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County-level characteristics associated with variation in end-stage kidney disease mortality in the United States, 2010-2018

By

Kylie Snow

Master of Public Health

Epidemiology

Dr. Jessica Harding

Committee Chair

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Kylie Snow

B.S., Georgetown University, 2019

Thesis Committee Chair: Jessica Harding, PhD

An abstract of
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Abstract

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Background: Once diagnosed with end-stage kidney disease (ESKD), mortality risk is high. Individual-level factors known to be associated with increased mortality in this patient population include age, race, gender, and multiple comorbidities. However, few studies have examined county-level characteristics associated with ESKD mortality. Therefore, using a national registry of ESKD patients receiving kidney replacement therapy (KRT) in the United States, we examined county-level variation in ESKD mortality and identified county-level characteristics associated with this variation.

Methods: Using the United States Renal Data System, we estimated county-level age-standardized mortality rates (ASMR) among all adults (N=1,516,742, aged 18-84) across 2,807 counties with ESKD receiving KRT between 2010 and 2018. County-level ASMRs were linked to county-level demographic (e.g., % female), socioeconomic (e.g., % unemployed), health care (e.g., % without health insurance), and health behavior (e.g., % current smokers) characteristics from publicly available census and survey data. Hierarchical linear mixed models, with a random intercept for state, identified county-level characteristics associated with ESKD-related ASMRs and quantified the percentage of variation explained by county-level characteristics.

Results: County-level ESKD-related ASMRs ranged from 25 to 509 per 1,000 person-years (PY). ASMRs were highest in counties located in the Tennessee Valley and Appalachia regions, and lowest in counties located in New England, the upper Midwest, and in some regions along the West coast. Overall, county-level characteristics explained 20% of variation in ESKD-related ASMRs. In fully adjusted models, a lower percentage of Black people (-5.33 deaths/1,000PY), higher health care expenditures (3.76 deaths/1,000PY), and lower percentage of people who drink excessively (-2.99 deaths/1,000PY) were significantly associated with ESKD mortality.

Conclusions: In this study, we show substantial variation in ESKD mortality by county, and find that approximately 20% of this variation is explained by county-level characteristics. Given that a large proportion of county-level variation (~80%) is unexplained, targeted vs. population-wide interventions may play a more important role in reducing ESKD mortality.

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Background

Epidemiology of end-stage kidney disease in the United States

In the United States, approximately 15% (37 million) of adults are estimated to have chronic kidney disease (CKD), the ninth leading cause of death.[1] In 2018, more than 785,000 patients had advanced to end-stage kidney disease (ESKD) – the most advanced stage of CKD – which requires kidney replacement therapy (KRT) for patient survival.[1,2]

The age, race, and sex adjusted incidence of ESKD in the United States has increased 46% since 1990, largely due to increases in the prevalence of diabetes and obesity **(Figure 1)**, though the risk of ESKD is not uniform across population subgroups.[2,3] For example, ESKD incidence is 2.7-times higher among Black vs. white populations,[4,5] and 1.3-times higher among Hispanic vs. non-Hispanic populations.[2] ESKD incidence increases with age such that people older than 75 years have a 13-fold increased risk for developing ESKD compared with people aged 18-44 years,[2] and males are 1.6 times more likely to develop ESKD compared with females.[2]

Once diagnosed with ESKD, the risk of mortality is high. For example, among patients on hemodialysis, 5-year survival is just 41.4%, and this increases to 84.5% for those who receive a kidney transplant.[2] Similar to ESKD incidence, ESKD mortality risk is not uniform across the population with the extant literature describing important variations by individual-level factors such as race, sex, underlying cause of ESKD, and socioeconomic status (SES). For example, adult white patients have, on average, higher mortality rates than Black patients.[2,5] The gap between mortality for white patients and Black patients also increases as age increases.[2] There are also known sex difference in ESKD mortality, in that females have higher mortality than males.[6,7] Furthermore, patients with comorbidities, including diabetes and cardiovascular disease, also have a higher risk of death.[8–10] Cause of ESKD also influences mortality risk, in that those with diabetic-ESKD have higher mortality, compared to those with ESKD from other causes.[11,12] Mortality is also higher among patients with low (vs. high) income and type of occupation.[13]

Despite a plethora of literature dedicated to understanding the individual-level drivers of ESKD mortality in people, few studies have examined the role that neighborhood-level factors and geographic variation may play.

