Chapter Seven

The transition to ESRD

The water you touch in a river is the last of that which has passed, and the first of that which is coming. Thus it is with time present.
Life, if well spent, is long.

Leonardo da Vinci
From the earliest stages of the disease, patients with chronic kidney disease (CKD) face many challenges. Control of salt intake, blood pressure, lipid levels, and weight, in addition to exercise, are needed to address the management of cardiovascular risk factors. And the disease’s progression, with the potential for accelerating cardiovascular disease and for reaching kidney failure, poses additional issues. Access to care is an important element in the management of this high-risk population, as is the detection and management of risk factors known to reduce cardiovascular event rates and the progression of CKD to end-stage renal disease (ESRD). At one year prior to starting ESRD therapy, 80 percent of Medicare patients have a CKD claim, considerably higher than the 56–57 percent seen in the younger employer group health (EGHP) populations. But only 40 percent of Medicare patients, and 23–34 percent of EGHP patients, see a nephrologist one year before ESRD. Given that 82 percent of ESRD patients start dialysis with a catheter, and that only 20 percent of these patients have a developing internal access, late referral may contribute to the high use of catheters, and thus to increased rates of infectious complications. The lack of preparation for ESRD in the younger population may also contribute to delays in living donor kidney transplants. Informing patients with Stage 4 CKD of the options for kidney replacement therapy, and planning for that therapy, are elements at the core of the new Medicare CKD education benefit, passed by Congress in 2008 and slated to begin in January, 2010. We next address laboratory testing during the transition to ESRD. Compared to the data shown in Chapter Four, on prospectively measured care of identified CKD patients, creatinine testing is less frequent in those who reach ESRD. Sixty-one percent of Medicare patients have a creatinine measured at two years prior to ESRD, compared to the 95 percent of CKD patients tested within a year after a CKD claim. Forty-four percent have bone and mineral metabolism testing within the two years before ESRD, while 27 percent have a serum parathyroid hormone level test. The level of assessment in the Ingenix i3 population is half that seen among Medicare patients, an area of concern in this younger population. These data, along with data on physician visits, suggest that patients progressing to ESRD are receiving less than optimal care. Information on the pre-ESRD use of prescription medications can also be compared to data in Chapter Four, on the management of the known CKD population. At two years prior to ESRD, 50–54 percent of patients are using ACE-Is, ARBs, or renin inhibitors, but this falls to 39–41 percent in the three months before initiation. It is not clear whether this decline arises from concern over rising creatinine levels as kidney failure progresses, or if complications such as hyperkalemia may contribute to these patterns. Interestingly, the use of beta blockers and dihydropyridine calcium channel blockers increases closer to ESRD, possibly reflecting increased treatment for hypertension in later stages of CKD. The use of thiazide diuretics, and the slight increase in the use of loop diuretics in the last year before ESRD, may reflect volume control treatment or treatment for hyperkalemia. The use
of other treatments, such as phosphate binders, accelerates in the last two quarters before ESRD, while vitamin D use reaches 20–25 percent in the quarter prior to ESRD. The continued use of certain medications after starting ESRD treatment is assessed on the following spread. In the three quarters before ESRD, 45 percent of EGHP patients receive an ACE-I, ARB, or renin inhibitor; this drops 10–20 percent in the quarter after ESRD. Since rates of heart failure and cardiovascular events are high in the ESRD population, these drugs may still have some benefit. The use of beta blockers is of particular interest, in that many investigators have shown high rates of sudden death in the ESRD population, possibly secondary to the high rates of heart failure, myocardial fibrosis, and arrhythmias, conditions which may be amenable to treatment. Beta blocker use increases by the first quarter after initiation, reaching half of the patients. It appears that at least one-fourth of the patients on beta blockers before ESRD are taken off, while others are started on the therapy. The use of diuretics is also interesting, in that some patients continue to use thiazide diuretics, while approximately one-third still use loop diuretics. Use of other medications may be difficult to interpret, given the small sample size. Prescription medication use in the Medicare population will be further assessed when Part D data becomes available to the USRDS. To conclude the chapter we address vascular access placement rates in patients reaching ESRD, examining patterns of care in the months prior to and following the initiation of therapy. Catheters are dominant in the Medicare population at the beginning of ESRD, while placements of arteriovenous fistulas reach only 15 percent in the month before initiation. In the MarketScan and Ingenix i3 data, catheter placements are noted in 15–19 percent of patients prior to ESRD, but this may reflect the lack of a clear registration system for these patients, since the start of dialysis is defined from three months of claims records rather than something like the Medical Evidence form used for Medicare patients. Fistula placement rates are slightly lower in the younger EGHP population reaching dialysis, but the numbers are still far below those needed for most patients to have a functioning access before ESRD. Attempts at placements after ESRD are considerably higher in all populations, yet the reported high failure rates noted by some investigators raise questions as to the falling rates of attempted graft placements, an alternative with lower rates of complications than catheters.

