It was the nature of the thing:
No moon outlives its leaving night,
No sun its day. And I went on
Rich in the loss of all I sing
To the threshold of waking light,
To larksong and the live, gray dawn.
So night by night, my life has gone.

WILLIAM DEWITT SNOGGRASS, “Orpheus”
Mortality of ESRD patients has been a subject of considerable debate over the past 25 years. Numerous investigators have examined risk factors for survival in both dialysis and transplant patients, and have reported trends in mortality. In this chapter we provide an overview of recent changes in mortality rates, and examine some of the patient characteristics and biochemical markers that can be used as predictors of mortality. In particular, we look at some of the clinical interventions that are part of the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (K/DOQI), such as anemia treatment and dialysis adequacy. Parallel spreads in Chapter Six address how these same interventions are associated with the risk of hospitalization.

To address these predictors of mortality we have developed outcome models that allow incident patients of all age groups to be characterized once they have survived a particular period of time. For that survival period we obtain data on hemoglobin levels and urea reduction ratios from the Medicare claims data. We then link these data to descriptive information from the Medical Evidence form, and to more detailed comorbidity information collected from the claims. Patient populations whose outcomes are known to differ significantly, such as diabetics and non-diabetics, are analyzed separately.

We adopted this approach in order to determine whether patient characteristics and biochemical markers are associated with similar risks of mortality in males and females, in whites and blacks, and in diabetics and non-diabetics.

Because one subgroup must be used as a baseline, comparisons across age, gender, race, and diagnosis groups are complex. We have therefore developed integrated survival models for several analyses.

To help readers understand the dramatic reductions in life expectancy of the ESRD population we compare the expected survival of the ESRD and general populations, and look as well at differences between dialysis and transplant populations.

In calculations of first-year mortality rates we use statistical models in which we compute the average survival probabilities of the patient population. Alternate models involve using the average characteristics of the population to compute the average survival. While

\[
\text{Adjusted one-year death rate per 1,000 patient years}
\]

\[
\text{Unadjusted one-year death rate per 1,000 patient years}
\]

\[
\text{Line: Mean age (years)}
\]

\[
\text{Bars: Percent of patients who are diabetic}
\]

\[
\text{Bars: Percent of patients who are diabetic}
\]

\[
\text{9.1 - Mortality rates in incident ESRD patients}
\]

adjusted first-year death rates are adjusted for age, gender, race, and primary diagnosis. All rates are standardized to 1995 incident ESRD patients.
the two approaches sound similar, the first method produces results closer to those of Kaplan-Meier analyses and is therefore, we believe, the better approach. A more detailed discussion of these methods is provided in Appendix A.

In Figures 9.1–2 we compare trends in unadjusted and adjusted death rates for incident and prevalent ESRD patients, also showing the mean age and percent of patients who are diabetic in each population. Patients in each cohort are followed for one year. In the incident population, unadjusted rates have been increasing since a low level in 1995 and 1996 (Figure 9.1). Rates that are adjusted for age, gender, race, and primary diagnosis, however, show a significantly different pattern. These rates were highest in the early 1990s, and declined steadily until 1997. In 1998 rates rose from a low of 226 deaths per 1,000 patient years to 233, remaining at approximately the same level in the following two years.

This analysis does not take into account the increasing cardiovascular comorbidity of the patient population, nor the fact that patients are beginning dialysis treatment earlier and with higher estimated glomerular filtration rates (see Figures 2.5 and 2.29–31). The stabilizing of the death rate since 1994 should, therefore, be viewed with caution.

Trends in adjusted and unadjusted mortality rates are closer in the prevalent population (Figure 9.2). During the 1990s the lowest adjusted death rate, 170 per thousand patient years, occurred in 1991. In 1999 the rate was at a high of 179, followed by 177 in 2000.

These figures are again adjusted for age, gender, race, and renal diagnosis. They are not, however, adjusted for increased comorbidity, nor for the earlier initiation of dialysis. Further trend analyses should be performed on cohorts for whom detailed information on pre-ESRD comorbidity can be determined. The Coordinating Center plans to develop these patient cohorts, but we are limited by the availability of Part B comorbidity data prior to 1992, and thus may only be able to use data from hospital services, available back to 1978.

