Chapter Nine
Special Studies

Everything comes from everything, and everything is made from everything, & everything can be turned into everything else; because that which exists in the elements is composed of those elements.

Leonardo da Vinci
For this year’s Annual Data Report we again present an expanded chapter for the Special Studies Centers, with assessments by the Cardiovascular, Rehabilitation/Quality of Life, and Nutrition centers. This year’s presentation by the Cardiovascular Special Studies Center concentrates on the development of new diagnoses for cardiovascular disease among patients with end-stage renal disease (ESRD) and on interventions such as revascularization procedures and implantable pacemakers and defibrillators. The first figures include data on new onset congestive heart failure, acute myocardial infarction, cerebrovascular accidents/transient ischemic attacks, cardiac arrest, and peripheral vascular disease. These events are less common among African American patients than among whites and, not surprisingly, the risk of these events rises with age. Compared to patients on hemodialysis, the peritoneal dialysis population has less newly diagnosed congestive heart failure, but more cardiac arrests and acute myocardial infarctions. But while patients treated with peritoneal dialysis tend to have less comorbidity, they are more likely to have surgical revascularization procedures and percutaneous interventions for revascularizations, and are also more likely to use implantable cardioverter defibrillators (ICDs) and cardiac resynchronization therapy defibrillators (CRT-Ds). These data may contribute to the observation that peritoneal dialysis patients have a changing hazard for morbidity and mortality over time, manifesting itself in cardiovascular disease and more frequent interventions. Survival after these events and procedures is generally best for the transplant population, which carries less disease, and slightly worse for those treated with peritoneal dialysis. Physician care during and after hospitalization for a cardiovascular diagnosis or event is illustrated in Figure 9.12. Generally, nephrology care of these patients is high, at 80–90 percent. Primary care physician involvement is lower, but still approaches 75–80 percent following a hospitalization. This year the Rehabilitation/Quality of Life Special Studies Center presents preliminary data from the Comprehensive Dialysis Study (CDS), assessing occupational status and patient employment at the initiation of ESRD treatment. Interestingly, 43 percent of incident patients in the CDS were employed in the administrative function and clerical sales area. Activity scores of patients who are employed and/or able to work are quite diverse, as expected. The Nutrition Special Studies Center of the USRDS also presents CDS data this year, looking at physical activity, nutritional status, and inflammation, and including data from participants in the nutrition substudy of the CDS. Data show that serum albumin and prealbumin are strongly associated with participation in physical activity, and suggest that the nutritional component of these markers, rather than the inflammatory one, may be the dominant correlate of physical activity.

Figure 9.1 Prevalent dialysis patients, 2005–2007; from Reference Table H.29.
Causes of death in prevalent dialysis patients, 2005–2007