Figure 7.1: see page 148 for analytical methods. Incident Medicare ESRD patients age 67 & older, & incident MarketScan & Ingenix i3 ESRD patients (all ages), 2007.
n the second year prior to ESRD initiation, 72–78 percent of Medicare patients have a CKD claim. Just 28–36 percent, however, see a nephrologist during this period. In the employed populations, 47–55 percent have a CKD claim 12–24 months prior to ESRD, but only 17–30 percent visit a nephrologist. Rates of referral do rise immediately prior to initiation, but still remain low. Ninety-six percent of Medicare patients, for example, have a CKD claim in the three months before starting ESRD therapy, but just 82 percent visit a nephrologist. And among MarketScan patients, 83 percent have a CKD claim, but only 39 percent see a nephrologist. Four in five Medicare patients, however, and approximately 60 percent of the employed population, see a physician of some type 12–24 months before ESRD. These data show that, while CKD is often recognized by a physician, many patients are not being referred for nephrologist care prior to the start of ESRD therapy, or far enough in advance to have a significant impact on outcomes. As we show in Volume Two, Chapter Three, patients without pre-ESRD nephrologist care are far more likely to use a catheter at initiation — an access associated with higher rates of complications and early mortality.

 Figures 7.2–4; see page 148 for analytical methods. Incident Medicare ESRD patients age 67 & older, & incident MarketScan & Ingenix i3 ESRD patients (all ages), 2007.
Medicare patients are more likely to visit a physician prior to ESRD than are their EGHP counterparts. Sixty-nine percent of Medicare patients, for example, visit a cardiologist in the three months prior to ESRD, compared to 37–38 percent of MarketScan and Ingenix i3 patients. And 85 percent of Medicare patients visit a primary care physician during this period, compared to 62–65 percent of their EGHP counterparts. *Figures 7.5–6*; see page 148 for analytical methods.

Incident Medicare ESRD patients age 67 & older, & incident MarketScan & Ingenix i3 ESRD patients (all ages), 2007.
Serum creatinine level is an important marker of kidney function. Sixty-one percent of Medicare ESRD patients (age 67 and older) incident in 2007 received testing eight quarters prior to initiating therapy, while 77.3 percent were tested in the quarter before ESRD initiation. When compared to Ingenix i3 patients, Medicare patients were twice as likely to be tested over the two-year period.

Calcium and phosphorus tests can identify potential bone and mineral problems. Early testing (eight quarters prior to ESRD) occurred in 19.5 percent of Medicare patients beginning ESRD therapy in 2007; this number reached 43.7 percent in the quarter prior to initiation. One in ten Ingenix i3 patients, in contrast, were tested in the early months, while 25 percent were tested in the quarter just prior to ESRD treatment.

Parathyroid hormone (PTH) tests can be used to determine causes of calcium imbalance. The likelihood of receiving at least one PTH test has increased in Medicare patients. Of 2003 incident patients, for example, only 2.2 percent were tested eight quarters prior to ESRD initiation, and 10.6 percent were tested just prior to initiating treatment. In the 2007 incident population, 8.9 and 26.7 percent, respectively, received testing. When compared to Medicare patients, fewer Ingenix i3 patients received testing — 3.8 percent at the two years prior, and 14.4 percent in the quarter just before ESRD treatment. Figures 7.7–91; see page 149 for analytical methods. Incident Medicare ESRD patients age 67 & older, & incident Ingenix i3 ESRD patients (all ages).
Lipid testing is used to identify abnormalities in cholesterol levels which can lead to hypertension and other cardiovascular diseases. In the 2007 incident population, only 27 percent of Medicare patients, and 16 percent of Ingenix i3 patients, had their lipid levels tested in the three months prior to ESRD — levels relatively unchanged from those in the previous seven quarters.

The monitoring of glycosylated hemoglobin (A1c) levels in patients with diabetes is important in the control and treatment of the disease. The American Diabetes Association recommends 2–4 tests per year, depending on treatment goals and changes in therapy. In the two years prior to ESRD, 42 percent of Medicare patients incident in 2007 received an A1c test, compared to 26 percent of those in the Ingenix i3 database.

