Chapter 16: Co-morbidity in Incident Patients

Summary

- Co-morbidity returns have improved and over 50% of renal units are submitting some information. 5,916 patients have had co-morbid data returns so far, which accounts for 39% of all incident dialysis patients.
- The incidence of co-morbidity increases with increasing age until age 75. In patients aged over 75, the percentage starting renal replacement therapy (RRT) with cardiovascular and cerebrovascular disease appears to reduce.
- 30% of diabetics were referred within 3 months of requiring dialysis.
- Diabetic patients starting RRT have a greater number of co-morbidities than non-diabetics and the majority were aged less than 65 years. Even after adjusting for co-morbidity in the Cox survival model, being diabetic was still a significant additional risk factor for impaired survival.
- HD patients were older and had more co-morbidity than those going onto PD.
- Most of the Registry co-morbid conditions influenced patient survival.
- In the multivariate analysis, diabetes was not a risk factor in the 90 day survival while as expected it is a risk factor in the longer term survival beyond day 90. Similarly smoking has a long term negative impact on survival rather than a short term impact.
- Comparisons of national registries show that age distribution of dialysis patients in the UK and the USA is similar. In the UK, history of a previous myocardial infarction (MI) is found in 50% more patients starting RRT over age 65 years than in the USA.
- In the USA the apparent higher rates of cardiac disease than the UK is misleading. It is due to the inclusion of congestive cardiac failure and dysrhthmias, which are not collected by the UK Registry.
- In the UK, patients starting RRT have a much higher incidence of cerebrovascular disease (CVA) than the USA (18% v 12% in patients aged 75+).
- The incidence of peripheral vascular disease (PVD) and chronic obstructive pulmonary disease (COPD) is similar in the UK to the USA, across all age bands.
- In the UK the incidence of diabetes in the transplanted cohort is 20% which is marginally lower than that seen in the incident RRT cohort (24%).
- Since, together with age, weight of co-morbidity determines survival on RRT, the completeness of co-morbidity recording by renal units needs to increase.

Co-morbidity data

The Registry has defined 15 'yes' (present) or 'no' questions relating to co-morbidity and asks clinicians to complete this record at the time of starting RRT. As an example, the screen made available to renal units using the CCL Proton system is shown in figure 16.1. A patient may therefore have a fully completed screen recording no co-morbid conditions to be present. Null entries are considered missing data rather than 'no'.

Beginning in 2004, the presence or absence of heart failure prior to the start of RRT was also recordable. Definitions for each co-morbidity are given at the end of this chapter.

Data on smoking at the time of starting RRT has been collected as a marker for vascular (cardiac, cerebral and peripheral) risk. It is not a co-morbid condition although for the purposes of these analyses, it has been treated as such.

Angina	Claudication
Previous MI within last 3 months	Ischaemic/neuropathic ulcers
Previous MI >3 months ago	Angioplasty vasc graft/aneurysm (non coronary)
Previous CABG or coronary angioplasty	Amputation for Periph Vasc disease
Heart failure	
Cerebrovascular disease	Smoking
Diabetes (not causing ESRF)	Malignancy
Chronic Obstructive Pulmonary Disease	
Liver Disease	

Figure 16.1: Co-morbidity entry screen for the CCL Proton system

Co-morbidity returns by renal units

15197 incident patients' details have been collected by the Renal Registry and the returns by renal units are shown in table 16.1. There are 41 renal units submitting information to the Registry, with an increasing number of patients with co-morbid information being available for analysis (table 16.2). The initial median co-morbid returns in 1999 were only 15%, but by 2003, it had risen to 57%. The proportion of renal units with a high return of co-morbidity (>67%) has increased from 25% in 1999 to 43% by 2003. The ideal situation would be to achieve co-morbid returns above 90% and the proportion of units achieving such a standard started at 6% in 1999, rising to 29% in 2001 and falling to 18% in 2003.

Unfortunately, many renal units (49%) are returning less than 50% of co-morbid information and the Renal Registry will have to explore mechanisms by which data returns can be improved.

Some centres like Bradford, Bristol, Leeds, Sheffield and York are showing declining co-morbidity returns. This contrasts with Hammersmith, Nottingham, Truro and Wolverhampton which show a sustained high return or improving return of co-morbidity.

Table 16.1: Co-morbidity data returns, by centre, at the start of RRT

Treatment centre	1999		2000		2001		2002		2003	
	No. incident patients	% returns co-morbidity	No. incident patients	% returns co-morbidity	No. incident patients	% returns co-morbidity	No. incident patients	% returns co-morbidity	No. incident patients	% returns co-morbidity
Bangor	–	–	–	–	–	–	29	55.2	38	39.5
Bradford	–	–	–	–	61	93.4	61	100.0	75	84.0
Bristol	118	89.8	149	94.0	152	91.4	123	79.7	168	67.9
Cambridge	–	–	–	–	103	4.9	75	4.0	104	–
Cardiff	137	0.7	139	0.7	153	–	157	–	154	1.3
Carlisle	26	46.2	27	40.7	26	3.8	29	20.7	30	–
Carshalton	111	9.9	119	11.8	119	15.1	172	2.9	203	2.5
Clwyd	–	–	–	–	–	–	19	–	9	–
Coventry	92	–	88	–	104	–	95	1.1	76	–
Derby	–	–	–	–	–	–	–		62	54.8
Exeter	82	31.7	72	36.1	98	30.6	82	47.6	98	43.9
Gloucester	59	1.7	48	97.9	50	98.0	57	66.7	55	87.3
Guys	–	–	126	0.8	111	–	141	–	95	–
Heartlands	82	–	86	–	85	–	60	–	103	–
HS & CX	–	–	–	–	–	–	177	99.4	152	100.0
Hull	64	1.6	81	2.5	74	–	105	4.8	78	88.5
Ipswich	–	–	–	–	–	–	42	38.1	35	28.6
Kings	–	–	–	–	–	–	117	86.3	114	94.7
Leeds	82	84.1	160	90.6	162	85.8	147	78.9	169	69.8
Leicester	164	79.9	177	75.7	184	90.2	152	88.2	168	83.9
Liverpool	–	–	–	–	186	55.9	150	46.0	119	52.9
Man-West	–	–	–	–	–	–	–	–	141	26.2
Middlesbrgh	92	1.1	86	69.8	81	90.1	111	100.0	104	–
Newcastle	–	–	–	–	–	–	105	1.0	91	3.3
Nottingham	128	24.2	114	71.1	121	66.1	87	98.9	114	97.4
Oxford	142	–	152	2.6	169	1.2	164	–	179	0.6
Plymouth	68	1.5	60	–	64	3.1	86	1.2	69	–
Portsmouth	–	–	–	–	144	56.3	142	45.1	137	30.7
Preston	106	0.9	117	0.9	136	0.7	112	–	99	1.0
Reading	–	–	49	–	63	–	42	–	69	–
Sheffield	133	20.3	137	81.0	152	85.5	156	57.7	158	51.9
Southend	43	2.3	39	7.7	37	24.3	35	45.7	43	37.2
Stevenage	103	–	101	–	125	0.8	89	1.1	114	–
Sunderland	46	–	46	–	38	5.3	56	46.4	57	59.6
Swansea	–	–	91	75.8	112	73.2	113	81.4	133	94.0
Truro	–	–	–	–	37	54.1	58	65.5	48	85.4
Wirral	–	–	–	–	–	–	38	–	49	–
Wolverhmptn	74	100.0	78	100.0	75	100.0	95	100.0	92	100.0
Wordsley	43	–	40	–	34	–	25	4.0	41	–
Wrexham	51	–	55	–	35	–	41	–	34	–
York	–	–	40	92.5	37	91.9	68	70.6	56	58.9
Totals	**2046**		**2477**		**3128**		**3613**		**3933**	

