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Trends in the Incidence, Demographics and Outcomes of End-Stage Renal Disease Due to Lupus Nephritis in the U.S., 1995–2006

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Abstract

Background—It is unknown whether recent advances lupus nephritis (LN) treatment have led to changes in the incidence of end-stage renal disease (ESRD) secondary to LN, or in the characteristics, therapies, and outcomes of patients with LN ESRD.

Methods—Patients with incident LN ESRD (1995–2006) were identified in the US Renal Datasystem. Trends in sociodemographic and clinical characteristics were assessed. We tested for temporal changes in standardized incidence rates (SIRs) for sociodemographic groups using Poisson regression. Changes in rates of waitlisting for kidney transplant, kidney transplantation, and all-cause mortality were examined using crude and adjusted time-to-event analyses.

Results—12,344 incident cases of LN ESRD were identified. Mean age at ESRD onset was 41 years; 81.6% were female and 49.5% African American. SIRs for LN ESRD among those ages 5–39, African Americans, and in the US Southeast increased significantly from 1995–2006. Increases in body mass index and the prevalence of both diabetes and hypertension were detected. Mean serum hemoglobin at ESRD onset increased, while that of serum creatinine decreased over time. More patients used hemodialysis and fewer peritoneal dialysis. There was a slight increase in pre-emptive kidney transplantation at ESRD onset, but kidney transplantation rates within the first three years of ESRD declined. Mortality did not change over 12 years of study.

Conclusions—The characteristics of LN ESRD patients and their initial therapies have changed in recent years. While SIRs rose in younger patients, among African Americans and in the South, outcomes did not improve in over a decade of evaluation.

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Disclaimer: Data for these analyses were provided by United States Renal Data System (USRDS), but the analysis and conclusions are those of the authors and do not represent the USRDS or National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

Keywords

incidence; dialysis; transplantation; survival; lupus; nephritis; end-stage renal disease; chronic kidney disease; systemic lupus erythematosus; African American; Hispanic; race; women

Introduction

Up to 60% of adults and 80% of children with systemic lupus erythematosus (SLE) develop nephritis[1, 2]. Of these, 10 to 30% progress to end-stage renal disease (ESRD) within 15 years of diagnosis, even with aggressive treatment[3–5]. Renal damage is the most important predictor of mortality for patients with SLE and five-year survival is significantly worse among individuals with lupus nephritis than among those without nephritis[5–7,8].

Advances in the treatment of lupus nephritis have been made within the past two decades, with the demonstration of effective immunosuppressive regimens including cyclophosphamide, azathioprine and mycophenylate mofetil[9–13]. The incidence of ESRD due to lupus nephritis, however, rose from 1.13 in 1982 to 3.20 cases per million in 1995[14], and showed no reduction between 1996 and 2004[15]. Advances in the ESRD treatment have also been made during these years. Kidney transplantation is now accepted as optimal therapy for the long-term treatment of most patients with ESRD[16, 17]. Living kidney transplantation has been demonstrated to offer all ESRD patients the best chance of dialysis-free survival[18]. Early evaluation for kidney transplantation and placement on the waiting list for allografts also has proven benefits, as rates of graft failure and mortality increase with dialysis wait times[19, 20]. For patients with lupus nephritis, as for other causes of ESRD, kidney transplantation has been associated with decreased mortality and improved quality of life[17, 21].

We examined recent trends in the incidence and outcomes of ESRD due to lupus nephritis in the entire U.S. population and in different sociodemographic groups, defined by age, sex, race, ethnicity, medical insurance type and geographic region of the country, between 1995 and 2006. The goals of these analyses were to investigate changes during these years in the populations affected by lupus ESRD, their clinical characteristics, treatments and rates of kidney transplantation and survival.

