# Outcomes Research in Dialysis

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**Worldwide, the number of patients with end stage renal disease (ESRD) and the number of ESRD patients receiving renal replacement therapy is growing. In the United States the number of patients enrolled in the Medicare-funded ESRD program has grown substantially, from approximately 10,000 beneficiaries in 1973 to 340,261 as of December 31, 1999. United States has the highest incidence ESRD of 317 per million population. Despite the magnitude of resources committed to the treatment of ESRD and the substantial improvements in the quality of dialysis therapy, these patients continue to experience significant mortality and morbidity, and reduced quality of life. Moreover, 50% of dialysis patients have 3 or more comorbid conditions, the mean number of hospital days per year is approximately 14 per patient, and self reported quality of life is far lower in dialysis patients than in general population. The most desirable interventions are those that specifically target measurable global outcomes such as mortality, morbidity, and health care costs. Nevertheless, patient outcomes that have shown links with these global outcomes may also be appropriate targets for intervention. This article will briefly review the available literature to discuss the role of important clinical indicators on dialysis outcomes and their impact on continuing care of ESRD population.**

WORLDWIDE, THE NUMBER of patients with end-stage renal disease (ESRD) and the number of ESRD patients receiving renal replacement therapy (RRT) is growing. In the United States, the number of patients enrolled in the Medicare-funded ESRD program has grown substantially, from approximately 10,000 beneficiaries in 1973 to 340,261 as of December 31, 1999. The United States has the highest incidence ESRD: 317 per million population.[1] The total cost of the ESRD program in the United States was $17.9 billion in 1999; up from $16.7 billion in 1998—a 7.2% increase.[1] The projected number of ESRD patients by the year 2010 has been estimated to be 661,330, and the total Medicare cost has been estimated to be in excess of $28 billion.[2]

Despite the magnitude of resources committed to the treatment of ESRD and the substantial improvements in the quality of dialysis therapy, these patients continue to experience significant mortality and morbidity, and reduced quality of life. In 1999 alone, 66,964 ESRD patients died. Survival probabilities for dialysis patients at 1, 2, 5, and 10 years were 79.2%, 64.9%, 34.4%, and 12.9%, respectively.[1] Moreover, 50% of dialysis patients have 3 or more comorbid conditions, their mean number of hospital days per year is approximately 14 per patient, and self-reported quality of life is far lower in dialysis patients than in the general population.[2-4]

In 1989, the Dallas symposium on morbidity and mortality of dialysis patients identified major differences in patient survival among the United States, Europe, Canada, Australia, and Japan. The United States had the highest rates of newly treated patients with ESRD, but also the highest gross mortality rate (22% to 24%).[5] Although some of the differences in survival and morbidity might be ascribed to differences in the populations at risk with respect to age, underlying disease, comorbidity, and race, these considerations, alone or in combination, could not explain the higher rates of undesired outcomes in the United States. Because of these findings, efforts to improve the quality of dialysis care in the United States were undertaken by the Health Care Financing Administration (now the Centers for Medicare and Medicaid Services),[6] the Association for the Advancement of Medical Instrumentation,[7] the Renal Physicians Association, and The National Institutes of Health in the 7 years immediately after the Dallas conference. These efforts culminated in the creation of the Dialysis Outcomes Quality Initiatives (DOQI) project, organized by the National Kidney Foundation (NKF).[8] The DOQI project was launched in 1995 and the first set of clinical practice guidelines developed as a result of the initiative were released in 1997.[8] These DOQI guidelines were focused mainly on dialysis adequacy, vascular access, and anemia. In late 1999, DOQI became K/DOQI, K standing for kidney and D for dialysis now representing D for disease. Recently, the recommenda-

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tions addressing the original 4 areas of concern were updated and released as K/DOQI guidelines in a supplement to the January 2001 issue of the *American Journal of Kidney Disease*.[9] In addition to these 4 categories, nutritional guidelines for patients with ESRD were released in 2000, also under the revised acronym K/DOQI.[10] The NKF/K-DOQI guidelines helped to develop a common language for communication among providers, patients and their families, investigators, and policy makers.

