Chapter Seven
pediatric esrd

Now you invent the boat of your flesh and set it
upon the waters
and drift in the gradual swell, in the laboring salt.
Now you look down. The waters of childhood are
there.

Mark Strand, "Where Are the Waters of Childhood?"

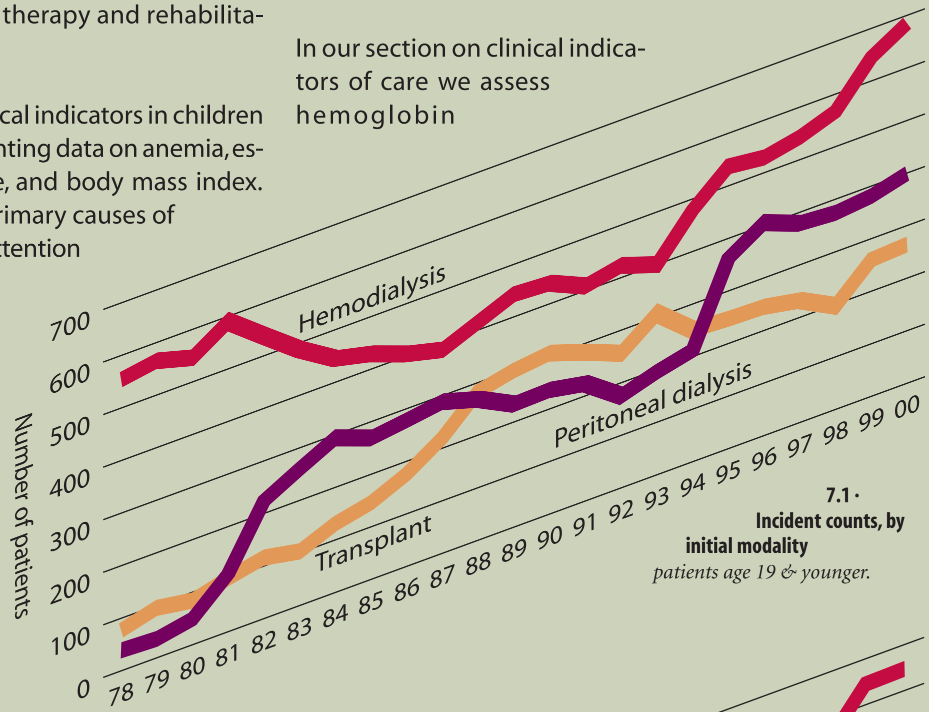
Since the Social Security Administration amendment in 1972, which entitled individuals younger than 65 to Medicare coverage for end-stage renal disease, pediatric patients with ESRD have constituted a unique population. Increased access to care for these children, and coverage from insurers other than Medicare, have provided opportunities for life-sustaining therapy and rehabilitation.

In this chapter we first look at clinical indicators in children beginning ESRD treatment, presenting data on anemia, estimated glomerular filtration rate, and body mass index. We then illustrate trends in the primary causes of pediatric ESRD, paying particular attention to racial differences and to the relation between primary diagnosis and body mass index. Since a large number of pediatric patients receive renal transplants, and graft failure is a common event, we also look at estimated glomerular filtration rates, hemoglobin levels, and erythropoietin use in patients who return to dialysis after a graft failure.

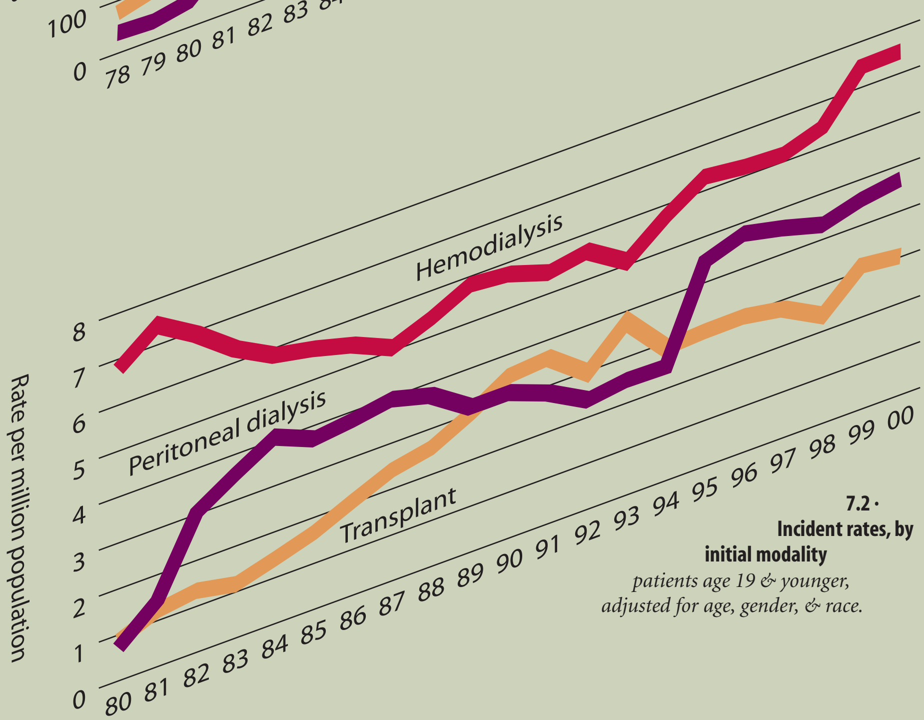
We then present information on treatment modalities that shows the frequent use of renal transplants in children, particularly in comparison to the adult population, and look as well at the number of cadaveric and living donor transplants performed since 1994. Data on five-year survival in dialysis and transplant patients illustrate differences by age and race.

Our next spread presents data on comorbidity and causes of death in pediatric patients. Since the USRDS has previously identified cardiomyopathy and heart failure as important factors in children, we look at the relationship between these comorbid conditions and hemoglobin levels. We also show the prevalence of diabetes and cancer in the transplant population, look at testing for the Epstein-Barr virus, an important complication in renal transplant recipients, and show rates of hospitalization and mortality.

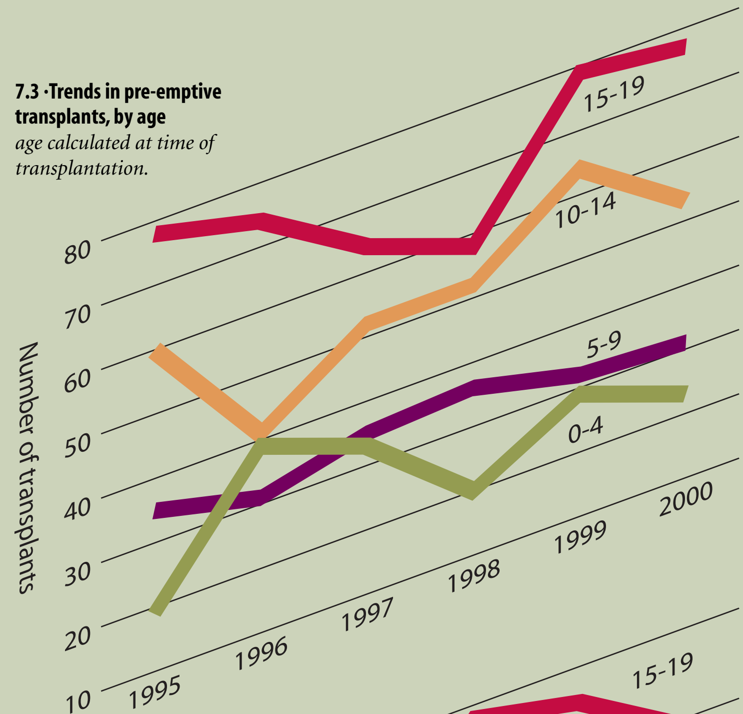
In our section on clinical indicators of care we assess hemoglobin



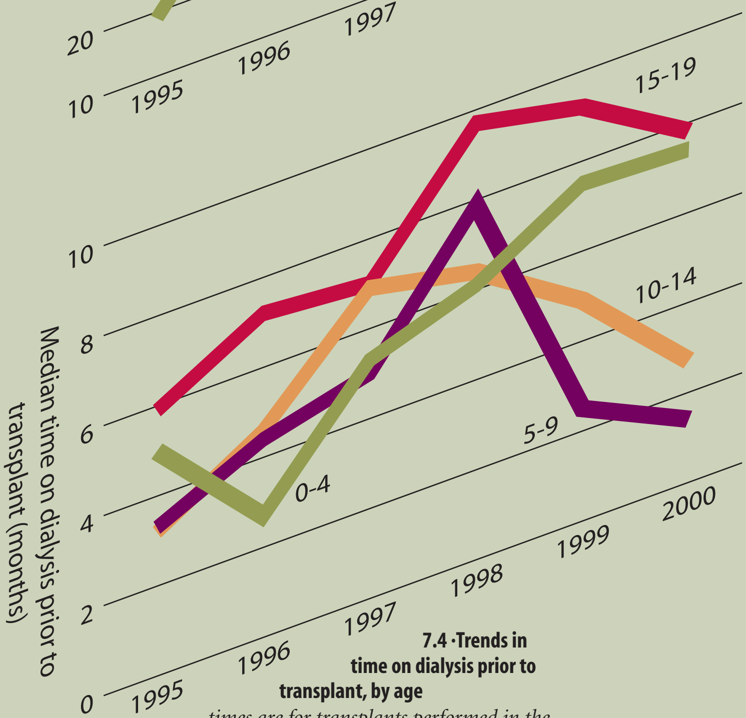
7.1 · Incident counts, by initial modality
patients age 19 & younger.



