LESS IS MORE

Predialysis Nephrology Care of Older Patients Approaching End-stage Renal Disease

Wolfgang C. Winkelmayer, MD, MPH, ScD; Jun Liu, MD; Glenn M. Chertow, MD, MPH; Manjula Kurella Tamura, MD, MPH

Background: Little is known about trends in the timing of first nephrology consultation and associated outcomes among older patients initiating dialysis.

Methods: Data from patients aged 67 years or older who initiated dialysis in the United States between January 1, 1996, and December 31, 2006, were stratified by timing of the earliest identifiable nephrology visit. Trends of earlier nephrology consultation were formally examined in light of concurrently changing case mix and juxtaposed with trends in 1-year mortality rates after initiation of dialysis.

Results: Among 323,977 older patients initiating dialysis, the proportion of patients receiving nephrology care less than 3 months before initiation of dialysis decreased from 49.6% (in 1996) to 34.7% (in 2006). Patients initiated dialysis with increasingly preserved kidney function, from a mean estimated glomerular filtration rate of 8 mL/min/1.73 m² in 1996 to 12 mL/min/1.73 m² in 2006. Patients were less anemic in later years, which was partly attributable to increased use of erythropoiesis-stimulating agents, and fewer used peritoneal dialysis as the initial modality. During the same period, crude 1-year mortality rates remained unchanged (annual change in mortality rate, +0.2%; 95% confidence interval, 0% to +0.4%). Adjustment for changes in demographic and comorbidity patterns yielded estimated annual reductions in 1-year mortality rates of 0.9% (95% confidence interval, 0.7% to 1.1%), which were explained only partly by concurrent trends toward earlier nephrology consultation (annual mortality reduction after accounting for timing of nephrology care was attenuated to 0.4% [0.2% to 0.6%]).

Conclusions: Despite significant trends toward earlier use of nephrology consultation among older patients approaching maintenance dialysis, we observed no material improvement in 1-year survival rates after dialysis initiation during the same time period.

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CURRENTLY, MORE THAN 570,000 US adults have end-stage renal disease (ESRD) and undergo maintenance dialysis or live with a functioning kidney transplant. More than 110,000 individuals initiate dialysis each year, almost half of whom are aged 65 years or older. Given the high risk of adverse outcomes from chronic kidney disease (CKD), timely referral to a nephrologist has long been recommended. The potential benefits of timely nephrology referral include identification of reversible causes of CKD, provision of treatments that may slow the progression of CKD, management of the metabolic complications of advanced CKD, coordination of education regarding ESRD treatment options, and optimal preparation for the chosen dialysis modality or kidney transplantation.

Delayed nephrology care has been associated with several unfavorable outcomes, including reduced access to peritoneal dialysis (PD) and kidney transplantation. Among patients who start hemodialysis, delayed nephrology care is associated with higher rates of dialysis initiation through a central venous catheter rather than an arteriovenous fistula or graft. Patients with CKD who consult a nephrologist relatively late or infrequently also experience a considerable excess mortality rate after starting maintenance dialysis, especially during the first few months. Older adults are particularly at risk for experiencing delayed nephrology care.

See Editor’s Note at end of article

For editorial comment see page 1317

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with a serum creatinine level of 1.5 mg/dL (to convert to micromoles per liter, multiply by 88.4) and men with a serum creatinine of 2.0 mg/dL or higher. Implementation of these guidelines was facilitated by the development of equations to estimate the glomerular filtration rate (GFR) from the serum creatinine concentration and by the development of a GFR-based CKD staging system. Subsequently, automatic reporting of estimated GFR (eGFR) by the Modification of Diet in Renal Disease formula has become routine in many health care systems and has increased recognition of CKD and referral of patients with CKD to nephrologists. However, referral practices among patients who are approaching ESRD have not been studied carefully. Furthermore, previous studies examining nephrology referral patterns before ESRD have relied primarily on patient self-report or on the judgment of dialysis facility personnel, which may not accurately reflect actual referral practices.

