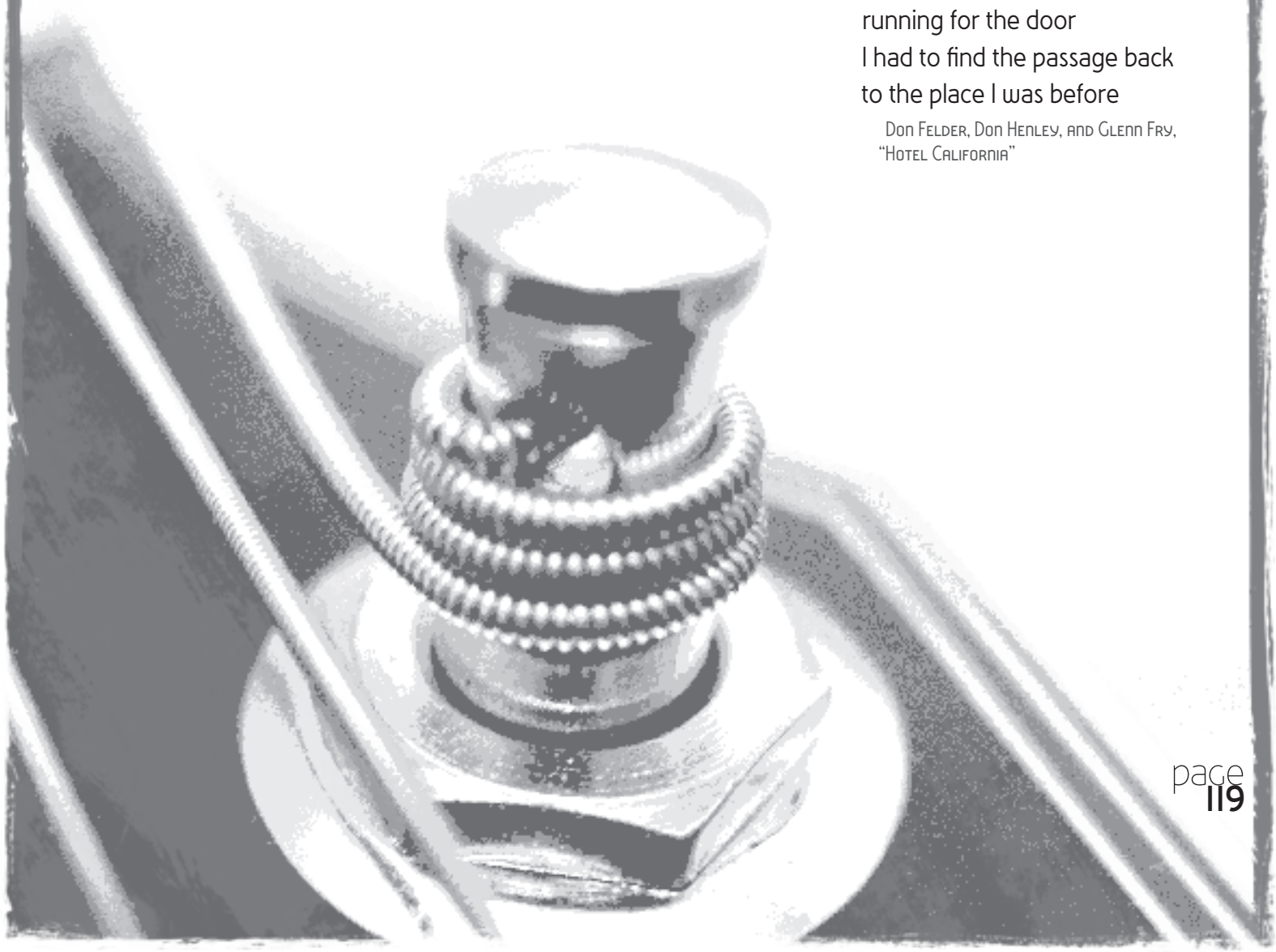
analytical methods: CKD

Last thing I remember I was
running for the door
I had to find the passage back
to the place I was before

Don Felder, Don Henley, and Glenn Fry,
"Hotel California"



In this appendix we describe the datasets and methods used for CKD analyses. Data management and preparation, database definitions, and the data sources used for ESRD analyses are described in the appendix of Volume Two.

data sources

The USRDS maintains a stand-alone database with data on diagnoses and demographic characteristics of CKD and ESRD patients, along with biochemical data, dialysis claims, and information on treatment and payor histories, hospitalization events, deaths, physician/supplier services, and providers.

CMS Medicare Enrollment Database

The Enrollment Database (EDB) of the Centers for Medicare and Medicaid Services (CMS) is the designated repository of all Medicare beneficiary enrollment and entitlement data, and provides current and historical information on residence, Medicare as secondary payor (MSP) and employer group health plan (EGHP) status, and Health Insurance Claim/Beneficiary Identification Code (HIC/BIC) cross-referencing.

ESRD Medical Evidence Form (CMS 2728)

The ESRD Medical Evidence (ME) form is the official form for registering ESRD patients, and must be submitted by dialysis or transplant providers within 45 days of ESRD initiation. The CMS, USRDS, and renal research communities rely on the ME form to ascertain basic patient demographic attributes, the primary cause of renal failure, major comorbidities, and biochemical test results at the time of ESRD initiation.

The third key revision of the ME form, released in May, 2005, was meant to remedy several shortcomings found in the 1995 form and its earlier version. Key additions target pre-ESRD care and vascular access use, and additional new fields collect information on glycosylated hemoglobin and lipid testing, on the frequency of hemodialysis sessions, and on whether patients are informed of transplant options.

ESRD Death Notification Form (CMS 2746)

The ESRD Death Notification form is used as the official form for reporting the death of individual patients with ESRD. According to CMS policy, this form must be submitted by dialysis or transplant providers within 30 days of a patient's death, and provides the date and causes of death (primary and secondary), reasons for discontinuation of renal replacement therapy, if applicable, and evidence of hospice care prior to death. It is the primary source of death information for CMS and the USRDS, identifying more than 99 percent of deaths. The USRDS also utilizes the Social Security Administration's (SSA) Death Master File as a supplemental data source for ascertaining death in a small group of lost-to-follow-up ESRD patients; this file, however, identifies only all-cause deaths.