7.2 · Incident rates, by initial modality
patients age 19 & younger, adjusted for age, gender, & race.



7.3 ·Trends in pre-emptive transplants, by age
age calculated at time of transplantation.



7.4 ·Trends in time on dialysis prior to transplant, by age
times are for transplants performed in the given year.

levels as they relate to treatment with erythropoietin and iron, and look as well at delivered dialysis therapy. We conclude by looking at vascular access use and preventive care.

Over the last two decades there has been a major shift in the use of ESRD treatment modalities in pediatric patients (Figures 7.1–2). During the 1980s there was a significant increase in the use of peritoneal dialysis, along with a rise in the number of children receiving pre-emptive renal transplants. But in the latter part of the 1990s, transplant use stabilized at 200–300 per year, while more patients were placed on hemodialysis.

Transplantation remains, however, the primary treatment modality in the pediatric population, as almost 75 percent of these patients ultimately receive a transplant. The number of patients receiving pre-emptive transplants is presented in Figure 7.3. Overall, there has been little change in this number since 1995, though the amount of time patients wait for a transplant has increased slightly, particularly for patients age 0–4 and 15–19. Despite this increase, children still wait considerably less time for a renal transplant than adults, usually fewer than ten months instead of the average two years for adult patients.

These continuing changes in the use of treatment modalities in young patients will be explored in more detail in future editions of the ADR.

This spread highlights differences between pediatric and adult patients at the initiation of dialysis, using data from the Medical Evidence form (CMS 2728). In both populations, a minority of patients receive erythropoietin (EPO) prior to the start of dialysis therapy (Figure 7.5). Despite evidence that increasing numbers of patients received the therapy between 1996 and 2001, inadequate use of EPO persists (see Figure 2.10).

Within all pediatric and adult age groups (except for 0–4 year-old females), peritoneal dialysis patients are more likely than hemodialysis patients to receive pre-dialysis EPO (Figure 7.5). By race/ethnicity, black and Asian hemodialysis patients and Hispanic and Native American peritoneal dialysis patients are the least likely to receive EPO prior to the start of ESRD therapy.

Compared to those of adults, hemoglobin levels in pediatric patients remain low, especially among non-white hemodialysis patients (Figure 7.6). By age, the dramatic anemia present at initiation in the 0–4 year-old group is the most striking. Hemoglobin levels at initiation are lower in hemodialysis than in peritoneal dialysis patients, and lower in females than in males. Female pediatric patients on hemodialysis display especially low levels, possibly explained by low EPO and iron use. As identified in previous ADRs, dysrhythmic disorders and cardiomyopathy occur frequently in young ESRD patients, and may be related to their high levels of anemia. Clear evidence, then, exists for more aggressive anemia management in children.

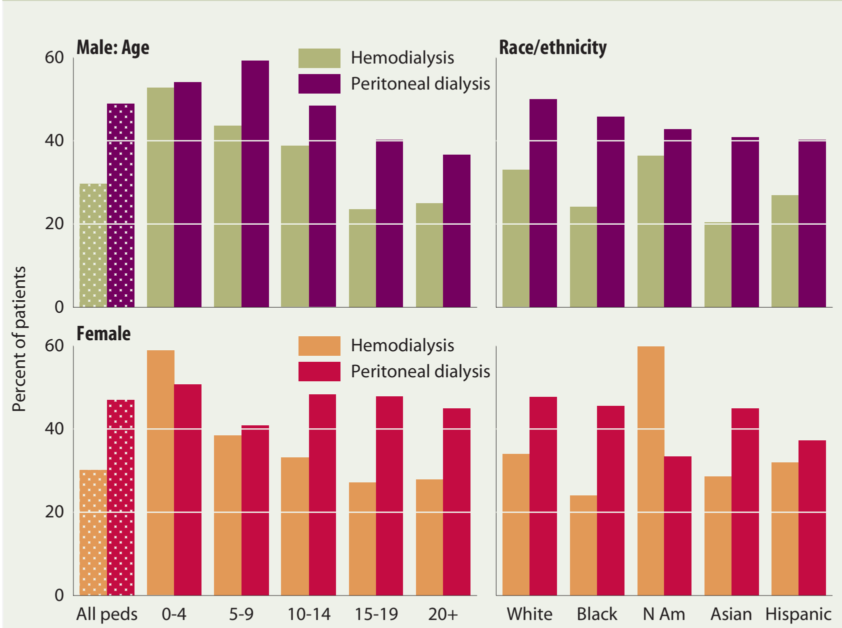
The percentage of children receiving EPO prior to initiation varies considerably throughout the nation (Figure 7.7). Some children are twice as likely to receive EPO than others, depending on the state in which they live. Mean hemoglobins also vary, and overall do not exceed 9.8 g/dl in any of the fifty states.

Estimated glomerular filtration rates (eGFRs) are higher in the pediatric than in the adult ESRD population (Figure 7.8). At the start of ESRD, nearly half of the children have eGFRs of ten or more ml per minute, while almost 20 percent of patients have eGRFs of less than six. As noted in Chapter Two (Figures 2.29–34), adult patients appear to be initiating dialysis at higher eGFR levels, which may reflect a greater level of pre-emptive treatment or more severe comorbidity. Such issues have not been evaluated in the pediatric population, and merit further consideration.

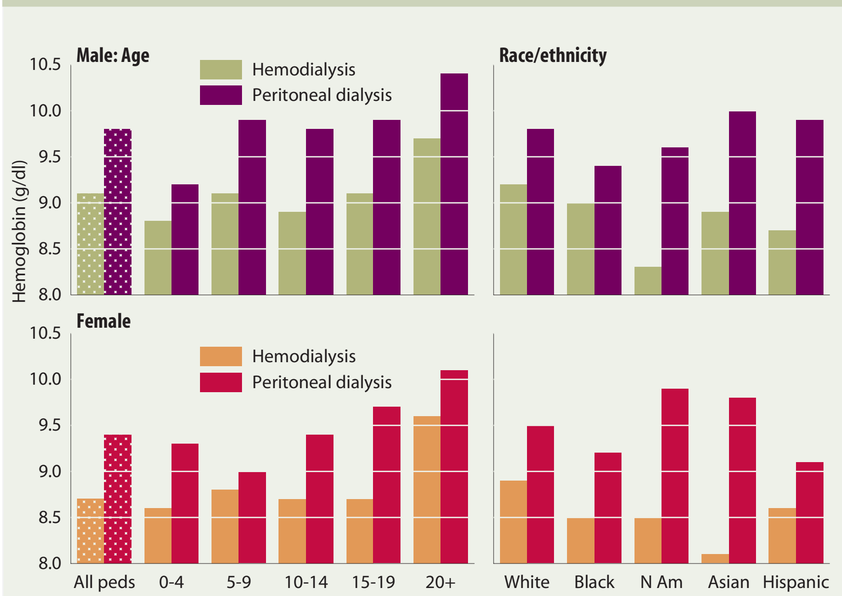
Patterns of estimated glomerular filtration rates are fairly similar when comparing patients younger than 10 to those age 10–19 years. Younger patients, however, do

Hemoglobin levels & erythropoietin use

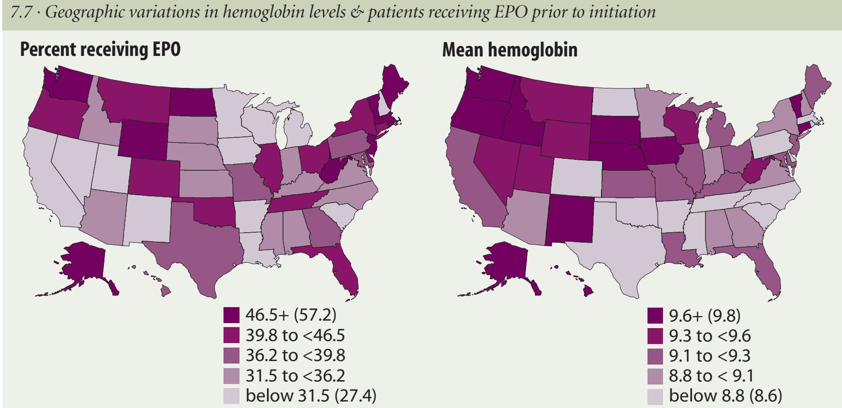
7.5 · EPO use prior to initiation, by age, race/ethnicity, gender, & modality



7.6 · Hemoglobin levels at initiation, by age, race/ethnicity, gender, & modality

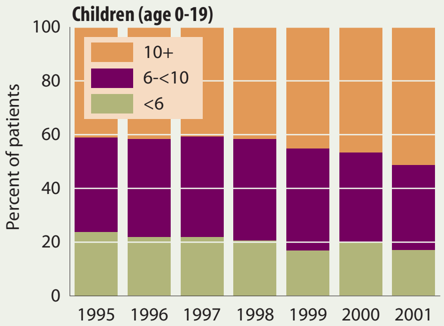


7.7 · Geographic variations in hemoglobin levels & patients receiving EPO prior to initiation

