Supplemental Material: Complete Methods

Data Source

Data were extracted from the United States Renal Data System (USRDS), a national data system funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the Center for Medicare & Medicaid Services (CMS) to collect data on ESRD in the U.S.[18] The USRDS contains detailed demographic and treatment information including date of dialysis initiation for all patients beginning renal replacement therapy. All Medicare Part A and B claims are also included within the USRDS dataset, including diagnosis and procedure codes for inpatient and outpatient visits. Institutional claims within Medicare Part A comprise all hospital inpatient, hospital-based outpatient, skilled nursing facility, home health agency, and hospice claims. Hospitalization data includes admission source, length of stay (LOS), discharge destination, and associated diagnoses and procedures for each patient. Medicare Part B Physician/Supplier claims include durable medical equipment charges along with physician and other outpatient healthcare provider services (e.g., office-based outpatient visits).

Identification of Fractures

Fractures were identified using International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) codes indicating fractures in any one of seven region-specific categories:

ICD-9 codes to identify fractures by site

Fracture Category	**ICD-9-CM Codes**
Vertebral	733.13, 805.xx, 806.xx

Pelvis/Hip	733.14, 808.xx, 820.xx
Femur	733.15, 821.xx
Lower Leg	733.16, 822.x, 823.xx, 824.xx
Ribs/Sternum	807.0x-807.1x, 807.2-807.3
Shoulder/Upper Arm	733.11, 810.xx, 811.xx, 812.xx
Forearm/Wrist	813.xx, 814.xx

This classification excluded fractures of the hands and feet (due to minimal consequences of these fractures), fractures of multiple areas and of the skull/trunk (likely indicative of severe or blunt trauma), and ill-defined, unspecified factures. Inpatient or outpatient fracture codes were identified in any diagnosis field.

Calculation of Unadjusted and Adjusted Fracture Incidence Rates

The study cohort consisted of incident and prevalent, in-center hemodialysis patients who received dialysis services between January 1, 2000 and December 31, 2009. Incident patients became eligible 90 days after their first service date to ensure stability in dialysis modality and to allow sufficient time for processing Medicare eligibility forms. Patients were required to be at least 18 years or older, have no history of renal transplant and have Medicare as a primary payer for the duration of the follow-up period.

Patients were at risk for a given fracture type until the time of the first identified inpatient or outpatient fracture of that type. The same patient, therefore, could contribute to more than one fracture rate. Patients were censored if one of the following events occurred: 1) death, 2) kidney

transplantation, 3) Medicare was no longer the primary payer, or 4) switch to peritoneal dialysis; and were administratively censored on the last date of available data up to December 31, 2009.

For each specific fracture type and overall, unadjusted quarterly incidence rates of fracture were estimated by dividing the total number of observed fractures during the quarter by the total patient time at risk (Supplemental Figure S1). Rates, expressed as fractures per 1000 patients per year, were calculated -overall and within strata of patient characteristics. Results were stratified by age (18-44, 45-64, 65-74 and ≥ 75 years old), sex, and race (white *versus* non-white), cause of ESRD, and years on dialysis.

We examined both inpatient and outpatient claims for fracture diagnoses in any field. To mitigate the likelihood of mistakenly classifying a "rule-out" fracture diagnosis in the outpatient setting as an actual fracture occurrence, patients were required to have at least two outpatient fracture diagnosis codes within a 28-day span. Only the first occurrence (inpatient or outpatient) of a particular fracture type (i.e., bone or joint area) contributed to the fracture incidence rate analyses. Patients were then no longer eligible to contribute data on that fracture type, but could contribute to other types of fracture.

To derive fracture rates adjusted for secular trends, we computed a standardized mortality ratio (SMR)-weighted model with a weight of 1 for patients hospitalized for a fracture in Q1 of 2000(the comparator group) and a weight of (p/[1-p]) for patients hospitalized for a fracture in all other quarters (Q2 of 2000-Q4 of 2009). Here, p represented the probability that the patient was hospitalized for a fracture in Q1 of 2000 given a combination of covariates used for adjustment. All trend lines were adjusted for age, race, sex, cause of ESRD, and years on dialysis.

