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Validation of Comorbid Conditions on the End-Stage Renal Disease Medical Evidence Report: The CHOICE Study

J. CRAIG LONGENECKER,* JOSEF CORESH,* MICHAEL J. KLAG,* ANDREW S. LEVEY,† ALICE A. MARTIN,† NANCY E. FINK,* and NEIL R. POWE,* FOR THE CHOICE STUDY

**The Johns Hopkins University, Baltimore, Maryland; and †The New England Medical Center, Boston, Massachusetts.*

Abstract. Since 1995, the Medical Evidence Report for end-stage renal disease (Form 2728) has been used nationally to collect information on comorbid conditions. To date, these data have not been validated. A national cross-sectional study of 1005 incident dialysis patients (734 hemodialysis and 271 peritoneal dialysis) enrolled between October 1995 and June 1998 was conducted using clinical data to validate 17 comorbid conditions on Form 2728. Sensitivity and specificity were calculated for each condition. The relationship between patient characteristics and sensitivity was assessed in multivariate analysis. Sensitivity was fairly high (0.67 to 0.83) for HIV disease, diabetes, and hypertension; intermediate (0.40 to 0.52) for peripheral vascular disease, neoplasm, myocardial infarction, cerebrovascular disease, coronary artery disease, cardiac arrest, and congestive heart failure; and poor (<0.36) for dysrhythmia, ambulation status, pericarditis, chronic obstructive pulmonary disease, and smoking. Sensitivity did not change significantly over calendar time. The sensitivity of Form 2728 averaged across all 17 conditions was 0.59 (95% confidence interval, 0.43 to 0.75). The average sensitivity was 0.10 greater in peritoneal dialysis than hemodialysis patients, 0.11 greater in diabetic patients than nondiabetic patients, and 0.04 less with each added comorbid condition. The specificity was very good for hypertension (0.91) and excellent (>0.95) for the other 16 conditions. Comorbid conditions are significantly underreported on Form 2728, but diagnoses are not falsely attributed to patients. Scientific research, quality of care comparisons, and payment policies that use Form 2728 data should take into account these limitations. Considerable effort should be expended to improve Form 2728 coding if it is to provide accurate estimates of total disease burden in end-stage renal disease patients.

The Health Care Financing Administration (HCFA) Medical Evidence Report for end-stage renal disease (ESRD), known as Form 2728, documents a patient's need for renal replacement therapy and provides important baseline data upon patient entry into the ESRD program. High mortality rates among dialysis patients, among other concerns, prompted the addition of a section on 20 comorbid conditions in 1995. Possible uses of these data are to determine case-mix severity, to adjust for confounding in clinical and epidemiologic studies, to sample subsets of individuals with particular conditions, to calculate the cost of comorbid illness in ESRD, and to potentially adjust reimbursement rates for comorbidity. Such uses require accurate and complete reporting. To date, the comorbidity data on Form 2728 have not been validated against medical record data. We conducted a study to validate 17 comorbid conditions reported on Form 2728 with clinical data obtained as part of the CHOICE (Choices for Healthy Outcomes in Caring for ESRD) Study (1), and to quantify the effect that inaccuracies on Form 2728 would have on clinical and statistical inferences.

Materials and Methods

Study Design and Research Population

This cross-sectional study is derived from the baseline data of CHOICE, a national prospective cohort study of incident dialysis patients initiated in 1995 to investigate treatment choices and outcomes of dialysis care. This study was possible because CHOICE collects sufficient baseline data allowing for clinical validation of 17 of the 20 comorbid conditions included on Form 2728. From October 1995 to June 1998, 1043 participants were enrolled from 80 participating dialysis clinics associated with Dialysis Clinic, Inc. (Nashville, TN), New Haven CAPD (New Haven, CT), or Saint Raphael's Hospital (New Haven, CT). The participating clinics were located in 19 states including Alabama, Arizona, California, Connecticut, Florida, Georgia, Kentucky, Louisiana, Massachusetts, Missouri, Montana, Nebraska, New Jersey, New Mexico, New York, Ohio, Pennsylvania, South Carolina, and Tennessee. Eligibility criteria for enrollment into CHOICE included initiation of chronic outpatient dialysis in the preceding 3 mo, ability to give informed consent for participation, age >17 yr, and ability to speak English or Spanish. The CHOICE Study protocol was approved by the Johns Hopkins University School of Medicine Institutional Review Board and the review boards for the clinical centers.

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Correspondence to Dr. J. Craig Longenecker, The Johns Hopkins University, Baltimore, MD 21205. Phone: 410-614-6928; Fax: 410-614-9793; E-mail: jlongene@jhsph.edu

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Table 1. Comorbidity definitions for Form 2728 and CHOICE data[a]

