chapter nine

special studies

If we long for our planet to be important, there is something we can do about it. We make our world significant by the courage of our questions and by the depth of our answers.

Carl Sagan, Cosmos
The Special Studies Centers (SSCs) of the USRDS provide focused assessments on cardiovascular disease, quality of life/rehabilitation, and the nutritional aspects of kidney disease, and each year present elements of their studies in the ADR. This year the Cardiovascular ssc addresses the use of defibrillators, pacemakers, and resynchronization therapy; prescription medication use; and obesity, heart failure, and bariatric surgery. The Quality of Life/Rehabilitation ssc explores patient access to information on kidney transplantation and its relation to the likelihood of reaching the transplant wait list, and the Nutrition ssc presents data on nutritional support provided to dialysis patients.

The Cardiovascular ssc has identified the ESRD population as a group at high risk for heart failure, noting that patients may become users of new types of pacemaker technology, such as resynchronization pacemakers/defibrillators, that are being employed in the general population. Data here show trends in the use of these devices, as well as survival probabilities associated with their primary and secondary use. Procedure use appeared to peak in 2007, and was reported in fewer than 0.6 percent of dialysis patients in 2008.

The ssc next explores the use of prescription drugs in dialysis patients with heart failure. The use of ACEIs/ARBs rises slightly with age, while combination therapy with ACEIs/ARBs and beta blockers reaches 40 percent in patients age 20–44, but falls to 30 percent in those 75 and older. Data on treatment of atrial fibrillation shows that warfarin is the most commonly used drug, with 33–36 percent of patients taking this medication alone. Warfarin plus clopidogrel, in contrast, is used in fewer than 6 percent of patients. There is little difference by medication use in unadjusted hospitalization and rehospitalization rates among patients with congestive heart failure or acute myocardial infarction; rehospitalization rates for those with atrial fibrillation or CVA/TIA, however, differ slightly. More comprehensive analyses will be needed to determine whether these differences are significant.
In its final spread the Cardiovascular SSC examines the relationship between body mass index (BMI) and survival. Here, as in many other publications, the probability of survival among dialysis patients with congestive heart failure is shown to be lowest in those with a low BMI, and greatest in those with a BMI of 35 kg/m<sup>2</sup> or above. Among ESRD patients undergoing bariatric surgery, the mean BMI is approximately 40 kg/m<sup>2</sup>, with 60–70 percent of these patients having a BMI greater than 40. In the 24 months following surgery, the mean BMI falls to less than 35. Although the total number of bariatric procedures performed in the ESRD population between 1999 and 2008 was less than 1,000, the number is increasing, and complications and long-term outcomes among these patients should be carefully evaluated.

The Quality of Life/Rehabilitation SSC looks at patients receiving information about their transplant options as they begin ESRD therapy, using data reported on the most recent revision of the Medical Evidence (ME) form. Patients with private insurance, particularly those younger than 40, are the most likely to receive this information, and there is remarkable similarity by geographic region. Further data examine the likelihood of being placed on the transplant wait list as it is associated with receiving or not receiving this information. While there may be important limitations to the questions on the ME form, the clear association with placement on the wait list suggests that improved access to kidney transplantation is needed, but may be limited by the marked shortage of organs.

The Nutrition SSC assesses the use of nutritional support — enteral and parenteral supplements, and anabolic steroids. There has for many years been a nutritional services benefit for kidney patients; few, however, have taken full advantage of these services. Variations in the geographic delivery of these services are remarkable, with a ten-fold difference across ESRD networks. Wider use of these supplements, when appropriate, may be coupled with the new CKD education benefit to improve the nutritional status of the incident dialysis population.

**Figure 9.1.** Prevalent dialysis patients, 2006–2008.
Cardiovascular disease is a predominant cause of death in dialysis patients. Deaths attributed to arrhythmic mechanisms are the largest single contributor to all-cause mortality, at 26 percent, while 39 percent are ascribed to cardiac causes, and 43 percent to cardiovascular causes. The number of deaths due to withdrawal, however, nearly matches total AMI and CHF deaths combined.