CMS 5 Percent Standard Analytical Files (SAFs)

These files contain billing data from final action claims, submitted by Medicare beneficiaries, in which all adjustments have been resolved. The claims data are selected randomly from general Medicare claims (i.e. final action claims) using five combinations of the last two digits of the CMS Health Insurance Claims (HIC) number: 05, 20, 45, 70, and 95. Since the same two-digit numbers are used each year to create the 5 percent general Medicare SAFs, one should

expect to see the same beneficiaries in these annual datasets. These claims are categorized into the inpatient (IP), outpatient (OP), home health agency (HHA), hospice (HS), skilled nursing facility (SNF), physician/supplier (PB), and durable medical equipment (DME) SAFs.

Files are updated each quarter through June of the next year, when annual files are finalized. Datasets for the current year are created six months into the year and updated quarterly until finalized at 18 months, after which they are not updated to include late arriving claims. Annual files are thus approximately 98 percent complete. The USRDS 2011 ADR includes all claims up to December 31, 2009.

Medicare Current Beneficiary Survey (MCBS)

The MCBS is a longitudinal survey of a nationally representative sample of aged, disabled, and institutionalized Medicare beneficiaries. It contains information on the health status, health care use and expenditures, drug prescriptions, health insurance coverage, and socioeconomic and demographic characteristics of the entire spectrum of Medicare beneficiaries. Data are made available by CMS in two datasets: Access to Care (1992–2008), and Cost and Use (1992–2007), with the 2008 and 2007 files, respectively, the latest updates for the 2011 ADR.

In the fall of 1991, the MCBS began to be conducted three times per calendar year (winter, summer, and fall), and in 1994 a sample rotation scheme was introduced. Survey participants are kept in the sample for four years, with approximately one-third rolling off, and new participants added each fall to keep the overall sample size at approximately 12,000 each calendar year.

CMS Prescription Drug Event (PDE) File

In December 2003, Congress passed the Medicare Prescription Drug, Improvement, and Modernization Act (MMA), amending the Social Security Act by adding Part D under Title XVIII. With this new Part D coverage, health plans must submit a summary record called the prescription drug event (PDE) record to CMS whenever a Medicare beneficiary fills a prescription. The PDE record contains 37 data elements; the USRDS receives PDE records with 30 elements, excluding a few non-critical fields. Each drug is identified by a National Drug Index (NDC) code; the record also contains prescription dosing information, drug costs above and below the out-of-pocket threshold, other true out-of-pocket (TrOOP) amounts, plan paid amounts, and low-income cost-sharing subsidy amounts.

Due to delays in the availability of the data, only the 2006 and 2007 PDE files were available for the 2010 ADR. PDE data from 2008 are included in this 2011 ADR.

Thomson Reuters MarketScan Data

The Thomson Reuters MarketScan Commercial Claims and Encounters Database includes specific health services records for employees and their dependents in a selection of large employers, health plans, and government and public organizations. The database includes nine files: Annual Enrollment Summary Table, Enrollment Detail Table, Inpatient Admissions Table, Inpatient Services Table, Outpatient Services Table, Outpatient Pharmaceutical Claims Table, Facility (Inpatient and Outpatient) Header Table, Aggregated Populations Table, and the Red Book (prescription drug information by National Drug Code). The strength of this database lies in the quality of its cost information, where claims data include actual paid dollars and net payments by the insurer.

The MarketScan database links billing and encounter data to detailed patient demographic and enrollment information across sites and types of providers, and includes commercial health data from approximately 100 payors; about 80 percent of those covered are self-insured. Each year the database contains health data for about 10.5 million people. For details about the MarketScan data, please visit www.usrds.org.

Ingenix i3 Data

The Ingenix i3 database is a commercial, non-capitated health plan database covering employees from multiple employers within a single insurer. In addition to the usual service encounter and drug data, it also includes laboratory data, allowing for comparisons between claims-based and lab-based definitions of diseases. To protect the discount structure of its business, the billing data of this single insurer discloses only charged dollars without actual paid amounts or the portion paid by the insurer.

The Ingenix i3 database links billing and encounter data to detailed demographic and enrollment information of individual employees from 2000 to 2009, and contains health data for about 14 million people annually. For details about what is contained in the Ingenix i3 data, please visit our website at www.usrds.org.

National Health and Nutrition Examination Survey (NHANES)

NHANES is a series of health examination surveys conducted by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC). Begun in 1959, NHANES is designed to monitor the health and nutritional status of the non-institutionalized civilian population in the United States. NHANES III was conducted in two phases between 1988 and 1994. In 1999, NHANES became a continuous annual survey to allow annual estimates, with release of public-use data files every two years. Both NHANES III and NHANES 1999–2008 were nationally representative cross-sectional surveys and used a complex, stratified, multistage probability cluster sampling design that included selection of primary sampling units (counties), household segments within the counties, and sample persons from selected households. Survey participants were interviewed in their homes and/or received standardized medical examinations in mobile examination centers. Both surveys over-sampled African Americans, Mexican Americans, and individuals age 60 or older to improve the estimates for these subgroups.

Payors

Information on payors is obtained from the CMS EDB. We also examine Medicare outpatient claims to identify patients for whom the EDB does not indicate Medicare as primary payor (MPP), but who have at least three consecutive months of dialysis treatment covered by Medicare; these patients are also designated as having MPP coverage. From these two data sources we construct a payor sequence file to define payor history, and, starting with the 2003 ADR, we use this file to identify Medicare eligibility status and other payors.

The construction of this file is similar to that of the treatment history file. Payor status is maintained for each ESRD patient from the first ESRD service date until death or the end of the study period. Payor data are used to categorize a patient as MPP, Medicare as secondary payer (MSP) with EGHP, MSP non-EGHP, Medicare Advantage (Medicare + Choice), Medicaid, or a combination of payors. With this approach, the USRDS is now able to apply payor status information in all outcome analyses using the "as-treated" model (see the discussion of Chapter Eleven in Volume Two).

