Predictors of End-stage Renal Disease in the Urban Poor

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Abstract

Background: Despite the disproportionate burden of end-stage renal disease (ESRD) among traditionally underserved populations, the influence of social and clinical factors on incident ESRD in the urban poor is poorly understood. We sought to examine the prognostic values of social and clinical factors on risk of progression of established chronic kidney disease (CKD) to ESRD in the urban poor.

Methods: We studied 15,353 individuals with moderate to advanced CKD who had received ambulatory care within a large public health system in northern California during 1996-2005. The primary outcome was progression to ESRD through December 31, 2005 as ascertained by the US Renal Data System registry.

Results: Overall, 559 cases of ESRD occurred during 55,538 person-years of follow-up. In this public healthcare setting, among traditional predictors of ESRD, younger age, male sex, non-white race-ethnicity, Medicaid or Medicare health insurance coverage, diabetes, lower kidney function, higher proteinuria, lower hemoglobin level and lower serum albumin concentration were significantly associated with a higher adjusted risk of progression to ESRD ($P<0.001$ for all variables). There was no significant association between HIV/AIDS ($P=0.07$), viral hepatitis ($P=0.11$), homelessness ($P=0.89$) or non-English language ($P=0.27$) and risk of incident ESRD after concomitant adjustment for age, sex, race-ethnicity, health insurance, kidney function, proteinuria, comorbid conditions, hemoglobin and serum albumin levels. In contrast, a history of substance abuse was associated with a significantly lower adjusted risk of progressing to ESRD ($P<0.001$).

Conclusions: In the urban healthcare safety net, we found no evidence that social factors including homelessness, substance abuse, non-English language status, or chronic viral diseases were associated with a higher risk of ESRD. Our results highlight the importance of addressing traditional risk factors for progressive CKD to reduce the disproportionate burden of ESRD among disadvantaged populations.

Introduction

In the US, end-stage renal disease (ESRD) disproportionately affects the poor and members of racial-ethnic minority groups.[1-4] Recent data from the US Renal Data System indicate that nearly one-third of persons initiating treatment for ESRD are now uninsured or covered by Medicaid, the US health insurance program for persons of severely limited financial means.[5]

Due to their relatively limited options for ongoing ambulatory care, many of America's poor and underinsured seek medical care from urban public hospitals and "safety net" health clinics. Collectively, these facilities provide healthcare to millions of uninsured and underserved individuals across the nation.[6,7] Because chronic kidney disease (CKD) has historically been poorly coded in administrative data and because there is no system for tracking the care of patients who are uninsured or covered by Medicaid within the US,[8,9] few studies have examined predictors of progression of CKD to ESRD in these underserved populations.[10] Prior studies in insured or universally screened populations have identified non-white race, hypertension, diabetes, proteinuria and index kidney function as the most important predictors of incident ESRD.[1,2,4,11,12] However, the influence of social or societally-driven clinical factors (i.e., factors that influence health by affecting exposure and vulnerability to disease, and access to health coverage or healthcare) such as poverty, substance abuse and homelessness on incident ESRD is unknown. Although kidney disease is a well-recognized consequence of infection with human immunodeficiency virus (HIV),[13,14] little is known about the role of chronic viral diseases on subsequent progression from established CKD to ESRD.

To better understand whether these social and clinical factors predict progression of established CKD to ESRD in the urban poor, we examined longitudinal data from a diverse cohort of adults with non-dialysis dependent CKD who received ambulatory care in the Community Health Network, a large safety net healthcare provider operated by the City and County of San Francisco, California. We hypothesized that in this population, chronic viral diseases, substance abuse, non-English language, and homelessness would be positively associated with an increased risk of ESRD independent of age, sex, race-ethnicity, kidney function, proteinuria, and other traditional ESRD risk factors.

Methods

Study design and setting

We conducted a retrospective cohort study of subjects with non-dialysis dependent CKD stages 3-5 who received ambulatory care in the Community Health Network (CHN) from January 1, 1996 to December 31, 2005. The CHN is the healthcare delivery system of the Department of Public Health of the City and County of San Francisco. Along with a consortium of not-for-profit primary care clinics (Consortium), the CHN forms the backbone of San Francisco's healthcare safety net system and offers an array of healthcare services including primary care, specialty care and acute care. The CHN includes an acute care hospital (San Francisco General Hospital) with on-site primary and specialty care clinics, as well as 11 community-based primary care clinics. Providers in these clinics, as well as those practicing in the Consortium clinics rely on San Francisco General Hospital for a significant portion of their laboratory testing, specialty referrals and inpatient care. All of the CHN and Consortium clinics have access to the San Francisco Department of Public Health's electronic health information system to assist in shared patient care. The CHN provides ambulatory and acute care to the majority of the estimated 130,000 uninsured residents of San Francisco. Services are available for free, or on a sliding scale based on income.[15]