In this year’s ADR the Cardiovascular Special Studies Center revisits the topics of AMI, CHF, atrial fibrillation, defibrillators, cerebrovascular disease, and coronary revascularization. Most content here, however, is entirely new, including an overview of Medicare Part D prescription drug therapy in relation to comorbid cardiovascular disease in dialysis patients. This is meant both to stimulate further analytic work and to provide the foundation for design of clinical trials. We also provide new data on bariatric surgery, a topic entirely new to the ADR. Despite the high prevalence of obesity in dialysis patients, there is little information on bariatric surgery and its outcomes in these individuals.

Of note, the data presented are observational, and caution should be exercised in their interpretation, particularly with respect to survival data in Figure 9.9 and data in Figure 9.10 on the probability of rehospitalization or rehospitalization/death, as these may be confounded by selection bias. As noted in our previous ADR analyses, AMI is associated with very high mortality; from an observational standpoint, however, survival is better in patients receiving beta blockers and ACEIs/ARBs. Similarly, medical therapy for congestive heart failure in the general population is associated with better outcomes than no therapy. This pattern is less evident in the observational data with respect to CVA/TIA and anticoagulant therapy. In these patients, there is no obvious benefit from warfarin regimens, but again this may reflect selection bias and confounding by indication. Although concerns have been expressed regarding the potential harm of warfarin in dialysis patients with atrial fibrillation (Chan et al.), this is not apparent in Figure 9.9, as overall survival is slightly better in patients with atrial fibrillation receiving warfarin compared to those not receiving anticoagulant therapy. It is difficult to discern trends related to rehospitalization and medication use in patients with CHF or AMI, in part because of the very high rehospitalization rate in these patients, and the fact that these are all-cause hospitalizations not related to specific cardiac conditions.
The previous trend of rising defibrillator use over time is no longer evident, with numbers beginning to plateau in 2005. Just over 1,800 dialysis patients received one of these devices in 2005; this dropped to 1,784 in 2008. Concerns related to the long-term efficacy of these devices (particularly as no dialysis patients were entered into clinical trials examining the utility of defibrillators) may have dampened the enthusiasm for their use in ESRD patients.

As noted in prior publications (Herzog et al.), there is a significant gender imbalance among ESRD patients receiving defibrillators; 70 percent of those on dialysis, and 84 percent of those with a transplant, are male. *Figures 9.2–5; see page 48* for analytical methods. Period prevalent dialysis patients (9.2); period prevalent ESRD patients (9.3); period prevalent ESRD patients, 1999–2008 (9.4–5).

One-year mortality in hemodialysis patients receiving ICDs/CRT-Ds for primary prevention is approximately 35 percent, compared to 39 percent for secondary prevention. The apparent reduction in defibrillator use in dialysis patients may in part reflect these sobering mortality data. One-year mortality among transplant patients is lower, at close to 20 percent. *Figure 9.6; see page 48* for analytical methods. Period prevalent ESRD patients, 1999–2008.
Table 9.a provides an overview of prescription drug therapy for the treatment of cardiovascular disease in dialysis patients. As only prescription drug data are available, data related to use of aspirin as a single agent are not shown.

Substantial numbers of patients receive an ACEI, ARB, or beta-blocker. As clinical trial results (4D, AURORA, and SHARP) pertaining to statins in ESRD patients are disseminated, it will be interesting to see if there are changes in the frequency of statin use in dialysis patients. + Table 9.a, see page 48 for analytical methods. January 1 point prevalent dialysis patients age 20 & older, with a first cardiovascular diagnosis or procedure between January 1 & November 30, 2007.

Among dialysis patients with CHF, 39 percent of those age 20–44 receive both an ACEI/ARB and a beta-blocker, compared to just 30 percent of those age 75 and older. There are no significant disparities by gender or race in the use of combined therapy. + Figure 9.7; see page 48 for analytical methods. January 1 point prevalent dialysis patients age 20 & older, with a first cardiovascular diagnosis or procedure between January 1 & November 30, 2007.

