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Kidney Failure and ESRD in the Atherosclerosis Risk in Communities (ARIC) Study: Comparing Ascertainment of Treated and Untreated Kidney Failure in a Cohort Study

Casey M. Rebholz, PhD, MS, MPH, **Josef Coresh, MD, PhD, MHS**, **Shoshana H. Ballew, PhD**, **Blaithin McMahon, MD, PhD**, **Seamus P. Whelton, MD, MPH**, **Elizabeth Selvin, PhD, MPH**, and **Morgan E. Grams, MD, PhD, MHS**
Johns Hopkins University, Baltimore, MD

Abstract

Background—Linkage to the US Renal Data System (USRDS) registry is commonly used to identify end-stage renal disease (ESRD) cases, or kidney failure treated with dialysis or transplantation, but it underestimates the total burden of kidney failure. This study validates a kidney failure definition that includes both kidney failure treated and not treated by dialysis or transplantation. It compares kidney failure risk factors and outcomes using this broader definition to USRDS-identified ESRD risk factors and outcomes.

Study Design—Diagnostic test study with stratified random sampling of hospitalizations for chart review.

Setting & Participants—Atherosclerosis Risk in Communities Study (N=11,530; chart review n=546).

Index Test—USRDS-identified ESRD; treated or untreated kidney failure defined by USRDS-identified ESRD or *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)/ICD-10-CM* code from hospitalization or death.

Corresponding author: Casey M. Rebholz, PhD, MS, MPH, 2024 E. Monument Street, Suite 2-600, Baltimore, MD 21287, Phone: 410-502-2049; Fax: 410-955-04876, crebhol1@jhu.edu.

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Reference Test—For ESRD, determination of permanent dialysis or transplantation; for kidney failure, determination of permanent dialysis, transplantation, or eGFR <15 mL/min/1.73 m^2.

Results—Over 13 years' median follow-up, 508 kidney failure cases were identified, including 173 (34.1%) from the USRDS registry. ESRD and kidney failure incidence were 1.23 and 3.66 cases per 1,000 person-years in the overall population, and 1.35 and 6.59 cases per 1,000 person-years among participants older than 70 years, respectively. Other risk factor associations were similar between ESRD and kidney failure, except diabetes and albuminuria which were stronger for ESRD. Survival at 1 and 5 years were 74.0% and 24.0% for ESRD and 59.8% and 31.6% for kidney failure, respectively. Sensitivity and specificity were 88.0% and 97.3% comparing the kidney failure *ICD-9-CM/ICD-10-CM* code algorithm to chart review; for USRDS-identified ESRD, sensitivity and specificity were 94.9% and 100.0%.

Limitations—Some medical charts were incomplete.

Conclusions—A kidney failure definition including treated and untreated disease identifies more cases than linkage to the USRDS registry alone, particularly among older adults. Future studies might consider reporting both USRDS-identified ESRD and a more inclusive kidney failure definition.

Index words

end stage renal disease (ESRD); chronic kidney disease (CKD); hospitalization; validation studies; chronic kidney failure; untreated renal failure; renal replacement therapy (RRT); sensitivity and specificity; Atherosclerosis Risk in Communities (ARIC) Study; US Renal Data System (USRDS)

Chronic kidney disease is recognized as an important public health issue because of the increasing prevalence and associations with morbidity and mortality.[1] The public health burden of kidney failure treated with dialysis or transplantation (ie, end-stage renal disease [ESRD]) is relatively well-characterized with respect to its prevalence, health care utilization, and cost. In 2011, there were 615,899 ESRD patients in the US population.[2] The overall hospitalization rate for hemodialysis patients was 1.84 admissions per year in 2011.[2] Total Medicare expenditures for ESRD were $34.3 billion in 2011, which is 5.4% higher than in 2010.[2] Less is known about kidney failure not treated with dialysis or transplantation, a disease entity encompassing estimated glomerular filtration rate (eGFR) <15 mL/min/1.73 m^2 without long-term renal replacement therapy, which may be particularly common in older adults.

In epidemiologic research, one strategy for identifying ESRD cases is to link to the US Renal Data System (USRDS) registry, a government-funded effort to collect information on all ESRD patients in the United States.[3-6] Since the USRDS registry only identifies individuals with treated kidney failure, it alone is inadequate for describing the full burden of kidney failure in the population. Prevalence and risk factor studies based on the USRDS registry may represent a healthier sub-group of the total population with kidney failure since the registry does not capture individuals who choose not to initiate renal replacement therapy or who experience pre- or early-dialysis mortality.[7]

In an effort to capture all cases of treated and untreated kidney failure in observational cohort data, we created a kidney failure definition that combined linkage to the USRDS registry, and an algorithm using billing codes abstracted from hospitalizations and deaths. The objectives of this study were: 1) to assess the validity of the proposed billing code algorithm against physician review of medical records, 2) to assess the validity of USRDS-identified ESRD against physician review of medical records, and 3) to investigate whether there are differences in risk factors and outcome associations with the broader definition of treated and untreated kidney failure compared with the USRDS-identified ESRD cases in the Atherosclerosis Risk in Communities (ARIC) Study.