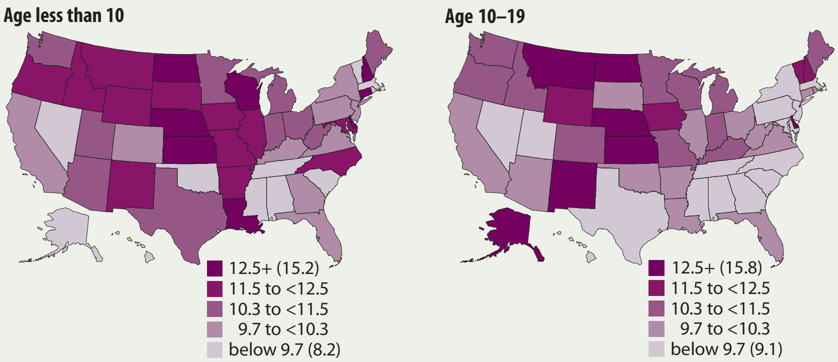


Estimated glomerular filtration rates (eGFR)

7.8 · Trends in eGFR: children versus adults



7.9 · Geographic variations in eGFR, by eGFR level



tend to have lower eGFRs overall (Figure 7.9).

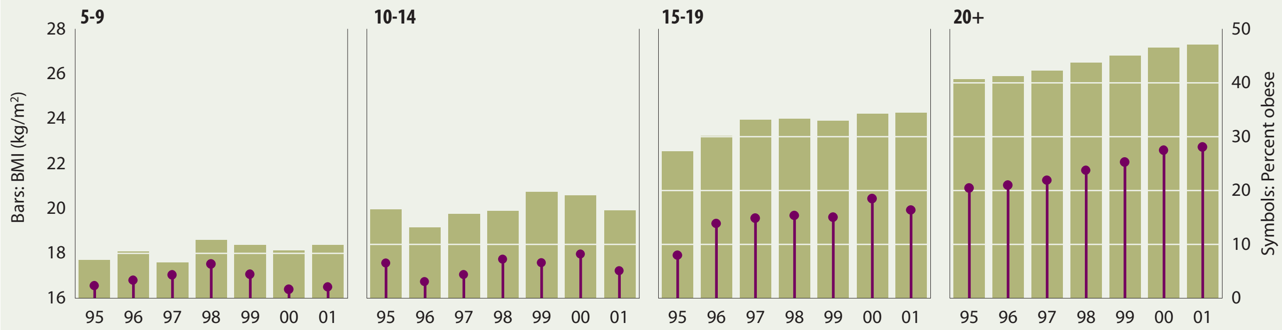
At the initiation of ESRD therapy, body mass index (BMI) appears low in 5–9 year olds, and increases slightly with older ages (Figures 7.10–11). While BMI consistently rises across cohort years in adults, the trend is less consistent in children. Males have higher BMIs than females for ages 5–9 and 10–14, but lower BMIs for ages 15 and older. Mean height and weight for males and females can be compared with estimated normal ranges of the general population, for previous studies have shown that children with ESRD have shorter stature and are underweight compared to children without the disease.

Figures 7.5–11 *incident ESRD patients; data obtained from the CMS Medical Evidence form.*

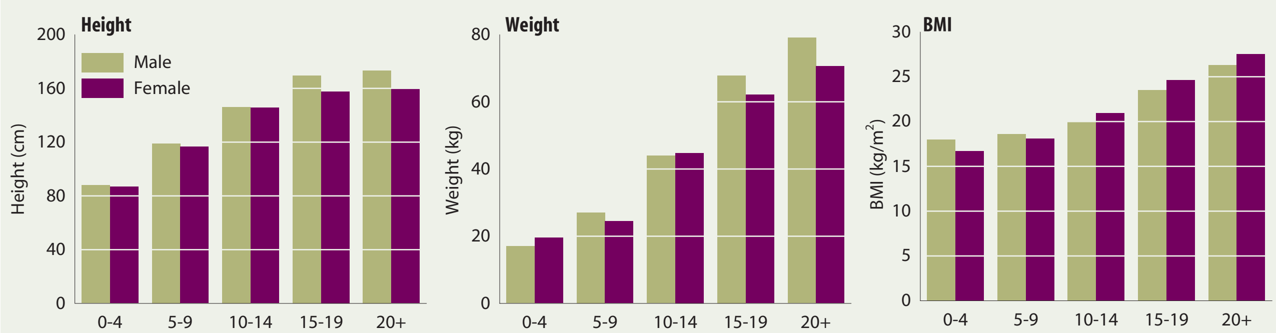
Figures 7.5–6 *1998–2000 combined.* ***Figures 7.7 & 7.9*** *1995–2000 combined, by state, unadjusted.* ***Figure 7.8*** *Schwartz formula used to calculate eGFR levels for pediatric patients age 0–19, & MDRD formula used for adults.* ***Figure 7.11*** *1998–2000 combined.*

Body mass index (BMI)

7.10 · Trends in BMI & obesity, by age



7.11 · Physical characteristics, by age & gender



For pediatric patients with glomerulonephritis as a primary diagnosis of ESRD, incident rates vary by race (Figure 7.12). For black patients and patients of races other than black or white, for example, rates have more than doubled in the last 20 years. Incident rates in the white population, however, have remained steady over the same period. For patients with cystic, heredity, and congenital diseases, rates have also increased over the last two decades. While these rates are generally low, the upward trends warrant further evaluation.

Figures 7.13–14 present the distribution of body mass index (BMI) in pediatric patients by primary diagnosis, age, gender, and race/ethnicity. A high percentage of pediatric patients have a low BMI, a trend especially evident among children age 0–9. The percentage of patients with low BMI decreases in older children.

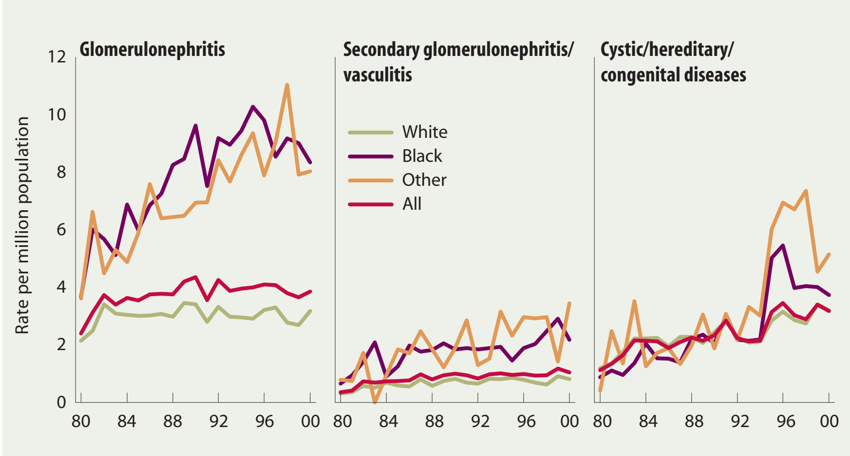
Since a high proportion of pediatric ESRD patients have a functioning graft, return to dialysis as a result of progressive graft failure is not uncommon. For Figure 7.15 we selected patients who returned to dialysis after a graft failure and who had a second Medical Evidence form filed at the time of this return, comparing data from these two periods.

Estimated glomerular filtration rates (eGFRs) are slightly higher at the time of graft failure than at the start of dialysis. At both times, eGFR is higher for pediatric than adult patients. Female pediatric patients initiate dialysis with eGFRs lower than those of males, and return to dialysis with slightly higher eGFRs. At both times, non-white children display lower eGFRs than white children, a difference that may reflect disparities in care. Racial differences in eGFR levels in the adult population are less striking.

