

## Chapter 16

# Kidney Diseases in Diabetes

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### SUMMARY

**D**iabetes now accounts for ~35% of all new cases of end-stage renal disease (ESRD) in the United States, and persons with diabetes make up the fastest growing group of renal dialysis and transplant recipients. In 1991, 48,274 persons with diabetes were receiving renal replacement therapy. The annual cost for this treatment exceeds \$2 billion, not including the costs associated with reduced productivity and unemployment. The magnitude of the problem and its economic impact have led to a dramatic increase in efforts to characterize the natural history of renal disease in diabetes and to identify more successful preventive and therapeutic options.

More than 40% of persons with diabetes have elevated urinary albumin excretion, and the prevalence is higher in those with diabetes of longer duration. In insulin-dependent diabetes mellitus (IDDM), the incidence of persistent proteinuria rises during the first 10 years of diabetes and begins to decline after ~15 years of diabetes. This pattern suggests that only a subset of persons is susceptible to renal disease and, once the majority of these have developed renal disease, the incidence declines. Improved control of hyperglycemia is credited for a secular decline in the incidence of proteinuria in IDDM, but a similar decline in non-insulin-dependent diabetes mellitus

(NIDDM) has not been reported.

Diabetic renal disease is more common in some families than in others, suggesting differences in genetic susceptibility. Other factors associated with the development of diabetic nephropathy include diabetes duration, hypertension, hyperglycemia, and smoking. Increased plasma prorenin activity, lipoprotein abnormalities, autonomic neuropathy, pregnancy, a high-protein diet, and drug nephrotoxicity have been implicated as risk factors in some studies.

Control of blood glucose and blood pressure reduce the rate of progression of renal disease in diabetes, and recent studies suggest that angiotensin converting enzyme (ACE) inhibitors may be renoprotective independent of their effects on blood pressure. Several studies also suggest that reduction of dietary protein may reduce the rate of progression. Most of these studies have been conducted in persons with IDDM, but little is known about the effectiveness of these treatment modalities in NIDDM.

Other renal diseases that occur with greater frequency in diabetic patients include asymptomatic bacteriuria, pyelonephritis, papillary necrosis, and radiocontrast-induced renal failure.

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### TERMINOLOGY

Diabetic nephropathy refers to the presence of elevated urinary protein excretion in a person with diabetes in the absence of other renal disease. The histologic changes accompanying this rise in protein excretion are referred to as diabetic glomerulosclerosis.

The primary constituent of urinary protein in diabetic nephropathy is albumin. Consequently, quantification

of urinary albumin excretion is central to any description of diabetic renal disease. Albumin excretion can be determined from timed urine collections, and 24-hour, overnight, or even shorter collection periods are used. Measurement of the urinary albumin-to-creatinine ratio in untimed urine specimens is a convenient alternative way to assess albumin excretion. Because of the relative constancy of urinary creatinine excretion, the albumin-to-creatinine ratio is highly correlated with the timed excretion rate. Several terms are used to describe the level of urinary albumin excre-

tion measured by these methods.

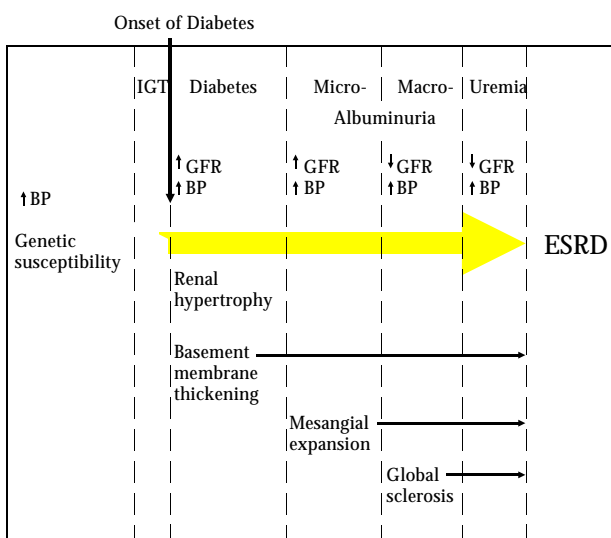
Microalbuminuria or incipient diabetic nephropathy generally refers to levels of urinary albumin excretion below those detected by standard dipstick methods, and macroalbuminuria refers to higher levels of urinary albumin excretion. Proteinuria refers to a positive dipstick test for protein or to a daily output of protein above a certain cutpoint, typically  $\geq 500$  mg protein/day. Thus, macroalbuminuria and proteinuria may be relatively equivalent measures of urinary protein excretion. Differences in methods of measurement and lack of standardized terminology often make comparisons between studies difficult.

## DIABETIC GLOMERULOSCLEROSIS

### PATHOPHYSIOLOGY

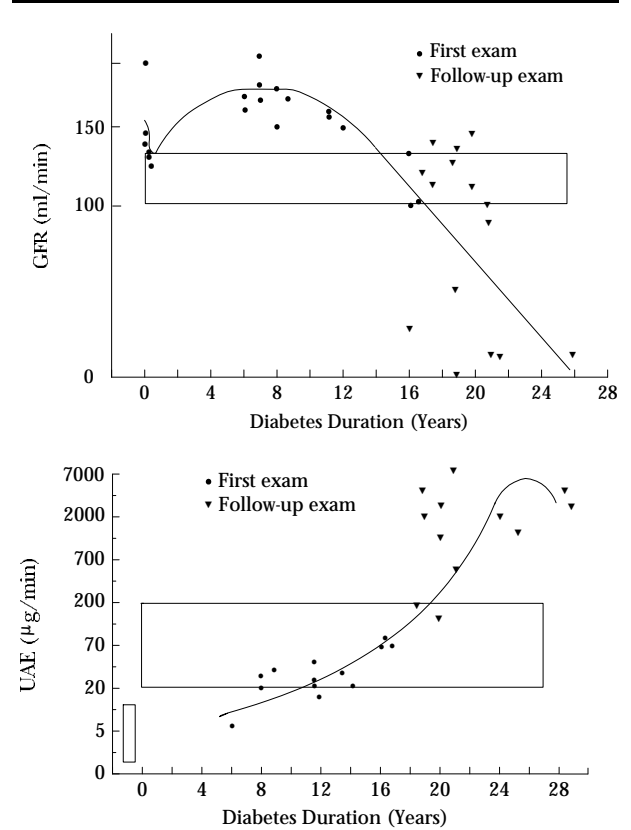
A diagram of the natural progression of diabetic renal disease, and some of the factors contributing to it, is shown in Figure 16.1. The natural history of diabetic glomerulosclerosis can be characterized by a number of phases in which albumin or protein excretion increases and glomerular filtration rate (GFR) rises and subsequently falls (Figure 16.2). As the disease progresses, characteristic morphologic and histologic changes occur in the kidney, which may eventually culminate in uremia or ESRD.

Figure 16.1  
Natural Course of Renal Disease in Diabetes



BP, blood pressure; IGT, impaired glucose tolerance; GFR, glomerular filtration rate; ESRD, end-stage renal disease.

Figure 16.2  
Outline of the Natural History of Diabetic Nephropathy in Patients with IDDM



GFR, glomerular filtration rate; UAE, urinary albumin excretion. Figure is based on data from 20 men, all of whom developed nephropathy; time between the first examination and followup averaged  $12 \pm 3$  years; not all patients had both examinations. Curved lines represent the typical course of GFR (log scale) and UAE; the box in the GFR panel represents the mean  $\pm$  SD of GFR in healthy subjects; the small vertical box in the UAE panel represents the normal range of UAE; and the large horizontal box represents the microalbuminuric range.

Source: Reference 2

### ■ Protein Excretion

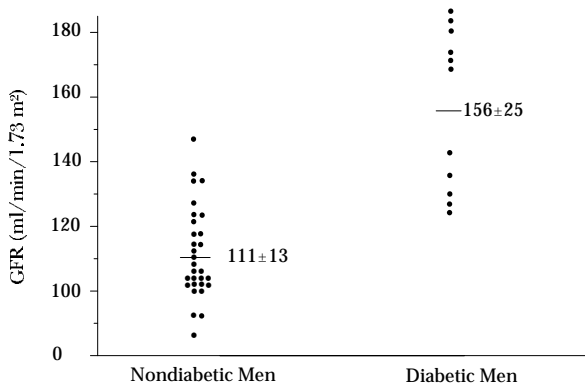
Urinary albumin excretion is often slightly elevated at the diagnosis of diabetes but frequently returns to normal with the institution of glycemic control<sup>1-4</sup>. After 7-15 years, 25%-40% of patients with IDDM develop microalbuminuria, and the vast majority of these patients (>90%) progress to proteinuria over the following years<sup>1</sup>. Development of persistent proteinuria often heralds a decline in renal function associated with even higher levels of protein excretion<sup>1</sup>. As the kidneys fail and glomerular filtration is severely compromised, the level of protein excretion declines. The course of urinary protein excretion in NIDDM may be similar, but its description is complicated by uncertainties in dating the onset of diabetes and by a higher frequency of nondiabetic renal disease contributing to the proteinuria<sup>5</sup>.

## Glomerular Hemodynamic Function

Considerable evidence, both human and experimental, suggests the onset of diabetes is associated with hemodynamic changes in the renal circulation that lead to increased renal plasma flow (RPF), glomerular capillary hyperperfusion, and an increased glomerular transcapillary hydraulic pressure gradient<sup>6-12</sup>. These hemodynamic alterations are hypothesized to cause functional and structural damage to the glomeruli that result in defects of selective glomerular capillary permeability, proteinuria, protein extravasation into the glomerular mesangium, expansion of mesangial matrix, and glomerulosclerosis<sup>13-17</sup>.

In one of the first studies of GFR with a suitable clearance marker in patients with diabetes, inulin or I<sup>125</sup>-iothalamate clearance was measured in 11 men with newly diagnosed untreated IDDM and 31 healthy nondiabetic men<sup>11</sup>. On average, GFR in the diabetic subjects was 40% higher than in the nondiabetic subjects (Figure 16.3). These findings have since been confirmed in studies of both men and women with IDDM, with the elevation of GFR averaging 20%-40%<sup>8,12</sup>. Although RPF was similar in the diabetic and nondiabetic subjects in the first study<sup>11</sup>, a significant elevation of RPF in IDDM has been reported subsequently<sup>12</sup>. Similar changes in GFR and RPF have been described in NIDDM<sup>18-21</sup>. Figure 16.4 shows the GFR and RPF in 110 normotensive whites with newly diagnosed NIDDM compared with 32 nondiabetic persons<sup>21</sup>. The GFR averaged 23% higher and the RPF 13% higher in NIDDM. Thus, hemodynamic changes

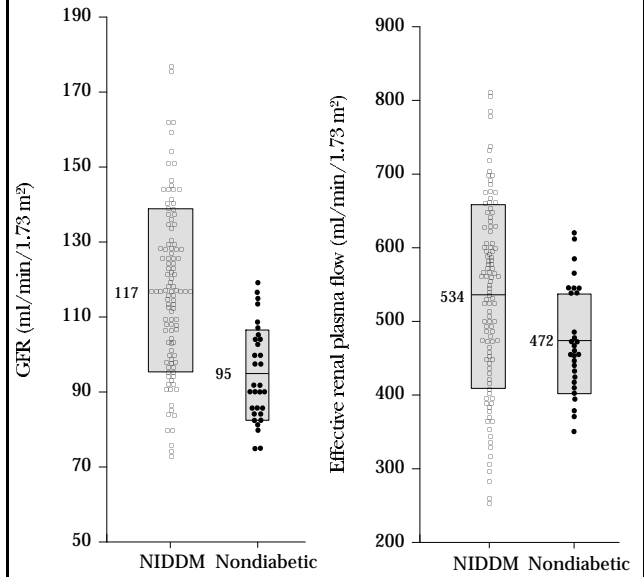
**Figure 16.3**  
Mean GFR in Newly Diagnosed IDDM and Nondiabetic Men



GFR, glomerular filtration rate. Subjects were 31 nondiabetic men and 11 men with newly diagnosed and untreated IDDM; horizontal lines are mean±SD. The mean GFR was 41% higher in the diabetic subjects than in the nondiabetic subjects.

Source: Reference 11

**Figure 16.4**  
GFR and Renal Plasma Flow in NIDDM and Nondiabetic Subjects



GFR, glomerular filtration rate. GFR and effective renal plasma flow were measured in 110 patients with NIDDM and 32 normal subjects; mean values are shown for each group. Mean GFR averaged 23% higher and renal plasma flow 13% higher in the diabetic subjects.

Source: Reference 21

in the glomerular circulation are found early in the course of both major types of diabetes. Increased renal blood flow is partly responsible for the elevation of GFR, but other factors, presently ill-defined, must be invoked to account for the magnitude of the hyperfiltration. Several investigators have reported a relationship between early hyperfiltration and the subsequent development of diabetic nephropathy<sup>22-24</sup>, but others have not<sup>25</sup>.

After the initial elevation at onset of diabetes, GFR decreases in response to metabolic control in both IDDM and NIDDM<sup>26-29</sup> but usually not to levels found in nondiabetic persons<sup>9,29-31</sup>. Coincidental with the initial elevation of GFR at the diagnosis of diabetes is slightly elevated urinary albumin excretion, but levels in the microalbuminuric range are usually seen only after some years of diabetes. The GFR in patients with microalbuminuria is higher, on average, than in those with normal urinary albumin excretion<sup>32,33</sup>, but in patients with clinical proteinuria it is lower, although in NIDDM it may still be within the normal range<sup>34,35</sup>. These cross-sectional data suggest that GFR declines in persons with clinical proteinuria, reflecting progressive glomerulosclerosis and loss of filtration surface area. Longitudinal studies confirm this hypothesis. Without antihypertensive therapy, GFR typically

declines by ~1 ml/min/month in persons with IDDM and clinical proteinuria<sup>36-40</sup>. This decline can be slowed by the initiation of effective antihypertensive treatment<sup>41-43</sup>. Similar rates of decline are noted in persons with NIDDM and clinical proteinuria<sup>44,45</sup>.

## Renal Morphology

Concurrent with the elevation of GFR at the onset of diabetes, there may be an increase in kidney size. Whether enlargement of the kidneys is due to hyperglycemia or other metabolic effects associated with diabetes or to altered circulating or tissue levels of hormones that affect renal growth is not known. Nevertheless, renal hypertrophy is a well-documented feature of IDDM, and the magnitude of hypertrophy correlates with the level of creatinine clearance or GFR<sup>26,29,31,46-48</sup>. The extent of renal hypertrophy in patients with uncomplicated NIDDM and good metabolic control, however, may be limited<sup>49</sup>. Figure 16.5 shows the kidney volume in patients with NIDDM and normal urinary albumin excretion compared with age- and sex-matched nondiabetic subjects. The difference in kidney size between these groups was not significant<sup>49</sup>. On the other hand, the kidneys are significantly larger in patients with elevated urinary albumin excretion, and the urinary albumin excretion rate has been shown to increase to a greater extent in subjects with nephromegaly than in those with kidneys of normal size<sup>50</sup>. This suggests that renal hypertrophy is a predictor of future progression of diabetic renal disease in NIDDM, but to our knowledge, no longitudinal studies have examined this relationship in IDDM. In a cross-sectional study, however, there

was no correlation between kidney size and histopathology in IDDM<sup>47</sup>. Reduction in kidney size has not been demonstrated consistently after initiation of metabolic control<sup>26-28,48,51</sup>.

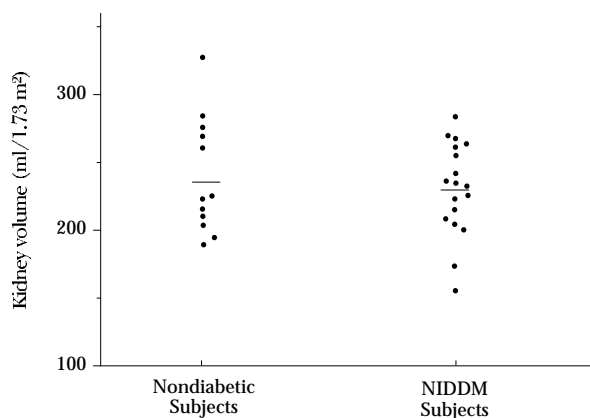
Renal hypertrophy may be due in part to glomerular hypertrophy, which has been noted both at the diagnosis of diabetes<sup>52</sup> and in patients with established nephropathy<sup>46,53-55</sup>. Reasons for the glomerular enlargement are uncertain, but hemodynamic changes in the glomerular circulation have been suggested.

The earliest structural abnormality of the glomerulus in diabetes is thickening of the glomerular basement membrane, a characteristic finding in nearly all patients<sup>17,56</sup>. This is followed by an increase in the fractional mesangial volume, i.e., mesangial volume per glomerulus. Mesangial matrix is the major component of this expansion, with an increase in the volume fraction of the mesangial cellular component playing a secondary role<sup>57</sup>. Nodular hyaline thickening of the intracapillary connective tissue within the glomerulus of diabetic patients with advanced renal disease was first described by Kimmelstiel and Wilson<sup>58</sup>. Most of the patients they described had NIDDM, but the advanced histologic lesions of diabetic nephropathy are indistinguishable between IDDM and NIDDM.

The clinical manifestations of diabetic renal disease do not correlate with thickening of the glomerular basement membrane but are highly correlated with the extent of mesangial expansion<sup>17</sup>. Occlusion of glomerular capillaries by expansion of the mesangium appears to lead to a loss of surface area available for filtration and thus contributes to the decline in renal function associated with diabetic nephropathy<sup>17,59</sup>. Glomerular hypertrophy may compensate for the loss of filtration surface area, providing a means by which GFR is maintained in progressive renal disease<sup>60</sup>. Thus, the rate of progression of diabetic renal disease may be limited by an individual's capacity for glomerular volume expansion<sup>55</sup>. The later stages of diabetic nephropathy are characterized by reduction in the number of functioning glomeruli and further enlargement of those that remain functional. This stage is associated with markedly reduced GFR.

Although much has been learned about the morphologic abnormalities that are associated with declining renal function in patients with established diabetic nephropathy, the degree of correlation between glomerular structure and function in early diabetic nephropathy is controversial. In one study, normotensive subjects with microalbuminuria could not be differentiated on the basis of structural parameters from those with normal urinary albumin excretion<sup>61</sup>.

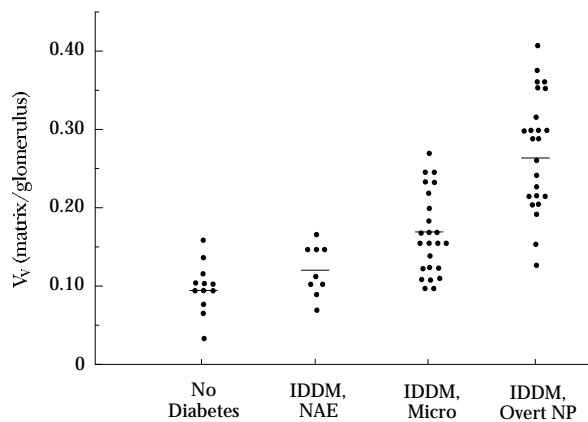
Figure 16.5  
Kidney Volume in Nondiabetic and NIDDM Subjects



Kidney volume measured by ultrasound in nondiabetic subjects and subjects with NIDDM; horizontal lines are means. The difference between the groups was not significant.

Source: Reference 49

**Figure 16.6**  
**Mesangial Matrix as Fraction of Total Glomerular Volume, by Diabetes Status and Albumin Excretion**



The mesangial matrix is expressed as fraction of total glomerular volume in a group of nondiabetic subjects and in patients with IDDM and normal albumin excretion (NAE), microalbuminuria (Micro), or proteinuria (overt nephropathy, Overt NP); horizontal lines are means. This parameter of glomerulopathy was increased in patients with microalbuminuria compared with diabetic patients with normal urinary albumin excretion. Thus, mesangial matrix volume fraction is a very sensitive indicator of renal function.

Source: Reference 62

However, several other studies have shown that both IDDM and NIDDM patients with microalbuminuria have more advanced structural lesions than those with normal urinary albumin excretion<sup>62-64</sup>. Figure 16.6 shows the matrix volume fraction according to the level of urinary albumin excretion in patients with IDDM. The volume fraction in the diabetic subjects with microalbuminuria is higher than in those with normal urinary albumin excretion, suggesting that microalbuminuria is a clinical indicator of structural damage in the diabetic kidney at a time when the GFR is usually elevated.

### ■ Selective Glomerular Permeability

The glomerular capillary wall serves as a filter that discriminates among molecules on the basis of size, charge, and configuration. Narrow size fractioning of exogenous polymers such as dextran, which are neither secreted nor reabsorbed by the renal tubule, is a standard method for measuring the size of the functional pores that perforate the glomerular capillary wall<sup>65-67</sup>. Mild impairment of barrier size selectivity has been demonstrated by this technique at the onset of NIDDM<sup>19</sup>. A comparison of the mean dextran sieving profiles for Pima Indians with NIDDM of <3 years duration and those with normal glucose tolerance is shown in Figure 16.7. The fractional dextran clearances in the diabetic subjects were uniformly elevated over the entire range of molecular radii tested, sug-

gesting a defect in the size-selective properties of the glomerular capillary wall soon after the onset of NIDDM<sup>19</sup>. A similar defect has been reported at the onset of IDDM by some investigators<sup>68</sup>, but not by others<sup>11,69</sup>. In both types of diabetes, established diabetic nephropathy is associated with substantial impairment of the glomerular barrier. The primary contributor to proteinuria at this stage of disease is a shunt resulting from the presence of large pores within the glomerular capillary wall through which plasma proteins can easily pass<sup>70-74</sup>.

The ratio of the clearance of IgG and IgG4, which are endogenous proteins of identical size but with different electrostatic charge, has been used to estimate the charge selectivity of the glomerular capillary wall<sup>70,75,76</sup>. However, because endogenous proteins undergo variable rates of tubular reabsorption, this selectivity index reflects the combined action of glomerular and tubular handling, thus limiting its utility and interpretation<sup>77-79</sup>. Nevertheless, data derived from this index suggest, at least in IDDM, that impairment of the electrostatic barrier within the glomerulus, consequent to a decrease in sialic acid and heparan sulfate content of the glomerular membrane<sup>80,81</sup>, precedes the development of a size-selective defect<sup>70,76</sup> and may contribute to enhanced filtration of plasma proteins in early diabetic renal disease. Other explanations proposed for the facilitated urinary clearance of anionic proteins such as albumin in early diabetic renal disease include modifications of molecular configuration of polyanions that favor en-

**Figure 16.7**  
**Fractional Dextran Clearance Profile in Diabetic and Nondiabetic Pima Indians**

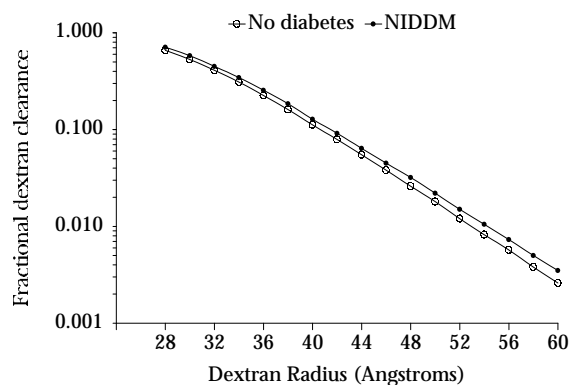


Figure compares the fractional dextran clearance profile in Pima Indians with NIDDM and those with normal glucose tolerance; fractional dextran clearances in the diabetic subjects were uniformly elevated over the entire range of molecular radii tested; the elevation was most marked at the large radius end of the profile, with statistically significant differences ( $p \leq 0.05$ ) for dextrans of  $\geq 48$  Å radius.

Source: Reference 19

hanced filtration, enhanced proximal tubular reabsorption of cationic species allowing preferential escape of filtered polyanions in the urine, or the presence of regions in the normal glomerular capillary wall that favor penetration by anionic over cationic proteins<sup>82</sup>.

## ELEVATED URINARY ALBUMIN EXCRETION

The normal kidney excretes small amounts of albumin, but the concentration is generally too low to be detected by the standard dipstick methods. With the development of sensitive immunoassays it has become possible to accurately measure the concentration within the normal range. The normal range of urinary albumin excretion is generally defined as an albumin excretion rate <30 mg/24 hours (<20 µg/min) or an albumin-to-creatinine ratio <30 mg/g.

Urinary excretion of protein is elevated in a number of kidney diseases that affect glomerular and tubular function. In diabetic nephropathy, the plasma protein excreted in the highest concentration is albumin. As noted above, urinary albumin excretion is often increased at the diagnosis of both types of diabetes but frequently returns to normal with the institution of glycemic control<sup>1-4</sup>. Persistent clinical proteinuria at the onset of NIDDM, however, may reflect diabetes that has remained undiagnosed for years<sup>4</sup> or the presence of renal disease unrelated to diabetes, since other renal diseases are common at the ages when NIDDM typically develops. Among 35 patients with NIDDM and elevated urinary albumin excretion who underwent kidney biopsy, 23% had nondiabetic glomerulopathies<sup>5</sup>. On the other hand, elevated urinary albumin excretion has been reported from several populations in persons with impaired glucose tolerance<sup>83-85</sup>, raising the possibility that hyperglycemia, even at

levels below those diagnostic of diabetes, is sometimes associated with renal abnormalities and that these abnormalities may precede the onset of diabetes.

## ■ Prevalence of Elevated Urinary Albumin Excretion

The prevalence of elevated urinary albumin excretion in a population-based study of 706 insulin-treated subjects in Wisconsin with diabetes onset at age <30 years, presumably mostly patients with IDDM, is shown in Table 16.1<sup>86</sup>. The overall prevalence of microalbuminuria (≥0.03 g albumin/L) was 21% and for proteinuria (≥0.30 g protein/L) was 21%. If the average urine volume is assumed to be 1 L per day, these rates are similar to the prevalence of 23% (31-299 mg albumin/24 hours) and 19% (≥300 mg albumin/24 hours) found in 876 clinic-based patients with IDDM in Denmark<sup>87</sup>. Figure 16.8 shows the prevalence of micro- and macroalbuminuria in this clinic-based population as a function of the duration of diabetes. The rates in both of these studies are higher than those reported in a nationwide cohort of Norwegian IDDM patients (12% for microalbuminuria, 15-199 µg/min; 0.3% for macroalbuminuria, ≥200 µg/min)<sup>88</sup>. This difference is due primarily to the shorter duration of diabetes among the subjects in the Norwegian study (see below).

Table 16.2 shows the prevalence of elevated urinary albumin excretion in a population-based study in Wisconsin of 798 subjects with diabetes diagnosed at age ≥30 years<sup>89</sup>. The majority of these patients presumably had NIDDM. The prevalence rates of microalbuminuria (≥0.03 g albumin/L) and proteinuria (≥0.30 g protein/L) were 29% and 21%, respectively, in those receiving insulin treatment. These were significantly higher than the rates of 22% and 10% found in those not treated with insulin. These differences in prevalence according to type of treatment may be due

Table 16.1

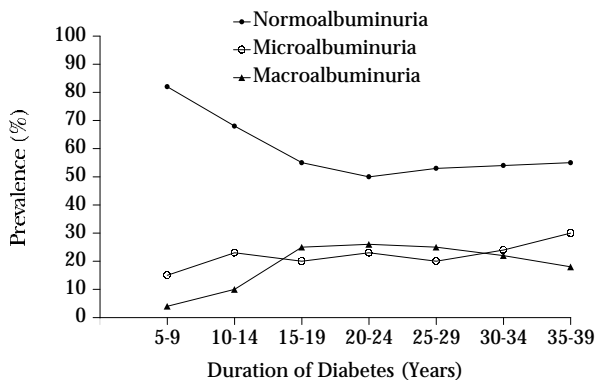
Prevalence of Microalbuminuria and Proteinuria in IDDM and Nondiabetic Males and Females in Wisconsin

|   | Diabetic group (%) |                  |                | Nondiabetic group (%) |                  |                |
|---|--------------------|------------------|----------------|-----------------------|------------------|----------------|
|   | Males<br>n=365     | Females<br>n=341 | Total<br>n=706 | Males<br>n=111        | Females<br>n=130 | Total<br>n=241 |
| Normoalbuminuria<br>(<0.03 g albumin/L)     | 53                 | 63               | 58             | 92                    | 95               | 94             |
| Microalbuminuria<br>(0.03-0.29 g albumin/L) | 21                 | 22               | 21             | 6                     | 4                | 5              |
| Proteinuria<br>(≥0.30 g protein/L)          | 26                 | 16               | 21             | 2                     | 1                | 1              |

IDDM defined as insulin-treated diabetic subjects diagnosed at age <30 years.

Source: Reference 86

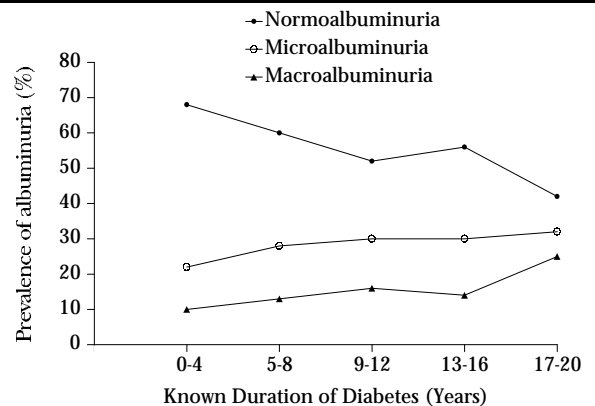
**Figure 16.8**  
**Prevalence of Elevated Urinary Albumin Excretion, by Duration of IDDM**



Microalbuminuria was defined as 31-299 mg/24 hours and macroalbuminuria as  $\geq 300$  mg/24 hours.

Source: Reference 87

**Figure 16.9**  
**Prevalence of Elevated Urinary Albumin Excretion, by Known Duration of NIDDM**



Microalbuminuria was defined as 31-299 mg/24 hours and macroalbuminuria as  $\geq 300$  mg/24 hours.

Source: Reference 90

to differences in duration of diabetes. Figure 16.9 shows the prevalence of elevated urinary albumin excretion in 507 clinic-based Danish patients with NIDDM<sup>90</sup> according to the known duration of diabetes. These patients were from the same clinic as the IDDM patients shown in Figure 16.8, and the same definitions for micro- and macroalbuminuria were used. The overall prevalence rates of microalbuminuria and macroalbuminuria were 28% and 14%, respectively. These were similar to the rates reported in Wisconsin for those receiving insulin, and rates of elevated urinary albumin excretion were higher among subjects with diabetes of longer duration. Higher prevalence rates of elevated urinary albumin excretion in NIDDM have been reported in two population-based studies. The overall rates of microalbuminuria and macroalbuminuria in Pima Indians<sup>84</sup> were 26% (albumin-to-creatinine ratio 30-299 mg/g) and 21% (albumin-to-creatinine ratio  $\geq 300$  mg/g), re-

spectively, and in the population on the Western Pacific island of Nauru<sup>85</sup> were 41% (30-299  $\mu\text{g/ml}$ ) and 31% ( $\geq 300$   $\mu\text{g/ml}$ ), respectively. Figure 16.10 shows the prevalence of micro- and macroalbuminuria in Pima Indians according to duration of diabetes. In both the Nauruan and Pima studies, the prevalence of elevated urinary albumin excretion was higher in subjects with longer duration of diabetes. Although different methods and definitions of urinary albumin excretion were employed, other factors must be invoked to explain the large differences in the prevalence of elevated urinary albumin excretion in these different groups. Additional contributing factors may include racial differences as well as differences in duration of diabetes, blood pressure and metabolic control, diet, and perhaps genetic susceptibility to diabetic renal disease.

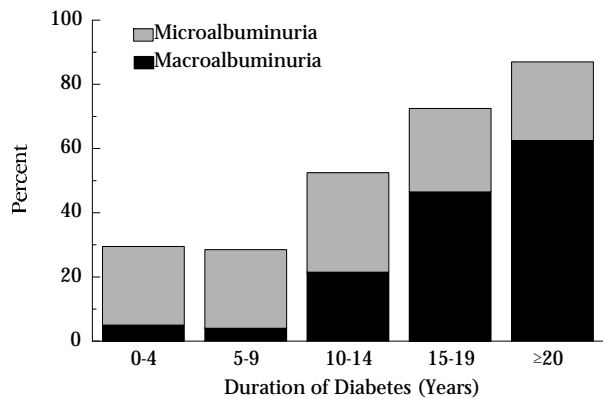
**Table 16.2**  
**Prevalence of Microalbuminuria and Proteinuria in NIDDM Subjects in Wisconsin, by Sex and Insulin Treatment**

|   | Taking insulin group (%) |                  |                | Not taking insulin group (%) |                  |                |
|---|--------------------------|------------------|----------------|------------------------------|------------------|----------------|
|   | Males<br>n=192           | Females<br>n=243 | Total<br>n=435 | Males<br>n=164               | Females<br>n=199 | Total<br>n=363 |
| Normoalbuminuria<br>( $< 0.03$ g albumin/L) | 43                       | 55               | 50             | 64                           | 71               | 68             |
| Microalbuminuria<br>(0.03-0.29 g albumin/L) | 33                       | 26               | 29             | 23                           | 22               | 22             |
| Proteinuria<br>( $\geq 0.30$ g protein/L)   | 23                       | 19               | 21             | 13                           | 8                | 10             |

NIDDM defined as diabetic subjects diagnosed at age  $\geq 30$  years.