Study subjects

The study cohort comprised 15,353 adults aged ≥ 20 years with non-dialysis dependent CKD stages 3-5 who received routine ambulatory care in the CHN from January 1, 1996 to December 31, 2005. We defined CKD based on at least two outpatient estimated glomerular filtration rate (eGFR) measurements <60 mL/min/1.73 m^2 as calculated by the re-expressed Modification of Diet in Renal Disease (MDRD) study equation based on calibrated serum creatinine, age, race and sex that were separated by at least one year.[16,17] We considered participants to be receiving regular ambulatory care if they had at least one additional CHN outpatient encounter subsequent to the index serum creatinine date. We imposed these restrictions to ensure that the study cohort comprised persons who meet the National

Kidney Foundation definition for CKD stages 3-5 and who had access to ambulatory care, rather than individuals with misclassified acute kidney injury or those who transiently visited the CHN.

Outcome Measures

The primary outcome measure was progression to ESRD, defined as having a first service date for maintenance dialysis or kidney transplantation. We defined survival time as the time from the second outpatient eGFR date until ESRD, death or the end of follow-up through December 31, 2005, whichever occurred first.

Independent Variables

We extracted data on important sociodemographic and clinical factors that we hypothesized might predict progression of established CKD to ESRD in the urban healthcare safety net based on prior studies.[1,2,11-14] Covariates were defined within the two-year period preceding and closest to the index qualifying eGFR measurement. Individual-level sociodemographic covariates included patient age, sex, race-ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, Asian/Pacific Islander, or other), health insurance coverage (uninsured, Medicaid, Medicare, or commercial/other), primary spoken language (English, Spanish, Cantonese, or other), housing status (domiciled or homeless), and annual household income based on administrative data. We ascertained comorbid conditions based on established algorithms using discharge diagnostic codes, ambulatory diagnostic codes and procedural codes (**Appendix A**) for diabetes, hypertension, cardiovascular disease (defined as coronary artery, cerebrovascular, or peripheral vascular disease), hepatitis B virus (HBV), hepatitis C virus (HCV), HIV or AIDS, alcoholism and drug abuse. Laboratory predictors included eGFR, hemoglobin and serum albumin concentrations, and the presence and severity of proteinuria. We classified proteinuria as normal (urine albumin-to-creatinine ratio [ACR] <30 mg/g or urine dipstick negative), mild (ACR 30-300 mg/g or urine dipstick trace-1+), or heavy (ACR >300 mg/g or urine dipstick ≥2+).[12,18]

Statistical analysis

We examined the distribution of covariates and outcomes using side-by-side boxplots and

histograms where appropriate. To examine the independent associations of these predictors on risk of incident ESRD, we used Cox proportional hazards regression models.[19] In the adjusted model, we incorporated fixed demographic factors (age, sex, and race-ethnicity), social factors (income, homeless status, health insurance coverage, and primary spoken language), comorbid conditions that were known to associate with the aforementioned social factors (HBV, HCV, HIV or AIDS, and substance abuse), established risk factors for death and progressive CKD (diabetes, hypertension, and cardiovascular disease) and laboratory measures associated with CKD severity (eGFR, proteinuria, hemoglobin, and serum albumin). To test whether the associations of proteinuria, index eGFR and risk of ESRD might differ according to age, race-ethnicity, sex or diabetes status, we incorporated interaction terms between proteinuria or eGFR and each covariate of interest and tested whether the estimated coefficients for the interaction terms differed from zero using the Wald test. We examined the adequacy of the functional form of each covariate by examining plots of Martingale residuals against each covariate. For all models, we tested for violations of the proportional hazards assumption by examining plots of -log(-log [survival rate]) against log (survival time). To reduce potential bias caused by excluding patients with missing data, we performed multiple imputation using the Markov chain Monte Carlo method with 10 imputations for these variables.[20] We considered a two-tailed P-value <0.05 as statistically significant without adjustment for multiple comparisons. We used Stata statistical software for all analyses (Stata MP version 11.0, Stata Corp, College Station, TX). The United States Renal Data System and the respective Institutional Review Boards at the University of Washington and University of California San Francisco approved the study protocol.

Results

Patient Characteristics

During the study period 15,353 adults with non-dialysis dependent CKD stages 3-5 received ambulatory care within CHN. In contrast with CKD cohorts from other North American studies, approximately one-half of subjects were younger than 60 and over one-fourth were younger than 50. The distribution of race-ethnicity (72% nonwhite) and health insurance coverage (41% uninsured or enrolled in Medicaid) were consistent with estimates of populations generally served by members of the National Association of Public Hospitals.[21] The prevalence of alcoholism (8%), drug abuse (16%), and chronic viral diseases including viral hepatitis (5%) and HIV (3%) were also notable as compared with the near absence of these comorbidities in prior CKD studies conducted in universally insured populations.[22,23]

As shown in Table 1, patients who eventually developed ESRD were younger and more likely to be male, homeless, of black race, covered by Medicaid and speak English as their primary language as compared with those who did not develop ESRD. Patients who developed ESRD also had a higher prevalence of diabetes and lower prevalence of hypertension, cardiovascular disease and substance abuse than those who did not progress to ESRD (**Table 1**). In contrast with subjects who did not progress to ESRD, many of whom had moderate CKD (eGFR of 30 to 59 ml/min/1.73 m^2) and little to no proteinuria, most subjects who progressed to ESRD had advanced CKD (eGFR <30 ml/min/1.73 m^2) and mild to heavy proteinuria at baseline. They also had lower mean levels of hemoglobin and serum albumin as compared with patients who did not progress to ESRD (**Table 1**).

