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# End-Stage Kidney Disease From Scleroderma in the United States, 1996 to 2012

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**Introduction:** Although the management of scleroderma continues to evolve, it is unknown whether the burden of end-stage kidney disease (ESKD) treated with maintenance renal replacement therapy from SD has changed.

**Methods:** We examined United States Renal Data System data (n = 1,677,303) for the years 1996 to 2012 to quantify the incidence and outcomes of ESKD from scleroderma treated with renal replacement therapy (n = 2398). Outcomes assessed through demography-matched scleroderma-positive/scleroderma-negative comparisons included recovery of kidney function, mortality, listing for transplant, renal transplantations, and graft failure.

**Results:** Overall ESKD rates from scleroderma were 0.5 per million per year. Adjusted incidence ratios fell over time, to 0.42 in 2012 (vs. 1996, 95% confidence interval [CI] = 0.32−0.54, $P < 0.001$). Adjusted incidence ratios for ESKD from scleroderma fell over time in both sexes, all age, race, and ethnicity categories except age < 20 years and Asian race, and in all regions of the United States. After initiating renal replacement therapy, patients with scleroderma had a greater likelihood of recovery of kidney function (hazards ratio [HR] = 2.67, 95% CI = 1.90−3.76, $P < 0.001$) and death (HR = 1.44, 95% CI = 1.34−1.54, $P < 0.001$) and a lower likelihood of transplantation (HR = 0.51, 95% CI = 0.44−0.59, $P < 0.001$) than demography-matched patients without scleroderma.

**Discussion:** The incidence of ESKD from scleroderma appears to have declined in the United States since 1996. ESKD from scleroderma is associated with an enhanced likelihood of recovery of kidney function and death, a reduced likelihood of transplantation, and similar outcomes after transplantation.

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Scleroderma, a rare disorder associated with considerable morbidity and mortality, has an estimated annual incidence of 10 to 12 per million in the United States.[1,2] End stage kidney disease (ESKD) is a feared complication that may occur abruptly as a scleroderma renal crisis, or as more indolent, progressive deterioration of kidney function.[3−11]

The therapeutic approach to scleroderma has evolved substantially in recent years, particularly with regard to angiotensin-converting enzyme inhibitor use in scleroderma renal crisis and vasodilator therapy for pulmonary hypertension.[12−14] As management of scleroderma has continued to evolve, it seems natural to question whether reductions in ESKD have occurred, and, if so, whether salutary trends have been generalized across major demographic subgroups. Hence, we set out to describe the clinical epidemiology of ESKD from scleroderma in the United States between 1996 and 2012.

## MATERIALS AND METHODS

### Study Objectives

The principal objective of this study was to evaluate trends in demography-adjusted incidence ratios of ESKD from scleroderma necessitating RRT in the United States between 1996 and 2012. For secondary outcomes after initiation of renal replacement therapy (RRT), we set out to compare likelihoods of renal recovery (where RRT was no longer necessary), listing for renal transplant, transplantation, death, and graft failure in matched patients with and without scleroderma. We further aimed to calculate hazards ratios for these outcomes, specific to the scleroderma population.

### Study Subjects

In this retrospective study, we used data from the United States Renal Data System (USRDS) for patients