Trends in mortality appear overall to have flattened over the last six years, with current differences that cannot be explained by variations in age, gender, race, or primary cause of renal failure.
Risk factors affecting the survival of ESRD patients are numerous and varied. We look here at patients from the ESRD (high-risk) and general Medicare (low-risk) populations who are age 65 and older, with or without cardiovascular disease, and compare all-cause mortality rates for these patients.

Unadjusted all-cause death rates for patients with primary diagnoses of diabetes or hypertension are similar, at 370 and 382 deaths per thousand patient years (Figure 9.3). Patients with chronic nephritis or with cystic kidney disease typically have lower mortality rates, 311 and 215, than those with diabetes or hypertension and those with other diagnoses such as renal cancers, vasculitis, and AIDS nephropathy. Cardiac mortality rates, while lower, follow a pattern similar to those in the all-cause category.

Patients with cardiovascular disease and on dialysis have five times the risk of all-cause mortality than those in the general Medicare population who do not carry a diagnosis of chronic kidney disease (CKD). Dialysis patients also have higher rates of all-cause mortality than patients who have CKD but are not yet in need of dialysis therapy (Figure 9.4). These relative differences are present even in populations without a diagnosis of cardiovascular disease, demonstrating that CKD patients carry a much higher risk of mortality than those not burdened with the disease.

All-cause mortality rates for the general Medicare and ESRD populations show varying geographic patterns (Figure 9.5). Although there are some similarities in the central part of the United States, overall patterns of mortality in dialysis patients do not match those for the general population. This suggests that factors which may have a positive impact, other than local access to care, may be not be available to the ESRD population.

When comparing all-cause mortality rates in the general Medicare population, in patients with chronic kidney disease but not yet on dialysis, and in dialysis patients, it is clear that dialysis patients have the highest risk of death regardless of diabetic status, gender, or age (Figures 9.6–9). This also holds true across racial and ethnic categories, with whites having the highest rates of death, closely followed by Hispanics and Native Americans.

**Figure 9.3** Period prevalent dialysis patients, 2000, unadjusted. **Figures 9.4 & 9.6–9** Period prevalent general Medicare & period prevalent dialysis patients, 1999, unadjusted. **Figure 9.5** Deaths per 1,000 patient years, period prevalent general Medicare & period prevalent dialysis patients, 1999, by HSA, unadjusted.
All-cause mortality in the general Medicare & dialysis populations, patients age 65+, by patient characteristics

9.6 - by diabetic status

9.7 - by gender

9.8 - by age

9.9 - by race/ethnicity
Patterns of mortality clearly vary by patient age, gender, and race/ethnicity (Figure 9.10). To adjust for these differences, and to analyze the influence on mortality of patient characteristics at the initiation of ESRD treatment, we ran separate Cox regressions for diabetic and non-diabetic patients (Table 9.a).

Many of the characteristics assessed on the Medical Evidence form are strong predictors of subsequent mortality. While gender, for instance, is not associated with mortality in the diabetic population, in non-diabetics males have lower risks of death than females. Regardless of diabetic status, blacks and patients of other races continue to have lower risks of death than whites. And, as a number of investigators have reported, lower risks are also associated with higher body mass indices.

Of particular interest is the increasing risk of mortality with higher estimated glomerular filtration rates. This is consistent with data presented in Chapter Two, showing that patients who initiate dialysis with higher eGFR levels also have higher Charlson scores and a history of more pre-ESRD hospitalization days. Such data suggest that, in contrast to patients able to delay dialysis until their eGFR levels fall, patients who begin treatment early do so because they have increased comorbidity, and need earlier control of fluid overload or other symptoms of progressive chronic kidney disease.

As reported more than a decade ago, albumin is also a strong predictor of mortality, as are the array of comorbid conditions reported on the Medical Evidence form. Congestive heart failure, for instance, is consistently associated with increased mortality in both diabetics and non-diabetics. A history of hypertension is paradoxically linked to lower risks, but this condition is associated with glomerulonephritis and cystic kidney disease, and patients with these diseases have lower rates of death (see Figure 9.3).