Progression to End-stage Renal Disease

In analyses adjusted for age group, sex, race-ethnicity, income, health insurance coverage, primary language, comorbid conditions, eGFR, proteinuria, and hemoglobin and serum albumin levels, several factors independently predicted progression to ESRD (**Table 2**). Lower eGFR category and higher degrees of proteinuria were the most potent predictors of progression to ESRD. Other covariates associated with a significantly higher adjusted risk of progression to ESRD included younger age, male

sex, nonwhite race-ethnicity, diabetes and Medicaid and Medicare health insurance coverage (P<0.001 for all comparisons). Substance abuse was the only ascertained comorbidity that was associated with a significantly lower risk of ESRD (P<0.001). There was no significant association between HIV/AIDS (P=0.07), viral hepatitis (P=0.11), homelessness (P=0.89) or non-English language (P=0.27) and risk of incident ESRD after adjustment (**Table 2**).

Modification of Progression

There was, however, strong evidence that the relations of eGFR category and time to ESRD differed according to age group (Wald test P-value=0.008) and race-ethnicity (P<0.001). The association of lower eGFR category and increased risk of ESRD was more pronounced among older as compared with younger individuals (**Figure 1**), and among Asian and Hispanic as compared with black and white patients (**Figure 2**). In contrast, there was no strong evidence that the relationship between eGFR category and time to ESRD differed significantly according to sex (P=0.16), proteinuria (P=0.96) or diabetes status (0.47). Similarly, there was no strong evidence that the relationship between proteinuria and time to ESRD differed significantly according to age (P=0.86), sex (P=0.99), or race-ethnicity (P=0.51), but there was strong evidence that this association differed by diabetes status (0.007). The association of higher proteinuria and increased risk of ESRD was more pronounced among patients without diabetes (HR [95%CI]: 1.86 [1.72, 2.02]) as compared with those with diabetes (1.63 [1.49, 1.79]).

Discussion

In the US, the rates of ESRD differ markedly by race-ethnicity and socioeconomic status.[5,24] Despite widespread recognition of these disparities, few studies have examined predictors of ESRD among disadvantaged populations.[5] In this public healthcare setting, we confirmed that younger age, male sex, non-white race-ethnicity, health insurance coverage, diabetes, lower eGFR, higher proteinuria, lower hemoglobin level, and lower serum albumin concentration were significantly associated with a higher adjusted risk of progression to ESRD. In contrast, we found no significant association between social or societally-determined clinical factors including homelessness, substance abuse, HIV/AIDS, viral hepatitis (HBV or HCV), and non-English language with higher risk of ESRD after concurrent adjustment for the aforementioned variables.

In a retrospective cohort study of 2,015,891 US Veterans with and without CKD, Choi et al. reported that HIV seropositivity was associated with a higher risk of developing ESRD among black but not among white patients after adjustment for age, sex, eGFR level and comorbid conditions.[25] Similar to Choi et al., we found no evidence of an overall association between HIV seropositivity and risk of ESRD. However, in contrast with Choi et al., we found no evidence that the association of HIV and risk of ESRD differed according to race or ethnicity. While the vast majority of patients with HIV who developed ESRD in our study (13 of 14) were black, our analyses were limited by the paucity of overall ESRD events in this subgroup. Differences in subject selection (i.e., only patients with moderate to advanced CKD were included in our study as compared with the largely non-CKD Veteran cohort of Choi et al.) may have also contributed to the disparate findings.

Similar to HIV, we found no significant association between the presence of HCV infection and higher risk of ESRD. In a retrospective cohort study of 474,369 US Veterans, Tsui et al. reported that HCV seropositivity was associated with an approximate three-fold higher adjusted risk of developing ESRD. In contrast with this national cohort of Veterans in which CKD was relatively uncommon (baseline prevalence <14%), all subjects in our study had moderate to advanced CKD. The more homogeneous nature of our study cohort with respect to kidney disease combined with shorter follow-up

(median 3.6 vs. 2.8 years in our cohort) and relative paucity of ESRD events among HCV-infected subjects (n=11) likely contributed to differences in study findings due to insufficient power to test this association. Likewise, we observed only a single case of ESRD among HBV-infected subjects in our study which precluded substantive inference.