Methods

Data Sources

The US Renal Data System (USRDS) is the U.S. national registry of patients with ESRD[22]. The USRDS database includes approximately 94% of the patients in the U.S who receive renal replacement therapy as dialysis or kidney transplantation, and in 2006 included information on 1.6 million individuals with ESRD since 1988[22]. For each new patient at enrollment, the attending nephrologist is required to complete the Medical Evidence Report form (CMS-2728). It serves to establish Medicare eligibility for those patients who were not previously Medicare eligible, reclassify previously eligible Medicare beneficiaries as ESRD patients, and provide demographic and diagnostic information, including the etiology of ESRD, on all new ESRD patients according to ICD-9-codes. The date of first service is derived from the earliest of dialysis start dates reported on the medical evidence form, the date of kidney transplant as reported on a CMS or Organ Procurement Transplant Network transplant, the Medical Evidence Report, a hospital inpatient claim, or the date of the first Medicare dialysis claim. Patients who were transiently dialyzed for acute renal failure, or who died before being enrolled in the database or who refused renal replacement therapy, may not be included. Completion of the CMS ESRD Death Notification Form (CMS-2746)

is also mandatory and enforced by CMS. Providers have 45 days to return the completed form to the ESRD networks and USRDS Coordinating Center[22].

From the U.S. Census Bureau[23], we obtained age-, sex-, race-, ethnicity- and state-specific population annual estimates (2000 U.S. Census, as well as annual intercensal population estimates for July of each year). Estimates of the Hispanic and non-Hispanic U.S. population were available only with the 2000 U.S. Census and thereafter.

Study Population

We identified all individuals ages 5 to 100 years with SLE (International Classification of Diseases, Ninth revision, ICD-9 code 710.0) identified as the cause of ESRD at enrollment in the USRDS from January 1, 1995 to December 31, 2006. From the USRDS, we obtained information concerning patient demographics, including age, sex, race (white, African American, Asian/Pacific Islander, or Native American), Hispanic ethnicity, and U.S. state or territory of residence at the time of initiation of ESRD treatment. The following data for each patient at ESRD onset was extracted: body mass index (BMI), serum creatinine, hemoglobin, and albumin, use of an erythropoiesis-stimulating agent, concomitant comorbidities (diabetes mellitus, hypertension, coronary artery disease, congestive heart failure, chronic obstructive pulmonary disease, peripheral vascular disease, cerebrovascular disease, inability to ambulate and inability to transfer), and type of medical insurance prior to ESRD (Medicare, Medicaid, Department of Veteran's Affairs, Employer group, or none), current employment status, and type of initial renal replacement (hemodialysis, peritoneal dialysis or pre-emptive kidney transplant). Updated USRDS data concerning dates of kidney transplant waitlisting, kidney transplantation and death were extracted. Patients with missing data on age or sex were excluded from all analyses.

Statistical analyses

A range of clinical and demographic characteristics were examined for lupus nephritis patients with incident ESRD in three year intervals. Two-sided Cochran-Armitage tests for categorical variables and general linear models for continuous variables were used to detect significant trends over time.

To account for changes in the underlying population composition of the U.S., we calculated standardized incidence rates (SIRs, per million individuals per year), employing age-, sex-, race-, ethnicity- and geography-specific population estimates for July of each year obtained from the U.S. Census, averaged in three year intervals. Poisson regression models were employed to test whether there were significant changes in SIRs and linear trends of SIRs over time were assessed in the models. The 95% confidence intervals for lupus nephritis ESRD SIRs were calculated. We investigated changes in incidence according to geographic region, classifying the U.S. states according to Federal Information Processing Standards (FIPS) codes into four geographic regions (Northeast, Midwest, South and West), as designated by the US Census[24]. (Data from U.S. islands and territories, including Puerto Rico, U.S. Virgin Islands, American Samoa and Guam, were excluded from SIR calculations as we were unable to find intercensal population estimates for each year.)

Incident lupus nephritis ESRD cases were stratified by year of ESRD onset into four three-year periods and we examined trends over time in three outcomes: kidney transplant waitlisting, kidney transplantation, and overall survival. Kaplan Meier survival analyses and log rank tests were employed to test for differences in rates of these three outcomes during the first three years after ESRD onset. The referent group for each pair-wise comparison was composed of individuals with onset in 1995–1997. We also calculated the proportion of individuals who had each outcome in each time period with 95% confidence intervals by the

exact method. (These proportions could not be calculated for the final period as fewer than three years of follow-up were captured in the available data.)

