Chapter 6: Co-morbidities in UK Patients at the Start of Renal Replacement Therapy

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Summary

- Co-morbidity returns have continued to improve, albeit slowly, with centres running Mediqal software having the highest rates of completeness.
- Diabetes as a primary renal diagnosis accounted for 20% of those starting RRT, but a further 7% had diabetes present as a co-morbid condition. The incidence of smoking remained high at 17% of diabetic patients, which was similar to that found in non-diabetics.
- 12% of patients starting RRT had a previous myocardial infarction (MI) and 31% of those aged over 65 years starting RRT had ischaemic heart disease (IHD).
- Patients starting on PD were on average nine years younger than those on HD and had fewer co-morbidities present.
- Patients starting RRT without any co-morbidity present had a lower median eGFR than those with co-morbid conditions.
- Patients with a previous MI or CABG, started RRT with slightly higher mean haemoglobin than those without co-morbid conditions or other co-morbid conditions.
- On univariate survival analysis, diabetes was not associated with an increased risk of death amongst patients aged over 65 years, possibly due to its close association with other co-morbidities in this age group.
- In the multivariate survival analysis the presence of ischaemic/neuropathic ulcers was the predictor of worst survival, followed by malignancy, previous MI and age per ten year increment.
- Smoking was less common in both South Asian and Black patients than Whites (7% vs 17%) starting RRT. 23% of both South Asian and White patients started RRT with IHD compared to only 12% of Black patients.

Introduction

Description of the extent of co-morbidity amongst patients starting treatment for established renal failure is important for a number of reasons.

1. Patients with significant co-morbidity may require more inpatient and outpatient care, and their treatment is therefore likely to cost more; information on co-morbidity may therefore help commissioners and providers to plan services.
2. Marked national and international variations in the take-on rate for Renal Replacement Therapy may partly be explained by differing policies and attitudes relating to provision of RRT to patients with significant co-morbidity. These differences may result from differences in referral, differences in acceptance for RRT, or both. Study of the outcomes of RRT amongst patients with and without co-morbidity may help explain and reduce these variations.
3. Co-morbidity may influence survival amongst patients on RRT and may affect survival differently depending on the modality of RRT. Differences in survival rates between patients on different modalities of RRT and differences in survival rates between different renal units, cannot therefore be fully understood unless data on co-morbidity are collected and analysed.

Methods

Clinical staff in each renal unit are responsible for recording (in yes/no format), on their renal unit IT system, the presence or absence of 14 co-morbid conditions and on current tobacco smoking (Table 6.1) in each patient starting

Table 6.1: Co-morbid conditions listed in the Registry dataset

Angina
Previous MI within 3 months
Previous MI over 3 months ago
Previous 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

RRT. Definitions of each of these conditions are given in web Appendix B Definitions, Statistical Methodology and Analysis Criteria (www.renalreg.org). Analyses are restricted to incident patients. Many other national Registries only collect data on patients who have survived the first 90 days of RRT and for the purposes of comparisons with their results, some analyses are restricted to patients surviving the first 90 days of RRT. Complete data on co-morbidity for a given patient is considered to have been provided if there is at least one yes/no answer to one of the 14 questions. For some analyses co-morbidities have been collapsed into broader categories.

- 'Ischaemic heart disease' is defined as the presence of a 'yes' to a history either of angina; MI in past 3 months; MI > 3 months; or coronary artery bypass grafting (CABG)/ angioplasty (or more than one of these).

- 'Peripheral vascular disease' is defined as the presence of a 'yes' to a history either of claudication; ischaemic or neuropathic ulcers; non-coronary angioplasty, vascular graft, or aneurysm; or amputation for peripheral vascular disease.

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

Data on completeness of co-morbidity returns from each renal unit may differ from those in previous reports because some renal units have provided additional data on co-morbidity of previous years' incident cohorts since original submission.

(Since 2004, the presence or absence of a clinical diagnosis of heart failure was also recordable. However, very few renal units are able to collect or submit this data item and it is not included in any of the analyses reported here).

Results

Completeness of co-morbidity returns from each participating renal unit

Table 6.2 shows that completeness of data returns still varies markedly from renal unit to renal unit with some units continuing to provide data on 100% of patients and others providing no data. There is no relationship between the size of the renal unit and the completeness of data returns. After excluding renal units that returned no data at all, the average completeness of data returns from units ranged from 1–100% (mean 63.6%) for 2005, a moderate improvement on a mean of 48.1% in 2000. Amongst all incident patients, data on co-morbidity was available on 39% of patients

Table 6.2: Completeness of co-morbidity data returns on incident patients from individual renal units (2000–2005)