Form 2728 Comorbidity Definition (Check all that apply currently or during last 10 years)	CHOICE Comorbidity Definition (Medical record documentation of a history of the condition, based on the listed criteria)[b]
a. Congestive heart failure	• Diagnosis of any CHF or history of pulmonary edema
b. Ischemic heart disease, CAD: includes prior CABG, angioplasty, and diagnoses of CAD/coronary heart disease.	• Diagnosis of CAD, or • Any history of MI, or • Prior CABG or coronary angioplasty, or • MI in the past 3 mo • (Although CHOICE obtains information regarding stable angina, exertional angina, rest angina, ischemia on EKG or other diagnostic test, and EKG evidence of old MI, we did not include these criteria in the definition for CAD.)
c. Myocardial infarction	• Any history of myocardial infarction, or • Myocardial infarction in the past 3 mo
d. Cardiac arrest	• Cardiac arrest in the past year
e. Cardiac dysrhythmia	• Arrhythmia or conduction problem (on EKG or in notes), or • Arrhythmias or conduction problem requiring medication or temporary pacemaker, or • Recurrent syncope (due to arrhythmia or conduction problem) while on medication, or • Requirement of a permanent pacemaker or defibrillator
f. Pericarditis	• Pericarditis in the past year
g. Cerebrovascular disease, CVA, TIA: includes history of stroke/CVA, and TIA	• Diagnosis of cerebrovascular disease, or • Multiple TIAs in past year, or • History of CVA with no or mild deficit (*e.g.*, hemiparesis, slurred speech, mild cognitive changes), or • CVA with major deficit (*e.g.*, paralysis, aphasia, blindness)
h. Peripheral vascular disease: includes absent foot pulses, prior typical claudication, amputations for vascular disease, gangrene, and aortic aneurysm.	• Diagnosis of PVD, or • Intermittent claudication, or • Amputation of toes or foot, or • Prior bypass graft, abdominal or thoracic aortic aneurysm repair, or • Pain at rest due to PVD, or • Inoperable disease, or • Amputation below or above the knee, or • Abdominal aortic aneurysm
i. History of hypertension	• Diagnosis of hypertension, or • Requirement of antihypertensive medication, or • Episode of malignant or accelerated hypertension in past 3 mo
j. Diabetes mellitus (primary or contributing)	• Diagnosis of diabetes mellitus (type I or II), or • Requirement of oral medication, or • Requirement of insulin, or • Uncontrolled diabetes: four or more hypoglycemic episodes or two or more hospitalizations for hyperglycemia or ketoacidosis
k. Diabetes mellitus, currently on insulin	• Insulin requirement
l. Chronic obstructive pulmonary disease	• Diagnosis of COPD (*e.g.*, chronic bronchitis, asthma, emphysema, or pulmonary fibrosis), or • Asthma or COPD requiring medications

Table 1 continues

Table 1. Continued

Form 2728 Comorbidity Definition (Check all that apply currently or during last 10 years)	CHOICE Comorbidity Definition (Medical record documentation of a history of the condition, based on the listed criteria)[b]
m. Tobacco use (current smoker)	• Patient questionnaire: Do you currently smoke cigarettes?
n. Malignancy neoplasm	• Diagnosis of malignancy, >5 yr since last treatment, or • Diagnosis of malignancy, <5 yr since treatment, but none in past year, or • Current malignancy or treatment within last year (Skin cancer other than melanoma was excluded)
o. Alcohol dependence	• No corresponding data
p. TDrug dependence	• No corresponding data
q. HIV-positive status	• Diagnosis of HIV (HIV-positive)
r. AIDS	• Diagnosis of AIDS
s. Inability to ambulate	• Index of physical impairment: Confined to wheelchair, bedridden (Does not include: "walks with assistance, uses cane or walker")
t. Inability to transfer	• No corresponding data

[a] The definitions listed here replicate the definitions used on Form 2728 and CHOICE data instruments.
[b] The CHOICE data were derived from a medical record review for all conditions except "Tobacco use," determined by patient questionnaire, and "Inability to ambulate," ascertained by the dialysis unit nurse using the Index of Physical Impairment. Conditions were considered present if any of the listed criteria were documented in the medical record. CHF, congestive heart failure; CAD, coronary artery disease; MI, myocardial infarction; CABG, coronary artery bypass graft; EKG, electrocardiogram; CVA, cerebrovascular accident; TIA, transient ischemic attack; PVD, peripheral vascular disease; COPD, chronic obstructive pulmonary disease.

Data Collection

CHOICE Clinical Data. Comorbidity assessment was performed using the Index of Co-Existent Disease (ICED) (2–6). The ICED includes the Index of Disease Severity, a 116-item chart-based review of 19 medical conditions, and the Index of Physical Impairment, an 11-item form completed by the local nurse or technician. An interobserver reliability study ($n = 49$) comparing ICED scoring technique of our nurse to an experienced nephrologist in the Mortality and Morbidity in Hemodialysis Patients (MMHD) Study yielded a kappa of 0.77. Upon each participant's enrollment into the study, the local study coordinator photocopied all history and physical data, discharge summaries, physician progress notes, medication records, and problem lists from the dialysis clinic chart. These were sent to the CHOICE Comorbidity Assessment Center at the New England Medical Center (Boston, MA). All records were abstracted by two experienced dialysis research nurses. The primary research nurse (who participated in the MMHD reliability study) abstracted 771 records and another, trained and supervised by the primary research nurse, abstracted 234. Clinic record mention of a condition (past or present) was sufficient for positive coding.