Table 16.2: Summary of the co-morbidity returns available for analysis

	Years					
	1999	2000	2001	2002	2003	Totals
Number of renal units	23	27	32	39	41	
Total number of new patients	2046	2477	3128	3613	3933	15197
Number of patients with co-morbid data entries	494	965	1300	1554	1603	5916
Percentage of co-morbid returns						
Mean of co-morbid returns for all centres (%)	24	39	41	43	41	39
Median of co-morbid returns per centre (%)	15	70	56	51	57	57

Frequency of co-morbidity returned

Of the 5,884 patients where co-morbid information was available by 90 days of RRT, table 16.3 outlines the total and age dependent incidence of co-morbidity. Cardiovascular diseases, COPD and malignancy were more common in patients aged over 65 years whilst diabetes, liver disease and smoking were more common in the younger patients.

Registry analyses from previous years indicate that the Registry is underestimating co-morbidity. Patients who die within 90 days were less likely to have their co-morbidity recorded and these patients would therefore have been excluded from analyses.

Table 16.3: Frequency of co-morbidity at the time of starting RRT

	Age <65 years		Age >65 years		Total % incidence
Co-morbidity	No. pts	%	No. pts	%	
Cardiovascular disease	470	15.7	987	34.0	24.7
Angina	355	11.9	773	26.6	19.2
MI in past 3 months	58	1.9	102	3.5	2.7
MI >3 months ago	188	6.3	478	16.5	11.3
CABG/angioplasty	124	4.5	176	6.6	5.5
Cerebrovascular disease	210	7.0	481	16.6	11.7
Diabetes (not a cause of ERF)	145	4.9	287	10.0	7.4
Diabetes as primary disease	660	22.0	450	15.4	18.8
Diabetes of either category	805	26.8	737	25.3	26.1
COPD	139	4.7	313	10.9	7.7
Liver disease	91	3.1	50	1.7	2.4
Malignancy	192	6.4	482	16.7	11.5
Peripheral vascular disease	301	10.1	538	18.5	14.2
Claudication	197	6.6	434	15.0	10.8
Ischaemic/neuropathic ulcers	125	4.2	117	4.1	4.1
Angioplasty/vascular graft	66	2.2	142	4.9	3.5
Amputation	76	2.5	57	2.0	2.3
Smoking	609	21.4	423	15.2	18.4
No co-morbidity present	1354	49.0	796	28.6	38.7

Abbreviations: MI – myocardial infarction; CABG – coronary artery bypass grafting; COPD – chronic obstructive pulmonary disease; ERF– established renal failure.

Table 16.4: Cumulative co-morbidity present at the commencement of RRT

	Number of co-morbidities					
Totals	0	1	2	3	4	5+
%	38.7	29.0	16.0	8.1	4.4	3.7

Co-morbidity totals

The presence of several co-morbid factors can influence patient survival[1,2]. Using the 14 fields available, an analysis of cumulative co-morbidity was performed (table 16.4). Of the data available, 39% had no co-morbidity and only 16% of patients had 3 or more conditions.

Frequency of co-morbidities by age band

Figures 16.2 and 16.3 outline the frequency of cardiac and vascular co-morbidity segregated by age bands. Cardiac and cerebrovascular disease incidence increases with age up to the 65 to 74 years age band, with the majority of patients receiving RRT being in this age band. Of patients aged above 75 years, the incidence of patients on RRT as well as the incidence of cardiac and cerebrovascular co-morbidities reduce. As the incidence co-morbidities: such as cardiac; cerebrovascular disease and COPD increases in the general population, this reduction in incidence of these co-morbidities in the older dialysis patients must be due to either patients not being referred for RRT; or patients being managed in a conservative manner and not commencing RRT.