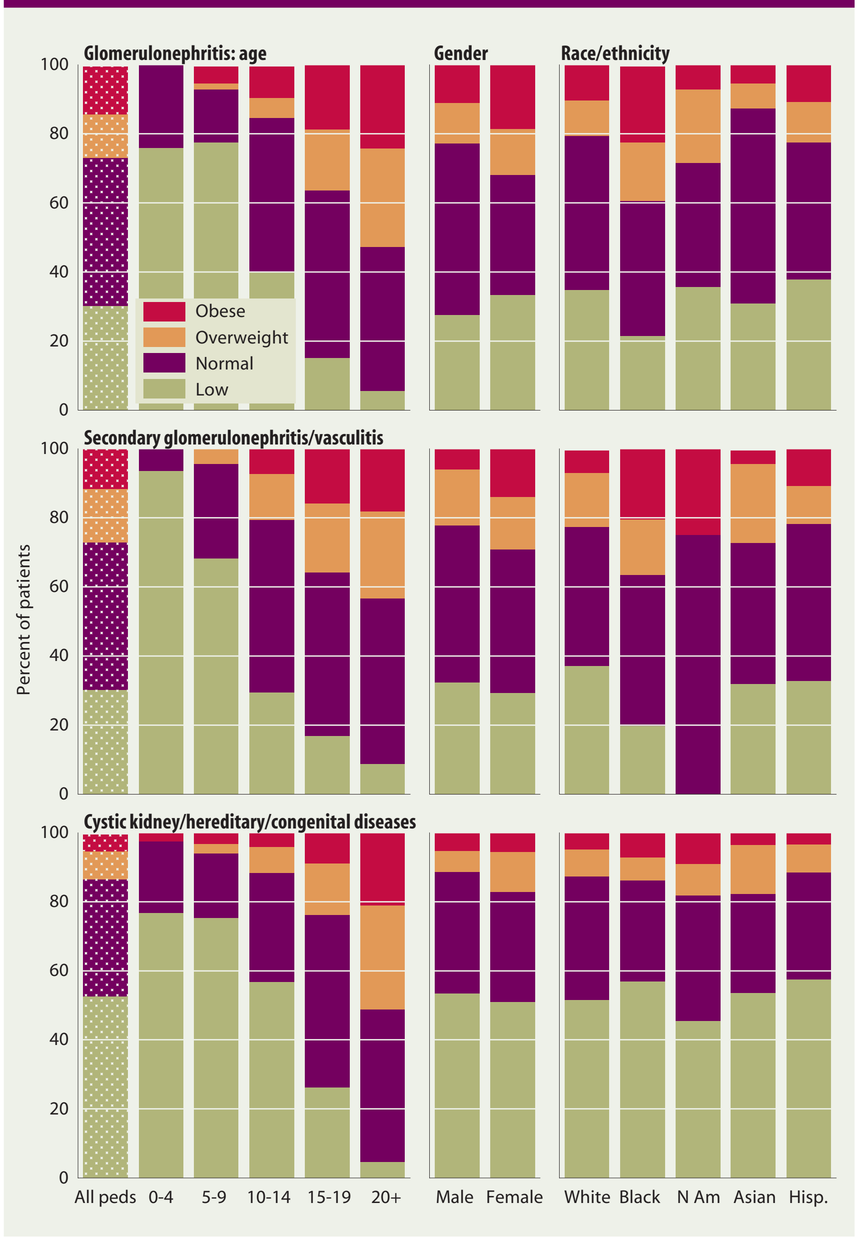
Hemoglobin levels at the initiation of dialysis are slightly lower in pediatric than in adult patients. After a graft failure, however, levels in both populations are equally low. While females have noticeably lower hemoglobin levels at initiation than their male counterparts, their levels tend to be slightly higher than those of males following graft failure. Levels show little change across racial groups. The fact that low hemoglobin levels persist at the return to dialysis after graft failure suggests that anemia treatment in renal transplant recipients with progressive graft loss may be inadequate.

Erythropoietin use during the period of graft failure prior to a return to dialysis is lower than at the initiation of dialysis. Given the scant improvement in hemoglobin levels, this decrease in EPO use during graft failure suggests either that EPO use

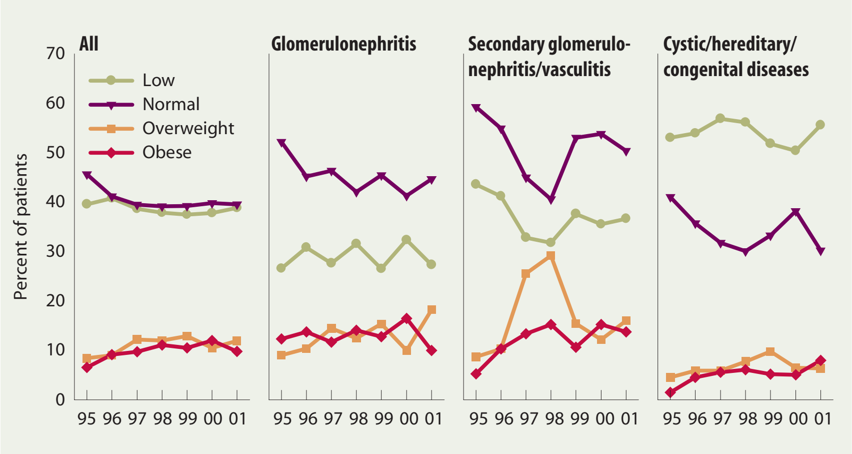
7.12 · Trends in incident rates, by primary diagnosis & race



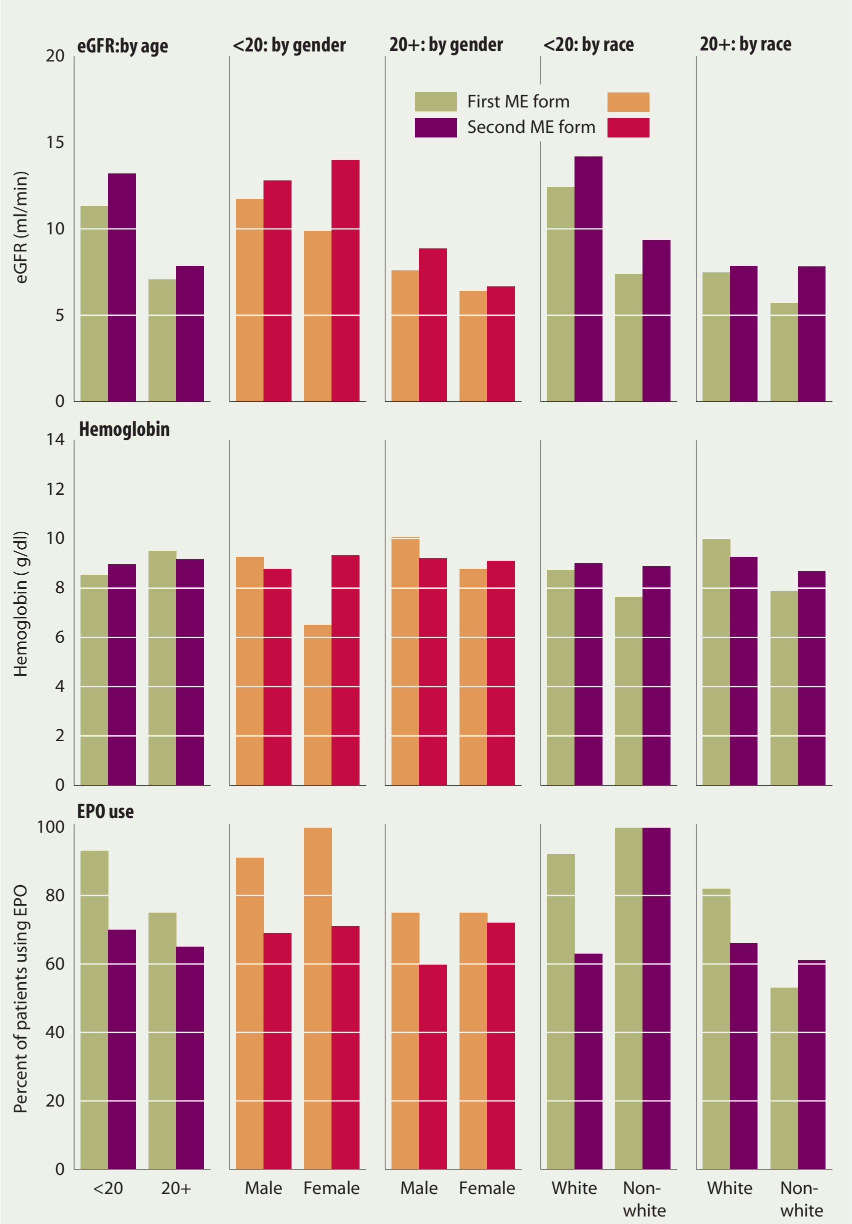
7.13 · Body mass index, by primary diagnosis, age, gender, & race/ethnicity



7.14 · Trends in body mass index, by primary diagnosis



7.15 · Characteristics of patients who return to dialysis after graft failure



is under-reported or that patients are under-treated, leading to comparable anemia upon re-initiation of dialysis.

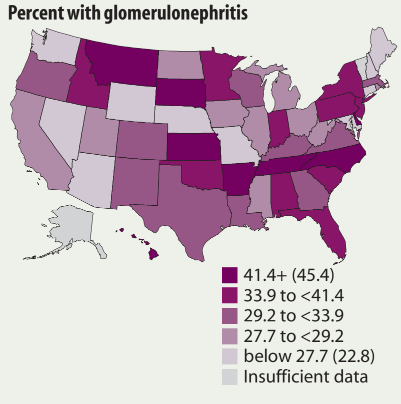
All figures *incident ESRD patients, data obtained from the CMS Medical Evidence form.*

Figure 7.12 *patients age 0–19, adjusted for age, gender, & race.* ***Figure 7.14*** *patients age 0–19.* ***Figure 7.15*** *patients transplanted in 1995 whose transplant functioned for at least four years. Schwartz formula used to calculate eGFR levels for pediatric patients, & MDRD formula used for adults.* ***Figure 7.16*** *patients age 0–19, 1995–2000 combined, by state, unadjusted.*

BMI categories
1 · Low · 0–<18.5
2 · Normal · 18.5–<25.0
3 · Overweight · 25.0–<30.0
4 · Obese · 30.0+

7.16 · Geographic variations in patients with GN

Percent with glomerulonephritis



The pediatric ESRD population is unique in that a large percentage of patients receive a renal transplant: 66 percent, compared to 46 percent of adults age 20–44 (see Table 3.f).