- AMI: 5.7%
- CHF: 5.3%
- Arrhythmia/cardiac arrest: 26.3%
- Other cardiac: 2.4%
- CVA: 4.0%
- Infection: 12.6%
- Withdrawal: 8.1%
- Malignancy: 3.7%
- All other: 32.0%
In this section we provide a detailed overview of cardiovascular disease (CVD) and cardiac procedures in prevalent ESRD patients, examining relative risk, incident rates, geographic variations, temporal trends, patient survival, patient care, and the costs of this care. It should be noted that this is a broad overview of CVD in ESRD patients, both dialysis and transplant; because of the lower risk of CVD in transplant recipients, overall rates and risks will be lower in these analyses when compared to those of dialysis patients alone. On the previous page we illustrate the distribution of attributed causes of death in dialysis patients, raising several important issues. Cardiac and cardiovascular causes have consistently dominated cause-specific mortality in dialysis patients, with approximately 40 and 44 percent of deaths, respectively, attributed to these causes. The percentage of deaths attributed to arrhythmic mechanisms has been remarkably constant over time; and the reported value of 26 percent is consistent with previously published data from both the HEMO and 4D studies (Herzog et al., Wanner et al.). There has, however, been a gradual decline in mortality attributable to acute myocardial infarction (AMI). Withdrawal from dialysis constitutes the third largest component of the pie chart, ranking behind infection but ahead of both AMI and congestive heart failure. Age is an important independent predictor of the risk of incident CVD, but, perhaps not surprisingly, is inversely related to the likelihood of cardiac intervention. Compared to an ESRD patient age 45–64, one age 75 or older is 32 percent less likely to receive percutaneous coronary intervention (PCI), 50 percent less likely to receive coronary artery bypass surgery, and 36 percent less likely to receive an implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy defibrillator (CRT-D). There is a strong relationship between gender and the likelihood of cardiac intervention. Women, for example, are less than half as likely as men to receive an ICD or CRT-D. This finding is similar to reported data on gender disparities in the use of device therapy in the general population. Although the magnitude is considerably less, a similar trend is noted by race and ethnicity. Compared to white patients, African Americans are less likely to receive coronary revascularization or an ICD/CRT-D, and Hispanic patients are less likely than non-Hispanics to receive an ICD/CRT-D. By modality, patients on peritoneal dialysis are 20 percent less likely than those on hemodialysis to develop congestive heart failure. The risk of CVA/TIA, in contrast, is essentially the same, while the risk of peripheral arterial disease is lower in peritoneal dialysis patients. Although the non-physiologic nature of thrice-weekly hemodialysis has been implicated in the overall high risk of cardiac arrest in hemodialysis patients, the overall risk of cardiac arrest is still 10 percent higher, after adjusting for other differences, in patients on peritoneal dialysis. Similarly, the risk of acute myocardial infarction is 19 percent higher for peritoneal dialysis patients (it should be remembered, however, that Cox models do not always adjust for important baseline differences between two populations); in this instance differential rates of transplantation related to dialysis vintage may make comparisons of hemodialysis and peritoneal dialysis populations somewhat problematic. The likelihood of both coronary revascularization and defibrillator use is higher in peritoneal dialysis patients. Transplant patients, in contrast, have markedly lower rates of incident CVD, likely reflecting their overall incident rates of cardiac disease, and a lower likelihood of coronary revascularization or device therapy.
Age is an important independent predictor of the risk of incident cardiovascular disease, but is inversely related to the likelihood of cardiac intervention. There is also a strong relationship between gender and the likelihood of receiving cardiac intervention, particularly for ICD/CRT-D, which women are 53 percent less likely to receive than men. In terms of modality, transplant patients are 80 percent less likely than those on hemodialysis to have a cardiac arrest, and 54–59 percent less likely to receive a cardiac intervention. Patients on peritoneal dialysis are 20 percent less likely than those on hemodialysis to have congestive heart failure; their likelihood of a cardiac arrest, however, is 10 percent greater, and they are 45 percent more likely to receive an ICD/CRT-D. \(\text{Table 9.1};\) see page 376 for analytical methods. January 1, 2005 point prevalent ESRD patients age 20 & older.

Event rates for congestive heart failure and peripheral arterial disease reach 270 and 260 per 1,000 patient years. Compared to dialysis patients, rates for the cardiovascular conditions and procedures examined here are markedly lower in transplant recipients. \(\text{Figure 9.2};\) see page 376 for analytical methods. January 1, 2005 point prevalent ESRD patients age 20 & older.
Maps on this spread present a population overview of geographic variations and temporal trends in rates of cardiovascular disease and interventions, looking at prevalent ESRD patients.

Since 1997, the overall rate of congestive heart failure (CHF) has dropped from 243 events per 1,000 patient years to 216. There remains, however, a clustering of CHF in the southern and eastern states. The overall rate of cerebrovascular disease has remained stable, at 105 events per 1,000 patient years in 1997 and 102 in 2007. Geographic variations in rates of CVA/TIA are qualitatively similar to those noted for CHF.