Data for 17 of the 20 conditions listed on Form 2728 were available in CHOICE Study documents. Data on 15 conditions were included in the Index of Disease Severity ($n = 1005$). Data regarding inability to ambulate were collected using the Index of Physical Impairment ($n = 1002$). Current smoking status was ascertained from the CHOICE baseline patient questionnaire ($n = 947$). Physician-reported data for three conditions (drug dependence, alcohol dependence, and inability to transfer) were not available. In this report, "clinical data" refers to the baseline CHOICE data for the 17 comorbid conditions.

Form 2728

The front page of Form 2728 lists 20 comorbid conditions without qualifying definitions. However, four conditions—ischemic heart disease, cerebrovascular disease, peripheral vascular disease (PVD), and substance abuse—have limited definitions listed on the back of the form (Table 1, first column). The attending nephrologist is instructed to indicate all concurrent conditions and those that have been present during the previous 10 yr.

Comparison of Form 2728 and Clinical Data Definitions

Table 1 directly compares the CHOICE comorbidity criteria with Form 2728. Each bulleted item in Table 1 represents a definitional criterion coded separately on the ICED. If any criterion was met, the record was considered positive for that comorbidity. For 15 of the 17 conditions studied, the CHOICE criteria were as specific (restrictive) or more specific than those on Form 2728. However, for cardiac dysrhythmia, the CHOICE definition included cardiac conduction abnormalities, and for chronic obstructive pulmonary disease (COPD), asthma was included. For these two conditions, the CHOICE definitions have the potential to identify conditions that would not necessarily fall within the Form 2728 definitions.

Statistical Analyses

Descriptive statistics using means or proportions and confidence intervals were performed on all variables where appropriate. The prevalence of each condition estimated by the clinical data was compared to Form 2728, and the difference in proportions was tested for significance

using McNemar χ^2 test for paired observations and the exact McNemar test for 2×2 tables with cells containing fewer than 10 observations (7). Sensitivity and specificity (8) were calculated by cross-tabulating Form 2728 data with the clinical data, which served as the gold standard. Agreement between Form 2728 data and the clinical data was evaluated with the kappa statistic (9). Although not a category on Form 2728, we created a new composite cardiovascular disease comorbidity (CVD), defined as the presence of PVD, myocardial infarction (MI), coronary artery disease (CAD), or cerebrovascular disease. CVD was included as a separate outcome variable in all analyses.

To identify the effect of various factors on Form 2728 sensitivity, we used generalized estimating equation (GEE) models constructed using a logit link and exchangeable correlation structure (10). GEE allowed us to adjust the standard error estimates by taking into account dialysis center effects on sensitivity (*i.e.*, clustering of coding patterns within clinic). Twelve conditions (those with sufficient sample size) were modeled separately. Only individuals with the condition (defined by the clinical data) were included in each respective model, and the logistic outcome was the presence or absence of the condition on Form 2728. Models included the following independent variables that were hypothesized to have an effect on sensitivity: age, race (White, African-American, other), gender, modality, calendar time (tested both as a continuous variable and a dichotomized variable), number of comorbid conditions, diabetes, and CVD. Each covariate's adjusted effect on sensitivity was determined by adjusting the sensitivity to the composition of the entire study population, using the method described by Lee (11). For example, to obtain the estimated sensitivity among African-Americans, the entire model population was restructured as all African-Americans without changing any other variables within individuals (*i.e.*, while holding all other variables within each individual constant). Conversely, to estimate the sensitivity among whites, the model population was restructured as all white while holding the other variables within each individual constant.

The average sensitivity of Form 2728 across all 17 conditions was modeled using multiple linear regression incorporating GEE (12). The percentage of clinical data conditions positively identified on Form 2728 was determined for each participant and was used as the outcome variable for average sensitivity across all 17 conditions. The eight independent variables included in the above models were also included in this model of average sensitivity. Models were also constructed including time from first nephrology consultation to enrollment, first dialysis to enrollment, and Form 2728 completion to enrollment.

To demonstrate the errors introduced into statistical analyses (*i.e.*, bias) when Form 2728 data are used instead of the clinical data, we constructed GEE models of the association of independent variables with the outcome of prevalent CVD, first using the clinical CVD data and then the Form 2728 CVD data. These models used clinical data for the independent variables (diabetes and dialysis modality). We then simulated 1-yr mortality data by applying an odds ratio of death equal to 2.0 for diabetes and 3.0 for CVD to our study population using a binomial distribution rule. The adjusted odds ratios of 1-yr mortality produced in the simulation for diabetes (1.7) and prevalent CVD (2.8) are similar to published reports of mortality risks for diabetes and CVD in dialysis patients (13–15). Using logistic regression models, the simulated odds ratios of death from the clinical data were compared with that predicted by Form 2728 data. In this analysis, GEE was not used because the simulated mortality was assigned randomly to individuals within the constraints of the odds of death associated with diabetes and CVD. All statistical analyses were performed using Stata 5.0 (Stata Corp., College Station, TX).

Table 2. Characteristics of CHOICE participants and the U.S. dialysis population (USRDS data)[a]

Characteristic	CHOICE (n = 1005)	1997 USRDS
Mean age at ESRD incidence (yr)	57.8	60.2
Gender (% female)	45.7	46.0
Race (% African-American)	28.4	31.9
Dialysis modality (% HD)[b]	73.0	83.2
Median no. of comorbid conditions	4.0	
ESRD cause		
diabetes mellitus (%)	46.7	37.4
HTN (%)	17.5	28.7
GN (%)	16.1	11.0
other (%)	19.7	22.9
Median time to enrollment (days)		
from first nephrology consultation	355	
from first dialysis	46	
from Form 2728 date	31	

[a] USRDS, U.S. Renal Data Study; ESRD, end-stage renal disease; HD, hemodialysis; HTN, hypertension; GN, glomerulonephritis.
[b] Excludes transplantation.