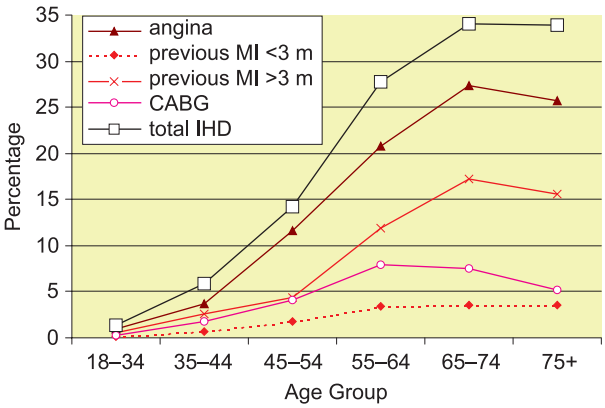

Figure 16.2: Frequency of cardiac co-morbidities in incident patients

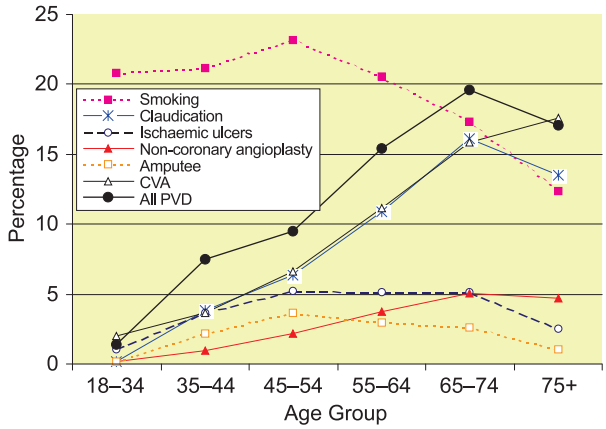

Figure 16.3: Frequency of vascular co-morbidity in incident dialysis patients

Figure 16.4 outlines the incidence of the conditions as COPD, diabetes not causing end stage renal failure, malignancy and liver disease. Smoking and liver disease incidence falls as patients age, whilst the incidence of malignancy rose. Diabetes as the primary cause of ERF starts to decline in those patients aged over 65 while diabetes as a co-morbidity continues to rise. This may be due to misclassification with 25% of patients classified with a primary diagnosis of 'uncertain' (EDTA diagnosis – 2 small kidneys) and a further 28% classified as renovascular disease. This highlights the potential for Registries to under record the incidence of diabetes unless collecting co-morbidity.

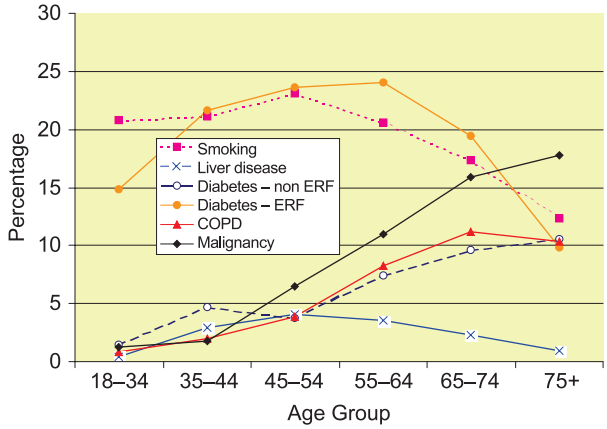

Figure 16.4: Frequency of other co-morbid conditions

Abbreviations: COPD – chronic obstructive pulmonary disease; non-ERF – not causing established renal failure

Table 16.5: Percentage of patients with and without diabetes and co-morbid conditions

	Non-diabetics	Diabetics
Cardiovascular disease	23.0	31.7
Cerebrovascular disease	10.6	16.5
Peripheral vascular disease	11.2	27.5
Smoking	18.4	18.2
COPD	8.1	6.3
Malignancy	13.3	4.4
Liver disease	2.4	2.2

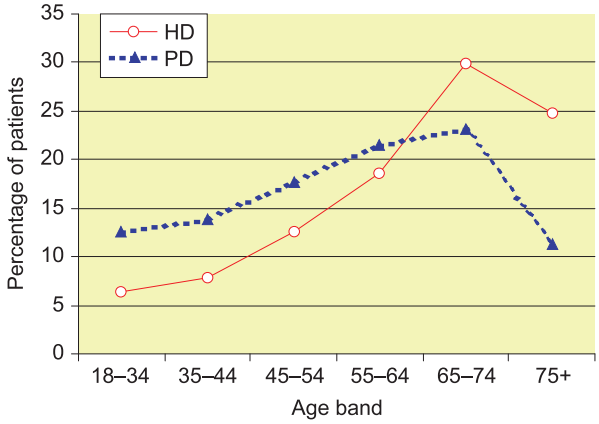

Figure 16.5: Age distribution of patients within each modality at day 90

Diabetes and co-morbidity

Using the available co-morbid data, patients with diabetes (1107) and those without diabetes (4648) were compared. Table 16.5 outlines the incidence of co-morbidity for patients with and without diabetes. Cardiac disease as a group including any case of angina; myocardial infarction; coronary artery angioplasty or bypass surgery was more common in diabetics even though diabetic patients were a younger age group than the non-diabetics (58% <65 years table 16.3). This was also similar for peripheral vascular disease (which included all cases of claudication; amputation; non coronary artery angioplasty, stenting or surgery) and for cerebrovascular disease.

It is disheartening to see that the incidence of smoking tobacco is similar in the diabetics to the non-diabetics, despite the well established increased risks in diabetics. Targeted smoking cessation programs may have a role to play.

The incidence of COPD and liver disease were similar in the two groups, whilst malignancy was more common in non diabetic patients.

Dialysis modality and co-morbidity

By 90 days after starting RRT (figure 16.5), those patients on PD were significantly younger than the HD patients (57 v 66 years respectively, $p < 0.0001$). The proportion of the PD patients aged 65 and over was 34.4% as compared with 54.7% in HD patients.

Dialysis modality selection for patients is not wholly dependent upon co-morbidity and is more dependent upon practical issues of patient choice, in some centres the availability of haemodialysis slots, the provision of space at home for storage of PD fluid, in addition to patients' physical and mental capacity to perform PD.

Following analysis of dialysis modality with co-morbid conditions and age, it was noted that patients with previous CABG surgery were more likely to start on PD. This contrasts with COPD, diabetes, angina, liver disease, malignancy, limb amputees, cerebrovascular disease and ischaemic/neuropathic ulcers where patients were more likely to start on HD. (Table 16.6).

A history of myocardial infarction, non coronary artery angioplasty/surgery and smoking tobacco did not differ significantly between dialysis modalities.

The median age of patients starting RRT is shown in table 16.6 and this shows that there is a complex relationship of age, co-morbidity and modality which is difficult to disentangle. As highlighted above, patients on PD are generally younger, although when analysed by co-morbidity the median age of patients with a previous MI are similar across modalities. This may indicate a preference for PD in this co-morbidity group.