All trend lines were adjusted for age, race, sex, cause of ESRD, and years on dialysis. Rates, expressed as fractures per 1000 patient-years (PYs), were calculated overall and within strata of patient characteristics (age, sex, race, cause of ESRD, and years on dialysis). Sensitivity analyses were conducted to examine adjusted fracture rates over time by diabetes status and results from these analyses can be found in Supplemental Figure S2.

Ascertainment of Post-Discharge Outcomes

We examined post-fracture outcomes for inpatient fractures only. Hemodialysis patients within the USRDS data set between January 1, 2000 and December 31, 2009 who were hospitalized during the study period were required to have survived at least 270 days post the initiation of dialysis therapy (90 days post the initiation of dialysis to allow for stability in Medicare claims processing and 180 days to allow for a 6 month baseline period). Patients whose first hospitalization during the period was for a fracture event formed the fracture cohort while patients whose first hospitalization for any reason other than fracture served as the comparator group. Demographic and clinical characteristics of both groups over time are described in Supplemental Table S1. The 180-day period immediately preceding the index hospitalization was used to identify comorbidities.

The following outcomes associated with the index inpatient admission for fracture were examined: median LOS and discharge destination (including death). For each index hospitalization, median hospital LOS was defined as the time in days from the date of hospital admission for fracture to the date of discharge or mortality (for patients who were discharged dead). The LOS was counted as one day if a patient was hospitalized and discharged on the same day or the day after admission. Hospitalizations on the same day, for the same patient, or a

hospitalization on the day subsequent to discharge from a short-term hospital were considered one contiguous hospitalization.

Discharge destination was reported as the percent of patients who either died in the hospital or were released/transferred to one of the following specified destinations post-fracture hospitalization: skilled nursing facility (SNF), other post-acute care facility (i.e., inpatient rehabilitation facility, swing bed, long term care), home or other. The table below describes the CMS discharge codes used to identify patients in each discharge destination category.

Discharge status codes comprising discharge destination categories

Discharge destination	CMS discharge status codes
Died	20, 41, 42
SNF	03
Post-acute care	61, 62, 63
Home	01, 06, 06, 71, 72
Other	All remaining CMS discharge codes

Patients hospitalized for an inpatient fracture who survived their inpatient stay were followed for one year following discharge to assess post-discharge outcomes. For all outcomes other than mortality, patients were censored if one of the following events occurred: 1) death, 2) kidney transplantation, 3) Medicare was no longer the primary payer, or 4) switch to peritoneal dialysis; and were administratively censored on the last date of available data up to December 31, 2009.

For those who survived and were discharged, we estimated both crude and adjusted rates of mortality, hospitalization and SNF admission during the 1-year following hospital discharge. Crude and adjusted mean hospital days/median SNF days during the follow-up year were also measured. To determine time at risk for our outcomes, we used the approach described in the USRDS Annual Data Report.[18] A patient's hospital days and SNF days were included in the time at risk for these measures given that patients institutionalized in a SNF or hospital were still at risk for additional days in each respective setting. A patient in a SNF or hospital during the observation period was not at risk for a new admission in that setting. Therefore, time at risk when calculating hospitalizations and SNF admission rates did not include a patient's hospital days or SNF days. No days were subtracted from the time at risk when a patient was discharged on the same day he or she was admitted. Hospitalizations and SNF admission rates were defined as the number of inpatient hospitalizations or SNF admissions per PY, respectively, occurring subsequent to discharge from the index fracture hospitalization event.

Unadjusted mean/median hospital days and SNF days during the follow-up year were measured (Supplemental Table S2). Rates and days were adjusted to the distribution of the comparator group using negative binomial regression models adjusting for age, sex, race, years on dialysis, cause of ESRD, comorbidities (the presence of an autoimmune disorder, anemia, cancer, COPD/asthma, diabetes, gastrointestinal bleeding, infections, heart diseases, ischemic stroke, hypertension, liver disease, acute myocardial infarction, neurological disorders, peptic ulcer disease, psychiatric disorders, pulmonary circulation disease, rheumatic heart disease, substance use disorders, blood transfusion), walking disability and the use of personal assistance aids. Post-discharge outcomes for pelvis/hip fractures were evaluated within patient strata.