Age-adjusted and multivariable-adjusted Cox proportional hazards models were developed to account for factors contributing to variation in successive time periods in rates of the three outcomes within three years of ESRD onset. Again, onset of incident ESRD within the years 1995–1997 was the comparison group for all subsequent three year periods. Multivariable Cox models were based upon the results of univariable trend and Kaplan Meier survival analyses, additionally adjusting for potential changes over time in the distributions of sociodemographic and clinical factors in incident patients. The final multivariable model included age, sex, race, ethnicity, medical insurance, and geographic region, as well as the presence of diabetes, hypertension, smoking, and the type of initial renal replacement therapy. Adjustment for other clinical factors, including other comorbidities, serum laboratory values, and use of erythropoiesis-stimulating agents, did not influence hazards ratios and thus were not included. Tests for proportionality of hazards over time were performed using interaction terms between the covariates and time, for each of the three outcomes of interest. (The final three year block 2004–2006 was not included in Cox proportional hazards analyses as the proportional hazards assumption did not hold for this incidence stratum with limited follow-up.) Tests for significant trends in the hazard ratios for these outcomes over successive three year blocks were assessed in separate models.

Individuals who received a kidney transplant before initiation of dialysis were excluded from waitlisting and kidney transplantation analyses, as were those who had been placed on the waiting list greater than 90 days prior to enrollment in the USRDS. However, we did include individuals who were placed on the waiting list within up to 90 days prior to the date of first service and imputed their date of waitlisting as day 1. Follow-up was censored at three years (or on December 31, 2006) for all subjects. Sensitivity analyses were performed in which all of the above survival analyses were repeated with the ESRD onset date delayed 90 days to assess for potential instability in ESRD reporting during that initial time. SAS version 9.2 was employed for all analyses. Data were obtained from the USRDS through a data use agreement and data are shown in accordance with their policy. The Partners' Healthcare Institutional Review Board reviewed this study protocol and granted it a waiver as non-human subjects research as no identifiable data were used.

Results

We identified a total of 12,344 incident cases of ESRD due to lupus nephritis in the U.S. from 1995–2006. Changes in the sociodemographic characteristics of individuals with incident ESRD due to lupus nephritis over this time period are shown in Table 1. Mean age at onset was relatively stable at approximately 40 years as was the proportion of women representing slightly more than 80% among all new patients. We did not observe any changes in the distribution of incident cases according to medical insurance type at ESRD onset. The proportion of individuals who were reported to be currently employed at the onset of ESRD due to lupus nephritis, however, rose over these years. The BMI of patients with ESRD due to lupus nephritis increased over time, while serum creatinine concentrations at the initiation of renal replacement therapy decreased. Serum albumin levels decreased slightly among patients with new onset ESRD due to lupus nephritis during these years. Serum hemoglobin concentrations at onset of ESRD, by contrast, rose steadily during this time, with a corresponding increase in use erythropoiesis-stimulating agents prior to initiation of dialysis. The prevalence of both concomitant diabetes mellitus and hypertension among incident ESRD patients increased steadily during these years, while the proportion of patients reported to have coronary artery disease and current smoking

remained unchanged. The proportions of patients who were reported to be unable to ambulate and unable to transfer at ESRD onset were small, but did increase over these years.

Hemodialysis was the initial type of dialysis offered to most patients during these years, but a marked decline in the proportion of patients initially begun on peritoneal dialysis was observed (from 16.4 to 9.9%). Three hundred and seventeen patients (2.6%) underwent elective kidney transplantation, as their initial form of ESRD treatment. This small percentage did grow over the years of the study, as did the small numbers of those who were already on the waiting list for kidney transplant at the time of ESRD onset.