UNITED STATES CENSUS

In rate calculations throughout this year's ADR we use data from the 2000 U.S. Census, and incorporate CDC population estimates by race.

Database definitions

EGHP DATA

To examine the demographic segment represented by the EGHP data, we use enrollment information to construct yearly cohorts of enrollees younger than 65. To ensure that we select enrollees with the potential to generate claims evidence appropriate to the demands of analytical methods, rules for inclusion also include 12 months of continuous coverage in a commercial fee-for-service plan, and, for medication analyses, continuous prescription drug coverage. Comorbidities are identified using claims. Patients with at least one inpatient claim or at least two outpatient claims during the period of interest and with a diagnosis code of a particular comorbidity are identified as having that comorbidity.

ESRD COHORT IN THE EGHP POPULATION

Because the MarketScan and Ingenix i3 databases do not provide identifiable data elements, we are unable to link them directly to the USRDS ESRD registry. To identify ESRD patients, we therefore use a process similar to that used in the registry. Transplant patients are identified by evidence of a kidney transplant procedure or an adverse graft event, and chronic dialysis patients by evidence of continuous history of dialysis therapy, with at least three consecutive months of dialysis service and with dialysis service claims in at least 70 percent of treatment months. Treatment months are defined by the period from the first dialysis claim to the earliest of kidney transplant, death, or end of enrollment. Both inpatient and outpatient claims are evaluated for evidence of dialysis service history.

The first ESRD service date is set to the earliest of the first dialysis service date or the transplant date. If neither is available, the start of enrollment is used. Incidence is defined by a first ESRD service date at least 60 days after the start of enrollment.

Identification of major comorbidities

According to a previously validated method for using Medicare claims to identify diabetic patients, a patient is diabetic if, within a one-year observation period, he or she has a qualifying ICD-9-CM diagnosis code of diabetes on one or more Part A institutional claims (inpatient, skilled nursing facility, or home health agency), or two or more institutional outpatient claims and/or physician/supplier claims. We employ this method to identify major comorbidities: diabetes, 250.xx, 357.2, 362.0x, and 366.41; hypertension, 362.11, 401.x–405.x, 437.2; CKD, 016.0, 095.4, 189.0, 189.9, 223.0, 236.91, 250.4, 271.4, 274.1, 283.11, 403.x1, 403.x0 (after October 1, 2006), 404.x2, 404.x3, 404.x0 and 404.x1 (after October 1, 2006), 440.1, 442.1, 447.3, 572.4, 580–588, 591, 642.1, 646.2, 753.12–753.17, 753.19, 753.2, and 794.4; congestive heart failure, 398.91, 402.x1, 404.x3, 422.xx, 425.xx 428.xx, V42.1; and CVD (other than CHF), 404.x1, 410–414, 420–421, 423–424, 426–427, 429, 430–438, 440–444, 447, 451–453, 557, 785.0–785.3, V42.2, V43.3, V45.0, V45.81, V45.82, and V53.3.

CKD IN THE GENERAL POPULATION

CHAPTER ONE

DATABASE DESIGN, SETTING, & STUDY PARTICIPANTS

Surveys used here include NHANES 1999–2000, NHANES 2001–2002, NHANES 2003–2004, NHANES 2005–2006, and NHANES 2007–2008, limited to participants age 20 and older. The public use NHANES 1999–2004 Linked Mortality File provides mortality follow-up data from the date of survey through December 31, 2006. Study populations using these data are limited to participants age 20 and older, and the mortality follow-up month is greater than zero.

MEASUREMENTS

In this chapter age is defined as the participant's age at the time of the household interview, and grouped into ages 20–39, 40–59, and 60 and older. Race/ethnicity is defined as non-Hispanic white, non-Hispanic African American, and other.

Obesity is defined as a BMI of 30 kg/m^2 or above.

Participants with self-reported diabetes are those ever told by a doctor that they have diabetes or sugar diabetes (other than during pregnancy). In NHANES 2001–2008, participants answering "borderline" are classified as non-diabetic. Participants with self-reported congestive heart failure are those ever told by a doctor that they have congestive heart failure. And participants with self-reported cardiovascular disease are those with at least one of the following self-reported diseases: coronary heart disease, angina/angina pectoris, heart attack, congestive heart failure, or stroke.

Smokers are identified by an affirmative answer to the question: "Have you smoked at least 100 cigarettes during your entire life?" then further classified by their answer to the question: "Do you smoke cigarettes now?" Those with affirmative answers are classified as smokers; others are defined as non-smokers.

Self-reported hypertension is identified by an affirmative answer to the question: "Have you ever been told by a doctor that you had hypertension, also called high blood pressure?"

Microalbuminuria is defined by the ratio of urinary albumin (mg/l) to urinary creatinine (mg/dl; ACR). Participants with a valid ACR are classified as having microalbuminuria if this value is not less than 30 mg/g. Based on an NCHS suggestion, urine creatinine value is adjusted to NHANES 2007–2008.

The glomerular filtration rate (eGFR; ml/min/1.73 m^2) is estimated by two methods. The first is the MDRD method, using the standardized creatinine value for NHANES 1999–2000, 2001–2002, 2003–2004, 2005–2006, and 2007–2008, separately, based on NCHS recommendations. The equation used to estimate the GFR is as follows (Levey et al.): estimated GFR = 175 * (standardized serum creatinine in mg/dl)**(-1.154) * age**(-0.203) * (0.742 if female) * (1.212 if African American).

Second is the CKD-EPI method, based on the standardized creatinine value for the NHANES cohorts, as listed above. The equation is as follows (Levey et al.): estimated GFR = 141 * min(Scr /κ, 1)**α * max(Scr/κ, 1)**(-1.209) * 0.993**age * 1.018 [if female] * 1.159 [if African American], where Scr is standardized serum creatinine in mg/dl, κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/ κ or 1, and max indicates the maximum of Scr/κ or 1.

