Chapter 5: Co-morbidities in UK Patients at the Start of Renal Replacement Therapy

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Summary

- This chapter contains an analysis of the available data on co-morbidity and smoking status at the start of Renal Replacement Therapy (RRT) in England and Wales between 2001 and 2006. Co-morbidity data completeness remained low and has improved little since 2001.

- Of all the patients starting RRT between 2001 and 2006 in centres reporting to the UK Renal Registry (after exclusion of data from centres from which data returns are considered unreliable) and for whom data on the presence or absence of co-morbid conditions was reported, 55% were reported to have one or more co-morbidities. Diabetes (either as primary renal disease or co-morbidity) and ischaemic heart disease were the most common conditions, seen in 29% and 24% of patients respectively.

- The prevalence of co-morbidity increased with increasing age up to the 65–74 age group. The prevalence of ischemic heart disease, cerebrovascular disease and peripheral vascular disease increased with increasing age, whereas the proportion of patients reported as being smokers declined with increasing age.

- The prevalence of most co-morbid conditions was much lower amongst patients of Black or South Asian origin compared to Whites, except for diabetes, which was more commonly observed in the ethnic minority populations.

- Patients who had a pre-emptive transplant had fewer co-morbidities compared to those whose first RRT modality was either haemodialysis (HD) or peritoneal dialysis (PD). Patients starting on PD were on average eight years younger and had fewer co-morbidities present compared to those on HD.

- The geometric mean eGFR was lower in those patients starting RRT without any co-morbidity compared to those starting RRT with at least one co-morbid condition (7.1 vs 7.9 ml/min/1.73 m^2, $p < 0.0001$).

- The presence of most co-morbidities were associated with a lower probability of being waitlisted for a deceased donor kidney transplant within the first year of RRT. The patient's smoking history did not affect waitlisting.

- In univariate Cox regression analysis, the association for most co-morbid conditions (except for chronic obstructive pulmonary disease and smoking) with mortality at 1 year after 90 days from start of RRT, was more pronounced for patients <65 years compared to those aged $\geqslant 65$ years.

- In multivariate Cox stepwise regression analysis, malignancy and ischaemic/neuropathic ulcers were the strongest predictors of poor survival at 1 year after 90 days from start of RRT, followed by liver disease, increasing age, previous MI and diabetes.

Introduction

Recording and reporting of the extent of co-morbidity amongst patients starting treatment for established renal failure (ERF) is important for a number of reasons.

1. Risk adjustment in reports of the outcomes of RRT: co-morbidity is associated with both early and long term mortality[1–4] and may also influence attainment of various clinical performance measures amongst patients on RRT. Case mix adjustment is therefore essential to quality reporting as differences in patient populations that exist across centres may affect process and outcome measures.

2. Resource allocation: patients with significant co-morbidity may require more inpatient[2] and outpatient care[5] and their treatment is therefore likely to cost more; information on co-morbidity may therefore help policy-makers, commissioners and providers to plan services.
3. Management of individual patients: the National Kidney Foundation and others have expanded clinical practice guidelines to include management of diabetes[6], dyslipidaemia[7] and cardiovascular disease[8] in patients with chronic kidney disease (CKD). It is therefore important as a first step, to document the presence of cardiovascular risk factors and other co-morbid illness to facilitate attainment of these goals.
4. Risk adjustment in clinical research: adjustment for differences in case mix is required in order to determine the true association of the treatment or other covariates with the outcome. For example, factors that may determine selection of peritoneal dialysis over haemodialysis such as young age and minimal co-morbidity are associated with better survival. Without adequate case mix adjustments, survival comparisons on PD versus HD will be biased in favour of PD.
5. International comparisons: there are marked national and international variations in the take-on rate for RRT with differences in underlying primary diagnoses. Comparisons of outcomes between countries require adjustment for the differences in co-morbidities. Many patients die before reaching ERF in Northern European countries with high rates of IHD in the general population.

The prevalence of various co-morbid conditions at the time of starting RRT and the association of these co-morbidities with patient demographics and early mortality are described in this chapter.

Methods

Study population

All adult ($\geqslant$18 years) patients who started RRT between 2001 and 2006 in centres reporting to the UK Renal Registry (UKRR) in these years and with data on co-morbidity were included. The total number of incident RRT patients in the centres included in a given year is described in Chapter 3. Scottish centres do not provide co-morbidity data to the UKRR and were not included in the analyses.

Data on completeness of co-morbidity returns from each centre and overall may differ from those in previous reports because of the exclusion of centres previously included (see below) and due to some centres backfilling previously missing co-morbidity data.

Centre exclusions

In the previous report[9] it was stated that centres using the Mediqal IT system had the highest co-morbidity data completeness. On more detailed investigation many of these centres seemed to have lower rates of co-morbidities present than expected for RRT patients. These high data completeness rates from the centres using Mediqal software were due to the IT system having a default setting to report missing co-morbidity data (data not entered) as an absence of co-morbidity. Therefore all six centres in Northern Ireland and four centres in England (Basildon, Chelmsford, Dorset and Norwich) have been excluded from these analyses.

Ipswich (Baxter software) was found to have an unusually low proportion (<15%) of patients with no co-morbidity present. They also had a low data completeness (<35%). One possible explanation was selective under-reporting of patients with no co-morbidity. This centre has been excluded from these analyses pending further investigation of reasons for this discrepancy.

Definition of co-morbidity and method of data collection

Clinical staff in each centre are responsible for recording (in yes/no format), on their renal IT system, the presence or absence of 13 co-morbid conditions and information on current tobacco smoking (Table 5.1) for each patient at the time of starting RRT. Definitions of each of these conditions are given elsewhere[10]. Complete data on co-morbidity for a given patient was considered to have been provided if there was a non-missing entry (yes/no) for at least one of the 14 co-morbid conditions. For some analyses co-morbidities have been collapsed into broader categories.

Table 5.1: Co-morbid conditions listed in the Registry dataset

Angina
Previous myocardial infarction (MI) within 3 months prior to start of RRT
Previous MI more than 3 months ago prior to start of RRT
Previous coronary artery bypass graft (CABG) or coronary angioplasty
(in some analyses the above four variables are combined under the term 'ischaemic heart disease')
Cerebrovascular disease
Diabetes (when not listed as the primary renal disease)
Chronic obstructive pulmonary disease (COPD)
Liver disease
Claudication
Ischaemic or neuropathic ulcers
Non-coronary angioplasty, vascular graft, or aneurysm
Amputation for peripheral vascular disease
(in some analyses these four variables are combined under the term 'peripheral vascular disease')
Smoking
Malignancy

- 'Ischaemic heart disease' was defined as the presence of one or more of the following conditions: angina, myocardial infarction (MI) in the 3 months prior to starting RRT, MI more than 3 months prior to starting RRT, or coronary artery bypass grafting (CABG)/angioplasty.