Figure 7.17 presents patient treatment modalities two years after the start of ESRD therapy. There are clear disparities across both age and racial groups. Black and Native American children, for example, are less likely to receive a renal transplant than patients of other races. And non-white girls are the least likely to receive a renal transplant. Since peritoneal dialysis is commonly used in children, and girls have more infectious complications than boys, the lower transplant rates may be explained by reduced access to transplantation. The low hemoglobin levels found in girls may also lead to more transfusions, thereby sensitizing these patients.

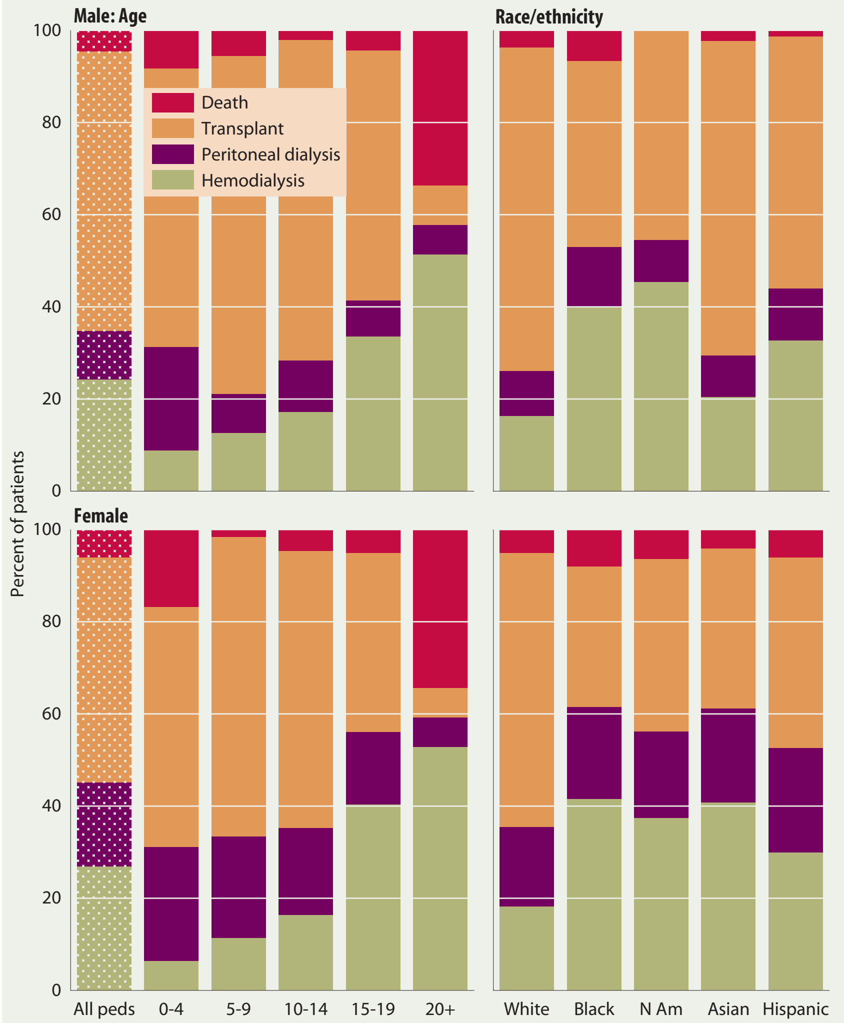
Other differences in transplant rates may be related to organ availability or access to care. Antigen-matched organs may, for instance, be of limited availability for blacks. Further work is needed to understand these differences.

Since 1995 living donors have become the dominant source of organs for children receiving their first renal transplant (Figure 7.18). Repeat transplants, however, are most commonly performed with cadaveric organs. Earlier declines in the rate of repeat transplants from cadaveric donors have leveled off, while the rate of repeat transplants from living donors has been stable. Since children appear to do well with transplants from either type of donor, the decline in cadaveric organ donations is a concern.

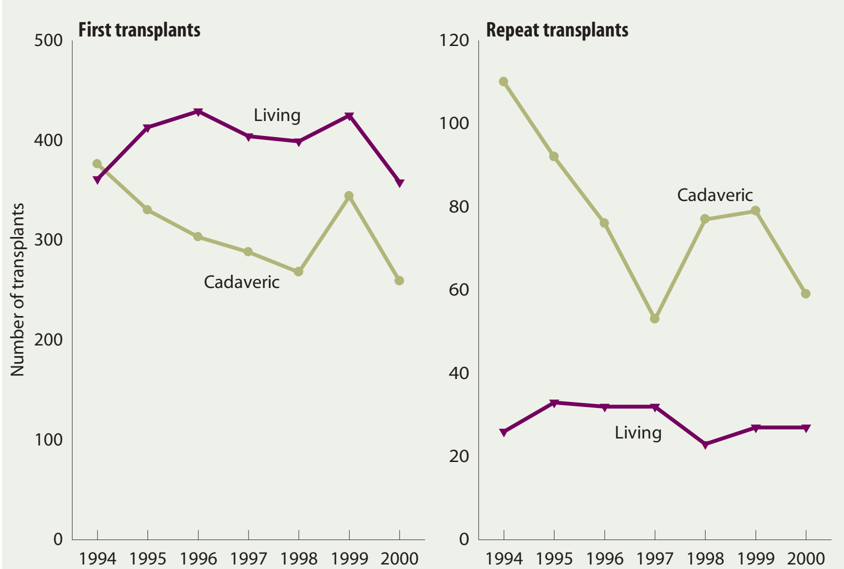
Survival of the pediatric population is highly dependant on the type of renal replacement therapy. Kaplan-Meier five-year survival estimates show a marked survival advantage for children with transplants compared to those on dialysis (Figure 7.19). Five-year survival estimates range from 94.1 to 97.2 percent in transplant patients, but 75 to 87 percent in patients treated with dialysis. These data strongly suggest that all possible efforts should be made to transplant children with ESRD. A number of factors, however interfere with the ability of children to receive renal transplants, including organ matching and the availability of living donors.

Figures 7.20–21 present five-year patient survival for transplanted patients. Children generally have excellent survival after transplantation with either type of donor organ. Survival of young black children, however, is less than that for white patients, raising concerns as to the sources of these disparities.

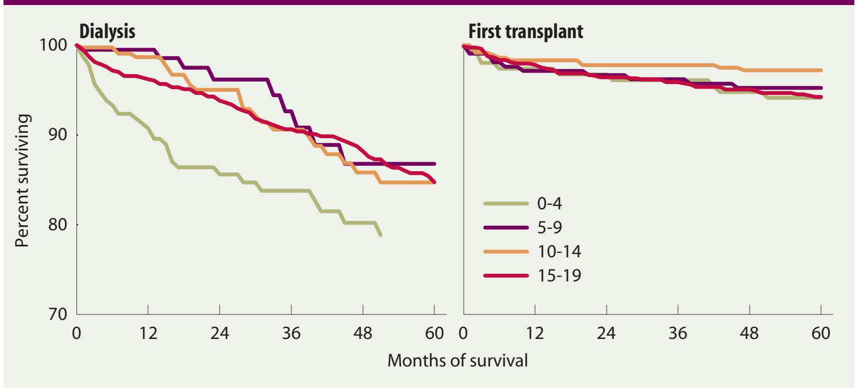
7.17 · Treatment modality two years following ESRD onset, by gender, age, & race/ethnicity



7.18 · Trends in total first & repeat transplants, by donor source

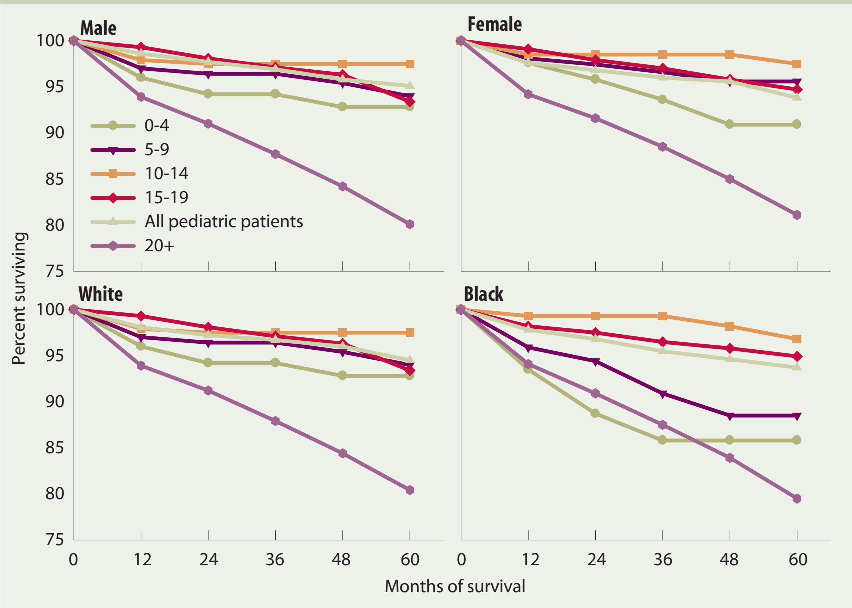


7.19 · Kaplan-Meier five-year patient survival, by modality & age



Kaplan-Meier five-year patient survival after first transplant, by gender, race, & age