Geographic variation in end-stage kidney disease in the United States

Geographic variation in ESKD incidence was first described in 1991 by Foxman et al.[14] In this descriptive study of the United States Renal Data System (USRDS) between 1983 and 1988, Foxman et al. identified geographic clusters of high and low ESKD incidence.[14] Regions of high ESKD incidence were found in the Southwest, Southeast, and in counties with a higher proportion of Native American reservations, while regions with low ESKD incidence were found in the West and Northwest. These patterns were similar in whites and nonwhites.[14]

Other studies have evaluated geographic variation in ESKD incidence while simultaneously examining demographic and socioeconomic factors that may contribute to this variation. For example, Mathur et al. identified high ESKD incidence rates in the southern and middle Atlantic regions using 2000-2008 data from Centers for Medicare & Medicaid Services and the Organ Procurement and Transplantation Network (OPTN) in a population of ESKD patients starting dialysis or pre-emptively placed on the OPTN kidney waitlist.[15] This study noted ESKD incidence was highest in regions with a greater density of Black and Native American people known to have higher rates of ESKD.[15] Volkova et al. identified patients starting KRT in Georgia, North Carolina, and South Carolina between 1998 and 2002 and found that higher neighborhood poverty (defined as the proportion of census tract living below the poverty level) was associated with higher ESKD incidence for both Black and white populations in a dose-response manner.[16] For example, compared to counties with <5% of the population below the poverty level, counties with 5-9.9%, 10-14.9%, 15-19.9%, and >20% of the population below the poverty level had a 1.5, 1.9, 2.6, and 3.0 times higher ESKD incidence rate, respectively. Furthermore, as neighborhood poverty increased, the disparity between ESKD incidence among Black vs. white populations increased, suggesting a significant interaction between poverty and race.[16] To date, no one has examined whether the geographic variation in ESKD incidence translates into geographic disparities in ESKD mortality.

Factors associated with geographic variation in end-stage kidney disease

It is feasible that the risk factors previously identified as factors associated with geographic variation in ESKD incidence – including demographic and socioeconomic factors – may also play a role in ESKD mortality. For example, in a study of mortality in the young adult dialysis population using United States Renal Data System data, lower neighborhood socioeconomic status was found to be associated with higher ESKD-related mortality.[17] Once diagnosed with ESKD, variation in treatment and access to healthcare across geographic regions may also contribute to variation in ESKD mortality. For example, it has previously been shown that dialysis facilities with a greater proportion of patients who receive recommended pre-ESKD care have lower ESKD mortality rates.[18] Treatment centers in the lowest quintile of pre-ESKD care were geographically clustered, notably in Southern states including Alabama and

Mississippi, and were more likely to be in urban (vs. rural) counties that, at the county-level, had larger Black populations and people of lower educational attainment.[18,19]

There are also well-known geographic disparities in access to kidney transplantation with important implications for mortality. Ashby et al. examined transplant rates using data from over 700,000 patients from 1996-2005 and identified high variability in living donor transplant rates (ranging from 57% lower to 166% higher than the national average) and deceased donor transplant rates (ranging from 60% lower to 150% higher than the national average).[20] States with both waitlisting and decreased donor transplant rates below the national average included Arizona, Connecticut, Hawaii, Mississippi, North Carolina, and New Mexico, again largely clustered in the Southern region of the United States.[20] Axelrod et al. also examined waitlisting, transplantation, and survival in solid organ transplants in rural versus urban areas between 1999 and 2004 and found substantially lower transplant rates in rural vs. urban residents.[21]

As for community-level characteristics, Schold et al. examined the impact of several community-level risk factors on kidney transplant access and kidney transplant outcomes.[22] In this study, researchers calculated a community risk score (range 0-40) for each U.S. county (including measures of the prevalence of comorbidities, access to and quality of healthcare, socioeconomic status, and self-reported physical and mental health) and determined that ESKD patients in the highest-risk communities had higher mortality (adjusted hazard ratio (aHR) 1.22, 95% Confidence Interval (CI):1.16-1.28) and decreased likelihood of living donor transplantation (adjusted odds ratio (aOR) 0.90, 95%CI: 0.85-0.94) compared to patients in lower-risk communities.[22] Plantinga et al. examined community-level characteristics related to dialysis facility transplant rates and determined that each standardized increase in the percentage of high school graduates in the community was associated with a 15% higher facility-level incidence of kidney transplant.[23] On the other hand, for each standardized increase in percentage of Black residents, married residents, unemployed residents, and households living in poverty in the community, there was a 2%, 7%, 3%, and 9% lower facility-level incidence of kidney transplant, respectively.[23]