Methods

Study Design and Participants

The ARIC Study is a prospective cohort study of 15,792 predominantly black and white men and women, aged 45-64 years at initial enrollment. The study has previously been described in detail elsewhere.[8] In brief, participants were recruited from four U.S. communities: Forsyth County, North Carolina; Jackson, Mississippi; suburban Minneapolis, Minnesota; and Washington County, Maryland. The initial study visit occurred in 1987-1989, and there have been four subsequent follow-up visits in 1990-1992 (n=14,348), 1993-1995 (n=12,887), 1996-1998 (n=11,656), and 2011-2013 (n=6,538). Participants have been contacted annually by phone since enrollment. For analyses of incident treated or untreated kidney failure and incident ESRD, ARIC Study visit 4 (1996-1998) was used as a baseline, with only those participants free of kidney failure and USRDS-identified ESRD included (N=11,530). Study participants provided informed consent and the study protocol was approved by the institutional review boards at all participating universities.

Data Collection

During the study visits, trained staff administered interviews to obtain information on demographics, clinical history, and health behaviors. Participants were asked about hospitalizations over the prior year during the annual follow-up phone interview. In addition, hospitalizations were identified through active surveillance of local hospital discharge lists. For each hospitalization, *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)*, diagnosis and procedure codes were abstracted from medical records and discharge summaries. Vital status was ascertained by annual follow-up phone interview with a proxy, hospital discharge status, local newspaper obituaries, state death records, and the National Death Index. All *International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM)*, codes, including the underlying cause of death, were abstracted from the death certificates obtained from the Department of Vital Statistics. Active surveillance of hospitalizations and deaths occurred continuously from enrollment through follow-up. Outcomes were assessed between February 1, 1996 (ARIC Study visit 4) and December 31, 2008 for validation, corresponding to the most recent data at the time at which charts were requested, and through December 31, 2010 for all other analyses in the present study.

Treated or Untreated Kidney Failure Definition

Details about the kidney failure definition is provided in Table S1 (provided as online supplementary material). The proposed definition for treated or untreated kidney failure was based on three sources: 1) linkage to the USRDS registry (treated kidney failure); 2) ICD-9-CM and ICD-10-CM codes from hospitalizations and deaths that represented kidney failure, transplantation, and dialysis (treated or untreated kidney failure); and 3) a study visit eGFR <15 mL/min/1.73 m^2 calculated with the Chronic Kidney Disease Epidemiology Collaboration creatinine equation. For the present study, there were no study visits during follow-up, and, as such, no incident cases were identified through the latter mechanism. To validate the diagnostic code algorithm, the reference kidney failure definition was physician-determined kidney failure (requirement for dialysis judged to be permanent, kidney transplantation, or eGFR <15 mL/min/1.73 m^2) based on medical chart review.

ESRD Definition

Linkage to the USRDS registry was performed for all ARIC Study participants. Those participants present in the registry were considered to have ESRD. To assess the validity of USRDS-identified ESRD, the reference definition was physician-determined treated kidney failure (incident or prevalent dialysis judged to be permanent, incident or prevalent living/ deceased donor kidney transplantation) based on medical chart review.

Chart Review Procedure

Chart review was conducted for a random sample of hospitalizations within each of the four ARIC Study communities, with oversampling for dialysis and transplantation records (Table S1).[9,10] For each hospitalization, the history and physical examination, nephrology consult (if available), discharge summary, and inpatient laboratory reports were collected in order to perform the chart review. All medical records were de-identified prior to chart review. Two physicians (?.?., ?.?.) independently reviewed charts for each selected participant. The reviewers were blinded to ICD-9-CM and ICD-10-CM codes and USRDS records. Discrepancies in kidney failure classification between the two reviewers were resolved through discussion, and consensus was obtained in all cases.

Statistical Analysis

Descriptive statistics, including means for continuous variables and proportions for categorical variables, were used to describe baseline (ARIC Study visit 4) characteristics of the case groups and of study participants free of ESRD and kidney failure at the end of follow-up. Incidence rates, overall and by age groups, were used to describe the burden of advanced kidney disease. Cox proportional hazards regression was used to estimate ESRD and kidney failure risk associated with participant characteristics. Seemingly unrelated regression was used to compare risk estimates from the two separate regression models for ESRD and kidney failure outcomes.[11] Kaplan-Meier curves were used to illustrate time from identification of ESRD and kidney failure cases until death. For the validation study, the kidney failure algorithm based on ICD-9-CM and ICD-10-CM diagnostic codes (treated or untreated kidney failure) and cases of USRDS-identified ESRD (treated kidney failure) were compared to chart review, weighting by the inverse probability of selection, to estimate sensitivity, specificity, positive predictive value, and negative predictive value across all ARIC Study participant hospitalizations, as done previously.[9,10] Analyses were performed using Stata version 13.1 (StataCorp LP, College Station, TX).