	2000		2001		2002		2003		2004		2005	
	No. incident patients	% return	No. incident patients	% return	No. incident patients	% return	No. incident patients	% return	No. incident patients	% return	No. incident patients	% return
Antrim	–	–	–	–	–	–	–	–	–	–	42	100
Bangor	–	–	0	0	29	55	33	42	36	53	38	47
Barts	–	–	–	–	–	–	–	–	187	71	180	79
Basildon	–	–	–	–	–	–	53	100	46	96	30	93
Belfast	–	–	–	–	–	–	–	–	–	–	138	99
Bradford	–	–	61	93	62	100	75	84	62	92	65	95
Brighton	–	–	–	–	–	–	–	–	119	0	108	0
Bristol	148	94	151	92	127	81	163	83	166	75	175	57
Cambridge	–	–	93	5	77	5	98	1	109	0	103	0
Cardiff	139	1	155	0	181	0	166	3	186	6	178	20
Carlisle	28	39	29	3	27	22	31	0	29	24	30	70
Carshalton	123	13	124	19	182	6	205	8	180	7	180	3
Chelmsford	–	–	–	–	–	–	–	–	55	96	40	100
Clwyd	–	–	0	0	20	0	12	0	14	0	27	0
Coventry	89	0	105	0	97	1	79	0	79	0	85	0
Derby	54	41	59	44	0	0	61	74	65	77	71	85
Dorset	–	–	–	–	–	–	71	94	62	98	51	98
Dudley	40	0	35	0	25	4	42	0	55	0	38	0
Exeter	71	39	98	35	82	50	99	51	113	44	111	25
Gloucester	47	96	50	96	55	67	53	87	54	89	62	97
Guys	126	2	115	3	146	2	100	2	104	2	111	3
H&CX	–	–	–	–	180	99	153	100	195	100	147	100
Heartlands	86	0	85	0	61	2	105	0	103	0	115	1
Hull	82	2	74	0	106	5	80	89	108	86	126	95
Ipswich	–	–	–	–	44	39	39	31	43	16	60	8
Kings	–	–	–	–	117	88	108	100	110	99	133	99
Leeds	163	90	166	88	151	85	190	83	182	77	164	59
Leicester	179	74	187	89	152	88	171	95	165	94	224	61
Liverpool	–	–	221	48	153	48	114	62	135	57	164	41
ManWst	–	–	–	–	–	–	142	30	110	35	109	24
Middlesbrough	86	70	82	90	111	100	104	0	102	1	74	0
Newcastle	–	–	–	–	109	1	106	3	106	0	93	2
Newry	–	–	–	–	–	–	–	–	–	–	28	100
Norwich	–	–	–	–	–	–	–	–	98	100	121	100
Nottingham	114	71	120	68	87	99	116	97	108	95	147	99
Oxford	159	3	172	1	171	0	186	44	170	52	156	15
Plymouth	59	0	64	3	79	3	67	1	62	16	57	0
Portsmouth	–	–	144	57	146	46	143	56	120	44	153	29
Preston	117	1	136	1	113	0	99	1	81	0	118	0
QEH	–	–	–	–	–	–	–	–	202	0	194	0
Reading	52	0	68	0	44	2	73	0	71	0	75	0
Royal Free	–	–	–	–	–	–	–	–	–	–	126	0
Sheffield	137	82	155	86	157	61	162	57	170	40	158	28
Shrewsbury	–	–	–	–	–	–	–	–	55	0	43	0
Southend	40	20	37	32	34	59	42	60	41	63	35	57
Stevenage	134	2	129	2	100	1	123	0	85	1	86	1
Sunderland	50	0	41	5	58	48	57	61	52	90	58	76
Swansea	92	79	114	74	114	82	130	96	93	92	97	96
Truro	–	–	41	51	62	63	53	83	67	81	32	84
Tyrone	–	–	–	–	–	–	–	–	–	–	24	100
Ulster	–	–	–	–	–	–	–	–	–	–	10	100
Wirral	–	–	–	–	43	0	53	0	68	0	55	0
Wolverhampton	80	100	78	99	101	99	89	100	103	95	92	70
Wrexham	53	0	35	0	42	0	33	0	29	0	43	0
York	41	90	37	92	63	81	58	84	49	92	43	91
Totals	**2,589**		**3,261**		**3,708**		**4,137**		**4,804**		**5,223**	

Table 6.3: Summary of completeness of incident patient co-morbidity returns 2000–2005

	Years						
	2000	2001	2002	2003	2004	2005	Totals
Number of renal units	28	33	39	43	49	55	
Total number of new patients	2,589	3,261	3,708	4,137	4,804	5,282	23,781
Number of patients with co-morbid data entries	1,006	1,362	1,622	2,014	2,266	2,309	10,579
Percentage of co-morbid returns							
Median percentage of centres returning co-morbidity	40.7	49.8	50.0	62.3	75.8	75.9	61.8

starting in 2000 and on only 43% in 2005 (Table 6.3).

An analysis of completeness of data returns by the type of renal unit IT system showed no pattern other than very high returns from all centres using the Mediqal system (nine centres: completeness 93.3%–100%). 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; in 2005, of entries that contained at least one entry on co-morbidity, 1.34% contained 11 answers, 1.21% contained 12 answers, 7.28% contained 13 answers, and 89.95% contained answers to all 14 questions.

Frequency of each co-morbidity condition

Table 6.4 gives the frequency of each co-morbidity (as a proportion of the total number of incident patients for whom data was available for that item) for patients aged <65 and ⩾65 as well as the total frequency of each co-morbidity in the incident population.

The denominator for each percentage reported is the number of patients for whom a yes/no answer was provided for that co-morbidity.

Frequency of multiple co-morbidity

Just under 50% of patients for whom co-morbidity data were available starting RRT in

Table 6.4: Frequency with which each condition was reported in incident RRT patients between 2000–2005

	Age <65 years		Age ⩾65 years		
Co-morbidity	No. patients	%	No. patients	%	Total % incidence
Ischaemic heart disease	673	14.1	1,377	30.9	22.2
Angina	476	9.9	1,029	23.0	16.2
MI in past 3 months	85	1.8	142	3.2	2.4
MI >3 months	271	5.6	654	14.6	9.9
CABG/angioplasty	220	4.6	300	6.7	5.6
Cerebrovascular disease	284	5.9	619	13.8	9.7
Diabetes (not a cause of ERF)	208	4.4	416	9.4	6.8
Diabetes as primary disease	1,115	23.0	751	16.6	19.9
Diabetes of either category	1,323	27.4	1,167	26.0	26.7
COPD	191	4.0	419	9.4	6.6
Liver disease	124	2.6	74	1.7	2.1
Malignancy	290	6.0	687	15.3	10.5
Peripheral vascular disease	417	8.7	701	15.6	12.0
Claudication	267	5.5	548	12.2	8.8
Ischaemic/neuropathic ulcers	160	3.3	129	2.9	3.1
Angioplasty/vascular graft	100	2.1	205	4.6	3.3
Amputation	106	2.2	67	1.5	1.9
Smoking	869	19.2	576	13.5	16.4
No co-morbidity present	2,807	57.9	1,746	38.7	48.6

Table 6.5: Number of reported co-morbidities in patients starting RRT, as a proportion of those for whom co-morbidity data was available (2000–2005)

	Number of co-morbidities					
Total	0	1	2	3	4	5+
%	47.8	25.2	13.5	7.0	3.6	2.9

2000–2005 were reported as having no co-morbidity present. More than one co-morbidity was reported as present in 27% (Table 6.5).