All statistical analyses were performed using SAS version 9.2 (SAS Institute, Inc., Cary, NC).

Supplemental Tables and Figures

Figure S1a. Inpatient and Outpatient Fractures

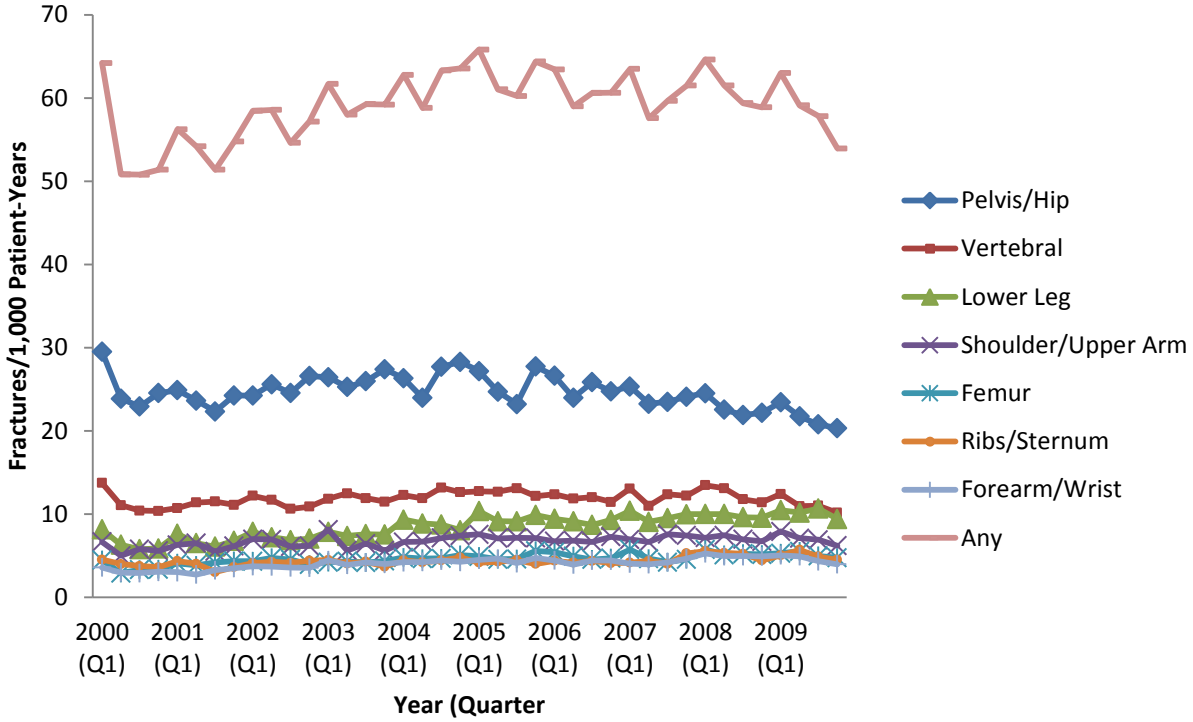

Figure S1b. Inpatient Fractures Only

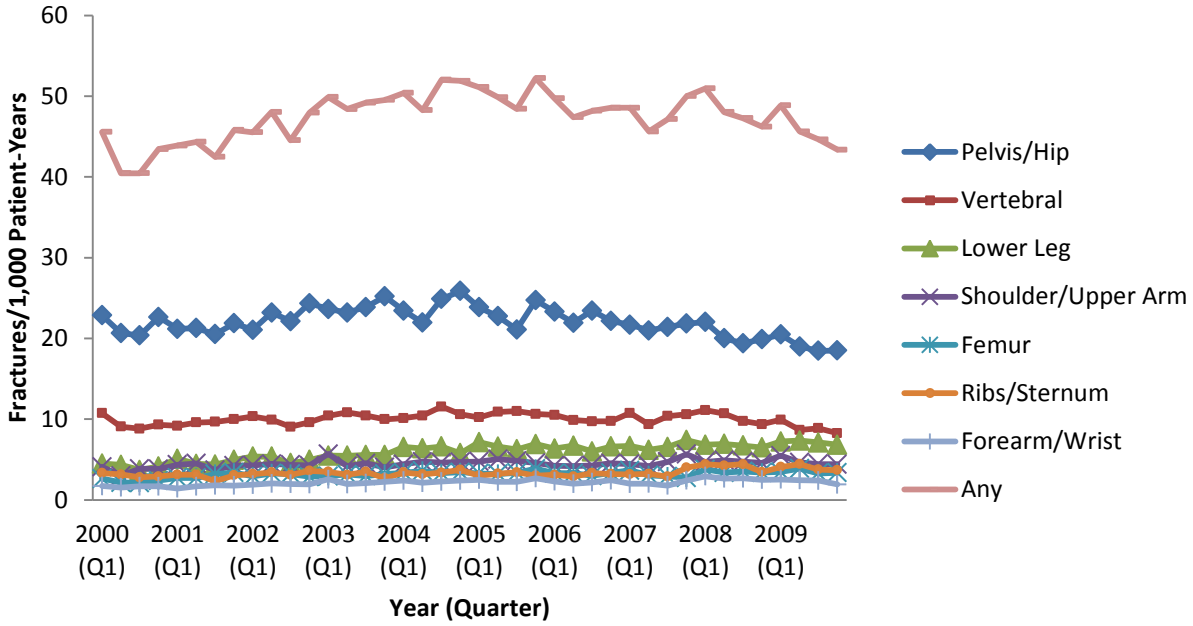