Source: Reference 89

**Figure 16.10**  
**Prevalence of Elevated Urinary Albumin Excretion in Pima Indians, by Duration of Diabetes**



Microalbuminuria was defined as 30-299 mg albumin/g creatinine and macroalbuminuria as  $\geq 300$  mg albumin/g creatinine.

Source: Reference 84

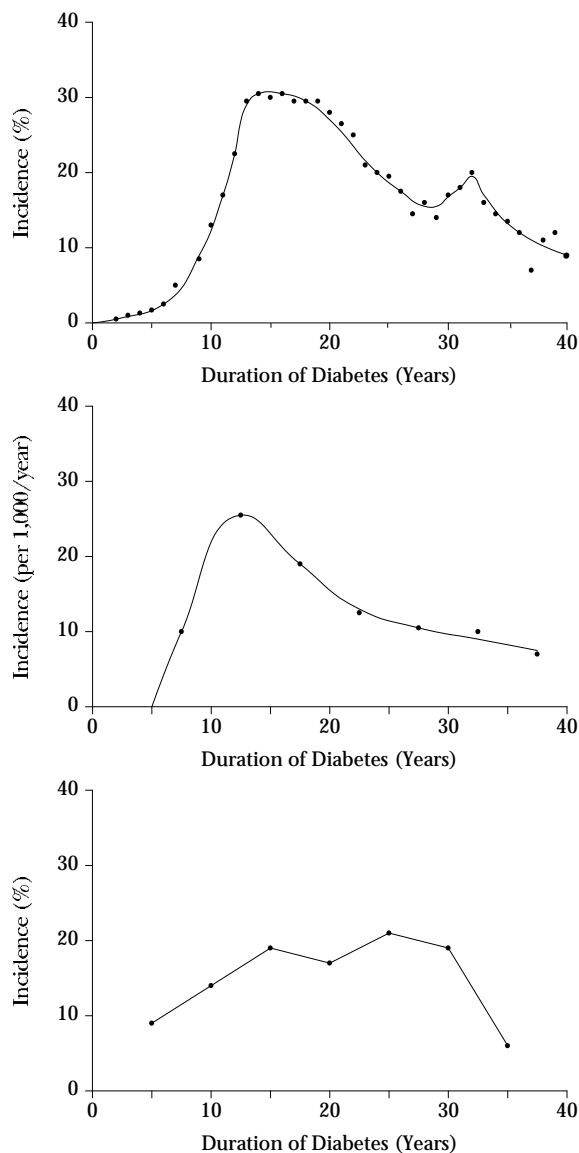
### Incidence of Elevated Urinary Albumin Excretion

Urinary albumin excretion within the microalbuminuric range predicts the development of clinical proteinuria in persons with IDDM<sup>24,91-94</sup> and NIDDM<sup>95-98</sup>, but the incidence of proteinuria in relation to diabetes duration is strikingly different in the two types of diabetes. Three longitudinal studies have examined the incidence of proteinuria in persons with IDDM. Two of these studies were clinic-based<sup>99,100</sup> and the third was population-based<sup>101</sup>. Figure 16.11 shows the incidence of persistent proteinuria as reported in each of these studies<sup>99-102</sup>. Although the rates differ slightly, all three studies show that the incidence of proteinuria rises during the early years of IDDM and then declines. This finding suggests that only a subset of persons with IDDM is susceptible to renal disease. As the duration of diabetes increases, the number of persons remaining who are susceptible to renal disease declines, resulting in the declining incidence of proteinuria.

During the past 50 years a secular decline in the incidence of diabetic nephropathy in IDDM has been described<sup>100,103,104</sup>, and the largest decline may have occurred in the past decade. For example, investigators in Sweden<sup>104</sup> reported that the cumulative incidence of persistent albuminuria ( $\geq 1+$  test by Albustix) after 20 years of diabetes decreased from 28% of patients in whom IDDM developed in 1961-65 to 6% of those in whom diabetes developed in 1980-85. Furthermore, none of the 51 patients in whom IDDM was diagnosed in 1976-80 developed persistent albu-

minuria during 12-16 years of followup. Figure 16.12 shows the cumulative incidence of persistent albuminuria in these cohorts according to the calendar year of diagnosis of diabetes. A declining cumulative incidence was noted throughout the study period, and improved glycemic control was credited for this finding<sup>104</sup>.

**Figure 16.11**  
**Incidence of Proteinuria in IDDM, by Duration of Diabetes**

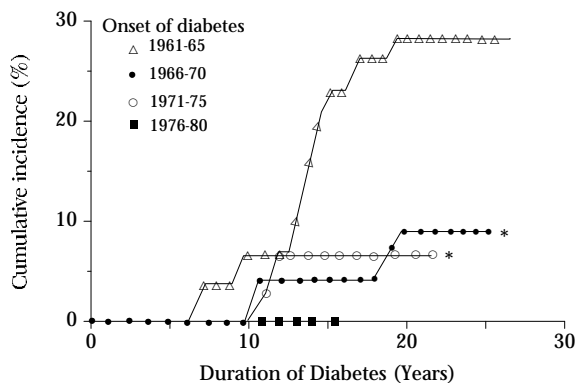


Incidence was defined as the annual percent of new cases in the upper panel, as cases per 1,000 person-years in the middle panel, and as 4-year incidence (%) in the lower panel. All three studies show an increase in the incidence during the early years of diabetes, followed by a decline as the duration of diabetes increases.

Source: References 99, 101, and 102



**Figure 16.12**  
**Cumulative Incidence of Persistent Albuminuria in Patients with IDDM Diagnosed at Age <15 Years, by Duration of Diabetes**



Persistent albuminuria was defined as  $\geq 1+$  by Albustix; subjects were divided into four groups based on the calendar years in which diabetes was diagnosed; the asterisks denote a significant difference in incidence ( $p=0.01$ ) between the two groups indicated and the group with onset of IDDM in 1961-65.

Source: Reference 104

The incidence of proteinuria in NIDDM is more difficult to characterize because of the uncertainty in dating the onset of diabetes in most studies. No relationship between duration of diabetes and the incidence of proteinuria was found in the Mayo Clinic population in Rochester, MN<sup>105</sup>, whereas in Wisconsin<sup>106</sup> a relationship between diabetes duration and incidence of proteinuria was stronger in persons who received

**Figure 16.13**  
**Incidence of Proteinuria in Diabetic Pima Indians Age  $\geq 25$  Years**

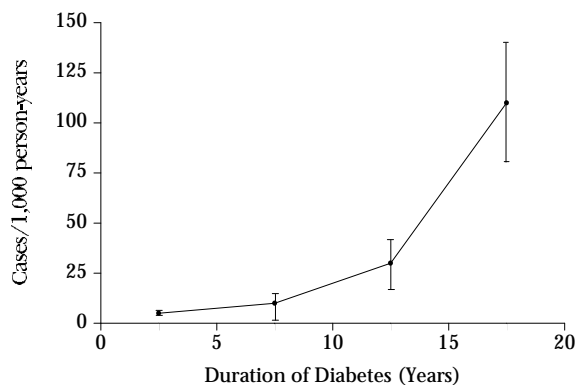


Figure shows the age- and sex-adjusted incidence rate (cases per 1,000 person-years) and 95% confidence intervals of proteinuria (protein-to-creatinine ratio  $\geq 1.0$  g/g).

Source: Reference 107

insulin than in those who did not. In Pima Indians<sup>107</sup>, in whom the duration of diabetes is known with greater accuracy because of systematic periodic glucose tolerance testing in the population, the incidence of proteinuria was strongly related to duration of diabetes and continued to rise with increasing duration of diabetes (Figure 16.13). No secular decline in the incidence of proteinuria in NIDDM has been reported. The calculated cumulative incidence of proteinuria in IDDM and in NIDDM are compared in Figure 16.14<sup>108</sup>. Based on incidence rates measured over short time intervals, 30%-50% of persons with IDDM would be expected to develop diabetic nephropathy after 40 years of diabetes<sup>99,100</sup>. However, contrary to previous widely held assumptions, for patients with a similar duration of diabetes the cumulative incidence in NIDDM is at least as high as in persons with IDDM<sup>107</sup>.

### ■ Elevated Urinary Albumin Excretion as a Risk Factor for Death

The presence of microalbuminuria in IDDM is associated with a nearly threefold risk of death from cardiovascular disease<sup>94</sup>. Both the overall death rate and death rates from cardiovascular disease are greatly increased in subjects with NIDDM and microalbuminuria<sup>95,109-112</sup>. Survival over 10 years in 407 subjects with NIDDM, according to the level of urinary albumin concentration at the baseline examination, is shown in Figure 16.15<sup>113</sup>. Significant reduction in survival was found in subjects whose urinary albumin excretion, although elevated, was below that detected

**Figure 16.14**  
**Cumulative Incidence of Proteinuria, by Duration of Diabetes**

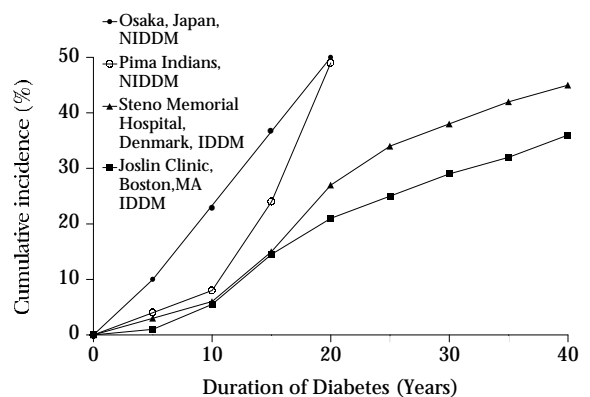
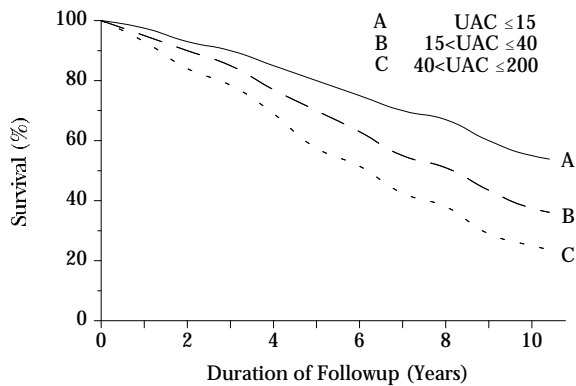


Figure shows cumulative incidence in Japanese subjects and Pima Indians with NIDDM and in two studies of white subjects with IDDM. The incidence in subjects with NIDDM was higher through 20 years of diabetes than in those with IDDM.

Source: Reference 108

**Figure 16.15**  
Survival in NIDDM Patients, by UAC



UAC, urinary albumin concentration. Figure shows 10-year survival by baseline UAC ( $\mu\text{g/ml}$ ) after correction for age, duration of diabetes, and serum creatinine concentration by a Cox regression analysis. Higher UAC at the baseline examination was associated with lower survival over the 10-year period.

Source: Reference 113

**Figure 16.17**  
Mortality in Pima Indians Age  $\geq 45$  Years, by Diabetes and Proteinuria Status

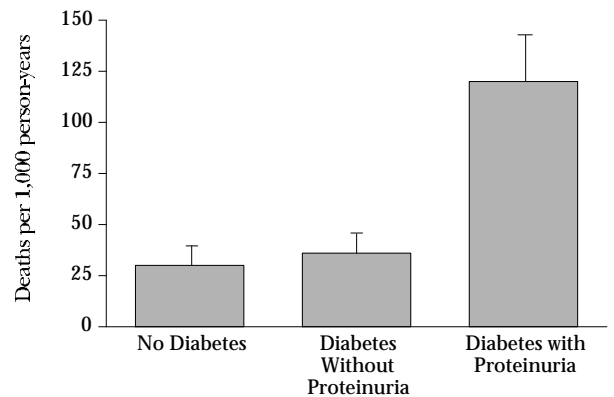


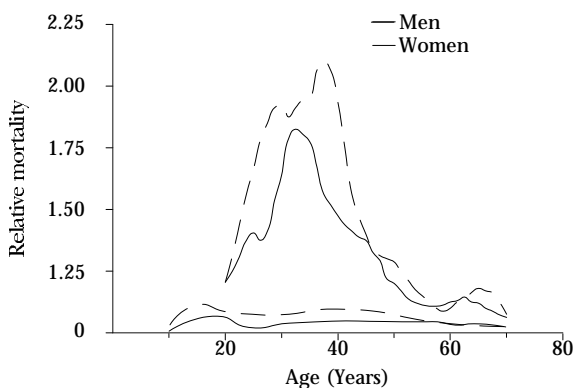
Figure shows age- and sex-adjusted death rates and standard errors for Pima Indians age  $\geq 45$  years for nondiabetic subjects without proteinuria and for diabetic subjects without and with proteinuria.

Source: Reference 115

by the usual dipstick methods.

Microalbuminuria also predicts the development of proteinuria in IDDM and NIDDM<sup>83,91-98</sup>, and mortality in patients with persistent proteinuria is very high<sup>99,114-117</sup>. Figure 16.16 shows the death rates in proteinuric ( $>0.5$  g/day) and nonproteinuric IDDM subjects relative to the nondiabetic population as a function of age, and Figure 16.17 shows the age-sex adjusted death rates in nondiabetic Pima Indians

**Figure 16.16**  
Relative Mortality in IDDM Patients, by Proteinuria, Age, and Sex



Relative mortality is calculated as mortality in IDDM patients divided by mortality in the nondiabetic population. Relative mortality for those with persistent proteinuria is shown in the upper curves and for those without proteinuria in the lower curves, as a function of current age.

Source: Reference 114

without proteinuria and in those with NIDDM according to the presence or absence of proteinuria (protein-to-creatinine ratio  $\geq 1.0$  g/g). Nearly all of the excess mortality associated with either type of diabetes is found in persons with proteinuria<sup>99,114,115</sup>, primarily from renal or cardiovascular disease in IDDM<sup>114,116</sup>; from cardiovascular disease in whites with NIDDM<sup>117</sup>, and from cardiovascular or renal disease in Pima Indians with NIDDM<sup>115</sup>.

## END-STAGE RENAL DISEASE

Clinical proteinuria in IDDM heralds a relentless decline of renal function that often leads to ESRD, but the decline of renal function may be slower in NIDDM. For example, the cumulative incidence of chronic renal failure in whites after 10 years of persistent proteinuria was 11% in patients with NIDDM in Rochester, MN<sup>118</sup> but was 50% in patients with IDDM at the Joslin Clinic in Boston, MA<sup>100</sup>. These differences are probably due mainly to the fact that in many populations NIDDM develops much later in life and the risk of death from nonrenal causes is much higher than in patients with IDDM of similar duration. Furthermore, a greater frequency of proteinuria of nondiabetic origin that may not lead to ESRD occurs in persons with NIDDM<sup>5</sup>. Among Pima Indians, in whom NIDDM often develops at a younger age than in other populations<sup>119</sup>, the cumulative incidence of ESRD after the diagnosis of proteinuria more closely resembles that in IDDM<sup>120</sup>.

Data for 93% of patients receiving treatment for ESRD in the United States are reported to the Health Care Financing Administration<sup>121</sup>. Consequently, reasonable estimates of the frequency of treated ESRD are available. Table 16.3 summarizes the prevalence, according to treatment modality, and incidence of treated ESRD in the United States in 1991<sup>121</sup>. In that year, 186,261 patients were receiving renal replacement therapy, of whom 48,274 (26%) of the prevalent cases had renal disease attributed to diabetes. The proportion of patients with treated diabetic ESRD has doubled from the 13% of total cases in 1982 (Table 16.4). On average, the prevalence of diabetic enrollees

has increased by nearly 16% annually and this category makes up the most rapidly growing group of patients in this program (Figure 16.18)<sup>121</sup>. Recent growth in the incidence of treated diabetic ESRD and improved survival among diabetic patients, who had almost twofold greater mortality than patients with other diagnoses in the mid-1980s, have contributed to the increase in the prevalence of diabetic ESRD<sup>121</sup>.

The annual number of new cases of renal replacement therapy for ESRD has risen substantially over the past decade, with the most rapid rise in the nonwhite population, as shown in Figure 16.19. In addition, the

**Table 16.3**  
**Summary Statistics on Reported ESRD Therapy, U.S., 1991**

| Patient characteristic | Incidence     |                | December 31 point prevalence |                |                     |               | Medicare kidney transplants performed by donor type |              |               |
|------------------------|---------------|----------------|------------------------------|----------------|---------------------|---------------|---|--------------|---------------|
|                        | Count*        | Adjusted rate† | Count*                       | Adjusted rate† | Counts by modality‡ |               | CAD   | LRD          | Deaths§       |
|                        |               |                |                              |                | Dialysis            | Transplant    |   |              |               |
| <b>Age (years)**</b>   |               |                |                              |                |                     |               |   |              |               |
| 0-19                   | 822           | 11             | 4,113                        | 55             | 1,629               | 2,544         | 321   | 350          | 97            |
| 20-44                  | 9,635         | 96             | 56,397                       | 557            | 29,850              | 27,199        | 3,779   | 1,288        | 3,302         |
| 45-64                  | 16,925        | 392            | 69,002                       | 1,576          | 51,627              | 18,496        | 2,695   | 464          | 9,860         |
| 65-74                  | 13,901        | 846            | 37,257                       | 2,292          | 35,565              | 2,122         | 304   | 20           | 11,166        |
| ≥75                    | 8,626         | 725            | 19,492                       | 1,643          | 19,606              | 107           | 5   | 0            | 8,808         |
| <b>Race</b>            |               |                |                              |                |                     |               |   |              |               |
| White                  | 33,337        | 150            | 120,707                      | 547            | 82,212              | 40,455        | 5,195   | 1,765        | 23,092        |
| Black                  | 14,211        | 595            | 56,508                       | 2,298          | 48,977              | 7,829         | 1,574   | 281          | 8,849         |
| Asian/Pacific          |               |                |                              |                |                     |               |   |              |               |
| Islander               | 1,023         | 205            | 3,885                        | 686            | 2,897               | 1,078         | 202   | 33           | 472           |
| Native American        | 619           | 464            | 2,272                        | 1,571          | 1,748               | 534           | 76  | 30           | 351           |
| Other                  | 631           |                | 2,364                        |                | 2,443               | 572           | 49  | 13           | 348           |
| Unknown                | 88            |                | 525                          |                |                     |               | 8   | 0            | 121           |
| <b>Sex</b>             |               |                |                              |                |                     |               |   |              |               |
| Male                   | 26,839        | 239            | 101,069                      | 860            | 72,063              | 30,539        | 4,341   | 1,205        | 17,763        |
| Female                 | 23,070        | 162            | 85,192                       | 607            | 66,214              | 19,929        | 2,763   | 917          | 15,470        |
| <b>Primary disease</b> |               |                |                              |                |                     |               |   |              |               |
| Diabetes               | 17,888        | 70             | 48,274                       | 188            | 39,997              | 9,072         | 1,623   | 453          | 11,361        |
| Hypertension           | 14,495        | 57             | 43,724                       | 171            | 38,486              | 5,625         | 1,092   | 204          | 9,987         |
| Glomerulonephritis     | 5,782         | 23             | 34,329                       | 134            | 20,813              | 14,110        | 1,804   | 591          | 3,509         |
| Cystic kidney disease  | 1,456         | 6              | 9,244                        | 36             | 5,641               | 3,679         | 582   | 104          | 773           |
| Urologic diseases      | 2,449         | 10             | 11,478                       | 45             | 7,952               | 3,668         | 423   | 172          | 1,797         |
| Other known cause      | 3,306         | 13             | 11,370                       | 44             | 7,696               | 3,757         | 480   | 248          | 1,864         |
| Unknown cause          | 2,651         | 10             | 12,312                       | 48             | 8,604               | 3,858         | 507   | 139          | 2,090         |
| Missing data           | 1,882         | 6              | 15,530                       | 55             | 9,088               | 6,699         | 593   | 211          | 1,852         |
| <b>Total</b>           | <b>49,909</b> | <b>195</b>     | <b>186,261</b>               | <b>721</b>     | <b>138,277</b>      | <b>50,468</b> | <b>7,104</b>  | <b>2,122</b> | <b>33,233</b> |

ESRD, end-stage renal disease; CAD, cadaver donor transplant; LRD, living-related donor transplant. \* Incidence count = number of new patients starting renal replacement therapy during 1991. Incidence and prevalence counts and rates include residents of the 50 states and the District of Columbia only. All other data in this table include residents of Puerto Rico and U.S. territories. † Rates are adjusted for age, race, and/or sex using the July 1, 1990, U.S. resident population as the standard population. All rates are per million population. Rates by age were adjusted for race and sex. Rates by sex were adjusted for race and age. Rates by race were adjusted for age and sex. Rates by disease group and total adjusted rate were adjusted for age, race, and sex. Adjusted rates do not include patients with other or unknown race. ‡ Patients were classified as receiving dialysis or having a functioning transplant. Those with unknown treatment modality on December 31 were assumed to be receiving dialysis. § Number of deaths among patients reported to have ESRD in 1991. \*\* Age was computed at start of therapy for incidence, on December 31 for point prevalence, at time of transplant for transplants, and on date of death for deaths.

Source: Reference 121

**Table 16.4**  
**Point Prevalence of Reported ESRD Therapy, U.S., 1982-91**

| Year | Total patients |        | Diabetes as primary diagnosis |
|------|----------------|--------|-------------------------------|
|      | No.            | No.    | Percent of total              |
| 1982 | 69,721         | 9,043  | 13.0                          |
| 1983 | 81,646         | 11,871 | 14.5                          |
| 1984 | 91,887         | 15,117 | 16.5                          |
| 1985 | 101,793        | 18,376 | 18.1                          |
| 1986 | 112,296        | 21,852 | 19.5                          |
| 1987 | 123,558        | 25,424 | 20.6                          |
| 1988 | 134,872        | 29,294 | 21.7                          |
| 1989 | 148,769        | 34,731 | 23.3                          |
| 1990 | 166,281        | 40,972 | 24.6                          |
| 1991 | 186,261        | 48,274 | 25.9                          |

ESRD, end-stage renal disease. A substantial number of patients with ESRD had no primary diagnosis listed, and some of these may have had diabetic ESRD. For example, in 1982, 25% of patients had missing diagnoses; this declined to 10% in 1991. In addition, a number of patients who entered the Medicare ESRD program during the year were lost to followup and are not included in this table, which lists only known patients who were alive on December 31 of each year. In 1982, the number lost to followup was 12,881; in 1991, the number was 10,408.

Source: Reference 121

proportion of new cases attributed to diabetes has risen from 23% to 36% during the same period (Figure 16.20)<sup>121</sup>. Diabetes is now the largest single cause of new cases of ESRD in the United States (Figure 16.21), and a majority of the new cases attributed to diabetes are in persons with NIDDM<sup>118,122</sup>. In 1982, 4,960 patients with diabetes began renal replacement therapy, and the number increased to 17,888 in 1991.

**Figure 16.18**  
**Percent Annual Increase in Point Prevalence of Reported ESRD, by Primary Diagnosis, U.S., 1987-91**

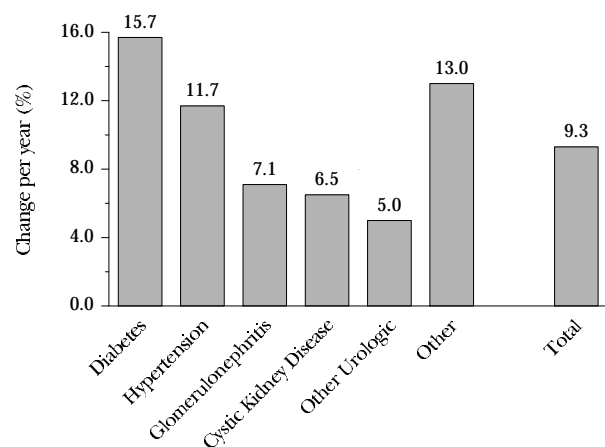
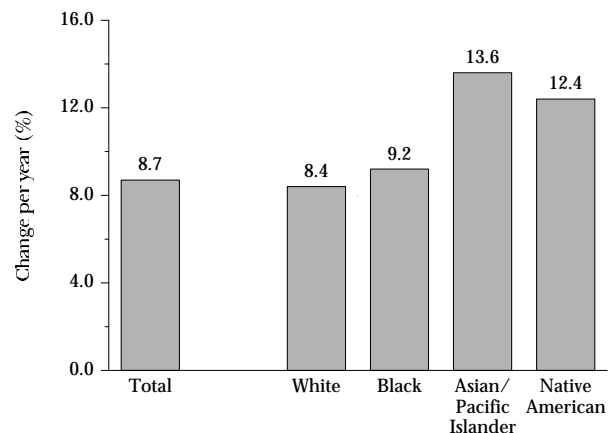


Figure shows annual compound rate of change; incidence rates are adjusted for age, sex, and race. Rates are for Medicare patients only and do not include patients from Puerto Rico or U.S. territories.

Source: Reference 121

**Figure 16.19**  
**Annual Change in Incidence of Treated ESRD, by Race, U.S., 1986-91**



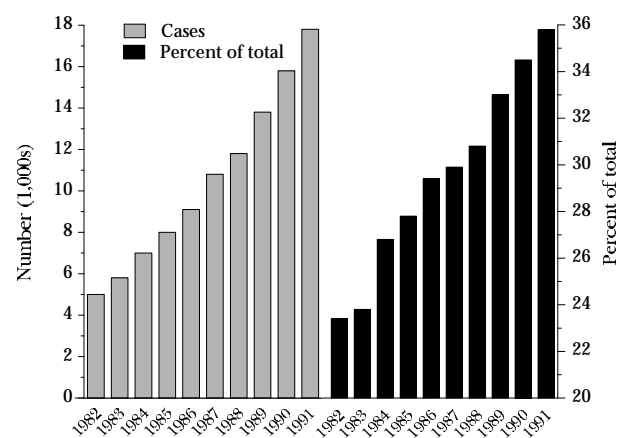
ESRD, end-stage renal disease. Annual change was calculated as the percent annual compound rate of change; total rate was adjusted for age, race, and sex; rates by race were adjusted for sex and age. Rates are for Medicare patients only and do not include patients from Puerto Rico or U.S. territories.

Source: Reference 121

Changing criteria for initiation of renal replacement therapy may contribute to the rising rate of treated ESRD in persons with diabetes.

Incidence rates of treated ESRD in diabetic patients vary by racial group (Table 16.5) and type of diabetes (Table 16.6)<sup>122-129</sup>. Racial differences in the incidence of ESRD in persons with NIDDM are almost certainly

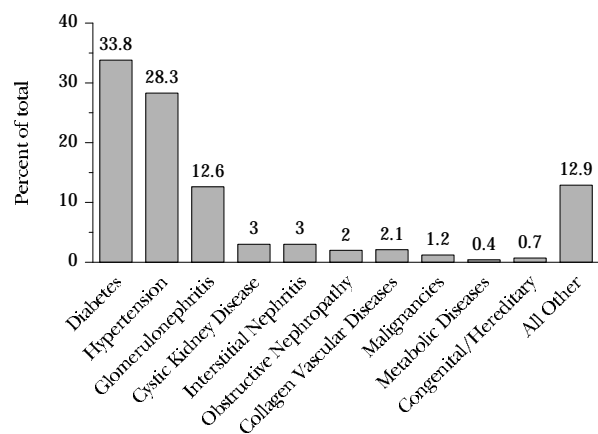
**Figure 16.20**  
**Time Trends in Incidence of Diabetic ESRD, U.S., 1982-91**



ESRD, end-stage renal disease. Figure shows number of new diabetic patients enrolled in the Medicare ESRD program and proportion of new enrollees with ESRD attributed to diabetes.

Source: Reference 121

**Figure 16.21**  
**Percent Distribution of New Cases of Treated ESRD, by Primary Diagnosis, U.S., 1988-91**



ESRD, end-stage renal disease. Data are for Medicare patients only.

Source: Reference 121

attributable in part to differences in the duration of diabetes. The incidence attributed to NIDDM is higher in blacks<sup>122,126</sup>, Mexican Americans<sup>127</sup>, Asians<sup>128</sup>, Pima Indians<sup>123</sup>, and other Native Americans<sup>129</sup> than in whites, with the highest rates being found in Native Americans. Data on racial differences in IDDM are sparse, and because many patients with NIDDM are treated with insulin, they are often misclassified as IDDM. For example, a study in which the type of diabetes was not verified reported that the incidence of ESRD in blacks with IDDM was 3.0 times the incidence in whites<sup>126</sup>. However, another study in which the type of diabetes was confirmed by review of

**Table 16.5**  
**Number of New Cases of ESRD, Percent Due to Diabetes, and Incidence of ESRD, by Race, U.S., 1989-91**

| Race            | No. of new cases per year | Percent of total | Percent due to diabetes | Adjusted total incidence of ESRD per million population |
|-----------------|---------------------------|------------------|-------------------------|---|
| White           | 30,739                    | 67.9             | 34.6                    | 140   |
| Black           | 13,043                    | 28.8             | 33.3                    | 550   |
| Asian/Pacific   |                           |                  |                         |   |
| Islander        | 924                       | 2.0              | 37.2                    | 186   |
| Native American | 573                       | 1.3              | 64.0                    | 437   |
| Total           | 45,279                    | 100.0            | 34.7                    | 181   |

ESRD, end-stage renal disease. Incidence rates are adjusted for age, sex, and race.

Source: Reference 121

**Table 16.6**  
**Incidence of ESRD in Diabetic Subjects, by Race and Type of Diabetes, Michigan, 1974-83**

|        | Average annual number of cases per 100,000 persons with diabetes |
|--------|--|
| IDDM   |  |
| Whites | 35   |
| Blacks | 36   |
| NIDDM  |  |
| Whites | 25   |
| Blacks | 108  |

Source: Reference 122

all available clinical records found that the incidence of ESRD in blacks and whites with IDDM was indistinguishable (Table 16.6)<sup>122</sup>.

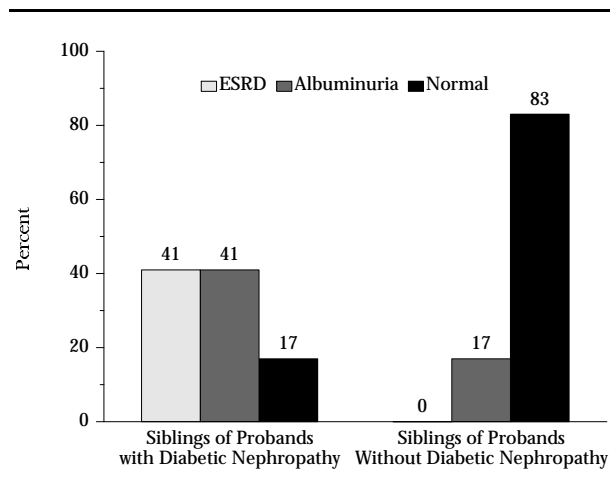
## RISK FACTORS FOR DIABETIC RENAL DISEASE

Duration of diabetes is one of the most important risk factors for diabetic nephropathy. The influence of duration is far greater than that of age, sex, or type of diabetes. For a given duration of diabetes, the cumulative incidence of diabetic nephropathy and ESRD are similar in IDDM and NIDDM<sup>118,123,130,131</sup>. Despite long duration of diabetes, only 30%-50% of patients with IDDM develop diabetic nephropathy<sup>99,100</sup>. Therefore, factors other than diabetes itself have been suggested as determinants of diabetic renal disease. In this section, other factors that influence the risk for diabetic renal disease are reviewed.

### ■ Familial and Genetic Factors

Supporting a role for genetic susceptibility in the development of diabetic renal disease are three studies that report familial clustering<sup>132-134</sup>. In one study, nephropathy was reported in 83% of the diabetic siblings of IDDM patients with nephropathy but in only 17% of the diabetic siblings of patients without nephropathy (Figure 16.22)<sup>132</sup>. Moreover, 41% of the affected siblings of patients with nephropathy had ESRD. A similar study found nephropathy in 33% of the diabetic siblings of diabetic patients with nephropathy but in only 10% of the diabetic siblings of patients without nephropathy<sup>133</sup>. Familial clustering is also found in NIDDM. In two generations of Pima Indians with NIDDM<sup>134</sup>, the frequency of proteinuria in the diabetic offspring was higher if both diabetic parents had proteinuria than if neither did, and if one parent had proteinuria, the prevalence was intermediate (Figure 16.23).