Use of warfarin-containing regimens in dialysis patients with AFIB is slightly more frequent among whites than African Americans, at 42 versus 35 percent. Despite the paucity of clinical data regarding its safety and efficacy in dialysis patients with AFIB, 16 percent also receive amiodarone. + Figure 9.8; see page 48 for analytical methods. January 1 point prevalent dialysis patients age 20 & older, with a first cardiovascular diagnosis or procedure between January 1 & November 30, 2007.
Among dialysis patients with cardiovascular disease, rates of rehospitalization after diagnosis are very high, particularly after AMI. Rates of rehospitalization and rehospitalization/death are both markedly lower after CABG than after PCI. *Figures 9.9-11; see page 481 for analytical methods. January 1 point prevalent dialysis patients age 20 & older, with a first cardiovascular diagnosis or procedure between January 1 & November 30, 2007; unadjusted.
In this sample of 86,470 prevalent dialysis patients with a cardiovascular diagnosis or cardiac intervention in 2008, more than half are classified as overweight or obese. Among those with diabetes, 36.7 percent have a BMI of 30 kg/m² or higher. Advanced age is associated with a lower mean BMI, and female gender with a higher one; by race, however, there are only minimal differences. *Table 9.8; see page 482 for analytical methods.* January 1 point prevalent dialysis patients age 20 & older with a first cardiovascular diagnosis or procedure in 2008.

Compared to patients with a BMI of 18.5–<25 kg/m², those with a lower BMI have a small but significant increased relative risk of incident CHF, while the risk is lower in patients with a BMI of 25 or above. This likely reflects the early identification of patients who can be characterized as showing “reverse epidemiology,” with a higher degree of underlying cardiomyopathy and disease severity.

Data on unadjusted survival probabilities in dialysis patients with CHF add to the large body of observational work on the paradox of improved survival associated with increased BMI. The most striking difference here is for patients with a BMI less than 18.5 kg/m², among whom one-year mortality is 46 percent; this falls with increasing BMI, reaching just 25–26 percent in patients with a BMI of 35 kg/m² or above. The increased mortality associated with low BMI may be a manifestation of malnutrition/inflammation, a wasting state which may potentially respond, at least in part, to nutritional or other medical intervention.

The phenomenon of reverse or confounded epidemiology is also demonstrated by adjusted data showing an increased risk of death in CHF patients with low BMI. It appears, however, that this relationship is attenuated for patients with a BMI of 40 kg/m² or above.

Observational data of this type do not provide a definitive answer as to what should be regarded as an ideal body weight for dialysis patients. Lifestyle modification, including weight reduction, has long been advocated as an appropriate intervention to reduce cardiovascular morbidity and mortality in the general population, and, by extension, patients with ESRD. *Figures 9.12–14; see page 482 for analytical methods.* January 1 point prevalent dialysis patients age 20 & older with a first cardiovascular diagnosis or procedure in 2008.
Minimal information exists on bariatric surgery in ESRD patients, and data here are intended to stimulate further research in this emerging area. In 1999–2008, 587 dialysis patients and 234 transplant patients received bariatric surgery. While the presence of patients with a BMI less than 30 kg/m² may seem paradoxical and at odds with clinical practice guidelines, data here are obtained from the Medical Evidence form at the initiation of ESRD therapy; patients with low reported BMIs may gain weight after initiation. Nearly two-thirds of ESRD patients receiving bariatric surgery during this period were women. Table 9.5; see page 482 for analytical methods. ESRD patients age 20 & older.

While bariatric surgery is relatively infrequent among ESRD patients, considering the number who are morbidly obese, its use has been increasing, concurrent with the recent introduction of the adjustable band technique.

As expected, outcomes after bariatric surgery are better for transplant patients than for their dialysis counterparts, with one-year survival of 88 compared to 78 percent. Surprising, however, is the high rate of survival in the dialysis cohort. While a selection bias for healthier patients is likely, one reasonable conclusion of these data is that it is possible to perform bariatric surgery in selected dialysis patients with reasonable long-term survival.