## QUALITY OUTCOMES IN THE ESRD POPULATION

Before the advent of hemodialysis treatments in the 1960s, patients with ESRD died of uremia. Once hemodialysis was recognized universally as an effective, but prohibitively expensive, means of extending the life of patients with kidney failure and securing rehabilitation, legislation establishing federal government financing of dialysis was passed in 1973. This action, and subsequent establishment of coverage for non-Medicare patients by state Medicaid programs, eventually extended dialysis treatment to nearly all Americans with ESRD.[11] Unfortunately, simply ensuring financial access to dialysis care has not been sufficient to ensure optimal patient outcomes. At present, one sixth of hemodialysis patients receive an inadequate dialysis dose, one-fourth use catheters for vascular access, and more than one-half are malnourished.[12] Despite Medicare ESRD expenditures of $11 billion annually, the mortality rate among American hemodialysis patients remains the highest in the industrialized world (22%/year).[2] The Institute of Medicine defines the quality of medical care as, “the degree to which health services for individuals and populations increase the likelihood of desirable health outcomes and are consistent with current professional knowledge.”[13] Quality in the dialysis setting is caring for dialysis patients (“the service”) in such a way that their health improves (“the outcome”). Value equals quality divided by cost. Therefore, quality and value should not be used synonymously. Quality can be measured and tracked by selecting indicators of particular health problem outcomes, called *outcome measures*. An outcome measure of quality must be valid, reproducible, actionable, and comparable over geographic, demographic, and temporal boundaries. To be useful for quality improvement purposes, a quality outcome measure must be based on evidence or expert consensus, readily quantifiable, sensitive to changes in treatment, and actionable by those held responsible for the outcome. Quality of life may be the most important patient outcome, encompassing survival rates and hospitalization rates. The treatment of dialysis patients is multifaceted and delivered by a multidisciplinary team. It is useful to group treatment processes into categories that are clinically coherent, although individual processes may span 2 or more categories.[14]

In the increasingly pragmatic and utilitarian climate in which nephrology is practiced, the most desirable interventions are those that specifically target measurable global outcomes such as mortality, morbidity, and health care costs. Nevertheless, patient outcomes that have shown links with these global outcomes also may be appropriate targets for intervention. For example, each 0.10 decrease in Kt/V (dialysis dose) is estimated to increase the relative risk for death by 7%, the likelihood of hospitalization by 11%, and Medicare inpatient expenditures by $1,880 per year.[15,16] Serum albumin, type of vascular access, and kidney transplantation are other examples of intermediate outcomes that have been linked clearly to global outcomes.[17-19] Finally, the improvement of patient quality of life also is viewed as a desirable target for intervention, although the extent to which this may be pursued and the cost appropriate to such pursuit is defined less easily.

This article briefly reviews the available literature to discuss the role of important clinical indicators on dialysis outcomes and their impact on continuing care of the ESRD population.

## ANEMIA MANAGEMENT

Anemia remains a common problem in the ESRD population. Currently, anemia is unrecognized or undertreated in a large number of patients in the United States. Obrador et al[20] found that only 28.1% of patients initiating dialysis in the United States have been treated with recombinant human erythropoietin (rHuEPO). Improved quality of life and sense of well-being are among the most important goals of drug therapy. For rHuEPO treatment, impressive gains have been shown.[21,22] Revicki et al[22] found that treatment of anemia resulted in improved energy, physical function, home management, social activity, and cognitive function. In

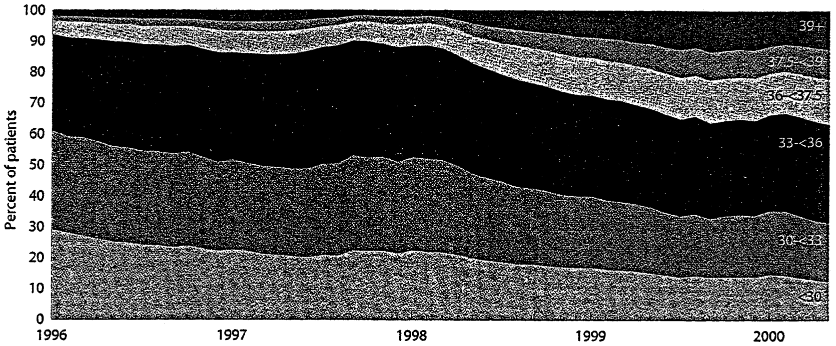

**Fig 1. Patient distribution, by mean monthly hematocrit. The percent of patients with hematocrits in the NKF-DOQI target range of 33-36% became stable between July 1999 and May 2000. (Data from the USRDS database).**

the hemodialysis population, rHuEPO treatment improves energy levels, global function, mood and stress,[23] sexual function, socializing, skin color, and mean Karnofsky score.[24] Patients with ESRD have an alarmingly high cardiovascular mortality rate.[25] At the time of starting RRT, 74% of ESRD patients already have left ventricular hypertrophy (LVH).[26] There is a reciprocal relationship between LVH and creatinine clearance.[27] Serum hemoglobin level predicts prevalent LVH and worsening of LVH over the course of a year among patients with chronic renal failure.[28] These studies suggest that anemia treatment in renal failure patients might reduce the very high prevalence of LVH in the ESRD population, and by extension also might reduce the great burden of cardiovascular morbidity and mortality of dialysis patients.