The percentage of patients receiving hemoglobin testing increases during the two years before initiation of ESRD therapy. Among Medicare patients incident in 2007, for example, 52 percent were tested eight quarters prior to ESRD, and 74 percent in the three months before initiation. These rates are twice as high as those in the Ingenix i3 population. \( \text{Figures 7.10–12; see page 149 for analytical methods. Incident Medicare ESRD patients age 67 & older, & incident Ingenix i3 ESRD patients (all ages).} \)
Little is known about medication use during the transition from CKD to ESRD. Angiotensin-converting enzyme inhibitors (ACE-Is), angiotensin receptor blockers (ARBs), and renin inhibitors are used to reduce blood pressure in the general population, but ACE-Is and ARBs are the preferred agents to reduce proteinuria and CKD progression in CKD patients. While 50–54 percent of MarketScan and Ingenix i3 patients have at least one claim for an ACE-I, ARB, or renin inhibitor in the eighth quarter prior to ESRD, only 39–41 percent have at least one claim for these medications in the three months before ESRD initiation. Use of dihydropyridine calcium channel blockers (CCBs), in contrast, rises from 30–34 percent to 44–45 percent in the same period, and to 50 percent in the three months following initiation. This may reflect misunderstanding among general practitioners on the use and monitoring of ACE-Is/ARBs/renin inhibitors in CKD patients, as well as increasing blood pressure and incidence of hyperkalemia as patients progress towards ESRD.

Beta blocker use rises from 25–29 percent in the eighth quarter before ESRD to 35–37 percent in the three months before initiation, and to 41–43 percent in the next three months, likely reflecting the increased incidence of congestive heart failure and coronary artery disease as CKD progresses. Use of lipid lowering agents is fairly low, and stable throughout the transition, despite the high rate of cardiovascular disease in this population. This may illustrate the current lack of evidence for the use of these agents in CKD and ESRD patients, or the low levels of lipid testing seen in Figure 7.10.

**Figures 7.13–16:** see page 149 for analytical methods.
Use of diuretics during the transition to ESRD, by year & dataset

- **Potassium-sparing diuretics**
  - MarketScan 2003
  - MarketScan 2007
  - Ingenix i3 2003
  - Ingenix i3 2007

- **Thiazide diuretics**

- **Loop diuretics**

Quarter prior to or after ESRD initiation

Use of diuretics is common in CKD patients, both for the treatment of hypertension and the management of fluid volume as CKD progresses. Thiazide or a combination of thiazide and potassium-sparing diuretics are typically given in the early stages of CKD, while loop diuretics are commonly needed when GFR falls below 30 ml/min/1.73 m². At 5 percent or lower, use of potassium-sparing diuretics is rare in the eighth quarter before ESRD. Thiazide or thiazide-like diuretics are used in 20–29 percent of patients in this period, and their use remains fairly stable until after initiation, at which time it falls to 12 percent. Loop diuretics, in contrast, are used in 28–36 percent of patients eight quarters prior to ESRD, and in 43–51 percent just prior to ESRD. Interestingly, about 30 percent of patients remain on loop diuretics in the first quarter after ESRD initiation.

As CKD progresses to ESRD, the use of specialty CKD medications such as erythropoietin (EPO), darbepoetin (DPO), vitamin D products, and phosphate binders all increase. EPO/DPO treatment, for instance, rises from 5–6 percent in the eighth quarter prior to ESRD to just 14–17 percent in the quarter before initiation.

Use of oral active vitamin D products (calcitriol, paricalcitol, and doxercalciferol) rose between 2003 and 2007. In 2007, use grew from 5 percent in the eighth quarter prior to ESRD to 20–25 percent just prior to ESRD. Interestingly, about 30 percent of patients remain on loop diuretics in the first quarter after ESRD initiation.
Here we examine the continuity of medication use at and prior to initiation of ESRD therapy, beginning with agents that block the renin-angiotensin system (RAS). Angiotensin-converting enzyme inhibitors (ACE-Is) or angiotensin receptor blockers (ARBs) are recommended by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) as primary agents for CKD patients with diabetes and hypertension, and for those with hypertension and micro- or frank albuminuria. Aliskiren, a direct renin inhibitor, has recently reached the marketplace, and practitioners may be using this drug for the same indications. Interestingly, only 44–45 percent of EGHP patients have claims for any RAS inhibitor three quarters before starting ESRD therapy, while 37–42 percent receive ACE-Is/ARBs or renin inhibitors in the quarter following initiation. And of patients on these medications three quarters prior to ESRD, only 50–58 percent remain on them in the quarter following initiation. This suggests that adverse effects of these agents, such as hyperkalemia or acute kidney injury, may be manifesting as CKD progresses. Given that many patients still have residual kidney function at the time of initiation, and may benefit, with appropriate monitoring, from the protective effects conferred by these agents, this requires further investigation.