Despite reportedly high prevalence among the homeless of risk factors for CKD such as diabetes mellitus and hypertension,[26,27] little is known about the adverse outcomes of CKD among this marginalized group. We observed similar adjusted rates of treated ESRD among homeless and housed adults in our study. While there are no official records of how many homeless individuals eventually progress to, and receive treatment for, ESRD in the US, our data suggest that this number may be considerable. Our findings require further confirmation as accurately classifying the homeless and capturing associated outcomes are extremely challenging tasks; homelessness is a dynamic process in which fleeting contact with medical resources represents the norm.[28]

Notably, one-third of individuals with CKD stages 3-5 in our study cohort spoke a primary language other than English. Prior studies in non-CKD populations have described suboptimal processes of care among adults with limited English proficiency such as poorer glycemic control among patients with diabetes.[29,30] In our study, we found no evidence to suggest that non-English speakers were at higher risk for progressing to ESRD compared with English speakers. The CHN provides a wide range of interpreter services and health information in several foreign languages, and it is possible that these services reduced linguistic barriers to care in our diverse patient population. In contrast with prior studies which were unable to account for differences in socioeconomic status and access to care among participants, we controlled for several measures of these important variables including household income and health insurance coverage. Based on our results, we posit that unfavorable outcomes associated with linguistic barriers might be attenuated in the presence of readily available interpreter services and access to ambulatory care as were available in the CHN.

In our study, having a history of substance abuse (drug use or alcoholism) was associated with an estimated 55% lower adjusted risk of progressing to ESRD. Several case-series and cross-sectional

studies have reported associations between intravenous drug use, higher levels of proteinuria and more severe kidney disease.[31-34] However, most of these reports preceded widespread testing and recognition of HIV: these reports may have actually been describing the renal manifestations of untreated HIV (i.e., HIV-associated nephropathy) rather than a true link between substance abuse and kidney function. It is unlikely that substance abuse actually "protects" against CKD progression outside of increasing the risk of premature death. Considering the higher prevalence of proteinuria among patients with versus those without a history of substance in our study, it is unlikely that differences in underlying cause of CKD (i.e., progressive vs. non-progressive CKD) accounted for this observation.

Consistent with prior reports, we found that more severe proteinuria and lower levels of kidney function were significantly associated with higher risk of ESRD.[11,35] Iseki et al. and Hsu et al. described independent, graded increases in ESRD risk associated with higher levels of dipstick proteinuria based on universally screened and insured cohorts from Japan and the US, respectively.[11,35] Our risk estimates for ESRD associated with more severe proteinuria or lower levels of kidney function were substantially higher than those reported in the aforementioned studies.[11,35] This observation was most likely due to differences in subject selection where younger patients with more advanced kidney disease were present in higher proportions in our cohort.

Even in this resource-poor environment, we also found that nonwhite race-ethnicity, and, in particular, black race was associated with higher risk of developing ESRD compared with white race. The risk estimates for ESRD among members of racial-ethnic minority groups in our study were consistent with those from CKD cohorts in other US healthcare settings.[23,36,37] However, the persistence of racial-ethnic differences in ESRD risk in this low-income population suggests that factors other than socioeconomic status may play an important role in the progression of established CKD to ESRD than previously suggested. Recent studies have linked *APOL1* gene mutations with certain types of progressive kidney disease.[38,39] Due partly to the protective effects conferred by *APOL1* mutations against trypanosomal disease, these mutations appear to be relatively common among individuals of African descent but virtually absent among those from Europe.[38] Similar associations between *APOL1*

mutations and American Indian race or Hispanic ethnicity have not been observed and reasons for the substantially higher risk of ESRD in these groups relative to whites remain unclear.

Consistent with prior studies, male sex and younger age were significant, independent predictors of progression to ESRD.[5,24,35] While the mechanisms underlying sex differences in ESRD risk among humans are inadequately understood, some investigators report that estrogen may have beneficial effects on collagen metabolism and mesangial cell biology.[40] With respect to age, we confirmed a strong stepwise association between younger age and higher risk of progression to ESRD in this largely poor clinical cohort.[24] Based on more pronounced attenuation of ESRD risk estimates among younger subjects after adjustment for baseline comorbidities (Table 2), the age-ESRD relations appear to be at least partly related to a higher frequency of risk factors for CKD progression among younger subjects. In the context of these findings, the high fraction of relatively young adults with moderate to advanced CKD in our study should prompt further inquiry into the potential impact of targeted CKD risk factor management interventions within public health systems. Lastly, the more pronounced association of lower eGFR and increased risk of ESRD among older patients and among Asians and Hispanics (relative to younger patients and blacks and whites, respectively) may reflect age or racial differences in CKD etiology, comorbid burden or perhaps tolerance of uremia among members of these groups at similar initial levels of eGFR.[24] It is also possible that these differences reflect some degree of eGFR misclassification as the MDRD equation has not been validated across the full range of age, racial groups and eGFR levels examined here.[17]