**Figure 16.22**  
**Renal Status of Siblings, by Diabetic Nephropathy of IDDM Probands**

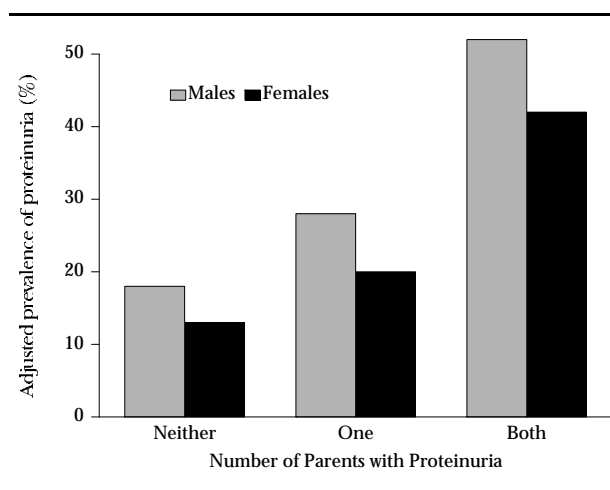


ESRD, end-stage renal disease. Siblings are categorized as those with ESRD, those with albuminuria (albumin excretion rates  $\geq 45$  mg/24 hours), and those with normal urinary albumin excretion ( $< 45$  mg/24 hours). The siblings of IDDM probands who were free of diabetic nephropathy ( $n=12$ ) had less evidence of renal disease than did the siblings of probands who had diabetic nephropathy ( $n=29$ ) ( $p<0.001$ ).

Source: Reference 132

Some reports have suggested that there is no convincing evidence that genetic factors are involved in the pathogenesis of diabetic renal disease<sup>135,136</sup>, but others have found differences in the distribution of HLA markers between IDDM patients with diabetic nephropathy and those with normal renal function<sup>137</sup>. In

**Figure 16.23**  
**Prevalence of Proteinuria in Offspring, by Sex and Number of Parents with Proteinuria**



Data are adjusted for age, systolic blood pressure, diabetes duration, and glucose concentration. Prevalence of proteinuria in offspring was significantly higher if both parents had proteinuria than if neither parent did; prevalence was intermediate if one parent had proteinuria.

Source: Reference 134

addition, both the major histocompatibility complex and the Gm loci have been associated with diabetic microvascular disease<sup>138</sup>, and the presence of diabetic nephropathy in IDDM has been related to DNA sequence differences in the angiotensin I-converting enzyme gene<sup>139</sup>. Although these findings are not universal<sup>140,141</sup>, they do suggest that genetic factors may predispose some individuals to a higher risk of diabetic nephropathy than others.

## ■ Hypertension

High blood pressure has been related to diabetic renal disease in many cross-sectional and longitudinal studies of both IDDM and NIDDM. To some extent, this relationship reflects elevation of blood pressure in response to the renal disease<sup>142,143</sup>, but several lines of evidence suggest that blood pressure contributes not only to the progression of renal disease but to its pathogenesis as well.

Sodium-lithium countertransport activity in red cells, a genetically influenced trait, is found in some studies to be higher in persons with essential hypertension and in those whose parents have essential hypertension<sup>144-147</sup>. In IDDM, elevated rates of countertransport activity are reported in persons with microalbuminuria or proteinuria and in those with elevated GFR<sup>148-152</sup>, suggesting that diabetic persons with hypertension and with elevated sodium-lithium countertransport activity are at greater risk for diabetic renal disease, although these findings and conclusions have been challenged<sup>152-154</sup>.

Parental hypertension is associated with renal disease in diabetic offspring<sup>148,155,156</sup>. Figure 16.24 shows the mean blood pressure in the parent with the higher blood pressure according to the presence or absence of proteinuria in offspring with IDDM. Parents of offspring with proteinuria had significantly higher mean blood pressure than those of offspring with normal urinary protein excretion<sup>155</sup>.

Patients with IDDM and diabetic nephropathy not only have a greater prevalence of parental hypertension but also have higher mean arterial pressures during adolescence<sup>156</sup>. The Microalbuminuric Collaborative Study Group<sup>157</sup> reported that blood pressure rises concomitantly with a rise in urinary albumin excretion in IDDM patients and that blood pressure elevation took place while the albumin excretion was rising within the normal range. Studies in Pima Indians revealed that high blood pressure before the onset of NIDDM was related to a higher prevalence of elevated urinary albumin excretion after the onset of NIDDM (Figure 16.25)<sup>158</sup>. These findings suggest a possible

**Figure 16.24**  
**Mean Blood Pressure in Parents of Proteinuric and Nonproteinuric Diabetic Patients**

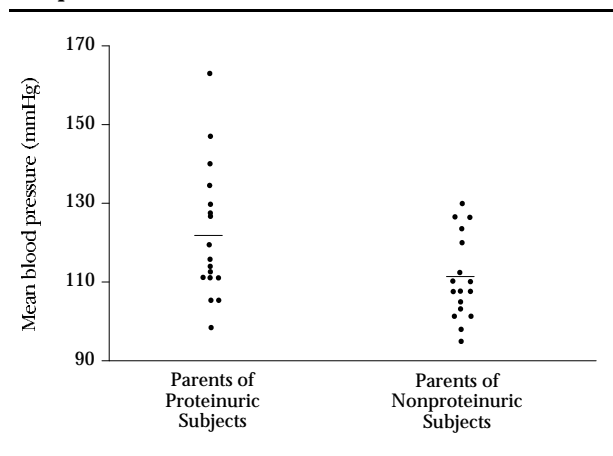


Figure shows mean blood pressure in the parent with higher arterial pressure of 17 proteinuric and 17 nonproteinuric diabetic patients; horizontal lines are means. Mean blood pressure of parents of proteinuric subjects averaged 11 mmHg (95% confidence interval, 1.7-20.3 mmHg) higher than in parents of diabetic subjects without proteinuria.

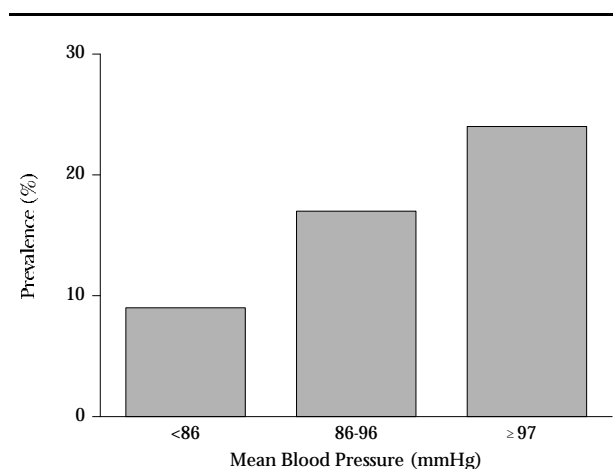
Source: Reference 155

causal role for blood pressure in the development of diabetic renal disease.

## ■ Hyperglycemia

The level of glycemic control is a major risk factor for elevated urinary albumin excretion and clinical prote-

**Figure 16.25**  
**Prevalence of Elevated UAE in Pima Indians After Diagnosis of NIDDM, by Blood Pressure Before Onset of NIDDM**



UAE, urinary albumin excretion. Figure shows prevalence (%) of elevated UAE (albumin-to-creatinine ratio  $\geq 100$  mg albumin/g creatinine). Pima Indians with the highest prediabetic blood pressure had the highest prevalence of elevated UAE after onset of diabetes.

Source: Reference 158

inuria in diabetes<sup>89,100,101,105-107,118,159-165</sup>. The relative risk of developing proteinuria ( $\geq 0.30$  g/L) after 4 years in subjects with IDDM in Wisconsin was three times as high for those with glycosylated hemoglobin in the highest quartile compared with those in the lowest quartile (Figure 16.26)<sup>101</sup>. Similarly, higher 2-hour post-load plasma glucose concentration in Pima Indians at diagnosis of NIDDM was associated with a higher incidence of proteinuria (Figure 16.27)<sup>107</sup>. Hyperglycemia also predicts the development of elevated urinary albumin excretion within the microalbuminuric range in both types of diabetes<sup>159,161</sup>.

A number of biochemical pathways affected by hyperglycemia may be responsible for many of the functional and structural abnormalities characterizing diabetic renal disease<sup>165</sup>. Hyperglycemia is associated with hyperfiltration, both in the early stages of diabetes before urinary albumin excretion becomes elevated<sup>48,166</sup> and in patients with overt diabetic nephropathy<sup>167,168</sup>. The rise in GFR may be mediated by changes in the permeability of the glomerular membrane<sup>167</sup> and by renal prostaglandin production<sup>168</sup>. Thus, several potential mechanisms have been identified by which hyperglycemia could lead to the development of diabetic renal disease.

## ■ Plasma Prorenin Activity

Prorenin is the precursor of renin, which is secreted into the blood by the juxtaglomerular cells of the

**Figure 16.26**  
**Four-Year Incidence of Proteinuria in IDDM, by Glycosylated Hemoglobin Level**

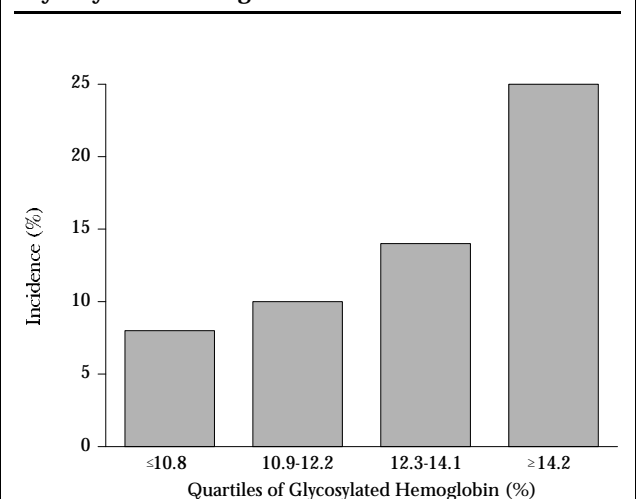


Figure shows incidence (%) of proteinuria ( $\geq 0.30$  g/L) after 4 years in 891 subjects from Wisconsin with IDDM (insulin-taking, diabetes onset at age <30 years) according to quartiles of glycosylated hemoglobin at baseline examination.

Source: Reference 101

Figure 16.27

**Incidence of Proteinuria in Pima Indians with NIDDM, by 2-Hour Post-Load Glucose and Diabetes Duration**

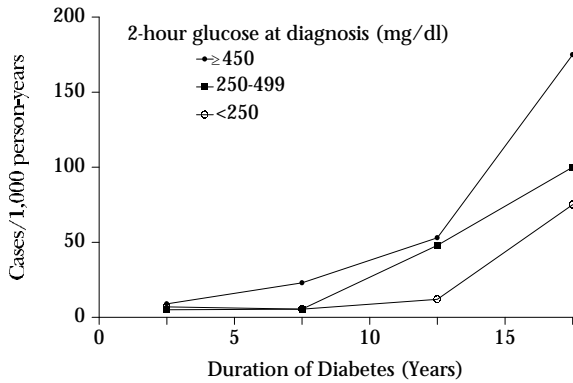


Figure shows incidence (cases/1000 person-years) of proteinuria (protein-to-creatinine ratio  $\geq 1.0$  g/g) by duration of diabetes in 480 Pima Indians with NIDDM, according to tertiles of 2-hour plasma glucose concentration after 75 g oral glucose, measured at diagnosis of NIDDM.

Source: Reference 107

kidneys and is converted ultimately to angiotensin II. Increased plasma prorenin activity is associated with the microvascular complications of diabetes<sup>169,170</sup>. Furthermore, an increase in prorenin activity precedes the development of these complications in children with IDDM<sup>171</sup>. The role of plasma prorenin in the pathogenesis of diabetic nephropathy, however, is unknown.

### ■ Lipids

Although it is generally assumed that many of the abnormalities in plasma lipoproteins associated with renal disease are sequelae of the renal dysfunction, hyperlipidemia may also play a role in the pathogenesis of glomerular injury<sup>172,173</sup>. Higher LDL cholesterol and triglyceride levels in IDDM<sup>159</sup> and higher total serum cholesterol concentration in NIDDM<sup>161</sup> predict the development of elevated urinary albumin excretion. In addition, among patients with IDDM and diabetic nephropathy, the rate of decline in GFR is lower in subjects with low serum cholesterol concentration than in those with high concentrations (Table 16.7), suggesting that higher cholesterol promotes the progression of renal disease<sup>174</sup>. Alternatively, the higher cholesterol concentration may simply reflect a more advanced stage of glomerulosclerosis. Studies in experimental animals have shown that glomerulosclerosis can be induced by a diet enriched with saturated fats and cholesterol<sup>175</sup>, and altered glomerular hemodynamics induced by the lipid-rich diet may be responsible<sup>175,176</sup>. Nevertheless, a definitive role for

Table 16.7

**Rate of Decline of GFR in Diabetic Patients, by Serum Cholesterol Concentration**

|  | Serum cholesterol (mmol/L) |                |
|--|----------------------------|----------------|
|  | $\leq 7$                   | $> 7$          |
| Number of patients                     | 17                         | 14             |
| Decline in GFR (ml/min/year)           | 2.3 $\pm$ 6.3              | 8.4 $\pm$ 5.3* |
| Urinary albumin excretion (g/24 hours) | 1.3 $\pm$ 0.9              | 1.5 $\pm$ 1.1  |
| Mean arterial pressure (mmHg)          | 102 $\pm$ 4                | 105 $\pm$ 3†   |
| Hemoglobin A <sub>1c</sub> (%)         | 8.8 $\pm$ 2.0              | 9.8 $\pm$ 1.8  |
| Enalapril/metoprolol treated           | 11/6                       | 8/6            |

\*p<0.01, †p<0.05. GFR, glomerular filtration rate. Values are means $\pm$ SD. All patients (n=31) had diabetic nephropathy and reduced renal function and are divided in the figure according to mean cholesterol concentration during the observation period. GFR declined more rapidly among those with higher serum cholesterol concentration, suggesting that either higher cholesterol promotes the progression of renal disease or may simply reflect a more advanced stage of glomerulosclerosis.

Source: Reference 174

hyperlipidemia in the development and progression of diabetic renal disease in humans remains to be established.

### ■ Autonomic Neuropathy

Autonomic neuropathy has been proposed as a predictor of deteriorating GFR in patients with IDDM<sup>177,178</sup>. Sympathetic neuropathy with ensuing alteration of vascular resistance in glomeruli has been suggested as the basis for the more rapid deterioration of renal function in patients with autonomic neuropathy<sup>178</sup>. Whether autonomic neuropathy per se is part of the pathogenetic process leading to diabetic renal disease or is a reflection of the severity of diabetes is unknown. Nonetheless, the two complications of diabetes occur together frequently. One study reported that half of the deaths of patients with IDDM and autonomic neuropathy are attributed to diabetic nephropathy<sup>179</sup>.

### ■ Pregnancy

Among women with normal kidney function, regardless of the presence or absence of diabetes, pregnancy is associated with a transient rise in GFR of 40%-60% that is accompanied by a moderate increase in urinary protein excretion<sup>180</sup>. By contrast, women with preexisting diabetic nephropathy may have a dramatic increase in proteinuria from the first to the third trimester, which often returns to prepregnancy levels after delivery<sup>181,182</sup>, suggesting that in most of them, pregnancy does not hasten the progression of diabetic



nephropathy<sup>183</sup>. Nevertheless, pregnancy may accelerate the rate of renal disease progression in some diabetic women. Among women with diabetic nephropathy who also have hypertension and impaired renal function (creatinine clearance <80 ml/min), pregnancy hastens the onset of ESRD<sup>184</sup>. Thus, although pregnancy does not affect adversely the course of early diabetic renal disease, women with more severe impairment, particularly those with hypertension, may be at greater risk of progression.

## ■ Diet

There is no clear evidence that dietary protein intake has any influence on the development of diabetic renal disease. No correlation was found between dietary protein intake and clinical proteinuria in a cross-sectional study of patients with NIDDM who were divided into high-, moderate-, and low-protein intake groups (Table 16.8)<sup>185</sup>. Indeed, although not statistically significant, the proportion of subjects with proteinuria was highest in those with the lowest protein intake. Similarly, no correlation was found between dietary protein intake and rate of decline in renal function in patients with IDDM<sup>186</sup>, and one study suggested that there was even a tendency for patients with the highest protein intake to have the lowest rate of decline in GFR (Figure 16.28)<sup>187</sup>. Nevertheless, excessive protein intake is thought to cause renal vasodilation and glomerular hyperperfusion. The resulting increase in the intraglomerular pressure is believed to precipitate proteinuria and glomerular damage in animals<sup>188,189</sup>, and experimental models of renal disease suggest that long-term high protein diets accelerate structural and functional injury, whereas

Table 16.8

### Proportion of Subjects with Diabetes Who Have Clinical Proteinuria, by Level of Dietary Protein Intake

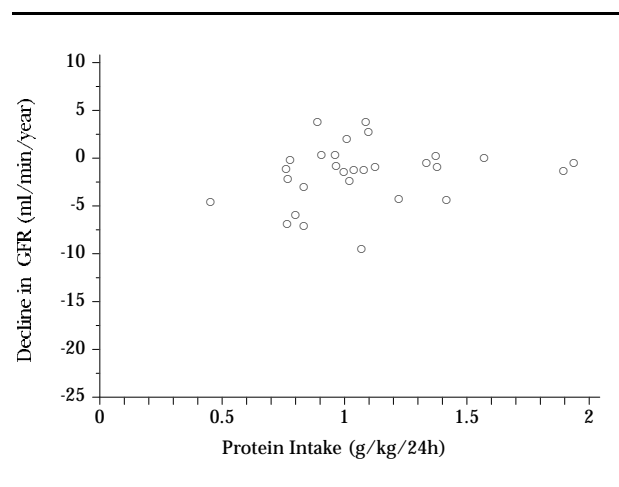
| Protein intake | Proteinuria  |                    | Total (n) | Proteinuria (%) |
|----------------|--------------|--------------------|-----------|-----------------|
|                | Positive (n) | Negative/trace (n) |           |                 |
| High           | 9            | 55                 | 64        | 14.1            |
| Moderate       | 43           | 240                | 283       | 15.2            |
| Low            | 6            | 23                 | 29        | 20.7            |
| Total          | 58           | 318                | 376       | 15.4            |

Subjects were stratified by their protein intake into high (mean protein intake >130 g/day for men and >86 g/day for women), moderate (mean protein intake 42-130 g/day for men and 28-86 g/day for women), and low (mean protein intake <42 g/day for men and <28 g/day for women). Proteinuria was defined by a dipstick test of  $\geq 1$ . The prevalence of proteinuria was not significantly related to the level of dietary protein intake ( $\chi^2=0.492$ ,  $p=0.48$ ), but those who reported the highest intake of protein tended to have the lowest prevalence of proteinuria.

Source: Reference 185

Figure 16.28

### Correlation Between Protein Intake and Decline in GFR in IDDM Patients



GFR, glomerular filtration rate. Figure shows correlation between protein intake (g/kg/24 hours) and decline in GFR (ml/min/year) in 34 patients with IDDM ( $r_s=0.43$ ,  $p=0.025$ ). Subjects reporting the lowest protein intake had the greatest decline in GFR.

Source: Reference 187

low-protein diets offer renoprotection<sup>190-192</sup>. Thus, although a theoretical case can be made for the impact of dietary protein on the development of diabetic renal disease, there are no observational data in humans to support such a role. On the other hand, a number of clinical interventions have reported beneficial effects of dietary protein restriction in persons with diabetes (see below).

## ■ Smoking

Smoking is associated with the progression of diabetic nephropathy in IDDM<sup>86,158,193-199</sup>, but no relationship was reported in patients with diabetes diagnosed at age  $\geq 30$  years<sup>89</sup>. In one study, patients with IDDM who smoked had twice the frequency of proteinuria ( $\geq 500$  mg/24 hours) of those who did not (Table 16.9)<sup>195</sup>. The smokers and nonsmokers were similar with regard to age, duration of diabetes, glycosylated hemoglobin, and prevalence of hypertension. Another study found that smoking was the most important risk factor for progression of both microalbuminuria and clinical diabetic nephropathy during a 1-year followup in IDDM patients already receiving intensified insulin and antihypertensive treatment<sup>199</sup>. In addition, one author noted that most patients with IDDM and ESRD in his study were either current or ex-smokers<sup>197</sup>. Although the precise mechanisms are unclear, tobacco smoking is known to cause vasoconstriction, impair platelets and coagulation, and alter blood pressure<sup>200,201</sup>. Given that patients with diabetes already incur widespread vascular damage as a consequence

Table 16.9

**Clinical Data and Prevalence of Proteinuria in IDDM Patients, by Smoking Status**

|                   | No. | Age (years) | Duration of diabetes (years) | HbA1c (%) | Hypertension (%) | Proteinuria (%) |
|-------------------|-----|-------------|------------------------------|-----------|------------------|-----------------|
| <b>Smokers</b>    |     |             |                              |           |                  |                 |
| Women             | 90  | 30±11       | 14±6                         | 7.9±1.6   | 11.1 (20.0)      | 14.4*           |
| Men               | 102 | 34±12       | 14±6                         | 8.4±2.2   | 14.7 (38.2)      | 23.5†           |
| Total             | 192 | 32±11       | 14±6                         | 8.2±1.9   | 13.0 (29.7)      | 19.3‡           |
| <b>Nonsmokers</b> |     |             |                              |           |                  |                 |
| Women             | 90  | 30±11       | 14±6                         | 8.3±2.2   | 7.8 (22.2)       | 5.6             |
| Men               | 102 | 33±11       | 14±6                         | 7.9±1.7   | 15.7 (34.3)      | 10.8            |
| Total             | 192 | 32±11       | 14±6                         | 8.1±2.0   | 12.0 (28.6)      | 8.3             |

Participants were recruited from an inpatient diabetes treatment and teaching program. Data for age, duration of diabetes, and HbA1c are mean±SD. Hypertension is defined as blood pressure values ≥165/95 mmHg or use of antihypertensive medication (percentages in parentheses are the prevalence of hypertension defined as blood pressure values ≥140/90 mmHg or use of antihypertensive medication). \*p<0.025. †p<0.01, ‡p<0.001, compared with nonsmoking group. Subjects who smoked had twice the prevalence of proteinuria (≥500 mg/24 hours) of nonsmokers.

Source: Reference 195

of their diabetes<sup>202</sup>, smoking may serve to accelerate the process. Reasons for a lack of association in NIDDM are unknown.

**Drug Nephrotoxicity**

Analgesic and nonsteroidal anti-inflammatory drugs, including aspirin, are used extensively in the United States<sup>203</sup>. Cumulative toxicity from prolonged exposure to these drugs has been proposed as a possible cause of chronic renal disease<sup>204,205</sup>. In the case of nonsteroidal anti-inflammatory drugs, changes in renal blood flow due to inhibition of prostaglandin synthesis may be responsible. Renal perfusion in persons with renal insufficiency is maintained, in part, by the local synthesis of vasodilating prostaglandins<sup>205-208</sup>. Tubulointerstitial changes associated with analgesic use may also influence the progression of a number of renal diseases<sup>209</sup>.

In a multicenter case-control study<sup>210</sup>, nonaspirin nonsteroidal anti-inflammatory drug use was associated with a twofold risk of chronic renal disease (serum creatinine concentration ≥1.5 mg/dl) (Table 16.10). The increased risk, however, was almost entirely confined to men, those age ≥65 years were at the greatest risk, and only 20% of the cases of renal disease in the study were attributed to diabetes. In another case-control study, involving 242 patients with diabetes, neither aspirin nor other nonsteroidal anti-inflammatory drugs significantly increased the odds of ESRD (Table 16.11)<sup>205</sup>. These studies suggest that nonsteroidal anti-inflammatory drugs, including aspirin, may have little effect on the progression of renal disease in diabetes. On the other hand, acetaminophen use increased the odds of ESRD in patients with

diabetic nephropathy<sup>205</sup>. Annual intakes of 105-365 acetaminophen pills doubled the odds of ESRD in 242 patients with diabetes, and a cumulative lifetime intake of ≥1,000 tablets nearly tripled the odds (Table 16.11)<sup>205</sup>.

Table 16.10

**Risk of Chronic Renal Disease Associated with Non-Aspirin Nonsteroidal Anti-Inflammatory Drugs**

| Frequency of use | Patients (no.) | Controls (no.) | Adjusted odds ratio (95% CI)* |
|------------------|----------------|----------------|-------------------------------|
| <b>Men</b>       |                |                |                               |
| Never            | 265            | 267            | 1.0                           |
| Occasionally     | 11             | 7              | 1.9 (0.7-4.9)                 |
| Weekly           | 4              | 5              | 0.8 (0.2-3.0)                 |
| Daily            | 17             | 4              | 4.6 (1.5-14.0)                |
| <b>Women</b>     |                |                |                               |
| Never            | 210            | 197            | 1.0                           |
| Occasionally     | 7              | 13             | 0.6 (0.2-1.5)                 |
| Weekly           | 9              | 5              | 1.8 (0.6-5.6)                 |
| Daily            | 11             | 9              | 1.1 (0.4-2.7)                 |

CI, confidence interval. \*Odds ratio comparing users with never users, adjusted for age, sex, race, proximity to study hospitals, and income. The risk was examined in 1,041 subjects (534 cases, 507 controls). Twenty percent of chronic renal disease cases were attributed to diabetic nephropathy. Men who regularly took nonsteroidal anti-inflammatory drugs had a higher risk of chronic renal disease than those who did not. This risk was not shared by the women. However, only a small portion of the study population regularly took these medicines, so the power to detect a significant difference in the odds ratio was small, as indicated by the wide CIs.

Source: Reference 210

**Table 16.11**  
**Risk of ESRD in Patients with Diabetes, by Use of Acetaminophen, Aspirin, and Nonsteroidal Anti-Inflammatory Drugs**

| Number of pills taken                             | Odds ratios of ESRD |
|---|---------------------|
| <b>Acetaminophen</b>                              |                     |
| <105 per year                                     | 1.0                 |
| 105-365 per year                                  | 2.1 (1.1-3.8)       |
| ≥366 per year                                     | 1.9 (0.9-3.8)       |
| <b>&lt;1,000 in lifetime</b>                      |                     |
| 1,000-4,999 in lifetime                           | 2.7 (1.6-4.7)       |
| ≥5,000 in lifetime                                | 2.6 (1.2-6.0)       |
| <b>Aspirin</b>                                    |                     |
| <105 per year                                     | 1.0                 |
| 105-365 per year                                  | 0.9 (0.5-1.5)       |
| ≥366 per year                                     | 0.9 (0.5-1.8)       |
| <b>&lt;1,000 in lifetime</b>                      |                     |
| 1,000-4,999 in lifetime                           | 0.5 (0.3-0.7)       |
| ≥5,000 in lifetime                                | 0.7 (0.3-1.4)       |
| <b>Other nonsteroidal anti-inflammatory drugs</b> |                     |
| <105 per year                                     | 1.0                 |
| 105-365 per year                                  | 0.9 (0.4-1.8)       |
| ≥366 per year                                     | 0.7 (0.3-1.8)       |
| <b>&lt;1,000 in lifetime</b>                      |                     |
| <1,000-4,999 in lifetime                          | 0.6 (0.3-1.4)       |
| ≥5,000 in lifetime                                | 5.8 (0.6-56.2)      |

ESRD, end-stage renal disease. Type of diabetes was not specified. Odds ratios are adjusted for age, sex, race, use of the other analgesic drugs in the table, and use of analgesic drugs possibly containing phenacetin. Values in parentheses are 95% confidence intervals.

Source: Reference 205

## RENAL DISEASE AND ITS RELATIONSHIP TO OTHER COMPLICATIONS

ESRD is a frequent consequence of elevated urinary albumin excretion in diabetes, but there are other consequences as well, including dyslipoproteinemias, cardiovascular disease, peripheral vascular disease, and retinopathy. The combination of these diabetic complications undoubtedly contribute to the increased morbidity and early mortality in diabetic patients with elevated urinary albumin excretion<sup>99,113-117,202</sup>. Death rates from cardiovascular disease are three times as high in IDDM patients with elevated urinary albumin excretion as in those with normoalbuminuria<sup>94</sup>, and similar findings have been reported in NIDDM<sup>95,109-112</sup> (see below). It is possible, although not proven, that the dyslipoproteinemia of diabetic renal disease<sup>211-216</sup> contributes to the higher rate of atherosclerosis in these patients. The risk of lower extremity amputations in diabetic subjects with proteinuria is two to four times that of those without proteinuria<sup>217,218</sup>.

The relationship between nephropathy and diabetic retinopathy is well established but is clearly not universal. In a study of renal pathology in 35 patients with NIDDM and persistent albuminuria, 41% of those with biopsy-proven diabetic glomerulopathy did not have retinopathy on review of fundus photographs that were taken through dilated pupils<sup>5</sup>. On the other hand, nearly 60% of them did have retinopathy. Moreover, the frequency of the more severe proliferative retinopathy is greater in those with elevated urinary albumin excretion than in those without<sup>86,87,89,90</sup>.

## TREATMENT OF DIABETIC RENAL DISEASE

Numerous studies have examined the effects of treatments on progression of renal disease in diabetic nephropathy. Few of them, however, offer more than a suggestion regarding the value of a given therapy, because methodologic issues such as small sample size, short duration of followup, poor patient compliance, inappropriate endpoint, or lack of a proper control group hinder their interpretation.

### ■ Metabolic Control

Epidemiologic studies indicate that hyperglycemia plays a role in the development of diabetic renal disease. A number of clinical trials have examined the effect of metabolic control on the course of diabetic renal disease<sup>219-224</sup>. The results of some of these trials in IDDM are presented in Table 16.12. Although many had small numbers of patients, were of short duration, or both, they all suggest that early in the course of diabetic renal disease, prior to the development of clinical proteinuria, aggressive control of blood glucose reduces the urinary albumin excretion rate. Improved blood glucose control also retards the progression of glomerular morphological changes in early diabetic nephropathy<sup>225</sup>. Once proteinuria is established, however, strict metabolic control appears to offer no benefit for preserving renal function<sup>220,226</sup>, unless it is accompanied by adequate control of hypertension<sup>227</sup>. Moreover, even in early diabetic renal disease, several years of strict control may be required for effective stabilization of renal function<sup>228</sup>. In one study, strict metabolic control had no effect on the rate of urinary albumin excretion after 1 year of therapy<sup>229</sup>, but a significant decline in albuminuria was demonstrated after 2 years of therapy in the same subjects<sup>221</sup>.

Two long-term studies involving large numbers of subjects with IDDM have examined the effect of intensified insulin treatment on the rate of development of diabetic renal disease<sup>223,224</sup>. The Stockholm Diabetes

Table 16.12

Clinical Trials of the Effect of Metabolic Control on the Course of Diabetic Nephropathy in IDDM

| Ref. | No. of patients | Extent of urinary protein excretion at baseline | Treatment duration | Intensive treatment method          | Outcome in intensive treatment group vs. conventional insulin therapy group |
|------|-----------------|---|--------------------|-------------------------------------|---|
| 219  | 70              | ≤500 mg protein/24 hours                        | 8 months           | CSII                                | Decreased urinary albumin excretion   |
| 220  | 12              | Albustix ≥1+                                    | 2 years            | CSII                                | No effect   |
| 221  | 36              | 30-300 mg albumin/24 hours                      | 2 years            | CSII                                | Decreased urinary albumin excretion   |
| 222  | 45              | 30-300 mg albumin/24 hours                      | 7 years            | CSII                                | Decreased urinary albumin excretion   |
| 223  | 102             | ≤200 µg albumin/minute*                         | 7.5 years          | Multiple insulin injections         | Decreased incidence of proteinuria  |
| 224  | 1,441           | <200 mg albumin/24 hours                        | 6.5 years          | CSII or multiple insulin injections | Decreased incidence of microalbuminuria and proteinuria                     |

\*Five of the 102 subjects had >200 µg albumin/minute. CSII, continuous subcutaneous insulin infusion. For all studies, intensive treatment is compared with conventional insulin therapy. In the study in Reference 223, the intensive treatment group took ≥3 insulin injections per day along with intensive education; by the end of the study, >60% of the conventionally treated group were receiving ≥3 insulin injections per day.