Results

Patient Characteristics

Table 2 presents the characteristics of the study population. Age, gender, race, and dialysis modality distributions were similar to the overall U.S. dialysis population (16). The proportion treated with hemodialysis (HD) was less than the U.S. Renal Data Study (USRDS) because peritoneal dialysis (PD) patients were oversampled for the CHOICE Study. Diabetes and hypertension together accounted for ESRD in two-thirds of the cohort, a figure similar to USRDS. However, the percentage attributed to hypertension in the study population was lower than in USRDS (16). The median time from first nephrology consultation to enrollment, first dialysis to enrollment, and Form 2728 completion to enrollment are also presented in Table 2.

Prevalence of Comorbid Conditions

Table 3 presents the prevalence for each condition as determined by Form 2728 data and the clinical data. Form 2728 prevalence was lower than the clinical data for all conditions except cardiac arrest (1.5% *versus* 0.6%; $P = 0.03$). The difference in prevalence was statistically significant for all conditions except HIV ($n = 6$) and AIDS ($n = 3$). Only seven of 947 (0.74%) individuals with data on all 17 conditions had no comorbid conditions identified in the clinical data. However, 106 (11.1%) of these 947 individuals had no comorbid conditions listed on Form 2728.

Sensitivity, Specificity, and Kappa

The sensitivity of Form 2728 (Table 3) was fairly high (0.67 to 0.83) for five conditions (AIDS, insulin use, diabetes, hypertension [HTN], and HIV). The sensitivity for seven condi-

Table 3. Prevalence, sensitivity, specificity, and the kappa statistic for 17 comorbid conditions on Form 2728 compared with CHOICE clinical data ($n = 1005$)[a]

Condition	*n*	Prevalence (%)		Sensitivity (95% CI)	Specificity (95% CI)	Kappa
		Form 2728	Clinical Data			
HIV	6	0.5	0.6	0.83 (0.36 to 0.99)	1.00 (1.00 to 1.00)	0.91
HTN	959	74.3	95.4[b]	0.77 (0.75 to 0.80)	0.91 (0.79 to 0.98)	0.22
Diabetes mellitus	536	40.5	53.3[b]	0.75 (0.71 to 0.79)	0.99 (0.98 to 1.00)	0.73
Insulin use	372	28.9	37.0[b]	0.71 (0.66 to 0.76)	0.96 (0.94 to 0.97)	0.70
AIDS	3	0.2	0.3	0.67 (0.09 to 0.99)	1.00 (1.00 to 1.00)	0.80
Any CVD	549	36.5	54.4[b]	0.61 (0.57 to 0.65)	0.95 (0.93 to 0.97)	0.54
CHF	443	24.9	44.1[b]	0.52 (0.47 to 0.56)	0.96 (0.94 to 0.98)	0.50
Cardiac arrest	6	1.5	0.6[c]	0.50 (0.11 to 0.88)	0.99 (0.98 to 0.99)	0.28
CAD	418	21.2	41.6[b]	0.48 (0.43 to 0.53)	0.98 (0.96 to 0.99)	0.49
CVA/TIA	139	7.5	13.8[b]	0.47 (0.39 to 0.56)	0.99 (0.98 to 1.00)	0.57
MI	182	9.2	18.1[b]	0.43 (0.36 to 0.50)	0.98 (0.97 to 0.99)	0.51
Neoplasm	95	4.5	9.5[b]	0.42 (0.32 to 0.53)	0.99 (0.99 to 1.00)	0.54
PVD	257	12.2	25.6[b]	0.40 (0.34 to 0.46)	0.97 (0.96 to 0.98)	0.45
Smoking	141	7.6	14.8[b]	0.35 (0.28 to 0.44)	0.97 (0.96 to 0.98)	0.41
COPD	172	5.9	17.1[b]	0.33 (0.26 to 0.40)	1.00 (0.99 to 1.00)	0.44
Pericarditis	34	1.7	3.4[b]	0.32 (0.17 to 0.50)	0.99 (0.99 to 1.00)	0.42
Nonambulatory	39	1.6	3.9[b]	0.23 (0.11 to 0.39)	0.99 (0.99 to 1.00)	0.31
Dysrhythmia	290	5.2	28.9[b]	0.15 (0.11 to 0.20)	0.99 (0.98 to 1.00)	0.19

[a] Rows are ordered by descending sensitivity. n = the number of cases of each condition identified by the medical record review. "Any CVD" combines CAD, CVA/TIA, MI, and PVD into a single definition (not defined as such on Form 2728). Sensitivity and specificity were calculated using the CHOICE data as the reference group. 95% CI values are binomial exact. The difference between Form 2728 and clinical data prevalence was tested using the McNemar χ^2 test for paired observations. For 2×2 tables with cells with fewer than 10 observations, the McNemar exact test was used. CI, confidence interval; CVD, cerebrovascular disease. Other abbreviations as in Tables 1 and 2.