Frequency of co-morbidity by age band

Figures 6.1 and 6.2 illustrate the rising frequency of co-morbidity with increasing age up to age 74 in incident patients; the lower rate

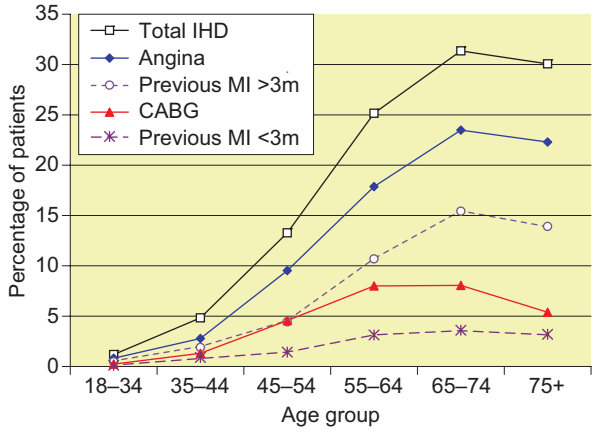

Figure 6.1: Frequency of ischaemic heart disease amongst incident patients 2000–2005 by age at start of RRT

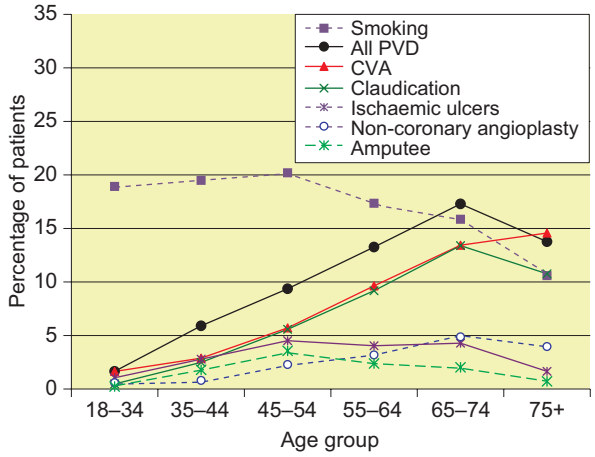

Figure 6.2: Frequency of peripheral vascular disease amongst incident patients 2000–2005 by age at start of RRT

Table 6.6: Frequency of co-morbidities in patients with diabetes as a cause of primary renal disease or as a co-morbidity compared to those without diabetes of either category

Co-morbidity	Non-diabetics	Diabetics
Ischaemic heart disease	18.6	32.6
Cerebrovascular disease	8.4	14.4
Peripheral vascular disease	8.3	23.6
Smoking	16.0	16.8
COPD	6.6	7.1
Malignancy	12.7	7.5
Liver disease	2.2	2.4

of reported co-morbidity amongst patients over 75 may reflect a 'healthy survivor effect' or decisions made by nephrologists and/or by patients aged >75 with cardiovascular co-morbidity not to embark on RRT. Smoking is less commonly reported amongst patients starting RRT aged 55 or older. Ischaemic heart disease, cerebrovascular disease and peripheral vascular disease are all more frequent amongst older compared to younger patients.

Frequency of co-morbidity amongst patients with diabetes

Diabetes was recorded as the primary renal disease in 20.2% of all patients starting RRT 2000–2005. Table 6.6 compares co-morbidity amongst patients with diabetes and patients without diabetes (as cause or co-morbidity), showing higher rates of ischaemic heart disease, cerebrovascular disease, and peripheral vascular disease amongst diabetic patients.

Age and co-morbidity in patients starting haemodialysis compared to those starting peritoneal dialysis

Figure 6.3 illustrates the younger age profile of patients being treated with peritoneal dialysis 90 days after the start of RRT, compared to those starting haemodialysis. The median age of patients on peritoneal dialysis at day 90 was 58.3 years, compared to 66.9 years for those on haemodialysis ($p < 0.001$, Kruskal-Wallis).

Table 6.7 compares the prevalence of each co-morbidity in patients on haemodialysis and peritoneal dialysis at day 0 of starting RRT, showing significantly higher prevalence (at a

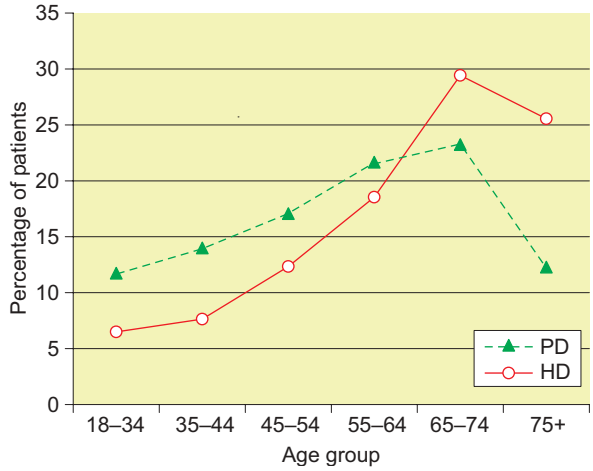

Figure 6.3: Percentage of patients in each age group starting RRT 01/01/00–30/09/05 on PD at 90 days compared to percentage on HD

higher age) amongst haemodialysis of all co-morbid conditions other than MI more than 3 months ago, CABG, smoking and non-coronary angioplasty. These data probably reflect a perception amongst UK nephrologists, nurses and their patients, that peritoneal dialysis is in general more suitable for younger and fitter patients.

The percentages out of total population of patients on that modality at 90 days, with data for that co-morbidity.

Frequency of co-morbidity by ethnic origin

For Registry returns, data on ethnic origin was retrieved from fields within renal unit IT systems that were completed by physicians or nurses. These were supplied either as 'old' Patient Administration System (PAS) codes (White = 0, Black Caribbean = 1, Black African = 2, Black/other/non-mixed origin = 3, Indian = 4, Pakistani = 5, Bangladeshi = 6, Chinese = 7) or as 'new' PAS codes (see web Appendix B www.renalreg.org). For purposes of analysis, 'new' PAS codes are collapsed into the 'old' PAS categories, and further collapsed into White (0), Black (1, 2, or 3), Asian (4, 5, or 6) and Chinese (7).

Figure 6.4 illustrates the presence or absence of co-morbidity by ethnic origin, showing a lower prevalence of co-morbid conditions amongst patients of Black or Asian origin compared to those of White origin. Figures 6.5, 6.6 and 6.7 show that the lower prevalence of co-morbidity amongst patients of Black or Asian origin is not attributable to younger age amongst these groups, as the prevalence of co-morbidity is lower even in the 18–34 year age group than in the White population. Table 6.8 shows the prevalence of major co-morbidities in each group; smoking was more common in the

Table 6.7: Percentage of patients with co-morbid conditions present in incident patients starting PD and HD 2000–2005