Source: References are listed within the table

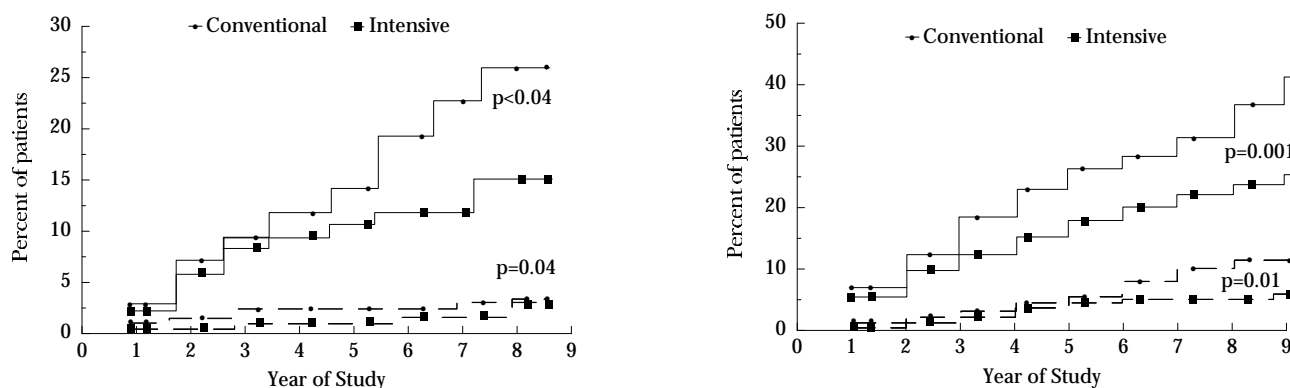
Intervention Study<sup>223</sup> reported a 16% reduction in the rate of development of nephropathy (≥200 µg albumin/minute) in 48 subjects undergoing intensified treatment, compared with 54 subjects undergoing standard insulin treatment during 7.5 years of followup. Similarly, in the Diabetes Control and Complications Trial (DCCT) of 1,441 IDDM patients followed for a mean of 6.5 years<sup>224</sup>, intensive insulin therapy reduced the risk of macroalbuminuria (≥300 mg/24 hours) and microalbuminuria (≥40 mg/24 hours) by 54% and 39%, respectively. Figure 16.29 shows the cumulative incidence of macroalbuminuria and microalbuminuria in patients in the DCCT.

The effect of metabolic control in NIDDM was examined in the University Group Diabetes Program<sup>230</sup>, a long-term clinical trial to determine whether insulin

treatment was better than diet alone in altering the course of vascular complications. Insulin treatment was administered either as a fixed dose or adjusted to maintain blood glucose levels within the normal range. The mean serum creatinine concentration was the same in each group at baseline. However, more patients in the placebo treatment group developed elevated serum creatinine levels than those in either of the two insulin treatment groups (Table 16.13), indicating that glycemic control with insulin reduced the rate of development of renal insufficiency in NIDDM. There was no relationship between type of diabetes treatment and development of proteinuria. A preliminary assessment of the effect of tolbutamide suggests that it did not significantly alter the course of microvascular complications in comparison with placebo, but treatment with tolbutamide was terminated

Figure 16.29

Cumulative Incidence of Elevated Urinary Albumin Excretion in IDDM Patients in the DCCT



DCCT, Diabetes Control and Complications Trial. Figure shows cumulative incidence (%) of two measures of elevated urinary albumin excretion: microalbuminuria (≥40 mg/24 hours, solid line) and macroalbuminuria (≥300 mg/24 hours, dashed line) in patients with IDDM receiving intensive or conventional insulin therapy. The left panel shows results for the primary-prevention cohort (patients who began the study with no retinopathy, n=726); in this cohort, intensive insulin therapy reduced the risk of microalbuminuria by 34% (p<0.04). The right panel shows results for the secondary-intervention cohort (patients with early retinopathy at the beginning of the study, n=715); intensive therapy reduced the risk of macroalbuminuria by 56% (p=0.01) and the risk of microalbuminuria by 43% (p=0.001), compared with conventional therapy.

Source: Reference 224

Table 16.13

**Percent of NIDDM Patients Who Developed Proteinuria or Elevated Serum Creatinine in the UGDP Followup**

| Specified event  | PLBO      | ISTD      | IVAR       |
|--|-----------|-----------|------------|
| Serum creatinine $\geq 1.5$ mg/dl  | 18.5 (34) | 8.3 (16)* | 10.2 (19)* |
| Urine protein $\geq 1$ g/L   | 4.2 (8)   | 2.1 (4)   | 5.8 (11)   |
| Urine protein $\geq 2+$ at two consecutive quarterly followup examinations | 11.8 (22) | 7.9 (15)  | 8.0 (15)   |

UGDP, University Group Diabetes Program; PLBO, diet plus placebo; ISTD, standard fixed-dose insulin therapy; IVAR, variable dose insulin therapy. The number of patients with a specified event are given in parentheses. Average length of followup was 12.5 years. \*  $p < 0.05$  vs. PLBO

Source: Reference 230

early because of increased numbers of cardiovascular deaths in this treatment group<sup>231</sup>.

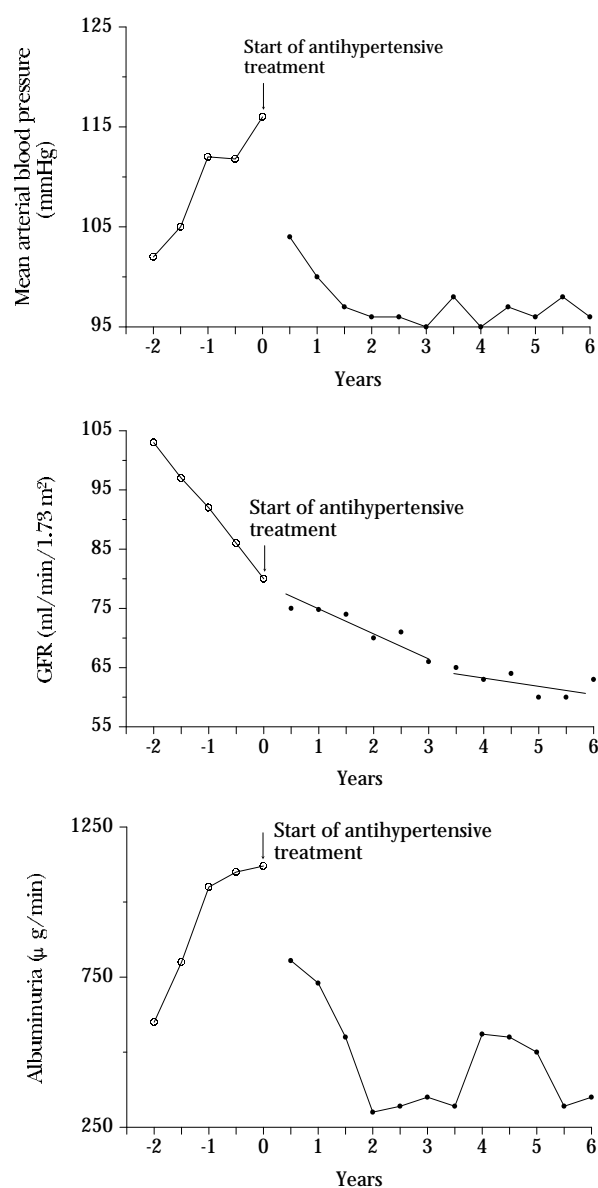
**Blood Pressure Control and ACE Inhibitors**

Reduction in blood pressure is a well-recognized means of delaying the progression of renal disease in diabetic patients with proteinuria, and a number of drugs have been shown to be effective, including  $\beta$ -blockers, calcium channel blockers, diuretics, and ACE inhibitors. Considerable reduction in the rate of decline of GFR was demonstrated in five men with IDDM, hypertension, and proteinuria who were treated with the  $\beta$ -blocker propranolol, alone or in combination with hydralazine or furosemide<sup>42</sup>. Similarly, treatment with metoprolol, hydralazine, and furosemide or thiazide reduced urinary albumin excretion and the rate of decline in renal function in young IDDM patients of either sex with diabetic nephropathy (Figure 16.30)<sup>43</sup>. Thus, effective antihypertensive therapy reduces blood pressure, albumin excretion, and the rate of decline in GFR in persons with established diabetic renal disease.

Although several types of antihypertensive drugs are effective in ameliorating the course of diabetic nephropathy, the purported relationship between increased intraglomerular pressure and diabetic renal disease has prompted many investigators to examine the effect of ACE inhibitors on the progression of diabetic renal disease. Studies of experimental diabetes in animals indicate that ACE inhibitors largely prevent the development of glomerular injury if administered continuously from the onset of diabetes<sup>232-234</sup>. ACE inhibitors also reduce the level of urinary protein excretion and the rate of decline of renal function in normotensive and hypertensive human subjects with either IDDM or NIDDM and with microalbuminuria

or proteinuria<sup>40,235-247</sup>. Moreover, patients with IDDM who have the greatest reduction in urinary albumin excretion shortly after the onset of treatment with an ACE inhibitor have the greatest attenuation in the rate of decline of GFR (Table 16.14)<sup>248</sup>.

Figure 16.30  
**Average Course of MABP, GFR, and Albuminuria in IDDM Patients with Nephropathy, by Antihypertensive Treatment**



MABP, mean arterial blood pressure; GFR, glomerular filtration rate. Figure shows average course before (open circles) and during (closed circles) long-term effective antihypertensive treatment of nine IDDM patients with nephropathy. Mean change in GFR during 2 to 0 years before start of treatment, 0.94 ml/min/month; at 0-3 years of treatment, 0.29 ml/min/month; and at 3-6 years, 0.10 ml/min/month.

Source: Reference 43

Table 16.14

**Effect of Relative Change in Urinary Albumin Excretion on Rate of Decline in GFR in IDDM Patients with Diabetic Nephropathy**

|  | Largest reduction<br>(n=6) | Intermediate<br>(n=6) | Lowest reduction<br>(n=6) |
|--|----------------------------|-----------------------|---------------------------|
| Range of percent change in urinary albumin excretion | -86% to -58%               | -57% to -26%          | -25% to +49%              |
| Rate of decline in GFR (ml/min/year)                 | 1.5<br>(-1.2 to 4.2)       | 4.0<br>(1.0 to 7.1)   | 8.3<br>(4.8 to 11.7)*     |

\* p<0.01 largest vs. lowest reduction. GFR, glomerular filtration rate; diabetic nephropathy was defined as urinary albumin >300 mg/24 hours; relative change in urinary albumin excretion was defined as: (albumin excretion during first year of treatment - baseline excretion)/(baseline excretion) x 100%; values in parentheses are 95% confidence intervals for mean rate of decline in GFR.

Source: Reference 248

ACE inhibitors have favorable effects in addition to their effect on peripheral blood pressure<sup>239-242,246</sup>, and it is believed that reduction of the transcapillary hydraulic pressure is the primary mechanism of action<sup>7</sup>. This class of drugs may also interfere with the promotion of cellular and glomerular hypertrophy by angiotensin II<sup>249-251</sup> and may have a modulating effect on the intrinsic membrane properties of the glomerular barrier with reduction in the size of glomerular pores<sup>246,247</sup>. The ensuing reduction in the filtration of macromolecules could diminish the accumulation of mesangial matrix<sup>252</sup>.

Despite the benefits of ACE inhibitors on protein excretion, demonstration of sustained preservation of glomerular filtration without serious side effects is needed before long-term treatment with these agents can be advocated. A study of 409 subjects with IDDM and urinary protein excretion  $\geq 500$  mg/24 hours, who were randomized to receive either captopril or placebo and were followed for a median of 3 years, found that the risk of doubling of serum creatinine concentration was 48% lower in the captopril group than in the placebo group<sup>253</sup>. Furthermore, the risk of the combined endpoints of death, dialysis, and transplantation was 50% lower (Figure 16.31)<sup>253</sup>. A significant renoprotective effect of captopril, however, was limited to those with baseline serum creatinine concentrations  $\geq 1.5$  mg/dl. Thus, the effects of captopril at lower creatinine concentrations is unclear. Moreover, ACE inhibitors may offer less renoprotection in blacks than in whites<sup>254</sup>. Long-term renoprotection by treatment with ACE inhibitors has not been demonstrated in NIDDM, and the renoprotective effects of treatment at an earlier stage of renal disease in either type of diabetes remain to be determined.

Figure 16.31

**Effect of Captopril on Incidence of Renal Disease in IDDM Patients with Nephropathy**

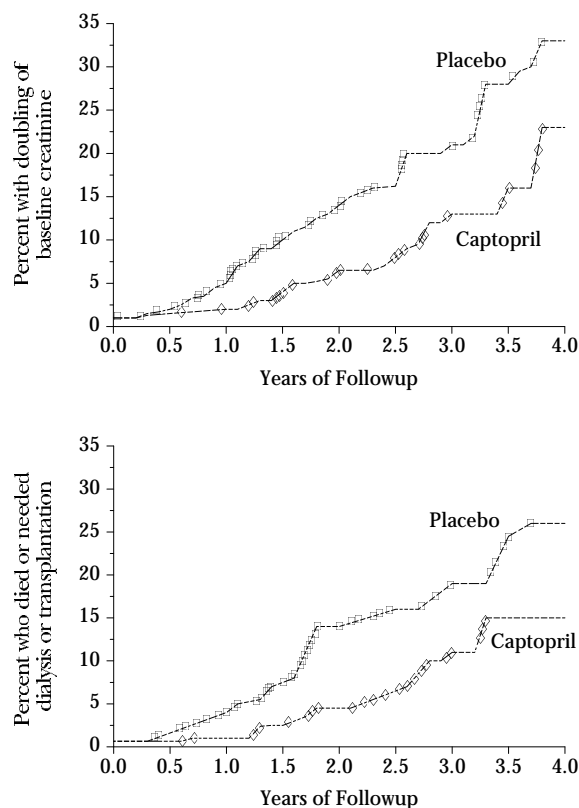


Figure shows cumulative incidence (%) of events in patients with IDDM and diabetic nephropathy in the captopril and placebo groups. Top panel shows the cumulative percentage of patients with the primary endpoint: a doubling of the baseline serum creatinine concentration and a final concentration  $\geq 2.0$  mg/dl. Bottom panel shows the cumulative percentage of patients who died or required dialysis or renal transplantation. Treatment with captopril was associated with a significant reduction of both endpoints.

Source: Reference 253

**■ Dietary Modification**

In animals with experimental diabetes, reduced protein intake protects against hyperfiltration and progressive sclerosis of functioning glomeruli<sup>255</sup>. In patients with IDDM and normal urinary albumin excretion, short-term dietary protein restriction favorably modifies glomerular hemodynamic function, and in those with microalbuminuria it also reduces urinary albumin excretion<sup>256-259</sup>.

The effects of reducing dietary protein have also been examined in patients with IDDM and clinical proteinuria<sup>260-263</sup>. Results of these studies, presented in Table 16.15, suggest that reduction in dietary protein lowers urinary protein excretion and reduces the rate of decline in GFR. In the largest of these studies<sup>263</sup>, protein restriction led to a significant amelioration in

Table 16.15

**Clinical Trials of the Effect of Dietary Protein Reduction on the Course of Diabetic Nephropathy in IDDM Patients with Clinical Proteinuria**

| Ref. | No. of patients | Treatment duration | Protein restriction | Outcome in treatment group   |
|------|-----------------|--------------------|---------------------|--|
| 260  | 16              | 4.5 months         | 0.7 g/kg/day        | Decreased urinary albumin excretion                                |
| 261  | 11              | 24 months          | 0.6 g/kg/day        | Decreased urinary protein excretion                                |
| 262  | 19              | 33 months          | 0.7 g/kg/day        | Decreased rate of GFR decline; decreased urinary albumin excretion |
| 263  | 35              | 34.7 months        | 0.6 g/kg/day        | Decreased rate of GFR decline; decreased urinary albumin excretion |

In the studies in References 260 and 263, a protein-restricted diet was compared with a standard diet; in Reference 261, there was no control group; in Reference 262, subjects were compared before and after dietary protein restriction.

Source: References are listed within the table

the rate of decline in GFR, as shown in Figure 16.32. The rates of decline in subjects receiving the standard diet averaged 1.0 ml/min/month, and 0.3 ml/min/month in those receiving the protein-restricted diet. Variability in the rate of GFR decline, however, was considerable, suggesting that the response to a low-protein diet is not homogeneous. Furthermore, the benefits of such therapy may not outweigh the inconveniences associated with a strict dietary regimen.

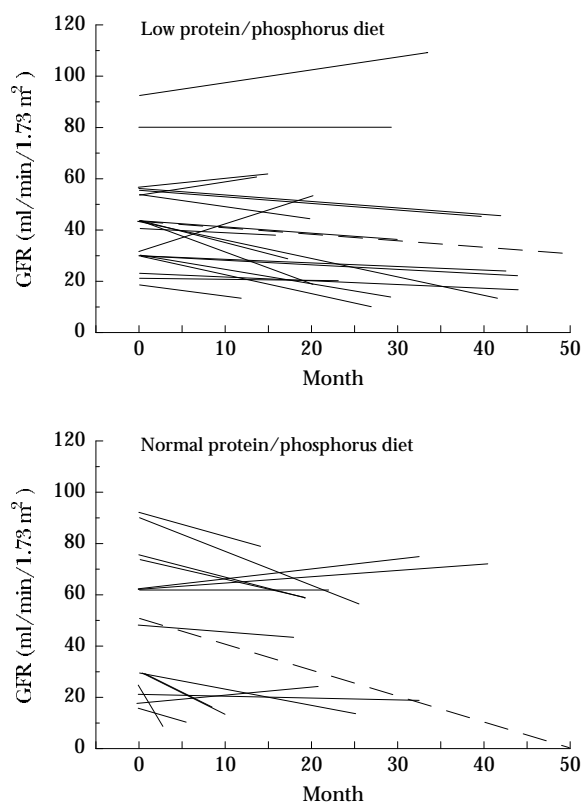
All of the studies reviewed above were conducted in patients with IDDM. No long-term trials assessing the effect of low-protein diets on the progression of renal disease have been done in NIDDM.

**Survival of ESRD Patients**

Once patients reach ESRD, death ensues unless renal replacement therapy is provided. Five-year survival in diabetic patients receiving dialysis is compared with that in all dialysis patients in Figure 16.33<sup>121</sup>. Survival is reduced in diabetic patients, as nearly half of the diabetic patients die within 2 years of beginning dialysis. However, diabetic blacks treated for ESRD survive longer than whites (Figure 16.34)<sup>264</sup>. The longer survival in blacks was found only in dialysis patients after adjusting for comorbidity and other factors that affect survival. For renal transplant patients, survival is much better both for cadaver donor and living-related donor transplant diabetic patients than for dialysis-treated patients (Figure 16.33)<sup>121</sup>, primarily because patients selected for transplant have fewer coexistent

conditions than those selected for dialysis. However, long-term survival among transplant recipients is significantly higher than in dialysis patients who are candidates for transplant, even though the transplant candidates are presumably similar in other respects to those who receive transplants. This suggests that the type of renal replacement therapy (transplant versus dialysis) may also influence long-term survival<sup>265</sup>. Nevertheless, regardless of the type of renal replacement therapy, survival is poorer in diabetic ESRD patients than in those with nondiabetic diseases, primarily because of co-existent diseases, mainly cardiovascular diseases<sup>266-269</sup>, which continue to advance during the course of renal replacement therapy. Even persons with renal failure due to hypertension, who are generally older than those with renal failure from diabetes, have better survival rates<sup>121</sup>. A noticeable

Figure 16.32  
**Progression of Renal Failure, by Dietary Protein Intake**



GFR, glomerular filtration rate. Figure shows progression of renal failure in 20 patients treated with a low-protein, low-phosphorus diet (top panel) and in 15 patients with diabetic nephropathy treated with normal dietary intake of protein and phosphorus (bottom panel). Diets were assigned at random. The GFR, based on measurements of iothalamate clearance, is shown as a function of time in months. Dashed lines indicate the mean regression for each group ( $p=0.22$  for the difference between groups in the slope of the mean regression line).

Source: Reference 263

improvement in survival, however, has occurred in all categories of ESRD, including diabetes, from 1982 through 1991 (Figures 16.35 and 16.36). Cause-specific death rates for patients receiving hemodialysis,

**Figure 16.33**  
Survival of Dialysis Patients, by Primary Cause of Renal Failure and Type of Therapy

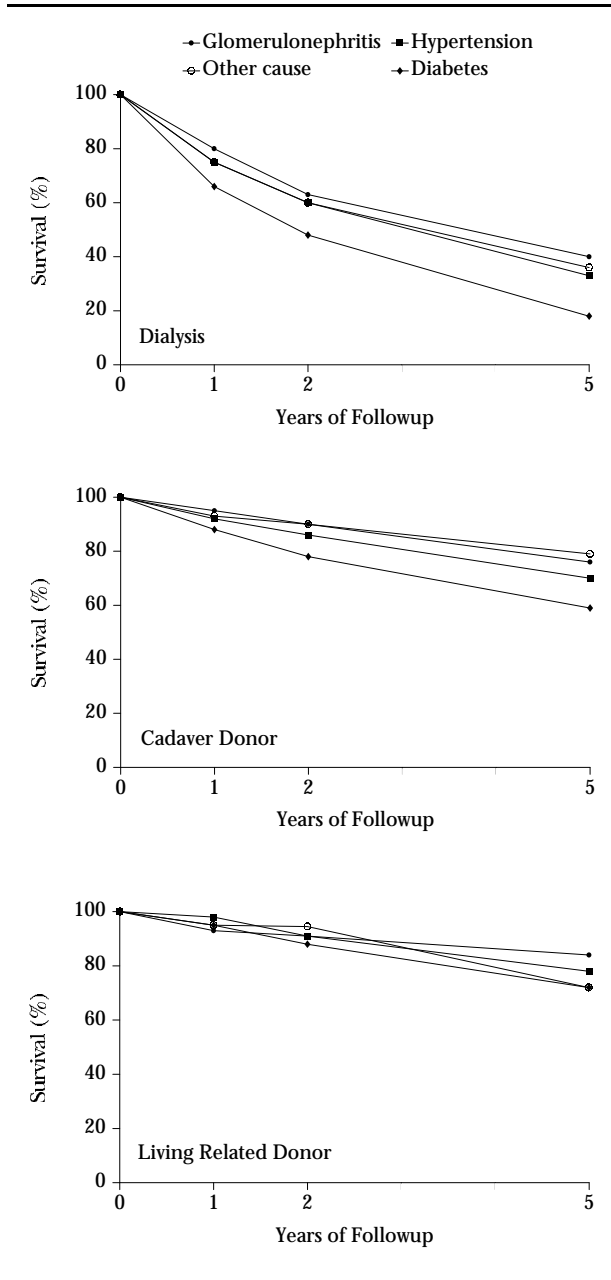


Figure shows Kaplan-Meier survival estimates (%) at 1, 2, and 5 years for dialysis patients by primary cause of renal failure and type of renal replacement therapy. Data are for Medicare patients in the 1987 incident cohort and are adjusted to the age, sex, and race of the 1991 incident cohort; patients in Puerto Rico and U.S. territories are included in the estimates; 5-year survival estimates are considered preliminary. Survival data for dialysis patients start at day 91 following the onset of end-stage renal disease and are censored at first transplant; survival data for transplant patients start at the day of transplant.

Source: Reference 121

**Figure 16.34**  
Survival of IDDM and NIDDM End-Stage Renal Disease Patients, by Race, Michigan, 1974-88

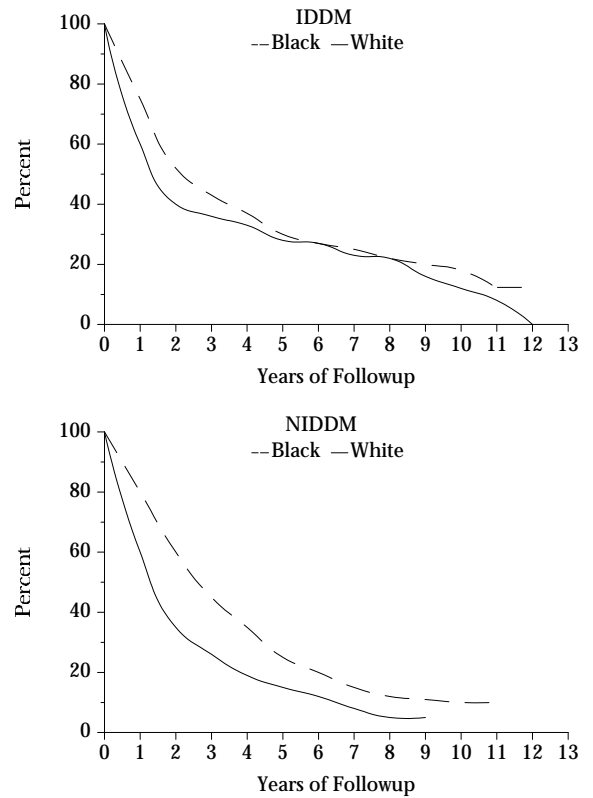
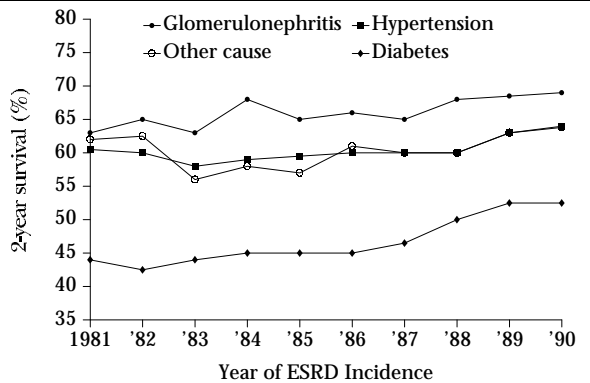


Figure shows Kaplan-Meier survival rates.

Source: Reference 264

**Figure 16.35**  
Time Trends in Survival of U.S. Dialysis Patients, by Primary Cause of Renal Failure and Year of ESRD Incidence



ESRD, end-stage renal disease. Figure shows Kaplan-Meier 2-year survival (%) of U.S. Medicare dialysis patients, by primary cause of renal failure and year of incidence. Data are calculated starting at day 91 following onset of ESRD and are censored at first transplant; data are adjusted for age, sex, and race; patients in Puerto Rico and U.S. territories are included in estimates; data for 1990 are preliminary.

Source: Reference 121



**Figure 16.36**  
**Time Trends in Survival of U.S. Transplant Patients, by Primary Cause of Renal Failure**

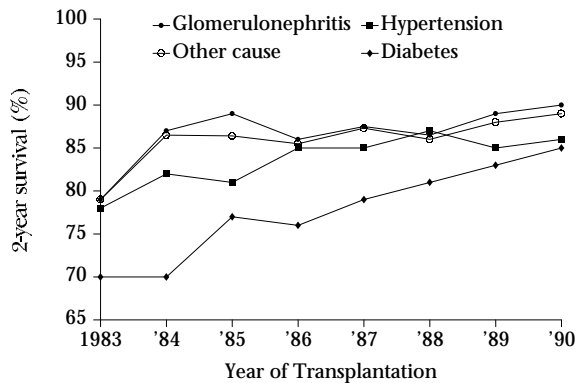


Figure shows Kaplan-Meier 2-year percent survival of U.S. Medicare patients with end-stage renal disease (ESRD) who received a first cadaveric transplant, by year of transplant and primary cause of renal failure. Data are adjusted for race, age, primary disease, and sex to the distribution of the 1991 ESRD incident population; data for 1990 are preliminary.

Source: Reference 121

peritoneal dialysis, and those with a functioning cadaveric transplant are shown in Tables 16.16-16.18. Additional data on renal replacement therapy in diabetes are found in the appendices.

## ■ Economic Impact of Renal Replacement Therapy

Medicare insures the majority of patients receiving renal replacement therapy in the United States, covering more than 92% of dialysis patients and 90% of kidney transplant recipients<sup>121</sup>. The total number of diabetic patients in the United States receiving renal replacement therapy through Medicare in 1990 was 39,904, 83% of whom were on dialysis, and the rest had functioning grafts<sup>270</sup>. Medicare expenditures per diabetic dialysis patient, excluding secondary-payer patients, averaged \$49,040 annually. Thus, the total cost of renal replacement therapy for persons with diabetes presently exceeds \$2 billion annually<sup>270</sup>, not including the additional costs associated with reduced productivity and unemployment. Although the cost of transplantation is high, maintenance costs are substantially less than for dialysis, averaging \$12,052 per patient in 1990<sup>270</sup>. Due to its lower overall cost, improved survival, and better quality of life than any form of dialysis, renal transplantation is the generally preferred treatment for diabetic patients with ESRD<sup>271</sup>.

## ■ Other Treatments

Modification of blood pressure, metabolic control, diet, and dialysis and transplantation have been the mainstays of treatment of renal disease in diabetic

**Table 16.16**  
**Cause-Specific Death Rates (per 1,000 Person-Years) for Medicare Hemodialysis Patients, by Age (Years), Race, and Diabetes Status, U.S., 1989-91**

| Cause of death              | Diabetic patients |        |        |       |        | Nondiabetic patients |        |         |        |        |
|-----------------------------|-------------------|--------|--------|-------|--------|----------------------|--------|---------|--------|--------|
|                             | Total             | Black  | White  | 20-44 | 45-64  | Total                | Black  | White   | 20-44  | 45-64  |
| Myocardial infarction       | 38.7              | 27.8   | 46.8   | 22.7  | 37.7   | 22.1                 | 16.1   | 26.5    | 4.1    | 17.4   |
| Pericarditis                | 1.2               | <1.0   | 1.4    | 1.1   | 1.2    | 1.0                  | 1.0    | 1.0     | <1.0   | <1.0   |
| Other cardiac               | 83.3              | 62.6   | 98.0   | 56.5  | 70.7   | 57.5                 | 45.7   | 66.4    | 17.2   | 40.5   |
| Cerebrovascular             | 15.8              | 15.4   | 16.4   | 11.0  | 13.2   | 10.0                 | 10.1   | 10.0    | 4.2    | 7.4    |
| Pulmonary embolism          | 1.0               | 1.0    | 1.1    | <1.0  | <1.0   | <1.0                 | <1.0   | <1.0    | <1.0   | <1.0   |
| GI hemorrhage               | 3.8               | 3.4    | 4.2    | 2.2   | 2.9    | 3.8                  | 3.0    | 4.4     | <1.0   | 2.9    |
| Other hemorrhage            | <1.0              | <1.0   | <1.0   | <1.0  | <1.0   | 1.6                  | 1.3    | 1.9     | <1.0   | 1.4    |
| Septicemia                  | 26.3              | 25.1   | 27.7   | 17.5  | 21.8   | 16.8                 | 16.4   | 17.1    | 7.5    | 13.7   |
| Pulmonary infection         | 5.7               | 4.4    | 6.4    | 3.8   | 3.9    | 6.6                  | 4.3    | 8.1     | 2.2    | 3.9    |
| Other infection             | 2.5               | 2.1    | 2.7    | 3.5   | 2.5    | 2.3                  | 3.0    | 1.7     | 3.5    | 1.8    |
| Hyperkalemia                | 3.4               | 2.0    | 4.5    | 8.0   | 2.7    | 2.6                  | 2.2    | 2.9     | 3.5    | 2.0    |
| Malignancy                  | 3.2               | 4.0    | 2.9    | <1.0  | 2.8    | 8.1                  | 6.8    | 9.1     | 1.5    | 7.0    |
| Withdrawal from dialysis    | 36.0              | 18.5   | 48.6   | 18.4  | 25.8   | 25.9                 | 11.7   | 36.0    | 4.1    | 12.3   |
| Unknown cause               | 20.6              | 19.4   | 21.6   | 21.5  | 17.8   | 13.2                 | 14.2   | 12.7    | 8.0    | 10.5   |
| Other                       | 19.1              | 15.6   | 22.0   | 18.5  | 15.2   | 17.9                 | 15.1   | 19.9    | 8.6    | 13.8   |
| Missing data                | 37.8              | 26.9   | 46.0   | 24.2  | 32.9   | 27.7                 | 20.5   | 33.1    | 10.4   | 19.5   |
| Total death rate            | 301.2             | 231.4  | 353.1  | 212.7 | 253.9  | 219.9                | 173.7  | 253.8   | 79.3   | 157.6  |
| Total patient years at risk | 68,238            | 25,821 | 38,124 | 9,957 | 32,500 | 173,889              | 67,069 | 100,587 | 39,584 | 59,966 |

Table includes dialysis patients with a prior kidney transplant unless the transplant failed during the year of study. Patients transplanted during the year of observation were censored on the day of transplantation. GI, gastrointestinal.