CKD is defined as an eGFR less than 60 ml/min/1.73 m^2, or an eGFR of 60 or greater in the presence of microalbuminuria. CKD stages are defined as follows: Stage 5, eGFR < 15; Stage 4, 15 ≤ eGFR < 30; Stage 3, 30 ≤ eGFR < 60; Stage 2, ACR ≥ 30 and 60 ≤ eGFR ≤ 89; and Stage 1, ACR ≥ 30 and eGFR ≥ 90. These are the standard CKD definitions used in this chapter.

STATISTICAL ANALYSIS

To obtain national estimates of each statistic, the odds ratios, sampling weights, and survey design are implemented by SUDAAN (Research Triangle Institute, Research Triangle Park, NC). Standard

errors are estimated using the Taylor Series Linearization method for NHANES 1999–2008. GFR is estimated by the method indicated in the figure titles. CKD includes Stages 1–5; all other comorbidities are self-reported.

Table 1.b presents data on awareness, treatment, and control of various metabolic markers by eGFR and ACR categories. eGFR is estimated using both the MDRD and CKD-EPI formulas. Patients are classified as hypertensive if measured systolic blood pressure is ≥ 140 mmHg (≥ 130 mmHg for CKD or diabetic patients) or measured diastolic blood pressure is ≥ 90 mmHg (≥ 80 mmHg for CKD or diabetic patients), or if the patient self-reports currently taking a prescription to control hypertension. Patients are classified as being aware of hypertension if they report having been told they have high blood pressure, are classified as being treated for hypertension if they report currently taking a prescription to control hypertension, and are considered in control of hypertension if current blood pressure is < 140/< 90 (< 130/< 80 for CKD or diabetic patients).

Control of hyperlipidemia is assessed similarly. Hyperlipidemia is defined as a measured LDL cholesterol above the ATP III target range (≥ 160 mg/dl for patients with 0–1 risk factors, ≥ 130 mg/dl for patients with two or more risk factors, ≥ 100 mg/dl for patients with coronary heart disease (CHD) and CHD risk equivalents). CKD is classified as a CHD risk equivalent. Awareness of hyperlipidemia is assessed by self-report of being told by a doctor that blood cholesterol level is high, and a patient is classified as being treated for hyperlipidemia if he or she reports currently taking a cholesterol medication or dieting to control cholesterol. Control is defined as meeting the ATP III LDL target for the appropriate risk category.

Diabetic patients are identified by self-report, as described above. Control of diabetes is assessed as a glycohemoglobin (A1c) of < 7 percent, as recommended by the American Diabetes Association.

Identification and Care of Patients with CKD

CHAPTER TWO

Figure 2.1 illustrates the extent of point prevalent diabetes, cerebrovascular accident/transient ischemic attack, congestive heart failure, and CKD in the general Medicare population. Methods are the same as those described at the beginning of Chapter Six.

Table 2.a compares the characteristics of prevalent general Medicare, MarketScan, and Ingenix i3 CKD patients by age, gender, and comorbidity in 2009. Figure 2.2 and Table 2.b include prevalent non-ESRD Medicare patients age 65 and older, alive at the end of 2009, and prevalent MarketScan and Ingenix i3 patients age 20–64. Each comorbidity is defined by medical claims (one inpatient or two outpatient claims) during each calendar year.

Figures 2.3–5 illustrate the prevalence of CKD in the Medicare, MarketScan, and i3 populations. The 5 percent Medicare sample includes patients age 65 and older, without ESRD, and who survive throughout the cohort year with Medicare as primary payor (and are not enrolled in Medicare Advantage). The MarketScan and Ingenix cohorts are constructed in a similar fashion, but are restricted to patients age 20–64, enrolled in a fee-for-service plan, and without ESRD.

Figure 2.6 shows the cumulative probability of non-CKD patients receiving a first urinary microalbumin or creatinine measurement, or both measurements, by month 12 of the second year of each two-year period. The general Medicare population includes patients continuously enrolled in the Medicare inpatient/outpatient and physician/supplier program during the first year. Patients are excluded if they are younger than 20 at the beginning at the second year, are enrolled in a managed care program (HMO), acquire Medicare as secondary payor, die, are diagnosed with CKD or ESRD during the first year, have a missing date of birth, or do not live in the 50 states, the District of Columbia, Puerto Rico, or the Territories. Patients are followed from January 1 to December 31 of the second year. The Kaplan-Meier method is used to calculate the cumulative probability, and patients are censored at death, development of ESRD, and change in payor status.

CPT codes used to define urinary microalbumin measurement are 82042, 82043, 82044, and 84156, while codes for creatinine measurement are 80047, 80048, 80049, 80050, 80053, 80054, 80069, and 82565. Diabetes and hypertension are defined in the first year. Methods of defining CKD, diabetes, and hypertension are the same as those described above in the section on identification of major comorbidities.

Table 2.c shows unadjusted and adjusted cumulative probabilities of non-CKD patients receiving a first urinary microalbumin or creatinine measurement, or both measurements, by month 12 of 2009. The cohort is the same as that described for 2008–2009 in Figure 2.6. Cardiovascular disease is defined as any combination of ASHD, CHF, CVD, PVD, dysrhythmia, or other cardiovascular disease, as described in the section on identification of major comorbidities. The Kaplan-Meier method is used to calculate the unadjusted cumulative probability, and the corrected groups prognosis methodology is used to calculate the adjusted cumulative probability for each patient characteristic category.

The Medicare and MarketScan columns of Tables 2.d–e include patients who are alive with full coverage for all of 2009. The CKD diagnosis code (all or 585.3–585.6), as well as the disease burden, are determined from claims in 2009. NHANES 2001–2008 data for those age 20 and older are also used in these tables, with CKD determined from the eGFR, estimated by the MDRD method. Table 2.f and Figures 2.7–9 reflect the results of adjusted logistic regression on the Medicare and MarketScan cohorts from Tables 2.d–e.