	HD		PD		
Co-morbidity	**%**	**Median age**	**%**	**Median age**	**p value***
Angina	17.6	71.3	14.0	67.6	<0.001
MI – more than 3 months ago	10.4	71.4	10.1	68.7	0.59
MI – within 3 months	2.9	69.8	1.7	68.4	<0.001
CABG	5.5	68.7	6.4	66.8	0.08
Cerebrovascular disease	11.0	71.6	7.4	66.5	<0.001
Diabetes non-ERF	8.0	71.4	4.5	68.1	<0.001
COPD	7.9	71.4	3.9	66.0	<0.001
Smoking	16.5	63.5	15.0	54.5	0.07
Liver disease	2.6	60.0	1.2	58.8	<0.001
Malignancy	13.0	72.1	6.5	69.6	<0.001
Claudication	9.6	70.7	7.3	66.6	<0.001
Ischaemic/neuropathic ulcers	3.8	65.4	1.9	56.7	<0.001
Angioplasty of non coronary vessels	3.5	71.5	2.9	65.6	0.18
Amputation	2.1	62.3	1.1	53.5	0.002

*p value compares the significance of the % patients in each modality

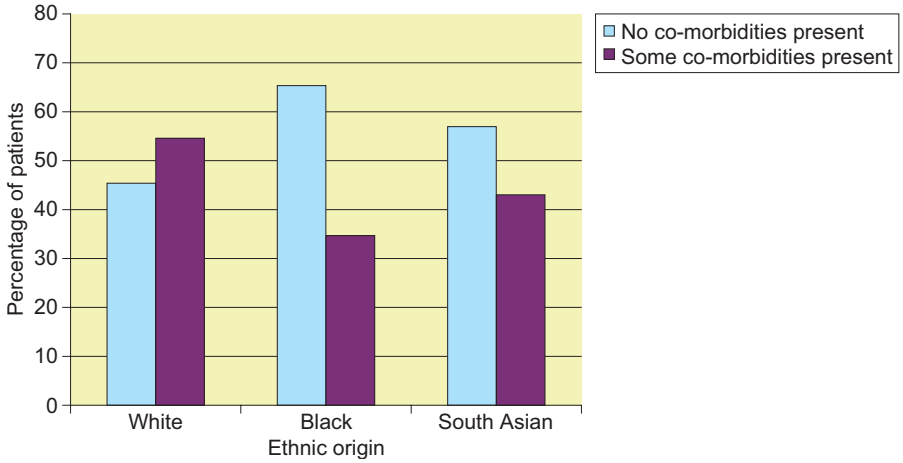

Figure 6.4: Presence or absence of co-morbid conditions at the start of RRT amongst patients starting RRT 2000–2005

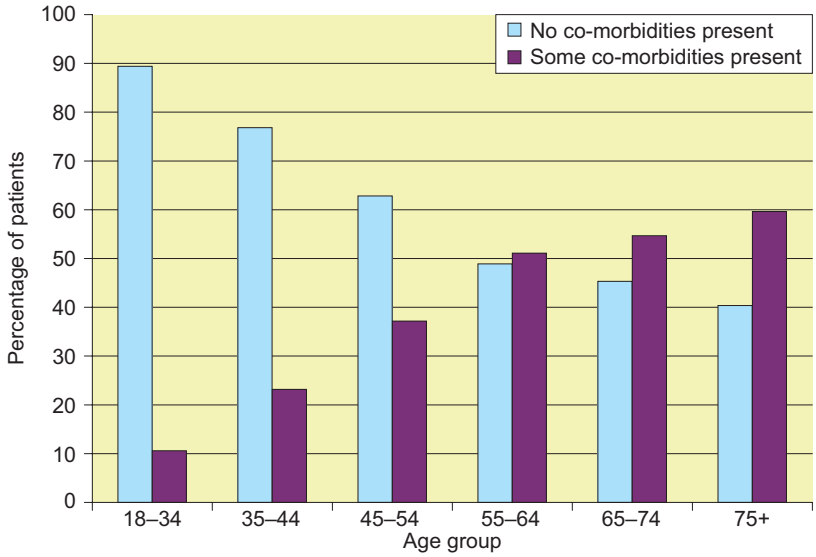

Figure 6.5: Presence or absence of co-morbid conditions at the start of RRT amongst patients of South Asian origin starting RRT 2000–2005

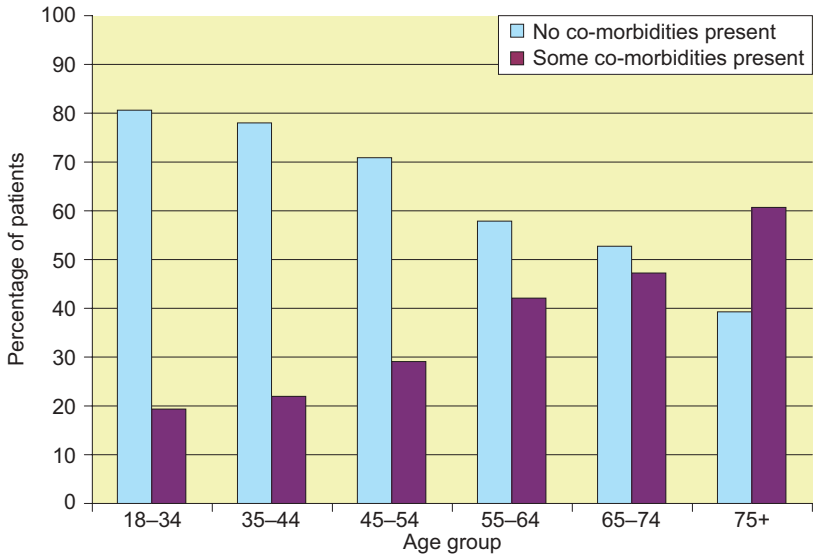

Figure 6.6: Presence or absence of co-morbid conditions at the start of RRT amongst patients of Black origin starting RRT 2000–2005

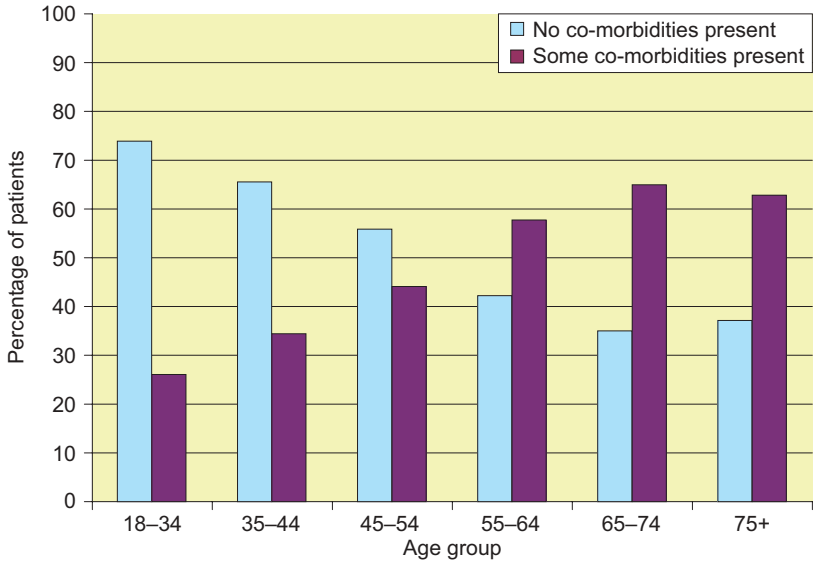

Figure 6.7: Presence or absence of co-morbid conditions at the start of RRT amongst patients of White origin starting RRT 2000–2005