7.20 · Cadaveric transplants



7.21 · Living donor transplants

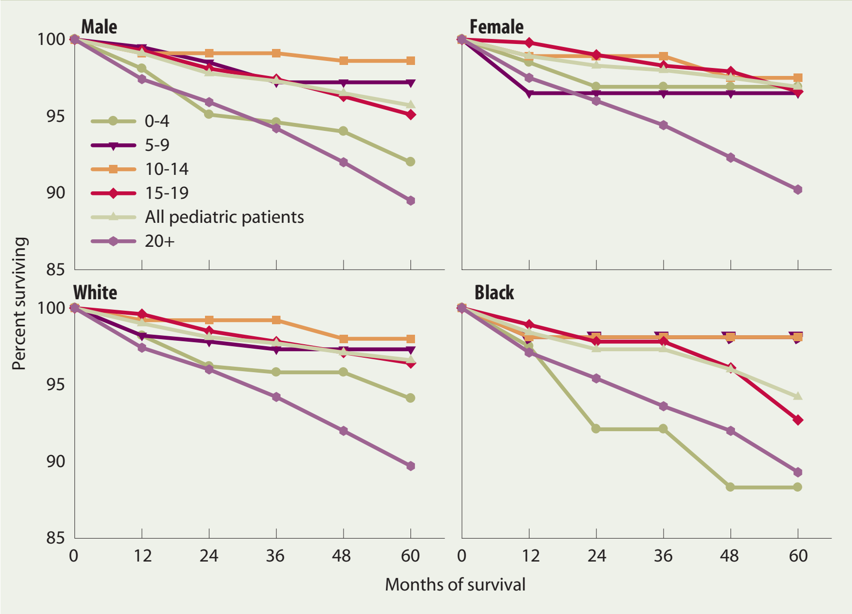
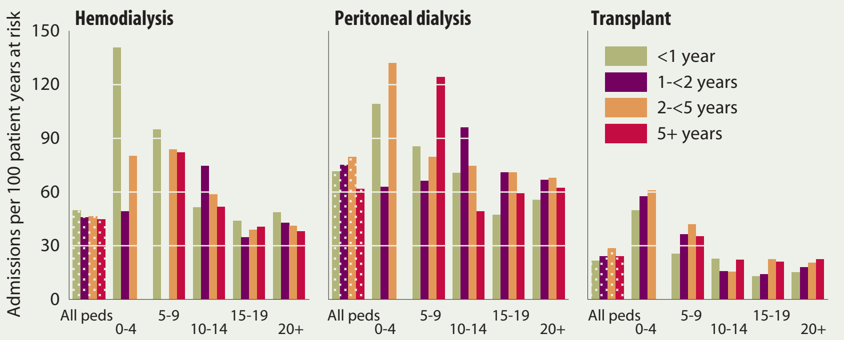


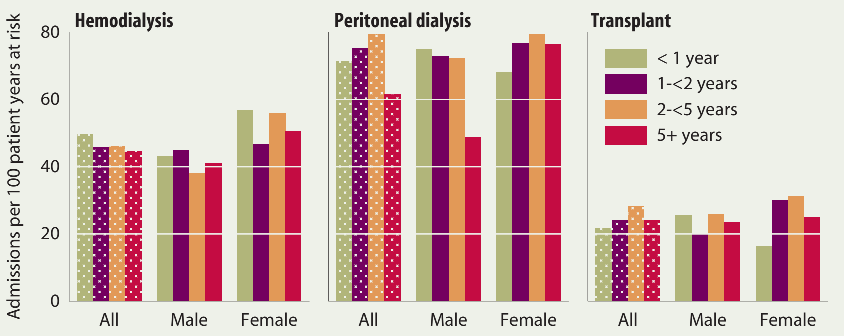
Figure 7.17 *incident Medicare patients who survive 90 days from the first ESRD date, 1996–1998 combined; data by race & ethnicity include pediatric patients only.* ***Figure 7.18*** *patients age 0–19.* ***Figure 7.19*** *incident dialysis & transplant patients, 1994–1995 combined.* ***Figures 7.20–21*** *1993–1994 combined.*

Hospital admissions for infection (overall), by modality & years after first ESRD service date

7.26 · by age

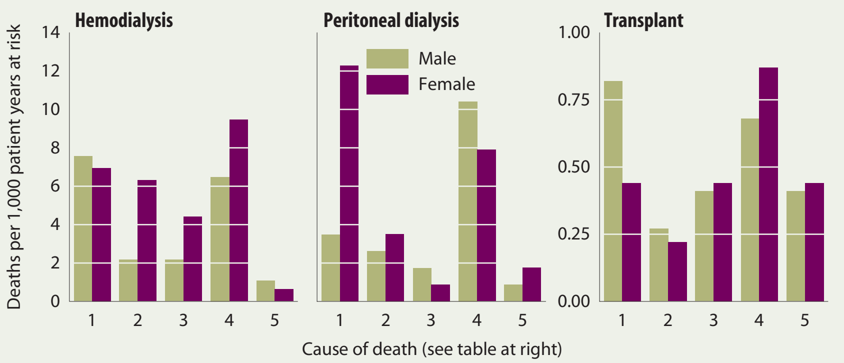


7.27 · by gender

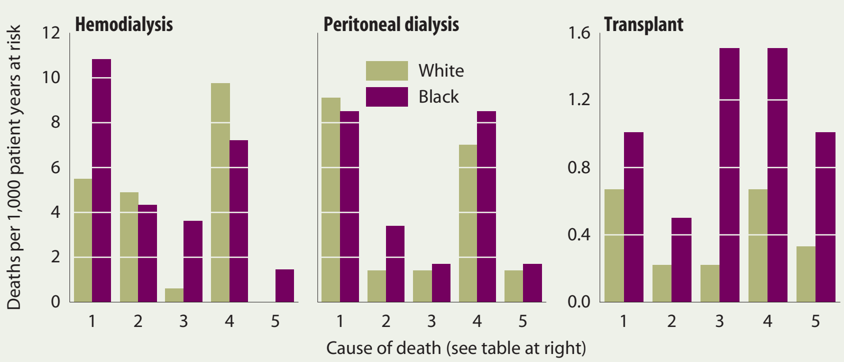


Causes of death, by modality

7.28 · by gender



7.29 · by race



Infection is the leading cause of mortality in young hemodialysis patients (Figures 7.28–29). And as noted in the two previous ADRs, rates of death from cardiac arrest in young female patients continue to be unusually high. Overall death rates in the transplant population are approximately one-tenth those of patients treated with dialysis.

By race, rates of death due to cardiac arrest are similar in whites and blacks on peritoneal dialysis, but are nearly twice as high for blacks on hemodialysis as for whites. Rates of death due to cardiovascular disease, infection, and malignancy are also far higher in black pediatric transplant patients than in their white counterparts.

Figure 7.22 *incident patients: dialysis patients age 0–19 at the start of ESRD, 1995–1999 combined; prevalent patients: dialysis patients age 0–19 as of July 1, 1999.* ***Figure 7.23*** *point prevalent patients on July 1, 1999 who survive the first six months of ESRD on dialysis. Comorbidities from claims (six-month entry period).* ***Figure 7.24*** *patients transplanted between 1996 & 2000.* ***Figure 7.25*** *incident patients age 0–19, 1994–1997 combined; followed for three years.* ***Figure 7.26*** *incident & prevalent ESRD patients, 1998–2000 combined (there are no patients age 0–4 with 5+ years on ESRD, & <10 hemodialysis patients age 5–9 with 1–<2 years on ESRD); "all" category includes pediatric patients (age 0–19) only.* ***Figure 7.27*** *incident & prevalent ESRD patients, age 0–19,1998–2000 combined.* ***Figures 7.28–29*** *prevalent patients, age 0–19, 1998–2000 combined.*

Causes of death

1 · Cardiac arrest
2 · Cardiac, other
3 · Cardiovascular disease
4 · Infection
5 · Malignancy

Hemoglobin levels in Medicare-insured pediatric patients tracked by the CMS Clinical Performance Measures project are similar, regardless of EPO treatment (Figure 7.30). In CPM non-Medicare patients, however, hemoglobin levels are nearly 0.5 g/dl lower in the EPO-treated than in the non-EPO-treated patients. In the USRDS Medicare claims data, EPO-treated patients have mean hemoglobin levels of 10.9 g/dl.

In all data sources, hemoglobin levels are substantially lower in patients who don't receive iron than in those who do. The greatest difference in hemoglobin levels between patients with and without iron (0.6 g/dl) occurs in USRDS Medicare patients. The magnitude of this difference suggests a need for more aggressive anemia treatment in patients not receiving iron.

The distribution of hemoglobin levels by patient age shows that a greater percent of pediatric than adult patients have hemoglobins in the lower ranges (Figure 7.31). Patients with low EPO doses (less than the median of 11,354 units per week) who receive iron are among those with the highest hemoglobin levels (Figure 7.32).