Relative to the population at risk, we found a significant increase in the SIRs of lupus ESRD among younger patients (ages 5–19 and 20–39 years), whereas the SIRs among patients aged ≥40 years did not change (Table 2). The SIRs also increased among African Americans and Native Americans. African Americans had a SIR of 6–7 times that of whites, and the *absolute* incidence rate of ESRD due to lupus nephritis has been higher among African Americans than among whites in every year since 1997 (data not shown). There has also been a significant increase in new cases occurring in the U.S. South.

Overall, 2167 lupus ESRD patients underwent kidney transplantation during the first three years of ESRD, 1298 (60.1%) of which were of kidneys from living donors. A substantial increase in the proportion of kidneys being donated by living rather than deceased donors was observed: in the 1995–1997 incidence cohort, approximately half of all transplants were obtained from living donors, which increased to over 70% of all kidney transplants in patients reaching ESRD in 2004–2006 (p for trend <0.0001). In Kaplan Meier survival analyses, we found that rates of waitlisting for kidney transplant within three years of ESRD onset increased slightly, but rates of kidney transplantation have significantly declined. (Table 3) Overall survival did not improve over the 12 years studied.

Age-adjusted and multivariable-adjusted Cox proportional hazards models for the three outcomes are shown in Table 4. The results of these models were similar to those of unadjusted Kaplan Meier analyses. Compared to ESRD onset in 1995–97, there was an indication of slightly increased waitlisting rates among patients with ESRD onset after 2000. However, there was a significant decrease in the rates of actual kidney transplantation within the first 3 years of ESRD and there was no change in survival rates. The results were similar in age-adjusted and multivariable-adjusted models. In sensitivity analyses in which the ESRD onset date for all survival analyses was delayed by 90 days, results were also unchanged.

Discussion

Several important changes in the sociodemographics, clinical characteristics, and outcomes of U.S. patients with ESRD due to lupus nephritis have occurred between 1995 and 2006. The SIRs of lupus nephritis ESRD among young patients, African Americans and in the U.S. South have increased. Although there have been increases in kidney transplantation preemptively at ESRD onset and waitlisting for kidney transplants since 2000, overall rates of kidney transplantation in the first three years of ESRD onset have declined. Despite advances in the treatment of lupus nephritis and ESRD in recent years, survival for lupus nephritis patients during the first three years of ESRD has not improved.

We found a significant and steady increase in patients' BMIs, likely reflective of increasing obesity in the U.S. population, and not necessarily overall health. We observed an increase in the proportion of concomitant diabetes mellitus and hypertension and some of these increases could be related to obesity. The increase in BMI is also important given recent findings that predictors of graft failure among lupus nephritis transplant recipients included

increasing weight, as well as African American compared with white race, and increasing Charlson comorbidity index[25]. Serum creatinine in more recent years has been slightly lower at the initiation of ESRD therapy, suggesting earlier start of kidney replacement therapy (i.e., with more preserved kidney function), while hemoglobin was higher, reflecting increasing use of injection erythropoiesis-stimulating agents, higher residual kidney function, and perhaps improved management of lupus nephritis. The growing use of erythropoiesis-stimulating agents has been observed for all types of ESRD in the past 15 years[26], but has since declined in response to several trials that raised concerns about the safety of erythropoiesis-stimulating agents in patients with chronic kidney disease, and corresponding changes in drug indications [27]. In our multivariable models, use of erythropoiesis-stimulating agents at ESRD onset was not associated with changes in survival over time.

Our findings of increases in the SIRs of ESRD due to lupus nephritis among individuals under age 40, among African Americans and Native Americans and in the U.S. South, are slightly different from those of Ward, who reported relatively stability through 2004[15]. That analysis, however, included only patients ages 15 years and older and did not investigate changes by U.S. region or adjust for annual population changes. We also found a growing absolute incidence in ESRD due to lupus nephritis among African Americans. Unfortunately, recent nationwide data on the incidence of SLE, overall and in specific racial and ethnic groups, are lacking[28]. Thus it is not known whether the observed changes are due to changes in the incidence of SLE or lupus nephritis. It is possible that observed increases in SIRs for ESRD due to lupus nephritis, particularly among children, reflect a decrease in early mortality due to SLE.