Knowledge gaps

Though several studies have documented geographic variation in ESKD incidence and kidney transplantation and identified some factors associated with this variation, no-one to date has examined geographic variation in ESKD mortality. This is likely owing to the need for large, national datasets with multiple of years of data to conduct such an analysis. Estimating geographic variation and identifying county-level factors associated with ESKD mortality may lead to the development of social, economic, and healthcare-based interventions to decrease ESKD-mortality and geographic disparities. Several similar studies have been conducted in cardiovascular disease,[24] diabetes,[25] cancer,[26] and drug-related mortalities.[27] Using a similar approach, this thesis will explore geographic variation in ESKD-mortality and identify the county-level demographic, socioeconomic, health care, and health behavior characteristics that may explain this variation.

Study aims

Using a national registry of ESKD patients receiving kidney replacement therapy (KRT), this study examines county-level variation in ESKD mortality and identifies county-level risk factors underpinning this variation. Specifically, we will:

1) describe the county-level distribution of age-standardized ESKD mortality rates throughout the United States

2) examine the county-level demographic characteristics, socioeconomic characteristics, health care characteristics, and health behavior characteristics associated with county-level variation in ESKD mortality.

Identifying county-level factors and geographic 'hot spots' associated with high ESKD-related mortality may be an important first step in designing and developing community-level interventions designed to reduce ESKD mortality.

Methods

Data sources

In this study, we combined county-level age-standardized ESKD-related mortality rates, estimated from the United States Renal Data System (USRDS) and described below, with several county-level characteristics, determined from multiple publicly available sources including the United States Census Bureau, the American Community Survey, the Behavioral Risk Factor Surveillance System, and Medicare, as described in **Table 1**, to create an ecological cross-sectional dataset. In all, 16 (73%) of these measures were accessed via the County Health Rankings and Roadmaps project,[28] 5 (23%) were accessed through the Area Health Resource File,[29] and 1 (5%) was accessed through the Dartmouth Atlas of Health Care.[30] Use of USRDS data was approved by the Institutional Review Board at Emory University (IRB00063645). All other data is publicly available and thus exempt from institutional review board approval.

Study population

County-level ESKD-related mortality was estimated from the USRDS. The USRDS is a national registry of all U.S. patients with ESKD initiating kidney replacement therapy (KRT).[2] The current study included all prevalent ESKD patients aged 18-84 between Jan 1, 2010 and Aug 23, 2018. We excluded patients with missing information on date of KRT initiation (n=4,321), date of birth (n=28), or county (n=1,610), those outside ages 18-84 (n=94,435), and those who died on the same day as KRT initiation (n=540). We also excluded patients who resided in counties, defined using the Federal Information Processing Standard (FIPS) code, with <10 deaths (n=319 counties) and in counties defined as U.S. territories, counties whose FIPS code have changed, or FIPS codes that are not county-specific (n=194 counties). The final study included 1,516,742 patients representing 2,807 counties **(Figure 2)**.

Mortality ascertainment

Mortality data in the USRDS is augmented by Social Security Death Master File data to the extent allowed by regulation. Further, universal reporting of ESKD patient deaths as well as date of death is required via Centers for Medicare and Medicaid (CMS) form 2746 as a condition of coverage for dialysis units and transplant centers.

County-level characteristics

County-level characteristics included in this study are described in **Table 1**. In brief, we considered four sets of characteristics to understand the contributions of county-level demographic, socioeconomic, health care, and health behavior characteristics to the variation in county-level ESKD-related mortality. For each variable, we included the most contemporaneously available data.

Statistical analyses

Individuals with ESKD were followed from date of KRT initiation, until date of death or end of follow-up (Aug 23, 2018), whichever occurred first. County-level ESKD-related mortality rates were defined as the number of deaths per 1,000 person-years per county and were age-standardized to the 2000 U.S. population[31] using age groups (18-44, 45-64, 65-74, and 75-84) and the direct method of standardization to calculate county-level ESKD-related age-standardized mortality rates (ASMR).