Source: Reference 121

Table 16.17

## Cause-Specific Death Rates (per 1,000 Person-Years) for Medicare CAPD/CCPD Patients, by Age (Years), Race, and Diabetes Status, U.S., 1989-91

| Cause of death              | Diabetic patients |       |       |       |       | Nondiabetic patients |       |        |       |       |
|-----------------------------|-------------------|-------|-------|-------|-------|----------------------|-------|--------|-------|-------|
|                             | Total             | Black | White | 20-44 | 45-64 | Total                | Black | White  | 20-44 | 45-64 |
| Myocardial infarction       | 43.9              | 32.1  | 46.9  | 23.1  | 48.2  | 21.9                 | 12.5  | 25.3   | 4.8   | 21.9  |
| Pericarditis                | 1.5               | <1.0  | 1.7   | 2.1   | 1.0   | 1.0                  | 1.5   | <1.0   | 1.2   | <1.0  |
| Other cardiac               | 92.6              | 73.3  | 97.6  | 51.5  | 83.1  | 51.6                 | 35.5  | 57.6   | 13.5  | 46.7  |
| Cerebrovascular             | 18.5              | 17.5  | 19.3  | 9.8   | 18.3  | 8.8                  | 7.2   | 9.6    | 2.0   | 6.5   |
| Pulmonary embolism          | 1.7               | <1.0  | 1.9   | <1.0  | 2.0   | <1.0                 | <1.0  | <1.0   | <1.0  | <1.0  |
| GI hemorrhage               | 3.3               | 1.4   | 4.0   | 1.5   | 2.9   | 2.7                  | 1.9   | 3.0    | <1.0  | 2.9   |
| Other hemorrhage            | <1.0              | <1.0  | 1.0   | <1.0  | 1.2   | 1.1                  | 1.0   | 1.0    | <1.0  | <1.0  |
| Septicemia                  | 35.2              | 36.9  | 35.4  | 21.9  | 33.8  | 19.2                 | 17.1  | 20.2   | 9.0   | 19.1  |
| Pulmonary infection         | 4.4               | 4.2   | 4.4   | 2.1   | 2.9   | 4.7                  | 2.9   | 5.3    | 2.3   | 3.3   |
| Other infection             | 4.1               | 3.7   | 4.3   | 3.0   | 3.5   | 4.8                  | 7.6   | 4.0    | 5.7   | 2.8   |
| Hyperkalemia                | 1.6               | 1.4   | 1.6   | 1.8   | 1.4   | <1.0                 | 1.0   | <1.0   | <1.0  | <1.0  |
| Malignancy                  | 1.8               | <1.0  | 2.0   | <1.0  | 2.0   | 4.6                  | 2.9   | 5.4    | <1.0  | 4.5   |
| Withdrawal from dialysis    | 39.6              | 20.8  | 45.2  | 20.0  | 34.7  | 23.4                 | 9.8   | 28.5   | 4.7   | 14.7  |
| Unknown cause               | 21.6              | 18.4  | 22.4  | 12.9  | 23.2  | 11.7                 | 11.3  | 12.0   | 4.8   | 9.8   |
| Other                       | 24.2              | 17.9  | 24.1  | 12.9  | 23.2  | 19.9                 | 17.4  | 21.0   | 11.1  | 19.8  |
| Missing data                | 38.8              | 27.9  | 42.8  | 17.6  | 39.9  | 22.1                 | 17.0  | 24.1   | 7.9   | 19.2  |
| Total death rate            | 334.8             | 259.7 | 357.6 | 183.4 | 322.3 | 200.4                | 148.4 | 220.9  | 71.8  | 175.3 |
| Total patient years at risk | 10,453            | 2,113 | 7,893 | 3,238 | 4,808 | 26,964               | 6,519 | 19,598 | 7,802 | 9,788 |

CAPD, continuous ambulatory peritoneal dialysis; CCPD, continuous cycling peritoneal dialysis; GI, gastrointestinal. Table includes dialysis patients with a prior kidney transplant, unless the transplant failed during the year of study; patients transplanted during the year of observation were censored on the day of transplantation.

Source: Reference 121

patients, and a majority of the research into new therapeutic approaches has focused on one or more of these therapies. Nevertheless, a growing body of evidence indicates that the development of diabetic complications is related to specific metabolic derange-

ments induced by hyperglycemia, such as formation of advanced glycosylation end-products, or the accumulation of polyols, such as sorbitol. No definitive studies on the role of these derangements and risk or progression of nephropathy are currently available.

Table 16.18

## Cause-Specific Death Rates (per 1,000 Person-Years) for Medicare Patients with a Functioning Cadaveric Transplant After 1 Year, by Age (Years), Race, and Diabetes Status, U.S., 1986-88

| Cause of death              | Diabetic patients |       |       |       |       | Nondiabetic patients |       |        |        |       |
|-----------------------------|-------------------|-------|-------|-------|-------|----------------------|-------|--------|--------|-------|
|                             | Total             | Black | White | 20-44 | 45-64 | Total                | Black | White  | 20-44  | 45-64 |
| Myocardial infarction       | 9.4               | 4.3   | 10.6  | 8.1   | 12.0  | 3.5                  | 5.1   | 3.0    | 2.0    | 5.8   |
| Pericarditis                | <1.0              | 1.0   | <1.0  | <1.0  | 1.0   | <1.0                 | <1.0  | <1.0   | <1.0   | <1.0  |
| Other cardiac               | 11.9              | 11.8  | 12.3  | 10.5  | 15.8  | 5.5                  | 7.2   | 5.0    | 4.5    | 7.5   |
| Cerebrovascular             | 5.8               | 3.2   | 6.4   | 5.4   | 7.1   | 1.1                  | 1.4   | 1.0    | <1.0   | 1.9   |
| Pulmonary embolism          | <1.0              | 2.1   | <1.0  | <1.0  | 1.0   | <1.0                 | <1.0  | <1.0   | <1.0   | <1.0  |
| GI hemorrhage               | <1.0              |       | <1.0  | <1.0  |       | <1.0                 | <1.0  | <1.0   | <1.0   | <1.0  |
| Other hemorrhage            | <1.0              | 1.0   | <1.0  | <1.0  | 1.6   | <1.0                 | <1.0  | <1.0   | <1.0   | <1.0  |
| Septicemia                  | 4.7               | 8.6   | 4.1   | 4.2   | 6.0   | 2.8                  | 3.8   | 2.6    | 2.1    | 4.0   |
| Pulmonary infection         | 1.1               |       | 1.3   | 1.1   | 1.0   | 1.3                  | 1.9   | 1.1    | <1.0   | 2.4   |
| Other infection             | 1.1               | 1.0   | 1.1   | 1.3   | <1.0  | <1.0                 | <1.0  | <1.0   | <1.0   | 1.0   |
| Hyperkalemia                | <1.0              | 1.0   | <1.0  | 1.3   |       | <1.0                 | <1.0  | <1.0   | <1.0   | <1.0  |
| Malignancy                  | <1.0              | 1.0   | <1.0  | <1.0  | 1.6   | 1.6                  | 1.3   | 1.7    | <1.0   | 2.9   |
| Withdrawal from dialysis    | 3.6               | 1.0   | 4.1   | 3.6   | 3.8   | <1.0                 | <1.0  | <1.0   | <1.0   | <1.0  |
| Unknown cause               | 6.4               | 9.7   | 5.6   | 6.5   | 6.0   | 2.4                  | 4.1   | 1.8    | 2.4    | 2.6   |
| Other                       | 5.3               | 8.6   | 4.7   | 4.0   | 8.7   | 4.3                  | 5.4   | 3.8    | 3.2    | 5.9   |
| Total death rate            | 70.6              | 72.4  | 71.2  | 64.3  | 85.7  | 35.8                 | 46.2  | 32.8   | 26.2   | 52.8  |
| Total patient years at risk | 6,340             | 925   | 5,274 | 4,443 | 1,830 | 25,187               | 6,035 | 18,104 | 13,731 | 8,701 |

GI, gastrointestinal.

Source: Reference 121

Studies in experimental diabetes in animals suggest that inhibition of aldose reductase may lead to preservation of kidney function<sup>272-275</sup>, and studies in humans with IDDM have demonstrated that aldose reductase inhibitors reduce GFR<sup>276,277</sup> and the rate of urinary albumin excretion in those with elevated excretion<sup>277</sup>. Nevertheless, much work remains in establishing a role for aldose reductase inhibitors in the treatment or prevention of diabetic nephropathy.

diabetic persons and the more frequent development of genitourinary tract infections has not been established<sup>283,296</sup>.

In most studies, the microorganisms causing asymptomatic bacteriuria in persons with diabetes are similar to those causing bacteriuria in nondiabetic persons<sup>283</sup>, but a survey of 514 diabetic and 405 nondiabetic subjects found that nearly half of the diabetic subjects with bacteriuria were infected by bacteria other than *E. coli*, whereas all but one case of bacteriuria in the nondiabetic subjects were caused by *E. coli*<sup>285</sup>. The prevalence of asymptomatic bacteriuria is not influenced by the type or duration of diabetes or by the level of glycemic control<sup>283</sup>.

## OTHER KIDNEY DISEASES ASSOCIATED WITH DIABETES

### INFECTION

Diabetic patients may be more susceptible to infections of the urinary tract. Autopsy studies from the pre-antibiotic era<sup>278-282</sup> reported a prevalence of histologic pyelonephritis of 10%-20% in persons with diabetes, five times that of nondiabetic persons. Not only was the frequency of urinary tract infection greater in diabetic patients at that time, but the infections were often more serious and protracted<sup>279</sup>. With the introduction of effective antimicrobial therapy, the frequency and severity of urinary tract infections may have diminished<sup>283</sup>. Tables 16.19 and 16.20 present the prevalence of asymptomatic bacteriuria in diabetic men and women from several different clinic- or hospital-based populations. Diabetic women have about three times the frequency of bacteriuria as nondiabetic women<sup>284-295</sup>, but among men most studies do not report a higher prevalence in those with diabetes<sup>285-296</sup>. A relationship between asymptomatic bacteriuria in

### RENAL PAPILLARY NECROSIS

Impaired blood flow to the inner medulla and papilla of the kidney can lead to anoxic damage and ultimately to renal papillary necrosis. Sloughing of the renal papilla may ensue, which can obstruct the renal pelvis. Patients may remain asymptomatic or develop flank pain and renal colic.

The prevalence of renal papillary necrosis at autopsy is 20-30 times as great in patients with diabetes as in those without<sup>297</sup>. Among diabetic patients, it occurs bilaterally in half of the cases and is 2.5 times as frequent in women as in men<sup>279,280,298</sup>. Moreover, diabetic patients with acute pyelonephritis are at particularly high risk. In one study, 27% of diabetic subjects with renal papillary necrosis at autopsy also had acute fulminant pyelonephritis<sup>280</sup>.

Table 16.19  
Prevalence of Asymptomatic Bacteriuria in Men, by Diabetes Status

| Ref.  | Diabetic men |                    |                           |                    | Nondiabetic men |                    |                           |                    |
|-------|--------------|--------------------|---------------------------|--------------------|-----------------|--------------------|---------------------------|--------------------|
|       | No.          | Type of population | Age range in years (mean) | Prevalence no. (%) | No.             | Type of population | Age range in years (mean) | Prevalence no. (%) |
| 286   | 67           | Clinic             | <20->70 (45)              | 5 (7.5)            | 67              | Clinic             | <20->70 (~45)             | 2 (3.0)            |
| 287   | 141          | Clinic             | 0->70 (44.4)              | 1 (0.7)            | 146             | Clinic             | 10->70 (38.6)             | 3 (2.1)            |
| 288   | 40           | Clinic             | 16-77 (54)                | 1 (2.5)            |                 |                    |                           |                    |
| 289   | 154          | Clinic             | 20-60 (~52)               | 2 (1.3)            | 159             | Clinic             | 20-60 (~52)               | 1 (0.6)            |
| 290   | 87           | Clinic             | Adult                     | 7 (8.0)            | 68              | Clinic             | Adult                     | 2 (2.9)            |
| 291   | 103          | Clinic             | Adult                     | 2 (1.9)            |                 |                    |                           |                    |
| 292   | 411          | Clinic             | 32-80 (55)                | 4 (1.0)            | 100             | Clinic             | (54)                      | 0                  |
| 293   | 9            | Hospital           | 17-79                     | 1 (11.1)           | 9               | Hospital           | 17-79 (>50)               | 2 (22.2)           |
| 294   | 58           | Clinic             | 0->60                     | 2 (3.4)            | 58              | Emergency room     | 0->60                     | 1 (1.7)            |
| 295   | 90           | Clinic             | 10-69 (~40)               | 3 (3.3)            | 90              | Clinic             | 10-69 (~40)               | 2 (2.2)            |
| 285   | 275          | Clinic             | 46 (18-80)                | 5 (1.8)            | 79              | Clinic             | 16-84 (30)                | 1 (1.3)            |
| Total | 1,435        |                    |                           | 33 (2.3)           | 776             |                    |                           | 14 (1.8)           |

Type of diabetes was not specified; for References 290 and 291, specific age data are not available; when all studies were combined, the prevalence in diabetic men was 1.3 times that in nondiabetic men.

Source: References are listed within the table

Table 16.20

## Prevalence of Asymptomatic Bacteriuria in Women, by Diabetes Status

| Ref.  | No.   | Diabetic women     |                          |                     | No.   | Nondiabetic women  |                          |                     |
|-------|-------|--------------------|--------------------------|---------------------|-------|--------------------|--------------------------|---------------------|
|       |       | Type of population | Age range in years, mean | Prevalence, no. (%) |       | Type of population | Age range in years, mean | Prevalence, no. (%) |
| 286   | 81    | Clinic             | <20->70 (~45)            | 15 (18.5)           | 81    | Clinic             | <20->70 (~45)            | 3 (3.7)             |
| 287   | 128   | Clinic             | 0->70 (31.1)             | 24 (18.8)           | 114   | Clinic             | 10->70 (38)              | 9 (7.9)             |
| 288   | 20    | Clinic             | 24-59 (42)               | 0                   | 36    | Clinic             | 61-88 (72)               | 1 (2.8)             |
| 288   | 40    | Clinic             | 61-82 (68)               | 8 (20.0)            |       |                    |                          |                     |
| 289   | 152   | Clinic             | 10-60 (~55)              | 24 (15.8)           | 152   | Clinic             | 20-60 (~55)              | 7 (4.6)             |
| 290   | 111   | Clinic             | Adult                    | 30 (27.0)           | 79    | Clinic             | Adult                    | 9 (11.4)            |
| 291   | 230   | Clinic             | Adult                    | 43 (18.7)           |       |                    |                          |                     |
| 284   | 400   | Clinic             | 15-65 (46)               | 38 (9.5)            |       |                    |                          |                     |
| 292   | 341   | Clinic             | 32-80 (55)               | 31 (9.1)            | 100   | Clinic             | (54)                     | 5 (5.0)             |
| 293   | 41    | Hospital           | 17-79                    | 12 (29.3)           | 41    | Hospital           | 17-79 (>50)              | 9 (22.0)            |
| 294   | 92    | Clinic             | 0->60                    | 18 (19.6)           | 92    | Emergency room     | 0->60                    | 17 (18.5)           |
| 295   | 100   | Clinic             | 10-69 (~40)              | 9 (9.0)             | 100   | Clinic             | 10-69 (~40)              | 8 (8.0)             |
| 285   | 239   | Clinic             | 20-80 (47)               | 12 (6.3)            | 326   | Clinic             | 17-85 (48)               | 10 (3.1)            |
| Total | 1,975 |                    |                          | 264 (13.4)          | 1,121 |                    |                          | 78 (7.0)            |

Type of diabetes was not specified; for References 290 and 291, specific age data are not available; when all studies were combined, the prevalence in diabetic women was 1.9 times that in nondiabetic women.

Source: References are listed within the table

## RADIOCONTRAST-INDUCED KIDNEY FAILURE

A well-documented complication of radiocontrast administration is acute and sometimes irreversible decrease in renal function. Such deterioration is probably more common in persons with diabetes than in those without<sup>299-305</sup> and may be influenced by poor hydration and the volume of contrast medium administered. Although some reports<sup>300,306</sup> suggest that diabetic patients with normal kidney function are not at greater risk of contrast-induced nephropathy than nondiabetic persons, more recent data indicate they are<sup>305</sup>. Nevertheless, azotemic diabetic patients are at substantially greater risk than azotemic nondiabetic patients or nonazotemic diabetic patients<sup>299,300,305</sup>, and patients with IDDM may be at greater risk than those with NIDDM<sup>301,305</sup>.

## CONCLUSIONS

The incidence of diabetic nephropathy in persons with IDDM appears to be declining<sup>100,103,104</sup>, and improvements in glycemic control may be a major contributing factor<sup>104</sup>. In addition, treatment with an ACE inhibitor dramatically reduces the rate of progression of renal disease in patients with IDDM, proteinuria, and elevated serum creatinine concentration<sup>253</sup>. On the other hand, the incidence of diabetic nephropathy in NIDDM does not appear to be declining and may actually be rising. An ever-increasing number of patients with diabetes, the majority of whom have NIDDM<sup>121</sup>, are requiring renal replacement therapy, at enormous cost to the patient and to society.

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APPENDICES

Appendices 16.1-16.19 contain selected tables adapted from the *USRDS 1994 Annual Data Report*<sup>121</sup> with data relevant to ESRD attributed to diabetes. The Hispanic population is not separated from the white population for racial comparisons. In the tables, the USRDS does not show data in cells that contain one to nine patients because of the possible ability to identify individual patients from the USRDS files.

Appendix 16.1

**Incidence Counts of Reported ESRD Therapy by Year, Age, Race, Sex, and Primary Disease Causing ESRD, U.S., 1982-91**

|                            | 1982   | 1983   | 1984   | 1985   | 1986   | 1987   | 1988   | 1989   | 1990   | 1991   |
|----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| <b>Age at ESRD (years)</b> |        |        |        |        |        |        |        |        |        |        |
| 0-4                        | 100    | 97     | 109    | 117    | 113    | 121    | 114    | 127    | 107    | 130    |
| 5-9                        | 100    | 81     | 102    | 90     | 109    | 114    | 88     | 104    | 131    | 101    |
| 10-14                      | 211    | 193    | 209    | 204    | 188    | 191    | 194    | 169    | 214    | 206    |
| 15-19                      | 428    | 425    | 393    | 402    | 418    | 451    | 432    | 477    | 445    | 385    |
| 20-24                      | 695    | 658    | 739    | 753    | 738    | 766    | 798    | 801    | 789    | 815    |
| 25-29                      | 1,078  | 1,054  | 1,133  | 1,197  | 1,292  | 1,221  | 1,308  | 1,413  | 1,444  | 1,437  |
| 30-34                      | 1,328  | 1,345  | 1,437  | 1,469  | 1,649  | 1,568  | 1,714  | 1,927  | 1,932  | 1,982  |
| 35-39                      | 1,270  | 1,347  | 1,450  | 1,668  | 1,807  | 1,860  | 2,092  | 2,178  | 2,315  | 2,439  |
| 40-44                      | 1,263  | 1,420  | 1,487  | 1,635  | 1,774  | 2,041  | 2,149  | 2,408  | 2,709  | 2,962  |
| 45-49                      | 1,421  | 1,621  | 1,696  | 1,896  | 1,954  | 2,140  | 2,368  | 2,694  | 2,776  | 3,113  |
| 50-54                      | 1,993  | 2,021  | 2,083  | 2,233  | 2,374  | 2,611  | 2,880  | 3,076  | 3,297  | 3,458  |
| 55-59                      | 2,423  | 2,543  | 2,791  | 2,998  | 3,093  | 3,313  | 3,580  | 3,871  | 4,142  | 4,425  |
| 60-64                      | 2,747  | 3,088  | 3,413  | 3,810  | 3,921  | 4,362  | 4,671  | 5,006  | 5,437  | 5,929  |
| 65-69                      | 2,588  | 3,278  | 3,408  | 3,829  | 4,225  | 4,803  | 5,177  | 6,054  | 6,707  | 7,253  |
| 70-74                      | 2,062  | 2,792  | 2,813  | 3,337  | 3,605  | 4,059  | 4,370  | 5,120  | 5,828  | 6,648  |
| 75-79                      | 1,181  | 1,774  | 1,906  | 2,183  | 2,593  | 2,902  | 3,276  | 3,912  | 4,328  | 5,048  |
| 80-84                      | 447    | 747    | 769    | 999    | 1,149  | 1,376  | 1,607  | 1,969  | 2,289  | 2,539  |
| ≥85                        | 167    | 249    | 273    | 341    | 408    | 487    | 578    | 760    | 919    | 1,039  |
| Total                      | 21,502 | 24,733 | 26,211 | 29,161 | 31,410 | 34,386 | 37,396 | 42,066 | 45,809 | 49,909 |
| <b>Race</b>                |        |        |        |        |        |        |        |        |        |        |
| White                      | 15,001 | 16,855 | 17,901 | 19,919 | 21,461 | 23,260 | 25,166 | 28,269 | 30,611 | 33,337 |
| Black                      | 5,859  | 7,061  | 7,445  | 8,241  | 8,730  | 9,714  | 10,532 | 11,958 | 12,960 | 14,211 |
| Asian                      | 303    | 311    | 380    | 496    | 505    | 565    | 650    | 781    | 967    | 1,023  |
| Native American            | 197    | 260    | 267    | 268    | 338    | 348    | 464    | 530    | 570    | 619    |
| Other                      | 95     | 138    | 143    | 151    | 240    | 367    | 476    | 434    | 614    | 631    |
| Unknown                    | 47     | 108    | 75     | 86     | 136    | 132    | 108    | 94     | 87     | 88     |
| Total                      | 21,502 | 24,733 | 26,211 | 29,161 | 31,410 | 34,386 | 37,396 | 42,066 | 45,809 | 49,909 |
| <b>Sex</b>                 |        |        |        |        |        |        |        |        |        |        |
| Male                       | 11,863 | 13,572 | 14,449 | 15,903 | 17,185 | 18,654 | 20,295 | 22,803 | 24,864 | 26,839 |
| Female                     | 9,639  | 11,161 | 11,762 | 13,258 | 14,225 | 15,732 | 17,101 | 19,263 | 20,945 | 23,070 |
| Total                      | 21,502 | 24,733 | 26,211 | 29,161 | 31,410 | 34,386 | 37,396 | 42,066 | 45,809 | 49,909 |
| <b>Primary diagnosis</b>   |        |        |        |        |        |        |        |        |        |        |
| Diabetes                   | 4,960  | 5,824  | 7,014  | 8,121  | 9,244  | 10,273 | 11,478 | 13,928 | 15,651 | 17,888 |
| Hypertension               | 5,438  | 5,849  | 6,585  | 7,513  | 7,962  | 9,139  | 10,220 | 12,059 | 13,176 | 14,495 |
| Glomerulonephritis         | 3,805  | 4,016  | 4,250  | 4,493  | 4,621  | 4,860  | 5,129  | 5,537  | 5,673  | 5,782  |
| Cystic kidney              | 1,016  | 1,050  | 1,071  | 1,144  | 1,210  | 1,236  | 1,236  | 1,266  | 1,381  | 1,456  |
| Other urologic             | 1,701  | 1,850  | 1,905  | 2,168  | 2,168  | 2,047  | 2,062  | 2,269  | 2,248  | 2,449  |
| Other cause                | 1,224  | 1,516  | 1,636  | 1,838  | 1,858  | 1,984  | 2,148  | 2,564  | 2,745  | 3,306  |
| Unknown cause              | 1,901  | 1,942  | 2,061  | 2,163  | 2,319  | 2,760  | 2,608  | 2,402  | 2,356  | 2,651  |
| Missing disease            | 1,457  | 2,686  | 1,689  | 1,721  | 2,028  | 2,087  | 2,515  | 2,041  | 2,579  | 1,882  |
| Total                      | 21,502 | 24,733 | 26,211 | 29,161 | 31,410 | 34,386 | 37,396 | 42,066 | 45,809 | 49,909 |
| <b>All ESRD patients</b>   |        |        |        |        |        |        |        |        |        |        |
| U.S.                       | 21,502 | 24,733 | 26,211 | 29,161 | 31,410 | 34,386 | 37,396 | 42,066 | 45,809 | 49,909 |
| Puerto Rico                | 303    | 308    | 379    | 391    | 399    | 431    | 477    | 529    | 533    | 552    |
| Other non-U.S.             | 14     | 19     | 15     | 25     | 26     | 25     | 46     | 41     | 53     | 56     |
| Unknown                    | 44     | 60     | 29     | 34     | 31     | 39     | 33     | 18     | 19     | 123    |
| Total                      | 21,863 | 25,120 | 26,634 | 29,611 | 31,866 | 34,881 | 37,952 | 42,654 | 46,414 | 50,640 |

ESRD, end-stage renal disease. The reporting and coding of race changed in 1982; age is as of start of ESRD therapy.

Source: Reference 121

Appendix 16.2

Incidence Counts of Reported ESRD Therapy Attributed to Diabetes, by Age, Sex, and Race, U.S., 1988-91

| Age at ESRD (years) | Males  |       |       |     |        | Females |       |       |     |        | Both sexes |        |       |       |        |
|---------------------|--------|-------|-------|-----|--------|---------|-------|-------|-----|--------|------------|--------|-------|-------|--------|
|                     | White  | Black | Asian | NA  | All    | White   | Black | Asian | NA  | All    | White      | Black  | Asian | NA    | All    |
| 0-4                 | 0      | 0     | 0     | 0   | 0      |         | 0     | 0     | 0   |        | 0          | 0      | 0     |       |        |
| 5-9                 |        | 0     | 0     | 0   |        | 0       | 0     | 0     | 0   | 0      |            | 0      | 0     | 0     |        |
| 10-14               | 0      | 0     | 0     | 0   | 0      |         | 0     | 0     | 0   |        |            | 0      | 0     | 0     |        |
| 15-19               | 14     |       | 0     | 0   | 19     | 12      |       |       |     | 16     | 26         |        |       |       | 35     |
| 20-24               | 163    | 40    | 0     | 0   | 203    | 173     | 64    |       |     | 243    | 336        | 104    |       |       | 446    |
| 25-29               | 748    | 120   |       |     | 877    | 632     | 144   |       |     | 789    | 1,380      | 264    |       | 15    | 1,666  |
| 30-34               | 1,203  | 208   | 10    | 11  | 1,432  | 830     | 165   | 12    | 13  | 1,020  | 2,033      | 373    | 22    | 24    | 2,452  |
| 35-39               | 1,439  | 293   | 19    | 24  | 1,775  | 834     | 228   | 11    | 15  | 1,088  | 2,273      | 521    | 30    | 39    | 2,863  |
| 40-44               | 1,526  | 435   | 28    | 49  | 2,038  | 1,009   | 388   | 19    | 30  | 1,446  | 2,535      | 823    | 47    | 79    | 3,484  |
| 45-49               | 1,537  | 632   | 44    | 77  | 2,290  | 1,121   | 650   | 17    | 61  | 1,849  | 2,658      | 1,282  | 61    | 138   | 4,139  |
| 50-54               | 1,808  | 828   | 72    | 104 | 2,812  | 1,468   | 962   | 45    | 96  | 2,571  | 3,276      | 1,790  | 117   | 200   | 5,383  |
| 55-59               | 2,136  | 908   | 86    | 97  | 3,227  | 2,158   | 1,395 | 82    | 129 | 3,764  | 4,294      | 2,303  | 168   | 226   | 6,991  |
| 60-64               | 2,718  | 1,063 | 89    | 79  | 3,949  | 3,096   | 1,684 | 132   | 148 | 5,060  | 5,814      | 2,747  | 221   | 227   | 9,009  |
| 65-69               | 2,942  | 887   | 116   | 71  | 4,016  | 3,659   | 1,886 | 141   | 154 | 5,840  | 6,601      | 2,773  | 257   | 225   | 9,856  |
| 70-74               | 2,116  | 558   | 58    | 45  | 2,777  | 2,588   | 1,215 | 86    | 79  | 3,968  | 4,704      | 1,773  | 144   | 124   | 6,745  |
| 75-79               | 1,188  | 291   | 47    | 29  | 1,555  | 1,447   | 642   | 72    | 43  | 2,204  | 2,635      | 933    | 119   | 72    | 3,759  |
| 80-84               | 407    | 115   | 19    |     | 546    | 513     | 239   | 13    | 12  | 777    | 920        | 354    | 32    | 17    | 1,323  |
| ≥85                 | 86     | 28    |       |     | 123    | 115     | 68    |       |     | 191    | 201        | 96     | 10    |       | 314    |
| All ages            | 20,032 | 6,411 | 598   | 599 | 27,640 | 19,657  | 9,733 | 640   | 798 | 30,828 | 39,689     | 16,144 | 1,238 | 1,397 | 58,468 |

ESRD, end-stage renal disease; NA, Native American. Table includes residents of 50 states and the District of Columbia only; cases where race is "other" or "unknown" are excluded from the table; incident cases for 1988-91 are combined to produce larger cell sizes; cells with no data shown are suppressed because they contain <10 patients.

Source: Reference 121

Appendix 16.3

Incidence per 10 Million Population of Reported ESRD Therapy Attributed to Diabetes, by Age, Sex, and Race, U.S., 1988-91

| Age at ESRD (years) | Specific rates (unadjusted) |       |       |       |         |       |       |        | Rates adjusted for |       |       |        |       |        |              |
|---------------------|-----------------------------|-------|-------|-------|---------|-------|-------|--------|--------------------|-------|-------|--------|-------|--------|--------------|
|                     | Males                       |       |       |       | Females |       |       |        | Sex                |       |       |        | Race  |        | Sex and race |
|                     | White                       | Black | Asian | NA    | White   | Black | Asian | NA     | White              | Black | Asian | NA     | Male  | Female |              |
| 0-4                 | 0                           | 0     | 0     | 0     |         | 0     | 0     | 0      |                    | 0     | 0     | 0      | 0     |        |              |
| 5-9                 |                             | 0     | 0     | 0     | 0       | 0     | 0     | 0      |                    | 0     | 0     | 0      |       | 0      |              |
| 10-14               | 0                           | 0     | 0     | 0     |         | 0     | 0     | 0      |                    | 0     | 0     | 0      | 0     |        |              |
| 15-19               |                             |       | 0     | 0     |         |       | 0     |        |                    |       | 0     |        |       |        |              |
| 20-24               | 50                          | 76    |       | 0     | 55      | 116   |       |        | 52                 | 97    |       |        | 51    | 62     | 57           |
| 25-29               | 209                         | 228   |       |       | 181     | 248   |       |        | 194                | 238   |       | 207    | 205   | 185    | 195          |
| 30-34               | 331                         | 416   | 71    | 319   | 230     | 289   | 79    | 361    | 279                | 351   | 76    | 340    | 333   | 234    | 283          |
| 35-39               | 438                         | 686   | 153   | 811   | 254     | 461   | 79    | 478    | 343                | 570   | 116   | 645    | 462   | 276    | 367          |
| 40-44               | 520                         | 1,280 | 271   | 1,966 | 341     | 975   | 161   | 1,144  | 427                | 1,119 | 212   | 1,542  | 616   | 418    | 514          |
| 45-49               | 663                         | 2,475 | 585   | 4,090 | 473     | 2,134 | 209   | 3,063  | 564                | 2,293 | 390   | 3,558  | 908   | 688    | 795          |
| 50-54               | 939                         | 3,898 | 1,226 | 6,987 | 730     | 3,708 | 719   | 6,002  | 832                | 3,798 | 959   | 6,459  | 1,359 | 1,138  | 1,246        |
| 55-59               | 1,196                       | 4,905 | 1,942 | 8,133 | 1,123   | 5,983 | 1,526 | 9,838  | 1,160              | 5,454 | 1,717 | 8,977  | 1,731 | 1,803  | 1,769        |
| 60-64               | 1,538                       | 6,361 | 2,428 | 8,087 | 1,552   | 7,638 | 2,732 | 13,451 | 1,543              | 7,003 | 2,557 | 10,811 | 2,207 | 2,427  | 2,322        |
| 65-69               | 1,826                       | 6,156 | 3,753 | 9,216 | 1,860   | 9,481 | 3,692 | 16,555 | 1,839              | 7,845 | 3,665 | 12,940 | 2,469 | 2,963  | 2,727        |
| 70-74               | 1,730                       | 5,518 | 2,761 | 8,973 | 1,581   | 7,934 | 3,331 | 11,827 | 1,648              | 6,738 | 3,025 | 10,408 | 2,277 | 2,489  | 2,390        |
| 75-79               | 1,388                       | 4,095 | 3,297 | 8,629 | 1,089   | 5,331 | 4,332 | 8,493  | 1,229              | 4,705 | 3,800 | 8,511  | 1,828 | 1,759  | 1,795        |
| 80-84               | 836                         | 2,960 | 2,386 |       | 556     | 3,211 | 1,541 | 4,077  | 690                | 3,062 | 1,935 | 3,444  | 1,154 | 933    | 1,042        |
| ≥85                 | 285                         | 1,066 |       |       | 146     | 1,108 |       |        | 212                | 1,076 | 961   |        | 425   | 287    | 355          |
| All ages            | 490                         | 1,116 | 422   | 1,489 | 461     | 1,521 | 433   | 1,950  | 475                | 1,330 | 428   | 1,721  | 571   | 605    | 588          |
| Age adj.            | 497                         | 1,583 | 684   | 2,408 | 420     | 1,855 | 639   | 2,952  | 456                | 1,738 | 660   | 2,714  | 610   | 566    | 589          |

ESRD, end-stage renal disease; NA, Native American. Table includes residents of 50 states and the District of Columbia only; cases where race is "other" or "unknown" are excluded from the table; incident cases for 1988-91 are combined to produce larger cell sizes; cells with no data shown are suppressed because they contain <10 patients. Note that rates are per 10 million population rather than per 1 million because of the small cell sizes; the population base is U.S. resident population on July 1 of each year; the standard population for adjustment is July 1, 1990, U.S. resident population.