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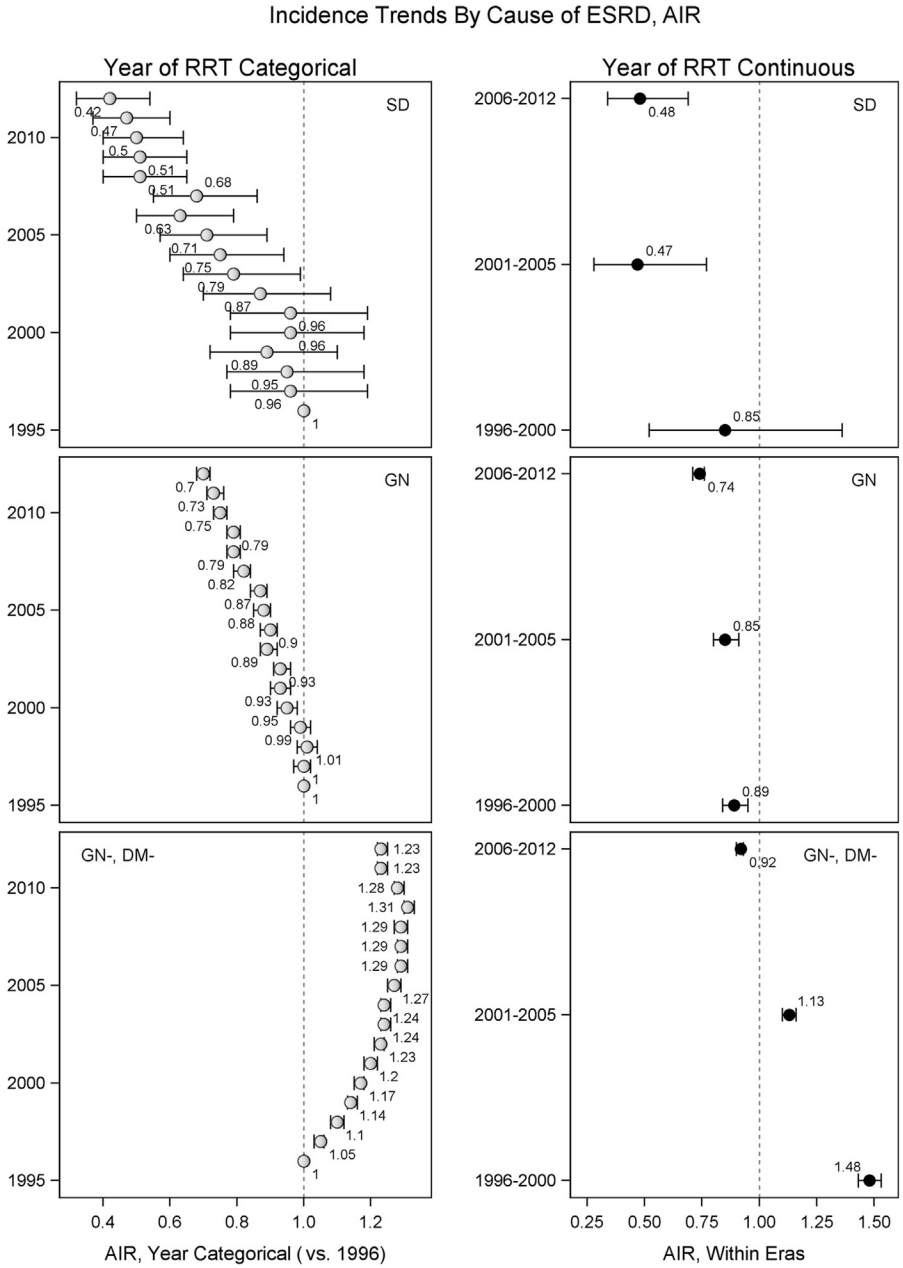


**Figure 1.** Trends in adjusted incidence ratios of end-stage kidney disease (ESKD) from scleroderma and other causes, 1996 to 2012. AIR, adjusted incidence ratio; DM, diabetes mellitus; GN, glomerulonephritis; RRT, renal replacement therapy.

who initiated maintenance RRT in the United States between 1996 and 2012 (N = 1,677,303). Baseline characteristics at initiation of RRT were determined from the Centers for Medicare & Medicaid (CMS) Medical Evidence Report (form CMS-2728). By federal requirement, this form must be submitted for all new patients starting RRT in the US. The Medical Evidence Form changed in 2005. On both forms, 1 of 82 causes is entered as the primary cause of ESKD, with identical options in the 1995 and 2005 forms. For this study, scleroderma cases were those with primary cause of ESKD listed as "Scleroderma" in the Medical Evidence Form. Dates of death, recovery of renal function, first listing for transplant, first renal transplantation, and graft failure were used to define clinical outcomes occurring after first RRT.

## Analysis

Mid-year US census data were used for population denominators for the years examined, with age in 5-year increments. Poisson regression was used to calculate incidence ratios of RRT-requiring ESKD from scleroderma, as well as for graphical illustration of annual trends of ESKD from glomerulonephritis or from causes other than diabetes and glomerulonephritis. The $\chi^2$ test was used for unadjusted comparisons of patients with and without scleroderma, and logistic regression for adjusted comparisons. For comparisons of clinical



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