Results

Validation of Kidney Failure and ESRD Definitions

Out of the stratified random sample of 655 medical charts that were requested, 546 (83%) had sufficient information to adjudicate treated or untreated kidney failure status (Figure S1). Compared to medical chart review, the sensitivity of the treated or untreated kidney failure algorithm based on ICD-9-CM and ICD-10-CM codes was 88.0% and specificity was 97.3% (Table 1, Table S2). Positive and negative predictive values were 70.2% and 99.1%, respectively, for the kidney failure algorithm.

Comparing USRDS-identified ESRD to medical chart review, sensitivity was 94.9%, and specificity was 100.0%. The one participant in the USRDS registry who was determined not to have ESRD by chart review required dialysis only temporarily. The 37 participants with ESRD by chart review but not yet included in the USRDS registry had the following characteristics: 27 died within six months of the reviewed hospitalization (25 of 27 within one month) and were never registered; 9 entered into the USRDS registry at a later date (6 within three months of the hospitalization); and 1 was never included in the USRDS registry (for unknown reasons, despite multiple hospitalizations for dialysis).

Baseline Characteristics of Participants Developing Kidney Failure and ESRD

Among 11,530 study participants, there were 173 (1.6%) ESRD cases identified by USRDS registry linkage and 508 (4.4%) treated or untreated kidney failure cases identified using the proposed definition during a median follow-up of 13 years (Table 2). At ARIC Study visit 4 (baseline), ESRD cases were younger and more likely to be black than treated or untreated kidney failure cases (Table 2, Table S3). Participants developing ESRD were also more likely to have worse kidney function and traditional kidney disease risk factors at baseline, including lower eGFR, moderately or severely increased albuminuria, hypertension, and diabetes. By definition, all of the USRDS- identified ESRD cases were also considered kidney failure cases.

Composition of Treated or Untreated Kidney Failure Cases

Approximately one-third of the kidney failure cases (173 of 508 [34.1%]) were identified as ESRD by linkage with the USRDS registry (Table 3), with the majority of these (164 [94.8%]) also identified through the billing code algorithm by having a kidney failure-related hospitalization or death. Ninety additional kidney failure cases (17.7%) were identified through ICD-9-CM and ICD-10-CM codes associated with a death. The remaining 245 were identified through a hospitalization: 16 (3.1%) had an untreated kidney failure code and a dialysis code, 207 (40.7%) had an untreated kidney failure code only, 21 (4.1%) had a dialysis code only, and 1 (0.2%) had a transplantation code. The composition of treated or untreated kidney failure cases varied by age, with a smaller proportion with

USRDS-identified ESRD and a larger proportion of kidney failure-related hospitalization or death among older participants (Figure 1, Table S3).

Incidence of ESRD and Kidney Failure by Age

The incidence rate of ESRD was relatively similar across age groups, ranging from 0.84 (95% confidence interval [CI], 0.50-1.42) to 1.35 (95% CI, 0.87-2.09) per 1,000 person-years among 51-to 55-year-olds and 71- to 75-year-olds, respectively (Figure 2). Conversely, there was a strong, positive, graded relationship between age group and treated or untreated kidney failure (incidence rates of 1.58 [95% CI, 1.08-2.33], 2.69 [95% CI, 2.24-3.25], 3.48 [95% CI, 2.93-4.14], 4.90 [95% CI, 4.17-5.76], and 6.59 [95% CI, 5.40-8.05] per 1,000 person-years for those aged 51-55, 56-60, 61-65, 66-70, and 71-75 years, respectively). Among participants in the oldest age group (71-75 years), the incidence of treated or untreated kidney failure was approximately five times higher than the incidence of ESRD.

Risk Factor Associations With ESRD and Kidney Failure

Traditional kidney disease risk factors, including sex, race, hypertension, diabetes, prevalent coronary heart disease, and albuminuria, were significantly associated with both kidney outcomes, i.e., USRDS-identified ESRD (treated kidney failure) and overall kidney failure (treated or untreated) (Table 4). The strength of the associations of risk factors with kidney outcomes differed between ESRD and kidney failure for age ($p<0.001$), diabetes ($p=0.01$), and albuminuria ($p<0.001$). In adjusted analyses, older age was significantly associated with higher risk of overall kidney failure (treated or untreated), but not ESRD (hazard ratios per 5-year increment older of 1.29 [95% CI, 1.20-1.40; $p<0.001$] and 1.11 [95% CI, 0.97-1.26; $p=0.1$] for kidney failure and ESRD, respectively). Participants with diabetes had a 3.77 times (95% CI, 2.65-5.36) higher risk of ESRD compared to 2.51 times (95% CI, 2.06-3.04) higher risk of overall kidney failure (treated or untreated). Relative to those with normal to mildly increased albuminuria, participants with severely increased albuminuria and moderately increased albuminuria, respectively, had a 30-fold and 6-fold higher risk of developing ESRD, and 11-fold and 3-fold higher risk of developing overall kidney failure (treated and untreated).