- 'Peripheral vascular disease' was defined as the presence of one or more of the following conditions: claudication, ischaemic or neuropathic ulcers, non-coronary angioplasty, vascular graft, aneurysm, or amputation for peripheral vascular disease.

- 'Vascular disease' was defined as the presence of cerebrovascular disease or any of the data items that comprise 'peripheral vascular disease'.

Ethnicity data reporting

Some centres electronically upload ethnicity coding to their renal IT system from the hospital Patient Administration Systems (PAS). Ethnicity coding in these PAS systems is based on self-reported ethnicity and uses a different coding system[11].

For the remaining centres, ethnic coding is performed by clinical staff and recorded directly into the renal IT system (using a variety of coding systems). For all these analyses, data on ethnic origin were grouped into Whites, South Asians, Blacks, Chinese and Others. The details of regrouping of the PAS codes into the above ethnic categories are provided in Appendix J at www.renalreg.org.

Renal function and haemoglobin at the start of RRT

The association of various co-morbidities with haemoglobin and with estimated glomerular filtration rate (eGFR) at start of RRT was studied amongst patients with data on these two variables within 14 days before the start of RRT.

Two-sample t-tests were used to compare the mean haemoglobin at start of RRT amongst patients with a specific co-morbidity with the mean for those with none of the co-morbidities. The eGFR was calculated using the abbreviated 4v MDRD study equation[12]. The eGFR values were log transformed in order to normalise the data and then two-sample t-tests were used to compare the means of the log eGFR of those patients with the specific co-morbidity against those with none of the co-morbidities present. As many tests were carried out, only p values <0.01 were considered statistically significant for these analyses.

There is no defined standard for a threshold eGFR at which patients should start RRT for ERF as this is weighted in conjunction with

other clinical parameters. However, there are defined thresholds for pre-emptive listing for a kidney transplant. The European Best Practice guidelines (EBPG) recommend that patients with progressive deterioration in renal function and a creatinine clearance of $<15\,ml/min/1.73\,m^2$ should be considered for pre-emptive transplantation; patients with ERF secondary to diabetes should be considered for an early and pre-emptive transplantation when their eGFR decreases to $<20\,ml/min/1.73\,m^2$ [13]. In the UK, the British Transplantation Society endorses the EBPG (www.bts.org.uk) and current UK Renal Association guidelines recommend that patients should be placed on the kidney transplant waiting list within six months of their anticipated dialysis start date[14]. There are no KDOQI guidelines for listing.

It is therefore possible that patients could have started RRT with a transplant and an eGFR value as high as $20\,ml/min/1.73\,m^2$. Patients with an eGFR $>20\,ml/min/1.73\,m^2$ were excluded from the eGFR analyses due to concerns on possible data errors. Patients starting RRT between 2001 and 2005 from one centre (London West) were also excluded due to errors in the data extraction process for this item. This extraction process had been rectified for the year 2006 and patients starting RRT in this centre in 2006 have been included.

The analyses excluded 3,104 patients who had no data on eGFR within 14 days prior to start of RRT, 365 who had eGFR values $>20\,ml/min/1.73\,m^2$ and 446 patients from London West leaving 6,896 patients in this analysis.

Activation on deceased donor transplant waiting list

There are no standards for the proportion of patients in a centre that should be waitlisted for a deceased donor transplant. It was previously reported that the proportion of patients on the active deceased donor transplant waiting list (TWL) varied widely across centres[15]. Both centre specific and patient specific factors including co-morbidity could have accounted for these variations. Therefore an analysis was undertaken to investigate if there were differences in co-morbidity amongst patients activated early on the TWL compared to those activated later or never.

Date of first activation on the deceased donor TWL for all patients starting RRT between 2001 and 2004 on the UKRR database were obtained from NHS Blood and Transplant (formerly UK Transplant), the independent organisation responsible for maintaining the national organ donor register. All patients were followed until 31st December 2005 to determine the date of activation on the TWL. The prevalence of various co-morbidities amongst patients activated on the deceased donor TWL within the first year of RRT was compared with those not activated on the TWL within the first year. Patients who died within the first year and were not on the active TWL at the time of death were included under the 'non-waitlisted' group.

Co-morbidity and survival

The Registry collected data with a 'timeline' entry on all patients who had started RRT for ERF. Patients who presented acutely and who were initially classified as acute renal failure requiring dialysis, but continued to require long-term dialysis can be re-classified as having had ERF from the date of their first RRT. Many other national Registries only collect data on patients who have survived the first 90 days of RRT. The UKRR, unlike these other registries, is able to collect and report data on factors affecting outcomes, including survival, in the first 90 days of RRT. However, the death rate is high in the first 90 days and highly variable between centres, due partly to individual clinical variation in the classification of patients with acute kidney injury who may be deemed from the start to be unlikely to recover renal function. To remove this centre variation and also allow comparison of results from other national Registries, the association of co-morbid conditions and survival 1 year after 90 days from start of RRT was also analysed.

For each of the follow up periods, the association of baseline co-morbidity with survival was studied using univariate and also multivariate Cox regression models. For analyses of survival within the first 90 days, the cohort included patients starting RRT between 1st January 2001 and 30th September 2006 to allow a minimum of three months follow-up from the start of RRT.

For the 1 year after 90 days survival analyses, the cohort included patients who survived at least 90 days on RRT and who started RRT between 1st January 2001 and 30th September 2005.

For each variable, the models estimated the hazard ratio of death comparing those with a particular co-morbidity with those who do not have the co-morbidity. The multivariate Cox models used a backward stepwise method that included all variables and then sequentially removed the variable with the largest p value (i.e. the one which added least to the model); the procedure was continued until all remaining variables were significant contributors to the model.