Table 6.8: Prevalence of co-morbidities amongst incident patients starting RRT 2000–2005 by ethnic group, as a proportion of the total number of patients in that ethnic group for whom co-morbidity data were available

	% with co-morbidity			
	South Asian n = 725	Black n = 375	White n = 7,566	p value
Smoking	7.0	7.4	17.7	<0.0001
Cerebrovascular disease	8.2	10.2	10.1	0.24
Peripheral vascular disease	10.0	5.4	12.9	<0.0001
Ischaemic heart disease	23.7	12.4	23.2	<0.0001
Liver disease	3.9	2.9	2.1	0.01
COPD	3.7	2.4	7.5	<0.0001
Malignancy	3.3	4.5	12.4	<0.0001

Comparisons were performed using the Chi square test.

White population and ischaemic heart disease and peripheral vascular disease less common in the Black population. Table 6.9 gives details of the age structure of each major ethnic group at the start of RRT. Figure 6.8 illustrates the lower prevalence of diabetes amongst 'White' patients starting RRT compared to that in other ethnic groups.

Table 6.9: Incident patients 2000–2005 in each age group by ethnic origin, as a percentage of all patients in that ethnic group

	South Asian	Black	Chinese	Other	White
18–34	9.9	15.0	13.5	16.5	8.1
35–44	11.4	21.3	12.5	11.2	9.8
45–54	21.6	15.5	18.8	15.2	12.8
55–64	23.8	17.5	22.9	16.5	18.8
65–74	25.3	23.7	22.9	23.9	27.2
75+	8.0	6.9	9.4	16.8	23.4

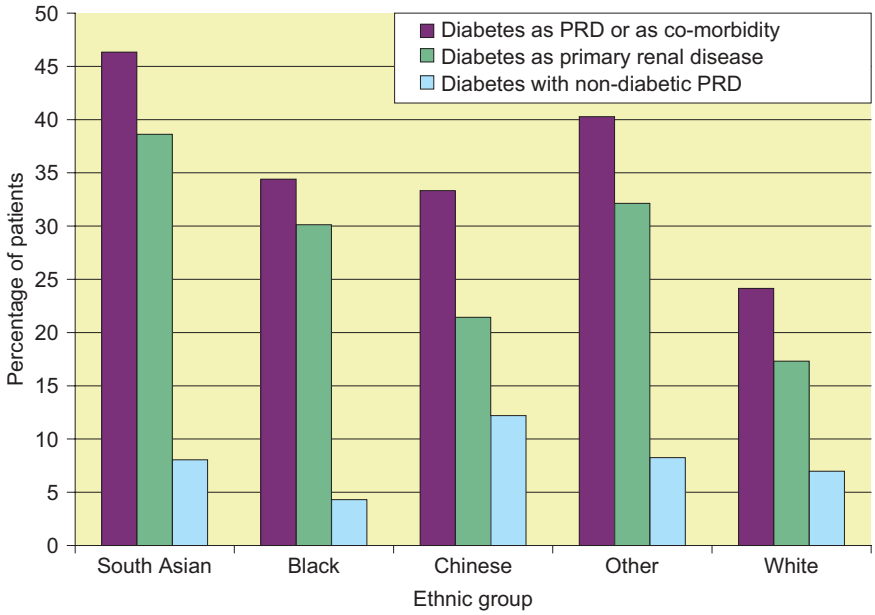

Figure 6.8: Prevalence of diabetes, either reported as the cause of primary renal disease, as a co-morbidity in patients with another reported PRD, or either of these, in each ethnic group at the start of RRT, 2000–2005

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

Using the abbreviated 4v MDRD calculation, the eGFR of patients starting RRT was calculated and is shown in Table 6.10. Data from patients with no available creatinine measurement within 14 days before the start of RRT were not used. Patients with an eGFR $> 20\,ml/min/1.73\,m^2$ were excluded from analysis (n = 553). Data from one centre (Hammersmith and Charing Cross) were excluded from analysis because of errors in the data extraction process of this item (n = 568), leaving 14,462 patients included in the analysis.

The log of the eGFR was taken to normalise the data and two-sample t-tests was used to

Table 6.10: eGFR within 2 weeks prior to the start of RRT 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
With any co-morbidity	7.8	7.7–7.9	<0.0001
Angina	8.2	8.0–8.4	<0.0001
MI in past 3 months	8.1	7.7–8.6	<0.0001
MI >3 months ago	8.3	8.1–8.6	<0.0001
CABG/angioplasty	8.6	8.3–8.9	<0.0001
Cerebrovascular disease	8.0	7.8–8.2	<0.0001
Diabetes (not cause of ERF)	8.0	7.8–8.3	<0.0001
Diabetes as primary disease	8.3	8.1–8.5	<0.0001
Diabetes of either category	8.2	8.1–8.4	<0.0001
COPD	8.2	7.9–8.5	<0.0001
Liver disease	7.8	7.3–8.3	0.01
Malignancy	7.4	7.2–7.7	0.01
Claudication	8.3	8.0–8.5	<0.0001
Ischaemic/neuropathic ulcers	8.3	7.9–8.8	<0.0001
Angioplasty/vascular graft	8.3	7.9–8.7	<0.0001
Amputation	8.8	8.2–9.4	<0.0001
Smoking	7.7	7.5–7.8	<0.0001

Table 6.11: Haemoglobin concentration at the start of RRT in patients, by co-morbidity

	Hb mean (g/dl)	Hb 95% CI	p value	% Hb >10 g/dl
Without co-morbidity	10.1	10.0–10.1	Ref	52.3
With any co-morbidity	10.0	10.0–10.1	0.093	49.8
Angina	10.1	10.0–10.2	0.54	51.6
MI in past 3 months	10.0	9.7–10.2	0.47	51.4
MI >3 months ago	10.3	10.2–10.5	<0.001	55.6
CABG/angioplasty	10.4	10.2–10.6	<0.001	57.5
Cerebrovascular disease	10.1	9.9–10.2	0.82	51.5
Diabetes (not cause of ERF)	10.0	9.9–10.2	0.49	50.2
Diabetes as primary disease	10.0	9.9–10.0	0.93	50.7
COPD	9.9	9.7–10.0	0.042	48.6
Liver disease	9.6	9.3–9.9	0.002	40.7
Malignancy	9.9	9.8–10.0	0.004	46.6
Claudication	10.0	9.9–10.1	0.45	50.5
Ischaemic/neuropathic ulcers	9.8	9.6–10.0	0.013	43.5
Angioplasty/vascular graft	10.2	10.0–10.5	0.19	54.3
Amputation	9.8	9.5–10.1	0.13	46.0
Smoking	10.0	9.9–10.1	0.07	47.8

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 being carried out, only a p value <0.01 was considered statistically significant. This should not imply that these differences imply a clinical significance as they may be only small variations.