County-level characteristics were described using mean ± standard deviation. We standardized county-level characteristics to have a mean of 0 and standard deviation of 1 so we could compare associations of county characteristics with mortality. We quantified the correlation between each county characteristics and county-level ESKD-related ASMRs. To avoid collinearity, when two similar characteristics had a correlation $r > 0.8$ or a variation inflation factor > 5, one variable was selected to include in regression models to avoid collinearity **(Tables S1 and S2)**.[32] We used hierarchical linear mixed models to estimate the association between county-level characteristics and ESKD-related ASMRs, in which counties were the level-1 unit and states were the level-2 unit with a random intercept. The purpose of allowing each state to have its own intercept was to eliminate the effect of state-level features that influence mortality and to account for clustering within states.

We sequentially fit four models by adding categories of county characteristics beginning with nonmodifiable demographic characteristics followed by socioeconomic characteristics, health care characteristics, and health behavior characteristics. Coefficients in the final model are interpreted as the association between each county-level characteristic and county-level ESKD ASMR, adjusting for all other county-level characteristics. We applied a Bonferroni correction to adjust for multiple testing and calculated the proportion of variance in county-level ESKD-related ASMRs explained by each set of county characteristics.

To examine state-level variation in ESKD-related ASMRs we estimated the random effect for each state in both a null model and in a final, fully adjusted model, including all non-collinear county-level characteristics. By comparing the random intercepts, we explored the extent to which county-level characteristics accounted for state-level variation in county-level ESKD-related ASMRs. In the null model, the random intercepts represent state deviation from the national mean county-level ESKD-related ASMR. In fully adjusted models, the random intercepts represent state deviation from the national mean county-level ESKD-related ASMR that is not explained by other county-level characteristics. All analyses were conducted using R software (version 4.0.2).

Results

Among 2,807 counties (representing 1,516,742 ESKD patients), the average ESKD ASMR between 2010 and 2018 was 79.1 (SD=25.8) per 1,000 person-years (PY) and ranged from 25.1 to 509.0 per 1,000 PY **(Figure 3)**. In general, higher ESKD ASMRs were seen among counties located in the Appalachia region, the Tennessee Valley, and the South, including Arkansas, Oklahoma, and Louisiana. Lower ESKD ASMRs were seen in counties located in New England, the upper Midwest, and along the West coast (in Washington state and southern California).

Table 2 shows the distribution of the demographic, socioeconomic, health care, and health behavior characteristics of the 2,807 counties included in the analysis. On average, the county-level proportions of people aged over 65, Black people, and people living in a rural area was 18.9%, 9.9%, and 54.8%, respectively. Further, the average county-level proportion of people unemployed, of low education, and without health insurance was 4.2%, 13.7%, and 11.1%, respectively. In addition, 64.0% and 17.7% of residents in the average county did not have access to exercise opportunities and smoked, respectively.

Table 3 shows crude and adjusted associations between county-level characteristics and ESKD ASMR. All independent variables were standardized; therefore, coefficients represent the average change in ESKD deaths per 1,000 person-years for each 1-standard-deviation increase in a county characteristic. In crude associations, the county-level characteristics most strongly associated with ESKD mortality were higher percentage current smokers (7.26/1,000PY), lower median income level (-6.68/1,000PY), lower percentage with excessive alcohol usage (-6.51/ 1,000 PY), and higher percentage living in a rural area (6.38 /1,000PY).

In fully adjusted models, county-level factors significantly and negatively associated with ESKD-related ASMR were the percentage of Black residents (-5.33/1,000 PY), percentage of the county residents who consumed excessive alcohol (-2.99/1,000 PY). In the same model, the only county-level factor significantly and positively associated with ESKD-mortality was health care expenditure (3.76/1,000 PY).

Overall, county-level characteristics explained 19.4% of the variation in county-level ESKD-related ASMR **(Table 3)**. Demographic characteristics alone explained 7.6% of the variation (model 1) and adding economic and social characteristics explained an additional 4.9% of the variation (model 2). Including health care characteristics explained an additional 3.7%

(model 3) and including health behavior characteristics explained an additional 3.2% (model 4), for a collective total of 19.4%.

Figure 4 shows state-level variation in ESKD-related ASMRs and illustrates changes in state deviation from the national mean county-level ESKD-related ASMR before and after adjustment for county-level characteristics. Before adjustment, state-level variation ranged from -12.8 per 1,000 PY in Minnesota to 21.0 per 1,000 PY in Kentucky, a difference of 33.8 per 1,000 PY. After adjustment, state-level variation ranged from -4.9 per 1,000 PY in Minnesota to 4.4 per 1,000 PY in Idaho, a difference of 9.3 per 1,000 PY. Thus, adjusting for county-level characteristics reduced the difference between the lowest and highest state intercepts by more than two-thirds. For most states, county-level characteristics reduced or eliminated state deviation from the national mean county-level ESKD-related ASMR.

