

Declining comorbidity-adjusted mortality rates in English patients receiving maintenance renal replacement therapy



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Benjamin C. Storey^{1,2,5}, Natalie Staplin^{2,5}, Charlie H. Harper^{1,2}, Richard Haynes^{1,4}, Christopher G. Winearls⁴, Raph Goldacre³, Jonathan R. Emberson^{1,2}, Michael J. Goldacre³, Colin Baigent^{1,2}, Martin J. Landray^{1,2,3,5} and William G. Herrington^{1,4,5}

¹Medical Research Council Population Health Research Unit, Nuffield Department of Population Health (NDPH), University of Oxford, Oxford, UK; ²Clinical Trial Service Unit and Epidemiological Studies Unit (CTSU), NDPH, University of Oxford, Oxford, UK; ³Unit of Healthcare Epidemiology, Big Data Institute, Li Ka Shing Centre for Health Information and Discovery, NDPH, University of Oxford, Oxford, UK; and ⁴Oxford Kidney Unit, Oxford University Hospitals NHS Foundation Trust, Oxford, UK

We aimed to compare long-term mortality trends in end-stage renal disease versus general population controls after accounting for differences in age, sex and comorbidity.

Cohorts of 45,000 patients starting maintenance renal replacement therapy (RRT) and 5.3 million hospital controls were identified from two large electronic hospital inpatient data sets: the Oxford Record Linkage Study (1965-1999) and all-England Hospital Episode Statistics (2000-2011). All-cause and cause-specific three-year mortality rates for both populations were calculated using Poisson regression and standardized to the age, sex, and comorbidity structure of an average 1970-2008 RRT population. The median age at initiation of RRT in 1970-1990 was 49 years, increasing to 61 years by 2006-2008. Over that period, there were increases in the prevalence of vascular disease (from 10.0 to 25.2%) and diabetes (from 6.7 to 33.9%). After accounting for age, sex and comorbidity differences, standardized three-year all-cause mortality rates in treated patients with end-stage renal disease between 1970 and 2011 fell by about one-half (relative decline 51%, 95% confidence interval 41-60%) steeper than the one-third decline (34%, 31-36%) observed in the general population. Declines in three-year mortality rates were evident among those who received a kidney transplant and those who remained on dialysis, and among those with and without diabetes. These data suggest that the full extent of mortality rate declines among RRT patients since 1970 is only apparent when changes in comorbidity over time are taken into account, and that mortality rates in RRT patients appear to have declined faster than in the general population.

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Correspondence: William G. Herrington, Clinical Trial Service Unit and Epidemiological Studies Unit, University of Oxford, Richard Doll Building, Old Road Campus, Oxford OX3 7LF, UK. E-mail: will.herrington@ndph.ox.ac.uk

⁵These authors contributed equally.

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Maintenance dialysis programs for end-stage renal disease (ESRD) began in the United Kingdom in the 1960s.¹⁻³ Until the 1980s, renal replacement therapy (RRT; i.e., dialysis or kidney transplantation) was restricted to ESRD patients who were considered the most economically active, and those with diabetes or other comorbidities were often not referred or treated.⁴ This contrasts with the situation 50 years later, when the median age of patients starting maintenance RRT is 65 years and diabetes is the leading cause of ESRD.⁵

Examining long-term temporal mortality trends helps describe past and current serious health risks. Interpreting these trends is difficult in RRT populations because comparisons between patients treated for ESRD and other populations need to take account of the substantial secular changes in the prevalence of comorbid illnesses that influence both mortality⁶⁻⁸ and the likelihood of receiving RRT. To date, no large study has standardized mortality rates in treated ESRD and general population cohorts to the same comorbidity as well as age and/or sex structure. Therefore, although data from ESRD registries in the United States from 1977 to 2007,⁹ Europe from 1998 to 2007,¹⁰ Australasia from 1992 to 2005,¹¹ and the UK from 2002 to 2011⁵ have all shown modest improvements in mortality for people with treated ESRD, it is unclear whether the magnitude of this change is comparable to that observed in the general population during the same period.¹²

The Oxford Record Linkage Study (ORLS) was established in 1963 and recorded information about all hospital inpatient admissions in Oxfordshire and surrounding counties covering about 5% of England (referred to as “Oxfordshire”).¹³ Hospital Episode Statistics (HES) succeeded ORLS and established nationwide coverage from 1998. Both data sets have been linked to national mortality

registers, so we aimed to study mortality trends among new maintenance RRT patients and controls from the general population between 1970 and 2008 using novel approaches to ensure all cohorts could correct for changes in comorbidity over time. We also consider the effects of temporal changes in the availability of transplantation on mortality trends.

RESULTS

Between 1970 and 2008, 44,922 new ESRD patients started maintenance RRT (2192 in ORLS 1970–1996 and 42,730 from all-England HES 2000–2008), and 5,360,712 general population controls (532,019 from ORLS and 4,828,693 from HES) were identified. Indirect validation included

observing closely matched numbers of kidney transplant operations recorded in HES and the UK Transplant Registry¹⁴ (Supplementary Table S1); closely matched cohort sizes, demographics and renal characteristics when HES data were compared with summary English data from the UK Renal Registry (Supplementary Table S2)^{15–18}; and similar age- and sex-adjusted 3-year mortality rates for ORLS/“HES Oxford” and for Oxford Kidney Unit (Supplementary Figure S1).