Source: Reference 121

## Appendix 16.4

## Incidence of Reported ESRD Therapy, by Detailed Primary Disease, Age, and Race, U.S., 1988-91

| Primary disease group                 | Total<br>1988-91* | Percent<br>distribution | Median age<br>(years) | White (%) | Black (%) | Asian (%) | Native<br>American (%) |
|---------------------------------------|-------------------|-------------------------|-----------------------|-----------|-----------|-----------|------------------------|
| All ESRD                              | 177,660           | 100.0                   | 62                    | 100.0     | 100.0     | 100.0     | 100.0                  |
| Diabetes                              | 60,052            | 33.8                    | 61                    | 34.0      | 32.5      | 36.8      | 63.9                   |
| Hypertension                          | 50,347            | 28.3                    | 68                    | 25.2      | 37.9      | 23.0      | 11.9                   |
| Glomerulonephritis (GN)               | 22,517            | 12.6                    | 54                    | 13.6      | 10.2      | 20.0      | 9.7                    |
| Goodpasture's syndrome                | 589               | 0.3                     | 64                    | 0.4       | <0.1      | 0.1       | 0.2                    |
| Focal glomerulosclerosis, focal GN    | 2,637             | 1.4                     | 40                    | 1.2       | 2.1       | 1.1       | 0.6                    |
| Membranous nephropathy                | 846               | 0.4                     | 55                    | 0.5       | 0.3       | 0.1       | 0.1                    |
| Membranoproliferative GN              | 692               | 0.3                     | 41                    | 0.4       | 0.1       | 0.5       | 0.5                    |
| All other glomerulonephritis          | 17,753            | 9.9                     | 56                    | 10.9      | 7.3       | 18.0      | 8.0                    |
| Cystic kidney diseases                | 5,394             | 3.0                     | 54                    | 3.9       | 1.1       | 2.3       | 1.8                    |
| Interstitial nephritis                | 5,464             | 3.0                     | 63                    | 3.7       | 1.5       | 3.0       | 1.9                    |
| Analgesic nephropathy                 | 1,449             | 0.8                     | 64                    | 0.9       | 0.4       | 0.6       | 0.5                    |
| All other interstitial nephritis      | 4,015             | 2.2                     | 62                    | 2.7       | 1.1       | 2.4       | 1.3                    |
| Obstructive nephropathy               | 3,716             | 2.0                     | 68                    | 2.5       | 1.1       | 1.4       | 1.3                    |
| Collagen vascular diseases            | 3,779             | 2.1                     | 41                    | 2.0       | 2.2       | 3.0       | 1.4                    |
| Lupus erythematosus                   | 2,406             | 1.3                     | 35                    | 1.0       | 1.9       | 2.7       | 1.0                    |
| Scleredema                            | 413               | 0.2                     | 58                    | 0.2       | 0.1       | 0.1       | <0.1                   |
| Wegener's granulomatosis              | 407               | 0.2                     | 62                    | 0.3       | <0.1      | <0.1      | 0.2                    |
| Hemolytic uremic syndrome/TTP         | 367               | 0.2                     | 48                    | 0.2       | <0.1      | <0.1      | 0.0                    |
| Polyarteritis                         | 97                | <0.1                    | 58                    | <0.1      | <0.1      | <0.1      | <0.1                   |
| Henoch-Schonlein purpura              | 68                | <0.1                    | 29                    | <0.1      | <0.1      | <0.1      | <0.1                   |
| Rheumatoid arthritis                  | 21                | <0.1                    | 63                    | <0.1      | <0.1      | <0.1      | 0.0                    |
| Malignancies                          | 2,248             | 1.2                     | 68                    | 1.5       | 0.7       | 0.5       | 0.4                    |
| Multiple myeloma, light chain disease | 1,502             | 0.8                     | 68                    | 0.9       | 0.5       | 0.4       | 0.3                    |
| Renal and urinary tract neoplasms     | 706               | 0.3                     | 66                    | 0.4       | 0.2       | 0.1       | <0.1                   |
| Lymphomas                             | 40                | <0.1                    | 66                    | <0.1      | <0.1      | 0.0       | 0.0                    |
| Metabolic diseases                    | 884               | 0.4                     | 62                    | 0.6       | 0.2       | 0.1       | 0.1                    |
| Amyloidosis                           | 630               | 0.3                     | 64                    | 0.4       | 0.1       | 0.1       | 0.1                    |
| Gouty/uric acid nephropathy           | 87                | <0.1                    | 63                    | <0.1      | <0.1      | 0.0       | 0.0                    |
| Oxalate nephropathy                   | 63                | <0.1                    | 53                    | <0.1      | <0.1      | 0.0       | 0.0                    |
| Cystinosis                            | 37                | <0.1                    | 12                    | <0.1      | <0.1      | 0.0       | 0.0                    |
| Fabry's disease                       | 36                | <0.1                    | 41                    | <0.1      | <0.1      | 0.0       | 0.0                    |
| Macroglobulinemia                     | 9                 | <0.1                    | 65                    | <0.1      | <0.1      | <0.1      | 0.0                    |
| Congenital/other hereditary disease   | 1,331             | 0.7                     | 22                    | 0.9       | 0.3       | 0.4       | 0.8                    |
| Congenital obstructive uropathy       | 348               | 0.1                     | 26                    | 0.2       | <0.1      | <0.1      | 0.2                    |
| Renal dysgenesis, agenesis, dysplasia | 338               | 0.1                     | 23                    | 0.2       | <0.1      | 0.1       | 0.1                    |
| Alport's syndrome                     | 645               | 0.3                     | 20                    | 0.4       | 0.1       | 0.1       | 0.4                    |
| Sickle cell disease                   | 154               | <0.1                    | 36                    | <0.1      | 0.2       | 0.0       | 0.0                    |
| AIDS-related                          | 586               | 0.3                     | 36                    | <0.1      | 1.0       | <0.1      | <0.1                   |
| Other ESRD                            | 1,879             | 1.0                     | 66                    | 1.3       | 0.5       | 0.3       | 0.5                    |
| Cause unknown                         | 10,145            | 5.7                     | 65                    | 6.0       | 4.9       | 6.7       | 4.7                    |
| Missing information                   | 9,175             | 5.1                     | 51                    | 4.2       | 4.9       | 1.8       | 1.0                    |

ESRD, end-stage renal disease. Table includes Medicare patients in the 50 states, the District of Columbia, Puerto Rico, and U.S. territories. \* Divide total by four to determine average annual counts.

Source: Reference 121



Appendix 16.5

**Point Prevalence Counts of Reported ESRD Therapy, by Year, Age, Race, Sex, and Primary Disease Causing ESRD, U.S., 1982-91**

| Characteristics     | 1982   | 1983   | 1984   | 1985    | 1986    | 1987    | 1988    | 1989    | 1990    | 1991    |
|---------------------|--------|--------|--------|---------|---------|---------|---------|---------|---------|---------|
| Age at ESRD (years) |        |        |        |         |         |         |         |         |         |         |
| 0-4                 | 155    | 187    | 212    | 241     | 257     | 262     | 259     | 267     | 269     | 296     |
| 5-9                 | 260    | 293    | 342    | 375     | 443     | 484     | 509     | 551     | 611     | 637     |
| 10-14               | 625    | 684    | 736    | 756     | 778     | 834     | 886     | 921     | 1,025   | 1,073   |
| 15-19               | 1,503  | 1,570  | 1,634  | 1,762   | 1,849   | 1,969   | 2,020   | 2,087   | 2,086   | 2,107   |
| 20-24               | 2,973  | 3,243  | 3,483  | 3,664   | 3,780   | 3,870   | 3,975   | 4,067   | 4,244   | 4,517   |
| 25-29               | 4,329  | 4,917  | 5,387  | 5,846   | 6,373   | 6,755   | 7,103   | 7,443   | 7,877   | 8,092   |
| 30-34               | 5,513  | 6,265  | 7,055  | 7,772   | 8,616   | 9,087   | 9,733   | 10,522  | 11,241  | 12,207  |
| 35-39               | 5,254  | 6,285  | 7,389  | 8,614   | 9,669   | 10,617  | 11,562  | 12,482  | 13,742  | 14,948  |
| 40-44               | 5,279  | 6,283  | 7,054  | 7,846   | 9,008   | 10,089  | 11,321  | 12,918  | 14,800  | 16,633  |
| 45-49               | 5,666  | 6,655  | 7,447  | 8,259   | 8,964   | 10,079  | 11,280  | 12,641  | 13,873  | 16,024  |
| 50-54               | 6,876  | 7,490  | 8,262  | 8,975   | 9,839   | 10,726  | 11,826  | 13,004  | 14,476  | 15,991  |
| 55-59               | 8,088  | 8,956  | 9,846  | 10,542  | 11,346  | 12,121  | 12,869  | 13,959  | 15,516  | 17,382  |
| 60-64               | 7,912  | 9,270  | 10,388 | 11,444  | 12,259  | 13,561  | 14,694  | 15,907  | 17,764  | 19,605  |
| 65-69               | 6,684  | 8,049  | 9,137  | 10,227  | 11,381  | 12,920  | 14,220  | 15,954  | 18,060  | 20,294  |
| 70-74               | 4,842  | 6,137  | 7,027  | 7,818   | 8,807   | 9,697   | 10,636  | 12,113  | 14,286  | 16,963  |
| 75-79               | 2,598  | 3,585  | 4,330  | 4,973   | 5,718   | 6,555   | 7,353   | 8,436   | 9,657   | 11,448  |
| 80-84               | 879    | 1,359  | 1,651  | 2,041   | 2,456   | 2,960   | 3,424   | 4,042   | 4,922   | 5,781   |
| ≥85                 | 285    | 418    | 507    | 638     | 753     | 972     | 1,202   | 1,455   | 1,832   | 2,263   |
| Total               | 69,721 | 81,646 | 91,887 | 101,793 | 112,296 | 123,558 | 134,872 | 148,769 | 166,281 | 186,261 |
| Race                |        |        |        |         |         |         |         |         |         |         |
| White               | 46,547 | 54,223 | 60,937 | 67,454  | 74,305  | 81,483  | 88,481  | 97,411  | 108,274 | 120,707 |
| Black               | 20,139 | 24,006 | 27,237 | 30,304  | 33,462  | 36,971  | 40,523  | 44,675  | 50,213  | 56,508  |
| Asian               | 554    | 798    | 1,045  | 1,335   | 1,611   | 1,905   | 2,235   | 2,694   | 3,257   | 3,885   |
| Native American     | 424    | 621    | 790    | 908     | 1,075   | 1,214   | 1,458   | 1,721   | 1,968   | 2,272   |
| Other               | 1,300  | 1,242  | 1,218  | 1,185   | 1,232   | 1,397   | 1,591   | 1,711   | 2,027   | 2,364   |
| Unknown             | 757    | 756    | 660    | 607     | 611     | 588     | 584     | 557     | 542     | 525     |
| Total               | 69,721 | 81,646 | 91,887 | 101,793 | 112,296 | 123,558 | 134,872 | 148,769 | 166,281 | 186,261 |
| Sex                 |        |        |        |         |         |         |         |         |         |         |
| Male                | 37,854 | 44,196 | 49,853 | 55,146  | 60,669  | 66,528  | 72,547  | 80,095  | 89,899  | 101,069 |
| Female              | 31,867 | 37,450 | 42,034 | 46,647  | 51,627  | 57,030  | 62,325  | 68,674  | 76,382  | 85,192  |
| Total               | 69,721 | 81,646 | 91,887 | 101,793 | 112,296 | 123,558 | 134,872 | 148,769 | 166,281 | 186,261 |
| Primary diagnosis   |        |        |        |         |         |         |         |         |         |         |
| Diabetes            | 9,043  | 11,871 | 15,117 | 18,376  | 21,852  | 25,424  | 29,294  | 34,731  | 40,972  | 48,274  |
| Hypertension        | 12,173 | 15,232 | 18,050 | 20,827  | 23,608  | 26,669  | 29,683  | 33,608  | 38,358  | 43,724  |
| Glomerulonephritis  | 13,311 | 15,940 | 18,323 | 20,615  | 22,848  | 24,858  | 26,803  | 29,034  | 31,504  | 34,329  |
| Cystic kidney       | 3,795  | 4,510  | 5,140  | 5,692   | 6,254   | 6,853   | 7,308   | 7,809   | 8,466   | 9,244   |
| Other urologic      | 5,281  | 6,308  | 7,154  | 7,985   | 8,598   | 8,964   | 9,359   | 9,918   | 10,615  | 11,478  |
| Other cause         | 2,423  | 3,306  | 4,160  | 5,039   | 5,848   | 6,579   | 7,400   | 8,528   | 9,704   | 11,370  |
| Unknown cause       | 6,595  | 7,388  | 8,184  | 8,785   | 9,505   | 10,515  | 10,926  | 11,039  | 11,493  | 12,312  |
| Missing disease     | 17,100 | 17,091 | 15,759 | 14,474  | 13,783  | 13,696  | 14,099  | 14,102  | 15,169  | 15,530  |
| Total               | 69,721 | 81,646 | 91,887 | 101,793 | 112,296 | 123,558 | 134,872 | 148,769 | 166,281 | 186,261 |
| All ESRD patients   |        |        |        |         |         |         |         |         |         |         |
| U.S.                | 69,721 | 81,646 | 91,887 | 101,793 | 112,296 | 123,558 | 134,872 | 148,769 | 166,281 | 186,261 |
| Puerto Rico         | 657    | 874    | 1,082  | 1,203   | 1,310   | 1,448   | 1,577   | 1,792   | 2,005   | 2,153   |
| Other non-U.S.      | 40     | 44     | 48     | 57      | 77      | 89      | 108     | 111     | 142     | 169     |
| Unknown             | 88     | 96     | 74     | 79      | 67      | 64      | 54      | 40      | 48      | 162     |
| Total               | 70,506 | 82,660 | 93,091 | 103,132 | 113,750 | 125,159 | 136,611 | 150,712 | 168,476 | 188,745 |
| Lost to followup    | 12,881 | 11,898 | 11,871 | 12,579  | 12,857  | 13,679  | 14,519  | 14,997  | 13,192  | 10,408  |

ESRD, end-stage renal disease. Table includes patients alive on ESRD therapy and not lost to followup on December 31 of each year (with exception of last row detailing lost to followup); the reporting and coding of race changed in 1982; age is as of December 31.

Source: Reference 121

Appendix 16.6

**Average Point Prevalence Rates per 10 Million Population of Reported ESRD Therapy Attributed to Diabetes, by Age, Sex, and Race, U.S., 1988-91**

| Age at ESRD (years) | Specific rates (unadjusted) |        |       |        |         |        |       |        | Rates adjusted for |        |       |        |       |        |              |
|---------------------|-----------------------------|--------|-------|--------|---------|--------|-------|--------|--------------------|--------|-------|--------|-------|--------|--------------|
|                     | Males                       |        |       |        | Females |        |       |        | Sex                |        |       |        | Race  |        | Sex and race |
|                     | White                       | Black  | Asian | NA     | White   | Black  | Asian | NA     | White              | Black  | Asian | NA     | Male  | Female |              |
| 0-4                 | 0                           | 0      | 0     | 0      |         | 0      | 0     | 0      |                    | 0      | 0     | 0      | 0     |        |              |
| 5-9                 |                             | 0      | 0     | 0      |         | 0      | 0     | 0      |                    | 0      | 0     | 0      |       |        |              |
| 10-14               | 0                           | 0      |       | 0      | 0       | 0      | 0     | 0      | 0                  | 0      |       | 0      |       | 0      |              |
| 15-19               |                             |        |       | 0      |         |        | 0     |        |                    |        | 11    |        |       |        |              |
| 20-24               | 89                          | 127    | 0     | 0      | 105     | 207    |       |        | 97                 | 168    |       |        | 90    | 116    | 103          |
| 25-29               | 553                         | 519    | 91    | 266    | 538     | 688    | 159   | 483    | 545                | 604    | 126   | 377    | 532   | 544    | 538          |
| 30-34               | 1,268                       | 1,288  | 232   | 1,000  | 1,001   | 997    | 295   | 1,176  | 1,130              | 1,137  | 264   | 1,085  | 1,236 | 979    | 1,104        |
| 35-39               | 1,836                       | 2,157  | 429   | 2,325  | 1,317   | 1,566  | 170   | 1,504  | 1,566              | 1,848  | 295   | 1,912  | 1,833 | 1,311  | 1,565        |
| 40-44               | 2,128                       | 3,995  | 608   | 5,008  | 1,310   | 2,781  | 557   | 3,112  | 1,703              | 3,360  | 576   | 4,001  | 2,327 | 1,477  | 1,890        |
| 45-49               | 2,280                       | 6,916  | 1,527 | 10,873 | 1,446   | 5,924  | 737   | 8,304  | 1,847              | 6,391  | 1,113 | 9,550  | 2,888 | 2,025  | 2,446        |
| 50-54               | 2,498                       | 11,660 | 2,795 | 20,078 | 1,744   | 10,746 | 1,857 | 16,034 | 2,110              | 11,175 | 2,300 | 17,873 | 3,769 | 2,965  | 3,357        |
| 55-59               | 2,839                       | 14,546 | 4,446 | 21,787 | 2,433   | 16,616 | 3,862 | 27,423 | 2,630              | 15,589 | 4,108 | 24,542 | 4,474 | 4,417  | 4,449        |
| 60-64               | 3,149                       | 17,388 | 6,086 | 18,974 | 3,160   | 22,385 | 5,360 | 37,276 | 3,150              | 19,907 | 5,655 | 28,218 | 5,101 | 5,853  | 5,494        |
| 65-69               | 3,310                       | 16,823 | 7,216 | 21,256 | 3,455   | 25,257 | 7,804 | 39,998 | 3,375              | 21,101 | 7,428 | 30,744 | 5,216 | 6,543  | 5,909        |
| 70-74               | 3,002                       | 14,343 | 5,909 | 20,087 | 3,057   | 22,963 | 7,709 | 38,090 | 3,018              | 18,699 | 6,754 | 29,139 | 4,602 | 5,902  | 5,282        |
| 75-79               | 2,208                       | 10,243 | 6,074 | 16,159 | 1,940   | 14,143 | 8,626 | 20,244 | 2,060              | 12,188 | 7,315 | 18,158 | 3,407 | 3,769  | 3,599        |
| 80-84               | 1,258                       | 5,585  | 5,787 | 7,064  | 1,037   | 7,807  | 4,321 | 12,695 | 1,138              | 6,676  | 4,940 | 9,833  | 1,957 | 2,047  | 2,007        |
| ≥85                 | 480                         | 2,342  | 2,349 |        | 278     | 2,561  |       |        | 374                | 2,433  | 1,655 |        | 761   | 598    | 678          |
| All ages            | 1,264                       | 3,133  | 956   | 3,781  | 1,114   | 4,276  | 1,007 | 5,287  | 1,187              | 3,735  | 982   | 4,540  | 1,497 | 1,543  | 1,521        |
| Age adj.            | 1,264                       | 4,389  | 1,500 | 5,887  | 1,040   | 5,204  | 1,452 | 7,968  | 1,149              | 4,858  | 1,479 | 7,065  | 1,576 | 1,455  | 1,520        |

ESRD, end-stage renal disease; NA, Native American. Table includes residents of 50 states and the District of Columbia only; it also includes only Medicare patients alive on ESRD therapy and not lost to followup on December 31 of each year; cases where race is "other" or "unknown" are excluded from the table; prevalent cases for December 31, 1988, 1989, 1990, and 1991 are combined to produce larger cell sizes; cells with no data shown are suppressed because they contain <10 patients. Note that rates are per 10 million population rather than per 1 million because of the small cell sizes; the population base is the U.S. resident population on December 31 of each year; the standard population for adjustment is the July 1, 1990, U.S. resident population.

Source: Reference 121

Appendix 16.7

**Patients with ESRD Who Were Alive on December 31, 1991, by Treatment Modality, Sex, Race, and Primary Disease Causing ESRD**

| Sex, race, and primary disease | Transplant |      | Other/unknown dialysis |      | Center hemodialysis |      | Home hemodialysis |     | CAPD and CCPD |      | Total   |     |
|--------------------------------|------------|------|------------------------|------|---------------------|------|-------------------|-----|---------------|------|---------|-----|
|                                | Count      | %    | Count                  | %    | Count               | %    | Count             | %   | Count         | %    | Count   | %   |
| Total                          | 50,468     | 26.7 | 5,950                  | 3.1  | 111,121             | 58.8 | 1,917             | 1.0 | 19,289        | 10.2 | 188,745 | 100 |
| Sex                            |            |      |                        |      |                     |      |                   |     |               |      |         |     |
| Male                           | 30,539     | 29.7 | 3,340                  | 3.2  | 57,468              | 56.0 | 1,098             | 1.0 | 10,157        | 9.8  | 102,602 | 100 |
| Female                         | 19,929     | 23.1 | 2,610                  | 3.0  | 53,653              | 62.2 | 819               | 0.9 | 9,132         | 10.6 | 86,143  | 100 |
| Race                           |            |      |                        |      |                     |      |                   |     |               |      |         |     |
| Native American                | 534        | 23.4 | 76                     | 3.3  | 1,387               | 60.7 | 32                | 1.4 | 253           | 11.0 | 2,282   | 100 |
| Asian                          | 1,078      | 27.1 | 76                     | 1.9  | 2,454               | 61.7 | 29                | 0.7 | 338           | 8.5  | 3,975   | 100 |
| Black                          | 7,829      | 13.7 | 1,468                  | 2.5  | 42,606              | 75.0 | 378               | 0.6 | 4,525         | 7.9  | 56,806  | 100 |
| White                          | 40,455     | 32.9 | 3,862                  | 3.1  | 62,960              | 51.3 | 1,441             | 1.1 | 13,949        | 11.3 | 122,667 | 100 |
| Other/unknown                  | 572        | 18.9 | 468                    | 15.5 | 1,714               | 56.8 | 37                | 1.2 | 224           | 7.4  | 3,015   | 100 |

Appendix 16.7—Continued next page

Appendix 16.7—Continued

| Sex, race, and primary disease | Transplant |      | Other/unknown dialysis |      | Center hemodialysis |      | Home hemodialysis |     | CAPD and CCPD |      | Total  |     |
|--------------------------------|------------|------|------------------------|------|---------------------|------|-------------------|-----|---------------|------|--------|-----|
|                                | Count      | %    | Count                  | %    | Count               | %    | Count             | %   | Count         | %    | Count  | %   |
| Disease groups                 |            |      |                        |      |                     |      |                   |     |               |      |        |     |
| Diabetes                       | 9,072      | 18.4 | 1,300                  | 2.6  | 32,764              | 66.7 | 319               | 0.6 | 5,614         | 11.4 | 49,069 | 100 |
| Hypertension                   | 5,625      | 12.7 | 858                    | 1.9  | 32,864              | 74.5 | 299               | 0.6 | 4,465         | 10.1 | 44,111 | 100 |
| Glomerulo-nephritis            | 14,110     | 40.4 | 755                    | 2.1  | 15,890              | 45.5 | 443               | 1.2 | 3,725         | 10.6 | 34,923 | 100 |
| Cystic kidney                  | 3,679      | 39.4 | 239                    | 2.5  | 4,241               | 45.5 | 187               | 2.0 | 974           | 10.4 | 9,320  | 100 |
| Other urologic                 | 3,668      | 31.5 | 262                    | 2.2  | 6,487               | 55.8 | 159               | 1.3 | 1,044         | 8.9  | 11,620 | 100 |
| Other cause                    | 3,757      | 32.8 | 353                    | 3.0  | 5,817               | 50.7 | 113               | 0.9 | 1,413         | 12.3 | 11,453 | 100 |
| Unknown cause                  | 3,858      | 30.9 | 268                    | 2.1  | 7,005               | 56.2 | 144               | 1.1 | 1,187         | 9.5  | 12,462 | 100 |
| Missing cause                  | 6,699      | 42.4 | 1,915                  | 12.1 | 6,053               | 38.3 | 253               | 1.6 | 867           | 5.4  | 15,787 | 100 |

ESRD, end-stage renal disease; CAPD, continuous ambulatory peritoneal dialysis; CCPD, continuous cycling peritoneal dialysis. Table includes all ESRD patients except those who were lost to followup on December 31. Age is computed as of December 31. The coding of race changed in 1982, with patients who entered the system before 1982 retaining the old coding scheme in later years; therefore, comparisons by race across years must be treated with caution.

Source: Reference 121

Appendix 16.8

**Counts of Renal Transplants, by Donor Type, Year of Transplantation, and Primary Disease Causing ESRD, U.S., 1982-91**

| Donor type and disease group | 1982  | 1983  | 1984  | 1985  | 1986  | 1987  | 1988  | 1989  | 1990  | 1991  |
|------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Cadaver donor                |       |       |       |       |       |       |       |       |       |       |
| Diabetes                     | 446   | 561   | 781   | 993   | 1,298 | 1,279 | 1,288 | 1,395 | 1,521 | 1,623 |
| Hypertension                 | 415   | 535   | 615   | 753   | 914   | 959   | 983   | 928   | 1,124 | 1,092 |
| Glomerulonephritis           | 893   | 1,054 | 1,414 | 1,457 | 1,787 | 1,777 | 1,701 | 1,643 | 1,838 | 1,804 |
| Cystic kidney                | 205   | 241   | 354   | 395   | 522   | 580   | 560   | 522   | 605   | 582   |
| Other urologic               | 212   | 303   | 329   | 400   | 475   | 446   | 355   | 381   | 385   | 423   |
| Other cause                  | 172   | 244   | 308   | 380   | 473   | 439   | 458   | 486   | 514   | 480   |
| Unknown cause                | 306   | 396   | 431   | 469   | 553   | 521   | 489   | 481   | 503   | 507   |
| Missing disease              | 625   | 582   | 568   | 511   | 608   | 547   | 595   | 630   | 582   | 593   |
| Total                        | 3,274 | 3,916 | 4,800 | 5,358 | 6,630 | 6,548 | 6,429 | 6,466 | 7,072 | 7,104 |
| Living-related donor         |       |       |       |       |       |       |       |       |       |       |
| Diabetes                     | 258   | 277   | 299   | 334   | 374   | 352   | 306   | 320   | 363   | 453   |
| Hypertension                 | 137   | 129   | 127   | 131   | 144   | 139   | 126   | 145   | 142   | 204   |
| Glomerulonephritis           | 483   | 550   | 508   | 523   | 500   | 529   | 497   | 504   | 541   | 591   |
| Cystic kidney                | 50    | 58    | 66    | 64    | 67    | 72    | 66    | 67    | 90    | 104   |
| Other urologic               | 124   | 139   | 119   | 159   | 148   | 132   | 115   | 132   | 156   | 172   |
| Other cause                  | 96    | 141   | 196   | 174   | 198   | 201   | 177   | 187   | 202   | 248   |
| Unknown cause                | 153   | 137   | 149   | 166   | 132   | 135   | 103   | 117   | 119   | 139   |
| Missing disease              | 281   | 207   | 139   | 164   | 180   | 177   | 221   | 201   | 202   | 211   |
| Total                        | 1,582 | 1,638 | 1,603 | 1,715 | 1,743 | 1,737 | 1,611 | 1,673 | 1,815 | 2,122 |
| Total                        |       |       |       |       |       |       |       |       |       |       |
| Diabetes                     | 704   | 838   | 1,080 | 1,327 | 1,672 | 1,631 | 1,594 | 1,715 | 1,884 | 2,076 |
| Hypertension                 | 552   | 664   | 742   | 884   | 1,058 | 1,098 | 1,109 | 1,073 | 1,266 | 1,296 |
| Glomerulonephritis           | 1,376 | 1,604 | 1,922 | 1,980 | 2,287 | 2,306 | 2,198 | 2,147 | 2,379 | 2,395 |
| Cystic kidney                | 255   | 299   | 420   | 459   | 589   | 652   | 626   | 589   | 695   | 686   |
| Other urologic               | 336   | 442   | 448   | 559   | 623   | 578   | 470   | 513   | 541   | 595   |
| Other cause                  | 268   | 385   | 504   | 554   | 671   | 640   | 635   | 673   | 716   | 728   |
| Unknown cause                | 459   | 533   | 580   | 635   | 685   | 656   | 592   | 598   | 622   | 646   |
| Missing disease              | 906   | 789   | 707   | 675   | 788   | 724   | 816   | 831   | 784   | 804   |
| Total                        | 4,856 | 5,554 | 6,403 | 7,073 | 8,373 | 8,285 | 8,040 | 8,139 | 8,887 | 9,226 |

ESRD, end-stage renal disease.

Source: Reference 121

Appendix 16.9

**Annual Death Rates for All Dialysis Patients Not Yet Transplanted per 1,000 Person-Years at Risk in 1989-91, by Age on January 1, Race, and Primary Disease**

| Age (years) | All   |       |       |       |       | Diabetes |       | Hypertension |       | Glomerulonephritis |       | Other/unknown |       |
|-------------|-------|-------|-------|-------|-------|----------|-------|--------------|-------|--------------------|-------|---------------|-------|
|             | All   | NA    | Asian | Black | White | Black    | White | Black        | White | Black              | White | Black         | White |
| Total       | 235.9 | 212.7 | 170.1 | 186.5 | 269.3 | 233.5    | 351.1 | 180.2        | 341.1 | 126.0              | 177.8 | 188.3         | 217.8 |
| 0-14        | 58.1  | 0.0   | 96.3  | 65.5  | 54.1  |          |       |              |       |                    |       |               |       |
| 15-19       | 32.4  | 64.5  | 19.0  | 50.2  | 22.3  | 111.7    | 62.3  | 31.9         | 15.4  | 43.2               | 24.3  | 62.5          | 20.0  |
| 20-24       | 56.7  | 56.1  | 15.2  | 61.9  | 53.4  | 135.5    | 153.7 | 56.5         | 31.2  | 37.1               | 29.8  | 83.7          | 56.5  |
| 25-29       | 79.6  | 94.6  | 41.6  | 95.1  | 71.4  | 192.7    | 154.0 | 70.4         | 59.6  | 56.0               | 42.4  | 124.6         | 45.2  |
| 30-34       | 103.9 | 110.2 | 62.3  | 105.2 | 105.5 | 167.0    | 198.0 | 69.0         | 64.5  | 92.9               | 53.3  | 130.8         | 76.8  |
| 35-39       | 114.8 | 117.3 | 35.6  | 116.4 | 116.9 | 165.5    | 219.1 | 88.0         | 82.9  | 104.3              | 59.8  | 153.2         | 72.3  |
| 40-44       | 124.3 | 103.1 | 56.9  | 110.5 | 139.3 | 172.9    | 254.0 | 79.1         | 100.3 | 102.6              | 70.7  | 140.1         | 99.3  |
| 45-49       | 136.5 | 131.2 | 83.9  | 117.0 | 154.0 | 168.0    | 270.6 | 93.9         | 125.1 | 104.8              | 87.1  | 119.3         | 104.8 |
| 50-54       | 165.6 | 153.1 | 122.5 | 141.2 | 188.1 | 175.6    | 279.1 | 122.0        | 167.2 | 109.3              | 127.3 | 150.2         | 139.9 |
| 55-59       | 198.6 | 206.1 | 146.7 | 159.8 | 228.9 | 194.6    | 315.1 | 137.4        | 221.4 | 137.3              | 162.1 | 147.8         | 170.8 |
| 60-64       | 243.9 | 225.4 | 190.1 | 192.9 | 278.4 | 212.5    | 372.9 | 186.1        | 275.9 | 153.1              | 197.0 | 178.3         | 219.3 |
| 65-69       | 295.4 | 298.7 | 218.5 | 248.1 | 320.9 | 273.0    | 417.9 | 227.3        | 321.9 | 221.2              | 236.0 | 260.2         | 271.2 |
| 70-74       | 352.9 | 304.8 | 294.7 | 288.9 | 381.8 | 316.8    | 481.0 | 268.0        | 395.4 | 267.0              | 307.1 | 309.4         | 332.1 |
| 75-79       | 426.1 | 458.6 | 352.4 | 364.2 | 450.5 | 386.4    | 551.4 | 350.7        | 457.2 | 316.5              | 373.6 | 392.0         | 423.4 |
| 80-84       | 498.4 | 459.8 | 372.4 | 423.3 | 527.0 | 476.9    | 614.0 | 414.6        | 547.7 | 411.5              | 476.8 | 396.7         | 486.2 |
| ≥85         | 607.7 | 525.9 | 492.0 | 524.2 | 640.7 | 589.8    | 647.0 | 506.5        | 655.4 | 404.3              | 558.4 | 579.9         | 647.5 |

NA, Native American. Table includes all patients who had reached day 91 of end-stage renal disease (ESRD) by the end of the year; cells with no data shown are suppressed because they contain <10 patients or have missing values; "0.0" represents a rate <0.1.