Discussion

In this study, we report for the first-time substantial variation in county-level ESKD mortality rates across the United States, with a 20-fold difference in the county with the highest vs. lowest ESKD-related ASMR. ESKD mortality rates were highest in counties in the Southern and Appalachian regions of the United States, and lowest in counties along the East and West coasts, and in the upper Midwest. In fully adjusted models, county-level factors significantly associated with higher ESKD-related ASMRs were a lower proportion of Black people, higher health care expenditures, and lower proportion of excessive drinkers. Overall, we found that county-level characteristics explained 19.4% of variation in ESKD-related ASMRs.

Comparison to previous literature

Our results are similar to previous studies of geographic variation in ESKD incidence. In studies such as Foxman et al. and Mathur et al., regions with highest ESKD incidence (e.g., Southeast) and lowest ESKD incidence (e.g., West and Northwest) were similar to those for ESKD mortality in the current study.[14,15] In these studies of ESKD incidence, authors identified factors including racial composition (including large populations of Native American or Black people) and higher neighborhood to be associated with ESKD incidence poverty, although these factors differ from those identified in this study.[14–16] In studies of access to kidney transplantation, a key driver of mortality rates in ESKD, studies showed that population-level characteristics including low education, rurality, and unemployment are associated with reduced access.[21–23] However, in the current study, most demographic, socioeconomic, health care, and health behavior characteristics were not significantly associated with county-level ESKD-related mortality. In fact, just 19.4% of the variation in county-level ESKD-related ASMR was explained by county-level demographic, socioeconomic, health care, and health behavior characteristics.

In this study, three factors were significantly associated with higher ESKD mortality rates in fully adjusted models. First, counties with a lower percentage of Black residents had lower ESKD-related ASMRs. This is perhaps a surprising finding given the well documented literature that Black populations, in general, have higher mortality rates as compared with White populations.[33,34] However, in ESKD, the opposite is true.[35–37] This so-called survival paradox has been previously described, and reasons postulated include: the younger age at which Black patients develop ESKD compared to white patients, reducing overall mortality rates;[38] a survival bias among Black ESKD patients who make it to KRT;[35] lower transplant rates in Black patients that artificially inflates the survival advantage of those on dialysis as well as transplant recipients, as they are a highly select population;[2,39] and higher body mass index (BMI) in Black adults (vs. white adults) mirroring the well-known obesity paradox whereby higher BMIs tend to have lower mortality rates.[38] While previous literature has examined this survival paradox at the individual-level, our results imply it may also hold true at the county-level.

Second, we found that an increase in the percentage of a county's population who drink excessively is associated with a decrease in ESKD mortality, an unexpected finding. Results from the Atherosclerosis Risk in Communities study, a community-based cohort study from four sites in the United States, suggests low or moderate alcohol consumption may be associated with a lower risk of CKD, compared to never drinkers.[40] Yet, a larger body of literature suggests that alcohol, particularly excessive alcohol consumption, may be a risk factor for CKD and subsequent ESKD.[41,42] It is therefore more plausible that high excessive drinking operates as a competing risk for ESKD-related mortality as excessive drinkers may die from other causes (e.g., liver disease, cardiovascular disease) before dying from ESKD.

Third, we show that higher health care expenditures were associated with higher ESKD mortality. In this study, health care expenditure was defined as average Medicare spending per enrollee in each county. All ESKD patients are eligible for Medicare coverage and thus a higher county-level Medicare expenditure may simply reflect a higher disease severity or burden. Further, increased healthcare expenditure does not necessarily indicate higher quality care or better access to care, but rather indicates regional differences in patterns of practice, such as more frequent physician visits, greater use of medical subspecialists, and more discretionary care.[43,44] This pattern has been demonstrated in other studies whereby increased Medicare spending was associated with increased mortality for diabetic patients with foot ulcers and amputations,[45] as well as patients with colorectal cancer.[46] Thus, given the Medicare coverage available to all ESKD patients, we postulate that increased Medicare spending in this study most likely reflects the increased county-level burden of ESKD.