Among dialysis patients undergoing this surgery, the mean BMI drops from 45.5 kg/m² to 33.7 at 24 months, apparently confirming the efficacy (when viewed from the perspective of weight reduction) of this surgery. This does not, however, address the issue of “ideal weight” (with or without surgical intervention) in this patient cohort.

Maps of variations in BMI in 2005 and 2008 across the country show no obvious geographic trends.

Based on the prevalence of obesity in dialysis patients, and the relatively favorable outcomes suggested here, it is likely that the number of bariatric surgical interventions will increase over time. This area merits further investigation. + Figures 9.13–19; see page 483 for analytical methods. ESRD patients age 20 & older (9.15–17), dialysis patients age 20 & older (9.18), & January 1 point prevalent dialysis patients who survive & receive dialysis for entire year (9.19).
Kidney transplantation increases the opportunity for rehabilitation and improved quality of life, and is the preferred therapy for many patients with treated chronic kidney disease. So that patients may be able to find a living donor or be placed on the waiting list to receive a kidney from a deceased donor, it is important for them to receive information as soon as possible about transplant as a treatment option.

The 2005 version of the ESRD Medical Evidence form (2728) includes the question “Has patient been informed of kidney transplant options?” Completion of the form is required when a patient is diagnosed as having ESRD and receives his/her first outpatient dialysis treatment. Data from this form are incorporated into the MEDEVID05 file of the USRDS Standard Analysis Files.

For patients starting dialysis between January 1, 2005, and September 30, 2008, MEDEVID05 data were used to examine the percent reported as having been informed of kidney transplant options. Patients included in this analysis (approximately 320,000) had started dialysis for the first time, had not had a prior kidney transplant, and had not been preemptively placed on a wait list for a kidney transplant before starting dialysis. Results were compared by age, gender, race, ethnicity, insurance status, and U.S. Census Division.

Among ESRD patients starting dialysis during the period, information recorded on the Medical Evidence form about whether they had been informed of kidney transplant options was associated with time to being wait listed for a kidney transplant. Informed patients had a shorter time to wait listing, suggesting that early discussion of kidney transplant options is valuable as a step toward transplant candidacy.

Among the 30 percent of patients reported as not receiving information on kidney transplant options at initiation, the most frequently reported reasons were that they were not assessed and/or they were medically unfit, and lack of suitability due to age was a more frequent reason as patient age increased.

Patient characteristics viewed as predicting post-transplant compliance may provide reasons for not informing patients about kidney transplant options. Drug dependence and language barriers, for instance, are two factors that may be associated with patients not being informed because they are deemed medically unfit. Comorbidity profiles associated with being termed medically unfit for kidney transplant merit study, as do the characteristics of patients not informed of transplant options for other reasons.
The percentage of females and males informed of their transplant options is similar by age, and for African Americans and whites. A small disadvantage in the likelihood of being informed is evident for Hispanics compared to non-Hispanics age 0–19; differences by ethnicity are not evident for the remaining ages. Among patients younger than 70, those with private insurance have a marked advantage of being informed compared to patients with Medicare, Medicaid, other types of insurance, and no insurance. Among patients age 80 and older, those with other types of insurance are most likely to have received information about kidney transplant options. And with respect to geographic location, the South Atlantic division has the lowest percentage of patients informed about kidney transplant options among those age 20–59, while the Pacific division has a markedly higher percent of patients age 70 and older receiving this information. *Figures 9.20–24; see page 483 for analytical methods. Incident dialysis patients, January 1, 2005, to September 30, 2008.*
Of patients not informed of their transplant options, no differences by gender are evident in the percent of patients not assessed. Not being assessed is a reason that African Americans more than whites have not been informed of transplant options in all age categories except 80 and older. Among patients age 0–39, not assessed is more often reported for non-Hispanic patients than for Hispanics, while ethnic differences are small for patients age 40–79.