We designed the present study to test whether access to and timing of nephrology care among Medicare-insured older adults approaching ESRD have changed during the past decade and whether these putative changes have translated into improved patient outcomes. We hypothesized that, after controlling for changes in demographic trends and comorbid conditions, putative trends toward earlier referral for nephrology services would be associated with lower mortality rates.

DATA SOURCES AND STUDY POPULATION

We used data from the United States Renal Data System spanning the years 1996 to 2007 for this study. Data for all patients who were aged 67 years or older at the start of dialysis were merged with data from Medicare claims (Part A and B) covering the previous 2 years. We ascertained the presence of fee-for-service Medicare coverage and at least minimal access to the health care system by requiring all patients to have had several recent medical encounters. Similar to previous work, we identified, the patient was considered to have had a nephrologist visit greater than 12 months, greater than 9 to 12 months, greater than 6 to 9 months, greater than 3 to 6 months, or 3 months or less or no nephrology consultation at all before starting dialysis. We hypothesized that, after controlling for changes in demographic trends and comorbid conditions, putative trends toward earlier referral for nephrology services would be associated with lower mortality rates.

OUTCOMES

From Medicare claims antedating the start of dialysis, we ascertained all consultations (ie, inpatient and outpatient) by a nephrologist billed to Medicare. We then defined the earliest of these claims relative to the start of dialysis. The main exposure for this study was whether a patient had consulted with a nephrologist at least 90 days before initiation of maintenance dialysis, in which case the patient was categorized as having experienced earlier nephrologist consultation. If the earliest recorded nephrology consultation occurred 90 days or less before dialysis initiation or if no such consultation could be identified, the patient was considered to have had later nephrologist consultation. Similar to previous work, we chose 90 days as the cutoff clinically and administratively because it is generally considered to be the minimum amount of time needed for adequate examination, information, and preparation for dialysis, as well as for preparation and maturation of vascular or peritoneal access. The main outcome was the 1-year rate of mortality from any cause after initiation of dialysis, which is recorded in the United States Renal Data System database.

VARIABLES

For each patient, we defined several potential determinants of access to nephrology care preceding the initiation of dialysis, including age, sex, race (ie, White, African American, Asian American, or Native American), and Medicaid coverage as a crude indicator of socioeconomic status. We categorized patients by US region (ie, Northeast, Midwest, West, South, or other; for details regarding geographic category assignment and timing of first nephrologist consultation, see the eAppendix and the eTable; http://www.archinternmed.com). We also ascertained a large number of comorbid conditions from 2 prior years of Medicare claims, using validated algorithms where available. Those conditions were diabetes mellitus, hypertension, heart failure, coronary artery disease, cerebrovascular disease, peripheral artery disease, chronic obstructive pulmonary disease, and cancer (excluding nonmelanoma skin cancer). These comorbid conditions were considered to be present if any 2 outpatient claims or 1 inpatient claim included a corresponding diagnosis code or if the specific condition was recorded on the patient’s medical evidence report (form CMS-2728). Certain procedure codes also qualified for the presence of some conditions (eg, a patient was considered to have had coronary artery disease if he or she had undergone coronary artery bypass surgery or percutaneous coronary intervention before the respective index date). From the medical evidence report, we also obtained information regarding each patient’s serum albumin, creatinine, and hemoglobin concentrations. We also recorded whether patients had received an erythropoiesis-stimulating agent before dialysis (as ascertained from the medical evidence report).

STATISTICAL ANALYSIS

We described patterns of nephrologist care by year, showing annual proportions of patients who had had their first recorded nephrologist visit greater than 12 months, greater than 9 to 12 months, greater than 6 to 9 months, greater than 3 to 6 months, or 3 months or less or no nephrology consultation at all before starting dialysis. Then, patient characteristics were tabulated or graphically presented by earlier vs later first nephrology consultation for each year. Categorical variables were presented as numbers and percentages and continuous variables as means and corresponding standard deviations.