Strengths and Limitations

Our study is strengthened by the inclusion of adults with moderate to advanced CKD from the urban healthcare safety net – a population rarely captured in US-based studies of kidney disease. In addition to providing detailed demographic and clinical data, we were able to link our cohort to statewide and national registries to obtain complete or nearly complete capture of treated ESRD and vital status. Our study also had several limitations. First, while diverse populations were well represented in our study, our cohort may not be fully reflective of persons receiving care from other US public hospitals

or safety net health systems.[41] Second, we were unable to account for changes in exposures such as health insurance coverage or laboratory measures over the period of follow-up. Third, our assessment of comorbid conditions was based on diagnostic codes and thus likely underestimates the prevalence of comorbidities such as cardiovascular disease, diabetes, and hypertension in this population; moreover, while we incorporated laboratory measures that often reflect disease severity, we could not directly determine the severity or duration of most of the comorbid conditions.[37, 38] Fourth, while it is possible that we have misclassified some persons with acute kidney injury or with near normal kidney function as having CKD, we attempted to reduce this potential misclassification by requiring at least two outpatient eGFR determinations for study inclusion. Misclassification of CKD and its severity using population-based GFR estimating equations may also be operative since the MDRD study equation was derived in a population of largely white and black patients with moderate to advanced CKD, very few of whom had diabetes.[17] Lastly, we were limited in our ability to examine the association of ESRD and certain exposures including chronic viral hepatitis and HIV due to the limited sample size of these groups.

Conclusions

In the urban healthcare safety net, we found no evidence that social and socially-determined clinical factors including homelessness, substance abuse, non-English language status and chronic viral diseases significantly predicted higher risk of progressing to ESRD. While the importance of these factors in predicting ESRD may differ in populations that include a wider-range of patients, our results reinforce the importance of addressing traditional risk factors for progressive CKD to reduce the disproportionate burden of ESRD among underserved populations.

Table 1. Baseline characteristics of 15,353 Community Health Network patients with moderate to advanced CKD who did and did not develop end-stage renal disease

Characteristic	No ESRD (n=14,794)	ESRD (n=559)
Age, mean (SD), years	59.5 (13.8)	52.7 (12.9)
Age category, N (%)		
< 40 years	1213 (8)	103 (18)
40-49 years	2512 (17)	137 (25)
50-59 years	3563 (24)	159 (28)
60-69 years	4402 (30)	106 (19)
≥ 70 years	3104 (21)	54 (10)
Female, N (%)	7935 (53)	216 (39)
Race-ethnicity, N (%)		
Non-Hispanic white	4243 (29)	58 (10)
Non-Hispanic black	2928 (20)	263 (47)
Hispanic	2759 (19)	84 (15)
Asian	4475 (30)	145 (26)
Other race-ethnicity	389 (3)	9 (2)
Primary spoken language, N (%)		
English	9863 (67)	435 (78)
Spanish	1721 (12)	50 (9)
Cantonese	1723 (12)	36 (6)
Other	1487 (10)	38 (7)
Annual income ≤$10 000 USD, N (%)	7968 (54)	254 (45)
Primary health insurance, N (%)		
Uninsured/none	2683 (18)	28 (5)
Medicaid	3405 (23)	154 (28)
Medicare	5890 (40)	214 (38)
Commercial or Other	321 (2)	8 (1)
Missing	2495 (17)	155 (28)
Homeless, N (%)	827 (6)	31 (6)
Comorbid conditions, %		
Diabetes	3154 (21)	210 (38)
Hypertension	6873 (46)	208 (37)
Cardiovascular disease	2604 (18)	62 (11)
AIDS/HIV	653 (4)	14 (3)
Hepatitis C virus infection	629 (4)	11 (2)
Hepatitis B virus infection	166 (1)	1 (0)
Alcoholism	1155 (8)	15 (3)
History of drug use	2365 (16)	56 (10)
Laboratory measures, %		
Estimated GFR category		
45-59 ml/min/1.73 m^2	12,062 (81)	200 (36)
30-44 ml/min/1.73 m^2	1926 (13)	123 (22)
15-29 ml/min/1.73 m^2	631 (4)	145 (26)
<15 ml/min/1.73 m^2	175 (1)	91 (16)
Proteinuria category		
Normal	6545 (44)	42 (5)
Mild	3891 (26)	391 (70)
Heavy (	202 (1)	88 (16)
Missing	4156 (28)	54 (10)
Hemoglobin, mean (SD), g/dL	12.9 (2.0)	11.4 (2.2)
Serum albumin, mean (SD), g/dL	4.0 (0.7)	3.3 (0.7)

Table 2. Unadjusted and adjusted hazard ratios (95% confidence intervals) among predictors of time to end-stage renal disease