Public health implications

In our study, we show that ~20% of the county-level variation in ESKD mortality is explained by county-level characteristics. In contrast to studies of other chronic diseases, this is a relatively small contribution. For example, in Patel et al. and Cunningham et al., county-level characteristics explained ~75% and ~42% of the variation in cardiovascular mortality and diabetes incidence, respectively.[24,25] The largest contributors to variation in cardiovascular disease mortality were county-level median income and education,[24] while variation in diabetes incidence was driven predominately by unemployment, poverty, and access to exercise opportunities and healthy foods.[25] The small contribution of county-level factors to the variation in ESKD-mortality may be explained by the fact that ESKD-mortality, compared to CVD mortality and diabetes incidence, is extremely rare, and so it is possible that population-level factors may not play a significant role. Compared to cardiovascular disease – whereby 48% of the population is affected[47] – only 0.2% of people have ESKD.[2] In 2016, over 840,000 people died from cardiovascular disease,[47] compared to just over 100,000 deaths from ESKD.[2] Taken together, this suggests that efforts to reduce ESKD-mortality may be more effective if targeted to the individual, rather than the broader population. Regardless, efforts to reduce ESKD incidence and subsequent mortality should consider the regional variations in the design and implementation of interventions to reduce geographic disparities.

Strengths and limitations

The key strengths of this study include the use of a large national registry of ESKD patients receiving KRT to estimate county-level ESKD mortality rates in the United States and the use of aggregated data from multiple sources to describe the impact of several county-level factors. However, there are several limitations that should also be considered. First, this is an ecological study (i.e., assessing the association between county-level risk factors and county-level ESKD-related mortality) and results cannot be extrapolated to the individual level. Second, the use of county averages, as was done in this study, does not account for variations within counties. Data at levels lower than the county (i.e., census tracts) are not available in USRDS. Third, to ensure adequate power to examine county-level ESKD-mortality, a rare outcome, we pooled ESKD mortality rates between 2010 and 2018, which may not reflect the most contemporary ESKD mortality rates. Regardless, we expect relative differences between counties to have remained relatively stable in this eight-year period. Last, there may be residual confounding by county-level characteristics not included in this analysis, such as the number of dialysis facilities, available organs, or transplant centers and surgeons.

Conclusion

In this national U.S. study, we demonstrate substantial variation in ESKD mortality across counties, and report that ~20% of this variation is explained by county-level characteristics, in particular percentage of Black people, percentage of people who drink excessively, and health care expenditures. Given that a large proportion of county-level variation (~80%) is unexplained, targeted vs. population-wide interventions may play a more important role in reducing ESKD mortality. Regardless, future studies are warranted to explore the substantial geographic variations in ESKD mortality and to develop interventions to mitigate these disparities that consider regional variations in ESKD mortality.

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Tables and Figures

Table 1. Definitions of county-level characteristics and data sources

Variable	Definition	Source	Year
Demographic			
Population size (N, in thousands)	County population	Census Population Estimates	2018
Female (%)	Percentage of the population who are female	Census Population Estimates	2018
Aged ≥ 65 years (%)	Percentage of population ages 65 and older	Census Population Estimates	2018
Hispanic (%)	Percentage of population who are Hispanic	Census Population Estimates	2018
Asian-American (%)	Percentage of the population who are Asian-American	Census Population Estimates	2018
Black (%)	Percentage of the population who are Black/African American	Census Population Estimates	2018
Native American/Alaskan Native (%)	Percentage of the population who are Native American/ Alaskan Native	Census Population Estimates	2018
Foreign born (%)	Percentage of the population who are foreign born	American Community Survey	2014-2018
Not proficient in English (%)	Percentage of the population who are not proficient in English	American Community Survey	2014-2018
Rural (%)	Percentage of the population living in a rural area	Census Population Estimates	2010
Economic/social			
Income level (median, $ in thousands)	Median income level	Small Area Income and Poverty Estimates	2018
Unemployed (%)	Percentage of residents aged 16–64 years who are unemployed	Bureau of Labor Statistics	2018
Without high school education (%)	Percentage of residents aged 24–65 years without a high school education	American Community Survey	2014-2018
In poverty (%)	Percentage of population living in poverty	Small Area Income and Poverty Estimates	2018
Health care			
Primary care physicians (N, per 100,000)	Number of primary care physicians per 100,000 population	American Medical Association	2018