Table 16.6: Proportions of co-morbid conditions present in PD and HD patients

Co-morbidity	HD		PD		p value
	%	Median age	%	Median age	
Angina	15.2	70	14.8	67	<0.001
MI – more than 3 months ago	7.8	69	9.9	70	0.9
MI – within 3 months	2.3	70	1.9	68	0.4
CABG	4.4	67	5.8	65	0.003
Cerebrovascular disease	9.9	72	8.2	66	<0.001
Diabetes non-ERF	10.3	68	8.5	63	<0.001
COPD	6.5	70	4.2	64	<0.001
Smoking	19.7	63	19.0	55	0.4
Liver disease	3.1	58	1.3	57	<0.001
Malignancy	9.2	71	6.7	65	<0.001
Claudication	8.7	70	10.5	67	0.054
Ischaemic/neuropathic ulcers	4.0	65	2.7	53	0.02
Angioplasty of non coronary vessels	2.9	72	3.4	67	0.1
Amputations	2.6	65	1.9	53	0.003

Patient early referral and co-morbidity

Nephrological follow up in the pre-dialysis phase is important in; addressing and modifying cardiovascular risk factors, the prevention of malnutrition, it enables the preparation of patients for renal replacement as well as ensuring the placement of appropriate forms of dialysis/vascular access and the prevention of uraemic emergencies.

In the Registry Report 2003 analysis of late referral in chapter 16 (unrelated to whether a centre was sending co-morbidity data) showed that <3 months, 3–12 months and >1 yr nephrological follow up was 30%, 21% and 49% respectively. Figure 16.6 shows that the younger and older patients were more likely to present late with a short period of nephrological follow up.

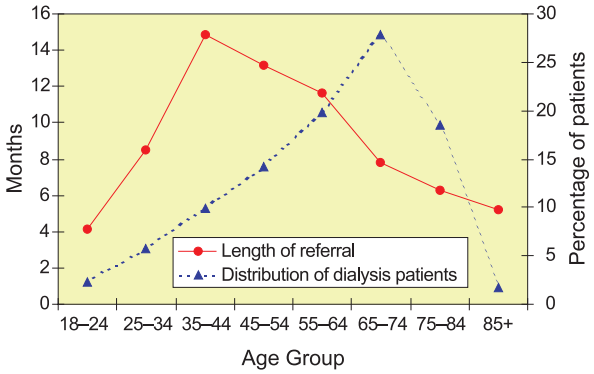

Figure 16.6: Duration of pre dialysis nephrological care and the proportions of the dialysis patients present per age band

Patients aged over 65 accounted for 48% of the total dialysis population and as expected, these individuals had a higher total co-morbidity in addition to the shorter period of nephrological follow up shown above.

Using information on co-morbidity and nephrological follow up from a cohort of 3981 patients, co-morbid conditions and referral were analysed (table 16.7). In the patients with specific co-morbid conditions, the referral pattern followed a similar trend: with 31% of

Table 16.7: Percentage of specific co-morbid conditions receiving pre dialysis follow up

	Referral period			
	3 m	3–6 m	6–12 m	>1 yr
Cardiovascular disease	27.7	8.7	11.3	52.3
Peripheral vascular disease	27.1	9.6	15.3	48.0
Cerebrovascular disease	27.3	9.7	13.5	49.6
Diabetes (not cause of ERF)	29.2	5.0	10.1	55.8
COPD	33.3	9.0	9.9	47.8
Liver disease	42.0	10.1	5.8	42.0
Malignancy	46.1	7.5	7.5	39.0
Smoking	32.9	10.3	13.1	43.7

Notes:
Heart disease included any instance of myocardial infarction, angina, coronary artery angioplasty or bypass surgery.
Peripheral vascular disease included any instance of claudication, the presence of ischaemic ulcers, limb amputation or angioplasty of non coronary vessels.

patients receiving less than 90 days of nephrological follow up and 49% receiving more than one year. In those patients with no co-morbidity present (who were also younger) 39% received less than 3 month nephrological follow up.

When analysed by number of co-morbid conditions present (either 1, 2, 3, 4+) the length of nephrological follow up was similar across the four groups. Only in those patients with three co-morbid conditions were patients likely to present >6 months prior to start of RRT.

In patients with diabetes, over 44% were referred within a year of requiring dialysis and 29% within 3 months, which is insufficient time to allow progression modifying treatment to have an effect or in the latter case to plan dialysis.

Frequency of co-morbidity by ethnicity

There were 4905 patients with data returns for both ethnicity and co-morbidity (table 16.8). For this analysis cardiovascular disease included angina, myocardial infarction, coronary angioplasty or coronary artery bypass grafting. In addition, PVD included claudication, non coronary artery angioplasty/stenting, amputations and the presence of ischaemic/neuropathic ulcers. The incidence of cardiac disease was similar in the South Asian and White populations, whilst vascular diseases (CVA + PVD) and smoking were more common in the White population.

When diabetes as a factor leading to diabetic nephropathy or diabetes as a coexistent condition was considered, as expected figure 16.7 shows that the incidence of diabetes was significantly greater in the ethnic minorities ($p < 0.0001$).

Analysing the data by age (figure 16.8), there were fewer patients in the age 75+ from the ethnic minorities. This is due to the fact that the ethnic minority community in the UK is a much younger population than the established population.

Table 16.8: Frequency of co-morbidity by ethnic group

	South Asian	Black	Chinese*	Other	White
Number of patients	369	145	18	100	4273
Ethnicity (%)	7.5	3.0		2.0	87.1
Smoking (%)	8.6	7.7		3.7	20.4
CVA (%)	8.4	10.4		3.7	11.9
PVD (%)	11.4	3.4		6.5	14.9
Cardiovascular disease (%)	24.1	17.4		14.8	25.1
Liver disease (%)	3.5	0.7		2.8	2.3
COPD (%)	4.2	3.5		4.7	8.5
Malignancy (%)	3.5	4.9		1.9	12.0