Predictor	Crude hazard ratio (95% confidence interval)	Adjusted hazard ratio* (95% confidence interval)
Sociodemographics		
Age group		
20-39 years	4.97 (3.58, 6.91)	2.90 (2.01, 4.18)
40-49 years	3.36 (2.45, 4.61)	2.59 (1.82, 3.68)
50-59 years	3.31 (2.43, 4.51)	2.40 (1.72, 3.37)
60-69 years	1.60 (1.15, 2.22)	1.50 (1.07, 2.11)
70+ years	Referent	Referent
Sex		
Men (vs. women)	1.69 (1.45, 1.97)	1.51 (1.26, 1.82)
Race-ethnicity		
Non-Hispanic white	Referent	Referent
Non-Hispanic black	5.67 (4.27, 7.54)	3.28 (2.42, 4.44)
Asian	2.43 (1.80, 3.30)	1.68 (1.14, 2.48)
Hispanic	2.30 (1.65, 3.21)	2.65 (1.88, 3.73)
Other	1.66 (0.82, 3.36)	1.91 (0.93, 3.94)
Health insurance coverage		
Uninsured/none	Referent	Referent
Medicaid	3.59 (2.40, 5.36)	2.34 (1.54, 3.54)
Medicare	2.48 (1.67, 3.67)	2.90 (1.92, 4.39)
Commercial	1.65 (0.58, 4.72)	1.57 (0.54, 4.59)
Other	2.87 (1.91, 4.29)	1.49 (0.51, 4.34)
Clinical predictors of ESRD		
Diabetes	2.59 (2.18, 3.08)	2.00 (1.64, 2.46)
Cardiovascular disease	0.69 (0.53, 0.90)	0.93 (0.70, 1.23)
Hypertension	0.86 (0.72, 1.02)	0.95 (0.77, 1.17)
Estimated GFR category		
45-59 ml/min/1.73 m^2	Referent	Referent
30-44 ml/min/1.73 m^2	3.01 (2.41, 3.78)	1.86 (1.47, 2.36)
15-29 ml/min/1.73 m^2	9.77 (7.86, 12.15)	4.98 (3.97, 6.25)
<15 ml/min/1.73 m^2	22.83 (17.20, 30.30)	8.68 (6.53, 11.54)
Log proteinuria per mg/g	2.02 (1.91, 2.13)	1.74 (1.64, 1.85)
Hemoglobin per g/L	0.76 (0.73, 0.48)	0.87 (0.83, 0.91)
Serum albumin per g/dL	0.44 (0.40, 0.48)	0.74 (0.65, 0.84)
Non-traditional predictors of ESRD		
HIV/AIDS	0.99 (0.80, 1.22)	0.58 (0.36, 1.04)
Hepatitis B or C virus	0.72 (0.40, 1.27)	0.61 (0.33, 1.12)
History of substance abuse	0.67 (0.51, 0.87)	0.45 (0.33, 0.60)
Homeless	1.11 (0.77, 1.60)	1.03 (0.70, 1.51)
Non-English speaker	0.63 (0.51, 0.76)	0.87 (0.67, 1.12)

*Model estimates are based on 10 imputations and are adjusted for baseline age group (referent group is 70+ years), sex, race-ethnicity (referent group is white), health insurance coverage (referent group is uninsured), diabetes, cardiovascular disease, hypertension, estimated glomerular filtration rate (EGFR referent group is 45-59 ml/min/1.73 m^2), log proteinuria, HIV/AIDS, viral hepatitis, substance abuse, housing status, non-English language, hemoglobin level and serum albumin concentration.

Figure 1. Adjusted hazard ratios (95% confidence intervals) for the association of initial eGFR category and time to end-stage renal disease stratified by age group