The (geometric) mean eGFR prior to starting RRT in patients who are recorded as starting without any co-morbidity present is 7.1 ml/min/1.73 m^2. Patients starting with different co-morbidities were compared against this value.

In each case, eGFR appears to have been slightly higher amongst patients with co-morbidity compared to patients without 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 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 52% of patients achieving a haemoglobin >10 g/dl. Patients starting with different co-morbidities were compared against this value (Table 6.11). Haemoglobin concentrations at the start of RRT were slightly higher amongst patients with ischaemic heart disease than in those without, and lower amongst those with liver disease or malignancy. In addition to the direct influence of co-morbidity, EPO prescribing patterns and late referral of patients will have an influence on these data.

Co-morbidity and subsequent kidney transplantation

This analysis was confined to incident patients in each of the years 2000–2005 from centres that had returned ⩾80% complete data for co-morbidity in that year (see Table 6.2). Table 6.12 shows that patients who underwent transplantation had less co-morbidity at the start of RRT than those who died or did not receive a transplant.

Figure 6.9 gives the age distribution of those who had received a transplant by the end of 2005 compared to those who remained untransplanted. Over the age of 65 years, the majority of incident patients are unlikely to undergo kidney transplantation, and this is very rare in patients starting RRT over the age of 75.

Table 6.12: Co-morbidity amongst incident patients 2000–2005 who underwent transplantation compared to those who remained on dialysis or died

	Not transplanted		Transplanted	
Co-morbidity	**Number**	**%**	**Number**	**%**
Patients with co-morbidity data	5,873		865	
Without co-morbidity	2,680	45.6	644	74.5
Ischaemic heart disease	1,423	24.3	40	4.6
Peripheral vascular disease	782	13.3	25	2.9
Cerebrovascular disease	615	10.5	26	3.0
Diabetes (not cause of ERF)	447	7.7	21	2.4
COPD	440	7.5	19	2.2
Liver disease	151	2.6	5	0.6
Malignancy	746	12.7	13	1.5
Smoking	861	15.1	126	15.6

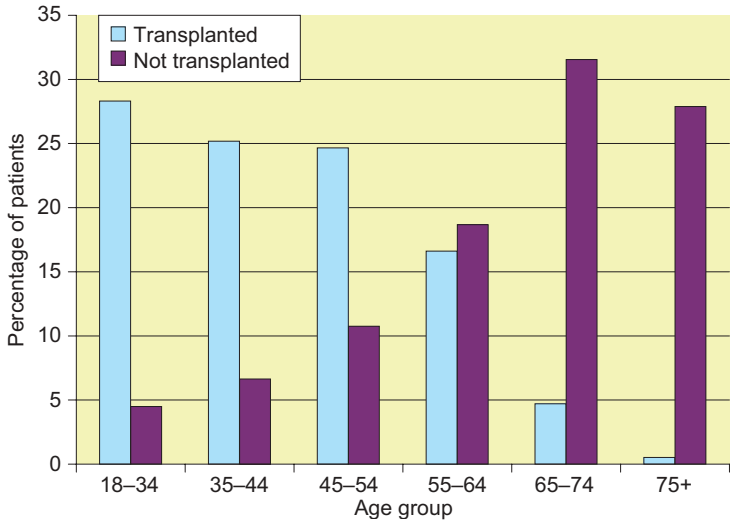

Figure 6.9: Age distribution of the incident cohort who received a transplant compared to those who remained on dialysis or died

Co-morbidity and subsequent survival – Introduction

These analyses were performed on patients starting RRT between 01/01/2000 and 30/09/2005, to allow at least three months follow-up from the start of RRT. The 1 year after 90 days analyses only include patients who survived at least 90 days on RRT. The death rate is high in the first 90 days and highly variable between centres, due for instance to variation in policies on inclusion of patients with acute kidney injury requiring dialysis. Use of this "90 day rule" also allows direct comparison of survival statistics with those from other national registries.

The effect within each renal unit of adjusting overall survival for co-morbidity can be found in Chapter 12.

Co-morbidity and survival within 90 days of commencing RRT

The Registry collects data on all patients with a 'timeline' entry that have started RRT for ERF. Patients who present acutely, and who are initially classified as Acute Renal Failure requiring dialysis, but continue to require long-term dialysis can be re-classified as having had ERF from the date of their first RRT. (Most other national registries only start the collection of data at 90 days after the first RRT.) This allows the UK Registry, unlike other registries, to collect data on factors affecting outcomes including survival, in the first 90 days of RRT.

The univariate model (Table 6.13), does not allow adjustment for age, so patients were first stratified by age group (less than 65 years and

Table 6.13: Univariate analysis of the risk of death within the first 90 days of RRT associated with co-morbid conditions at the start of RRT

	Age <65		Age ⩾65	
Co-morbidity	**Hazard ratio**	**p value**	**Hazard ratio**	**p value**
Angina	2.5	<0.0001	1.2	0.10
Ischaemic heart disease	2.2	<0.0001	1.1	0.19
Claudication	1.8	0.04	1.1	0.28
Ischaemic/neuropathic ulcers	3.4	<0.0001	1.8	0.002
Peripheral vascular disease	2.9	<0.0001	1.2	0.16
Cerebrovascular disease	2.2	0.0036	1.3	0.01
Vascular disease (IHD, PVD, CVA)	2.5	<0.0001	1.2	0.06
Diabetes as primary disease	1.5	0.04	0.7	0.009
Diabetes (not as cause of ERF)	1.4	0.33	1.2	0.22
Diabetes of either category	1.5	0.02	0.9	0.16
Liver disease	5.5	<0.0001	1.0	0.94
Malignancy	4.2	<0.0001	1.7	<0.0001
COPD	2.4	0.004	1.3	0.09
Smoking	0.8	0.37	1.2	0.16