In the univariate models, patients were first stratified by age group (<65 years and ⩾65 years) to account for the increasing incidence of certain co-morbidities with age, which may otherwise obscure the analysis. The variables included in the multivariate model were: age per 10 years, angina, MI within 3 months prior to starting RRT, MI more than 3 months prior to starting RRT, coronary artery bypass grafting (CABG) or coronary angioplasty, cerebrovascular disease, diabetes mellitus (whether as a cause of primary renal disease or as a co-morbidity), chronic obstructive pulmonary disease (COPD), liver disease, malignancy, claudication, ischaemic/neuropathic ulcers, angioplasty/vascular graft, amputation and smoking.

The effect within each centre of adjusting overall survival for co-morbidity is reported in Chapter 6.

Results

Completeness of co-morbidity returns from each participating centre

Table 5.2 shows that completeness of data returns still varies markedly between centres with one centre providing data on 100% of patients but 22 providing data for less than 5% of their new patients. There was no relationship between the size of the centre and the completeness of data returns. Amongst all incident patients, data on co-morbidity has declined from 42.3% of patients starting in 2001 to only 35.1% in 2006 (Table 5.3). After excluding centres that returned no data at all, the average completeness of data returns from centres ranged from 1–100% (mean 52%) for 2006, a moderate improvement on a mean of 47.8% in 2001. As stated above, a return was considered to be 'complete' if there was at least one answer to the 14 questions on the co-morbidity screen. However, most records that contained at least one answer contained answers to most or all of the other questions; only 0.4% had 10 or fewer questions answered, 1.2% contained 11 answers, 1.2% contained 12 answers, 7.7% contained 13 answers and 89.6% contained answers to all 14 questions.

Prevalence of multiple co-morbidity

Of patients for whom co-morbidity data were available, 54.6% had at least one co-morbidity present and 28.4% had more than one co-morbid condition (Table 5.4).

Frequency of each co-morbidity condition

Table 5.5 gives the frequency of each co-morbidity and the percentage this was of the total number of incident patients (for whom data was available for that item) for patients aged <65 and ⩾65 years in addition to the overall percentage who had each co-morbidity in the incident population.

Prevalence of co-morbidity by age band

Figures 5.1 and 5.2 illustrate the rising prevalence of co-morbidity with increasing age up to the 65–74 age group in incident patients; the levelling off or slight reductions in reported co-morbidity amongst patients aged over 75 years may reflect a 'healthy survivor effect' or decisions made by nephrologists and/or patients aged >75 years with cardiovascular co-morbidity not to embark on RRT. The prevalence of smoking reported amongst patients starting RRT decreased as age increases above age 55. Ischaemic heart disease, cerebrovascular disease and peripheral vascular disease all become more common as age group increases.

Table 5.2: Completeness of co-morbidity data returns on incident patients from individual centres (2001–2006)

	2001		2002		2003		2004		2005		2006	
	No. incident patients	% return	No. incident patients	% return	No. incident patients	% return	No. incident patients	% return	No. incident patients	% return	No. incident patients	% return
B Heart	85	0	66	2	104	0	102	0	116	1	119	0
B QEH							195	0	195	1	187	0
Bangor			29	59	33	42	36	56	40	53	40	40
Bradfd	61	93	62	100	74	85	62	92	66	95	49	100
Brightn							119	0	110	0	131	1
Bristol	153	92	124	82	163	83	164	79	176	88	173	84
Camb	92	5	74	4	99	1	112	0	160	0	92	0
Cardff	154	1	181	0	166	3	187	6	183	20	206	3
Carlis	29	3	26	23	31	19	29	66	31	90	27	81
Carsh	123	18	175	6	201	8	167	7	182	4	190	2
Chestr	2	0	3	0	4	0	5	0			4	0
Clwyd			20	0	12	0	14	0	27	0	17	0
Covnt	106	0	96	1	75	0	76	0	84	0	104	0
Derby	59	44			60	73	67	78	71	90	72	69
Dudley	34	0	25	8	41	0	55	0	38	0	45	2
Exeter	97	35	82	50	98	51	110	45	111	28	114	25
Glouc	49	96	54	67	53	87	53	89	60	97	73	88
Hull	74	0	105	5	80	89	109	86	126	95	98	95
L Barts							187	74	183	84	179	73
L Guys	111	2	141	2	93	2	104	3	133	3	133	0
L Kings			116	88	108	100	114	99	136	99	111	99
L Rfree									131	2	206	0
L West			234	77	230	67	272	72	267	55	272	67
Leeds	165	88	152	86	185	86	174	82	164	66	186	52
Leic	184	90	152	88	168	96	162	94	225	63	241	61
Liv Ain							3	0	29	3	36	0
Liv RI	217	50	153	49	114	62	129	60	139	59	142	46
ManWst					143	32	113	41	111	34	127	6
Middlbr	81	90	111	100	103	0	102	1	84	0	97	0
Newc			107	1	108	3	106	0	94	3	110	1
Nottm	120	68	87	99	115	98	107	95	146	99	136	90
Oxford	170	2	170	1	187	44	172	53	163	17	163	1
Plymth	65	6	79	11	64	5	62	18	58	14	93	9
Ports	144	58	146	47	141	57	118	58	151	46	174	34
Prestn	135	1	110	0	98	1	79	0	118	0	121	0
Redng	62	0	39	3	63	0	59	0	74	0	72	0
Sheff	153	88	156	62	159	61	169	46	158	33	167	46
Shrew							55	0	43	0	54	0
Stevng	127	4	101	3	119	3	88	3	91	3	115	0
Sthend	36	33	33	61	42	64	40	70	34	68	44	95
Sund	39	5	57	47	56	64	51	88	59	92	58	84
Swanse	113	73	113	82	128	97	93	92	97	97	113	95
Truro	40	55	59	66	53	83	67	81	32	84	50	78
Wirral			40	18	49	12	63	14	58	7	56	2
Wolve	75	99	99	100	88	100	105	96	93	84	93	45
Wrexm	35	0	42	0	32	3	29	0	41	0	25	0
York	37	92	63	81	57	84	48	92	43	91	47	87
Totals	**3,227**		**3,682**		**3,997**		**4,533**		**4,931**		**5,162**	

Blank cells – no data returned to the Registry for that year.