The overall rate for peripheral arterial disease has dropped from 238 per 1,000 patient years in 1997 to 208 in 2007. And the rate of cardiac arrest has fallen from 96 to 88. Some geographic clustering is noted in the southern states and in Appalachia. \textbf{Figures 9.3–6;} see page 376 for analytical methods. January 1 point prevalent ESRD patients age 20 & older.
There has been a slight growth in the rate of acute myocardial infarction (AMI), from 42 per 1,000 patient years in 1997 to 46 in 2007. Although this is a relatively small difference, it is a trend distinctly opposite that reported among patients with chronic kidney disease (see Chapter Six of Volume One) and in the general population. There has been a progressive decline in the overall rate of AMI in the United States, and this finding of an actual increase among ESRD patients raises concern. It may also, however, reflect in part the changing demographics of ESRD patients over time.

From 1997 to 2007, the overall rate of percutaneous coronary intervention (PCI) increased from 15 to 26 events per 1,000 patient years, while the rate of surgical coronary revascularization has fallen from 12 to 10. Use of defibrillators in ESRD patients is low, but has increased from 4.6 per 1,000 patient years in 2003 to 6.6 in 2007.

Much attention has been given recently to geographic variations in the use and delivery of medical care — particularly as related to expensive procedures — in the general population; this variation is apparently mirrored in the ESRD population as well. \(\text{Figures 9.7–10; see page 376 for analytical methods. January 1 point prevalent ESRD patients age 20 & older.}\)
This figure illustrates survival, by modality, after a diagnosis of incident cardiovascular disease and after cardiac intervention. Across diagnoses and procedures, survival is greatest among transplant recipients, and lowest among those treated with peritoneal dialysis. The one-year survival associated with congestive heart failure, for example, is 0.8 for transplant patients, compared to 0.57 among peritoneal dialysis patients. As in the non-renal population, survival after acute myocardial infarction (AMI) is poor, regardless of modality. As reported in previous ADRs, despite improved survival after AMI in the general population, the unadjusted survival of dialysis patients sustaining an AMI has changed little over the past three decades. (Figure 9.11; see page 376 for analytical methods. January 1 point prevalent ESRD patients, 2005, age 20 & older, with a first cardiovascular diagnosis or procedure in 2005–2007.)
Not surprisingly, nephrologists play a key role in the delivery of medical care to ESRD patients during a cardiovascular hospitalization and its subsequent follow-up. What is surprising, however, is that neurologists contribute to the care of just 42 percent of ESRD patients hospitalized with cerebrovascular disease, and 36 percent after discharge. These data also indirectly provide a rough gauge of the error associated with certain specialty codes. In the U.S., essentially 100 percent of percutaneous coronary interventions are performed by cardiologists; the reported value of 96.6 percent is close to this expected value.

Figure 9.12; see page 376 for analytical methods. January 1 point prevalent dialysis patients age 20 & older, 2005, with a first cardiovascular diagnosis or procedure in 2005–2007.

Comparably, transplant patients, dialysis patients have higher per person per month costs for cardiovascular conditions and procedures. The overall financial cost related to cardiovascular disease and treatment in ESRD patients is considerable. Figure 9.13; see page 377 for analytical methods. January 1 point prevalent ESRD patients, 2005, age 20 & older, with a first cardiovascular diagnosis or procedure in 2005–2007.
Overview of employment among incident dialysis patients: Data from the Comprehensive Dialysis Study