Figures 2.10–13 and Tables 2.g–i include patients who are alive with full coverage for all of 2008, to allow for up to one year of follow-up for physician claims. The date on the earliest CKD claim (all or 585.3–585.6) of 2008 is used as the date of CKD diagnosis, and physician claims are searched for 365 days following that date. The cumulative probability in Figure 2.10 represents unadjusted Kaplan-Meier estimates, while in Tables 2.g–h the adjusted cumulative probability is obtained from the corrected group prognosis method, implementing proportional hazards regression. Adjusted hazard ratios in Table 2.i and Figures 2.11–13 are obtained from proportional hazards regression.

Figures 2.14–21 include CKD patients in the 2007 entry period, and show the cumulative probability of medication use during the twelve-month study period in 2008. The study cohort includes MarketScan patients (age 20–64) and patients from the Medicare 5 percent sample (age 65 and above); MarketScan patients have fee-for-service coverage during the entry period and medical coverage and drug insurance during the study period. All comorbidities are defined by medical claims (one inpatient or two outpatient) during the entry period.

Morbidity and Mortality in Patients with CKD

CHAPTER THREE

HOSPITALIZATION

Adjusted admission rates in this chapter include adjustment for baseline comorbidities and prior hospitalization in addition to patient demographics.

A model-based adjustment method is used with a Poisson assumption, and includes data from the current and previous two years, with respective weights of 1, ¼, and ⅛. Adjusted rates reflect the distribution of a reference cohort, specified below in the discussion of the respective figures. With this method, the parameter estimates from the model are used to calculate an estimated admission rate for each patient in the reference cohort. Adjusted rates are then computed as the weighted average of these individual rates, using as the weight the time at risk of each patient in the reference cohort.

Figure 3.1 compares all-cause hospital admission rates for CKD and non-CKD patients in prevalent Medicare and MarketScan cohorts. The study design consists of a one-year period during which CKD, comorbidities, and prior hospitalization are defined from claims, followed by the cohort year when follow-up for admissions begins on January 1. The Medicare cohort includes patients who are age 66 and older on December 31 of the prior year, are residents of the 50 states, the District of Columbia, Puerto Rico, or the Territories, are continuously enrolled in Medicare inpatient/outpatient and physician/supplier coverage, are without HMO coverage, are without ESRD, and who survive the complete year prior to follow-up. The MarketScan cohort includes patients age 50–64 on December 31 of the prior year who remain without ESRD and enrolled in a fee-for-service commercial health plan during the prior year. Patients are followed for admissions from January 1 of the follow-up year, and are censored at ESRD initiation, end of plan coverage, or December 31; Medicare patients are also censored at death. Rates are adjusted for gender, prior hospitalization, diabetes, COPD, hypertension, liver disease, gastrointestinal disease, cancer, anemia, peripheral vascular disease, CVA/TIA, atherosclerotic heart disease, congestive heart failure, dysrhythmia, and other cardiac disease. The reference cohort includes Medicare patients in 2005, age 66 and older.

Table 3.a and Figures 3.2–3 show adjusted all-cause admission rates in Medicare patients age 66 and older. Study design, censoring, and inclusion criteria generally follow those described for the Medicare cohort in Figure 3.1. Groups for diabetes and cardiovascular disease are mutually exclusive. Follow-up for hospital admissions starts on January 1, 2009, with the model-based adjustment method described above. Adjustment factors include age, gender, race, prior hospitalization, COPD, hypertension, liver disease, gastrointestinal disease, cancer, and anemia, and with diabetes and cardiovascular disease combinations rather than as separate factors. Rates presented by one factor are adjusted for the others. The reference cohort includes Medicare patients in 2009, age 66 and older.

Figures 3.4–7 show adjusted all-cause and cause-specific admission rates by CKD diagnosis code and dataset. Again, study design, censoring, and inclusion criteria generally follow the description for the Medicare and MarketScan cohorts in Figure 3.1. Additionally, Ingenix i3 data include point prevalent patients on January 1, 2009, continuously enrolled in a fee-for-service or commercial health plan and without ESRD during 2008, and age 50–64 on December 31, 2008. The group labeled "CKD" includes those with claims-based evidence of CKD in 2008, while "non-CKD" is defined as patients without claims-based evidence of CKD. Rates are adjusted for the same factors listed for Figure 3.1. Cause-specific rates reflect hospital admissions for the purpose of the stated condition, and are identified by the principal ICD-9-CM diagnosis codes for cardiovascular and infectious admissions listed in the description of Figure 3.1 in Volume Two. The reference cohort includes Medicare patients in 2009, age 66 and older.

Figure 3.8 and Table 3.b show rates of infectious admissions by major organ system and CKD stage. Rates include Medicare patients in 2009, age 66 and older. Methods again follow those described for Medicare patients in Figure 3.1. Rates are adjusted for age, gender, race, prior hospitalization, diabetes, COPD, hypertension, liver disease, gastrointestinal disease, cancer, anemia, peripheral vascular disease, CVA/TIA, atherosclerotic heart disease, congestive heart failure, dysrhythmia, and other cardiac disease. The reference cohort includes Medicare patients in 2009, age 66 and older. Major organ systems are defined by principal ICD-9-CM diagnosis codes listed for Figure 3.6 and Table 3.c in Volume Two. The "other" infection group here includes nervous and cardiac infections in addition to infections other than those of the organ system groups shown in 3.8 and 3.b. In Table 3.b, rates presented by one factor are adjusted for the others.

MORTALITY

Figure 3.9 illustrates trends, by CKD status, in unadjusted and adjusted all-cause mortality. The study cohort for 1995 includes point prevalent Medicare patients on January 1, 1995, age 66 or older. CKD status is identified from 1994 Medicare claims, and the cohort excludes patients enrolled in an HMO, with Medicare as secondary payor, or diagnosed with ESRD in 1994. Follow-up extends from January 1, 1995, to December 31, 1995, and is censored at ESRD and the end of Medicare entitlement. Patients not living in the 50 states or the District of Columbia are excluded. Cohorts for 1996–2009 are constructed in a similar manner. Adjusted mortality is based on a Cox regression model and adjusted for demographics, hospitalization in the prior year, and comorbidities and sources of comorbidities defined in the prior year. Medicare patients from 2005 are used as the reference cohort.