Another strong trend observed was a decline in the initial use of peritoneal dialysis, already used in a minority in the earlier years of our study. Limited geographic access to peritoneal dialysis services and a national transition to chain-affiliated hemodialysis facilities are thought responsible for increasing the proportion of all ESRD patients started on hemodialysis in the U.S. in the past two decades[29]. Pre-transplant use of peritoneal dialysis compared with hemodialysis has been associated with 51% better allograft survival among lupus nephritis ESRD recipients[25]. Further understanding of the initial choice of dialysis modality and associated outcomes in ESRD patients with lupus is becoming increasingly relevant given the relatively lower cost of peritoneal dialysis and the new capitated reimbursement program for dialysis services which starts in 2011[30, 31].

Our analyses detected only slight recent increases in kidney transplant waitlisting for lupus nephritis ESRD patients, but kidney transplant rates declined. This decrease may be due to changes in the demographics of the lupus nephritis ESRD population, or to the increase in living (versus deceased) donor kidney transplants and a relative shortage of organs for transplant. In an analysis of access to kidney transplantation among adult individuals with lupus nephritis ESRD from 1987–1995, younger age, white race, and living in the Midwest were all significant predictors of receiving a living transplant[32]. At that time, however, only 11% of transplanted patients received a living donor kidney, compared a much higher proportion in recent years.

The limitations of this study include the use of data reported by the attending nephrologist and staff on the USRDS Medical Evidence Report at the onset of ESRD for many baseline variables. Consistent completion of this form is expected as it is a U.S. government document establishing the onset of ESRD and qualification for Medicare coverage, but missing data do exist for some of the baseline clinical characteristics, including albumin, hemoglobin and BMI, and some underreporting of comorbidities is also known to occur[33]. Furthermore, the validity of the cause of ESRD as reported on the Medical Evidence Report

has not been studied. By contrast, the outcomes studied -- waitlisting for kidney transplant, transplantation and death --are well documented in the national databases that serve as the basis for the USRDS data, including the United Network of Organ Sharing (UNOS). Data regarding lupus disease activity and damage in other organ systems are not available for these patients, limiting our interpretation about the observed changes in standardized incidence, transplantation and mortality rates in different population subgroups. Lastly, patients who were transiently dialyzed for acute renal failure or who died before being enrolled in the database or who refuse renal replacement therapy may not be included in USRDS data.

As it includes virtually all new onset ESRD cases in the U.S. for a span of 12 years, these analyses of changes over time in incidence, therapies and outcomes in lupus nephritis have important strengths. The slightly growing incidence of ESRD and lack of improvements in important outcomes among patients with ESRD due to lupus nephritis over the past 12 years is disappointing. Despite slightly increased waitlisting for kidney transplant, kidney transplantation rates have fallen and survival has not changed. This may reflect the changing sociodemographics of lupus nephritis with more cases occurring among minority populations, in younger individuals and in the U.S. South, where waitlisting and kidney transplantation rates have been lower in recent years[34]. It may also reflect limited use or effectiveness of current treatments, non-adherence to therapies, barriers to healthcare access, or the increasing demand and shrinking supply of donor organs. Taken together with other recent findings of increased risks of graft failure, recurrent lupus nephritis and death after kidney transplant[25, 35], the changing sociodemographics and the lack of improvement in survival in ESRD due lupus nephritis underscore the ongoing challenge of caring for these patients. There is pressing need to identify the potentially modifiable contributing factors and to intervene to improve both incidence and outcomes of ESRD due to lupus nephritis.