While alcohol dependence does not appear to predict subsequent death, drug dependence in non-diabetic patients is a strong predictor. The inability to ambulate and the inability to transfer independently are also strongly linked to poor outcomes.

Because the Medical Evidence form has been shown to under-report comorbidity, caution should be used in interpreting the absolute level of comorbid conditions.

Remaining figures illustrate, by age, gender, and race/ethnicity, the association of mortality with eGFR, with body mass index, and with age. As expected, death rates increase for all populations as eGFR levels rise, though patients of Hispanic origin...
appear to be less sensitive to the influence of eGFR than patients of other races or ethnicities (Figure 9.11).

The association of mortality and body mass index is equally clear, with the highest mortality rates occurring in patients with BMIs less than 20 (Figure 9.12). But while a BMI of 30 or above is associated with the lowest mortality in most patient groups, in patients of other races mortality rates increase at this level, to a rate comparable to that seen with BMIs of 20–25.

Increasing age is associated with higher mortality, regardless of gender, race/ethnicity, or diabetic status (Figure 9.13). Such data suggest that primary patient characteristics are consistently associated with mortality rates, and that these rates can be computed across all types of primary renal disease. Clinical markers such as estimated glomerular filtration rate and body mass index do not, in contrast, have the same relationship to mortality across racial and ethnic groups.

Figures 9.10–13 incident dialysis patients, 1998–1999 combined. Rates by race are also adjusted for ethnicity, rates by ethnicity are also adjusted for race, and rates for all patients are also adjusted for race & ethnicity. Direct comparison of adjusted rates is appropriate only between rates within the “all” group, the three race groups, or the two ethnicity groups; see Appendix A for details.

Figure 9.10 adjusted for diabetic status, eGFR, & BMI. Table 9.a incident dialysis patients, 1998–1999 combined. Results are from separate main effects models for diabetics & non-diabetics, containing the following covariates: age, gender, race, Hispanic ethnicity, BMI, eGFR, albumin (a continuous variable), & Medical Evidence form comorbidities. Reference: 20–44 years old, female, white, non-Hispanic, BMI 20–<25 kg/m², eGFR<5 ml/min, no comorbidity. Figure 9.11 adjusted for age, diabetic status, & BMI. Figure 9.12 adjusted for age, diabetic status, & eGFR. Figure 9.13 adjusted for eGFR & BMI.
M any factors can influence patient survival. We look here at two major predictors of mortality—anaemia and dialysis adequacy—and show that, within separate groups of patients, covariates such as hemoglobin levels, urea reduction ratios, and body mass indices are strong predictors of subsequent death.

A higher body mass index is associated with a lower risk of death in both males and females (Table 9.b). Higher hemoglobin levels are also associated with a lower risk, with levels greater than 12 having a significant impact on mortality in males. Urea reduction ratios (URRs) in males have little effect—only those with a URR of less than 16 percent have an increased risk of death—while there is a consistent decrease in the risk of death as URR levels increase in females.

As is the case with males and females, higher body mass indices and increasing hemoglobin levels are also associated with a lower risk of death in whites and blacks (Table 9.c). Hemoglobin levels greater than twelve do not, however, appear to have any positive impact in blacks. Urea reduction ratios of less than 60 percent are associated with an increased risk of death for both whites and blacks, and the risk is also higher in whites with URRs between 60 and 64 percent.

Within diabetics and non-diabetics, body mass indices and hemoglobin levels are associated with a consistent monotonic decrease in mortality risk as levels rise (Table 9.d). Urea reduction ratios above 70 percent are associated with a lower risk of death in non-diabetics, but not in diabetics.

Adjusted one-year death rates with interactions between gender, race, and diabetic status are shown in Figures 9.14–15. When an interactive model is used, death rates for females are higher than those for males, and decrease in both genders as urea reduction ratios increase until a ratio of 75+ percent is reached, when the risk of death increases for males. The pattern of risk is similar across the races, with the same U-shaped curve as URRs reach levels greater than 75 percent. These trends are not as strong in comparisons of diabetics and non-diabetics.