*Due to small numbers no analysis has been performed on this data

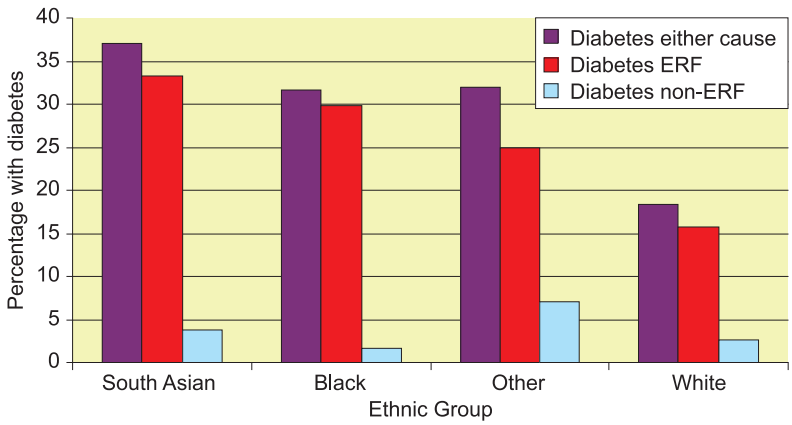

Figure 16.7: Frequency of diabetes by ethnic group

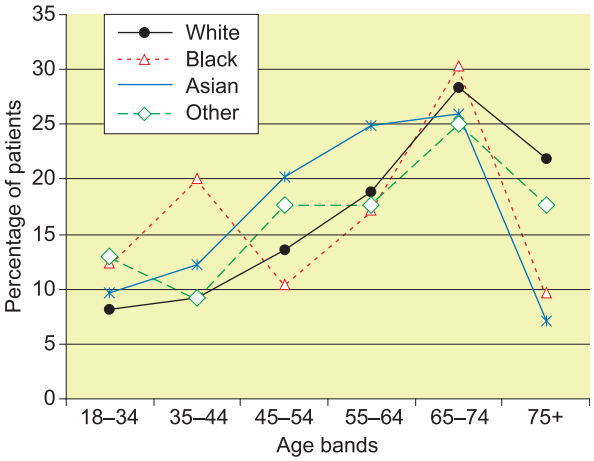

Figure 16.8: Age distribution of incident patients by ethnic group

Renal function at commencement of dialysis and co-morbidity

Using the abbreviated MDRD calculation, the eGFR of patients starting dialysis was calculated and is shown in table 16.9. The Tukey multiple comparison test was used to test the mean 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.

Patients with diabetes had a slightly higher eGFR at commencement of dialysis (table 16.9), although this may not be a clinically important difference. As diabetic patients had more co-morbidity (table 16.5) it is possible that factors such as heart disease, heart failure/resistant oedema may have prompted earlier dialysis initiation in these individuals.

This data is similar to that of the United States Renal Data System (USRDS) which shows a mean eGFR of 9.6 ml/min at the start of RRT.

Table 16.9: Mean eGFR and presence of co-morbidity

	Co-morbidity present		
	Mean	**95% CI**	**p value**
No co-morbidity	8.7	8.4–9.1	0.070
Angina	9.3	8.9–9.6	0.005
MI in past 3 months	9.9	8.5–11.3	0.055
MI >3 months ago	8.9	8.5–9.3	0.161
CABG/angioplasty	9.7	9.0–10.3	0.075
Cerebrovascular disease	9.0	8.6–9.4	0.178
Diabetes (not cause of ERF)	9.4	8.7–10.0	0.016
Diabetes as primary disease	10.2	9.6–10.7	<0.0001
Diabetes of either category	9.9	9.5–10.4	<0.0001
COPD	9.2	8.7–9.8	0.036
Liver disease	9.4	8.3–10.4	0.077
Malignancy	9.1	8.4–9.7	0.421
Claudication	9.5	9.0–10.0	0.010
Ischaemic/neuropathic ulcers	9.8	8.9–10.8	0.030
Angioplasty/vascular graft	9.5	8.6–10.5	0.050
Amputation	9.8	8.8–10.8	0.051
Smoking	8.4	8.1–8.7	0.516

Table 16.10: Mean haemoglobin by co-morbidity

	Mean	95% CI	p value
No co-morbidity	10.0	10.0–10.1	0.911
Angina	10.1	10.0–10.2	0.259
MI in past 3 months	10.2	9.9–10.5	0.675
MI >3 months ago	10.3	10.1–10.4	0.004
CABG/angioplasty	10.2	10.1–10.4	0.064
Cerebrovascular disease	10.0	9.8–10.1	0.998
Diabetes (not cause of ERF)	10.2	10.0–10.3	0.223
Diabetes as primary disease	9.9	9.8–10.0	0.265
Diabetes of either category	10.0	9.9–10.1	0.422
COPD	9.9	9.7–10.0	0.114
Liver disease	9.7	9.3–10.1	0.022
Malignancy	10.0	9.8–10.1	0.488
Claudication	10.0	9.9–10.2	0.349
Ischaemic/neuropathic ulcers	9.7	9.5–10.0	0.092
Angioplasty/vascular graft	10.2	9.9–10.5	0.048
Amputation	9.8	9.5–10.1	0.237
Smoking	10.0	9.8–10.1	0.594

Haemoglobin at commencement of dialysis and co-morbidity

The mean haemoglobin at commencement of dialysis was analysed (table 16.10) and median haemoglobin (1–14 days prior to RRT) for those without co-morbidity present was 10 g/dl. Only patients with a myocardial infarction >3 m previously had a slightly higher haemoglobin.

Renal transplantation and co-morbidity

Patients benefit significantly from renal transplantation and which patients are listed on the waiting list and receive a transplant is of interest. A more detailed analysis of access to the transplant waiting list is in chapter 11. Utilising information from centres with a high return of co-morbid information (>67%), an analysis of patients who had been transplanted (Tx) and those that remained on dialysis by the end of 2004 was performed. Of a cohort of 4,132 patients, just over 10% of patients (425) had been transplanted.

Renal transplant patients were significantly younger, however a small number of patients had been transplanted from the older age bands (figure 16.9). As expected there was a higher level of co-morbid conditions in those patients who remained on dialysis (table 16.11).

In the future, more detailed analysis of patient selection for transplant listing will be possible in conjunction with UKTransplant.