Internal medicine subspecialists (N, per 100,000)	Number of internal medicine subspecialists per 100,000 population, including nephrologists	American Medical Association	2018
Without health insurance (%)	Percentage of persons aged 40–64 years without health insurance	Small Area Health Insurance Estimates	2017
Health-care expenditures ($ in thousands)	County-level price-, age-, sex-, and race/ethnicity- adjusted Medicare expenditures per enrollee	Centers for Medicare & Medicaid Services	2018
Health behaviors			
Access to exercise opportunities	Percentage of the county population residing within one-half mile (0.8 km) of a park or within 1 mile (1.6 km) (urban) or 3 miles (4.8 km) (rural) of a recreational facility	Business Analyst, Delorme map data, ESRI, & US Census Tigerline File	2010 & 2019
Food environment index	Food availability index, a composite score (ranging from 1 to 10) describing limits on access to healthy foods and food insecurity	USDA Food Environment Atlas, Map the Meal Gap from Feeding America	2015 & 2017
Current smoking (%)	Percent of adults that reported currently smoking	Behavioral Risk Factor Surveillance System	2017
Excessive drinking (%)	Percent of adults that report excessive drinking	Behavioral Risk Factor Surveillance System	2017

Table 2. Summary of U.S. county-level characteristics among 2,807 counties included in this analysis

County Characteristic	Mean (SD)[1]	Range
Demographic		
Population size (N, in thousands)	116.0 (350.9)	1.6 – 10105.5
Female (%)	50.0 (2.1)	31.5 – 56.9
Aged ≥ 65 years (%)	18.9 (4.4)	4.8 – 57.6
Hispanic (%)	9.5 (13.9)	0.6 – 96.4
Asian-American (%)	1.6 (2.9)	0.0 – 43.0
Black (%)	9.9 (14.8)	0.1 – 85.4
Native American/Alaskan Native (%)	2.1 (6.8)	0.1 – 85.7
Foreign born (%)	4.8 (5.7)	0.0 – 53.3
Not proficient in English (%)	1.7 (2.8)	0.0 – 30.4
Rural (%)	54.8 (30.2)	0.0 – 100.0
Economic/social		
Income level (median, $ in thousands)	52.7 (14.1)	25.4 – 140.4
Unemployed (%)	4.2 (1.4)	1.5 – 18.1
Without high school education (%)	13.7 (6.2)	1.2 – 48.5
In poverty (%)	15.4 (6.2)	2.6 – 48.4
Health care		
Primary care physicians (N, per 100,000)	52.5 (33.8)	0.0 – 559.2
Internal medicine subspecialists (N, per 100,000)	6.6 (14.8)	0.0 – 350.9
Without health insurance (%)	11.1 (5.0)	2.3 – 33.8
Health-care expenditures ($ in thousands)[2]	10.4 (1.4)	5.5 – 18.4
Health behaviors		
Access to exercise opportunities (%)[3]	64.0 (22.2)	0.0 – 100.0
Food environment index[4]	7.5 (1.1)	0.0 – 10.0
Current smoking (%)	17.7 (3.5)	5.9 – 41.5
Excessive drinking (%)	17.4 (3.2)	7.8 – 28.6

[1] Mean and standard deviation (SD) of counts, proportions, medians, or indices, as appropriate
[2] County-level price-, age-, sex-, and race/ethnicity- adjusted Medicare expenditures per enrollee, in thousands of dollars
[3] Percentage of the county population residing within one-half mile (0.8 km) of a park or within 1 mile (1.6 km) (urban) or 3 miles (4.8 km) (rural) of a recreational facility
[4] Food environment index, a composite score (ranging from 1 to 10) describing limits on access to healthy foods and food insecurity; 19 counties were missing data

Table 3. Associations of U.S. county-level characteristics with end-stage kidney disease (ESKD) mortality, 2010-2018[1]