Figure S1. Crude fracture incidence rates by fracture type in years 2000-2009.

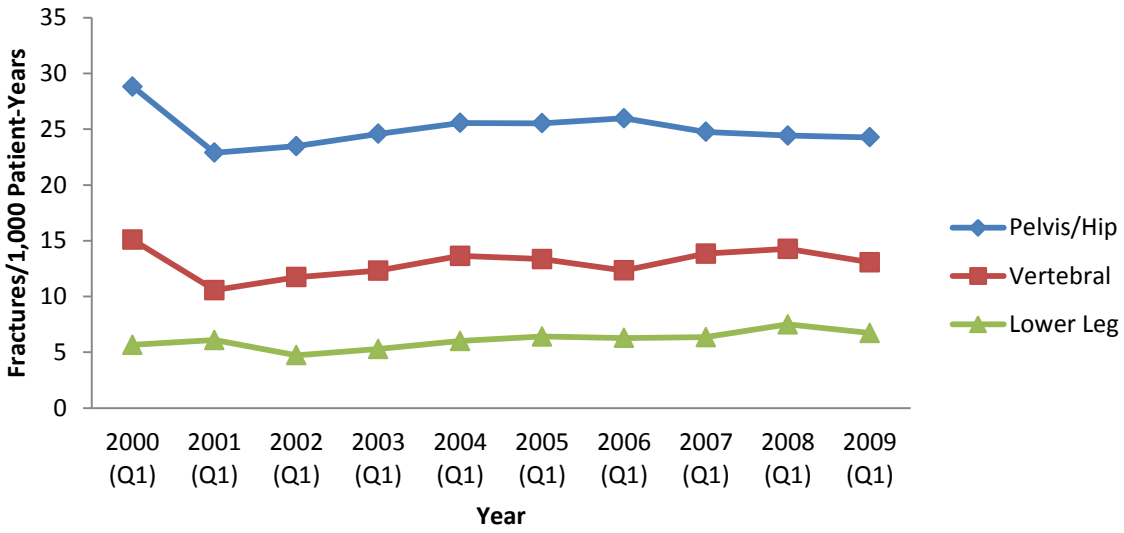

Figure S2. Adjusted fracture rates among only patients with diabetes as the cause of end-stage renal disease. Trend lines adjusted for age, sex, race, and years on dialysis.