For Figures 3.10–12 and Table 3.c, the cohort definitions are same as those defined in Figure 3.9. Adjusted mortality is based on a Cox regression model; rates by age are adjusted for gender, race, and comorbidities; rates by gender are adjusted for age, race, and comorbidities; and rates by race are adjusted for age, gender, and comorbidities. All 2009 patients are used as the reference cohort.

CARDIOVASCULAR DISEASE IN PATIENTS WITH CKD

CHAPTER FOUR

Table 4.a describes the prevalence of cardiovascular disease and treatment in Medicare enrollees. Cardiovascular disease include acute myocardial infarction (AMI), atrial fibrillation (AF), cerebrovascular accident/transient ischemic attack (CVA/TIA), congestive heart failure (CHF), and peripheral arterial disease (PAD), while treatment include percutaneous coronary interventions (PCI), coronary artery bypass graft surgery (CABG), and use of implantable cardioverter defibrillators and cardiac resynchronization therapy with defibrillator (ICD/CRT-D). The study cohort includes point prevalent Medicare enrollees on December 31, 2009 who are age 66 and older, residing in the 50 states, the District of Columbia, Puerto Rico, or the Territories, continuously enrolled in Medicare inpatient/outpatient and physician/supplier coverage, and not enrolled in an HMO in 2009. Patients diagnosed with ESRD are excluded.

Patients with CKD are identified using the same methodology described above in the section on data sources (referred to in this chapter as the claims-based method). CKD stage is defined based on the fourth digit of ICD-9-CM diagnosis code 585.x. Using the claims-based method, we identify those with AMI, AF, CVA/TIA, or CHF in 2009. Various sources of claims and types of codes are used to identify cardiovascular treatments. CABG is

defined through ICD-9-CM procedure codes in inpatient claims only, ICD/CRT-D is defined through ICD-9-CM procedure codes in inpatient/outpatient claims, and PCI is identified through ICD-9-CM procedure codes in inpatient/outpatient claims or CPT codes in outpatient revenue claims or physician/supplier claims. PAD is defined through either diagnosis codes or procedure codes; if defined through diagnosis codes, we use the claims-based method; if defined through procedure codes, we employ the method used for PCI. The codes used to identify cardiovascular diseases and procedures are as follows:

- AF: 427.3 (ICD-9-CM diagnosis codes)
- AMI: 410 and 412 (ICD-9-CM diagnosis codes)
- CHF: 398.91, 422.xx, 425.x, 428.xx, 402.x1, 404.x1, 404.x3, and V42.1 (ICD-9-CM diagnosis codes)
- CVA/TIA: 430–438 (ICD-9-CM diagnosis codes)
- PAD: 440–444, 447, and 557 (ICD-9-CM diagnosis codes); 84.0, 84.1, 84.91, 39.25, 39.26, and 39.29 (ICD-9-CM procedure codes); 24900, 24920, 25900, 25905, 25920, 25927, 27295, 27590, 27591, 27592, 27598, 27880, 27881, 27882, 27888, 27889, 28800, 28805, 34900, 35131, 35132, 35141, 35142, 35151, 35152, 34051, 34151, 34201, 34203, 34800–34834, 35081–35103, 35331, 35341, 35351, 35355, 35361, 35363, 35371, 35372, 35381, 35450, 35452, 35454, 35456, 35459, 35470, 35471, 35472, 35473, 35474, 35480, 35481, 35482,35483, 35485, 35490, 35491, 35492, 35493, 35495, 35521, 35531, 35533, 35541, 35546, 35548, 35549, 35551, 35556, 35558, 35563, 35565, 35566, 35571, 35583, 35585, 35587, 35621, 35623, 35646, 35647, 35651, 35654, 35656, 35661, 35663, 35665, 35666, and 35671 (CPT codes)
- CABG surgery: 36.1x (ICD-9-CM procedure codes)
- PCI: 00.66, 36.01, 36.02, 36.05, 36.06, and 36.07 (ICD-9-CM procedure codes); 92980–92982, 92984, 92995–92996, G0290, and G0291 (CPT/HCPCS codes)
- ICD/CRT-D: 37.94 and 00.51 (ICD-9-CM procedure codes)

The overall prevalence and age-, gender-, and race-specific prevalence of each cardiovascular disease and treatment in 2009 is calculated for patients with CKD (by CKD stage) and without CKD, respectively. Prevalence is represented per 100 patients.

Figure 4.1 presents the burden of prevalent AMI, CHF, and CVA/TIA in the Medicare CKD and non-CKD population with cardiovascular disease in 2009. Methods are the same as those described for Table 4.a.

Figures 4.2 and 4.5 illustrate geographic variations in the prevalence of CHF and CVA/TIA in 1999 and 2009. Methods are the same as those described for Table 4.a. The unadjusted prevalence of CHF and CVA/TIA is calculated for each HSA, and presented per 1,000 patients.

Figure 4.3 describes the percentage of patients with incident CHF receiving diagnostic testing at or up to 90 days after CHF diagnosis in 1999 and 2009. The cohort of incident CHF patients in 2009 includes point prevalent Medicare enrollees on January 1, 2009, with their first CHF diagnosis (index event) during 2009, continuously enrolled in Medicare inpatient/outpatient and physician/supplier coverage, not enrolled in an HMO during the one-year period before the index event, age 66 or older on the date of the index event, and residing in the 50 states, the District of Columbia, Puerto Rico, or the Territories. Patients with incident CHF are identified through ICD-9-CM diagnosis codes 398.91, 425.x, 428.xx, 402.x1, 404.x1, and 404.x3 using the claims-based method, and the index date is defined on the date of the first appearance of a claim with the qualifying diagnosis codes. The twelve-month period prior to the index event is the baseline period. Patients with CKD and pre-existing CHF are identified during the baseline period using the method described for Table 4.a. We exclude patients who are diagnosed with ESRD prior to the index event and those with pre-existing CHF. Follow-up for testing begins on the CHF diagnosis date and ends on the earliest of death, ESRD diagnosis, change of enrollment status, 90 days after CHF diagnosis, or December 31, 2009.