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Table 1

Demographic and Clinical Characteristics at Onset of ESRD due to Lupus Nephritis

Demographic Characteristics		Years of ESRD Onset				
		1995–1997	1998–2000	2001–2003	2004–2006	p trend*
Total N new cases, (% of 12,344 total new cases)		2600 (21.1)	3115 (25.23)	3232 (26.2)	3397 (27.5)	
Age	Mean, in years	40.5 (15.2)	40.6 (15.4)	40.6 (15.6)	40.1 (15.3)	0.25
Sex	Female, (%)	2131 (82.0)	2552 (81.9)	2637 (81.6)	2750 (81.0)	0.29
Medical Insurance**	Medicare, (%)	659 (26.5)	795 (25.8)	802 (24.9)	848 (25.1)	0.16
	Medicaid, (%)	571 (23.0)	715 (23.2)	729 (22.6)	844 (25.0)	0.10
	Private, (%)	1012 (40.7)	1263 (41.0)	1331 (41.3)	1351 (40.0)	0.56
	Uninsured, (%)	243 (9.8)	307 (10.0)	361 (11.2)	339 (10.0)	0.49
Employment status	Employed at onset ESRD, (%)	549 (21.1)	757 (24.3)	793 (24.5)	889 (26.2)	**<0.0001**
Mean Values at ESRD Onset**	BMI, kg/m^2 (SD)	23.5 (±7.2)	25.0 (±7.2)	26.0(±6.9)	26.5 (±7.1)	**< 0.0001**
	Creatinine, mg/dl (SD)	8.6 (±3.5)	8.0 (±3.5)	7.6 (±3.5)	7.1 (±3.4)	**< 0.0001**
	Hemoglobin, g/dl (SD)	8.9 (±1.8)	9.2 (±1.9)	9.5 (±1.8)	9.6 (±1.8)	**< 0.0001**
	Albumin, g/dl (SD)	3.0 (±0.8)	2.9 (±0.8)	2.9 (±0.8)	2.9 (±0.8)	**0.03**
Erythropoiesis-stimulating agent use at ESRD onset **, (%)		688 (28.5)	983 (32.2)	1184 (36.7)	1221 (35.9)	**< 0.0001**
Comorbid Conditions	Diabetes mellitus, (%)	139 (5.4)	199 (6.4)	225 (7.0)	308 (9.1)	**<0.0001**
	Hypertension, (%)	1724 (66.3)	2244 (72.0)	2435 (75.3)	2735 (80.5)	**< 0.0001**
	Coronary Artery Disease, (%)	132 (5.1)	175 (5.6)	201 (6.2)	191 (5.6)	0.28
	Congestive Heart Failure, (%)	439 (16.9)	457 (14.7)	506 (15.7)	476 (14.0)	**0.01**
	Chronic Obstructive Pulmonary Disease, (%)	59 (2.3)	75 (2.4)	71 (2.2)	66 (1.9)	0.29
	Peripheral Vascular Disease, (%)	75 (2.9)	102 (3.3)	115 (3.6)	108 (3.2)	0.48
	Cerebrovascular disease, (%)	122 (4.7)	164 (5.3)	170 (5.3)	169 (5.0)	0.71
	History of malignancy, (%)	32 (1.2)	39 (1.3)	58 (1.8)	51 (1.5)	0.18
	Current smoking, (%)	101 (3.9)	108 (3.5)	128 (4.1)	122 (3.6)	0.82
	Current alcohol abuse, (%)	16 (0.6)	10 (0.3)	18 (0.5)	12 (0.5)	0.76
	Current drug abuse, (%)	14 (0.5)	19 (0.6)	23 (0.7)	27 (0.8)	0.19
	Unable to ambulate, (%)	51 (2.0)	61 (2.0)	68 (2.1)	90 (2.7)	0.05

Demographic Characteristics		Years of ESRD Onset				
		1995–1997	1998–2000	2001–2003	2004–2006	p trend*
	Unable to transfer, (%)	15 (0.6)	23 (0.7)	29 (0.9)	39 (1.2)	0.01
Initial Type of ESRD Treatment**	Hemodialysis, (%)	1974 (75.9)	2482 (79.7)	2625 (81.2)	2850 (83.9)	**<0.001**
	Peritoneal dialysis, (%)	426 (16.4)	370 (11.9)	355 (11.0)	337 (9.9)	**<0.001**
	Pre-emptive transplant,(%)	42 (1.6)	74 (2.4)	84 (2.6)	117 (3.4)	**<0.001**
On waiting list for renal transplant at ESRD onset date***		37 (1.5)	42 (1.4)	50 (1.6)	72 (2.2)	**<0.001**

* Cochran-Armitage 2-sided test for trend for categorical variables and by general linear models for continuous variables.