65 years and over) to make some account for the increasing incidence of co-morbidity with age which would otherwise obscure the analysis. On univariate analysis stratified for age, most co-morbidities were associated with an increased risk of death both amongst patients aged <65 years and those aged ⩾65 years. However, there was no increased risk of death associated with diabetes mellitus as a co-morbidity in the absence of diabetes as a cause of primary renal disease; and smoking was not associated with an increased risk of death (Table 6.13). Some co-morbidities may appear not to be associated with an increased risk of death because of low numbers – for instance, liver disease aged ⩾65. The observation that the risk of death amongst those ⩾65 is not greater in the presence of ischaemic heart disease may be down to either competing risks or to negative selection caused by clinicians or patients opting not to start RRT in the presence of severe ischaemic heart disease. Of special interest in this univariate survival analysis was that diabetes was not associated with an increased risk of death amongst patients aged ⩾65 years, possibly due to its close association with other co-morbidities in this age group.

On multivariate analysis using the stepwise Cox proportional hazards model, age, and six of the co-morbid conditions were identified as significant independent predictors of the risk of death (Table 6.14). 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.

There were 9,047 patients included in the analysis. Variables included in the model

Table 6.14: Cox proportional hazards model for predictors of death within the first 90 days of starting RRT during 01/01/00–30/9/05

Variable	**Hazard ratio**	**95% CI**	**p value**
Ischaemic/neuropathic ulcers	2.3	1.7–3.3	<0.0001
Liver disease	2.1	1.3–3.2	0.001
Malignancy	1.8	1.5–2.2	<0.0001
MI in past 3 months	1.7	1.2–2.5	0.003
Age (per 10 years)	1.6	1.5–1.8	<0.0001
MI more than 3 months ago	1.3	1.0–1.6	0.03
Angioplasty/vascular graft	0.6	0.4–1.0	0.034

Table 6.15: 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

	Age <65		Age ⩾65	
Co-morbidity	**Hazard ratio**	**p value**	**Hazard ratio**	**p value**
Angina	1.8	0.0001	1.3	0.0008
Ischaemic heart disease	2.0	<0.0001	1.4	<0.0001
Claudication	2.2	<0.0001	1.2	0.07
Ischaemic/neuropathic ulcers	3.2	<0.0001	2.1	<0.0001
All peripheral vascular disease	2.2	<0.0001	1.3	0.00
Cerebrovascular disease	1.7	0.0118	1.5	<0.0001
Vascular disease (IHD, PVD, CVA)	2.1	<0.0001	1.4	<0.0001
Diabetes as primary disease	2.0	<0.0001	1.0	0.73
Diabetes (not as cause of ERF)	2.7	<0.0001	1.3	0.01
Diabetes of either category	2.5	<0.0001	1.1	0.18
Malignancy	5.0	<0.0001	1.5	<0.0001
Liver disease	2.6	0.0001	1.3	0.29
COPD	1.4	0.19	1.4	0.002
Smoking	1.1	0.41	1.3	0.011

included: age per 10 years, angina, myocardial infarction <3 months ago, myocardial infarction more than 3 months ago, coronary artery bypass grafting or coronary angioplasty, cerebrovascular disease, diabetes (whether as a cause of primary renal disease or as a co-morbidity), chronic obstructive pulmonary disease, liver disease, malignancy, claudication, ischaemic/neuropathic ulcers, angioplasty/vascular graft, amputation and smoking.

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

In all analyses, patients starting RRT are only included if they survived at least 90 days on RRT. The death rate is high in the first 90 days, and highly variable between centres, due for instance to variation in policies on inclusion of patients with acute kidney injury requiring dialysis. Use of this "90 day rule" also allows direct comparison of survival statistics with those from other national registries.

On univariate analysis (Table 6.15) stratified for age, most co-morbidities were associated with an increased risk of death both in patients starting RRT aged <65 years and in those ⩾65 years. Diabetes as a primary cause of renal failure was not associated with an increased risk of death amongst patients over 65 years, possibly due to its close association with other co-morbidities in this age group. COPD was not associated with an increased risk of death in patients <65 years.

On multivariate analysis using the stepwise Cox proportional hazards model, eight variables were identified as independent predictors of death (Table 6.16). Recent MI was no longer

Table 6.16: Cox proportional hazards model for predictors of death in the first year after completion of 90 days of starting RRT during 01/01/00–30/9/04

Variable	**Hazard ratio**	**95% CI**	**p value**
Ischaemic/neuropathic ulcers	2.0	1.5–2.7	<0.0001
Malignancy	1.9	1.6–2.3	<0.0001
Liver disease	1.5	1.0–2.3	0.03
MI more than 3 months ago	1.5	1.3–1.8	<0.0001
Age per 10 years	1.5	1.4–1.6	<0.0001
COPD	1.3	1.1–1.6	0.01
Diabetes of either category	1.3	1.1–1.5	0.0002
Cerebrovascular disease	1.3	1.1–1.6	0.006

significantly associated with an increased risk of death, possibly because the prognostic importance of this marker is 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.

There were 6,535 patients included in the analysis. Variables in the model included: age per 10 years, angina, myocardial infarction less than 3 months ago, myocardial infarction more than 3 months ago, coronary artery bypass grafting or coronary angioplasty, cerebrovascular disease, diabetes (whether as a cause of primary renal disease or as a co-morbidity), chronic obstructive pulmonary disease, liver disease, malignancy, claudication, ischaemic/neuropathic ulcers, angioplasty/vascular graft, amputation and smoking.

Discussion

These analyses demonstrate that co-morbidity is common amongst UK patients starting RRT, with over 50% of all patients having some recorded co-morbidity (using data from centres with >80% returns). Reporting of the presence or absence of these simple markers of co-morbidity to the Registry is still poor in many centres, although this situation is gradually improving. Unlike many data items recorded in renal unit IT systems, the recording of the presence or absence of co-morbidity is probably not required for the routine day-to-day care of these patients. It is anticipated however, that the introduction of a system of tariff-based payment by results in England might act to encourage clinicians to improve the systematic recording of co-morbidity. The Registry is also exploring the possibility of linking to the Hospital Episode Statistics dataset within the Secondary Users Service, which would allow data to be obtained on hospital discharge codes, very much along the lines of the approach used by the United States Renal Data System.