A summary from the Rehabilitation/Quality of Life Special Studies Center

The USRDS Comprehensive Dialysis Study (CDS) obtained patient-reported behavior and health status assessments from individuals age 19–94 who initiated maintenance dialysis between 2005 and 2007. Participants in the CDS had been receiving regular dialysis for an average of four months, and were affiliated with 295 randomly sampled dialysis units across the U.S. The dialysis unit sample matched the overall population closely on facility type, chain/non-chain status, and ESRD Network location. Based on data from the Medical Evidence (ME) form, CDS participants were similar with respect to gender, race/ethnicity, and treatment modality (hemodialysis/peritoneal dialysis) to all incident dialysis patients who began treatment during the same period, but were more likely to be younger than 65. Participants also appeared to have higher educational status than patients who participated in the USRDS DMMS Wave 2 study. In a phone interview, CDS participants were asked “Are you now working for pay (receiving taxable wages)?” Twelve percent answered affirmatively — slightly higher than the 10.7 percent of patients starting dialysis in 2005–2007 and reported by dialysis staff as employed on the ME form, possibly reflecting younger age and higher educational status among CDS participants than the overall incident dialysis population. The CDS employment rate of 12 percent must be interpreted in relation to the study population denominator: patients age 19–94 who started dialysis in 2005–2007. Employment rates are likely to be higher when the study population is restricted to younger patients. National data from the 2004 ESRD Facility Survey File, for example, indicated that 18.9 percent of prevalent dialysis patients age 18–54 were employed. Two-thirds of CDS patients who reported that they were working were insured by an employer group health plan (EGHP). If a patient is covered by an EGHP through his or her own employment or a family member’s current employment, the plan remains the primary payor for the first 30 months of ESRD treatment, with Medicare the secondary payor. After 30 months of eligibility or Medicare entitlement, Medicare becomes the primary payor, and the group health plan the secondary payor.

Job characteristics of patients who report being employed in the first year of dialysis

Of CDS participants, 7.2 percent reported working full-time and 4.8 percent part-time. A smaller proportion — 1.9 percent — of all incident patients in 2005–2007 were listed on the ME form as being employed part-time. It is possible that staff who complete the form may not be aware of patients’ part-time employment. CDS patients employed part-time were significantly older and were more likely to have COPD than patients employed full-time. The two groups did not, however, differ significantly in education level, number of cardiovascular conditions, hemoglobin level, or albumin level. Participants who reported employment were asked what kind of work they were doing, and the jobs listed were classified into occupational status categories ranging from 1 (high) to 7 (low) using the Hollingshead scale (a modification of the Edwards-Census occupational classification scheme). Table 9.b shows the distribution of CDS patients’ jobs using the Hollingshead occupational status categories. Mean (SD) occupational status was not significantly different for patients working full-time [3.8 (1.7)] and those working part-time [4.0 (1.8)].

Characteristics of patients who report not being employed

Chronic kidney failure requiring dialysis conveys entitlement to disability benefits, which can create a disincentive to gainful employment. This makes it difficult to estimate the extent of “true” inability to work among dialysis patients. Employment and receipt of disability income overlapped for some CDS participants. Among patients who reported working full-time, 5 percent received disability income, compared to 29 percent of those who reported working part-time.
government programs provide benefits based on disability: the Social Security Disability Insurance (SSDI) program and the Supplemental Security Income (SSI) program. Individuals are eligible to receive compensation for lost employment under SSDI if they are “insured” under the Social Security Act by virtue of the Social Security tax on their earnings, or if they are disabled dependents of insured individuals. Individuals are eligible for SSI payments if they are disabled and have limited income and resources; in most states these individuals are also automatically entitled to Medicaid. 

Of patients who reported not working, 9.8 percent said they were able to work (143/1,450). When compared to patients who were employed, these patients (not working but able to work) were significantly older, had a lower average educational level, and had a higher number of cardiovascular conditions. They were also more than twice as likely to be receiving disability income compared to patients who reported employment (37 versus 15 percent). Among all CDS participants, 44.2 percent were unemployed and receiving disability income (728/1,645). Compared to patients who were working and not receiving disability income (166/1,645 or 10 percent), unemployed disability income recipients had a significantly lower educational level, were significantly more likely to have diabetic ESRD and COPD, had a higher number of cardiovascular conditions, and had significantly lower hemoglobin and albumin levels. They did not differ in age from patients who were working, however, and 7.3 percent of unemployed disability income recipients said that they considered themselves able to work (53/728).