[b] $P < 0.001$.

[c] $P < 0.05$.

tions (PVD, neoplastic disease, MI, cerebrovascular disease, CAD, cardiac arrest, and congestive heart failure) was intermediate (0.40 to 0.52). The combined sensitivity for all CVD diagnoses was 0.61. The sensitivity for the remaining five conditions (dysrhythmia, inability to ambulate, pericarditis, COPD, and smoking) was poor (<0.36). Form 2728 specificity was very good for hypertension (0.91) and excellent (>0.95) for the other 16 conditions. Agreement between Form 2728 and the clinical data, as measured by the kappa statistic, was greater than that expected by chance alone for all comorbid conditions, although the agreement was only slight to fair for dysrhythmia (0.19), hypertension (0.22), cardiac arrest (0.28), and ambulation status (0.31).

Factors Associated with Form 2728 Sensitivity

Table 4 presents the independent effects of race, gender, modality, diabetes, and CVD on the sensitivity of Form 2728 for the 12 conditions with a prevalence above 25%. In addition to the characteristics listed in Table 4, other variables included in the multivariate models included age, number of comorbid conditions, and calendar time. Each row displays a separate regression model, and the columns present each characteristic's independent effect on the adjusted sensitivity for the 12 conditions examined. Form 2728 sensitivity was significantly higher for African-Americans than whites for hypertension (0.84 *versus* 0.75; $P = 0.009$), but was lower in African-Americans than whites for CAD (0.34 *versus* 0.49; $P = 0.04$) and smoking (0.24 *versus* 0.42; $P = 0.05$). Sensitivity was significantly higher in men than women only for CVD (0.65 *versus* 0.54; $P = 0.02$). Sensitivity was lower in HD patients than PD patients for nine of the 12 models, although these differences were statistically significant only for diabetes and CVD. Form 2728 sensitivity was significantly higher for diabetic patients (0.58) than nondiabetic patients (0.42; $P = 0.007$) only for CHF. No consistent effect of CVD on Form 2728 sensitivity was found.

The average sensitivity of Form 2728 across all 17 conditions was 0.59 (95% confidence interval, 0.43 to 0.75). Variables having a statistically significant effect on the average sensitivity included dialysis modality (0.10 higher in PD than HD), number of comorbid conditions (0.04 lower for each added comorbid condition), and diabetes (0.11 higher in diabetic patients than nondiabetic patients) (Table 5). No significant differences in average sensitivity were seen for race, gender, age, calendar time (both as a continuous variable and dichotomous variable), or the presence or absence of CVD.

Table 4. Adjusted Form 2728 sensitivity for 12 comorbid conditions by race, gender, modality, diabetes mellitus, and CVD[a]

Condition	*n*	Overall Sensitivity	Adjusted Form 2728 Sensitivity									
			Race		Gender		Modality		Diabetes Mellitus		CVD	
			A-A	White	Male	Female	HD	PD	DM−	DM+	CVD−	CVD+
HTN	904	0.78	0.84	0.75[b]	0.78	0.77	0.76	0.82	0.80	0.75	0.75	0.80
Diabetes mellitus	507	0.76	0.80	0.74	0.74	0.77	0.73	0.83[c]			0.75	0.76
Insulin use	349	0.72	0.66	0.75	0.72	0.72	0.70	0.79			0.70	0.74
Any CVD	516	0.60	0.58	0.62	0.65	0.54[c]	0.57	0.74[d]	0.66	0.58		
CHF	414	0.53	0.49	0.55	0.52	0.53	0.53	0.52	0.42	0.58[b]	0.45	0.55
CAD	399	0.46	0.34	0.49[c]	0.49	0.41	0.44	0.50	0.45	0.46		
CVA/TIA	127	0.47	0.41	0.47	0.47	0.47	0.49	0.43	0.43	0.48		
MI	173	0.42	0.47	0.42	0.48	0.32	0.39	0.54	0.47	0.40		
PVD	236	0.41	0.44	0.40	0.43	0.38	0.37	0.55	0.43	0.40		
Smoking	141	0.36	0.24	0.42[c]	0.39	0.31	0.35	0.42	0.42	0.27	0.37	0.36
COPD	166	0.33	0.26	0.35	0.33	0.33	0.34	0.33	0.40	0.26	0.23	0.37
Dysrhythmia	217	0.14	0.18	0.13	0.14	0.15	0.13	0.18	0.14	0.15	0.26	0.11

[a] Each row represents a separate generalized estimating equation regression model, and the columns describe the effect of each covariate on the adjusted sensitivity. All models were adjusted for race, gender, modality, age, calendar time, number of comorbid conditions, and the presence of diabetes or CVD. *n* = number of individuals in each model who have the condition as defined by medical record review. A-A, African-American; PD, peritoneal dialysis. "Any CVD" includes CAD, MI, CVA/TIA, and PVD. Other abbreviations as in Tables 1 and 2.
[b] $P < 0.01$.
[c] $P < 0.05$.