Overall, relatively few patients are reported not informed of kidney transplant options because the patient declined information. This is reported most often in patients age 0–19 with Medicare coverage, at 5.3 percent.

Among patients younger than 40, females are more likely than males not to receive transplant information due to being medically unfit; the reverse, however, is true among patients age 80 and older. In the two younger age categories, being medically unfit is a more common reason among African Americans than whites, but the reverse is true for all other ages. And for all ages, it is a more common reason among non-Hispanic patients than among Hispanics.

No differences by gender are evident across age categories in the percentage of patients not informed of transplant options because the patient is psychologically unfit. Although differences are generally small, this reason is reported more for African Americans than for whites in all age categories, and more for non-Hispanics than for Hispanics among those younger than 70. In those younger than 80, it is a more common reason among Medicaid patients compared to those with other insurance; it is especially likely to be a reason in patients age 0–19.

Among patients 70 and older, women more than men, and Hispanics more than non-Hispanics, are not informed of transplant options for the reason “unsuitable due to age.” This reason is more common among boys than girls, and among whites, non-Hispanics, and those with Medicare coverage than African Americans, Hispanics, and those with other insurance.

Among those not informed of transplant options for other reasons, gender differences are small across ages. For ages younger than 60, this reason is more common among whites than African Americans; it is also more common across ages among Hispanics than non-Hispanics, and it is far more frequently reported among uninsured children than among those with insurance. Having no insurance is associated in all ages with not having been informed of transplant options for other reasons.

For all patients in the study population, time from the start of dialysis to placement on a kidney transplant wait list was examined as a function of whether or not the patient was informed of kidney transplant options; patients receiving a transplant without being wait-listed were censored at the transplant date. Informed patients were placed on a wait list sooner than were non-informed patients and, by six months after initiation of therapy, were about twice as likely to have been wait-listed.

Among patients not informed of transplant options, time to wait listing was then examined as a function of the reason for not being informed, with patients receiving a transplant without being wait-listed again censored at the transplant date. Patients not assessed for transplant eligibility, followed by those with other reasons for not having been informed, were more likely to be subsequently wait-listed than were those for whom another reason for not being informed was reported. Patients termed medically unfit, psychologically unfit, or unsuitable age were the least likely to be wait-listed. It should be noted that persons younger than 65 and with Medicare coverage have that coverage because of disability, increasing the likelihood that they are designated as medically unfit for kidney transplantation. + Figures 9.29–30; see page 483 for analytical methods. Incident dialysis patients, January 1, 2005, to September 30, 2008.
We used Medicare claims data to track the use of intradialytic parenteral nutrition (IDPN), enteral nutrition delivered by tube feeding, and injectable androgens among prevalent dialysis patients from 2003 through 2007. For each calendar year, we assembled a cohort of January 1 point prevalent adult patients who had received any form of dialysis therapy for more than 90 days and had Medicare as their primary payor. Medicare claims data for each year were then searched for claims for enteral nutrition supplements (B4149–B4155; B4164–B5200), parenteral nutrition supplements (B4164–B4199), or anabolic agents, including testosterone or nandrolone decanoate (J0900, J1060, J1070, J1080, J2320, J2321, J2322, J3120, J3130, J3140, and JT3150).

Figure 9.33 shows the number of patients with at least one claim for each type of nutritional therapy per 1,000 patients. Overall rates of nutritional or anabolic support are extremely low. Enteral nutrition is prescribed far more frequently than parenteral nutrition or anabolic therapies, at 11.3–12.6 per 1,000 patients. Use of enteral nutrition increased from 2003 to 2004, then remained stable until a decline in 2007 to approximately 2003 levels. Use of parenteral nutrition was 2.1–3.6 per 1,000 patients; it appeared to increase from 2003–2005, but then decreased substantially from 2005–2007. Anabolic therapy showed a steady decline throughout the period of 2003–2007, from 2.3 to 1.5 per 1,000 patients.