Diagnostic testing for patients with CHF includes resting echocardiogram, coronary angiography, or any stress test including stress echocardiograms, stress nuclear imaging, stress test, and stress electrocariograms (ECGs). Patients received these tests are identified through ICD-9-CM procedure codes in inpatient/outpatient claims or CPT/HCPCS codes in outpatient revenue claims or physician/supplier claims. Codes used to define these tests are as follows:

- resting echocardiogram: 93303, 93304, 93306–93308, 93312-93318, 93320, 93321, and 93325 (CPT codes)
- coronary angiography and/or catheterization: 37.22–37.23 and 88.53–88.57 (ICD-9-CM procedure codes); 93508, 93510, 93511, 93524, 93526, 93527, 93529, 93531–93533, 93539, 93540, 93543, 93545, and 93555 (CPT codes)
- stress echocardiograms: 93350 (CPT code)
- stress nuclear imaging: 78459–78461, 78464, 78465, 78469, 78472, 78473, 78478, 78480, 78481, 78483, 78491, and 78492 (CPT codes)
- stress test: 89.41–89.44 (ICD-9-CM procedure codes)
- stress ECGs: 93015–93018 (CPT codes)

The percentage of patients receiving each test is calculated as the number of patients tested during the follow-up period divided by the total number of patients at the beginning of follow-up. The same methods are used to obtain the percentage of patients with a first diagnosis of CHF in 1999 who received diagnostic testing at or up to 90 days after the diagnosis.

Figure 4.5 describes the percentage of patients first hospitalized for CVA/TIA and receiving diagnostic test at or up to 90 days after admission in 1999 and 2009. Methods are similar to those described for Figure 4.3, and the codes used to define a CVA/TIA event are 430–437.

Diagnostic testing for patients with CVA/TIA include transesphogeal echo (TEE), transthoracic echo (TTE), vascular ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), non-invasive angiography, and invasive angiography. Patients receiving these tests are identified through ICD-9-CM procedure codes in inpatient/outpatient claims or CPT codes in outpatient revenue claims or physician/supplier claims. Codes used to define these tests are as follows:

- TEE: 93312–93318 (CPT codes)
- TTE: 93303, 93304, and 93306–93308 (CPT codes)
- vascular ultrasound: 93875, 93880, 93882, 93886, 93888, 93890, 93892, and 93893 (CPT codes)
- CT or MRI: 70450, 70460, 70470, and 70551–70555 (CPT codes)
- non-invasive angiography: 70496, 70498, 70541, and 70544–70549 (CPT codes)
- invasive angiography: 88.41 (ICD-9-CM procedure code); 75660, 75662, 75665, 75671, 75676, 75680, and 75685 (CPT codes)

Table 4.b and Figures 4.6–11 include Medicare enrollees with a CVD event (as described for Table 4.a) between January 1, 2008, and November 30, 2008, discharged within two weeks of the date

of the index event (if the enrollee was hospitalized at the time of the event), remaining outside the hospital at one month after the date of the index event, and carrying continuous Medicare Part D coverage during the interval from one month before to one month after the date of the index event; use of a particular drug is defined by at least one fill of a prescription for the drug during this interval. Drugs are identified from National Drug Codes included on Part D claims, and linked with the 2010 edition of the MediSpan Master Drug Data Base. For each of the CVD events, a study cohort is constructed based on the 2007–2008 Medicare claims, using the same method described for Figure 4.3. With the exception of AMI, data sources and methods used to define each event are the same as those described for Table 4.a; the AMI event is defined as the first appearance of the diagnosis code on an inpatient claim. The same codes described for Table 4.a are used to identify AF, PAD, PCI, CABG, and ICD/CRTD, while different codes are used to identify patients with first diagnosis of AMI, CHF, and CVA/TIA:

- AMI: 410, 410.x0, and 410.x1 (ICD-9-CM diagnosis codes)
- CHF: 398.91, 425.x, 428.xx, 402.x1, 404.x1, and 404.x3 (ICD-9-CM diagnosis codes)
- CVA/TIA: 430–437 (ICD-9-CM diagnosis codes)

Figure 4.6 illustrates geographic variations in prescription drug use in Medicare CKD and non-CKD patients with a first diagnosis for CHF in 2008. Methods for cohort construction and identification of prescription drug use are those used in Table 4.b. CHF medications include angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, beta blockers, digoxin, and spironolactone.

Prescription Drug Coverage in CKD Patients

CHAPTER FIVE

In figures and tables regarding enrollment and utilization of Medicare Part D, we analyze cohorts of Medicare enrollees in 2006, 2007, and 2008 without chronic kidney disease (CKD), with non-dialysis-dependent CKD, receiving dialysis, or with a functioning kidney transplant. For enrollees without CKD or with non-dialysis-dependent CKD, we require continuous enrollment in Medicare Parts A and B during the previous calendar year, no participation in Medicare Advantage during the previous year, and Medicare enrollment in January of the index year. CKD is identified from diagnosis codes on claims during the previous calendar year. For the dialysis and kidney transplant cohorts we retain all patients who were alive and enrolled in Medicare on January 1 of the index year and whose ESRD onset was at least 90 days earlier; treatment modality is identified on January 1.

In Figure 5.1, diagnoses of hypertension, cardiovascular disease (arrhythmia, cerebrovascular disease, congestive heart failure, ischemic heart disease, peripheral vascular disease, or valvular disease), and diabetes are ascertained from claims during 2007. Here, and in Figures 5.2–4, type of prescription drug coverage is defined sequentially. That is, we first classify patients as "Part D with LIS" if there exists at least one calendar month in 2008 with Part D enrollment and receipt of low-income subsidy (LIS). In patients without one such month, we classify remaining patients as "Part D without LIS" if there exists at least one calendar month with Part D enrollment. In patients without one such month, we classify remaining patients as "retiree drug subsidy" if there exists at least one calendar month with employer receipt of the subsidy. In patients without one such month, we classify remaining patients as "other creditable coverage" if there exists at least one calendar month with enrollment in military, government employee, or employer group health plans.