Table 5. Relationship of demographic and clinical characteristics to average sensitivity of Form 2728 (aggregated across 17 conditions) ($n = 940$)[a]

Explanatory Variable	Comparison Groups	Difference in Average Sensitivity	95% CI
African-American race	A-A *versus* white	+0.03	(−0.02 to 0.08)
Hispanic ethnicity	Hispanic *versus* white	−0.02	(−0.10 to 0.05)
Gender	Male *versus* female	+0.04	(−0.00 to 0.08)
Age	+10 yr	0.00	(0.00 to 0.00)
Modality	PD *versus* HD	+0.10[b]	(0.03 to 0.17)
Calendar time	≥1/97 *versus* <1/97	+0.02	(−0.03 to 0.07)
Comorbid conditions	+1 comorbid condition	−0.04[c]	(−0.06 to −0.03)
Diabetes mellitus	Present *versus* not present	+0.11[c]	(0.07 to 0.15)
CVD	Present *versus* not present	−0.01	(−0.04 to 0.06)

[a] The difference in average sensitivity is the linear regression coefficient for the model after adjustment for race, gender, age, modality, enrollment period, number of comorbid conditions at baseline, the presence of diabetes, and the presence of any CVD. Abbreviations as in Tables 1, 3, and 4.
[b] $P < 0.01$.
[c] $P < 0.001$.

Exclusion of individuals with a blank Form 2728 ($n = 99$ of 940) did not significantly alter the results shown in Table 5. Results of models incorporating time from first nephrology consultation to enrollment, first dialysis to enrollment, or Form 2728 completion to enrollment also did not differ significantly from the model in Table 5; these three time-to-enrollment effects were negligible and statistically not significant. Because Form 2728 sensitivity was significantly higher among African-Americans than whites for HTN, but lower for CAD and smoking, we created a model excluding HTN from the calculation of average sensitivity. The average sensitivity among African-Americans in this model was 0.04 lower than among whites, but this difference was not statistically significant ($P = 0.22$).

Effect of Form 2728 Underestimation of Comorbidity on Statistical Analyses

Underestimation of comorbid conditions on Form 2728 could result in erroneous estimates of disease prevalence and

Table 6. Odds ratios of prevalent CVD associated with diabetes and modality: comparison of assessment of the dependent variable (prevalent CVD) by clinical data *versus* Form 2728[a]

Model	Independent Variables	(a) Dependent Variable based on Clinical Data		(b) Dependent Variable based on Form 2728	
		OR of Prevalent CVD	95% CI	OR of Prevalent CVD	95% CI
Models 1a and 1b	Diabetes mellitus (+ *versus* −)	3.03[b]	(2.34 to 3.92)	1.99[b]	(1.52 to 2.59)
Models 2a and 2b	Modality (PD *versus* HD)	0.69[c]	(0.52 to 0.92)	1.06	(0.79 to 1.42)
Models 3a and 3b	Diabetes mellitus (+ *versus* −)	3.00[b]	(2.32 to 3.90)	2.00[b]	(1.52 to 2.60)
	Modality (PD *versus* HD)	0.71[c]	(0.53 to 0.95)	1.10	(0.82 to 1.48)
Models 4a and 4b (adjusted for age, gender, and race)	Diabetes mellitus (+ *versus* −)	3.16[b]	(2.38 to 4.12)	2.06[b]	(1.55 to 2.73)
	Modality (PD *versus* HD)	0.85	(0.62 to 1.18)	1.27	(0.92 to 1.74)

[a] Prevalent CVD (defined as CAD, MI, CVA/TIA, or PVD). Clinical data were used for all independent variables. Models 1a, 1b, 2a, and 2b are simple logistic regression models. Models 3a, 3b, 4a, and 4b are multiple regression models. OR, odds ratio. Other abbreviations as in Tables 1 to 4.
[b] $P < 0.001$.
[c] $P < 0.05$.

associations with risk factors (*i.e.*, bias). We performed two sets of analyses to quantify the bias introduced by such underestimation. First, we compared the association of diabetes and modality with prevalent CVD when CVD (the outcome variable) is defined by the clinical data *versus* Form 2728 (Table 6). In these models, all independent variables were defined by the clinical data. The odds ratio for prevalent CVD associated with diabetes was 3.0 when CVD was defined by the clinical data (model 1a) compared to 2.0 when CVD was defined on the basis of Form 2728 (model 1b). This difference persisted even after adjusting for modality, age, gender, and race (models 4a and 4b). PD was associated with a lower risk of prevalent CVD than HD when CVD was defined by the clinical data (models 2a, 3a, and 4a), but was associated with a higher risk of CVD when defined on the basis of Form 2728 (models 2b, 3b, and 4b). This differential bias results from the higher sensitivity of Form 2728 for any CVD among PD patients than HD patients (Table 4).