Source: Reference 121

Appendix 16.10

**Annual Death Rates for Hemodialysis Patients Not Yet Transplanted per 1,000 Person-Years at Risk in 1989-91, by Age on January 1, Race, and Primary Disease Causing ESRD**

| Age (years) | All   |       |       |       |       | Diabetes |       | Hypertension |       | Glomerulonephritis |       | Other/unknown |       |
|-------------|-------|-------|-------|-------|-------|----------|-------|--------------|-------|--------------------|-------|---------------|-------|
|             | All   | NA    | Asian | Black | White | Black    | White | Black        | White | Black              | White | Black         | White |
| Total       | 238.0 | 213.1 | 181.6 | 187.5 | 275.3 | 231.4    | 353.1 | 181.2        | 343.8 | 130.1              | 184.8 | 188.2         | 226.8 |
| 0-14        | 54.6  |       | 153.5 | 57.6  | 48.3  |          |       |              |       |                    |       |               |       |
| 15-19       | 31.5  | 0.0   | 0.0   | 54.8  | 19.7  | 134.6    | 0.0   | 20.5         | 19.6  | 50.0               | 20.9  | 70.1          | 17.6  |
| 20-24       | 56.1  | 71.4  | 18.1  | 60.6  | 52.8  | 133.9    | 193.2 | 48.9         | 33.9  | 36.0               | 30.4  | 85.3          | 49.6  |
| 25-29       | 79.8  | 116.5 | 45.5  | 86.7  | 75.5  | 198.9    | 181.7 | 57.6         | 60.6  | 52.1               | 45.7  | 117.2         | 46.1  |
| 30-34       | 104.3 | 118.0 | 66.4  | 103.3 | 108.3 | 171.5    | 221.8 | 69.1         | 68.1  | 95.5               | 52.9  | 123.5         | 82.0  |
| 35-39       | 112.9 | 112.3 | 36.3  | 112.0 | 117.3 | 169.0    | 246.2 | 86.8         | 88.1  | 102.5              | 60.1  | 143.8         | 72.4  |
| 40-44       | 120.4 | 114.2 | 55.4  | 108.3 | 135.6 | 175.3    | 250.5 | 79.9         | 114.2 | 99.3               | 73.0  | 132.8         | 97.0  |
| 45-49       | 134.2 | 141.7 | 86.6  | 115.9 | 153.0 | 164.1    | 274.5 | 93.7         | 125.5 | 116.4              | 86.3  | 115.5         | 105.7 |
| 50-54       | 159.8 | 154.7 | 133.6 | 138.2 | 181.3 | 175.8    | 264.6 | 120.2        | 164.0 | 104.3              | 126.3 | 136.7         | 140.7 |
| 55-59       | 192.0 | 198.7 | 157.9 | 158.2 | 221.5 | 189.5    | 301.1 | 137.7        | 217.1 | 138.6              | 153.7 | 144.0         | 170.9 |
| 60-64       | 236.1 | 206.2 | 198.3 | 189.1 | 272.0 | 206.9    | 359.6 | 182.9        | 276.2 | 147.8              | 193.3 | 177.3         | 216.8 |
| 65-69       | 288.6 | 286.3 | 221.4 | 244.4 | 315.4 | 265.6    | 400.8 | 225.0        | 315.8 | 227.1              | 234.8 | 258.7         | 272.0 |
| 70-74       | 345.3 | 281.6 | 303.9 | 282.4 | 377.0 | 306.4    | 465.3 | 263.7        | 392.8 | 259.8              | 307.2 | 304.3         | 327.8 |
| 75-79       | 417.8 | 436.2 | 347.3 | 357.8 | 443.7 | 377.6    | 529.4 | 344.9        | 452.4 | 312.9              | 369.3 | 385.7         | 420.6 |
| 80-84       | 490.5 | 490.1 | 368.2 | 419.9 | 519.3 | 471.4    | 601.3 | 409.6        | 531.1 | 416.5              | 478.1 | 394.8         | 486.7 |
| ≥85         | 588.8 | 549.2 | 485.4 | 499.4 | 624.7 | 546.6    | 633.5 | 487.4        | 639.6 | 392.5              | 542.4 | 555.6         | 633.6 |

ESRD, end-stage renal disease; NA, Native American. Table includes all patients who had reached day 91 of ESRD by the end of the year; cells with no data shown are suppressed because they contain <10 patients or have missing values; "0.0" represents a rate <0.1.

Source: Reference 121

Appendix 16.11

**Annual Death Rates for CAPD/CCPD Patients Not Yet Transplanted per 1,000 Person-Years at Risk in 1989-91, by Age on January 1, Race, and Primary Disease**

| Age (years) | All   |       |       |         |       | Diabetes |       | Hypertension |       | Glomerulonephritis |       | Other/unknown |       |
|-------------|-------|-------|-------|---------|-------|----------|-------|--------------|-------|--------------------|-------|---------------|-------|
|             | All   | NA    | Asian | Black   | White | Black    | White | Black        | White | Black              | White | Black         | White |
| Total       | 238.3 | 243.7 | 118.3 | 176.4   | 260.6 | 259.7    | 357.6 | 156.9        | 335.1 | 106.1              | 166.2 | 176.3         | 187.9 |
| 0-14        | 68.0  | 0.0   | 75.2  | 116.4   | 57.0  |          |       |              |       |                    |       |               |       |
| 15-19       | 33.3  | 138.2 | 0.0   | 43.2    | 25.8  |          |       | 89.8         | 0.0   | 38.6               | 30.0  | 42.7          | 17.9  |
| 20-24       | 53.1  | 0.0   | 0.0   | 52.1    | 53.5  | 167.9    | 69.3  | 30.0         | 32.1  | 45.7               | 22.4  | 57.1          | 72.2  |
| 25-29       | 68.7  | 36.7  | 38.7  | 110.8   | 53.3  | 111.2    | 94.2  | 108.0        | 46.6  | 78.6               | 23.8  | 144.3         | 35.5  |
| 30-34       | 96.9  | 91.3  | 59.1  | 99.8    | 96.5  | 171.9    | 156.5 | 48.0         | 63.7  | 66.7               | 48.5  | 153.0         | 46.5  |
| 35-39       | 116.0 | 134.0 | 18.1  | 111.1   | 123.2 | 132.1    | 194.1 | 73.7         | 65.4  | 105.4              | 65.1  | 158.0         | 64.6  |
| 40-44       | 137.2 | 53.9  | 59.8  | 113.9   | 152.6 | 189.1    | 263.7 | 70.6         | 68.4  | 104.9              | 61.7  | 137.2         | 109.2 |
| 45-49       | 151.4 | 106.5 | 91.2  | 122.3   | 167.9 | 192.0    | 273.3 | 100.1        | 130.0 | 51.3               | 98.3  | 157.5         | 110.2 |
| 50-54       | 202.4 | 179.3 | 98.4  | 157.1   | 227.2 | 176.3    | 354.3 | 120.1        | 191.7 | 140.1              | 147.7 | 228.2         | 140.6 |
| 55-59       | 236.4 | 306.9 | 63.6  | 174.3   | 260.2 | 237.7    | 356.5 | 125.7        | 244.8 | 131.3              | 208.9 | 178.1         | 181.7 |
| 60-64       | 289.2 | 359.1 | 114.5 | 241.7   | 303.2 | 279.3    | 457.1 | 226.8        | 282.7 | 206.9              | 213.5 | 194.8         | 230.0 |
| 65-69       | 346.2 | 516.1 | 228.9 | 292.3   | 355.3 | 364.9    | 546.6 | 234.7        | 354.9 | 212.7              | 247.2 | 299.8         | 269.2 |
| 70-74       | 410.7 | 614.8 | 249.2 | 406.2   | 411.7 | 589.5    | 596.1 | 339.1        | 414.2 | 393.6              | 304.1 | 382.2         | 358.3 |
| 75-79       | 495.2 | 879.7 | 440.2 | 456.3   | 496.7 | 714.6    | 756.8 | 402.3        | 484.2 | 140.0              | 430.4 | 483.6         | 426.2 |
| 80-84       | 573.4 |       | 390.5 | 514.3   | 580.8 | 504.9    | 654.3 | 660.2        | 666.9 |                    | 500.8 | 440.4         | 489.9 |
| ≥85         | 830.9 |       |       | 1,171.3 | 782.3 |          | 834.8 | 1,088.0      | 764.7 |                    | 762.3 |               | 778.0 |

CAPD, continuous ambulatory peritoneal dialysis; CCPD, continuous cycling peritoneal dialysis; NA, Native American. Table includes all patients who had reached day 91 of end-stage renal disease by the end of the year; cells with no data shown are suppressed because they contain <10 patients or have missing values; "0.0" represents a rate <0.1.

Source: Reference 121

Appendix 16.12

**Death Rates for All Patients with Functioning Cadaveric Donor Transplants per 1,000 Person-Years at Risk in First 3 Years Post-Transplant (1986-88), by Age on January 1, Race, and Primary Disease**

| Age (years) | All   |       |       |       |       | Diabetes |       | Hypertension |       | Glomerulonephritis |       | Other/unknown |       |
|-------------|-------|-------|-------|-------|-------|----------|-------|--------------|-------|--------------------|-------|---------------|-------|
|             | All   | NA    | Asian | Black | White | Black    | White | Black        | White | Black              | White | Black         | White |
| Total       | 86.9  | 127.6 | 72.2  | 81.6  | 88.8  | 141.0    | 127.4 | 75.9         | 94.1  | 64.7               | 67.6  | 60.6          | 74.0  |
| 0-4         | 147.3 |       |       | 73.8  | 170.2 |          |       |              |       |                    | 121.9 | 0.0           | 131.5 |
| 5-9         | 89.3  |       |       | 119.0 | 79.9  |          |       |              |       |                    | 102.4 | 197.4         | 67.3  |
| 10-14       | 34.4  |       |       | 71.1  | 27.7  |          |       |              |       | 123.0              | 13.2  | 37.2          | 34.9  |
| 15-19       | 28.7  |       | 0.0   | 35.9  | 26.2  |          |       |              | 0.0   | 62.6               | 10.7  | 15.3          | 32.3  |
| 20-24       | 42.3  |       | 0.0   | 54.0  | 39.7  | 120.8    | 55.7  | 24.4         | 0.0   | 31.2               | 31.8  | 56.5          | 42.8  |
| 25-29       | 59.8  | 0.0   | 21.8  | 61.5  | 62.2  | 177.0    | 95.1  | 38.5         | 45.2  | 9.2                | 44.2  | 63.8          | 54.4  |
| 30-34       | 60.3  | 0.0   | 48.7  | 38.8  | 68.3  | 37.9     | 118.6 | 33.5         | 0.0   | 41.8               | 35.4  | 33.0          | 48.9  |
| 35-39       | 74.6  | 117.7 | 109.4 | 59.5  | 78.7  | 109.5    | 112.6 | 39.4         | 91.5  | 41.8               | 39.6  | 93.7          | 60.9  |
| 40-44       | 79.9  | 77.3  | 35.3  | 70.1  | 84.6  | 125.8    | 116.5 | 61.7         | 56.4  | 71.2               | 76.9  | 38.9          | 64.0  |
| 45-49       | 103.3 | 347.2 | 122.6 | 103.4 | 98.8  | 135.7    | 166.8 | 93.4         | 63.7  | 145.5              | 90.6  | 53.4          | 65.7  |
| 50-54       | 105.9 | 192.9 | 36.0  | 97.7  | 111.1 | 159.7    | 163.8 | 99.5         | 110.1 | 81.4               | 83.9  | 65.0          | 96.0  |
| 55-59       | 151.2 | 163.2 | 268.3 | 186.0 | 137.6 | 247.6    | 153.0 | 181.0        | 173.6 | 147.6              | 125.3 | 77.3          | 133.7 |
| 60-64       | 146.3 | 246.1 | 64.6  | 147.7 | 146.8 | 154.7    | 203.9 | 139.5        | 162.4 | 404.2              | 176.1 | 105.5         | 104.4 |
| 65-69       | 197.4 |       |       | 146.4 | 215.1 |          | 594.8 | 68.6         | 288.1 |                    | 116.5 | 204.7         | 169.1 |
| 70-74       | 210.5 |       |       |       | 206.3 |          |       |              | 363.0 |                    | 121.7 |               | 266.1 |
| 75-79       |       |       |       |       |       |          |       |              |       |                    |       |               |       |

NA, Native American; cases with primary disease unknown/missing are included in the "All" category and are excluded from the "Other/unknown" category. Patients at risk from transplant to death or 1 year. Cells with no data shown are suppressed because they contain <10 patients or have missing values; "0.0" represents a rate <0.1.

Source: Reference 121

Appendix 16.13

**Death Rates for All Patients with Functioning Living-Related Donor Transplants per 1,000 Person-Years at Risk in First 3 Years Post-Transplant (1986-88), by Age on January 1, Race, and Primary Disease**

| Age (years) | All   |      |       |       |       | Diabetes |       | Hypertension |       | Glomerulonephritis |       | Other/unknown |       |
|-------------|-------|------|-------|-------|-------|----------|-------|--------------|-------|--------------------|-------|---------------|-------|
|             | All   | NA   | Asian | Black | White | Black    | White | Black        | White | Black              | White | Black         | White |
| Total       | 34.5  | 54.3 | 56.2  | 37.9  | 33.6  | 50.5     | 54.1  | 42.8         | 41.0  | 11.4               | 25.2  | 60.9          | 29.8  |
| 0-4         | 53.8  |      |       | 0.0   | 59.2  |          |       |              |       |                    | 46.9  |               | 59.7  |
| 5-9         | 7.5   |      |       | 0.0   | 8.7   |          |       |              |       |                    | 0.0   |               | 16.8  |
| 10-14       | 25.0  |      |       | 51.7  | 24.0  |          |       |              |       |                    | 18.7  | 75.1          | 8.3   |
| 15-19       | 14.7  |      |       | 0.0   | 17.7  |          |       |              | 90.5  | 0.0                | 8.9   | 0.0           | 23.4  |
| 20-24       | 13.7  |      |       | 15.3  | 14.0  |          | 19.0  |              | 0.0   | 0.0                | 16.6  | 55.2          | 15.5  |
| 25-29       | 21.4  |      |       | 15.5  | 22.4  |          | 29.0  | 70.0         | 0.0   | 0.0                | 18.9  | 0.0           | 27.8  |
| 30-34       | 36.1  |      | 0.0   | 101.9 | 30.0  |          | 58.3  | 50.1         | 28.5  | 36.3               | 16.9  | 181.5         | 0.0   |
| 35-39       | 32.0  |      | 65.7  | 13.6  | 34.4  | 0.0      | 69.7  | 0.0          | 0.0   | 0.0                | 13.9  | 81.3          | 30.4  |
| 40-44       | 49.2  |      |       | 36.9  | 53.1  |          | 60.8  | 49.8         | 72.5  | 0.0                | 51.1  |               | 63.3  |
| 45-49       | 50.3  |      |       | 66.1  | 38.9  | 0.0      | 66.6  | 118.7        | 0.0   |                    | 35.9  |               | 38.8  |
| 50-54       | 83.8  |      |       | 65.1  | 75.3  |          | 82.7  | 0.0          | 127.2 |                    | 49.8  |               | 59.8  |
| 55-59       | 52.9  |      |       | 0.0   | 64.3  |          | 110.5 | 0.0          | 66.0  |                    | 71.1  |               | 43.8  |
| 60-64       | 108.1 |      |       | 180.0 | 95.4  |          |       |              |       |                    | 42.9  |               | 118.4 |
| 65-69       | 91.7  |      |       |       | 91.7  |          |       |              |       |                    |       |               |       |
| 70-74       |       |      |       |       |       |          |       |              |       |                    |       |               |       |
| 75-79       |       |      |       |       |       |          |       |              |       |                    |       |               |       |

NA, Native American; cases with primary disease unknown/missing are included in the "All" category and are excluded from the "Other/unknown" category. Patients at risk from transplant to death or 1 year. Cells with no data shown are suppressed because they contain <10 patients or have missing values; "0.0" represents a rate <0.1.

Source: Reference 121

Appendix 16.14

**Annual Death Rates for All ESRD Patients per 1,000 Person-Years at Risk in 1989-91, by Age on January 1, Race, and Primary Disease**

| Age (years) | All   |       |       |       |       | Diabetes |       | Hypertension |       | Glomerulonephritis |       | Other/unknown |       |
|-------------|-------|-------|-------|-------|-------|----------|-------|--------------|-------|--------------------|-------|---------------|-------|
|             | All   | NA    | Asian | Black | White | Black    | White | Black        | White | Black              | White | Black         | White |
| Total       | 176.4 | 166.0 | 126.9 | 164.2 | 184.0 | 221.6    | 265.8 | 163.0        | 292.8 | 100.9              | 105.8 | 158.0         | 142.0 |
| 0-14        | 26.8  | 0.0   | 42.9  | 36.9  | 24.2  |          |       |              |       |                    |       |               |       |
| 15-19       | 20.0  | 35.4  | 24.5  | 39.9  | 13.8  | 87.2     | 50.5  | 32.2         | 6.7   | 40.1               | 15.4  | 44.7          | 13.4  |
| 20-24       | 32.3  | 33.2  | 16.7  | 48.2  | 26.5  | 123.9    | 88.1  | 45.8         | 14.6  | 31.8               | 16.8  | 61.1          | 27.9  |
| 25-29       | 43.9  | 41.9  | 26.4  | 73.5  | 35.1  | 148.7    | 87.1  | 56.4         | 32.0  | 43.1               | 20.2  | 97.3          | 23.2  |
| 30-34       | 58.7  | 59.4  | 36.1  | 80.6  | 51.5  | 135.5    | 103.7 | 56.2         | 33.9  | 66.7               | 25.5  | 101.3         | 37.2  |
| 35-39       | 68.5  | 87.9  | 21.7  | 91.6  | 59.7  | 140.6    | 112.4 | 72.5         | 51.7  | 78.0               | 29.9  | 118.5         | 37.5  |
| 40-44       | 83.0  | 77.4  | 39.2  | 91.8  | 80.3  | 146.7    | 148.6 | 71.7         | 71.4  | 77.4               | 39.5  | 115.3         | 60.1  |
| 45-49       | 99.5  | 111.0 | 59.4  | 102.2 | 99.0  | 158.3    | 191.7 | 81.9         | 92.5  | 83.8               | 54.5  | 102.4         | 68.8  |
| 50-54       | 128.6 | 115.2 | 101.1 | 127.1 | 130.8 | 167.4    | 229.9 | 109.7        | 128.1 | 99.0               | 77.4  | 124.0         | 96.1  |
| 55-59       | 165.6 | 184.4 | 129.6 | 149.5 | 175.1 | 188.2    | 280.9 | 131.2        | 179.1 | 122.9              | 117.6 | 129.7         | 121.6 |
| 60-64       | 217.6 | 204.6 | 179.0 | 185.1 | 236.6 | 207.8    | 354.9 | 179.8        | 250.1 | 145.7              | 157.5 | 168.1         | 175.0 |
| 65-69       | 281.8 | 293.0 | 209.1 | 244.3 | 300.8 | 272.4    | 410.3 | 223.4        | 309.8 | 217.6              | 215.1 | 253.6         | 249.1 |
| 70-74       | 347.7 | 295.5 | 290.2 | 287.7 | 374.2 | 315.4    | 479.9 | 266.9        | 391.9 | 266.1              | 297.6 | 308.7         | 322.6 |
| 75-79       | 424.2 | 456.1 | 351.7 | 363.4 | 448.0 | 386.2    | 551.4 | 350.4        | 455.3 | 314.3              | 370.6 | 390.7         | 420.5 |
| 80-84       | 498.1 | 459.8 | 372.4 | 423.3 | 526.6 | 476.9    | 614.0 | 414.6        | 547.7 | 411.5              | 476.1 | 396.7         | 486.4 |
| ≥85         | 607.0 | 525.9 | 492.0 | 524.2 | 639.6 | 598.6    | 647.0 | 506.5        | 655.4 | 404.3              | 559.4 | 579.9         | 644.6 |

ESRD, end-stage renal disease; NA, Native American. Table includes all ESRD patients who had reached day 91 of ESRD by the end of the year; cells with no data shown are suppressed because they contain <10 patients or have missing values; "0.0" represents a rate <0.1.

Source: Reference 121

Appendix 16.15

Death Rates for All Dialysis Patients Not Yet Transplanted with ESRD Attributed to Diabetes per 1,000 Person-Years at Risk in 1989-91, by Cause of Death, Age on January 1, Sex, and Race

| Cause of death                  | All ages |        |        |       |        |       |        | Age 0-19 years | Age 20-44 years |        |        |       |        | Age 45-64 years |        |        |        |        | Age ≥65 years |        |        |        |        |
|---------------------------------|----------|--------|--------|-------|--------|-------|--------|----------------|-----------------|--------|--------|-------|--------|-----------------|--------|--------|--------|--------|---------------|--------|--------|--------|--------|
|                                 | All      | Male   | Female | Asian | Black  | NA    | White  | All            | All             | Male   | Female | Black | White  | All             | Male   | Female | Black  | White  | All           | Male   | Female | Black  | White  |
| Total                           | 304.5    | 308.0  | 301.7  | 245.0 | 233.5  | 246.6 | 351.1  | 131.9          | 202.3           | 209.0  | 193.2  | 170.4 | 215.2  | 263.6           | 274.0  | 254.8  | 192.7  | 320.8  | 410.6         | 439.3  | 393.4  | 316.3  | 472.0  |
| Pericarditis                    | 1.2      | 1.5    | <1     | <1    | <1     | 1.3   | 1.4    |                | 1.3             | 1.3    | 1.4    | 1.4   | 1.4    | 1.2             | 1.4    | <1     | <1     | 1.5    | 1.1           | 1.6    | <1     | <1     | 1.2    |
| Myocardial infarction           | 39.2     | 43.8   | 35.4   | 33.4  | 28.1   | 25.4  | 46.3   | 0.0            | 23.2            | 23.4   | 22.9   | 15.3  | 26.3   | 38.9            | 44.9   | 33.8   | 26.1   | 48.7   | 47.5          | 57.5   | 41.4   | 35.5   | 55.5   |
| Other cardiac                   | 84.3     | 88.1   | 81.1   | 80.9  | 63.4   | 72.7  | 97.2   | 32.9           | 54.0            | 56.4   | 50.8   | 41.1  | 58.9   | 72.2            | 76.5   | 68.5   | 51.6   | 87.5   | 115.7         | 131.3  | 106.3  | 88.9   | 132.7  |
| Cerebrovascular                 | 16.2     | 14.3   | 17.7   | 11.7  | 15.8   | 12.2  | 16.9   |                | 10.6            | 10.8   | 10.4   | 9.3   | 11.2   | 14.0            | 13.2   | 14.7   | 12.6   | 15.6   | 22.0          | 19.0   | 23.8   | 22.8   | 21.9   |
| Embolism, pulmonary             | 1.1      | <1     | 1.3    | 1.1   | 1.0    | <1    | 1.2    |                | <1              | <1     | <1     | <1    | <1     | <1              | <1     | 1.3    | <1     | 1.1    | 1.5           | 1.4    | 1.6    | 1.4    | 1.7    |
| GI hemorrhage                   | 3.6      | 4.0    | 3.3    | 4.4   | 3.1    | <1    | 4.0    |                | 2.0             | 2.3    | 1.6    | <1    | 2.5    | 2.8             | 3.4    | 2.3    | 2.6    | 3.2    | 5.5           | 6.4    | 5.0    | 4.8    | 5.9    |
| Hemorrhage, other               | <1       | <1     | 1.1    | 1.1   | <1     | <1    | <1     |                | <1              | <1     | <1     | <1    | <1     | <1              | <1     | 1.2    | <1     | <1     | 1.0           | 1.1    | 1.0    | <1     | 1.1    |
| Pulmonary infection             | 5.5      | 6.7    | 4.4    | 4.4   | 4.4    | 7.8   | 5.9    | 0.0            | 3.2             | 3.2    | 3.2    | 1.9   | 3.8    | 3.8             | 4.8    | 2.9    | 3.1    | 4.2    | 8.9           | 12.7   | 6.6    | 7.2    | 9.4    |
| Septicemia                      | 27.4     | 24.5   | 29.7   | 21.2  | 26.0   | 17.0  | 28.8   | 0.0            | 17.6            | 16.7   | 18.7   | 18.4  | 17.4   | 23.6            | 22.1   | 25.0   | 21.8   | 26.1   | 37.3          | 34.5   | 39.0   | 35.0   | 39.1   |
| Infection, other                | 2.8      | 2.6    | 2.9    | 2.7   | 2.3    | 3.9   | 3.0    |                | 3.3             | 3.6    | 2.9    | 3.9   | 3.2    | 2.7             | 2.4    | 2.9    | 2.3    | 2.8    | 2.7           | 2.1    | 3.0    | 1.7    | 3.2    |
| Hyperkalemia                    | 3.1      | 3.4    | 3.0    | 1.1   | 2.0    | 2.1   | 3.9    |                | 6.2             | 6.5    | 5.7    | 6.8   | 5.9    | 2.6             | 2.6    | 2.5    | 1.2    | 3.8    | 2.5           | 2.3    | 2.6    | 1.5    | 2.9    |
| Malignancy                      | 3.0      | 3.3    | 2.7    | <1    | 3.7    | 2.1   | 2.8    | 0.0            | <1              | <1     | <1     | <1    | <1     | 2.6             | 3.1    | 2.3    | 3.3    | 2.4    | 4.7           | 6.0    | 3.9    | 5.4    | 4.5    |
| Withdrawal from dialysis        | 36.3     | 32.2   | 39.7   | 23.4  | 18.5   | 34.6  | 47.6   | 32.9           | 18.6            | 18.2   | 19.0   | 9.0   | 22.4   | 27.1            | 25.8   | 28.1   | 13.2   | 37.7   | 57.6          | 53.4   | 60.2   | 29.6   | 75.3   |
| Suicide                         | <1       | 1.1    | <1     | 0.0   | <1     | 0.0   | 1.0    |                | <1              | <1     | <1     | <1    | <1     | <1              | 1.2    | <1     | <1     | 1.3    | <1            | 1.1    | <1     | <1     | <1     |
| Accident, not treatment related | <1       | <1     | <1     | 0.0   | <1     | 0.0   | <1     |                | <1              | <1     | <1     | <1    | <1     | <1              | <1     | <1     | <1     | <1     | <1            | <1     | <1     | <1     | <1     |
| Unknown cause                   | 20.6     | 21.4   | 19.9   | 17.8  | 19.2   | 19.7  | 21.6   |                | 19.2            | 20.9   | 16.9   | 20.4  | 18.5   | 18.4            | 18.5   | 18.2   | 15.5   | 20.7   | 24.4          | 26.7   | 23.0   | 24.3   | 24.6   |
| Other                           | 19.6     | 20.1   | 19.2   | 13.3  | 15.9   | 13.5  | 22.3   | 32.9           | 16.7            | 17.6   | 15.4   | 17.3  | 16.9   | 16.2            | 16.6   | 15.9   | 12.6   | 19.5   | 25.6          | 27.7   | 24.4   | 20.3   | 28.9   |
| Missing data                    | 37.9     | 38.1   | 37.8   | 26.7  | 27.0   | 31.1  | 45.2   | 32.9           | 22.6            | 24.3   | 20.3   | 21.8  | 22.6   | 34.0            | 35.1   | 33.0   | 23.1   | 42.6   | 50.9          | 53.4   | 49.3   | 34.7   | 62.1   |
| Years at risk                   | 82,516   | 37,103 | 45,413 | 1,791 | 28,839 | 2,282 | 48,766 | 30             | 14,352          | 8,216  | 6,136  | 3,525 | 10,331 | 39,175          | 18,015 | 21,159 | 15,137 | 21,395 | 28,958        | 10,860 | 18,097 | 10,168 | 17,019 |
| No. of patients                 | 118,912  | 54,403 | 64,509 | 2,562 | 38,470 | 3,117 | 73,597 | 53             | 21,496          | 12,397 | 9,099  | 4,785 | 15,995 | 54,922          | 25,672 | 29,250 | 19,834 | 31,478 | 42,441        | 16,313 | 26,128 | 13,839 | 26,085 |

ESRD, end-stage renal disease; NA, Native American; GI, gastrointestinal. Table includes all patients who had reached day 91 of ESRD by the end of the year; the "Other" cause group includes air embolism, vascular access hemorrhage, viral hepatitis, pancreatitis, and treatment-related accidents, each of which has a rate <1; cells with no data shown are suppressed because they contain <10 patients or have missing values; "0.0" represents a rate <0.1.