Table 5.3: Summary of completeness of incident patient co-morbidity returns (2001–2006)

	Years						Combined years
	2001	2002	2003	2004	2005	2006	
Number of centres included	34	39	41	46	46	47	
Total number of new patients	3,227	3,682	3,997	4,533	4,931	5,162	25,532
Number of patients with co-morbid data entries	1,365	1,622	1,912	2,078	2,023	1,811	10,811
Percentage of patients from all centres	42	44	48	46	41	35	42
Median percentage amongst only centres returning co-morbidity	50	50	62	71	57	56	59

Table 5.4: Number of reported co-morbidities in patients starting RRT, as a proportion of those for whom co-morbidity data was available (2001–2006)

Number of co-morbidities	0	1	2	3	4	5+
%	45.4	26.2	13.8	7.6	4.0	2.9

Table 5.5: Frequency with which each condition was reported in incident RRT patients 2001–2006

	Age <65 years		Age ⩾65 years		
Co-morbidity	No. patients	%	No. patients	%	Overall incidence (%)
Ischaemic heart disease	799	14.8	1,756	33.6	24.0
Angina	551	10.1	1,310	25.0	17.4
MI in past 3 months	94	1.7	211	4.0	2.8
MI >3 months ago	333	6.1	853	16.2	11.0
CABG/angioplasty	266	4.9	412	7.9	6.4
Cerebrovascular disease	340	6.2	776	14.7	10.4
Diabetes (not cause of ERF)	271	5.1	565	10.9	7.9
Diabetes as primary disease	1,340	24.3	932	17.6	21.0
Diabetes of either category	1,611	29.3	1,497	28.2	28.8
COPD	217	4.0	536	10.2	7.1
Liver disease	154	2.8	96	1.8	2.3
Malignancy	351	6.4	913	17.3	11.7
Peripheral vascular disease	490	9.0	851	16.2	12.5
Claudication	292	5.3	646	12.2	8.7
Ischaemic/neuropathic ulcers	207	3.8	183	3.5	3.6
Angioplasty/vascular graft	101	1.8	249	4.7	3.3
Amputation	136	2.5	77	1.5	2.0
Smoking	964	19.0	688	13.8	16.4
No co-morbidity present	3,121	56.7	1,792	33.8	45.4

Prevalence of co-morbidity amongst patients with diabetes

Diabetes was recorded as the primary renal disease in 21% of all patients starting RRT between 2001 and 2006. Only 10,556 patients who had data on co-morbidity and had a non-missing code for primary renal disease were included in this analysis. Table 5.6 compares co-morbidity amongst patients with diabetes and without diabetes (either as primary renal disease or co-morbidity) who had at least one other co-morbidity present, showing higher rates of ischaemic heart disease, cerebrovascular disease and peripheral vascular disease amongst diabetic patients.

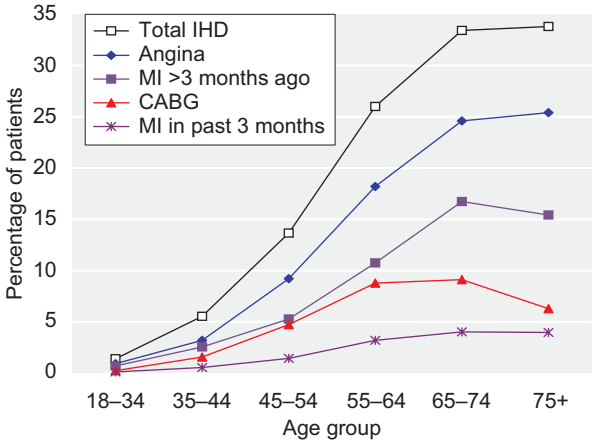

Figure 5.1: Prevalence of ischaemic heart disease amongst incident patients 2001–2006 by age at start of RRT

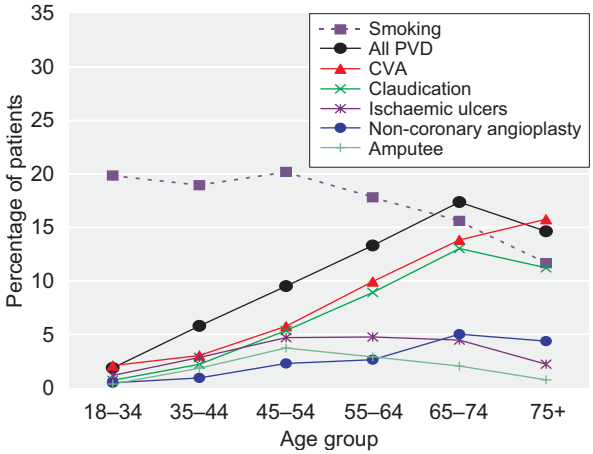

Figure 5.2: Prevalence of vascular disease amongst incident patients 2001–2006 by age at start of RRT

Age and co-morbidity in patients by treatment modality at start of RRT

Amongst all patients with data on co-morbidity, 1.7% started RRT with a pre-emptive transplant. This compared with a UK average of 4% of patients being pre-emptively transplanted. This must reflect a tendency to not report co-morbidity on some patients who have no co-morbid conditions present.

The proportion of patients aged less than 65 years who had at least one co-morbidity was 44.2% amongst those who started with either HD or PD compared to 16.3% amongst patients who had a pre-emptive transplant (Fischer's exact test, $p < 0.0001$). The number of pre-emptive transplants was too small to undertake comparisons for individual co-morbidities.

The median age of patients on PD at the start of RRT was 66.6 years compared with 59.0 years for those starting HD (Kruskal Wallis test, $p < 0.0001$). Table 5.7 compares the prevalence of individual co-morbidities in patients on HD and PD at the start of RRT, showing significantly higher prevalence amongst HD patients of all co-morbid conditions other than MI more than 3 months ago and previous CABG. The percentages shown are out of the total population of patients on that modality at the start of RRT with data for that co-morbidity. These findings probably reflect a perception amongst UK nephrologists, nurses and patients that PD is in general more suitable for younger and fitter patients. In addition, the presence of certain co-morbid conditions such as cerebrovascular disease, liver disease and COPD that adversely affect the ability of patients to perform PD exchanges or to tolerate large volumes of dialysate in the peritoneum could have favoured the choice of HD in these patients. Some centres in the UK are starting to provide assisted APD (by a carer) which may alter this patient distribution in future.

Table 5.6: Percentage of patients with and without diabetes (either as primary diagnosis or co-morbidity) who have other co-morbid conditions

Co-morbidity	Non-diabetics	Diabetics	p value*
Ischaemic heart disease	19.8	33.6	<0.0001
Cerebrovascular disease	8.7	14.4	<0.0001
Peripheral vascular disease	8.2	23.1	<0.0001
Smoking	16.6	16.4	0.82
COPD	7.0	7.2	0.71
Malignancy	13.5	7.6	<0.0001
Liver disease	2.2	2.6	0.30

*p values from Chi-squared test for differences in the % with the co-morbidities, between diabetics and non-diabetics.