The second set of analyses used simulated 1-yr mortality models (Table 7) to compare the use of explanatory variables based on the clinical data *versus* Form 2728. The univariate models for diabetes (models 1a and 1b) show that using Form

Table 7. Odds ratios of simulated 1-yr mortality, associated with diabetes and CVD: comparison of assessment of independent variables (diabetes and CVD) by clinical data *versus* Form 2728[a]

Model	Independent Variables	(a) Independent Variables based on Clinical Data		(b) Independent Variables based on Form 2728	
		OR of Mortality	95% CI	OR of Mortality	95% CI
Models 1a and 1b	Diabetes mellitus	2.18[b]	(1.64 to 2.90)	1.43[c]	(1.08 to 1.90)
Models 2a and 2b	CVD	3.22[b]	(2.39 to 1.33)	1.59[d]	(1.20 to 2.10)
Models 3a and 3b	Diabetes mellitus	1.72[b]	(1.28 to 2.31)	1.33[c]	(1.00 to 1.75)
	CVD	2.82[b]	(2.08 to 3.84)	1.51[d]	(1.14 to 2.00)
Model 4	Diabetes mellitus			1.15	(0.86 to 1.53)
	CVD	3.12[b]	(2.31 to 4.24)		

[a] Models compare diabetes and CVD data from the CHOICE clinical data (a) *versus* Form 2728 (b). Simulated 1-yr mortality is the dichotomous outcome. Models 1a, 1b, 2a, and 2b are simple logistic regression models. Models 3a, 3b, and 4 are multiple logistic models. Model 4 incorporates clinical data for CVD and Form 2728 data for diabetes. Abbreviations as in Tables 1 and 3.
[b] $P < 0.001$.
[c] $P < 0.05$.
[d] $P < 0.01$.

2728 to define diabetes underestimates the risk of dying associated with diabetes compared to that found when the clinical data are used (odds ratio [OR] 1.43 *versus* 2.18, respectively). Similarly, the univariate models including only CVD (models 2a and 2b) also demonstrate that using Form 2728 data severely underestimates the 1-yr mortality risk associated with CVD compared to the clinical data (OR 1.59 *versus* 3.22, respectively). Model 3a, a multivariate model using clinical data for both diabetes and CVD, shows strong adjusted associations for both diabetes and CVD with mortality (OR 1.72 and 2.82). When Form 2728 data are used for both diabetes and CVD (model 3b), both the adjusted risk of mortality and statistical significance for diabetes and CVD are underestimated compared to the clinical data (model 3a).

Use of Form 2728 data also attenuates the degree of adjustment attainable in multivariate models. Model 3a, using clinical data for both diabetes and CVD, illustrates that adjustment for the confounding effect of diabetes lowers the OR of mortality associated with CVD from 3.22 (unadjusted in model 2a) to 2.82 (adjusted for diabetes in model 3a). Model 4, a hybrid model incorporating the diabetes variable based on Form 2728 and the CVD variable based on the clinical data, demonstrates that the risk of dying associated with CVD is adjusted only minimally from 3.22 to 3.12: $<25\%$ of the full adjustment effect. Furthermore, the OR of mortality associated with diabetes is greatly attenuated in model 4 and not statistically significant when Form 2728 is used to define diabetes (OR 1.15; $P = 0.34$).

Discussion

This cross-sectional study of 1005 dialysis patients compares data for 17 comorbid conditions on Form 2728 to clinical data contained in the outpatient dialysis clinic record. The study sample was national and representative of ESRD patients in the United States.

The prevalence of all conditions except cardiac arrest was lower for Form 2728 compared to the clinical data, and the difference in prevalence for all conditions except HIV and AIDS was statistically significant. The specificity of Form 2728 was greater than 0.91 for all 17 conditions. The sensitivity of Form 2728 ranged from 0.15 to 0.83, being highest for HIV disease, hypertension, and diabetes and lowest for dysrhythmia, ambulation status, pericarditis, COPD, and smoking. The condition-specific sensitivity did not change significantly even after adjustment for eight independent variables.

The average sensitivity of Form 2728 across all 17 conditions was 0.59. Regression analysis of average sensitivity demonstrated significant differences in sensitivity by modality (PD higher than HD), diabetes status (diabetic patients higher than nondiabetic patients), and number of comorbid conditions (lower with higher number of conditions). These results suggest that comparing the Form 2728 comorbid conditions of PD to HD patients or diabetic patients to nondiabetic patients may produce spurious results simply because these conditions are even more underreported in HD than in PD, and in nondiabetic patients than diabetic patients. The strongest association that emerged in the model was the lower sensitivity with more comorbid conditions. One could speculate that the extra effort required to fill out the form for patients with more comorbid conditions discourages completion of the form. This type of underreporting may result in differential bias by selectively misclassifying those with the greatest comorbidity and mortality risk. Assuming continuity of care by a single physician, one might expect that the longer the relationship of the physician with the patient, the better the reporting of comorbid illness. However, models incorporating the above independent variables and time from first nephrology consultation to date of Form 2728 completion found no effect of time on Form 2728 sensitivity. In addition, time from first nephrology consultation to enrollment, first dialysis to enrollment, or Form 2728 completion to enrollment also had no effect on Form 2728 sensitivity.

The average sensitivity did not improve over the 3 years of the study, a time frame corresponding to the first 3 years the form was in use. This lack of improvement over time suggests that lack of familiarity with the form may not be the primary cause of the low sensitivity, and that efforts should be made to improve the coding of Form 2728. Wider availability of electronic patient records may contribute to an improved sensitivity of Form 2728 in the future.

Our findings are similar to validation studies of other administrative databases (17–24). Most studies evaluating administrative data sources report that they underestimate the prevalence of comorbid conditions (17,18,22,23). Although the specificity of administrative data tends to be very good (>0.90), the sensitivity of these data for some conditions can be 0.50 or even lower (18,22). These studies suggest that while diagnoses reported in administrative databases do not generally attribute diagnoses to those without the condition, many diagnoses are often significantly underreported.