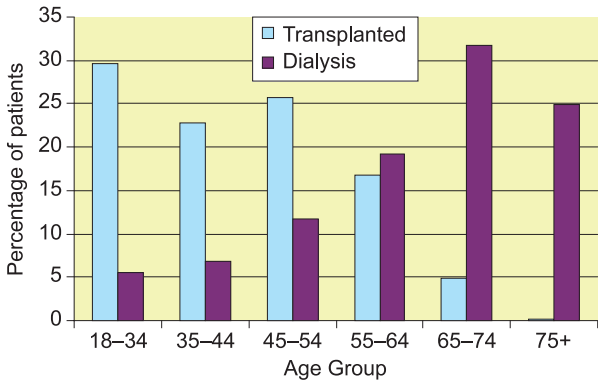

Figure 16.9: Distribution of incident RRT cohort that received a transplant and those that remained on dialysis

Table 16.11: Incidence of co-morbidity in transplanted and not transplanted patients

Co-morbidity	Not transplanted	Transplanted
Patient number	3707	425
Cardiovascular disease	26.5%	6.8%
Peripheral vascular disease	15.5%	2.1%
Cerebrovascular disease	12.3%	3.5%
Diabetes (not cause of ERF)	8.1%	2.6%
COPD	8.5%	1.4%
Liver disease	2.3%	0.7%
Malignancy	12.7%	1.9%
Smoking	17.9%	16.8%

Survival analysis and co-morbidity

Survival within 90 days of commencing dialysis

The univariate model (table 16.12), does not allow adjustment for age, so patients were first stratified by age group (less than 65 years and 65 years and above) to make some account for the increasing incidence of co-morbidity with age which would otherwise obscure the analysis.

Important risk factors for both age groups for survival in the first 90 days were malignancy and vascular disease: (which includes at least one of cerebrovascular disease; claudication; ischaemic/neuropathic ulcer; angioplasty/vascular graft; or amputation). As liver disease was more common in patients aged less than 65, it was noted as an important risk factor in this group. Patients aged less than 65 with cardiovascular disease faced a significant risk as compared to others within this age group who did not have this co-morbid condition. Cardiovascular disease was not significant in those patients aged over 65 and this may indicate a clinical decision not to start RRT in older patients with severe cardiovascular disease who were thought unlikely to survive the first 3 months or patients who died before starting RRT.

The multivariate analysis using a Cox proportional hazards model for the first 90 days after dialysis initiation (table 16.13) was performed. The variables considered in the model were:

age, angina, myocardial infarction (MI) in previous 3 months, MI more than 3 months ago, CABG/angioplasty, cerebrovascular

Table 16.12: Univariate analysis, co-morbidity hazards of death by day 90

	age <65		age 65+	
Co-morbidity	Hazard ratio	p-value	Hazard ratio	p-value
Angina	2.3	0.003	1.0	0.744
Cardiovascular disease*	2.1	0.003	1.2	0.244
Vascular disease**	3.3	<0.0001	1.3	0.018
Diabetes (not as cause of ERF)	0.8	0.694	1.3	0.189
Diabetes as primary disease	1.5	0.131	0.8	0.138
Diabetes of either category	1.3	0.227	1.0	0.725
COPD	1.5	0.409	1.1	0.639
Liver disease	6.0	<0.0001	1.1	0.828
Malignancy	3.8	<0.0001	1.7	<0.000
Claudication	2.1	0.029	1.1	0.534
Ischaemic/neuropathic ulcers	4.9	<0.0001	2.0	0.002
Smoking	0.5	0.095	1.3	0.128

*At least one of angina, myocardial infarction at any time, angioplasty/vascular graft
**At least one of cerebrovascular disease, claudication, ischaemic/neuropathic ulcer, angioplasty/vascular graft, amputation

Table 16.13: Cox regression survival analysis of the first 90 days of RRT

Variable	p-value	Hazard ratio	95% CI
Age per 1 year increase	<0.0001	1.05	1.04–1.07
MI in past 3 months	0.033	1.76	1.05–2.97
Cerebrovascular disease	0.026	1.41	1.04–1.90
Malignancy	<0.0001	2.14	1.63–2.82
Liver disease	0.001	2.60	1.45–4.66
Ischaemic/neuropathic ulcers	<0.0001	2.58	1.72–3.86

disease, diabetes of either category, COPD, liver disease, malignancy, claudication, ischaemic/neuropathic ulcers, angioplasty/vascular graft, amputation and smoking.

The results showed that age as a linear variable, a history of a recent myocardial infarction in the previous 3 months, cerebrovascular disease, malignancy, liver disease and ischaemic ulcers were all significant factors associated with impaired survival.

Survival 1 yr after 90 days of commencing RRT

Many other countries are unable to collect data on survival within the first 90 days of starting RRT. For this reason a 1 year survival analysis has been performed excluding the first 90 day period.

Similar to the previous analysis, the univariate analysis was performed after stratifying the patients into 2 age bands (table 16.14). In the younger patients (<65 years): the presence of heart disease; diabetes and liver disease were important risk factors within this age group compared to those without these co-morbidities. The lack of importance of cardiovascular disease in the older age group either indicates that other factors are more important or there is a selection bias through death prior to starting RRT or acceptance on to the program.

In the multivariate analysis (table 16.15), age, cerebrovascular disease and malignancy were important. Smoking and diabetes were added into the model only after first testing all the other co-morbidities because many co-morbid conditions will be correlated with these two factors. Smoking and diabetes remained an important prognostic factor even after adjusting for all the other co-morbid conditions.