Recent improvements in patient hematocrit levels parallel the improvement in death rates in hemodialysis patients. Hematocrit levels have increased steadily in the past decade, with 8% of patients having hematocrit levels greater than 33% in 1990, and 67% of patients at this level in 1998. During this period the first-year death rate dropped from 274 per 1,000 patient treatment years to 246, a decrease of 10%. Second-year deaths also decreased 10%, from 287 per 1,000 patient treatment years in the 1990 cohort to 258 in the 1997 cohort.[1] The hematocrit levels of prevalent patients have increased since 1996, and have reached a plateau near the 33% to 36% level recommended by NKF/DOQI (Fig 1). As of May 2000, the percent of patients with a hematocrit level less than 30% had decreased to 12% from 29% in January 1996 (Fig 1). The number of patients with a hematocrit level of less than 33% decreased from 61% to 31% in May of 2000, and approximately 12% of patients had a hematocrit level of 39% or higher in May of 2000.[1] Unfortunately, there has been a widening gap in hematocrit levels between the hemodialysis and peritoneal dialysis patients treated with erythropoietin (EPO), as shown in Figure 2. Peritoneal dialysis patients treated with EPO have lower hematocrit levels than their counterparts on hemodialysis, and the gap has increased from 0.4% in 1994 to 1.4% in 1999. In 1999, peritoneal dialysis patients had an average hematocrit level during EPO treatment of 32.8%, as compared with 34.2% in hemodialysis patients. Across all racial groups, EPO-treated patients on peritoneal dialysis are less likely to meet the NKF/DOQI target hematocrit level (>33%) than those on hemodialysis. The

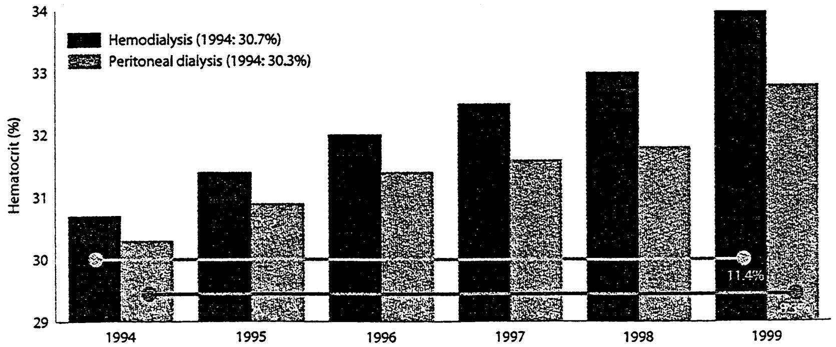

**Fig 2. Mean hematocrit, by modality. (Data from the USRDS database). Peritoneal Patients treated with EPO have lower hematocrits than their counterparts on hemodialysis. The gap has increased from 0.4% in 1994 to 1.4% in 1999.**

percent of hemodialysis patients meeting the NKF/DOQI target hematocrit ranges from 61.3% to 81.3%—a 32% difference by geographic region. Among peritoneal dialysis patients, only 38.4% to 67.4% reach the target hematocrit level, a difference of 76% between the lowest and highest quintiles.[1]The effect of the promulgation of evidenced-based and expert panel consensus guidelines on measurable patient outcomes is shown readily by the response to the DOQI guidelines for hematocrit level. The 3-month rolling average hematocrit value for the overall ESRD population increased consistently after the release of the DOQI guidelines and discontinuation of the hematocrit measurement audit (HMA) prepayment review.

The percentage of patients with 3-month rolling average hematocrit levels of 36% or greater increased from 4.1% in January 1996 to 10.2% in June 1998, and to 29.9% by April 2000. During the last quarter of 1999 and the first quarter of 2000, the percentage of patients with 3-month rolling average hematocrit levels less than 33% and 36% or greater stabilized, with approximately 30% of patients falling within each of these groups. The percentage of patients with a rolling 3-month average hematocrit level of 33% to less than 36%, and with one or more monthly hematocrit values of 36% or greater or 39% or greater, increased over time from 33.8% in January 1996 to 62.6% in April 2000 and from 3.2% in January 1996 to 8.9% in April 2000, respectively.[1] The long-term improvement in the intermediate outcome of serum hematocrit level on the targeted outcome of long-term survival is still pending. Hypertension is the major serious side effect of erythropoietin therapy. Blood pressure increases in 30% of rHuEPO-treated patients.[29-32] An early animal study[33] found that rHuEPO treatment accelerated the course of kidney disease, but no such evidence has been found in human studies.[34-37] Recently, there even have been reports of a retardation of renal disease progression with rHuEPO treatment.[38,39]