Interactions between urea reduction ratios and body mass indices within URR groups are presented in Figure 9.16. In patients with a BMI less than 25, an increase in URR is associated with a consistent decrease in death rates. Patients with a body mass index greater than 25 and a URR greater than or equal to 75 percent, however, have a higher risk of death than those with URRs between 70 and 75 percent. This pattern exists among the races and in the Hispanic population, suggest-
Effect of hemoglobin & urea reduction ratio on one-year mortality rates

9.14 - One-year mortality rates, by hemoglobin, gender, race, & diabetic status, adjusted for URR

9.15 - One-year mortality rates, by URR, gender, race, & diabetic status, adjusted for hemoglobin

9.16 - Mortality rates, by urea reduction ratio, race/ethnicity, & body mass index

Tables 9.1.4–9.1.6 & Figures 9.1.4–1.6 incident hemodialysis patients, 1998–1999 combined.

Table 9.1.b results are from separate main effects models for males & females, containing the following covariates: age, race, diabetic status, Hispanic ethnicity, comorbidities, transfusions, hospitalization days, vascular access procedures, BMI, hemoglobin, & URR. Reference: 20–44 years old, white, non-diabetic, non-Hispanic, no comorbidity, no blood transfusions, no hospitalization days, no vascular access procedures, BMI 20–<25 kg/m², hemoglobin 11–<12 g/dl, URR 65–<70 percent. Table 9.1.c results are from separate main effects models for white & black patients, containing the following covariates: age, gender, Hispanic ethnicity, comorbidities, transfusions, hospitalization days, vascular access procedures, BMI, hemoglobin, & URR. Reference: 20–44 years old, female, non-diabetic, non-Hispanic, no comorbidity, no blood transfusions, no hospitalization days, no vascular access procedures, BMI 20–<25 kg/m², hemoglobin 11–<12 g/dl, URR 65–<70 percent. Table 9.1.d results are from separate main effects models for diabetic & non-diabetic patients, containing the following covariates: age, gender, race, Hispanic ethnicity, comorbidities, transfusions, hospitalization days, vascular access procedures, BMI, hemoglobin, & URR. Reference: 20–44 years old, female, non-diabetic, non-Hispanic, no comorbidity, no blood transfusions, no hospitalization days, no vascular access procedures, BMI 20–<25 kg/m², hemoglobin 11–<12 g/dl, URR 65–<70 percent. Figure 9.1.4 adjusted for age, ethnicity, BMI & URR. Figure 9.1.5 adjusted for age, ethnicity, BMI & hemoglobin. Figure 9.1.6 adjusted for age, gender, diabetic status, & hemoglobin. Rates by race are also adjusted for ethnicity, rates by ethnicity are also adjusted for race, & rates for all patients are also adjusted for race & ethnicity. Direct comparison of adjusted rates is appropriate only between rates within the “all” group, the three race groups, or the two ethnicity groups; see Appendix A for details.
On these pages we present five-year survival curves, by age and gender, for patients whose ESRD is caused by one of the less commonly occurring diseases. As expected, survival consistently decreases with advancing age. Survival curves for men and women are almost identical, though men with IgA or IgM nephropathy, systemic lupus erythematosus, secondary glomerulonephritis, or scleroderma have slightly lower survival rates than women with the same diseases.

Among the rare diseases examined here, the highest five-year survival rates are found in patients with Alport’s or with IgA or IgM nephropathy (Figures 9.22 and 9.17). The lowest rates are found in patients with multiple myeloma/light chain nephropathy—fewer than ten percent of these patients are still alive five years after beginning ESRD treatment—and in patients with AIDS nephropathy, only one-fifth of whom live at least five years after the start of ESRD (Figures 9.23–24).

Patient age has the most influence on survival in patients with IgA or IgM nephropathy and in those with Goodpasture’s syndrome. While fewer than 20 percent of ESRD patients age 75 or older live five years with one of these diseases, more than 80 percent of those younger than 45 survive for the same period of time. For patients with multiple myeloma/light chain nephropathy or AIDS nephropathy, in contrast, age has the least influence on survival.