To assess crude and adjusted temporal trends of the proportion of incident patients who underwent later nephrology consultations, we conducted unadjusted and multivariable-adjusted modified Poisson regression models, which permit direct estimation of risk ratios even for frequent (ie, nonrare) outcomes. We studied the univariate association of calendar year with the outcome of study and then built case mix–adjusted models in which we incorporated demographics, Medicaid coverage, and geographic region, as well as 8 comorbid conditions. We did so in an iterative fashion to examine the influence of changes in the demographics and case mix of annual cohorts of patients initiating dialysis over time.

We also studied the association of calendar year on 1-year all-cause mortality rates after the start of maintenance dialysis using crude and adjusted Cox proportional hazard models. Data from patients were censored at the end of the database but not for receipt of a kidney transplant. Having hypothesized the presence of secular trends toward improved access to nephrology care before the need for dialysis, we were interested specifically in examining the association of calendar year with mortality rate and the change of the effect estimate of calendar year after additional control for the variable regarding timing for first nephrology consultation. All estimates of association were presented with their corresponding 95% confidence intervals (CIs).
The study was approved by the institutional review boards at Brigham and Women’s Hospital and Stanford University School of Medicine, and active data use agreements with the National Institute of Diabetes and Digestive and Kidney Diseases were in place (no. 2007-2019). We used SAS for Windows, version 9.2, statistical software (SAS Institute, Inc, Cary, North Carolina) for all analyses.

## RESULTS

### STUDY PATIENTS

We identified 323,977 patients who were aged 67 years or older when they initiated dialysis between January 1, 1996, and December 31, 2006, and who had fee-for-service Medicare coverage before initiation of dialysis and Medicare claims in the first and second year before their start date of maintenance dialysis. The annual incident count increased by 36.8% from 23,777 in 1996 to 32,529 in 2006 (Table 1). During that time, the mean age at initiation increased by 1.5 years, from slightly more than 75 years to almost 77 years on average, and the proportion of women decreased from 49.9% to 47.5%. The prevalence of most comorbidities increased; most important, diabetes increased from 58.5% to 70.1%. Fewer patients established PD as their initial treatment modality, from 8.5% to 4.2%. The proportion of dually eligible patients (ie, Medicare and Medicaid) increased slightly from 18.2% to 20.0%.

### TEMPORAL TRENDS IN PATTERNS OF NEPHROLOGY CARE

In 1996, 49.6% of older patients initiated maintenance dialysis without having received care by a nephrologist for 3 months or longer. Over time, however, this proportion decreased to only 34.7% in 2006 (Figure 1). Conversely, the proportion of patients who had seen a nephrologist for at least 1 year before renal replacement therapy increased from 30.0% (1996) to 48.5% (2006). Using regression analysis, the proportion of patients with delayed nephrology care decreased by approximately 4% (95% CI, 3%-4%) per year, which remained essentially unchanged after adjustment for sociodemographic factors and comorbid conditions (Table 2). Across all years, older age and female sex also were associated with delayed nephrology care but older African Americans and those of Asian American race were slightly less likely to experience later nephrology care compared with whites. Some geographic differences also were observed in predialysis nephrology care patterns, with patients in the Midwest being most likely to receive delayed nephrology care.
the 1996 incident cohort was 35.4%. Unadjusted Cox product limit estimator for the 1-year mortality rate among patients translated into better survival with dialysis. The timing of predialysis nephrology care among older patients was surprising and requires differentiated consideration.

Next, we studied whether the observed differences in the timing of predialysis nephrology care among older patients translated into better survival with dialysis. The product limit estimator for the 1-year mortality rate among the 1996 incident cohort was 35.4%. Unadjusted Cox regression analysis suggested that the 1-year mortality rate remained unchanged during the 11 years of study (annual change in mortality rate, +0.2%; 95% CI, 0 to +0.4; P=.07), but adjustment for sociodemographic characteristics showed a slight improvement in mortality of 0.6% (0.4%-0.8%) per annum. Additional adjustment for comorbidities yielded an estimated 0.9% (95% CI, 0.7% to 1.1%) reduction in the 1-year mortality rate per calendar year. (Figure 3 shows the results from analyses that categorized incidence year rather than using it as a continuous variable.) Additional introduction of the later nephrology referral variable, which was associated with mortality (hazard ratio, 1.36; 95% CI, 1.35 to 1.38), yielded a highly attenuated association between year and mortality (annual change in mortality, −0.4% to −0.2% to −0.6%). These findings were essentially unchanged in time-stratified models examining the first 90 days after start of dialysis or days 91 to 365 after initiation (not shown).