Outcomes After Kidney Failure and ESRD

Within the first two years, mortality was higher for kidney failure (1-year survival, 59.8%; 2-year survival, 51.8%) than ESRD (1-year survival, 74.0%; 2-year survival, 58.0%) (Figure 3A, Figure 3B). However, after a longer follow-up period, mortality was higher for ESRD (5-year survival, 24.0%; 10-year survival, 13.5%) than kidney failure (5-year survival, 31.6%; 10-year survival, 16.5%). The median survival time was 2.2 years after kidney failure designation (treated or untreated) and 2.4 years after ESRD designation.

Discussion

In the present study, we evaluated a definition for kidney failure that encompasses both treated and untreated kidney failure utilizing billing code data from hospitalizations and deaths, as well as linkage to the USRDS registry. We described differences between the more traditional outcome of USRDS-identified ESRD and the more inclusive outcome of treated or untreated kidney failure. Kidney failure was increasingly common in older age, whereas ESRD was more strongly associated with traditional risk factors such as diabetes and albuminuria. We compared the billing code algorithm and the USRDS ESRD definition to medical chart review of a stratified random sample of all participants, reporting good agreement with both, and a sensitivity of 88% and specificity of 97% for the billing code algorithm. Thus, both the ESRD and overall kidney failure (treated or untreated) outcomes appear valid and important. Selection of one outcome over the other should be determined by research purpose.

Many prospective cohorts, including the ARIC Study, have used billing code-identified kidney failure almost interchangeably with ESRD defined by entry into the USRDS registry.[12] In the present study, we reported similarities between ESRD and treated or untreated kidney failure cases. In particular, traditional risk factors, including sex, race, hypertension status, diabetes status, history of coronary heart disease, and albuminuria, were significantly associated with both outcomes. In addition, there was a high rate of mortality for both ESRD and kidney failure. However, there were also some differences between ESRD and the more inclusive kidney failure definition.

We found that many more individuals developed kidney failure than ESRD as identified by USRDS registry linkage, particularly among the oldest segment of the population. Likewise, in the Alberta Kidney Disease Network, rates of untreated kidney failure were five times higher among the oldest (85 years or older: adjusted rate per 1,000 person-years, 20.0 [95% CI: 15.8-25.2]) compared to the youngest (18-44 years: adjusted rate per 1,000 person-years, 3.5 [95% CI, 1.6-8.0; $p<0.001$]) individuals.[7] This age disparity was also reported in a case-control study nested within the Second National Health and Nutrition Examination Survey (NHANES II), in which younger adults (30- to 59-year-olds) were five times more likely to receive renal replacement therapy compared to those 60 years of age or older (odds ratio, 5.57; 95% CI, 1.72-18.0).[13] Reasons for this disparity are unknown, but it may be driven by patient and/or provider preference: older people may choose not to initiate dialysis and physicians may not recommend such treatment to patients due to their older age.[14] Studies that define kidney failure based on initiation of renal replacement therapy alone may underestimate the incidence of late kidney disease among older individuals, a large and growing segment of the US population.

In some cases, the proposed kidney failure definition incorporating diagnostic codes may be a more useful outcome than treated kidney failure based on USRDS-identified ESRD. For instance, the kidney failure algorithm may be preferable for assessing the overall burden of treated and untreated advanced kidney disease, for more accurately determining the date of incident kidney disease, and for enumerating deaths due to kidney failure. In our analysis, sometimes there was a delay between the date of treated kidney failure-related hospitalization and incorporation into the USRDS registry. This lag time was usually only a couple weeks, but ranged up to 1.5 years, an unexpected finding given the 45-day deadline for filing the Centers for Medicare & Medicaid Services Medical Evidence Report.[15] In addition, the kidney failure definition captured data about many people who died within months of initiating dialysis. Thus, the kidney failure definition addresses a known limitation of the USRDS registry, the survival bias introduced by only registering those individuals who survive for a period of time after initiating renal replacement therapy.[16,17] Furthermore, the kidney failure definition based on diagnostic codes and the USRDS registry incorporates the competing event of death in advanced kidney disease that precedes renal replacement therapy.[18,19]

There may be situations in which USRDS-identified ESRD is the more appropriate outcome definition. When data on hospitalizations and deaths are not accessible, then linkage to the USRDS registry may be more efficient. Additionally, treated cases of advanced kidney disease may be the intended study population. Those who reach eGFR <15 mL/min/1.73 m^2 may never go on to require renal replacement therapy, or the times until initiation of renal replacement may be quite heterogeneous, as demonstrated in the African American Study of Kidney Disease and Hypertension (AASK) cohort study.[20] Enumeration of ESRD cases may be more relevant than that of overall (treated and untreated) kidney failure cases for projecting Medicare spending or assessing kidney transplantation demand.