Pediatric hemodialysis patients have a mean URR of 69.5 percent and a mean Kt/V of 1.5, above the K/DOQI target Kt/V of 1.2 for adults (Figure 7.33). Whether pediatric patients should require therapy targets similar to those of adults is still unclear.

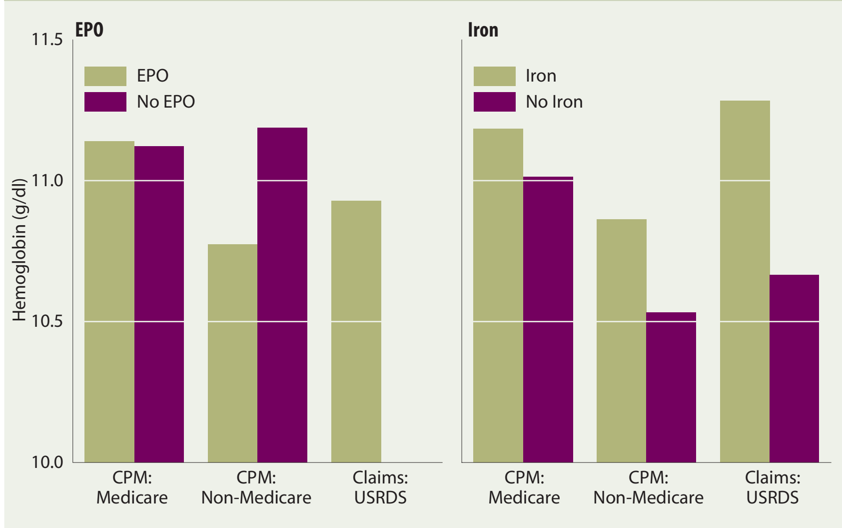
Dialysis catheters are used in the majority of pediatric hemodialysis patients (Figure 7.34). Gender differences in vascular access use are minimal, while a slightly lower percent of black and Native American patients use catheters. Insertion rates for temporary and permanent catheters are considerably higher than those for arteriovenous fistula and graft placements. Rates of catheter days per patient year are higher for pediatric than adult patients (46 versus 31), while the number of days per insertion is similar (151 and 149). High rates of catheter use in pediatric patients may influence levels of anemia and infectious complications, including hospitalizations and mortality.

While few prevalent adult ESRD patients receive vaccinations, the number is even lower for pediatric patients (Figure 7.35). Respectively, the percentages of adult and pediatric patients vaccinated are 44 and 16 percent for influenza, 18 and five percent for hepatitis B, and 11 and four percent for pneumococcal pneumonia. Native American and Asian pediatric patients have particularly low vaccination rates.

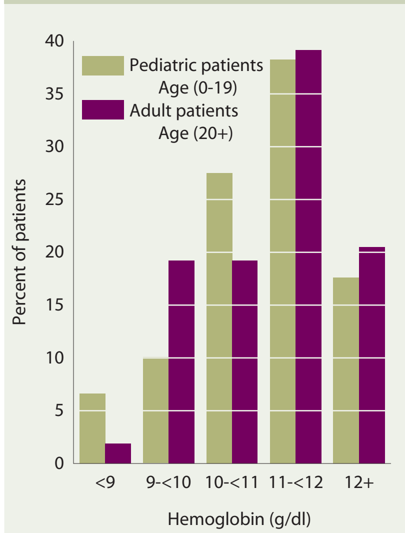
Glycosylated hemoglobin testing occurs in 45 percent of pediatric and 63 percent of adult diabetic patients (Figure 7.36). Because some guidelines have suggested a

Anemia treatment

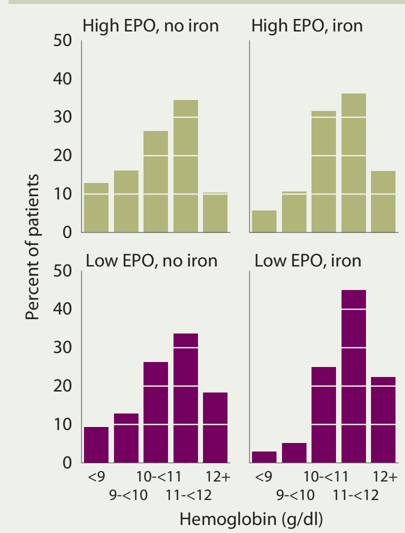
7.30 · Hemoglobin levels, by data source & by EPO & iron use



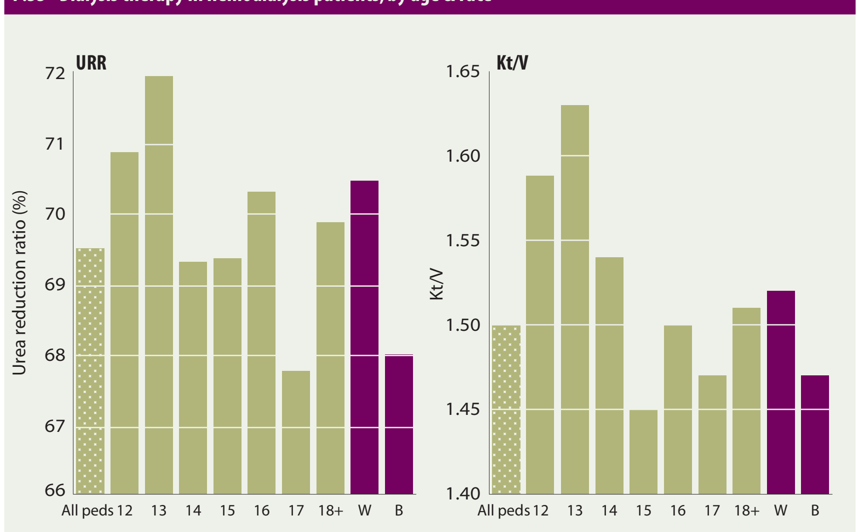
7.31 · Hemoglobin levels, by patient age



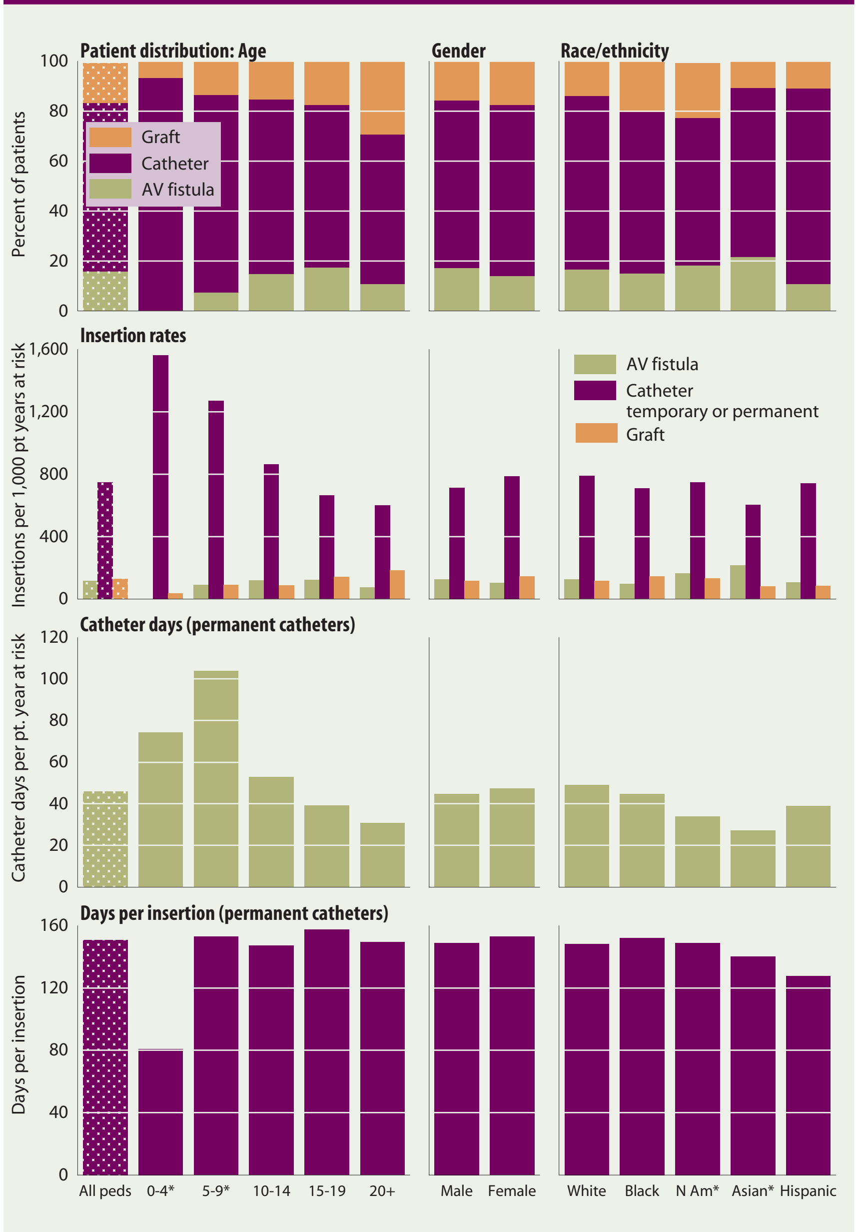
7.32 · Hemoglobin levels, by iron & EPO dose