**TRENDS IN 1-YEAR MORTALITY**

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In this study of older US patients approaching ESRD during a period longer than a decade, we found that the proportion of patients who had consulted with a nephrologist at least 1 year before initiation of dialysis increased by 62.0%, from 30.0% in 1996 to 48.5% in 2006. Correspondingly, the proportion of patients who first consulted with a nephrologist less than 3 months before initiation of dialysis decreased by 30.1%, from 49.6% in 1996 to 34.7% in 2006. Given the existing literature reporting associations among later nephrology care and poor outcomes for these patients, one would have expected that these significant shifts in practice during the past decade would have resulted in meaningful improvements in patient outcomes. However, we found only small improvements in 1-year mortality rates. This observation is surprising and requires differentiated consideration.

The contrast between increasing adoption of practice guidelines that recommend early nephrology referral and the apparent lack of a meaningful improvement in survival raises the question of whether earlier is necessarily better. Generally, it has been assumed that earlier nephrology referral improves dialysis outcomes and may reduce the cost of care by reducing CKD-related complications and improving preparation for ESRD and access to transplantation. However, recent studies have raised questions regarding the efficacy of several costly interventions provided to patients with advanced CKD, including more aggressive erythropoiesis-stimulating agent use, aggressive blood pressure lowering, revascularization of atherosclerotic renovascular disease, secondary cardiovascular prevention using statins and initiation of dialysis with more preserved kidney function. Furthermore, guidelines for management of CKD-associated metabolic bone disease, although based on compelling observational studies, have not been rigorously tested. Thus, in hindsight, it may be that many of the interventions touted as benefits of early referral were less efficacious than previously thought. It is even possible that nephrologists, unknowingly, contributed to worse outcomes in patients new to dialysis.
We found that mean hemoglobin concentrations at initiation of dialysis increased quite a bit during the decade of the study (Figure 2), which may be attributable partly to initiation with increasingly preserved kidney function. However, erythropoiesis-stimulating agents were also increasingly used, with use and corresponding hemoglobin concentrations increasing more among patients experiencing earlier nephrology care. In light of the recent evidence regarding the potential harms from increasing use of these drugs, it is possible that increasing use of these agents may have offset potential trends toward lower mortality rates during the past decade. It is also remarkable that the use of PD as the initial dialysis modality decreased during the study period from 8.3% to 4.2% of incident patients. The opposite could have been expected because earlier studies had shown an association between earlier nephrology care and more PD use in new dialysis patients. Our study is not designed to dissect the reasons for this paradoxical observation.

Several factors should be considered in the interpretation of our findings. It is unlikely that the modest improvement in survival after dialysis initiation we observed over time is directly attributable to changes in nephrology referral. The incidence of ESRD has increased during the past decades, partly driven by demographic trends toward an older society with a higher prevalence of risk factors for ESRD, such as diabetes mellitus and obesity, and improved survival of cardiovascular diseases. Also, it appears that increasingly sicker patients, who might not have been considered acceptable candidates in earlier years, are initiating dialysis. Instead, the modest improvement we observed is more likely to represent lead-time bias from the co-occurring trend of dialysis initiation earlier in CKD (ie, with a higher eGFR) over time. Most likely, our findings can be attributed to trends toward initiating dialysis with more preserved kidney function, at least as determined by conventional metrics (ie, eGFR). It is remarkable that initiation of dialysis occurred at a mean eGFR of 8 mL/min/1.73 m² in 1996 but of 12 mL/min/1.73 m² in 2006. Using progression rates from other cohorts (ranging from 2 to 4 mL/min yearly), these trends seem to indicate that patients may have started dialysis at least 1 year earlier, on average, in 2006 compared with 1996. When translating the relative 1-year mortality reduction of 6.6% between 1996 and 2006 (Figure 3) into an estimated absolute survival gain, median survival for similar patients may have improved less than 2 months. It is clear that this marginal survival benefit may have come at the cost of several additional months or years of maintenance dialysis treatment and its attendant burdens. If patients with advanced CKD more strongly prefer to spend time without dialysis, following a watchful waiting strategy, rather than to initiate dialysis relatively early, the net effects from this marginal survival benefit may have come at the cost of several additional months or years of maintenance dialysis treatment and its attendant burdens. If patients with advanced CKD more strongly prefer to spend time without dialysis, following a watchful waiting strategy, rather than to initiate dialysis relatively early, the net effects from such a strategy actually may be negative.