## MANAGEMENT OF VASCULAR ACCESS

Efficient initiation of RRT requires preemptive placement of a hemodialysis vascular access or peritoneal dialysis catheter. Hemodialysis is the primary mode of RRT in the United States. According to recent US Renal Data System (USRDS) data, prevalence of hemodialysis patients is 62%.[1] Access-related problems are the major cause of the morbidity and mortality in the hemodialysis population. Access issues account for 16% to 25% of hospital admissions and cost in excess of $1 billion annually.[40,41] NKF/DOQI guidelines recommend the use of native arteriovenous fistula (AVF) be the vascular access of the choice.[42] Unfortunately, it has been estimated that only one third of hemodialysis patients have native AVF.[43] Late referrals to nephrologists and the high prevalence of diabetes and vascular disease in the ever-aging ESRD population make establishment of AVF a very difficult task.[44,45] Therefore, reliance on less-reliable modes of vascular access such as synthetic grafts and tunneled catheters has increased. These 2 methods are very prone to thrombosis and infection. During the past decade, catheters have played an increasingly important role in providing dialysis. Analysis of 1993 USRDS data showed that less than 10% of patients were using a catheter at the initiation of dialysis. By 1996 this number had doubled, so that 19% were using a catheter at the initiation of dialysis and 13% were still catheter dependent at 60 days. Moreover, in recent reports, 60% of new patients and 30% of prevalent patients are now using a catheter for dialysis access.[1]

Because of the excess morbidity and mortality associated with catheter use, NKF/DOQI guidelines decry catheter use.[42] The guidelines state that cuffed, tunneled central venous catheters should be discouraged as permanent vascular access and should be reserved for temporary access for periods longer than 3 weeks or in patients who have exhausted other conventional means of vascular access. A target of less than 10% of patients undergoing chronic maintenance hemodialysis should be maintained on catheters. Access infection rates of 10% at 3 months and less than 50% at 1 year have been proposed as outcome goals. Dialysis catheter use rates changed radically between 1996 and 1999. Insertion rates for temporary catheters declined 17.5% whereas insertion rates for permanent catheters increased 71% in the same period. Insertion rates for simple fistulas have increased 35%, consistent with the NKF/DOQI objective of increasing the use of this access.[1] Although it has been suggested that the continued use of dialysis catheters may be related to increased placement of simple fistulas, geographic patterns do not support this hypothesis. The highest fistula placement rates only occasionally correspond to

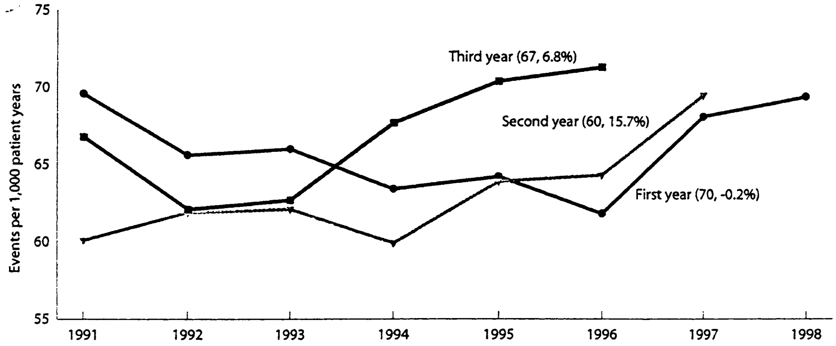

**Fig 3. Acute myocardial infarction rates. (Incident Medicare dialysis patients, 1991-98 combined adjusted for age, gender, race and primary diagnosis). (Data from the USRDS database). The highest rate occurs in the first year after dialysis initiation and did not change from 1991-98. Second and third year acute myocardial infarction rates increased during this period.**

areas with high catheter rates, suggesting that other factors influence catheter use. These may include thrombosis in native and synthetic accesses, or late referrals for the initiation of hemodialysis.[1]