Table 5.7: Percentage of patients with co-morbid conditions present in incident patients starting PD and HD 2001–2006

	HD		PD		
Co-morbidity	**%**	**Median age**	**%**	**Median age**	**p value***
Angina	19.0	71.5	13.5	67.7	< 0.0001
MI >3 months ago	11.4	71.5	10.4	68.5	0.15
MI in past 3 months	3.3	70.3	1.6	70.7	<0.0001
CABG/angioplasty	6.3	68.7	6.7	66.6	0.47
Cerebrovascular disease	11.5	71.6	7.5	66.0	<0.0001
Diabetes (not cause of ERF)	9.1	71.0	4.9	66.9	<0.0001
COPD	8.2	71.2	4.1	68.3	<0.0001
Smoking	17.1	62.5	14.8	55.3	0.008
Liver disease	2.7	60.1	1.1	59.3	<0.0001
Malignancy	13.5	72.0	6.9	70.0	<0.0001
Claudication	9.5	70.5	6.8	66.8	<0.0001
Ischaemic/neuropathic ulcers	4.2	64.8	2.0	58.6	<0.0001
Angioplasty/vascular graft	3.6	71.8	2.4	66.8	0.005
Amputation	2.2	62.1	1.5	55.0	0.019

*p values from Chi-squared tests for differences between modalities in the % with the co-morbidities.

Prevalence of co-morbidity by ethnic origin

Of the incident patients starting RRT between 2001 and 2006, there were 9,277 patients with data returns on both ethnicity and co-morbidity who were included in this analysis.

Figure 5.3 illustrates the presence or absence of co-morbidity by ethnic origin, showing a lower prevalence of co-morbidity amongst patients of ethnic minority compared with those of White origin. Figures 5.4, 5.5 and 5.6 show that the lower prevalence of co-morbidity amongst patients of Black or Asian origin is not entirely attributable to younger age amongst these groups, as the prevalence of co-morbidity was lower than in the White population even in the 18–34 year age group. Table 5.8 shows the prevalence of major co-morbidities in each group; compared to Whites, Blacks and South Asians had lower prevalence of most co-morbid conditions (with the exception of liver disease and diabetes).

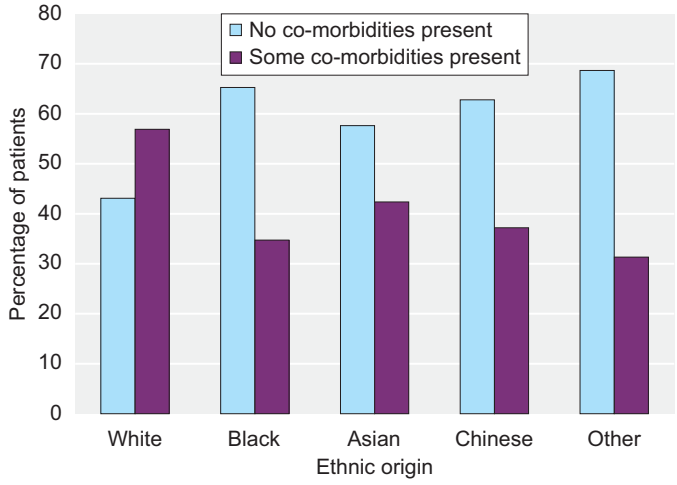

Figure 5.3: Presence or absence of co-morbid conditions at the start of RRT amongst patients starting RRT 2001–2006

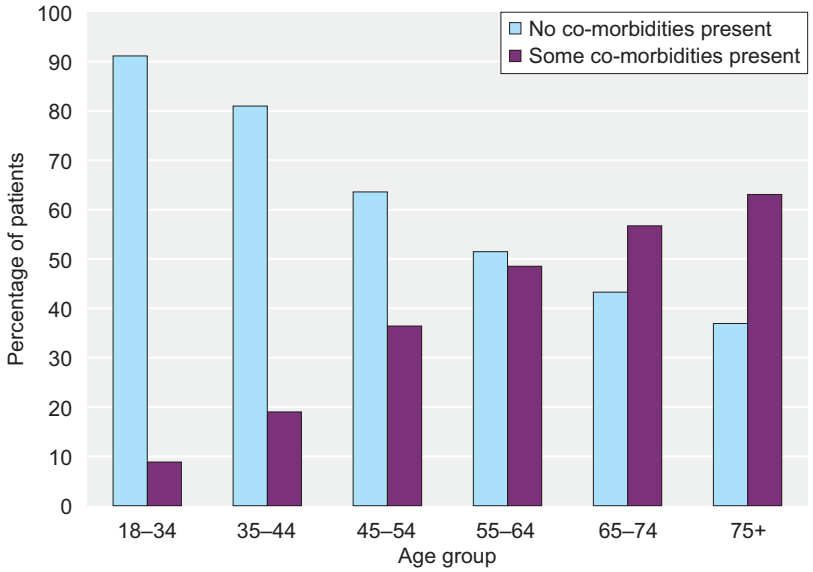

Figure 5.4: Presence or absence of co-morbid conditions at the start of RRT amongst patients of South Asian origin starting RRT 2001–2006

Renal function at the time of starting RRT and co-morbidity

The (geometric) mean eGFR prior to starting RRT in patients who are recorded as starting without any co-morbidity present was 7.1 ml/min/1.73 m^2 (Table 5.9). Patients starting with each of the co-morbidities were compared against the no co-morbidity present group. Due to multiple testing, caution needs to be exercised while interpreting the significance of the associations and a p value of <0.01 would be considered statistically significant. This however may not indicate any clinical significance as there may only be a small variation in values between the two groups.