The strengths of this study include its use of a large and comprehensive national registry of patients with ESRD with more than a decade of data. Our population was restricted to older individuals, who are particularly at risk for dialysis patients. Our study is not designed to dissect the reasons for this paradoxical observation.

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### Table 2. Associations With Later Nephrology Consultation (≥90 Days Before Initiation of Long-term Dialysis)†

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
<th>Adjusted for Demographics</th>
<th>Additionally Adjusted for Region and Medicaid Status</th>
<th>Fully Adjusted</th>
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<tr>
<td>Calendar year, continuous</td>
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<td>0.96 (0.96-0.97)</td>
<td>0.96 (0.96-0.96)</td>
<td>0.97 (0.97-0.97)</td>
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<td>Age per year</td>
<td>1.01 (1.01-1.01)</td>
<td>1.01 (1.01-1.01)</td>
<td>1.01 (1.01-1.01)</td>
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<td>Female vs male sex</td>
<td>1.04 (1.03-1.05)</td>
<td>1.04 (1.03-1.06)</td>
<td>1.04 (1.03-1.05)</td>
<td>1.06 (1.05-1.07)</td>
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<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>African American</td>
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<td>0.92 (0.90-0.93)</td>
<td>0.93 (0.92-0.94)</td>
<td>0.94 (0.93-0.96)</td>
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<tr>
<td>Asian American</td>
<td>0.91 (0.88-0.95)</td>
<td>0.92 (0.89-0.96)</td>
<td>0.92 (0.89-0.95)</td>
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<td>Native American</td>
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<td>1.19 (1.13-1.26)</td>
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<td>1.20 (1.13-1.27)</td>
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<td>Medicaid beneficiary, yes vs no</td>
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<td>NA</td>
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<td>1 [Reference]</td>
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<td>1.03 (1.01-1.05)</td>
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<td>Diabetes mellitus</td>
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<td>1.06 (1.04-1.07)</td>
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<td>NA</td>
<td>1.94 (1.02-1.05)</td>
</tr>
</tbody>
</table>

Abbreviation: NA, not applicable.

* Categorical comparison of data from 2006 with those from 1996 in fully adjusted models showed a 28% (95% confidence interval, 26% to 30%) reduction in the risk of late nephrologist consultation.
for later referral to nephrologists and also are at higher risk for adverse outcomes from dialysis. Studying older adults with advanced CKD provides important information for health care planning because in older patients with advanced CKD (ie, those with stage 4 and 5 disease who are not yet receiving dialysis), the risk of death exceeds the risk of progression toward ESRD.35 Of importance, we were able to reliably identify nephrology consultations from billing claims to Medicare, which preceded the onset of ESRD by as long as 2 years, as opposed to relying on nephrologists’ or dialysis facility staff’s self-report on the medical evidence report, which has not been validated and may be subject to recall bias. We ascertained comorbidities from billing claims preceding ESRD rather than relying on the medical evidence report.36 Although increases were observed in the prevalences of several comorbidities over time, it is also known that comorbid conditions are being coded more aggressively in recent years in response to financial incentives inherent in reimbursement rules.37 Thus, it is possible that the true trends are overestimated. For our analyses, this means

Figure 2. Trends in laboratory measurements at initiation of renal replacement therapy by timing of first nephrologist consultation (January 1, 1996–December 31, 2006). A, serum creatinine concentration (to convert to micromoles per liter, multiply by 88.4). B, estimated glomerular filtration rate (eGFR). C, hemoglobin concentration (to convert to grams per liter, multiply by 10). D, reported receipt of an erythropoiesis-stimulating agent (ESA) before initiation of renal replacement therapy. E, serum albumin concentration (to convert to grams per liter, multiply by 10).