In Figures 5.6–7 and Table 5.a, we classify Part D enrollees as LIS recipients if there exists at least one calendar month in 2008 with LIS receipt. In Figures 5.8–10, we consider only those Part D enrollees who were not LIS recipients during any calendar month of the index year. In all figures, patients enrolled in Medicare Advantage Part D (MA-PD) plans are excluded.

In Figures 5.15–17 and Tables 5.c–d, we consider only those Part D enrollees who were not LIS recipients during any calendar month of 2008. In all figures, patients enrolled in employer group waiver plans or national Programs of All-inclusive Care for the Elderly (PACE) are excluded, as these types of plans do not report data concerning coverage phase progression of enrollees. In Figure 5.16, follow-up begins on January 1, 2008, and in Figure 5.17, follow-up begins on the date of entry into the coverage gap. In Table 5.c, diagnoses of hypertension, cardiovascular disease, diabetes, and cancer are ascertained from claims during 2007. In the final analysis in Table 5.c, regarding the association of fills per month in 2007 with probability of entry into the coverage gap in 2008, we necessarily limit analysis to the subset of patients enrolled in Part D in 2007. Here and in Table 5.d, a fill is simply defined as a transaction billed to Part D.

Part D costs for several different populations are presented in this chapter. The general Medicare population includes all Part D enrollees (estimated from the 5 percent Medicare sample), while the CKD population includes only persons who survive all of year one, are continuously enrolled in Medicare inpatient/outpatient and physician/supplier coverage for this period, are not enrolled in an HMO, and have a qualifying CKD diagnosis (but do not have ESRD) during year one; this cohort is also drawn from the 5 percent Medicare sample. CKD stage is defined from claims. Costs are aggregated for year two for all Part D enrollees with CKD, with censoring at the earliest of death, development of ESRD, or the end of year two. The general Medicare population used in Figure 5.14 is constructed in the same fashion as the CKD population (without the requirement of CKD diagnosis) to ensure the presence of Part A and B claims. The ESRD population (Figure 5.11) and dialysis populations (Figure 5.13) are drawn from the 100 percent ESRD population. ESRD includes all ESRD patients enrolled in Part D, while the dialysis population includes only those individuals who are enrolled in Part D and on dialysis during the year of interest.

Costs are presented as total Part D expenditures, which are estimated as the sum of the Medicare covered amount and the low income subsidy (LIS) amount (Figure 5.11 and Tables 5.e–g), or as per person per year expenditures (Figures 5.12–14, 5.19, and 5.21), also estimated as above. Figure 5.12 also presents out-of-pocket expenditures obtained from the prescription drug event record.

Tables 5.e–g show the top Part D drugs by frequency, as judged from the total days supply (obtained from the prescription drug event record), as well as by cost. Figures 5.18 (general Medicare) and 5.20 (CKD) show the frequency of prescriptions for Part D drugs, by generic name and cumulative frequency, while the parallel figures (5.19 and 5.22) present cumulative costs.

Costs of CKD

CHAPTER SIX

The general Medicare point prevalent cohort used in Figures 6.1–8 includes persons age 65 and older who survive all of year one, are continuously enrolled in Medicare inpatient/outpatient and

physician/supplier coverage for this period, are not enrolled in an HMO, and do not have ESRD during year one. Costs are aggregated for year two, with censoring at the earliest of death, development of ESRD, change in payor status, or the end of year two. Figure 6.2 also features the MarketScan point prevalent CKD population, constructed in a similar fashion, but limited to patients age 50–64.

Costs are categorized in several ways throughout this chapter. For Figures 6.1 and 6.5–7, costs are simply total claims-based expenditures, while those in 6.2–4 are claims-based expenditures on a per person per year (PPPY) basis. Figure 6.8 and Table 6.a display costs as per person per month (PPPM) claims-based totals. Costs are further broken down for Table 6.a, using diagnosis-related groupings (DRGs) for inpatient claims; revenue codes, current procedural terminology (CPT) codes, and healthcare common procedure coding system (HCPCS) codes for outpatient claims; and CPT, HCPCS, provider specialty, and place of service codes for physician/supplier claims.

Important comorbidities (diabetes, CKD, and CHF) are determined for these cohorts from Medicare claims using a previously validated method, as described earlier in the section on identification of major comorbidities. Costs in Figures 6.5–8 are presented for the 1992–2008 cohorts; the cost year is always the year after the cohort year.

The MarketScan population used in Figure 6.2 includes patients age 50–64, and is constructed in the same fashion as that described for the Medicare population, requiring continuous enrollment in a fee-for-service health plan. Patients identified as having ESRD are excluded, and the cohorts are from 2006–2008 (cost years 2007–2009).

Figures 6.9–22 and Table 6.b present Medicare Part D costs. Populations used in these figures are derived from the point prevalent Medicare population (described above), with the further restriction that each individual included in the population is enrolled in Part D for the full 12 months of the analysis year (Figures 6.9–11). Table 6.b and Figures 6.12–22 also require a qualifying diagnosis of CKD. Costs are estimated Medicare net pay, which is the sum of plan covered payments and low income subsidy payments. Costs do not include out-of-pocket expenditures. Table 6.b and Figures 6.12–14 show total Part D expenditures, while other figures use PPPY expenditures.

Reference Tables: CKD

Tables B.1–6 present estimated point prevalent (December 31) counts of the general Medicare non-ESRD population, based on the 5 percent Medicare sample.

Tables K.1–5 present estimates of per person per year costs for general Medicare patients, also derived from the 5 percent Medicare sample. The cohorts include those who survive all of year one, are continuously enrolled with Medicare inpatient/outpatient and physician/supplier coverage, are not enrolled in Medicare Advantage, and do not have ESRD during year one. Costs are aggregated for year two, with censoring at the earliest of death, development of ESRD, change in payor status, or the end of year two. Important comorbidities are determined for these cohorts from Medicare claims using a previously validated method, as described earlier in the section on identification of major comorbidities. Expenditures are presented for the 1992–2008 cohorts, and the cost year is always the calendar year after the cohort year.