

Treatment modality on day 90 of starting RRT

This was obtained from the treatment modality of the take-on population after 90 days of being on RRT. For this reason, patients who started treatment between 1 October 2005 and 31 September 2006 were used in this analysis.

The sample used was that defined by the take-on population.

Patients were counted at their take-on hospital centre rather than at their hospital centre on day 90. This is important as some patients had transferred out of their initial hospital centre by day 90.

Patients who died before they reached 90 days were excluded.

One-year survival of the take-on population

The sample used was the same as that defined for the take-on population except for recovered renal function patients, who were excluded.

Patients who transferred out of their initial treatment centre were censored on the day they transferred out if there was no further information in the timeline.

Analysis of 1 year survival of prevalent patients

The death rate within the year was calculated separately for the patients established on dialysis and with a functioning transplant on 1 January 2006. As there is an increased death rate in the first 3 months following transplantation, patients were included in the analysis only if they had not received a transplant between 1 October 2005 and 31 December 2005. The sample criteria thus became:

1. Patients who had been receiving RRT for more than 90 days on 1 January 2006.

2. Patients who had a transplant between 1 October 2005 and 31 December 2005 were excluded.

3. Patients who transferred into a Registry centre were excluded if information was not available to confirm that they had not received a transplant between 1 October 2005 and 31 December 2005.

4. The few patients who recovered renal function in 2006 were excluded.

5. Patients who transferred out of a Registry centre to a non-Registry centre were censored at that date.

6. A transplant patient whose transplant failed was censored at the time of restarting dialysis and dialysis patients who received a transplant were censored at the time of transplantation.

7. Patients who died, received a transplant, or transferred out on 1 January 2006 were included and were counted as being at risk for 1 day.

8. Patients who died on the day of the transplant were censored on this day rather than counted as a dialysis death.

Co-morbidity definitions

Angina

History of chest pain on exercise with or without ECG changes, ETT, radionucleotide imaging or angiography.

Previous MI within last 3 months

The rise and fall of a biomarker (CK, CK-MB or Troponin) together with one of either: ischaemic symptoms, pathologic Q waves, ischaemic ECG changes or a coronary intervention.

The definition is from the European Society of Cardiology and American College of Cardiology.

Previous MI > 3 months ago

Any previous MI at least 3 months prior to start of renal replacement therapy.

Previous CABG or coronary angioplasty

Previous episode of heart failure

Whether or not due to fluid overload.

Cerebrovascular disease

Any history of strokes (whatever cause) and including transient ischaemic attacks caused by carotid disease.

Diabetes (not causing ESRF)

This includes diet controlled diabetics.

Chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) is characterised by airflow obstruction. The airflow obstruction is usually progressive, not fully reversible and does not change markedly over several months.

- Airflow obstruction is defined as a reduced FEV1 (forced expiratory volume in 1 second) and a reduced FEV1/FVC ratio (where FVC is forced vital capacity), such that FEV1 is less than 80% predicted and FEV1/FVC is less than 0.7.

- The airflow obstruction is due to a combination of airway and parenchymal damage.

- The damage is the result of chronic inflammation that differs from that seen in asthma and which is usually the result of tobacco smoke.

There is no single diagnostic test for COPD. Making a diagnosis relies on clinical judgement based on a combination of history, (exertional breathlessness, chronic cough, regular sputum production, frequent winter 'bronchitis', wheeze) physical examination and confirmation of the presence of airflow obstruction using spirometry (source: British Thoracic Society guidelines).

Liver Disease

Persistent enzyme evidence of hepatic dysfunction or biospy evidence or HbeAg or hepatitis C antigen (polymerase chain reaction) positive serology.

Malignancy

Defined as any history of malignancy (even if curative) eg removal of melanoma, excludes basal cell carcinoma.

Claudication

Current claudication based on a history, with or without Doppler or angiographic evidence.

Ischaemic/neuropathic ulcers

Current presence of these ulcers.

Angioplasty, stenting, vascular graft (all non coronary)

This category now includes vascular grafts (eg aortic bifurcation graft) and renal artery stents.

Amputation for Peripheral Vascular Disease

Smoking

Current smoker or history within the last year.