** Number missing from each category: 174 for medical insurance; 5 for geographic region, 445 for BMI, 2944 for albumin, 199 for creatinine, 1424 for hemoglobin, 267 for erythropoietin use, 608 for initial type of renal replacement therapy.

*** among 12,033 incident ESRD patients not pre-emptively transplanted

Table 2

Standardized Incidence Rates (SIRs) for ESRD due to Lupus Nephritis in the US, 1995–2006

Sociodemographic Group		Total N 12,198*	Year of ESRD Onset				p trend*
			1995–1997	1998–2000	2001–2003	2004–2006	
Age at ESRD Onset	5–19 years	810	0.84 (0.66, 1.06)*	1.05 (0.85, 1.28)	1.26(1.04, 1.51)	1.35 (1.13, 1.62)	**<0.0001**
	20–39 years	5648	5.06 (4.67, 5.48)	5.68 (5.19, 6.44)	5.86 (6.18, 7.21)	6.31 (5.87,6.78)	**0.005**
	40–59 years	4309	4.55 (4.13, 5.00)	5.08 (4.66, 5.53)	5.00 (4.61, 5.43)	4.88 (4.50, 5.30)	0.38
	≥60 years	1431	2.35 (2.00, 2.76)	2.66 (2.29, 3.09)	2.75 (2.38, 3.17)	2.53 (2.19, 2.93)	0.45
Sex	Female	9951	5.54 (5.19, 5.92)	6.40 (6.03,6.80)	6.42 (6.05, 6.81)	6.52 (6.15, 6.91)	**0.007**
	Male	2247	1.28 (1.11, 1.48)	1.48 (1.30,1.68)	1.51 (1.33,1.71)	1.59 (1.41,1.79)	**0.007**
Race**	White	5344	1.96 (1.83, 2.10)	2.15 (2.01, 2.30)	2.12 (1.99, 2.27)	2.11 (1.98, 2.25)	0.22
	African American	5923	12.80 (11.92, 13.74)	15.04 (14.12, 16.03)	15.24 (14.33, 16.21)	15.55 (14.64, 16.51)	**0.008**
	Asian	629	4.51 (3.62, 5.62)	4.74 (3.88, 5.80)	4.39 (3.61, 5.35)	5.52 (4.67, 6.52)	0.09
	Native American	128	2.46 (1.36, 4.46)	3.99 (2.57, 6.20)	4.16 (2.75, 6.30)	5.10 (3.53, 7.35)	**0.002**
Ethnicity***	Hispanic	1918	-	5.55 (4,57, 6.74)	5.21 (4.66, 5.83)	5.47 (4.92, 6.08)	0.84
Geographic Region*	Northeast	2017	2.98 (2.63, 3.39)	3.46 (3.08, 3.88)	3.51 (3.14, 3.94)	3.41 (3.04,3.83)	0.15
	Midwest	2319	2.69 (2.38,3.03)	3.48 (3.13, 3.87)	3.32 (2.99, 3.70)	3.34 (3.00, 3.72)	0.09
	South	5323	4.19 (3.87, 4.53)	4.71 (4.38, 5.07)	4.77 (4.44, 5.12)	5.13 (4.79,5.48)	**0.002**
	West	2539	3.39 (3.03, 3.79)	3.61 (3.25, 4.01)	3.73 (3.38,4.13)	3.56 (3.22,3.94)	0.21

Poisson regression models with 95% confidence intervals for standardized incidence (per million population per year) according to the U.S. Census population estimates for each particular demographic group in July of corresponding years.

* SIRs for U.S. island territories (n=146) could not be calculated as intercensal population estimates not available, thus these individuals were excluded from this analysis.

** p for trend from Poisson regression models

** 174 missing race data.

*** SIRs for Hispanic population from 2000 on as estimates of the U.S. Hispanic population available with 2000 U.S. Census forward.