7.33 · Dialysis therapy in hemodialysis patients, by age & race



7.34 · Vascular access use & insertion rates, by age, gender, & race/ethnicity

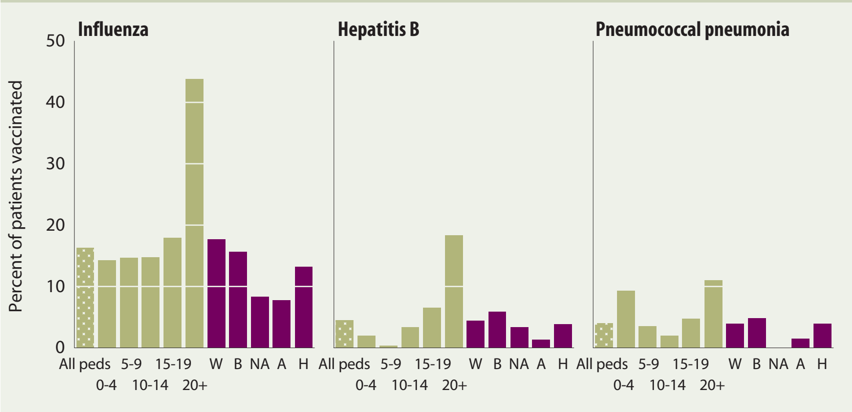


minimum of two tests per year, this measure of patients with at least one test during the year may over-represent the number of patients receiving recommended testing.

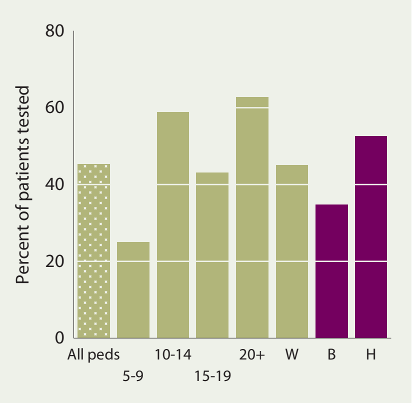
Figure 7.30 *claims data: period prevalent hemodialysis patients age 12–17 as of September 30, 1999, initiating dialysis on or before April 1, 1999 & alive & still on hemodialysis as of December 31,1999; mean hemoglobin is from claims during October–December of 1999, & patients are designated as receiving iron if they have at least one iron claim during this period. CPM data obtained from the CMS Clinical Performance Measures project report, which collected information on all known pediatric patients regardless of insurance payor status.* ***Figure 7.31*** *period prevalent hemodialysis patients, 1998–2000 combined.* ***Figure 7.32*** *period prevalent hemodialysis patients age 0–19 as of January 1 of the prevalent year, 1998–2000 combined.* ***Figure 7.33*** *hemodialysis patients, 2000, CPM data (collected October–December 1999).* ***Figure 7.34*** *period prevalent hemodialysis patients age 0–19 as of January 1 of the prevalent year, 1998–2000 combined; breakdowns by gender & race include pediatric patients only. Graphs of percent of patients: starred categories contain fewer than ten patients.* ***Figure 7.35*** *influenza vaccinations: prevalent ESRD patients, age 0–19, initiating therapy 90 days prior to September 1, 2000, living through December 31, 2000, & with Part B eligibility during the last four months of 2000; age on September 1, 2000. Hepatitis vaccinations: prevalent ESRD patients, age 0–19, initiating therapy 90 days prior to January 1, 2000, living through December 31, 2000, & with Part B eligibility during 2000; age on December 31, 2000. Pneumococcal vaccinations: prevalent ESRD patients, age 0–19, initiating therapy 90 days prior to January1,1999, living through December 31, 2000, & with Part B eligibility during 1999–2000; age on December 31, 2000. Pre-transplant vaccinations billed to Medicare are not included. Patients with Medicare as secondary payor, or enrolled in an HMO, are excluded.* ***Figure 7.36*** *prevalent diabetic ESRD patients, age 0–19, initiating therapy 90 days prior to January 1, 2000 & living through December 31, 2000; age on December 31, 2000. Patients with Medicare as secondary payor, or enrolled in an HMO, are excluded. The number of patients age 0–5, & the number of Native American & Asian patients, are too small to include in the analysis.*

Preventive healthcare, by age & race/ethnicity

7.35 · Vaccinations



7.36 · Glycosylated hemoglobin testing



Maps: National means & patient populations

Figure number	7.7	7.7	7.9	7.9	7.16
	EPO	Hgb	<10	10+	
Overall value for all patients	36.9	9.1	10.6	9.9	32.2
Total patients	5,780	5,471	1,202	4,291	1862
Overall value for patients mapped	36.9	9.1	10.6	9.9	32.2
Patients dropped due to missing HSA/state	2	2	1	1	4

Patient populations & analytical methods

- Figures 7.2 and 7.12 include only patients age 0–19 residing in the 50 states or the District of Columbia. Patients with unknown age, gender, or race are excluded. Adjustments are made using the direct method, with 1999 as the standard population.
- Figures 7.5–7.16, 7.22, and 7.23 include counts and percents of incident patients age 0–19 with a new CMS Medical Evidence form, certified within one year of the first service date.
- Rates in Figures 7.26–27 are unadjusted total admission rates per 100 patient years for hospitalizations with a principal ICD-9-CM diagnosis code of infection; patients with missing age or gender information are excluded. Time on ESRD is calculated as the time from the first ESRD service date until the first of the year for prevalent patients, or as less than one year for incident patients. Principal ICD-9-CM diagnosis codes used for overall infection are listed in the discussion of Figures 6.7–8.
- Age groups used for the analyses of anemia treatment were chosen to match those used in the CPM data.
- For Figure 7.34, percentages represent the distribution of prevalent hemodialysis patients age 0–19 as of January 1 of the prevalent year, and the most recent access claim in the prevalent year or prior years back to 1996. Patients with Medicare as a secondary payor at any time during the period between their most recent access claim and the end of their prevalent year are excluded. Rates for insertions, catheter days, and days per insertion are aggregated across all three prevalent years (1998, 1999, and 2000), and exclude patients with Medicare as a secondary payor during their prevalent year.
- In Figure 7.35 the patient cohort excludes patients with Medicare as a secondary payor and those enrolled in an HMO. Influenza vaccination percentages are based on prevalent patients age 0–19 as of September 1, 2000, initiating ESRD therapy 90 days prior to September 1, 2000, living through December 31, 2000, and with Part B eligibility during this time. Hepatitis B percentages are based on prevalent patients age 0–19 as of December 31, 2000, initiating ESRD therapy 90 days prior to January 1, 2000, living through December 31, 2000, and with Part B eligibility during that period. Pneumococcal vaccination percentages are based on prevalent patients age 0–19 as of December 31, 2000, initiating ESRD therapy 90 days prior to January 1, 1999, living through December 31, 2000, and with Part B eligibility during this time.

Conclusions

- During the last two decades the use of pre-emptive transplants in pediatric patients has more than tripled. Hemodialysis use declined, but has now reappeared as the primary dialytic modality in these patients.
- Mean waiting times for transplants have increased for patients age 0–4 and 15–19. Overall, however, pediatric patients wait an average of only ten months for a transplant, compared to two years in the adult population.
- Erythropoietin use in the pediatric population continues to be low, particularly in context of the severe degree of anemia noted in patients younger than five. Increased attention should be given to pre-ESRD anemia treatment in this population.
- Pediatric patients tend to initiate dialysis with higher estimated glomerular filtration rates than their adult counterparts. Almost half of pediatric patients, however, still begin dialysis with eGFRs less than ten, and 17 percent have levels lower than six. These data suggest that earlier referral to treatment is needed to prevent some of the major comorbid complications, particularly severe anemia and secondary heart failure, from emerging later in the course of ESRD.
- Body mass index appears to be low within the pediatric population, consistent with prior reports of slow growth and with the potential for malnutrition.
- Trends in the primary causes of renal insufficiency show that rates of glomerulonephritis in blacks and patients of other races have more than doubled over the past 20 years. Rates of cystic, hereditary, and congenital diseases have also almost doubled.
- Data on patients returning to dialysis after a transplant failure show that these patients re-enter dialysis with a similar degree of anemia, similar estimated glomerular filtration rates, and the same under-utilization of EPO compared to those beginning dialysis for the first time.
- After two years of ESRD treatment, almost two-thirds of pediatric patients have received a renal transplant. Use of peritoneal dialysis is increasing in the youngest patients, while more adolescents are being placed on hemodialysis.
- Organs used for first transplants in pediatric patients are more likely to come from living donors, though cadaveric donors are more common in repeat transplants.
- Survival of pediatric patients is highly dependent on treatment modality. More than 95 percent of transplanted patients survive at least five years, while children who are do not to receive a renal transplant have significantly lower survival rates.
- Patient survival is generally comparable in children receiving cadaveric and living donor grafts.
- Black pediatric patients have lower overall survival after a renal transplant than whites.