Source: Reference 121

Appendix 16.16

Death Rates for Hemodialysis Patient Not Yet Transplanted with ESRD Attributed to Diabetes per 1,000 Person-Years at Risk in 1989-91, by Cause of Death, Age on January 1, Sex, and Race

|                                 | All ages |        |        |       |        |       |        | Age 0-19 years | Age 20-44 years |       |        |       |        | Age 45-64 years |        |        |        |        | Age ≥65 years |        |        |        |        |
|---------------------------------|----------|--------|--------|-------|--------|-------|--------|----------------|-----------------|-------|--------|-------|--------|-----------------|--------|--------|--------|--------|---------------|--------|--------|--------|--------|
|                                 | All      | Male   | Female | Asian | Black  | NA    | White  | All            | All             | Male  | Female | Black | White  | All             | Male   | Female | Black  | White  | All           | Male   | Female | Black  | White  |
| Total                           | 301.2    | 307.1  | 296.6  | 253.0 | 231.4  | 244.1 | 353.1  | 91.9           | 212.7           | 218.1 | 205.0  | 173.9 | 232.4  | 253.9           | 265.4  | 244.6  | 189.1  | 311.4  | 395.1         | 427.8  | 376.5  | 308.2  | 456.3  |
| Pericarditis                    | 1.2      | 1.5    | <1     | <1    | <1     | 1.5   | 1.4    |                | 1.1             | 1.0   | 1.2    | 1.0   | 1.2    | 1.2             | 1.6    | 1.0    | <1     | 1.6    | 1.1           | 1.6    | <1     | <1     | 1.2    |
| Myocardial infarction           | 38.7     | 43.7   | 34.8   | 33.7  | 27.8   | 24.8  | 46.8   | 0.0            | 22.7            | 22.5  | 23.1   | 14.1  | 26.9   | 37.7            | 43.1   | 33.3   | 25.9   | 47.9   | 46.1          | 57.9   | 39.5   | 34.5   | 54.6   |
| Other cardiac                   | 83.3     | 86.6   | 80.7   | 83.5  | 62.6   | 68.7  | 98.0   | 0.0            | 56.5            | 58.1  | 54.2   | 41.7  | 63.6   | 70.0            | 74.0   | 66.8   | 50.0   | 86.1   | 110.4         | 124.0  | 102.7  | 86.5   | 127.3  |
| Cerebrovascular                 | 15.8     | 14.1   | 17.1   | 12.8  | 15.4   | 12.9  | 16.4   |                | 11.0            | 10.8  | 11.3   | 10.3  | 11.4   | 13.2            | 12.3   | 13.9   | 12.1   | 14.7   | 21.0          | 19.0   | 22.1   | 21.6   | 20.8   |
| Embolism, pulmonary             | 1.0      | <1     | 1.2    | 1.2   | 1.0    | <1    | 1.1    |                | <1              | <1    | <1     | 1.0   | <1     | <1              | <1     | 1.1    | <1     | <1     | 1.4           | 1.3    | 1.5    | 1.4    | 1.5    |
| GI hemorrhage                   | 3.8      | 4.2    | 3.4    | 4.9   | 3.4    | 1.0   | 4.2    |                | 2.2             | 2.4   | 1.9    | 1.0   | 2.8    | 2.9             | 3.4    | 2.5    | 2.9    | 3.2    | 5.5           | 6.7    | 4.9    | 4.8    | 6.0    |
| Hemorrhage, other               | <1       | <1     | 1.1    | 1.2   | <1     | 1.0   | <1     |                | <1              | <1    | <1     | <1    | <1     | <1              | <1     | 1.3    | <1     | <1     | 1.0           | 1.1    | <1     | <1     | 1.2    |
| Pulmonary infection             | 5.7      | 7.2    | 4.6    | 4.9   | 4.4    | 7.7   | 6.4    | 0.0            | 3.8             | 4.1   | 3.3    | 2.4   | 4.6    | 3.9             | 5.0    | 3.0    | 3.2    | 4.6    | 8.7           | 12.5   | 6.6    | 6.9    | 9.2    |
| Septicemia                      | 26.3     | 24.3   | 27.8   | 22.1  | 25.1   | 14.4  | 27.7   | 0.0            | 17.5            | 16.6  | 18.8   | 18.2  | 17.3   | 21.8            | 21.6   | 22.0   | 20.6   | 23.8   | 35.3          | 33.5   | 36.4   | 33.5   | 36.8   |
| Infection, other                | 2.5      | 2.3    | 2.7    | 3.0   | 2.1    | 4.1   | 2.7    |                | 3.5             | 3.9   | 2.8    | 4.1   | 3.4    | 2.5             | 2.2    | 2.7    | 2.0    | 2.6    | 2.2           | 1.6    | 2.6    | 1.6    | 2.5    |
| Hyperkalemia                    | 3.4      | 3.8    | 3.1    | 1.2   | 2.0    | 2.0   | 4.5    |                | 8.0             | 8.4   | 7.4    | 8.2   | 7.8    | 2.7             | 2.8    | 2.7    | 1.1    | 4.3    | 2.6           | 2.5    | 2.6    | 1.4    | 3.2    |
| Malignancy                      | 3.2      | 3.7    | 2.9    | <1    | 4.0    | 2.0   | 2.9    |                | <1              | <1    | <1     | <1    | <1     | 2.8             | 3.2    | 2.5    | 3.6    | 2.5    | 4.8           | 6.3    | 3.9    | 5.6    | 4.5    |
| Withdrawal from dialysis        | 36.0     | 32.1   | 39.0   | 25.1  | 18.5   | 35.6  | 48.6   | 45.9           | 18.4            | 18.5  | 18.3   | 9.3   | 23.4   | 25.8            | 24.7   | 26.7   | 12.9   | 37.1   | 55.7          | 52.1   | 57.7   | 29.2   | 73.5   |
| Suicide                         | <1       | 1.0    | <1     | 0.0   | <1     |       | <1     |                | <1              | <1    | 0.0    | <1    | <1     | <1              | 1.2    | <1     | <1     | 1.3    | <1            | <1     | <1     | <1     | <1     |
| Accident, not treatment related | <1       | <1     | <1     | 0.0   | <1     | 0.0   | <1     |                | <1              | <1    | <1     | <1    | <1     | <1              | <1     | <1     | <1     | <1     | <1            | <1     | <1     | <1     | <1     |
| Unknown cause                   | 20.6     | 21.7   | 19.8   | 17.8  | 19.4   | 19.6  | 21.6   |                | 21.5            | 23.4  | 19.0   | 22.0  | 21.0   | 17.8            | 17.5   | 18.0   | 15.3   | 19.8   | 23.9          | 27.1   | 22.0   | 24.4   | 24.0   |
| Other                           | 19.1     | 20.0   | 18.5   | 12.8  | 15.6   | 12.9  | 22.0   |                | 18.5            | 19.1  | 17.8   | 17.9  | 19.4   | 15.2            | 16.0   | 14.5   | 12.4   | 18.1   | 24.4          | 26.7   | 23.0   | 19.3   | 27.8   |
| Missing data                    | 37.8     | 38.2   | 37.5   | 27.0  | 26.9   | 34.6  | 46.0   | 45.9           | 24.2            | 25.4  | 22.4   | 20.3  | 25.4   | 32.9            | 34.5   | 31.6   | 23.1   | 41.3   | 49.3          | 52.0   | 47.8   | 34.1   | 60.6   |
| Years at risk                   | 68,238   | 29,771 | 38,466 | 1,628 | 25,821 | 1,933 | 38,124 | 21             | 9,957           | 5,811 | 4,145  | 2,897 | 6,641  | 32,500          | 14,611 | 17,888 | 13,375 | 16,862 | 25,759        | 9,341  | 16,417 | 9,541  | 14,608 |
| No. of patients                 | 96,838   | 43,065 | 53,773 | 2,324 | 34,186 | 2,625 | 56,688 | 34             | 14,579          | 8,594 | 5,985  | 3,913 | 10,064 | 44,955          | 20,567 | 24,388 | 17,384 | 24,484 | 37,270        | 13,892 | 23,378 | 12,879 | 22,118 |

ESRD, end-stage renal disease; NA, Native American; GI, gastrointestinal. The "Other" cause group includes air embolism, vascular access hemorrhage, viral hepatitis, pancreatitis, and treatment-related accidents, each of which has a rate <1; patients at risk from transplant to death or 1 year; cells with no data shown are suppressed because they contain <10 patients or have missing values.

Source: Reference 121



Appendix 16.17

Death Rates for CAPD/CCPD Patients with ESRD Attributed to Diabetes per 1,000 Person-Years at Risk in 1989-91, by Cause of Death, Age on January 1, Sex, and Race

| Cause of death                  | All ages |       |        |       |       |       |        | Age 0-19 years | Age 20-44 years |       |        |       |       | Age 45-64 years |       |        |       |       | Age ≥65 years |       |        |       |       |
|---------------------------------|----------|-------|--------|-------|-------|-------|--------|----------------|-----------------|-------|--------|-------|-------|-----------------|-------|--------|-------|-------|---------------|-------|--------|-------|-------|
|                                 | All      | Male  | Female | Asian | Black | NA    | White  | All            | All             | Male  | Female | Black | White | All             | Male  | Female | Black | White | All           | Male  | Female | Black | White |
| Total                           | 334.8    | 322.4 | 348.2  | 228.4 | 259.7 | 306.9 | 357.6  | 296.6          | 183.4           | 190.8 | 174.4  | 159.5 | 187.9 | 322.3           | 322.9 | 321.6  | 224.6 | 366.6 | 564.1         | 516.2 | 611.2  | 461.4 | 594.0 |
| Pericarditis                    | 1.5      | 1.8   | 1.1    |       | <1    |       | 1.7    |                | 2.1             | 2.8   | 1.3    | 2.2   | 2.1   | 1.0             | <1    | 1.2    |       | 1.5   | 1.6           | 2.5   | <1     | 2.2   | 1.6   |
| Myocardial infarction           | 43.9     | 46.5  | 41.0   | 45.6  | 32.1  | 37.9  | 46.9   |                | 23.1            | 26.0  | 19.6   | 20.5  | 23.6  | 48.2            | 55.7  | 40.2   | 29.9  | 55.0  | 63.3          | 58.0  | 68.5   | 50.5  | 67.6  |
| Other cardiac                   | 92.6     | 97.2  | 87.8   | 73.0  | 73.3  | 106.1 | 97.6   | 148.3          | 51.5            | 55.5  | 46.8   | 45.5  | 52.7  | 83.1            | 88.1  | 77.9   | 63.0  | 92.7  | 167.0         | 177.4 | 156.9  | 130.8 | 173.1 |
| Cerebrovascular                 | 18.5     | 16.0  | 21.3   | 0.0   | 17.5  | 11.3  | 19.3   |                | 9.8             | 11.3  | 8.1    | 2.2   | 11.2  | 18.3            | 18.1  | 18.4   | 15.3  | 20.0  | 30.8          | 18.4  | 42.9   | 39.0  | 30.2  |
| Embolism, pulmonary             | 1.7      | 1.4   | 1.9    |       | <1    | 3.7   | 1.9    |                | <1              | 1.1   | <1     | 0.0   | 1.0   | 2.0             | 1.6   | 2.5    | <1    | 2.4   | 2.0           | 1.6   | 2.4    | 2.2   | 2.1   |
| GI hemorrhage                   | 3.3      | 3.8   | 2.7    |       | 1.4   |       | 4.0    |                | 1.5             | 1.6   | 1.3    | 0.0   | 1.8   | 2.9             | 4.4   | 1.2    | <1    | 3.9   | 6.6           | 5.8   | 7.4    | 4.5   | 7.5   |
| Hemorrhage, other               | <1       | <1    | 1.1    |       | <1    |       | 1.0    |                | <1              |       | 1.3    |       | <1    | 1.2             | 1.2   | 1.2    | <1    | 1.5   | <1            | <1    | <1     | 2.2   | <1    |
| Pulmonary infection             | 4.4      | 4.4   | 4.5    |       | 4.2   | 11.3  | 4.4    |                | 2.1             | 1.1   | 3.3    | 0.0   | 2.5   | 2.9             | 3.2   | 2.5    | 2.4   | 2.4   | 10.8          | 11.7  | 9.9    | 13.7  | 10.8  |
| Septicemia                      | 35.2     | 27.9  | 43.2   | 9.1   | 36.9  | 34.1  | 35.4   |                | 21.9            | 21.5  | 22.4   | 25.0  | 21.4  | 33.8            | 25.4  | 42.8   | 35.5  | 34.3  | 56.2          | 42.8  | 69.3   | 52.8  | 58.4  |
| Infection, other                | 4.1      | 3.1   | 5.1    |       | 3.7   | 3.7   | 4.3    |                | 3.0             | 2.8   | 3.3    | 2.2   | 3.2   | 3.5             | 2.0   | 5.1    | 4.0   | 3.3   | 6.6           | 5.8   | 7.4    | 4.5   | 7.5   |
| Hyperkalemia                    | 1.6      | 1.2   | 1.9    |       | 1.4   | 3.7   | 1.6    |                | 1.8             | 1.6   | 2.0    | 0.0   | 2.1   | 1.4             | 1.2   | 1.7    | 1.6   | 1.5   | 1.6           | <1    | 2.4    | 2.2   | 1.0   |
| Malignancy                      | 1.8      | 2.0   | 1.5    |       | <1    | 3.7   | 2.0    | 0.0            | <1              | 0.0   | 1.3    |       | <1    | 2.0             | 2.8   | 1.2    | <1    | 2.7   | 2.9           | 3.3   | 2.4    | 2.2   | 2.7   |
| Withdrawal from dialysis        | 39.6     | 33.6  | 45.9   | 9.1   | 20.8  | 34.1  | 45.2   |                | 20.0            | 18.1  | 22.4   | 9.1   | 21.4  | 34.7            | 32.7  | 36.8   | 15.3  | 42.2  | 75.8          | 58.8  | 92.5   | 48.2  | 86.0  |
| Suicide                         | 1.3      | 2.0   | <1     |       |       |       | 1.7    |                | 1.2             | 1.6   | <1     |       | 1.4   | 1.2             | 1.6   | <1     |       | 1.8   | 1.6           | 3.3   |        |       | 2.1   |
| Accident, not treatment related | <1       | <1    | <1     |       |       |       | <1     |                | <1              | <1    |        |       | <1    | <1              | <1    |        |       | <1    | <1            | <1    | <1     |       | 1.0   |
| Unknown cause                   | 21.6     | 21.1  | 22.0   | 27.4  | 18.4  | 22.7  | 22.4   |                | 12.9            | 14.7  | 10.8   | 9.1   | 13.8  | 23.2            | 24.6  | 21.8   | 19.3  | 26.1  | 30.0          | 23.5  | 36.3   | 25.2  | 28.6  |
| Other                           | 22.9     | 20.8  | 25.2   | 27.4  | 17.9  | 22.7  | 24.1   | 148.3          | 11.7            | 12.4  | 10.8   | 13.6  | 11.6  | 22.0            | 18.1  | 26.1   | 13.7  | 25.5  | 39.5          | 38.6  | 40.4   | 34.4  | 40.0  |
| Missing data                    | 38.8     | 37.5  | 40.2   | 36.5  | 27.9  | 11.3  | 42.8   | 0.0            | 17.6            | 17.5  | 17.6   | 29.6  | 15.6  | 39.9            | 40.4  | 39.4   | 21.0  | 48.9  | 65.4          | 61.3  | 69.3   | 45.9  | 72.4  |
| Years at risk                   | 10,453   | 5,430 | 5,022  | 109   | 2,113 | 263   | 7,893  | 6              | 3,238           | 1,765 | 1,472  | 438   | 2,750 | 4,808           | 2,473 | 2,334  | 1,237 | 3,289 | 2,399         | 1,189 | 1,210  | 435   | 1,848 |
| No. of patients                 | 15,606   | 8,063 | 7,543  | 162   | 2,941 | 372   | 12,031 | 12             | 4,686           | 2,563 | 2,123  | 588   | 4,030 | 6,997           | 3,606 | 3,391  | 1,678 | 4,933 | 3,911         | 1,890 | 2,021  | 673   | 3,058 |

CAPD, continuous ambulatory peritoneal dialysis; CCPD, continuous cycling peritoneal dialysis; ESRD, end-stage renal disease; NA, Native American; GI, gastrointestinal. Table includes all patients not yet transplanted who had reached day 91 of ESRD by the end of the year; the "Other" cause group includes air embolism, vascular access hemorrhage, viral hepatitis, pancreatitis, and treatment-related accidents, each of which has a rate <1; cells with no data shown are suppressed because they contain <10 patients or have missing values; "0.0" represents a rate <0.1.

Source: Reference 121

Appendix 16.18

Death Rates for All Patients with Functioning Cadaveric Transplants with ESRD Attributed to Diabetes per 1,000 Person-Years at Risk in 1986-88, by Cause of Death, Age at Transplant, Sex, and Race

| Cause of death                  | All ages |       |        |       |       |       |       | Age 0-19 years | Age 20-44 years |       |        |       |       | Age 45-64 years |       |        |       |       | Age ≥65 years |       |        |       |       |
|---------------------------------|----------|-------|--------|-------|-------|-------|-------|----------------|-----------------|-------|--------|-------|-------|-----------------|-------|--------|-------|-------|---------------|-------|--------|-------|-------|
|                                 | All      | Male  | Female | Asian | Black | NA    | White | All            | All             | Male  | Female | Black | White | All             | Male  | Female | Black | White | All           | Male  | Female | Black | White |
| Total                           | 130.7    | 132.3 | 128.1  | 86.6  | 141.0 | 331.3 | 127.4 | 0.0            | 109.4           | 102.7 | 118.9  | 110.5 | 109.8 | 172.9           | 180.8 | 154.9  | 172.3 | 166.5 | 468.0         | 460.8 |        | 108.3 | 647.1 |
| Pericarditis                    | <1       | <1    |        |       | 1.9   |       |       |                |                 |       |        |       |       | <1              | 1.3   |        | 3.8   |       |               |       |        |       |       |
| Myocardial infarction           | 17.1     | 19.0  | 14.0   | 28.8  | 13.3  | 30.1  | 17.6  |                | 16.6            | 18.7  | 13.7   | 11.8  | 17.5  | 17.9            | 20.3  | 12.3   | 15.3  | 17.1  | 36.0          |       |        |       | 53.9  |
| Other cardiac                   | 23.6     | 20.8  | 28.1   |       | 24.7  | 60.2  | 23.3  |                | 23.1            | 18.0  | 30.4   | 27.6  | 23.0  | 24.5            | 25.8  | 21.6   | 22.9  | 23.7  | 36.0          | 41.8  |        |       | 53.9  |
| Cerebrovascular                 | 4.2      | 4.0   | 4.4    |       | 1.9   |       | 4.7   |                | 4.0             | 3.4   | 4.9    | 3.9   | 4.1   | 4.7             | 5.4   | 3.0    |       | 6.6   |               |       |        |       |       |
| Embolism, pulmonary             | 5.0      | 5.8   | 3.7    |       | 5.7   |       | 5.0   |                | 4.0             | 4.1   | 3.9    |       | 4.6   | 6.6             | 8.1   | 3.0    | 11.4  | 5.2   | 36.0          | 41.8  |        |       | 53.9  |
| GI hemorrhage                   | <1       | <1    |        |       |       |       | <1    |                |                 |       |        |       |       | 1.8             | 2.7   |        |       | 2.6   |               |       |        |       |       |
| Hemorrhage, other               | 1.1      | <1    | 1.4    |       | 3.8   |       | <1    |                | <1              |       | <1     |       | <1    | 2.8             | 2.7   | 3.0    | 7.6   | 1.3   |               |       |        |       |       |
| Pulmonary infection             | 6.1      | 7.7   | 3.7    |       | 3.8   |       | 6.4   |                | 4.8             | 6.2   | 2.9    | 3.9   | 5.0   | 8.5             | 9.5   | 6.1    | 3.8   | 9.2   | 36.0          | 41.8  |        |       | 53.9  |
| Septicemia                      | 14.9     | 12.6  | 18.5   |       | 24.7  | 150.6 | 11.8  |                | 8.9             | 6.9   | 11.7   | 11.8  | 8.7   | 25.5            | 19.0  | 40.2   | 38.2  | 15.8  | 144.0         | 167.5 |        |       | 215.7 |
| Infection, other                | 2.8      | 2.7   | 2.9    |       | 1.9   |       | 3.0   |                | 2.4             | 2.0   | 2.9    | 3.9   | 2.3   | 3.7             | 4.0   | 3.0    |       | 5.2   |               |       |        |       |       |
| Hyperkalemia                    | 1.1      | <1    | 2.2    |       | 1.9   |       | 1.0   |                | <1              |       | 1.9    |       | <1    | 1.8             | 1.3   | 3.0    | 3.8   | 1.3   |               |       |        |       |       |
| Malignancy                      | <1       | 1.3   |        |       |       |       | 1.0   |                | <1              | <1    |        |       | <1    | 1.8             | 2.7   |        |       | 2.6   |               |       |        |       |       |
| Withdrawal from dialysis        | 4.4      | 4.5   | 4.4    |       | 1.9   | 30.1  | 4.7   |                | 4.0             | 3.4   | 4.9    | 3.9   | 3.6   | 5.6             | 6.7   | 3.0    |       | 7.9   |               |       |        |       |       |
| Accident, not treatment related | <1       | <1    |        |       | 1.9   |       | <1    |                | <1              | 1.3   |        | 3.9   | <1    |                 |       |        |       |       |               |       |        |       |       |
| Unknown cause                   | 7.8      | 8.6   | 6.6    |       | 9.5   | 30.1  | 7.4   |                | 6.9             | 6.9   | 6.8    | 7.8   | 6.9   | 10.3            | 12.2  | 6.1    | 11.4  | 9.2   |               |       |        |       |       |
| Other                           | 10.9     | 10.8  | 11.1   | 57.7  | 7.6   | 30.1  | 10.8  |                | 9.3             | 9.7   | 8.8    | 7.8   | 8.7   | 14.1            | 12.2  | 18.5   | 7.6   | 15.8  | 36.0          | 41.8  |        |       | 53.9  |
| Missing data                    | 28.9     | 30.3  | 26.6   |       | 36.2  |       | 28.4  |                | 22.3            | 20.8  | 24.5   | 23.6  | 22.6  | 41.5            | 46.2  | 30.9   | 45.9  | 42.2  | 144.0         | 125.6 |        | 108.3 | 161.7 |
| Years at risk                   | 3,556    | 2,206 | 1,349  | 34    | 524   | 33    | 2,951 | 12             | 2,457           | 1,440 | 1,017  | 253   | 2,166 | 1,058           | 735   | 322    | 261   | 756   | 27            | 23    |        | 9     | 18    |
| No. of patients                 | 3,865    | 2,403 | 1,462  | 36    | 571   | 39    | 3,206 | 12             | 2,637           | 1,539 | 1,098  | 270   | 2,328 | 1,179           | 826   | 353    | 290   | 842   | 37            | 32    |        | 10    | 27    |

ESRD, end-stage renal disease; NA, Native American; GI, gastrointestinal. The "Other" cause group includes air embolism, vascular access hemorrhage, viral hepatitis, pancreatitis, and treatment-related accidents, each of which has a rate <1; patients at risk from transplant to death or 1 year; cells with no data shown are suppressed because they contain <10 patients or have missing values.

Source: Reference 121

Appendix 16.19

**Death Rates for Patients with Functioning Living-Related Donor Transplants with ESRD Attributed to Diabetes per 1,000 Person-Years at Risk in 1986-88, by Cause of Death, Age at Transplant, Sex, and Race**

| Cause of death           | All ages |      |        |       |       |       | Age 0-19 years | Age 20-44 years |      |      |        |       | Age 45-64 years |      |       |        |       | Age ≥65 years |     |      |       |
|--------------------------|----------|------|--------|-------|-------|-------|----------------|-----------------|------|------|--------|-------|-----------------|------|-------|--------|-------|---------------|-----|------|-------|
|                          | All      | Male | Female | Asian | Black | NA    | White          | All             | All  | Male | Female | Black | White           | All  | Male  | Female | Black | White         | All | Male | White |
| Total                    | 55.9     | 60.7 | 49.8   |       | 50.5  | 160.7 | 54.1           |                 | 50.5 | 49.0 | 52.2   | 52.4  | 51.1            | 89.1 | 124.5 | 34.8   | 47.3  | 75.3          |     |      |       |
| Myocardial infarction    | 10.9     | 10.7 | 11.3   |       | 16.8  |       | 10.8           |                 | 10.5 | 10.6 | 10.4   | 26.2  | 9.9             | 13.7 | 11.3  | 17.4   |       | 16.7          |     |      |       |
| Other cardiac            | 10.9     | 5.3  | 18.1   |       | 16.8  | 80.3  | 9.7            |                 | 11.7 | 4.2  | 20.9   | 26.2  | 11.2            | 6.8  | 11.3  |        |       |               |     |      |       |
| Cerebrovascular          | 3.9      | 7.1  |        |       |       |       | 4.3            |                 | 2.3  | 4.2  |        |       | 2.4             | 13.7 | 22.6  |        |       |               |     | 16.7 |       |
| Embolism, pulmonary      | 1.9      | 1.7  | 2.2    |       |       |       | 2.1            |                 | 2.3  | 2.1  | 2.6    |       | 2.4             |      |       |        |       |               |     |      |       |
| Hemorrhage, other        | <1       | 1.7  |        |       |       | 80.3  |                |                 |      |      |        |       |                 | 6.8  | 11.3  |        |       |               |     |      |       |
| Pulmonary infection      | 2.9      | 5.3  |        |       |       |       | 3.2            |                 | 3.5  | 6.4  |        |       | 3.7             |      |       |        |       |               |     |      |       |
| Septicemia               | 1.9      | 1.7  | 2.2    |       |       |       | 2.1            |                 | 2.3  | 2.1  | 2.6    |       | 2.4             |      |       |        |       |               |     |      |       |
| Infection, other         | 1.9      | 3.5  |        |       |       |       | 2.1            |                 | 2.3  | 4.2  |        |       | 2.4             |      |       |        |       |               |     |      |       |
| Withdrawal from dialysis | 1.9      |      | 4.5    |       |       |       | 2.1            |                 | 1.1  |      | 2.6    |       | 1.2             | 6.8  |       | 17.4   |       |               |     |      | 8.3   |
| Suicide                  | 1.9      | 3.5  |        |       |       |       | 2.1            |                 | 1.1  | 2.1  |        |       | 1.2             | 6.8  | 11.3  |        |       |               |     |      | 8.3   |
| Unknown cause            | 2.9      | 5.3  |        |       |       |       | 3.2            |                 | 3.5  | 6.4  |        |       | 3.7             |      |       |        |       |               |     |      |       |
| Other                    | 2.9      | 3.5  | 2.2    |       |       |       | 3.2            |                 | 3.5  | 4.2  | 2.6    |       | 3.7             |      |       |        |       |               |     |      |       |
| Missing data             | 9.9      | 10.7 | 9.0    |       | 16.8  |       | 8.6            |                 | 5.8  | 2.1  | 10.4   |       | 6.2             | 34.2 | 56.5  |        | 47.3  | 25.1          |     |      |       |
| Years at risk            | 1,000    | 559  | 441    |       | 59    | 12    | 923            |                 | 851  | 468  | 382    | 38    | 800             | 145  | 88    | 57     | 21    | 119           |     |      |       |
| No. of patients          | 1,032    | 578  | 454    |       | 62    | 14    | 950            |                 | 875  | 480  | 395    | 40    | 823             | 153  | 95    | 58     | 22    | 124           |     |      |       |

ESRD, end-stage renal disease; NA, Native American. The "Other" cause group includes air embolism, vascular access hemorrhage, viral hepatitis, pancreatitis, and treatment-related accidents, each of which has a rate <1; patients at risk from transplant to death or 1 year; cells with no data shown are suppressed because they contain <10 patients or have missing values.

Source: Reference 121

Appendix 16.20

Death Rates for All Patients with ESRD Attributed to Diabetes per 1,000 Person-Years at Risk in 1989-91, by Cause of Death, Age on January 1, Sex, and Race

|                                 | All ages |        |        |       |        |       |        | Age 0-19 years | Age 20-44 years |        |        |       |        | Age 45-64 years |        |        |        |        | Age ≥65 years |        |        |        |        |
|---------------------------------|----------|--------|--------|-------|--------|-------|--------|----------------|-----------------|--------|--------|-------|--------|-----------------|--------|--------|--------|--------|---------------|--------|--------|--------|--------|
|                                 | All      | Male   | Female | Asian | Black  | NA    | White  | All            | All             | Male   | Female | Black | White  | All             | Male   | Female | Black  | White  | All           | Male   | Female | Black  | White  |
| Total                           | 251.3    | 242.2  | 259.8  | 231.9 | 221.6  | 227.3 | 265.8  | 82.0           | 121.1           | 126.9  | 113.5  | 142.3 | 117.2  | 236.4           | 235.5  | 237.3  | 185.2  | 272.0  | 407.8         | 433.0  | 392.3  | 315.4  | 467.5  |
| Pericarditis                    | <1       | 1.1    | <1     | <1    | <1     | 1.1   | 1.0    |                | <1              | <1     | <1     | 1.0   | <1     | 1.0             | 1.1    | <1     | <1     | 1.2    | 1.1           | 1.6    | <1     | <1     | 1.2    |
| Myocardial infarction           | 32.1     | 34.1   | 30.3   | 30.4  | 26.5   | 23.8  | 34.8   | 16.4           | 13.6            | 14.4   | 12.5   | 12.4  | 13.9   | 34.6            | 38.0   | 31.4   | 25.0   | 41.0   | 47.0          | 56.5   | 41.3   | 35.3   | 54.9   |
| Other cardiac                   | 67.8     | 66.6   | 68.8   | 75.1  | 59.3   | 66.1  | 71.3   | 16.4           | 29.7            | 30.8   | 28.2   | 34.1  | 28.7   | 62.7            | 63.1   | 62.4   | 48.3   | 71.7   | 114.6         | 128.7  | 105.9  | 88.3   | 131.1  |
| Cerebrovascular                 | 13.4     | 11.5   | 15.3   | 10.6  | 14.9   | 11.3  | 13.0   |                | 6.5             | 6.5    | 6.4    | 7.8   | 6.2    | 12.6            | 11.6   | 13.6   | 12.0   | 13.5   | 21.9          | 18.9   | 23.7   | 22.7   | 21.8   |
| Embolism, pulmonary             | 1.2      | 1.0    | 1.3    | 1.0   | 1.0    | <1    | 1.3    |                | 1.1             | 1.1    | 1.1    | 1.0   | 1.1    | 1.0             | <1     | 1.3    | <1     | 1.1    | 1.5           | 1.4    | 1.5    | 1.4    | 1.6    |
| GI hemorrhage                   | 2.9      | 3.0    | 2.8    | 4.0   | 2.9    | <1    | 2.9    |                | 1.1             | 1.2    | <1     | <1    | 1.2    | 2.4             | 2.7    | 2.1    | 2.4    | 2.6    | 5.5           | 6.3    | 5.0    | 4.7    | 5.9    |
| Hemorrhage, other               | <1       | <1     | 1.0    | 1.0   | <1     | <1    | <1     |                | <1              | <1     | <1     | <1    | <1     | <1              | <1     | 1.2    | <1     | <1     | 1.0           | 1.0    | 1.0    | <1     | 1.1    |
| Pulmonary infection             | 4.6      | 5.4    | 3.9    | 5.0   | 4.3    | 7.0   | 4.6    | 0.0            | 2.3             | 2.4    | 2.1    | 1.9   | 2.4    | 3.5             | 4.1    | 2.9    | 3.1    | 3.7    | 8.8           | 12.5   | 6.6    | 7.2    | 9.3    |
| Septicemia                      | 22.4     | 19.2   | 25.3   | 19.2  | 24.6   | 16.4  | 21.5   | 0.0            | 10.0            | 9.7    | 10.3   | 14.8  | 9.0    | 21.1            | 18.9   | 23.1   | 21.0   | 21.8   | 37.1          | 34.2   | 38.8   | 34.8   | 38.9   |
| Infection, other                |          |        |        |       |        |       |        |                |                 |        |        |       |        |                 |        |        |        |        |               |        |        |        |        |
| Hyperkalemia                    | 2.5      | 2.5    | 2.5    | 1.0   | 1.9    | 1.9   | 2.8    |                | 3.1             | 3.3    | 2.8    | 5.2   | 2.6    | 2.2             | 2.1    | 2.3    | 1.2    | 3.0    | 2.4           | 2.2    | 2.6    | 1.5    | 2.8    |
| Malignancy                      | 2.6      | 2.8    | 2.4    | 2.0   | 3.5    | 2.3   | 2.3    | 0.0            | <1              | <1     | <1     | <1    | <1     | 2.5             | 2.9    | 2.2    | 3.1    | 2.3    | 4.7           | 5.9    | 3.9    | 5.4    | 4.4    |
| Withdrawal from dialysis        | 29.0     | 24.3   | 33.4   | 21.8  | 17.3   | 31.3  | 34.6   | 16.4           | 10.2            | 10.2   | 10.0   | 7.0   | 10.9   | 23.4            | 21.1   | 25.6   | 12.4   | 30.7   | 57.1          | 52.5   | 59.9   | 29.6   | 74.4   |
| Suicide                         | <1       | 1.0    | <1     | 0.0   | <1     |       | <1     |                | <1              | <1     | <1     | <1    | <1     | <1              | 1.1    | <1     | <1     | 1.1    | <1            | 1.0    | <1     | <1     | <1     |
| Accident, not treatment related | <1       | <1     | <1     | 0.0   | <1     | 0.0   | <1     |                | <1              | <1     | <1     | <1    | <1     | <1              | <1     | <1     | <1     | <1     | <1            | <1     | <1     | <1     | <1     |
| Unknown cause                   | 17.0     | 17.0   | 17.0   | 16.7  | 18.3   | 17.9  | 16.4   |                | 11.0            | 12.5   | 8.9    | 17.5  | 9.5    | 16.4            | 16.0   | 16.7   | 14.8   | 17.5   | 24.1          | 26.1   | 23.0   | 24.2   | 24.3   |
| Other                           | 16.4     | 15.8   | 16.9   | 13.7  | 15.2   | 13.3  | 17.1   | 16.4           | 10.2            | 10.4   | 9.9    | 14.4  | 9.4    | 14.7            | 14.3   | 15.0   | 12.4   | 16.6   | 25.4          | 27.3   | 24.3   | 20.2   | 28.6   |
| Missing data                    | 33.5     | 33.0   | 34.0   | 26.3  | 26.6   | 28.5  | 37.1   | 16.4           | 17.3            | 18.7   | 15.3   | 19.2  | 16.7   | 32.9            | 33.7   | 32.2   | 23.5   | 39.7   | 51.0          | 53.6   | 49.5   | 34.9   | 62.1   |
| Years at risk                   | 105,376  | 50,851 | 54,525 | 1,970 | 31,220 | 2,555 | 68,693 | 60             | 29,789          | 16,992 | 12,796 | 4,566 | 24,482 | 46,263          | 22,738 | 23,524 | 16,412 | 26,924 | 29,263        | 11,095 | 18,167 | 10,230 | 17,241 |
| No. of patients                 | 140,153  | 67,197 | 72,956 | 2,724 | 40,618 | 3,359 | 92,193 | 79             | 35,801          | 20,522 | 15,279 | 5,719 | 29,145 | 61,541          | 30,105 | 31,436 | 20,984 | 36,693 | 42,732        | 16,538 | 26,194 | 13,900 | 26,296 |

ESRD, end-stage renal disease; NA, Native American; GI, gastrointestinal. Table includes all patients who had reached day 91 of ESRD by the end of the year; the "Other" cause group includes air embolism, vascular access hemorrhage, viral hepatitis, pancreatitis, and treatment-related accidents, each of which has a rate <1; cells with no data shown are suppressed because they contain <10 patients or have missing values; "0.0" represents a rate <0.1.

Source: Reference 121