Table 3

Three-year outcomes among individuals with incident ESRD due to Lupus Nephritis, 1995–2006

	Waitlisting for Kidney Transplant		Kidney Transplantation		Mortality	
Year of ESRD onset	**Kaplan Meier estimates (%, 95%CI)***	**p****	**Kaplan Meier estimates (% 95%CI)***	**p****	**Kaplan Meier estimates (%, 95% CI)***	**p****
1995–1997	35.7% (33.8, 37.6)	Ref.	21.5% (19.9, 23.1)	Ref.	27.6% (25.9, 29.3)	Ref.
1998–2000	36.2% (34.5, 37.9)	0.60	20.5% (19.1, 22.0)	0.70	27.6% (26.0, 29.2)	0.65
2001–2003	37.2% (35.5, 39.0)	0.09	18.0% (16.7, 19.4)	**0.002**	27.1% (25.6, 28.7)	0.79
2004–2006***	-	**0.04**	-	**0.005**	-	0.23
p for 1995–2006****		0.11		**0.0008**		0.35

Waitlisting for kidney transplantation and kidney transplantation were calculated among all incident dialysis patients (n=12,027) and mortality among all incident ESRD patients (including 317 pre-emptively transplanted, n=12,344). All follow-up was censored on December 31, 2006. Total waitlisted = 4,237; total transplants= 2,167; total deaths= 4,901. Values are for % of individuals with ESRD onset in those years having the outcome within 3 years.

* 95% confidence interval by exact method.

** p values for pair-wise log rank tests comparing survival curves to the 1995–1997 curve

*** For patients with incident ESRD in 2004–2006, we provided the p-value from log rank tests compared with the 1995–1997 cohort, but did not provide estimates of 3-year failure rates due to <3 years of follow up.

**** p values for overall log rank tests for the four three-year incidence cohorts, 1995–2006

Table 4

Cox Proportional Hazard Ratios (HRs) for Outcomes within Three Years of ESRD Onset according to Incident Year, 1995–2003

	Kidney Transplantation Waiting list*		Kidney Transplantation*		Mortality*	
Year of ESRD onset	**Age-adjusted HR (95% CI**)**	**MV-adjusted *** HR (95% CI**)**	**Age-adjusted HR (95% CI**)**	**MV-adjusted *** HR (95% CI*)**	**Age-adjusted HR (95% CI**)**	**MV-adjusted *** HR (95% CI**)**
1995–1997	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
1998–2000	1.02 (0.94, 1.12)	1.05 (0.96, 1.15)	0.97 (0.86, 1.10)	1.01 (0.89, 1.15)	1.03 (0.92, 1.14)	0.94 (0.84, 1.07)
2001–2003	1.07 (0.98, 1.17)	**1.09 (1.00, 1.20)**	**0.82 (0.72, 0.93)**	**0.87 (0.76, 0.99)**	1.02 (0.91, 1.13)	0.95 (0.85, 1.07)
p for trend** **over intervals**	0.12	0.05	**0.001**	**0.03**	0.80	0.44

* Waiting list for kidney transplantation and kidney transplantation were calculated among all incident dialysis patients (n=8,830) and mortality among all incident ESRD patients (including pre-emptively transplanted, n=8,947). All follow-up was censored on December 31, 2006. Total waitlisted = 3,405; total transplants= 1,859; total deaths= 4,390.

** 95% Confidence Interval by Wald method

*** Multivariable model: Age, sex, race (white, African American, Asian, Native American, other/missing), ethnicity (Hispanic, non-Hispanic), medical insurance (Medicaid, Medicare, private, none, other/missing) and region (Northeast, Midwest, South, West, Puerto Rico and U.S. Islands, missing), diabetes, hypertension, smoking and initial ESRD therapy (hemodialysis, peritoneal dialysis, other/missing, and pre-emptive transplant for mortality analyses only).

**** p for trend over 3 year intervals by Cox regression models. Parameter estimates indicated positive trends for kidney transplantation waiting list HRs over time intervals, but negative trends for kidney transplantation and mortality HRs.