In each case, average eGFR was slightly higher amongst patients with co-morbidity compared to patients without any co-morbidity, suggesting that patients with more co-morbidity tend to be advised to start dialysis earlier than those without co-morbidity. If trying to compare patient survival between these groups, then

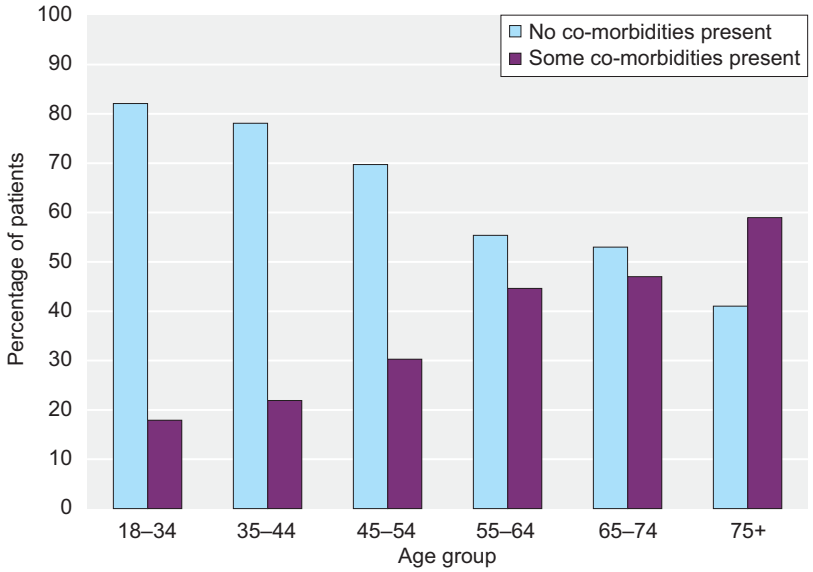

Figure 5.5: Presence or absence of co-morbid conditions at the start of RRT amongst patients of Black origin starting RRT 2001–2006

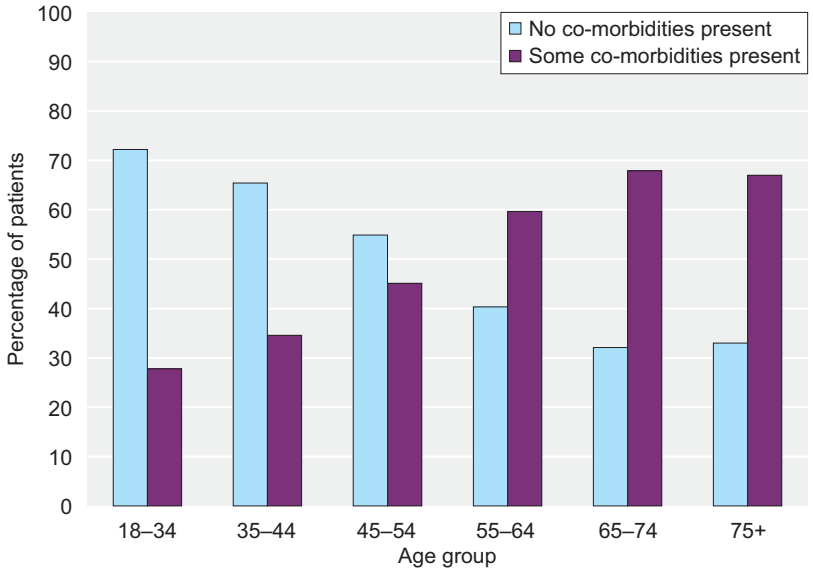

Figure 5.6: Presence or absence of co-morbid conditions at the start of RRT amongst patients of White origin starting RRT 2001–2006

the potential of an 'earlier start' may need to be adjusted for in the analyses.

Haemoglobin concentration at the time of starting RRT and co-morbidity

The mean haemoglobin prior to starting RRT in patients who are recorded as starting without any co-morbidity present is 10.1 g/dl, with 53% of these patients achieving a haemoglobin >10 g/dl. Patients starting with each of the co-morbidities were compared against this group (Table 5.10). Again due to multiple testing, a p value of <0.01 would be considered statistically significant. This however may not indicate clinical significance as they may be only small variations. Haemoglobin concentrations at the start of RRT were slightly higher amongst patients with previous CABG and MI more than 3 months prior to starting RRT than in those without any co-morbidities and lower amongst those with ischaemic/neuropathic ulcers. In addition to the

Table 5.8: Prevalence of co-morbidities amongst incident patients starting RRT 2001–2006 by ethnic group, as percentages of the total number of patients in that ethnic group for whom co-morbidity data were available

	% with co-morbidity					
	South Asian	Black	White	Chinese	Other	p value*
Number of patients with data	859	452	7,674	43	249	
Smoking	6.6	8.2	18.0	5.4	5.2	<0.0001
Cerebrovascular disease	8.7	9.8	10.3	9.3	6.8	0.26
Peripheral vascular disease	9.7	5.1	13.0	14.0	7.7	<0.0001
Ischaemic heart disease	24.2	11.6	24.7	9.5	13.2	<0.0001
Liver disease	3.5	3.1	2.2	7.0	0.8	0.010
COPD	3.5	2.4	7.9	0.0	3.3	<0.0001
Malignancy	2.9	5.1	13.0	4.7	4.8	<0.0001
Diabetes of either category	49.0	35.0	25.7	30.2	41.0	<0.0001
Diabetes (not cause of ERF)	9.0	4.5	7.8	7.1	7.8	0.071
Diabetes as primary disease	40.4	30.5	18.0	23.3	33.3	<0.0001

*p values from Chi-squared tests for differences between ethnic groups in the % with the co-morbidities.

Table 5.9: eGFR within 2 weeks prior to the start of RRT (2001–2006) by co-morbidity

	eGFR geometric mean (ml/min/1.73 m^2)	eGFR 95% CI	p value*
Without co-morbidity	7.1	7.0–7.2	Ref
Some co-morbidity present	7.9	7.8–8.0	<0.0001
Angina	8.4	8.2–8.5	<0.0001
MI in past 3 months	8.3	7.9–8.8	<0.0001
MI >3 months ago	8.4	8.2–8.6	<0.0001
CABG/angioplasty	8.6	8.4–8.9	<0.0001
Cerebrovascular disease	8.0	7.8–8.3	<0.0001
Diabetes (not cause of ERF)	8.2	7.9–8.4	<0.0001
Diabetes as primary disease	8.3	8.1–8.5	<0.0001
Diabetes of either category	8.3	8.1–8.4	<0.0001
COPD	8.2	7.9–8.5	<0.0001
Liver disease	7.8	7.3–8.3	0.009
Malignancy	7.5	7.3–7.7	0.003
Claudication	8.4	8.2–8.7	<0.0001
Ischaemic/neuropathic ulcers	8.3	8.0–8.7	<0.0001
Angioplasty/vascular graft	8.5	8.1–8.9	<0.0001
Amputation	8.7	8.1–9.2	<0.0001
Smoking	7.9	7.7–8.1	<0.0001

*Two-sample t-test compares log (eGFR) for each co-morbidity against those without co-morbidity.