Beta blockers are used in 39 percent of patients three quarters before ESRD, and in 50 percent in the first quarter after initiation. Of the first group, 73–75 percent remain on the medication in the quarter after beginning ESRD therapy. This trend seems reasonable, given the increasing prevalence of congestive heart failure and hypertension as CKD progresses.

Use of a dihydropyridine calcium channel blocker (CCB) also rises over time; 28–33 percent of patients are on this class of CCB three quarters before ESRD, and 41–43 percent in the quarter after initiation. Of the first group, 63–71 percent remain on these drugs in the quarter after ESRD initiation. Given increasing hypertension as kidney disease progresses, and the difficulty controlling it, this is not surprising. Dihydropyridine CCBs are effective antihypertensive agents in CKD patients, despite the fact that they have not been shown to reduce proteinuria as effectively as ACE-Is or ARBs.

The percentage of patients using lipid-lowering agents remains stable throughout the transition to ESRD, at 33–38 percent, and two in three patients receiving these agents three quarters before ESRD continue to use them after initiation. This low amount of use, and its lack of increase in the year before ESRD, may reflect low levels of lipid monitoring and/or a current lack of evidence on outcomes in the CKD population.

Forty-five to 47 percent of patients with diabetes have claims for insulin three quarters before ESRD; of these patients, 72–78 percent continue to receive it in the quarter following initiation. Sulfonylureas, in contrast, are used by just 15–19 percent of diabetic patients three quarters before ESRD initiation, and use falls to 12–16 percent in the quarter after. This may reflect a decreasing use of sulfonylureas in the general population, with metformin becoming a first-line agent. In addition, most sulfonylureas or their active metabolites accumulate as kidney function declines, making their use challenging.

Only 3–4 percent of patients receive potassium-sparing diuretics three quarters before ESRD, and, as expected, virtually none receive them after initiation. Only 16–22 percent receive thiazide diuretics in the early period, and 23–30 percent of these patients remain on the agents after initiation. Patients on thiazide diuretics at initiation might also be receiving loop diuretics in combination. Loop diuretics, in contrast, are used by 44–47 percent of patients in the three quarters prior to ESRD, and 44–47 percent of these patients, in turn, have claims for this diuretic class in the quarter following initiation.

### Table 7.1 & Figures 7.21–7.23

<table>
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<tr>
<th>Medications</th>
<th>MarketScan</th>
<th>% on drug at 1 qtr ESRD</th>
<th>% on drug at 3 qtr ESRD</th>
<th>% of 3 qtr group on drug at 1 qtr ESRD</th>
<th>Ingenix i3</th>
<th>% on drug at 1 qtr ESRD</th>
<th>% on drug at 3 qtr ESRD</th>
<th>% of 3 qtr group on drug at 1 qtr ESRD</th>
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<tr>
<td>ACE-Is/ARBs/renin inhibitors</td>
<td>230</td>
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<td>33.4</td>
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<td>62.8</td>
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<td>68.5</td>
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<td>Insulin</td>
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<td>155</td>
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<td>Loop diuretics</td>
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<td>37.5</td>
<td>238</td>
<td>43.8</td>
<td>111</td>
<td>46.6</td>
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*Values for cells with ten or fewer cases.

Dihydropyridine CCBs are effective antihypertensive agents in CKD patients, despite the fact that they have not been shown to reduce proteinuria as effectively as ACE-Is or ARBs.
Medication continuation in the transition to ESRD, 2007

### 23. Medication use in the quarter after ESRD initiation in patients on the drug three quarters prior to ESRD, by dataset, 2007