Figure 9.20 Other secondary GN/vasculitis includes polyarteritis, Wegener’s granulomatosis, Henoch-Schoenlein syndrome, & vasculitis & its derivatives.
Scleroderma

9.21 · Survival curves, by age & gender

![Scleroderma survival curves](image)

Alport's, other hereditary/familial disease

9.22 · Survival curves, by age & gender

![Alport's, other hereditary/familial disease survival curves](image)

Multiple myeloma & light chain nephropathy

9.23 · Survival curves, by age & gender

![Multiple myeloma & light chain nephropathy survival curves](image)

AIDS nephropathy

9.24 · Survival curves, by age & gender

![AIDS nephropathy survival curves](image)

Scleroderma, Alport's, other hereditary/familial disease, Multiple myeloma & light chain nephropathy, AIDS nephropathy.
Long-term survival of dialysis and transplant patients, particularly when compared to that of the general population and of other risk populations, continues to be an area of concern. In the general U.S. population, expected remaining lifetimes are four to five times higher than for dialysis patients (Table 9.e). Transplant patients have far higher survival rates than patients on dialysis, but their expected remaining lifetimes are still considerably lower than those in the general population.

Figures 9.25–26 show the impact on survival of increasing comorbidity in the general Medicare population. Patients with neither chronic kidney disease nor diabetes have, as expected, the greatest expected remaining lifetimes, while in the presence of one or both of these diseases expected lifetimes decrease toward those seen in the dialysis population. A similar pattern is seen with diabetes, chronic kidney disease, and chronic heart failure. With each additional disease, expected lifetimes for patients in the general Medicare population decrease, again reaching levels close to those of dialysis patients.

Maps of expected remaining lifetimes again illustrate the higher survival times for patients in the general Medicare population (Figure 9.27). Across age groups, expected lifetimes for dialysis patients are consistently greater for patients in Montana, Wyoming, Colorado, New Mexico, and Texas than in the surrounding states. They are also higher in most of the southeastern states, an area in which remaining lifetimes for general Medicare patients are, in contrast, some of the lowest in the country.

These geographic differences suggest that dialysis patient outcomes and those in the general Medicare population may not be related to the same local elements of the healthcare system.

Table 9.e ESRD data: prevalent dialysis & transplant patients, 2000. U.S. data from the National Vital Statistics Reports, Expectation of Life, 1999, Table A (www.cdc.gov/nchs/data/nvss/nvss50/ nvss50_06.pdf; provides information only for whites & blacks). Figures 9.25–26: prevalent dialysis patients, 2000; general Medicare: period prevalent non-ESRD Medicare patients age 65 or older with at least one Medicare entitlement in 1999 & who are residents of the 50 states, the District of Columbia, Puerto Rico, or the Territories. Diabetes, CKD, & CHF status based on a two-year entry period, 1997–1998. Figure 9.27: prevalent dialysis patients, 2000; general Medicare: period prevalent non-ESRD Medicare patients age 65 or older with at least one Medicare entitlement in 1999 & who are residents of the 50 states or the District of Columbia, by state, unadjusted.
## Maps: National means & patient populations

<table>
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<th>Figure number</th>
<th>M/care ESRD 0–19</th>
<th>M/care General 0–19</th>
<th>Dialysis ESRD 0–19</th>
<th>Dialysis General 0–19</th>
<th>Tx ESRD 20–44</th>
<th>Tx General 20–44</th>
<th>45–64</th>
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</thead>
<tbody>
<tr>
<td>Overall value for all patients</td>
<td>54.7 375.4 19.7</td>
<td>48.3 54.6 11.4</td>
<td>33.0 39.7 5.7</td>
<td>17.9 24.2</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<td>NA</td>
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</tr>
<tr>
<td>Total patients</td>
<td>198,267 153,143</td>
<td>2,716 406 53,429</td>
<td>38,349 77,140 121,431</td>
<td>43,999 230,771</td>
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</tr>
<tr>
<td>Overall value for patients mapped</td>
<td>54.7 374.7</td>
<td>48.3 54.6 11.4</td>
<td>33.0 39.7 5.7</td>
<td>17.9 24.2</td>
<td>NA</td>
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<td>NA</td>
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<tr>
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<td>1,915</td>
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## Patient populations & analytical methods