Table 5.10: Haemoglobin concentration at the start of RRT (2001–2006) by co-morbidity

	Hb mean (g/dl)	Hb 95% CI	p value*	% Hb >10 g/dl
Without co-morbidity	10.1	10.0–10.2	Ref	53.0
Some co-morbidity present	10.1	10.0–10.1	0.410	51.5
Angina	10.2	10.1–10.3	0.231	54.0
MI in past 3 months	10.0	9.8–10.3	0.575	53.6
MI >3 months ago	10.4	10.2–10.5	0.001	57.8
CABG/angioplasty	10.4	10.2–10.5	0.006	56.6
Cerebrovascular disease	10.2	10.0–10.3	0.493	53.3
Diabetes (not cause of ERF)	10.0	9.9–10.1	0.231	50.4
Diabetes as primary disease	10.0	9.9–10.1	0.602	51.4
COPD	10.0	9.9–10.2	0.295	51.8
Liver disease	9.8	9.5–10.0	0.025	43.4
Malignancy	10.0	9.8–10.1	0.026	48.5
Claudication	10.0	9.9–10.1	0.170	50.7
Ischaemic/neuropathic ulcers	9.8	9.6–10.0	0.005	43.0
Angioplasty/vascular graft	10.3	10.0–10.5	0.231	56.7
Amputation	9.9	9.6–10.1	0.121	46.2
Smoking	10.1	10.0–10.2	0.547	50.6

*Two-sample t-test compares mean Hb for each co-morbidity against those without co-morbidity.

direct influence of co-morbidity, EPO prescribing patterns and the late referral of patients will also affect haemoglobin levels.

Co-morbidity and subsequent activation on deceased donor transplant waiting list

Table 5.11 shows that patients starting dialysis as their first RRT modality and who were activated on the TWL within the first year, were younger and had significantly less co-morbidity (except smoking) at the start of RRT than those who were not activated within the first year. Hence, when time taken to activate patients on the transplant waiting list is used as a marker of quality of care provided by the centres, adjustments for differences in co-morbidity should be made for meaningful comparisons of the performance of each centre in listing patients for a transplant.

Co-morbidity and survival within 90 days of starting RRT

On univariate analysis stratified for age, most co-morbidities were associated with an increased risk of death in the first 90 days, both amongst patients aged <65 years and those aged ⩾65 years, the associations being more profound for those aged <65 years. There was no increased risk of death within the first 90 days associated with diabetes mellitus as a co-morbidity in the absence of diabetes as a cause of primary renal disease; and smoking was also not associated with an increased 90 day risk (Table 5.12). Both these factors are associated with longer term increased risk.

Some co-morbidities may appear not to be associated with an increased risk of death because of the low number of patients in these groups – for instance, liver disease in those aged 65 or over. Table 5.13 shows the hazard of death within 90 days of RRT associated with various co-morbid conditions grouped into broader categories.

On multivariate analysis using the stepwise Cox proportional hazards model, age and eight of the co-morbid conditions were identified as significant independent predictors of the risk of death (Table 5.14). Diabetes did not emerge as an independent predictor, probably due to the close association between diabetes and ischaemic heart disease, cerebrovascular disease and peripheral vascular disease.

Co-morbidity and survival 1 year after 90 days of commencing RRT

On univariate analysis (Table 5.15) stratified for age, most co-morbidities were associated with

Table 5.11: Co-morbidity amongst incident patients 2001–2004 who were activated on the transplant waiting list within the first year compared to those who were not activated within the first year of RRT

	Not on waiting list			On waiting list			
Co-morbidity	**%**	**N**	**Median age**	**%**	**N**	**Median age**	**p value***
Angina	21.6	1187	70.7	3.8	51	56.3	<0.0001
MI >3 months ago	13.5	743	70.6	1.9	25	55.6	<0.0001
MI in past 3 months	3.6	200	69.9	0.4	6	52.5	<0.0001
CABG/angioplasty	6.8	371	68.0	2.4	31	56.3	<0.0001
Cerebrovascular disease	12.4	685	71.5	2.7	36	55.6	<0.0001
Diabetes (not cause of ERF)	8.5	463	71.6	2.5	33	49.7	<0.0001
COPD	8.8	480	71.5	2.1	28	54.4	<0.0001
Smoking	17.8	925	65.4	16.8	212	44.0	0.381
Liver disease	2.7	149	62.1	0.9	12	49.2	<0.0001
Malignancy	14.4	796	71.8	1.6	21	57.3	<0.0001
Claudication	11.8	648	70.1	1.8	24	48.2	<0.0001
Ischaemic/neuropathic ulcers	4.5	249	64.4	1.0	13	50.0	<0.0001
Angioplasty/vascular graft	4.1	224	71.0	0.3	4	55.3	<0.0001
Amputation	2.4	134	59.6	0.4	5	51.7	<0.0001

*p values from Chi-squared tests for differences between transplant waiting list groups in the % with the co-morbidities.

Table 5.12: Univariate analysis of the risk of death within the first 90 days of RRT associated with co-morbid conditions at the start of RRT during 01/01/01–30/9/06

	Age <65		Age ⩾65	
Co-morbidity	**Hazard ratio**	**p value**	**Hazard ratio**	**p value**
Angina	2.9	<0.0001	1.4	0.001
MI >3 months ago	2.2	0.004	1.5	0.001
MI in past 3 months	3.8	0.001	2.5	<0.0001
CABG/angioplasty	1.2	0.626	1.0	0.970
Cerebrovascular disease	2.7	0.001	1.4	0.009
Diabetes (not cause of ERF)	1.2	0.609	1.2	0.130
COPD	2.2	0.016	1.5	0.003
Smoking	1.1	0.675	1.2	0.197
Liver disease	5.7	<0.0001	1.1	0.772
Malignancy	5.3	<0.0001	1.6	<0.0001
Claudication	2.1	0.009	1.2	0.096
Ischaemic/neuropathic ulcers	2.6	0.002	2.0	0.001
Angioplasty/vascular graft	0.9	0.853	0.8	0.350
Amputation	2.9	0.004	0.9	0.819

Table 5.13: Univariate analysis of the risk of death within the first 90 days of RRT associated with co-morbid conditions at the start of RRT (during 01/01/01–30/09/06) grouped into broader categories