Multiple studies have shown that native AVF placement improves access patency and longevity. These goals currently are achievable as several countries in Europe such as France, Germany, Italy, Spain, and the United Kingdom have shown. The Dialysis Outcomes and Practice Patters Study compared these countries with the United States in terms of vascular access placement. There is a significant difference in the usage of AVF, 47% to 83% in Europe as compared with 15% in the United States. The study cited the difference in population characteristics such as race, diabetes status, peripheral vascular disease status, and angina history that may contribute to the differences in AVF placement. Further, 69% of European patients initiated on hemodialysis were seen by a nephrologist for more than 1 year compared with 44% in the United States ($P < 0.0001$).[46] These important comparisons certainly suggest that early referral to a nephrologist is critical for the optimization of pre-ESRD care. Presently, up to 30% of dialysis patients are referred in the final month before needing hemodialysis.[45] A significant difference also persisted with the placement of more temporary accesses in the United States than in Europe. Both had similar percentages of patients under the care of a nephrologist for greater than 30 days, suggesting that the type of access placement should become more of priority in the US nephrology practice than it currently is. Finally, it has been suggested that a pre-ESRD program in which the patient is educated on the importance of a functional permanent access at the time of hemodialysis initiation may increase the placement. Once the access has been placed and hemodialysis initiation is declared, serial monitoring of the access should be an important part of the care provided by the hemodialysis unit. This only can be achieved by communication between the nephrologist and the team at the dialysis unit, the interventional radiologist, and the access surgeon.[47]

## MORBIDITY AND HOSPITALIZATION

Cardiovascular disease is the major cause of morbidity and mortality in patients with ESRD. The mortality rates owing to cardiovascular disease are 10 to 20 times higher among ESRD patients treated with dialysis compared with the general population,[48] and cardiovascular disease accounts for nearly one half of deaths among ESRD patients.[2]

Morbidity caused by cardiovascular disease is substantial. The Canadian Hemodialysis Morbidity Study reported a probability of hospital admission for nonfatal myocardial infarction, angina, or pulmonary edema among incident patients of 8% to 10% per year,[49] and in the Hemodialysis Study, approximately one third of first hospitalizations were related to cardiovascular complications.[48] The burden of cardiovascular disease is greatest in older patients and in those with diabetic nephropathy. Because the trend of older diabetic patients is expected to continue, it is also likely that the absolute burden of cardiovascular disease present in ESRD patients in the United States will mirror this increase as well.[1] The rates of all events related to cardiovascular disease also have increased. There is an increased incidence of acute myocardial infarction, especially after the first year of starting dialysis (70 events/1,000 patient years). This rate did not change from 1991 to 1998 (Fig 3). There also are increases in second- and third-year acute

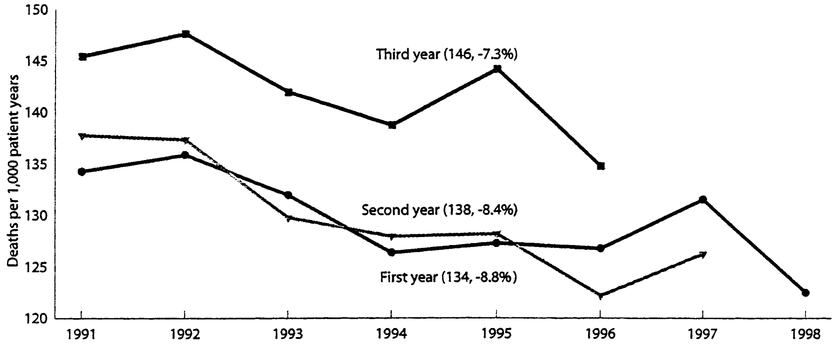

**Fig 4. Cardiac death rates. (Incident Medicare dialysis patients, 1991-98 combined adjusted for age, gender, race and primary diagnosis). (Data from the USRDS database). The cardiac death rate is highest in the third year of the dialysis. There has been an overall decline in the rates of cardiac deaths overtime.**

myocardial infarction rates during this period. This is supported by reports of increased coronary revascularization rates during the same period. The number of cardiac deaths is highest in the third year of dialysis. There has been an overall decline in the rates of cardiac death over time (Fig 4). Compared with the base year of 1991, there was an overall decrease in all-cause mortality rates between 1991 and 1998, with a 7.6% reduction in the first year and a 7.1% reduction in the second year. These decreases are mirrored by decreases in cardiac death rates occurring in the first, second, and third years after dialysis initiation. There is an increased rate of new cerebrovascular accidents (18.2%), transient ischemic attacks (23.3%), and major amputations and peripheral revascularizations (51.2%) after the first year of initiating dialysis treatment from 1991 to 1998. This risk remains elevated even in the second and third year after starting dialysis.[1]