- Figure 9.3 shows rates for period prevalent (December 31, 2000) dialysis patients, age 65 and older, followed from January 1, 2000 for patients incident prior to 2000, and from the incident date for patients incident in the year 2000. Patients are followed through December 31, 2000, and cause-specific rates are determined by the cause of renal failure.
- Figure 9.4 includes 1999 period prevalent dialysis patients age 65 and older, followed from January 1, 1999 (for patients incident prior to 1999) or from the date of incidence (for patients incident in 1999) to the end of 1999. Rates for patients without CKD are based on the 1999 period prevalent population of patients age 65 years and older as of January 1, with at least one month of Medicare entitlement in 1999, and residing in the fifty states, the District of Columbia, Puerto Rico, or the Territories.
- Figures 9.9.9, 9.6–7, and 9.9 include rates for dialysis patients age 65 or older who are point prevalent as of July 1, 1999; patients are followed to December 31, 2000. The last six months of 1999 are used as the entry period.
- Figures 9.10–16 and Tables 9.a–d include rates and descriptive statistics for incident dialysis patients from 1998–1999. Patients are characterized during a six-month entry period and followed for up to one year.
- For Figure 9.27, expected remaining lifetimes for dialysis patients are calculated from GLIMMIX models, with age group and state as the main effect. Only fixed effects by age and state, and their interactions, are considered in the model. The general Medicare population is based on 1999 period prevalent non-ESRD patients with at least one month of Medicare entitlement in 1999.

## Conclusions

- Adjusted first-year death rates have not improved since 1994 in either incident or prevalent populations.
- The stability of first-year death rates does not reflect the increasing comorbidity of the population.
- Earlier initiation of dialysis and its increased associated comorbidity may mask improvements in the death rates.
- The primary causes of renal failure are associated with important differences in mortality, particularly in patients with chronic nephritis and hereditary kidney diseases.
- All-cause death rates are almost four times higher in dialysis patients age 65 or older than in the general Medicare population. Medicare patients with CKD have twice the risk of death as those without the disease.
- Variations in death rates between the general Medicare population and patients on dialysis are present regardless of diabetic status, gender, age, and race.
- Geographic patterns of death in the general Medicare population differ from those in the ESRD population, suggesting that factors other than local healthcare resources may influence outcomes in ESRD patients.
- Comorbidity, estimated glomerular filtration rate, and albumin at initiation are all strong predictors of mortality in the dialysis population.
- Patients with impaired mobility have a significant risk of death.
- Death rates associated with body mass index differ by race.
- Comorbidity and disease severity are both strong predictors of death in patients who survive nine months on dialysis. These findings are present regardless of gender, race, or diabetic status.
- The association of body mass index to the risk of death is consistent across gender, race, and diagnosis groups.
- Higher hemoglobin levels are associated with a lower risk of mortality, but have the least effect in females and blacks.
- Higher urea reduction ratios are associated with differential risks of death within gender, race, and diagnosis groups.
- Interactions among body mass index, urea reduction ratio, and race/ethnicity show different patterns based on BMI.
- The risk of death for patients with BMIs <25 kg/m² generally decreases with higher URRs. The pattern of mortality risk for patients with higher BMI levels, however, shows a “U” shape as URRs increase.
- As expected, patients with AIDS nephropathy and multiple myeloma have the poorest survival of patients whose ESRD is caused by less common diseases. Patients with IgA nephropathy or Alport’s, in contrast, fare among the best survival rates.
- Expected remaining lifetimes of dialysis patients are one-quarter to one-fifth those of the general population, while expected lifetimes in the transplant population are 20–30 percent less.
- In the general Medicare population, expected remaining lifetimes in patients with chronic kidney disease and chronic heart failure—regardless of diabetic status—are only slightly higher than those in the dialysis population. General Medicare patients without these complications, in contrast, have expected remaining lifetimes that are four to five times higher than those of dialysis patients.