Figure 3. Trends in 1-year survival rates of older patients initiating treatment for end-stage renal disease in the United States (January 1, 1996–December 31, 2006). Hazard ratios without confidence limits are presented. Adjusted for demographics indicates model adjusted for age, sex, and race; fully adjusted, model additionally adjusted for Medicaid beneficiary, region, and 8 comorbid conditions; plus later nephrologist visit, inclusion of indicator variable regarding whether a patient had consulted with a nephrologist at least 90 days before the start of dialysis.
that adjustment of temporal trends for comorbidities may yield estimates that are biased away from the null. Therefore, the already small improvements in mortality rate over time actually may be overestimated.

This study needs to be considered in light of its limitations. We lacked information regarding the severity of CKD and of comorbid diseases at the time of nephrology referral, as well as regarding relevant laboratory variables and vital signs that might have enabled us to further explore other important trends in these patients’ characteristics. We did not assess other outcomes that may have been affected by the timing of nephrology referral, including hospitalization rates, nutritional status, patient-reported functional status or health-related quality of life, patient satisfaction, or the cost of care. Finally, it appears that in the most recent years, a nascent trend may have begun toward better mortality rates in older patients starting dialysis (Figure 3). Whether this impression is caused by a sustained trend or random variation will need to be carefully tracked during the coming years.

In conclusion, in a large cohort of older adults initiating dialysis in the United States, we found an increasingly higher proportion of patients consulting a nephrologist earlier in their disease (ie, for a longer time before dialysis initiation), meeting the often-recommended goal of “timely referral.” Independent of the timing of predialysis nephrology care, a strong trend was observed toward earlier initiation of dialysis based on eGFR. Despite this significant shift in practice, we did not observe meaningful improvements in survival. New approaches to improving care will need to be identified and tested to justify the additional expense, effort, and potential burden of nephrologist-driven health care interventions, including dialysis.

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Author Contributions: Drs Winkelmaier, Chertow, and Tamura had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Winkelmaier and Chertow. Acquisition of data: Winkelmaier. Analysis and interpretation of data: Winkelmaier, Chertow, and Tamura. Drafting of the manuscript: Winkelmaier. Critical revision of the manuscript for important intellectual content: Winkelmaier, Chertow, and Tamura. Statistical analysis: Winkelmaier and Chertow. Administrative, technical, and material support: Chertow and Tamura. Study supervision: Winkelmaier.

Financial Disclosure: Dr Winkelmaier reports having served as a scientific adviser or consultant to Affymix Inc, Amgen Inc, Astellas Pharma USA Inc, Vifor-Fresenius Medical Care Renal Pharma Ltd, GlaxoSmithKline plc, and Sanofi. He has received unrestricted research support from Fibrogen Inc. Dr Chertow has served as a consultant to Amgen Inc.

Disclaimer: Data reported herein were supplied by the United States Renal Data System (USRDS). Interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as official policy or interpretation of the US government.

Online-Only Material: The eAppendix and eTable are available at http://www.archinternmed.com.

REFERENCES

Earlier Nephrology Consultation Is Not Associated With Improved Survival

Timely nephrology referral potentially could have many benefits in allowing earlier identification and treatment of reversible causes of chronic kidney disease. Winkelmayer and colleagues analyze data from January 1, 1996, through December 31, 2006, and report that although early nephrology consultation is increasing, no associated decrease in mortality has been observed. However, as part of a national trend toward earlier diagnosis (and treatment) of disease in the past decade, Americans have been starting dialysis with increasingly preserved kidney function and are being prescribed higher dosages of erythropoietin. Because this article identifies an area of increased nephrology care and increasingly early dialysis with no material mortality benefit, it has been given our “Less Is More” designation.

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