The low sensitivity of Form 2728 raises concern regarding two types of statistical bias. First, an underreporting bias would result in lower estimates of disease burden. For example, an estimate of the prevalence of CHF (sensitivity = 0.52) would be biased downward to 52% of its true prevalence if Form 2728 data were used. Second, when sensitivity is as low as seen in this study, potential exists for a differential bias that is important when comparing two groups (*e.g.*, HD *versus* PD). If underreporting occurs to a greater degree in one group compared with another, associations with other comorbid conditions may be masked (as shown with the OR estimates of CVD associated with modality in Table 6), or spurious relationships may be created.

To illustrate these biases, we tested the association of diabetes and dialysis modality with prevalent CVD and found that these associations were underestimated when Form 2728 CVD data were used (Table 6). When comparing PD to HD, use of Form 2728 CVD data created a bias that produced a point estimate for the OR for CVD in the opposite direction as that generated by the clinical data and eliminated the significant association between modality and CVD seen with the clinical data.

We also tested the association of diabetes and prevalent CVD with simulated 1-yr mortality and found similar biases

(Table 7). Use of Form 2728 data for diabetes and prevalent CVD significantly underestimated the OR of mortality compared with the clinical data, and resulted in <25% adjustment for confounding. The degree of underestimation was similar to that found by Romano *et al.*, who compared coronary artery bypass graft hospital discharge data from two populations with clinical data from two other populations (17). In that study, the administrative data underestimated the relative risk of 30-d mortality by 40 to 80% for various conditions, including previous MI, angina, hypertension, hyperlipidemia, cardiomegaly, bundle branch block, and premature ventricular contractions. It was not significantly different, however, for tobacco use, diabetes, CHF, or PVD (17).

Implications for Use of Form 2728 Data

The low sensitivity of Form 2728 has implications for its potential uses. For example, the prevalence and economic burden of comorbidity in ESRD patients may be underestimated when determined using Form 2728. Reimbursement for patient care may be insufficient if rates of provider payment were to be linked to comorbidity defined by Form 2728. However, the results of this study could be used to adjust prevalence and cost estimates. More importantly, bias may be introduced if Form 2728 data are used to study associations between comorbid conditions, treatment, and mortality or other outcomes. Use of Form 2728 data will bias such associations toward null findings and will result in incomplete adjustment for confounding, as seen in Tables 6 and 7. Differential bias (described above) could bias estimates in either direction. Furthermore, biased sampling could occur if Form 2728 were used to identify specific subgroups of patients for study.

Limitations

There are limitations to our study. The criteria used to identify conditions in both data sets are crucial when comparing diagnoses. Overall, the CHOICE criteria were as restrictive or more restrictive than the definitions presented on Form 2728. For example, to avoid including CAD diagnoses having lower specificity in the ESRD population, we excluded from the definition of CAD those with only angina ($n = 3$), ischemia diagnosed by clinical tests such as electrocardiogram or stress test ($n = 1$), or electrocardiogram evidence of old MI ($n = 2$) without other physician documentation of CAD. Such diagnoses may be reported on Form 2728; thus, our definition of CAD provides a conservative estimate of Form 2728 sensitivity for CAD. There are two important exceptions. First, for most conditions CHOICE identified any history of a condition as sufficient for inclusion. In contrast, Form 2728 requires a history of the condition within the past 10 yr. Thus, the CHOICE data may include conditions that occurred before the Form 2728 10-yr window. We suspect the effect of this difference is probably minimal.

Second, the sensitivity presented for dysrhythmia and COPD may be biased downward because our definitions included conduction problems and asthma, respectively, which were not explicitly included in the Form 2728 definitions. Although these effects would spuriously lower the calculated sensitivity for these conditions, it is improbable that they would introduce errors on the order of magnitude seen in this study.

While deriving the clinical data directly from medical records is a primary strength of this study, an independent validation of these records using other sources—such as the records or reports of primary care physicians—was not performed. However, the high specificity of Form 2728 in the face of the low sensitivity provides an internal validation of the data. To produce spuriously low Form 2728 sensitivity values of the magnitude found by this study, the clinical data itself would need to have an extraordinarily high rate of false positives. Such high false positive rates are extremely unlikely; other studies have shown that medical record data generally have very low false positive rates (between 0 and 8%) (22,25). We therefore conclude that the low sensitivity of Form 2728 is more likely due to errors on Form 2728 than in the clinical data.

Summary

This study found generally low sensitivity but high specificity for 17 prevalent comorbid conditions on Form 2728 when compared with the medical records of 1005 dialysis patients. The sensitivity was higher in PD compared with HD, in diabetic patients compared with nondiabetic patients, and in those with fewer comorbid conditions. This differential reporting of comorbid conditions could result in either under- or overestimation of risk estimates when Form 2728 data are used. Incomplete adjustment for confounding variables also results when defined using Form 2728. Scientific research and policy initiatives that use Form 2728 data should take into account the inherent limitations of these data. Considerable effort should be expended to improve Form 2728 coding if it is to be used to provide accurate estimates of comorbid diseases in ESRD patients.

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