Characteristics of patients treated with nutritional therapies are shown in Figures 9.34–38. Women are more likely to receive enteral and parenteral nutrition than men, but men, not surprisingly, are overwhelmingly more likely to receive androgen treatment (84–89 percent of androgen recipients are male). African American race is associated with a higher likelihood of receiving enteral nutrition, but a lower likelihood of receiving parenteral nutrition support. While patients who receive enteral or parenteral nutrition have significantly lower serum albumin concentrations at dialysis initiation than those not prescribed nutritional supplementation, there is no relationship between serum albumin and receipt of anabolic agents.

Patients receiving enteral nutrition are older than those not receiving tube feeding, but their average age has not changed substantially with time. Patients receiving parenteral nutrition in 2003 were younger than those not prescribed IDPN, but their age increased steadily from 2003 to 2007 so that, by 2007, they...
were older than those not receiving IDPN. Patients receiving anabolic agents are consistently younger than those not receiving this therapy. And patients with diabetes are more likely to receive enteral nutrition, but less likely to receive parenteral nutrition or androgens.

There is substantial geographic variation in nutritional support, particularly in the use of parenteral and anabolic therapies, which vary by more than ten-fold across ESRD networks. Use of enteral nutrition therapy varies by more than three-fold across networks as well. Use of enteral nutrition within networks is related to use of parenteral nutrition ($r=0.58$), but there is no relationship between use of nutritional therapy and androgen use.

Few dialysis patients received nutritional/anabolic therapies billed to Medicare during 2003–2007. Although age, gender, race, albumin, and diabetes were all associated with receipt of specific types of nutritional support, none was associated with all types. Analysis of Medicare claims data unfortunately does not allow for determination of all types of nutritional support, as oral nutritional supplements and transdermal forms of androgens were not included in the Medicare claims data for these years. The full extent of nutritional support thus cannot be quantified. In addition, anabolic agents may be prescribed for indications other than malnutrition and wasting, including androgen deficiency and anemia. On the other hand, use of these agents in women, albeit in small numbers, would suggest that androgen deficiency is not the only reason for their use, and since treatment of anemia with these agents has been largely supplanted by erythropoiesis stimulating agents, wasting may be an indication for some patients. It is unfortunate that an important therapeutic tool such as nutritional support cannot be fully captured and described within the Medicare data, because if use cannot be reliably ascertained, studies of outcomes are limited. The introduction of Medicare Part D may allow for better tracking of some nutritional support, but the proposed bundling of all dialysis-associated medications with the facility payment will eliminate the need for specific claims for IDPN and any other therapy delivered through the dialysis unit, making them more difficult to quantify.

*Figure 9.33. Prevalent dialysis patients, 2003–2007.*
Serum albumin concentration among recipients & non-recipients of nutritional support

Mean age of recipients & non-recipients of nutritional support

Gender distribution of patients receiving & not receiving nutritional support
Figure 9.34–38 & Table 9.d. Prevalent dialysis patients, 2003–2007 (9.34–38); prevalent dialysis patients, 2007 (9.d).
As noted in prior publications, there is a significant gender imbalance among ESRD patients receiving defibrillators; 70 percent of those on dialysis, and 84 percent of those with a transplant, are male. FIGURE 9.15

Data on unadjusted survival probabilities in dialysis patients with congestive heart failure add to the large body of observational work on the paradox of improved survival associated with increased body mass index. FIGURE 9.13

In 1999–2008, 587 dialysis patients and 234 transplant patients received bariatric surgery. TABLE 9.C

Patients informed of their transplant options at the initiation of ESRD therapy have a shorter time to wait-listing, suggesting that early discussion of kidney transplant options is valuable as a step toward transplant candidacy. FIGURE 9.31

Overall rates of nutritional or anabolic support are extremely low, with enteral nutrition prescribed far more frequently than parenteral nutrition or anabolic therapies, at 11.3–12.6 per 1,000 patients. FIGURE 9.33

African American race is associated with a higher likelihood of receiving enteral nutrition, but a lower likelihood of receiving parenteral nutrition support. FIGURE 9.37