### Physical activity status & work status

The Human Activity Profile (HAP) is an instrument that assesses participation in 94 common activities with a known average energy expenditure requirement. The Adjusted Activity Score from the HAP provides an estimate of a person’s normal daily energy expenditure, after subtracting activities the person has stopped doing. The higher the Adjusted Activity Score, the greater the range of activities an individual performs; the lower the score, the greater an individual’s impairment. The possible score range is 1–94. As shown in Table 9.c, the average Adjusted Activity Score was significantly different in all of the employment status comparisons among CDS participants. Participants who reported that they were “able to work” had significantly higher scores than those who said that they were not able to work. These scores, therefore, may provide a useful marker of “true” ability or inability to work.
A major goal of the nutrition substudy of the Comprehensive Dialysis Study (CDS) was to measure markers of nutritional status and inflammation among participants who also completed the Patient Questionnaire, in which they were asked about their health-related quality of life, physical functioning, and participation in physical activity, as well as about the symptoms and burden of kidney disease. These data could then be linked to information from the Medical Evidence form (2728) to obtain additional information about body size and comorbidity at the initiation of dialysis, creating a rich dataset in which to explore relationships among physical activity, physical functioning, nutritional status, and inflammation. The Patient Questionnaire, including all items of the Human Activity Profile (HAP), was completed by 1,628 CDS participants. Three hundred sixty-one patients from 68 dialysis units participated in the nutrition substudy. Serum samples were obtained for 269 (76 percent) of these individuals, and were assayed for nutritional and inflammatory markers, including albumin, prealbumin, C-reactive protein (CRP), and alpha-1 acid glycoprotein (AAG). This report highlights the univariate correlates of physical activity within the entire CDS cohort, and of nutritional and inflammatory status among nutrition substudy participants. We also examine the relationships among physical activity, nutritional status, and inflammation within the nutrition substudy cohort. Participants in the CDS had lower levels of physical activity than healthy individuals. Among CDS participants, physical activity was lower among women and older individuals, as has been observed in the general population. Dialysis-specific variables, such as modality and type of hemodialysis vascular access, were also related to the level of physical activity, with greater levels of activity among peritoneal dialysis patients and those with a permanent vascular access at dialysis initiation. Participants who were more physically active reported better physical functioning. Data on laboratory markers of nutritional status and inflammation show that serum albumin and prealbumin were somewhat lower among older participants, but CRP and AAG were not associated with age. Serum albumin and prealbumin were higher among men than women, while AAG was higher among women; CRP, in contrast, was not associated with gender. Only prealbumin was associated with dialysis modality, with higher levels among those initiating on peritoneal dialysis. Only albumin was higher among those initiating dialysis using a fistula compared to other access types. Albumin and prealbumin were both lower among patients with diabetes than those without this diagnosis, and were both higher among patients reporting better physical functioning. No marker was associated with body mass index. Demographic, clinical, and functional variables were, overall, more likely to be related to albumin or prealbumin and less likely to be associated with CRP or AAG, suggesting that these factors are more closely related to nutritional status than to inflammation. Data on the intersection of physical activity, nutritional status, and inflammation show that serum albumin and prealbumin were strongly associated with participation in physical activity, but there was no significant relationship with either CRP or AAG and physical activity, suggesting that the nutritional rather than the inflammatory component of albumin and prealbumin may be the dominant correlate of physical activity.
The Maximal Activity Score (MAS) and Adjusted Activity Score (AAS) of the Human Activity Profile (HAP) are lower among older CDS participants. Physical activity is not significantly different between white and non-white CDS participants, but is greater among men than women. Figs 9.14–16; see page 378 for analytical methods. Incident patients included in the Comprehensive Dialysis Study, 2005–2007.