An interesting finding was the stronger association of diabetes and albuminuria with risk of ESRD than with treated or untreated kidney failure. This may signify that the USRDS registry captures a more severe form of disease, since both diabetes and albuminuria are associated with kidney disease progression.[21-23] On the other hand, it might reflect treatment differences, whereby providers might be more likely to initiate renal replacement therapy, or to do so sooner, in persons with diabetes and/or albuminuria. This is consistent with previous studies demonstrating that persons with diabetes were more likely to initiate dialysis and preemptive kidney transplantation at higher eGFR levels than those without diabetes.[24,25]

Strengths of this study include the large, broadly generalizable study population with a considerable number of kidney disease events over a lengthy follow-up period. The findings from the validation study are comprehensive, in that the proposed method for ascertaining kidney disease outcomes via active surveillance of hospitalizations and deaths was compared to both medical chart review as well as the USRDS registry. We sampled records from a stratified random sample of all study participants with and without kidney disease, which allows for greater generalizability than a single nephrology clinic-based study.

A limitation is that some medical records had insufficient information to adequately assess kidney disease status. However, the vast majority of requested records was retrieved and included in the present analysis. Furthermore, the missing data would be expected to be non-differential by kidney disease status. If the proposed kidney failure definition is applied to a population with a low prevalence of kidney disease, then the positive predictive value would be lower than estimated in the current study. Another limitation is that we did not have access to information about kidney function recovery for those who were included in the USRDS registry. It is possible that there was misclassification of acute kidney injury cases and in determining the cause of death to be kidney failure based on death certificate information.

In conclusion, we propose the use of a kidney failure definition based on billing code information from hospitalizations and deaths, linkage to the USRDS registry, and ascertainment of eGFR at planned study visits. This definition could be utilized within ongoing prospective cohort studies as well as studies of clinic-based populations with access to electronic medical records. Use of the USRDS registry alone to define ESRD cases only identified one third of all kidney failure cases but might be preferable for efficiency and cost-effectiveness, or when the study outcome of interest is long-term renal replacement therapy. Use of the proposed kidney failure definition may be preferable in studies intending to generalize to both treated and untreated kidney failure cases, when accuracy of kidney failure incidence is important, and for inclusion of deaths due to kidney failure. Future research studies might consider reporting this kidney failure outcome based on ICD-9-CM and ICD-10-CM codes for hospitalizations and deaths in addition to USRDS-identified ESRD cases.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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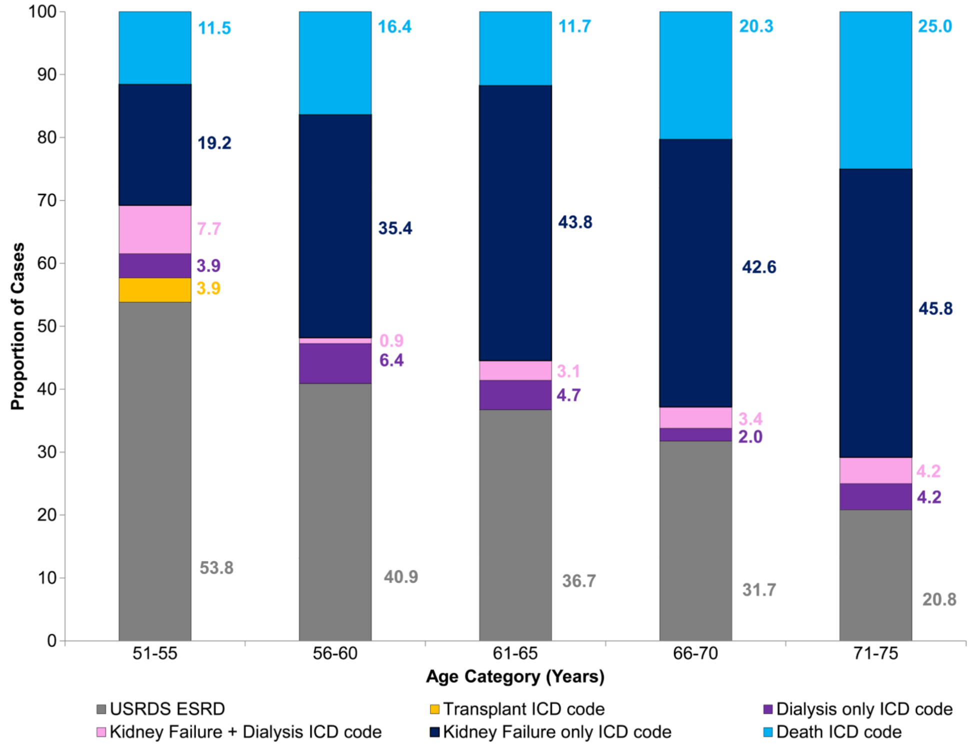