In Oxfordshire, the median age at start of maintenance RRT increased from 49 years (interquartile cut-offs 36–60 years) in 1970 to 1990 to 61 years (46–72 years) by 2006 to 2008. Consequently, while only one-quarter of patients starting RRT from 1970 to 1990 were aged ≥60 years, by

Table 1 | Baseline characteristics of newly treated end-stage renal disease patients, by year

Characteristics	Year groups							
	Oxfordshire					All-England		
	Oxford Record Linkage Study		Hospital Episode Statistics (Oxford)			Hospital Episode Statistics (All-England)		
	1970–1990	1991–1996	2000–2002	2003–2005	2006–2008	2000–2002	2003–2005	2006–2008
N	1220	972	700	750	878	13,178	13,606	15,946
Demographics								
Female	40.2%	38.0%	41.1%	35.9%	37.7%	39.5%	37.9%	38.5%
Median age (yr)	49 (36–60)	59 (44–69)	61 (45–72)	61 (45–72)	61 (46–72)	61 (47–71)	62 (47–72)	63 (49–73)
18–40	30.2%	18.7%	18.7%	18.7%	15.9%	15.8%	14.8%	13.0%
40–50	21.2%	15.6%	13.6%	13.1%	14.7%	13.5%	13.4%	12.9%
50–60	23.5%	17.2%	15.4%	16.4%	17.1%	17.8%	16.6%	17.2%
60–70	16.8%	24.2%	20.7%	20.8%	22.1%	23.1%	22.9%	22.7%
70–80	7.9%	20.5%	24.4%	23.5%	19.8%	23.6%	24.1%	24.5%
≥80	0.3%	3.8%	7.1%	7.6%	10.4%	6.1%	8.2%	9.7%
Ethnicity^{a,c}								
White	-	-	86.8%	86.4%	84.0%	82.1%	81.2%	79.9%
Black	-	-	3.5%	3.5%	4.7%	6.3%	6.5%	6.9%
South Asian	-	-	7.4%	6.3%	7.2%	8.2%	8.3%	8.7%
Other	-	-	2.3%	3.8%	4.0%	3.4%	3.9%	4.4%
Unknown	-	-	131	36	35	1,694	962	745
Comorbidities								
Diabetes	6.7%	16.8%	24.4%	29.2%	33.9%	25.7%	29.9%	34.3%
Vascular	10.0%	18.3%	22.3%	24.7%	25.2%	25.2%	26.5%	28.3%
Major coronary disease	2.6%	4.2%	5.1%	7.2%	8.3%	6.1%	7.0%	7.7%
Congestive heart failure	5.2%	8.5%	9.9%	10.8%	10.5%	11.7%	12.3%	12.8%
Cerebrovascular disease	1.4%	2.2%	3.1%	2.8%	3.5%	3.3%	3.4%	3.4%
Peripheral arterial disease	3.0%	7.8%	11.3%	11.5%	12.9%	12.0%	12.5%	14.2%
Nonvascular ^b	7.8%	14.4%	18.3%	21.7%	24.9%	21.7%	25.0%	27.5%
Liver disease	0.5%	0.4%	1.7%	1.1%	2.3%	1.6%	2.0%	2.8%
Cancer	2.9%	4.6%	5.3%	8.9%	7.6%	6.4%	7.8%	8.3%
Chronic obstructive pulmonary disease	1.3%	2.9%	6.3%	6.5%	10.3%	8.3%	10.0%	12.1%
Peptic ulcer disease	1.6%	2.3%	2.7%	1.9%	1.9%	2.3%	2.3%	2.0%
Connective tissue disease	2.0%	4.3%	3.1%	4.4%	4.9%	4.7%	5.0%	4.8%
Renal characteristics^c								
Initial renal replacement therapy modality								
Dialysis	94.6%	92.6%	93.7%	92.7%	91.6%	94.5%	94.3%	93.6%
Transplant	5.4%	7.4%	6.3%	7.3%	8.4%	5.5%	5.7%	6.4%
Primary renal diagnosis (presumed)								
Diabetic kidney disease	1.6%	8.4%	20.0%	22.5%	22.1%	19.1%	20.1%	20.4%
Glomerulonephritis	9.3%	14.1%	9.3%	10.8%	14.5%	10.8%	12.2%	14.1%
Polycystic kidney disease	10.5%	8.4%	8.6%	7.5%	10.4%	9.2%	8.6%	8.9%
Other known diagnosis/unknown	78.5%	69.0%	62.1%	59.2%	53.1%	60.9%	59.1%	56.6%

Excludes patients dying within 90 days. Data are n or % or median (interquartile range).

^aEthnicity only recorded in Hospital Episode Statistics (92% complete) with percentages quoted only for those with a known ethnicity.

^bAlso includes hemiplegia or paraplegia.

^cNot used for standardization. Baseline characteristics of general population hospital controls are in Supplementary Table S3.

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