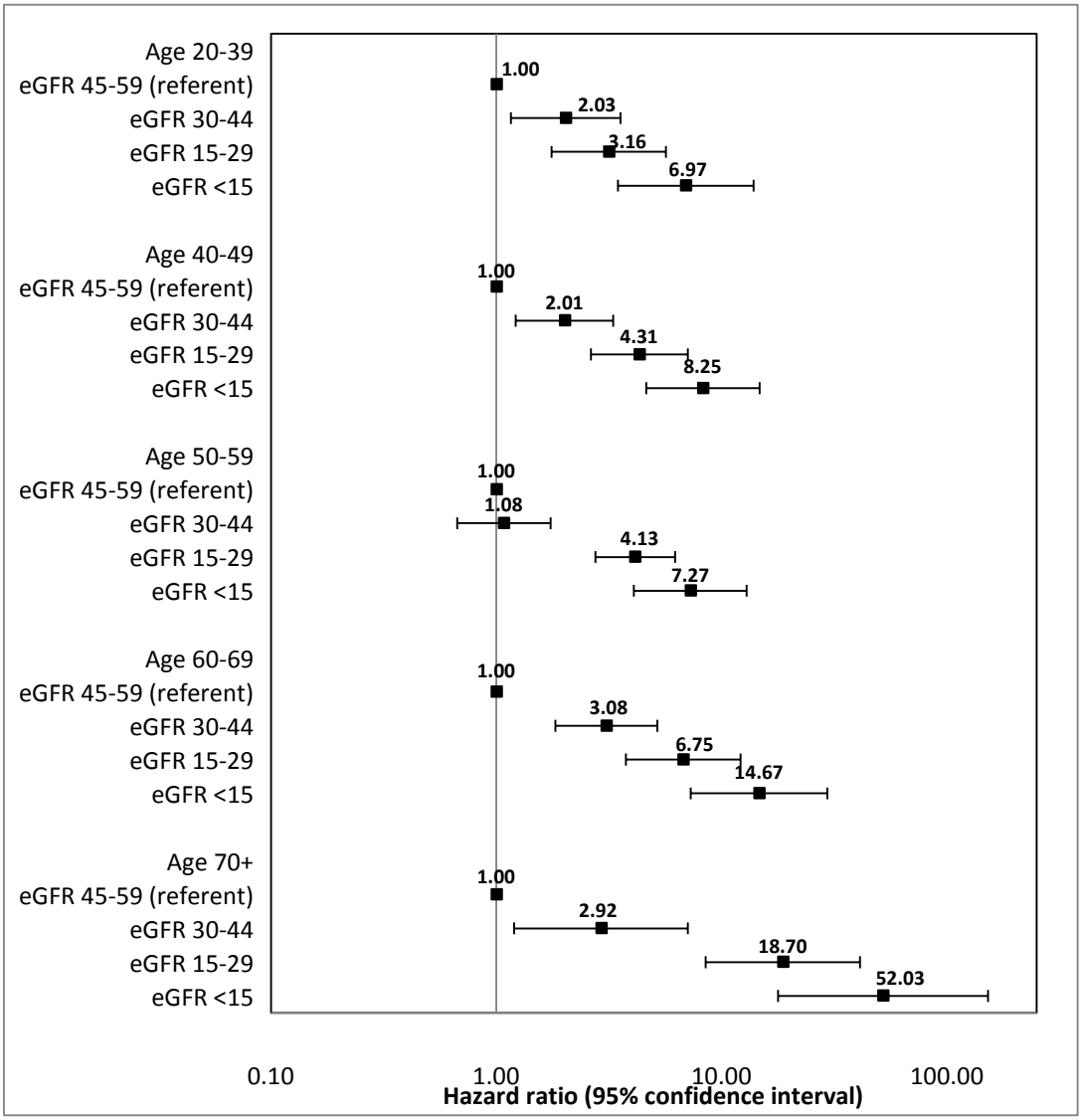
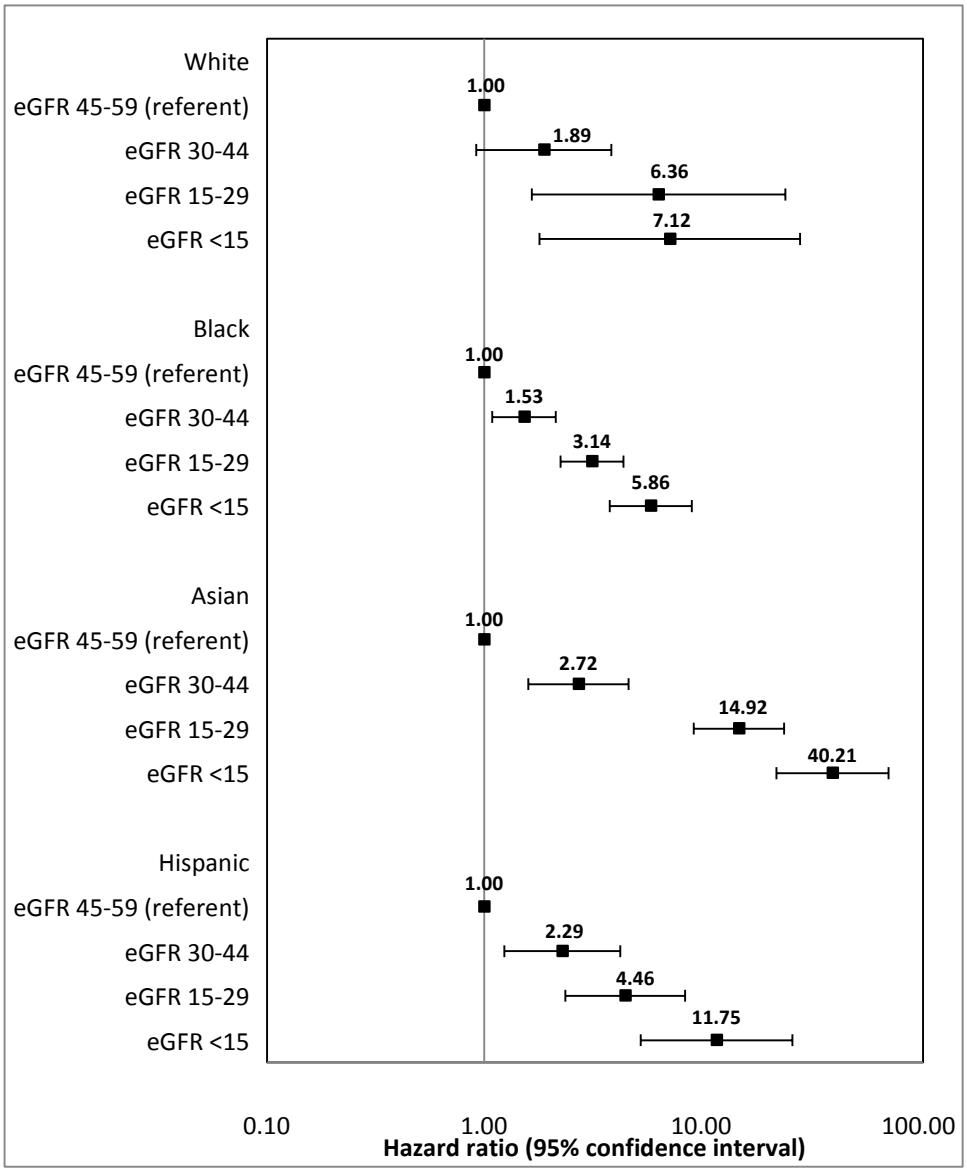