The morbidity associated with ESRD is most clearly evident in hospitalizations and acute events, which are both documented extensively. The USRDS database provides the most important data in this regard. The number of hospital days per admission and days per patient year at risk has remained relatively steady over the past 5 years, with the greatest decreases seen in the transplant patients, regardless of race and ethnicity. Geographic illustration shows that hospital days per admission are slightly higher for non-whites than for whites, and hospital days per patient year at risk are higher for peritoneal dialysis patients than for patients on hemodialysis. Hospital days per patient year at risk are noticeably higher for diabetics compared with nondiabetics. Some of these differences are likely owing to age and race, but adjustments for these factors do not completely account for the variations. Diabetes also might be considered a factor, but areas of the country with high rates of diabetes, such as the Southwest, do not have equivalently high rates of hospitalization.[1] Hospital admissions per patient year at risk are slightly lower for patients aged 20 to 44 than for those in other age groups. Asian patients have dramatically lower admission rates than patients of other races or ethnicities, and diabetic patients are hospitalized more frequently than their nondiabetic counterparts.[1]

Anemia plays an important role in causing morbidity. The relative risk for first all-cause hospitalization is highest for both black and white patients with a hematocrit level of less than 30% and decreases steadily with higher hematocrit levels irrespective of their diabetic status. There also is increased cardiovascular first hospitalization in patients with a hematocrit levels less than 30%. Relative risk for first infectious hospitalization is increased with hematocrit levels less than 33%. A urea reduction ratio less than 60% is associated with increased risk for first all-cause hospitalization irrespective of diabetic status.[1]

## QUALITY OF LIFE

Quality-of-life assessment has become increasingly important in clinical research, especially for chronic conditions such as ESRD.[50] Measurement of health related quality of life in patients on RRT began in 1964, with a comparison of the Karnofsky scores of 4 patients about to begin hemodialysis therapy, with their scores 2 to 5 weeks later.[51] Interest in quality-of-life measurement has grown considerably in recent years. Many researchers, anxious to add a quality-of-life assessment to their battery of clinical measures or to examine quality of life as a primary outcome, have selected from among currently available measures. However, some of these measures have not been subjected to rigorous testing and evaluation.[52] Disease and treatment complications affect the patients' ability to function and limit their lifestyles but often are not captured by conventional biologic and clinical measures of disease and treatment effectiveness.

The Medical Outcomes Study 36-Item Short Form Survey (SF-36), a generic measure of health status, probably has been administered to more dialysis patients than any other questionnaire. Its use in dialysis has provided information that supplements conventional clinical assessment.[50,53,54] The SF-36 is a well-documented health-related quality-of-life instrument consisting of 36 questions compressed into 8 scales and 2 primary dimensions: the physical and mental component scores. This tool was used to evaluate quality of life among peritoneal dialysis (PD) and hemodialysis (HD) patients. The results of 16,755 HD and 1,260 PD patients (728 continuous ambulatory PD [CAPD] and 532 continuous cycling PD [CCPD]) completing an SF-36 during 1996 were analyzed. HD and PD patients scored similarly for scales reflecting physical processes. PD patients scored higher for mental processes, but only after statistical adjustment for the laboratory measures. Scores on scales reflecting physical processes were worse, and those reflecting mental processes were better among CCPD than CAPD patients. HD and CAPD patient scores were similar. CCPD patients perceived themselves as more physically impaired but better adjusted than HD or CAPD patients. These descriptive data show that perception of quality of life between PD and HD patients is similar before adjustment, but PD patients score higher for mental processes with adjustment. CCPD patients score worse for physical function and better for mental function than either CAPD or HD patients. One cannot, however, exclude the influence of therapy selection.[55] Because disease-specific quality-of-life instruments include domains affected most by a particular disease or treatment, they may be more sensitive to the effects of interventions than generic measures. Some domains are not included in the SF-36 that might be salient for patients undergoing dialysis and may vary with treatment modality and dose. These include eating behaviors (eg, dietary restrictions are stricter on HD), sexual functioning, specific treatment side effects (eg, peritonitis), or disease-related symptoms (eg, nausea and vomiting). In addition, the SF-36 may have a floor effect in seriously ill populations, particularly in role functioning and physical functioning domains.[56-59]