<table>
<thead>
<tr>
<th>Medication</th>
<th>MarketScan</th>
<th>Ingenix i3</th>
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</thead>
<tbody>
<tr>
<td>Dihydropyridine CCBs</td>
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<tr>
<td>Lipid lowering agents</td>
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<tr>
<td>Insulin</td>
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<td>orange</td>
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<td>Sulfonylureas</td>
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<tr>
<td>Loop diuretics</td>
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<td>orange</td>
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<tr>
<td>ACE-Is/ARBs/RIs</td>
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<td>orange</td>
</tr>
<tr>
<td>Beta blockers</td>
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<td>orange</td>
</tr>
<tr>
<td>Potassium-sparing diuretics</td>
<td>purple</td>
<td>orange</td>
</tr>
</tbody>
</table>

Percent of patients

0 10 20 30 40 50

ACE-Is/ARBs/RIs  Beta blockers  Lipid lowering agents  Insulin  Sulfonylureas  Potassium-sparing diuretics  Thiazide diuretics  Loop diuretics

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Catheter placement rates prior to ESRD have generally fallen since 2001, and most often peak in the month following initiation of ESRD therapy. In 2006, the highest rates during this month were in the Medicare database, at 106 per 100 patient months for hemodialysis patients, compared to 47 and 53, respectively, for dialysis patients in the MarketScan and Ingenix i3 databases. (Figure 7.24; see page 149 for analytical methods. Medicare: incident hemodialysis patients age 67 & older. MarketScan & Ingenix i3: all dialysis patients. (Type of dialysis is not available in the MarketScan & Ingenix i3 databases.)

Like catheter placement rates, rates of arteriovenous fistula placement peak in the month after the initiation of ESRD therapy. Rates have increased overall since 2001, in the first month of treatment reaching 22.2 per 100 patient months for 2006 Medicare hemodialysis patients, compared to 9.7 and 13.6, respectively, in MarketScan and Ingenix i3 dialysis patients. (Figure 7.25; see page 149 for analytical methods. Medicare: incident hemodialysis patients age 67 & older. MarketScan & Ingenix i3: all dialysis patients. (Type of dialysis is not available in the MarketScan & Ingenix i3 databases.)
Use of arteriovenous grafts, like that of catheters, has been falling. In 2001, placements in the first month after ESRD initiation reached 26.4 per 100 patient months among Medicare hemodialysis patients, and 6.8 and 10.0, respectively, among MarketScan and Ingenix i3 dialysis patients. By 2006, rates during this month had decreased 66, 55, and 77 percent, respectively. (See Figure 7.26; see page 149 for analytical methods. Medicare: incident hemodialysis patients age 67 & older. MarketScan & Ingenix i3: all dialysis patients. (Type of dialysis is not available in the MarketScan & Ingenix i3 databases.)

Between 2001 and 2006, placement rates for peritoneal dialysis catheters in the month prior to initiation of ESRD therapy increased 84 percent, from 66 placements per 100 patient months to nearly 121. Rates are highest in this month before ESRD initiation, in contrast to rates found for dialysis accesses, which peak in the month following the start of ESRD therapy. (See Figure 7.27; see page 149 for analytical methods. Medicare: incident peritoneal dialysis patients age 67 & older. (Type of dialysis is not available in the MarketScan & Ingenix i3 databases, so these datasets are not included here.)
Only 17–30% of EGHP patients see a **Nephrologist** 22–24 months prior to ESRD, though 47–54% have a **CKD Claim** in that period. • 7.2 & 7.4

In the three months prior to ESRD, 69% of Medicare patients, compared to 37–38% of MarketScan & Ingenix i3 patients, visit a **Cardiologist**. • 7.5

Medicare patients are generally twice as likely as their Ingenix i3 counterparts to receive **Laboratory** testing in the two years prior to ESRD. • 7.7–12

At two years prior to ESRD, **50–54% of EGHP patients receive an ACE-I, ARB, or renin inhibitor; this falls to 39–41% in the quarter before ESRD.** • 7.13

Use of **Calcium Channel Blockers** rises from 30–34% eight quarters before ESRD initiation to 50% in the three months after. • 7.15

**Loop Diuretics** are used in 28–36% of patients eight quarters prior to ESRD, & in 43–51% just prior to ESRD. • 7.17

Of the 44–45% of patients on ACE-1s, ARBs, or renin inhibitors three quarters before ESRD, **50–58% remain on them in the quarter after initiation.** • 7.a

**Beta Blockers** are used in 39% of patients three quarters before ESRD; 3 in 4 patients remain on the medication in the quarter after initiation. • 7.a

The placement rate for **AV Fistulas** is 13.9 per 100 patient months in Medicare hemodialysis patients, compared to 6.1–6.4 in EGHP dialysis patients. • 7.25

**Summary**