Figure 1. Classification* of Kidney Failure Cases by Age Category

* Categories are mutually exclusive and hierarchical in the following order: USRDS ESRD; ICD code for kidney failure death; ICD code for kidney failure hospitalization (586, 585.5, 585.6, 403.01, 403.91, N18.5, N18.6, N19, I12.0); ICD code for dialysis hospitalization (V45.1, V56, 39.95, 54.98, Z99.2, Z49, Z45.2); ICD code for transplantation hospitalization (V42.0, 55.6, 996.81, Z94.0).

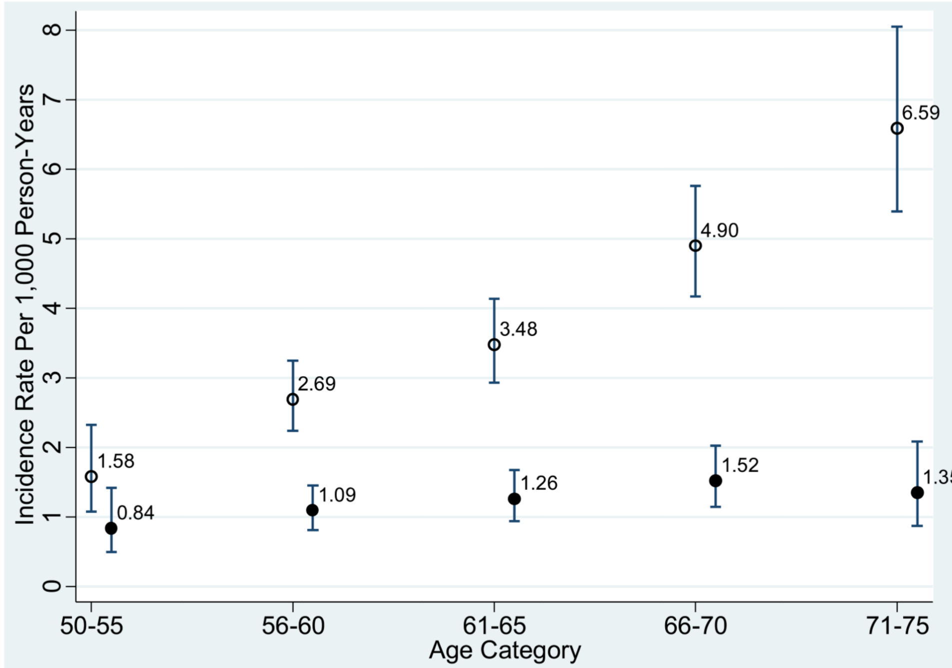

Figure 2. Incidence Rates per 1,000 Person-Years (95% Confidence Interval) for Kidney Failure and End-Stage Renal Disease by Age Categories

$p<0.001$ for test of difference in hazard ratio for kidney failure vs. hazard ratio for end-stage renal disease associated with age using seemingly unrelated regression; hollow circle: kidney failure; solid circle: end-stage renal disease; bar: 95% confidence intervals