	Age <65		Age ⩾65	
Co-morbidity	**Hazard ratio**	**p value**	**Hazard ratio**	**p value**
Diabetes as primary disease	1.4	0.109	0.8	0.043
Diabetes of either category	1.4	0.081	0.9	0.502
Ischaemic heart disease	2.6	<0.0001	1.4	0.001
Peripheral vascular disease	3.3	<0.0001	1.2	0.064
Vascular disease	3.1	<0.0001	1.3	0.004
Cardio-vascular disease	2.9	<0.0001	1.4	0.000

Table 5.14: Multivariate Cox proportional hazards model for predictors of death within the first 90 days of starting RRT during 01/01/01–30/9/06

Variable	**Hazard ratio**	**95% CI**	**p value**
Ischaemic/neuropathic ulcers	2.1	1.5–2.9	<0.0001
Liver disease	2.0	1.3–3.1	0.002
Malignancy	1.9	1.6–2.3	<0.0001
MI in past 3 months	1.9	1.4–2.7	0.001
Age (per 10 yrs)	1.6	1.5–1.8	<0.0001
COPD	1.4	1.1–1.8	0.019
MI >3 months ago	1.4	1.1–1.7	0.012
Angina	1.3	1.0–1.6	0.027
Angioplasty/vascular graft	0.6	0.3–0.9	0.021

an increased risk of death in the 1st year after 90 days, both in patients starting RRT aged <65 years and in those ⩾65 years, the associations being more profound for patients aged <65 years. COPD and smoking were not significantly associated with increased risk of death in patients under 65 years of age. Table 5.16 shows the hazard of death in the year after the first 90

Table 5.15: Univariate analysis of the risk of death one year after completion of the first 90 days of RRT associated with co-morbid conditions at the start of RRT during 01/01/01–30/9/05

	Age <65		Age ⩾65	
Co-morbidity	**Hazard ratio**	**p value**	**Hazard ratio**	**p value**
Angina	1.9	<0.0001	1.4	<0.0001
MI >3 months ago	2.5	<0.0001	1.4	0.000
MI in past 3 months	2.5	0.002	1.5	0.022
CABG/angioplasty	2.0	0.000	0.9	0.337
Cerebrovascular disease	1.8	0.001	1.4	<0.0001
Diabetes (not cause of ERF)	2.4	<0.0001	1.3	0.015
COPD	1.4	0.185	1.4	0.002
Smoking	1.2	0.169	1.3	0.003
Liver disease	2.6	<0.0001	1.6	0.040
Malignancy	4.8	<0.0001	1.4	<0.0001
Claudication	1.9	0.001	1.2	0.085
Ischaemic/neuropathic ulcers	3.0	<0.0001	1.8	0.001
Angioplasty/vascular graft	1.9	0.035	1.3	0.078
Amputation	3.1	<0.0001	1.8	0.017

Table 5.16: Univariate analysis of the risk of death in the one year after the first 90 days of RRT associated with co-morbid conditions at the start of RRT (during 01/01/01–30/09/06) grouped into broader categories

	Age <65		Age ⩾65	
Co-morbidity	**Hazard ratio**	**p value**	**Hazard ratio**	**p value**
Diabetes as primary disease	2.0	<0.0001	1.0	0.647
Diabetes of either category	2.4	<0.0001	1.1	0.224
Ischaemic heart disease	1.9	<0.0001	1.4	<0.0001
Peripheral vascular disease	2.1	<0.0001	1.3	0.011
Vascular disease	2.0	<0.0001	1.4	<0.0001
Cardio-vascular disease	2.0	<0.0001	1.5	<0.0001

days of RRT associated with various co-morbid conditions grouped into broader categories.

On multivariate analysis using the stepwise Cox proportional hazards model, age and eight other variables were identified as independent predictors of death (Table 5.17). Recent MI was no longer significantly associated with an increased risk of death, possibly because the prognostic importance of this marker is

Table 5.17: Cox proportional hazards model for predictors of death in the first year after completion of 90 days of starting RRT during 01/01/01–30/9/05

Variable	**Hazard ratio**	**95% CI**	**p value**
Malignancy	1.9	1.6–2.2	<0.0001
Ischaemic/neuropathic ulcers	1.8	1.4–2.4	<0.0001
Liver disease	1.8	1.3–2.6	0.001
Age (per 10 yrs)	1.5	1.4–1.6	<0.0001
MI >3 months ago	1.4	1.2–1.6	0.000
Diabetes of either category	1.3	1.2–1.5	<0.0001
Cerebrovascular disease	1.3	1.1–1.6	0.003
COPD	1.2	1.0–1.5	0.050
Smoking	1.2	1.0–1.4	0.021

time-dependent and so would not be any more powerful a predictor than other markers of atherosclerotic vascular disease a year later. Diabetes was a powerful predictor of increased risk of death after the first 90 days.

Discussion

These analyses demonstrate that co-morbidities are common amongst UK patients starting RRT, with over 54% of patients with co-morbidity data having some recorded co-morbidity. Furthermore, these analyses demonstrate that co-morbidity is associated with increased mortality in patients on RRT in the UK. This is consistent with the findings of many other studies elsewhere using a variety of co-morbidity scores[3,4,16–39]. Data completeness remained poor in many centres. Unlike many data items that are transferred electronically from the local laboratory systems to the renal IT systems, the recording of co-morbidity on the renal IT system by clinical staff requires appreciation of the advantages of such data reporting, plus considerable manpower and resources. It is anticipated however, that the introduction in England of a system of tariff-based payment by results might act to encourage clinicians to improve the systematic recording of co-morbidity.

The publication, from 2006 onwards, of de-anonymised survival statistics for each centre and demonstrating the centre effect on survival of adjusting for these co-morbidities may provide some stimulus to clinical directors to improve collection of co-morbidity data.

The prevalence and severity of co-morbidity increases with time on RRT and this change in co-morbidity over time has been reported to be associated with mortality[4]. The Registry, in addition to collecting baseline co-morbidity data, is therefore hoping to stimulate collection of annual co-morbidity data on RRT patients. The Registry is also exploring the possibility of linking to the Hospital Episode Statistics dataset within the Secondary Uses Service (http://www.connectingforhealth.nhs.uk/), which would provide an alternative way of providing some of these data from inpatient diagnosis discharge codes, along the lines of the approach used by the United States Renal Data System.

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