In the multivariate analysis, the contrast between important risk factors in survival up to day 90 and the 1 year after 90 days period shows that diabetes is not a risk factor in the 90 day survival while as expected it is a risk factor in

Table 16.14: Univariate analysis, co-morbidity hazards of death by 1 year after 90 days

	age <65		age 65+	
Co-morbidity	Hazard ratio	p-value	Hazard ratio	p-value
Angina	1.6	0.027	0.9	0.577
Cardiovascular disease*	1.9	0.000	1.1	0.550
Vascular disease**	2.9	<0.0001	1.3	0.030
Diabetes (not as cause of ERF)	2.3	0.003	1.4	0.043
Diabetes as primary disease	2.5	<0.0001	1.2	0.236
Diabetes of either category	2.9	<0.0001	1.3	0.018
COPD	2.0	0.021	1.2	0.414
Liver disease	3.3	0.000	1.6	0.196
Malignancy	3.9	<0.0001	1.3	0.093
Claudication	2.8	<0.0001	1.3	0.099
Ischaemic/neuropathic ulcers	3.0	<0.0001	1.8	0.007
Smoking	1.5	0.030	1.3	0.111

*At least one of angina, myocardial infarction at any time, angioplasty/vascular graft

**At least one of cerebrovascular disease, claudication, ischaemic/neuropathic ulcer, angioplasty/vascular graft, amputation

Table 16.15: Cox regression survival analysis for the 1 year after 90 days

Variable	p-value	Hazard ratio	95% CI
Age per 1 year increase	<0.0001	1.04	1.04–1.05
Cerebrovascular disease	0.008	1.39	1.09–1.78
Liver disease	0.009	1.99	1.19–3.34
Malignancy	<0.0001	1.69	1.32–2.15
Ischaemic/neuropathic ulcers	0.002	1.75	1.23–2.49
Smoking	0.010	1.36	1.08–1.72
Diabetes of either category	<0.0001	1.65	1.35–2.02

the longer term. Whether this lack of importance in the first 90 days is due to the absence of a short term impact or that diabetic patients with a high co-morbidity load die prior to start of RRT is unknown. Similarly smoking has a long term negative impact on survival rather than a short term impact.

International comparisons of renal registries and co-morbidity

The number of national renal registries which produce a comprehensive list of co-morbid conditions of dialysis patients is small. A comparative analysis between countries, was available using publications from the USA, Australia/New Zealand and the Netherlands. As discussed earlier in this chapter, UK data is probably under reporting co-morbidity.

The USRDS generates a large amount of data which is easily accessible through its website (www.usrds.org). The Australian and New Zealand (ANZDATA) Registry had published co-morbid information in a paper discussing late referral and data is on their website (www.anzdata.org)[3]. The Necosad group[4] discussing dialysis have published information of a prospective cohort of patients from the 36 renal units in the Netherlands. Using all this information, it was possible to make a number of observations regarding co-morbidity.

Analysis by the proportions of the incident UK and US RRT patients within specific age bands shows a similar distribution (figure 16.10).

Definitions of cardiac disease, peripheral vascular disease and diabetes vary between countries. **Methods of recording other co-morbidity may also be different within these Registries, therefore these comparisons should be interpreted cautiously**.

Cardiac disease, cerebrovascular disease, peripheral vascular disease and COPD appear to be more common in Australia and New Zealand (table 16.16). Diabetes was most common in the USRDS population, followed by Australia and New Zealand. The USA was the only other country with data on smoking history and this was 1/3 the rate seen in the UK (5.2% v 18.4%).

The incidence of peripheral vascular disease, and COPD were similar in the USA, UK and Netherlands.

The Necosad data from the Netherlands shows a similarity to that in the UK for the incidence of diabetes, peripheral vascular disease, malignancy and COPD in the renal replacement therapy population. This may also relate to the similar incidence of RRT in the Netherlands in 2002 (100 p.m.p) to that of the UK (103 p.m.p). The Necosad data set is complete and this close agreement with the UK

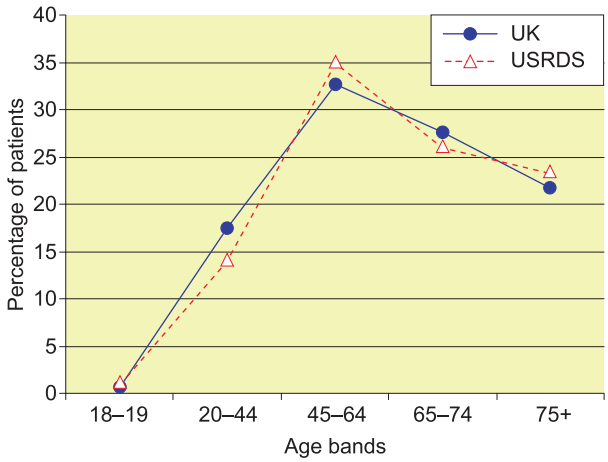

Figure 16.10: Percentage of patients on dialysis by age distribution, for UK and USA

Table 16.16: Summary of co-morbidity from differing national registries

	National registries			
Study period	**ANZDATA Apr 1995–Mar 2000**	**USRDS 1995–2003**	**Renal Registry 1999–2003**	**Necosad 2 Jan 1997– Nov 2000**
Number of patients	4243	696043	15197*	1041
Ischaemic heart disease inc MI	38.6%	23.8%	24.7%	11.1%
Cerebrovascular disease	15.1%	9.0%	11.7%	7.2%
Peripheral vascular disease	25.9%	14.3%	14.2%	13.0%
COPD	15.6%	7.1%	7.7%	7.2%
Diabetes**	30.7%	41.2%	18.8%	19.5%
Malignancy	–	5.3%	11.5%	10.1%
Smoking	not collected	5.2%	18.4%	not collected
Congestive cardiac failure	not collected	32.0%	not collected	12.3%
Patients with no co-morbidity at start of RRT***	39.0%	9.4%	38.7%	not collected

Notes:
*comprehensive co-morbid information was only available in 5916 patients.
**countries may sometimes include those patients who were diabetic not as a primary cause of renal failure in this total.
***US data includes hypertension (74%) and also congestive cardiac failure as a co-morbidity

data may suggest that while the Renal Registry data is badly incomplete it is reasonably representative of the UK.

The USRDS includes hypertension as a separate risk factor which is present in 74% of patients starting RRT and this explains why the percentage of patients in the USA reported as having no co-morbidity was low.

The incidence of cardiac co-morbidity was less in patients aged over 75 in the UK renal replacement therapy population than those in the 65–74 age band. A more detailed analysis of UK co-morbidity by age band, compared to the USA is shown in table 16.17.