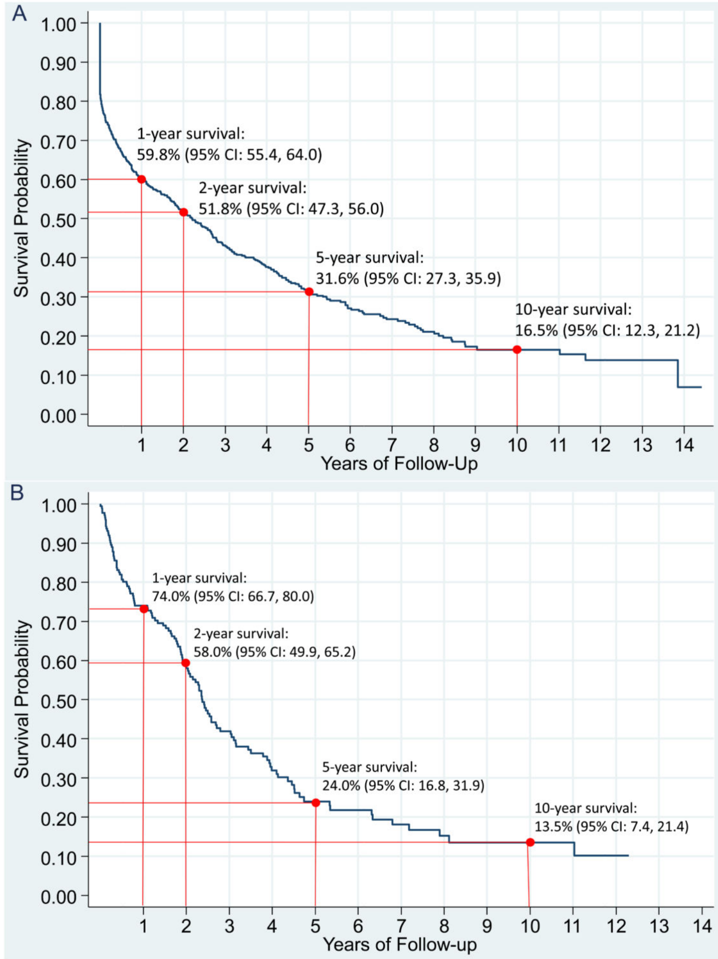

Figure 3. Kaplan-Meier Plots of Time from Kidney Disease Event until Death for (A) Kidney Failure Cases and (B) End-Stage Renal Disease Cases

Table 1

Validity of Kidney Failure-Related Diagnostic Codes Compared with Chart Review

	Estimate (95% CI)
Sensitivity	88.0% (67.6%-96.3%)
Specificity	97.3% (96.0%-98.3%)
Positive Predictive Value	70.2% (55.8%-81.5%)
Negative Predictive Value	99.1% (97.3%-99.7%)

Note: Chart review criteria for classification as kidney failure case were: incident or prevalent renal replacement therapy judged to be permanent, incident or prevalent living/deceased donor kidney transplantation, estimated glomerular filtration rate <15 mL/min/1.73 m^2 (as described in Table S1).

Validity estimates calculated based on review of 546 charts which were randomly selected within each of the four ARIC Study communities, with oversampling for dialysis and transplantation records.

Hospitalizations for medical chart review were selected from ten strata corresponding to disease status using *International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM)* and *ICD-10-CM* codes. Sampling fractions per stratum are as follows: 1) AKI only, 32/686=4.7%; 2) AKI and CKD, 35/547=6.4%; 3) AKI with receipt of dialysis, 22/31=71.0%; 4) AKI with receipt of dialysis and CD, 58/86=67.4%; 5) CKD only, 66/2,927=22.5%; 6) CKD with receipt of dialysis, 151/1,041=14.5%; 7) dialysis only, 13/57=22.8%; 8) transplantation, 6/32=18.8%; 9) cardiovascular disease only, 105/15,416=0.7%; 10) none of the above, 58/13,356=0.4%. For stratum 6 (CKD with receipt of dialysis) and stratum 7 (dialysis only), separate weights were used for first hospitalizations and all other hospitalizations.

AKI, acute kidney injury; CI, confidence interval; CKD, chronic kidney disease

Table 2

Baseline Participant Characteristics According to Kidney Failure Status

	No Kidney Failure or ESRD	ESRD[a]	Kidney Failure[b]
No. of participants	11,022 (95.6)	173 (1.6)	508 (4.4)
Incidence rate (95% CI)*	--	1.23 (1.06-1.42)	3.66 (3.36-3.99)
Age (y)	62.7 ±5.7	63.6 ±5.6[c]	64.8 ±5.6[c]
Female sex	56.4% (6,213)	51.4% (89)	44.1% (224)[c]
Black race	21.6% (2,382)	46.2% (80)[c]	34.6% (176)[c]
BMI (kg/m^2)	28.7 ±5.6	31.1 ±6.1[c]	30.5 ±6.3[c]
History of CHD	7.9% (861)	22.1% (38)[c]	22.5% (113)[c]
Current smoker	14.7% (1,608)	19.8% (34)	18.6% (94)[c]
Current drinker	50.0% (5,476)	31.4% (54)[c]	33.1% (167)[c]
High school education or higher	81.5% (8,968)	65.7% (113)[c]	65.2% (330)[c]
Medicaid insurance[d]	7.6% (742)	18.1% (23)[c]	17.9% (72)[c]
Married[e]	76.1% (8,332)	69.9% (121)	72.3% (365)
Annual household income ≤$25,000[f]	30.9% (3,252)	53.7% (88)[c]	49.2% (237)[c]
Professional/management occupation	30.1% (3,286)	25.0% (43)	22.4% (113)[c]
Total cholesterol (mg/dL)	200.9 ±36.9	208.3 ±49.4[c]	199.1 ±41.6
LDL cholesterol (mg/dL)	122.7 ±33.4	126.1 ±38.7	122.2 ±35.0
HDL cholesterol (mg/dL)	50.2 ±16.5	44.6 ±16.7[c]	44.0 ±14.8[c]
Triglycerides (mg/dL)	142.5 ±84.0	195.4 ±190.4[c]	171.8 ±138.7[c]
Hypertension	46.2% (5,075)	80.9% (140)[c]	77.4% (390)[c]
Diabetes	15.4% (1,686)	63.7% (109)[c]	46.4% (234)[c]
eGFR (mL/min/1.73 m^2)	87.0 ±15.1	65.9 ±26.9[c]	71.5 ±23.6[c]
Albuminuria			
<30 mg/g	93.1% (10,163)	41.5% (71)[c]	63.8% (319)[c]
30-300 mg/g	5.9% (645)	26.3% (45)	20.2% (101)
>300 mg/g	1.0% (111)	32.2% (55)	16.0% (80)