Physical activity & patient demographics: CDS participants

- **Fig 9.14**: Association of age & physical activity
- **Fig 9.15**: Association of race & physical activity
- **Fig 9.16**: Association of gender & physical activity

Physical activity is higher among CDS patients initiating ESRD therapy on peritoneal dialysis than among those starting on hemodialysis, and also higher among patients initiating hemodialysis with a permanent vascular access than with a catheter. Physical activity is lower among patients with diabetes. Figs 9.17–19; see page 378 for analytical methods. Incident patients included in the Comprehensive Dialysis Study, 2005–2007.
Patients with higher self-reported physical functioning, as measured by the Physical Component Summary of the SF-12, have higher levels of physical activity. \(\text{Figure 9.20};\) see page 378 for analytical methods. Incident patients included in the CDS, 2005–2007.

Physical activity is highest among CDS participants with a body mass index (BMI) in the normal weight category, and lower among underweight and overweight participants. Physical activity is associated with serum albumin level, with greater participation in physical activity among participants who have a higher serum albumin concentration. \(\text{Figures 9.21–22};\) see page 378 for analytical methods. Incident patients included in the Comprehensive Dialysis Study, 2005–2007.

In the CDS nutrition substudy, albumin and prealbumin are lower among older participants; C-reactive protein (CRP), and alpha-1 acid glycoprotein (AAG) are not associated with age. None of the markers of nutritional status or inflammation varies significantly between white and non-white participants. Serum albumin and prealbumin are higher among men than women, CRP is not associated with gender, and AAG is higher among women.

In terms of clinical parameters, prealbumin is higher among patients starting ESRD therapy on peritoneal dialysis than among those initiating on hemodialysis; no other marker of nutritional status or inflammation is significantly related to dialysis modality. Serum albumin is higher among patients initiating hemodialysis with a fistula compared to those using a graft or catheter; there are no associations between access type and other markers of nutrition or inflammation. And while albumin and prealbumin are lower among participants with diabetes, CRP and AAG are not related to this diagnosis.

Patients with higher self-reported physical functioning, as measured by the Physical Component Summary (PCS) of the SF-12, have higher serum albumin and prealbumin levels. There is no significant association between physical functioning and CRP or AAG. And none of the laboratory markers of nutrition or inflammation are associated with body mass index. \(\text{Table 9.3};\) see page 378 for analytical methods. Incident patients included in the nutrition substudy of the Comprehensive Dialysis Study, 2005–2007.
For participants in the nutrition substudy of the CDS, physical activity is associated with both serum albumin level and serum prealbumin level, with greater participation in physical activity among participants with higher concentrations. CRP level is not significantly associated with physical activity in this cohort, nor is AAG level. \textbf{Figures 9.23–26}; see page 378 for analytical methods. Incident patients included in the nutrition substudy of the Comprehensive Dialysis Study, 2005–2007.
AGE is an important independent predictor of the risk of incident CVD, but is inversely related to the likelihood of cardiac intervention. • 9.5

WOMEN are less than HALF AS LIKELY as men to receive an ICD or CRT-D. • 9.1

Across cardiovascular diagnoses & procedures, SURVIVAL is greatest among transplant recipients, & lowest among those treated with peritoneal dialysis. • 9.11

The overall rate of ACUTE MYOCARDIAL INFARCTION has increased from 42 per 1,000 patient years in 1997 to 46 in 2007. • 9.7

Twelve percent of CDS participants reported that they were now WORKING for pay.

TWO-THIRDS of CDS patients who reported that they were working were insured by an EMPLOYER GROUP HEALTH PLAN.

Among CDS patients who reported working full-time, 5% received DISABILITY income, compared to 29% of those who reported working part-time.

More than 44% of CDS participants were UNEMPLOYED & receiving disability income.

Among CDS participants, PHYSICAL ACTIVITY was greater among those on peritoneal dialysis & those with a permanent access at initiation. • 9.17–18

In the CDS nutrition substudy, serum ALBUMIN & prealbumin were strongly associated with participation in physical activity. • 9.23–24