These and other previously published analyses using a variety of co-morbidity scores[1–26] also demonstrate that co-morbidity is a powerful predictor of survival in patients on RRT. The publication of de-anonymised survival statistics for each renal unit in this year's report should also provide a stimulus to renal unit Directors to ensure that they collect and report complete data on co-morbidity.

References

1. Comorbid conditions and correlations with mortality risk among 3,399 incident hemodialysis patients. *Am J Kidney Dis* 1992;20(5 Suppl 2):32–8.
2. Avram MM, Mittman N, Bonomini L, Chattopadhyay J, Fein P. Markers for survival in dialysis: a seven-year prospective study. *Am J Kidney Dis* 1995; 26(1):209–19.
3. Beddhu S, Zeidel ML, Saul M, Seddon P, Samore MH, Stoddard GJ, *et al*. The effects of comorbid conditions on the outcomes of patients undergoing peritoneal dialysis. *Am J Med* 2002;112(9):696–701.
4. Byrne C, Vernon P, Cohen JJ. Effect of age and diagnosis on survival of older patients beginning chronic dialysis. *Jama* 1994;271(1):34–6.
5. Davies SJ, Phillips L, Naish PF, Russell GI. Quantifying comorbidity in peritoneal dialysis patients and its relationship to other predictors of survival. *Nephrol Dial Transplant* 2002;17(6):1085–92.
6. Di Iorio B, Cillo N, Cirillo M, De Santo NG. Charlson Comorbidity Index is a predictor of outcomes in incident hemodialysis patients and correlates with phase angle and hospitalization. *Int J Artif Organs* 2004;27(4):330–6.
7. Fried L, Bernardini J, Piraino B. Charlson comorbidity index as a predictor of outcomes in incident peritoneal dialysis patients. *Am J Kidney Dis* 2001; 37(2):337–42.
8. Ganesh SK, Hulbert-Shearon T, Port FK, Eagle K, Stack AG. Mortality differences by dialysis modality among incident ESRD patients with and without coronary artery disease. *J Am Soc Nephrol* 2003; 14(2):415–24.
9. Goldwasser P, Mittman N, Antignani A, Burrell D, Michel MA, Collier J, *et al*. Predictors of mortality in hemodialysis patients. *J Am Soc Nephrol* 1993;3(9): 1613–22.
10. Goodkin DA, Bragg-Gresham JL, Koenig KG, Wolfe RA, Akiba T, Andreucci VE, *et al*. Association of comorbid conditions and mortality in hemodialysis patients in Europe, Japan, and the United States: the Dialysis Outcomes and Practice Patterns Study (DOPPS). *J Am Soc Nephrol* 2003;14(12):3270–7.
11. Held PJ, Pauly MV, Diamond L. Survival analysis of patients undergoing dialysis. *Jama* 1987;257(5): 645–50.
12. Hemmelgarn BR, Manns BJ, Quan H, Ghali WA. Adapting the Charlson Comorbidity Index for use in patients with ESRD. *Am J Kidney Dis* 2003;42(1): 125–32.
13. Hutchinson TA, Thomas DC, MacGibbon B. Predicting survival in adults with end-stage renal disease: an age equivalence index. *Ann Intern Med* 1982;96(4): 417–23.

14. Iseki K, Kawazoe N, Osawa A, Fukiyama K. Survival analysis of dialysis patients in Okinawa, Japan (1971–1990). *Kidney Int* 1993;43(2):404–9.
15. Johnson JG, Gore SM, Firth J. The effect of age, diabetes, and other comorbidity on the survival of patients on dialysis: a systematic quantitative overview of the literature. *Nephrol Dial Transplant* 1999;14(9): 2156–64.
16. Khan IH. Comorbidity: the major challenge for survival and quality of life in end-stage renal disease. *Nephrol Dial Transplant* 1998;13 Suppl 1:76–9.
17. Lacson E, Jr., Teng M, Lazarus JM, Lew N, Lowrie E, Owen W. Limitations of the facility-specific standardized mortality ratio for profiling health care quality in dialysis. *Am J Kidney Dis* 2001;37(2):267–75.
18. Miguel A, Garcia-Ramon R, Perez-Contreras J, Gomez-Roldan C, Alvarino J, Escobedo J, *et al*. Comorbidity and mortality in peritoneal dialysis: a comparative study of type 1 and 2 diabetes versus nondiabetic patients. Peritoneal dialysis and diabetes. *Nephron* 2002;90(3):290–6.
19. Miskulin DC, Martin AA, Brown R, Fink NE, Coresh J, Powe NR, *et al*. Predicting 1 year mortality in an outpatient haemodialysis population: a comparison of comorbidity instruments. *Nephrol Dial Transplant* 2004;19(2):413–20.
20. Miskulin DC, Meyer KB, Athienites NV, Martin AA, Terrin N, Marsh JV, *et al*. Comorbidity and other factors associated with modality selection in incident dialysis patients: the CHOICE Study. Choices for Healthy Outcomes in Caring for End-Stage Renal Disease. *Am J Kidney Dis* 2002;39(2):324–36.
21. Miskulin DC, Meyer KB, Martin AA, Fink NE, Coresh J, Powe NR, *et al*. Comorbidity and its change predict survival in incident dialysis patients. *Am J Kidney Dis* 2003;41(1):149–61.
22. Schrander-v d Meer AM, van Saase JL, Roodvoets AP, van Dorp WT. Mortality in patients receiving renal replacement therapy, a single center study. *Clin Nephrol* 1995;43(3):174–9.
23. van Manen JG, Korevaar JC, Dekker FW, Boeschoten EW, Bossuyt PM, Krediet RT. How to adjust for comorbidity in survival studies in ESRD patients: a comparison of different indices. *Am J Kidney Dis* 2002;40(1):82–9.
24. Van Manen JG, Korevaar JC, Dekker FW, Boeschoten EW, Bossuyt PM, Krediet RT. Adjustment for comorbidity in studies on health status in ESRD patients: which comorbidity index to use? *J Am Soc Nephrol* 2003;14(2):478–85.
25. Vonesh EF, Snyder JJ, Foley RN, Collins AJ. The differential impact of risk factors on mortality in hemodialysis and peritoneal dialysis. *Kidney Int* 2004;66(6):2389–401.
26. Weller JM, Port FK, Swartz RD, Ferguson CW, Williams GW, Jacobs JF, Jr. Analysis of survival of end-stage renal disease patients. *Kidney Int* 1982; 21(1):78–83.