Table S1. Demographic and clinical characteristics of patients' index hospitalization for any fracture versus the comparator group in 2000, 2004 2009

Characteristic	2000		2004		2009	
	Any Fracture	Comparator Group[a]	Any Fracture	Comparator Group	Any Fracture	Comparator Group
Patients (N)	3,008	65,771	7,460	46,519	7,283	45,125
Age (%)						
18-44	5.0	11.9	24.0	35.0	4.1	10.6
45-64	22.3	35.0	28.9	27.2	26.3	37.9
65-74	30.8	28.8	43.3	27.3	26.5	25.5
>74	42.0	24.4	33.2	64.8	43.0	26.0
Male	37.3	49.0	41.8	53.0	43.0	54.8
White	62.7	51.0	72.3	59.1	72.6	60.3
Years on dialysis ()						
0-1	28.7	33.2	33.2	64.8	32.3	62.9
2-5	51.3	48.8	49.8	29.8	49.7	33.1
>5	20.0	18.0	17.0	5.4	18.0	4.1
Cause of ESRD is diabetes	43.7	46.2	48.6	48.9	50.2	49.9
Autoimmune disorder	5.3	4.5	4.6	4.2	5.4	4.9
Blood loss anemia	11.7	10.5	6.7	5.5	6.0	4.9
Cancer	15.4	12.0	17.5	13.3	17.9	13.8
Chronic obstructive pulmonary disease/Asthma	25.0	23.4	30.9	25.4	33.6	26.9
Diabetes	57.6	60.2	65.2	64.5	69.4	67.9
Gastrointestinal bleeding	9.6	9.0	8.7	7.3	9.0	7.0
Infection	20.5	30.0	22.9	28.4	24.1	30.9
Heart diseases/heart procedure performed diseases	83.5	81.4	86.9	81.3	88.4	82.5
Ischemic stroke	18.9	16.3	18.7	14.9	25.1	19.9
Hypertensive disease	91.2	92.2	95.5	95.2	98.3	97.5
Liver disease	4.1	4.3	5.4	4.7	5.6	5.4
Acute myocardial infarction	6.8	7.7	7.5	7.8	8.3	7.7
Other neurological disorders	15.1	12.5	15.9	11.6	20.2	13.3
Peptic ulcer disease	6.5	6.7	5.3	4.6	4.6	3.6
Psychiatric disorder	7.6	6.2	7.7	5.5	9.7	6.6
Pulmonary circulation disease	5.3	4.5	5.9	4.5	10.5	7.5
Rheumatic heart disease	5.3	5.0	6.8	5.0	5.9	4.5

Substance use disorder	7.2	8.7	8.5	10.5	10.8	12.3
Blood transfusion	18.8	13.1	23.3	12.5	27.3	14.0
Walking disability/history of falls	21.2	8.5	48.5	12.9	55.6	16.7
Use of wheelchair	25.3	20.4	20.6	14.6	18.4	12.6
Use of walker/cane	8.8	5.2	7.0	3.9	7.2	3.9
Use of modified bathroom equipment	4.7	3.5	3.8	2.3	3.7	2.1

[a]Patients hospitalized for the first time for any cause (except for fracture)
[b]ESRD, End-stage renal disease

Table S2. Unadjusted mean/median hospitals days/year and skilled nursing facility days/year

Fracture Type	Mean hospital days/yr	Mean skilled nursing facility days/yr	Median hospital days/yr (Q1-Q3)	Median skilled nursing facility days/yr (Q1-Q3)
Comparator Group	29.3	19.0	9.5 (0.0-33.0)	0.0 (0.0-0.0)
Pelvis/Hip	54.4	78.5	24.0 (5.0-67.0)	38.0 (0.0-118.6)
Vertebral	56.1	59.7	26.0 (5.2-72.4)	8.0 (0.0-97.1)
Lower leg	45.7	63.7	20.0 (4.0-56.0)	21.0 (0.0-99.1)
Shoulder/Upper Arm	47.1	70.6	20.0 (3.0-58.0)	24.0 (0.0-104.9)
Ribs/Sternum	44.5	49.1	20.3 (3.0-55.6)	0.0 (0.0-68.9)
Femur	56.3	77.6	24.0 (5.0-71.0)	39.0 (0.0-117.1)