The Choices for Healthy Outcomes In Caring for ESRD (CHOICE) Study was designed to evaluate the effectiveness of alternative dialysis prescriptions.[61] As part of CHOICE, a patient-reported measure of health-related quality of life defined as "the value assigned to duration of life as modified by the impairments, functional states, perceptions, and social opportunities that are influenced by disease, injury, treatment, or policy."[61] This instrument, the CHOICE Health Experience Questionnaire, was designed to: (1) complement the generic SF-36, (2) be sensitive to the effectiveness of alternative dialysis modalities and dosing regimens, and (3) be useful for longitudinal collection in routine practice. Successful renal transplantation generally is accepted as the preferred treatment for ESRD. Among all RRTs, successful transplantation most closely replicates the normal process of waste removal and precludes known shortcomings of maintenance dialysis (eg, medical complications, such as hyperparathyroidism and transient azotemia). In addition, it eliminates the constraints imposed by maintenance dialysis and, as a result, many assert that successful transplantation affords a better quality of life.[62] One meta-analysis corroborates the growing consensus that the potential for a high quality of life differs across RRTs. Synthesizing data from 49 published comparative studies, including 77 comparisons involving emotional distress and 66 involving psychologic well-being, renal transplant recipients reported significantly less emotional distress and more psychologic well-being than patients on either hospital-based chronic hemodialysis (CHD) or CAPD. CAPD patients reported more psychologic well-being than those on hospital-based CHD, and those on CHD reported more emotional distress than those receiving HHD. This meta-analysis found significant differences among RRTs with respect to 2 fundamental quality-of-life dimensions: psychologic well-being and emotional distress. Although the results corroborated existing clinical impressions, their validity generally was threatened by the potential existence of unpublished studies showing no significant differences across treatment groups. Validity also was threatened by the observation that important case-mix

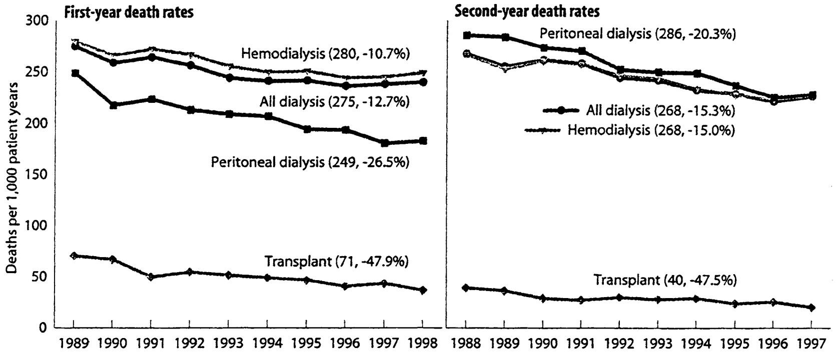

**Fig 5. First and second year death rates, by modality: Overall (Incident Medicare dialysis patients, adjusted for age, gender, race and primary diagnosis). (Data from the USRDS database). Overall first-year death rates have decreased since 1989 for all modalities. Rates are highest in the first year for hemodialysis patients, and in the second year for patients on peritoneal dialysis.**

variables differed across the treatment groups. Because these variables also are related importantly to psychosocial outcomes in ESRD, the existing literature cannot rule out the competing hypothesis that observed quality-of-life differences across RRTs are attributable to preexisting nonrenal and/or no treatment differences. Research should address the problem of case mix directly and consistently, reporting relevant data for each treatment group in sufficient detail to facilitate future meta-analyses. Although the best available evidence to date indicates that quality of life differs systematically across patients receiving alternative RRTs, it is not clear whether this occurs because of valid differences across treatment modalities, preexisting differences among patients, or a combination of these 2 alternatives.[63]

## MORTALITY

The 5-year survival of men older than 64 years starting RRT is worse than those with colon or prostate cancer. The same is true for women at that age with breast or colon cancer. Almost half of all deaths in dialysis patients result from cardiovascular disease.[2] The annual mortality from cardiovascular disease in dialysis patients is substantially higher than in the general population.[64] The average expected remaining lifetime for dialysis and transplant patients is highly dependent on age. White male dialysis and transplant patients aged 60 to 64, for example, are expected to live 3.6 and 4.3 years, respectively. White men aged 50 to 54, in contrast, are expected to live 5.0 and 10.8 additional years, and for those aged 30 to 34 the numbers are 9.2 and 24.3. Comparable differences are seen in female white patients. Such discrepancies are less in black patients because they have better overall survival on dialysis.[1]

First-year death rates for HD patients decreased 11% between 1989 and 1998, but remained relatively flat in 1996 to 1998 (Fig 5). First-year death rates for patients on PD, in contrast, decreased 27% over a 10-year period. The decrease in second-year death rates for dialysis patients was more consistent at 15% to 20%.[1]