Figure 2. Adjusted hazard ratios (95% confidence intervals) for the association of initial eGFR category and time to end-stage renal disease stratified by race-ethnicity



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Supplementary Appendix A: Criteria used to define coexisting illnesses based on data recorded in the Lifetime Clinical Records of the Community Health Network.

Condition	Criteria	ICD-9 or CPT codes
Coronary artery disease	Primary discharge diagnosis or procedural code in hospitalization databases.[2]	**ICD-9:** 414.0, 414.8, 414.9, 36.01–36.02, 36.05, 36.06, 36.09, 36.10–36.17, 36.19 **CPT:** 92980–92981, 92982, 92984–92996, 33510–33519, 33521–33523, 33533–33536
Cerebrovascular Disease	Primary discharge diagnosis or procedural code in hospitalization databases.[2]	**ICD-9:** 433.x1, 434.x1, 436.0, 435
Congestive heart failure	Primary discharge diagnosis or procedural code in hospitalization databases.[2]	**ICD-9:** 398.91, 402.01, 402.11, 402.91, 428.0, 428.1, 428.9
Chronic obstructive lung disease	Primary discharge diagnosis of chronic obstructive pulmonary disease or chronic bronchitis in hospitalization databases, or physician-assigned diagnoses in ambulatory-visit databases.[2]	**ICD-9:** 491.x, 492.x, 493.x, 496, 518.1, 518.2
Depression	Primary discharge diagnosis in hospitalization databases, or physician-assigned diagnoses in ambulatory-visit databases.[2, 3]	**ICD-9:** 296.20-26, 296.30-36, 296.40-46, 296.50-56, 296.60-66, 296.7, 296.80-82, 296.89, 296.90, 296.99, 298.0, 311.
Diabetes mellitus	Two or more physician-assigned diagnoses in ambulatory-visit or hospitalization databases.[4-6]	**ICD-9:** 250, 357.2, 362.0, 366.41
Alcoholism	Primary discharge diagnosis in hospitalization databases, or physician-assigned diagnoses in ambulatory-visit databases.[3, 4]	**ICD-9:** 291, 303, 303.0, 303.00-303.03, 303.9, 303.90-303.93, 305.0, 305.00-305.03, 357.5, 425.5, 535.3, 571.0-531.3, 790.3, 980.0, 980.8, 980.9, V11.3, E860.0, E860.1, E860.8, E860.9
Drug abuse	Primary discharge diagnosis in hospitalization databases, or physician-assigned diagnoses in ambulatory-visit databases.[3, 4]	**ICD-9:** 292, 292.0, 292.1, 292.11, 292.12, 292.2, 304, 304.00-03, 304.10-304.13, 304.20-23, 304.30-33, 304.40-43, 304.50-53, 304.6, 304.60-63, 304.7, 304.70-73, 304.8, 304.80-304.83, 304.9, 304.90-93, 305.1, 305.20-23, 305.30-33, 305.40-43, 305.50-53, 305.60-63, 305.70-73, 305.80-305.83, 305.9, 305.90-93
Hepatitis C virus infection	Primary discharge diagnosis in hospitalization databases, or physician-assigned diagnoses in ambulatory-visit databases, or laboratory diagnosis based on American Association for the Study of Liver Diseases Guidelines.[7, 8]	**ICD-9:** 070.41, 070.44, 070.51, 070.54, V02.62
HIV/AIDS	Two or more physician-assigned diagnoses in ambulatory-visit or hospitalization databases.[3]	**ICD-9:** 042.0-044.9, V08
Hypertension	Two or more physician-assigned diagnoses in ambulatory-visit databases.[2]	**ICD-9:** 401–405
Tobacco Smoking	Primary discharge diagnosis in hospitalization databases, or physician-assigned diagnoses in ambulatory-visit databases.[10, 11]	**ICD-9:** 305.1, V15.82, 649.0, 989.84

Supplementary Appendix References

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