Note: Unless otherwise indicated, values for categorical variables are given as number (percentage); values for continuous variables are given as mean ± standard deviation. Conversion factors for units: cholesterol in mg/dL to ×mmol/L, 0.02586; triglycerides in mg/dL to mmol/L, ×0.01129. BMI, body mass index; CHD, coronary heart disease; CI, confidence interval; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein;

[a] ESRD = US Renal Data System registry (treated kidney failure).

[b] Kidney failure = kidney failure-related International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)/ICD-10-CM code from hospitalization or death or U.S. Renal Data System registry (treated or untreated kidney failure).

[c] p <0.05 for difference between participant characteristic compared to those with neither kidney failure nor ESRD

[d] After excluding missing data for medical insurance, n=9,749 for neither kidney failure nor ESRD, n=127 for ESRD, and n=402 for kidney failure.

[e]After excluding missing data for marital status, n=10,955 for neither kidney failure nor ESRD, n=173 for ESRD, and n=505 for kidney failure.

[f]After excluding missing data for income, n=10,519 for neither kidney failure nor ESRD, n=164 for ESRD, and n=482 for kidney failure.

[*]Incidence rate is per 1,000 person-years in overall population.

Table 3
Clinical Outcomes According to Kidney Failure Status

	No Kidney Failure or ESRD	ESRD[a]	Kidney Failure[b]
No. of participants	11,022 (95.6)	173 (1.6)	508 (4.4)
No. hospitalizations	3.4 ±3.8	12.0 ±7.5	10.5 ±7.6
No. hospitalizations/y	0.4 ±1.5	1.3 ±0.9	1.4 ±3.2
Kidney failure	0.0% (0)	100.0% (173)	100.0% (508)
USRDS ESRD	0.0% (0)	100.0% (173)	34.1% (173)
Death	19.5% (2,146)	68.8% (119)	72.6% (369)

Note: Unless otherwise indicated, values for categorical variables are given as number (percentage); values for continuous variables are given as mean ± standard deviation.
ESRD, end-stage renal disease; SD, standard deviation; USRDS, US Renal Data System registry

[a]ESRD = identified from USRDS

[b]Kidney failure = identified from kidney failure-related International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)/ICD-10-CM code from hospitalization or death or USRDS registry (treated or untreated kidney failure)

Table 4

Association between Baseline Participant Characteristics, Incident Kidney Failure, and Incident ESRD

	Kidney Failure[a]		ESRD[b]		P for HR difference[d]
	HR[c] (95% CI)	P	HR[c] (95% CI)	P	
Age, per 5-y older	1.29 (1.20-1.40)	<0.001	1.11 (0.97-1.26)	0.1	<0.001
Male sex	1.70 (1.41-2.05)	<0.001	1.40 (1.02-1.93)	0.04	0.08
Black race	1.48 (1.21-1.80)	<0.001	1.92 (1.38-2.67)	<0.001	0.1
Hypertension	2.21 (1.77-2.77)	<0.001	1.81 (1.19-2.74)	0.006	0.3
Diabetes	2.51 (2.06-3.04)	<0.001	3.77 (2.65-5.36)	<0.001	0.01
Prevalent CHD	2.02 (1.62-2.53)	<0.001	2.03 (1.39-2.97)	<0.001	0.7
Albuminuria					
<30 mg/g	1.00 (reference)		1.00 (reference)		
30-300 mg/g	2.93 (2.31-3.72)	<0.001	5.56 (3.73-8.28)	<0.001	<0.001
>300 mg/g	11.2 (8.55-14.6)	<0.001	29.5 (19.8-44.2)	<0.001	<0.001

HR, hazard ratio; CI, confidence interval; CHD, coronary heart disease; ESRD, end-stage renal disease; USRDS, US Renal Data System

[a]ESRD = identified from USRDS registry (treated kidney failure)

[b]Kidney failure = identified from kidney failure-related International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM)/ICD-10-CM code from hospitalization or death or USRDS registry (treated or untreated kidney failure)

[c]Adjusted HRs from regression model including all characteristics listed in table.

[d]P for test of difference in HR for kidney failure vs. HR for ESRD for the respective characteristic using seemingly unrelated regression