In the UK, the incidence of previous myocardial infarction rises with age and falls slightly in

Table 16.17: Percentage of co-morbidity present, per age group, UK and USA populations

		Age bands			
Registry	**Conditions**	**⩽44**	**45–64**	**65–74**	**75+**
UK	Myocardial infarction	1.9	10.8	19.5	18.4
USRDS	Myocardial infarction	1.8	7.6	11.7	12.4
UK	Ischaemic heart disease	3.8	22.1	34.0	33.9
USRDS	Ischaemic heart disease	4.1	19.8	32.1	35.2
USRDS	Cardiac dysrhythmia	1.0	3.6	7.7	10.8
USRDS	Congestive heart failure	11.7	28.5	39.2	43.8
UK	COPD	1.5	6.4	11.2	10.4
USRDS	COPD	1.3	5.7	10.2	10.4
UK	Smoking	21.0	21.7	17.3	12.4
USRDS	Smoking	7.5	6.9	4.4	2.3
UK	Malignancy	1.5	9.1	15.9	17.8
USRDS	Malignancy	1.3	3.9	7.0	9.0
UK	Cerebrovascular disease	2.9	9.2	15.9	17.6
USRDS	Cerebrovascular disease	2.5	8.1	11.8	12.3
UK	Peripheral vascular disease	4.6	13.0	19.6	17.1
USRDS	Peripheral vascular disease	4.0	13.1	18.8	18.3

those aged over 75 years. This contrasts with the USA, where the incidence of a previous myocardial infarction is much lower than the UK in patients starting renal replacement therapy. Although in the USA it continues to rise in patients aged over 75 (probably at less than the expected rate seen in the general population), the rate is still only 2/3 that seen in the UK (12% v 18%). This higher incidence of previous MI would have a detrimental effect on survival in the UK and partly accounts for the lower incidence rates, with many patients in the UK dying before reaching the stage of requiring RRT.

The incidence of ischaemic heart disease is similar between the UK and USA at 34% and 35% of patients aged over 75 years respectively. The apparent similar incidence of cardiac disease in the USA when compared to the UK (table 16.16) is due to the inclusion of cardiac dysrhythmia. Congestive cardiac failure is not collected in the UK which also accounts for the apparent higher co-morbidity rate in the USA.

Cerebrovascular disease in UK patients was more common than the USA across all age bands, rising to almost 50% higher in those aged over 75 years. In contrast the incidence of peripheral vascular disease was similar in the UK to that of the USA, across all age bands.

Discussion

Since 1999, 15,197 patients' details have been recorded by the Renal Registry and 39% of these individuals did have co-morbid returns. There are still difficulties with data returns from the majority of renal units, although a number of renal units have managed to submit a sustained high data return. It is likely that these renal units have invested in administrative and IT systems to aid data collection and the lessons learnt by these units need to be shared. This incompleteness of data returned leads to potential unreliability in analyses. Surprisingly therefore the incidence of several co-morbidities seemed to correlate closely with that of the USA and Netherlands.

The current datasets collected by the Renal Registry have been useful and a number of analyses investigating patient survival as well as patient demography have been performed. There are a number of differing systems of co-morbid data collection[1,2,4,5,6,7]. As mortality is associated with cardiac and vascular disease, all the differing methods do collect information associated with these topics. To date, co-morbidity has been used by the Registry to analyse the outcomes of dialysis and transplant patients. It has been noted that elderly patients (aged 75+) have less co-morbidity than patients aged 65 to 74 years.

The Renal Registry has advocated that all renal units should collect information on patients with severe renal disease managed conservatively, without dialysis. It is likely that this group will account for the apparent disparity in the incidence of co-morbidity in the elderly patients. In general, there are patients with severe renal failure who do not start dialysis as a consequence of multiple co-morbidity, age and disability. There is debate as to whether the current information collected by the Renal Registry will aid the analysis in this group of patients. It is likely that severity of individual or collective co-morbidities or entirely different factors such as dementia and mental illness, which are not collected by the Renal Registry, may influence the decision on whether to start on renal replacement therapy or opt for conservative management.

In the past, cardiac failure as a co-morbid condition was not collected by the Renal Registry, but its importance has been noted and the dataset has been adjusted to collect heart failure information. Similarly there may be a need to further adapt the current dataset to account for other co-morbid conditions that may prove to be of importance.

The functional ability of patients can influence patient survival[1], and the collection of Karnovsky scores may be useful in the long term, although it is unlikely that renal units would cope with this added burden of work.

In summary, an understanding of the co-morbidity burden faced by patients is necessary to support future analyses, and all renal units have been encouraged to submit a complete dataset of their patients.

Appendix to Chapter 16

Important changes to co-morbidity definitions in 2003

The non-coronary angioplasty group has been widened to include other vascular grafts and arterial stents. The new definitions are given below:

Angioplasty, stenting, vascular graft, aneurysm (all non-coronary)

This category now includes vascular grafts (e.g. aortic bifurcation grafts), arterial stents and aneurysms.

Episode of heart failure (right or left) prior to RRT

This is whether or not it was only the result of fluid overload.

Co-morbidity definitions

Angina

A history of chest pain on exercise with or without ECG changes, exercise tolerance test, radionucleotide imaging or angiography.

Previous MI within the past 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. This definition is from both the European Society of Cardiology and the American College of Cardiology.

Previous MI more than 3 months ago

From the time of the start of RRT.

Previous CABG or coronary angioplasty

Episode of heart failure (right or left)

This is whether or not it was only caused by fluid overload.

Cerebrovascular disease

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

Diabetes (not causing established renal failure)

This includes diet-controlled diabetics.

Chronic obstructive pulmonary disease

This is defined as a slowly progressive airways disorder characterised by obstruction of the expiratory airflow, which does not change markedly over several months, it may be accompanied by airway hyper-reactivity and may be partially reversible.

N.B. Chronic bronchitis and emphysema may occur in the absence of airflow obstruction. Asthma patients may rarely develop airflow obstruction that does not improve with steroids.

Liver disease

Persistent enzyme evidence of hepatic dysfunction or biopsy evidence or hepatitis B e antigen or hepatitis C antigen (polymerase chain reaction) positive serology.

Malignancy

Defined as any history of malignancy (even if curative), for example the removal of a melanoma; excludes basal cell carcinoma.

Claudication

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

Ischaemic/neuropathic ulcers

The current presence of these ulcers.

Angioplasty, stenting, vascular graft, vascular aneurysm (all non-coronary)

This category now includes vascular grafts (e.g. aortic bifurcation grafts) and renal artery stents.

Amputation for peripheral vascular disease

Smoking

Being a current smoker or having a history of smoking within the previous year.

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