Mortality rates in the first and second years increase with the age of the HD patient population, with first-year death rates for patients 75 and older being more than 9 times more than those for pediatric patients in 1999. Rates have declined for patients in all age groups except those aged 0 to 19, in whom they have increased slightly. However, death rates in PD patients decreased in all age groups except for patients aged 0 to 19, for whom second-year rates increased 29.4% between 1988 and 1997. Second-year death rates are higher than first-year death rates for all age categories.[1]

Gender and race also affect the mortality, both first- and second-year death rates for male HD patient have decreased slightly more than they have for female patients, in contrast to PD patients, in whom there is decreased death rates in women as compared with men in the first year. The greatest decline in second-year death rates has been in Native Americans and Asians, 32.4% and 30.3%, respectively.[1] Diabetes and hypertension as a primary diagnosis remain a leading cause of death in both HD and PD patients. However, PD patients have higher rates of death from myocardial infarction, cardiac arrest, cerebrovascular accident/transient ischemic attack (CVA/TIA), infection as compared with HD patients. Prevalent transplant patients have the lowest mortality rates in all categories.[1] In nondiabetic patients, death rates in most categories are either comparable or slightly higher in HD patients as compared with PD patients. Rates of death owing to infection, however, are slightly higher in PD patients. Mortality rates for nondiabetic transplant patients are lower than those of their diabetic counterparts.[1] A strong association exists between nutritional status and morbidity and mortality in patients with ESRD who are treated with HD.

Hypoalbuminemia at initiation of dialysis is a strong predictor of early death on dialysis. Studies involving US and Canadian patients have revealed a strong association of low serum albumin levels at the start of dialysis with subsequent increased risk for death on dialysis.[65] Described here is the predictive value for mortality over 5 years of follow-up of a number of risk factors, recorded at baseline, in a national sample of 3,607 HD patients. Among the variables studied were case-mix covariates, caregiver classifications of nutritional status, serum albumin concentration, and body mass index (BMI). The Case Mix Adequacy special study of the USRDS provided these measurements as of December 31, 1990. Caregiver classification refers to documentation in a patient's dialysis facility medical records that stated an individual to be "undernourished/cachectic," "obese/overweight," or "well- nourished." The mean serum albumin was 3.7 ± 0.45 (SD) g/dL, and the mean BMI was 24.4 ± 5.3 (SD) kg/m$^2$. By caregiver classification, 20.1% of patients were undernourished, and 24.9% were obese. In hazard regression models, including but not limited to the Cox proportional hazards model, low BMI, low serum albumin, and the caregiver classification "undernourished" were independently and significantly predictive of increased mortality. In analyses allowing for time-varying relative mortality risks (ie, nonproportional hazards), the greatest predictive value of all 3 variables occurred early during follow-up, but the independent predictive value of baseline serum albumin and BMI measurements on mortality risk persisted even 5 years later. No evidence of increasing mortality risk was found for higher values of BMI. Serum albumin was confirmed to be a useful predictor of mortality risk in HD patients; BMI was established as an independently important predictor of mortality; both serum albumin level and BMI, measured at baseline, continue to possess predictive value 5 years later; the subjective caregiver classification of nutritional status "undernourished" has independent value in predicting mortality risk beyond the information gained from the 2 other markers of nutritional status—BMI and serum albumin.[66] Anemia also plays an important role in determining mortality. The relative risk for all-cause death is highest in HD patients with hematocrit levels of less than 30%, which parallels the increased relative risk from cardiac death at that level of hematocrit. A urea reduction ratio below 60% is associated with increased relative risk for all-cause death, increased relative risk from cardiac death, and increased relative risk from infectious death.[1]

## SUMMARY

Unfortunately, care of patients with CKD in the United States is fragmented, with suboptimal delivery of care and inadequate use of existing resources. Patients often reach end-stage kidney disease in poor health without adequate preparation for dialysis or transplantation.

The caring for the renal patient should begin early in the course of disease. Only with early intervention can nephrologists attempt to slow the progression of kidney disease, treat the complications of chronic kidney diseases, and prepare patients for transplantation or dialysis. National Kidney Foundation K/DOQI guidelines are a road map for practicing nephrologists to help assess the degree of renal insufficiency and to risk-stratify patients for continued loss of renal function as well as the development of CKD complications.

Just as the benefits of the current DOQI guidelines require putting them into practice, it is only when the insights gained from these new initiatives are incorporated into the practice of primary care providers that the fruits of these budding efforts will be reaped. Thus, both promotion of growth in our understanding of renal disease and optimal management of it, and helping to put what we already know into practice, are critical to accomplishment of this goal.

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