County Characteristic	Bivariate Associations[2]		Model 1		Model 2		Model 3		Model 4	
	Coeff	95% CI	Coeff	95% CI	Coeff	95% CI	Coeff	95% CI	Coeff	95% CI
Demographic										
Population size (N, in thousands)	**-3.37**	**-4.31, -2.43**	-0.41	-1.92, 1.09	-0.10	-1.63, 1.43	-0.73	-2.33, 0.85	-0.46	-2.09, 1.16
Female (%)	**-1.81**	**-2.75, -0.89**	-0.60	-1.97, 0.77	-0.10	-1.49, 1.30	-0.08	-1.50, 1.35	-0.56	-2.07, 0.94
Aged ≥ 65 years (%)	**3.36**	**2.42, 4.29**	0.13	-1.50, 1.75	-1.04	-2.79, 0.71	-0.32	-2.16, 1.50	-0.40	-2.43, 1.59
Hispanic (%)	**-3.05**	**-4.32, -1.78**	-0.31	-3.23, 2.61	-1.94	-4.88, 0.99	-1.48	-4.38, 1.43	-0.96	-3.89, 2.00
Asian-American (%)	**-4.83**	**-5.83, -3.83**	**-1.99**	**-3.70, -0.29**	-0.08	-1.88, 1.73	0.46	-1.38, 2.33	0.17	-1.70, 2.08
Black (%)	**-2.72**	**-3.97, -1.45**	-1.36	-3.12, 0.41	**-3.82**	**-5.74, -1.89**	**-3.58**	**-5.53, -1.66**	**-5.33**	**-7.53, -3.17**
Native American/Alaskan Native (%)	**1.22**	**0.26, 2.18**	1.20	-0.26, 2.65	0.05	-1.48, 1.57	-0.16	-1.84, 1.49	-1.26	-3.13, 0.59
Not proficient in English (%)	**-3.07**	**-4.12, -2.03**	-0.68	-3.13, 1.77	-2.67	-5.39, 0.03	-2.56	-5.43, 0.24	-1.96	-4.85, 0.86
Rural (%)	**6.38**	**5.45, 7.31**	**4.65**	**2.89, 6.41**	**2.81**	**0.87, 4.73**	2.05	-0.07, 4.13	1.78	-0.69, 4.16
Economic/social										
Income level (median, $ in thousands)	**-6.68**	**-7.68, -5.68**			**-4.10**	**-6.28, -1.91**	**-3.68**	**-5.92, -1.43**	-1.69	-4.40, 1.08
Unemployed (%)	**3.38**	**2.30, 4.45**			0.44	-1.38, 2.26	0.50	-1.39, 2.42	-0.06	-1.99, 1.91
Without high school education (%)	**4.50**	**3.41, 5.61**			**3.72**	**1.11, 6.40**	**2.34**	**-0.51, 5.05**	1.04	-1.94, 4.12
Health care										
Primary care physicians (N, per 100,000)	**-4.60**	**-5.55, -3.67**					-1.32	-3.38, 0.71	-1.14	-3.26, 0.96
Internal medicine subspecialists (N, per 100,000)	**-3.63**	**-4.54, -2.72**					0.26	-1.61, 2.13	0.26	-1.65, 2.17
Without health insurance (%)	**5.53**	**3.84, 7.21**					1.58	-1.44, 4.56	0.99	-1.77, 3.74
Health-care expenditures ($ in thousands)	**5.56**	**4.40, 6.74**					**4.06**	**2.34, 5.80**	**3.76**	**2.03, 5.52**
Health behaviors										
Access to exercise opportunities (%)	**-5.41**	**-6.40, -4.44**							-0.75	-2.74, 1.22
Food environment index[3]	**-2.95**	**-4.03, -1.89**							-1.78	-4.24, 0.65
Current smoking (%)	**7.26**	**6.06, 8.46**							2.32	-0.65, 5.27
Excessive drinking (%)	**-6.51**	**-7.88, -5.14**							**-2.99**	**-5.46, -0.50**
Marginal variance modeled[4]			7.6%		12.5%		16.2%		19.4%	

Abbreviations: Coeff, coefficient; CI, confidence interval
Bolded coefficients and confidence intervals indicate $p < 0.05$
[1] We modeled age-standardized county-level ESKD mortality rates per 1,000 person-years using four sequential linear regression models with county-level characteristics, so that model 1 includes demographic characteristics, model 2 includes model 1 characteristics plus economic and social characteristics, model 3 includes model 2 characteristics plus health care characteristics, and model 4 includes model 3 characteristics plus health behavior characteristics
[2] Coefficients for bivariate associations are from linear regression models and indicate the change in county-level ESKD mortality per 1,000 person-years associated with a 1-standard-deviation increase in each county-level characteristic
[3] Missing data: n=19 for food environment index
[4] The marginal variance modeled is the percentage of variation in ESKD mortality explained by the contribution of the county-level characteristics, including only the fixed effects

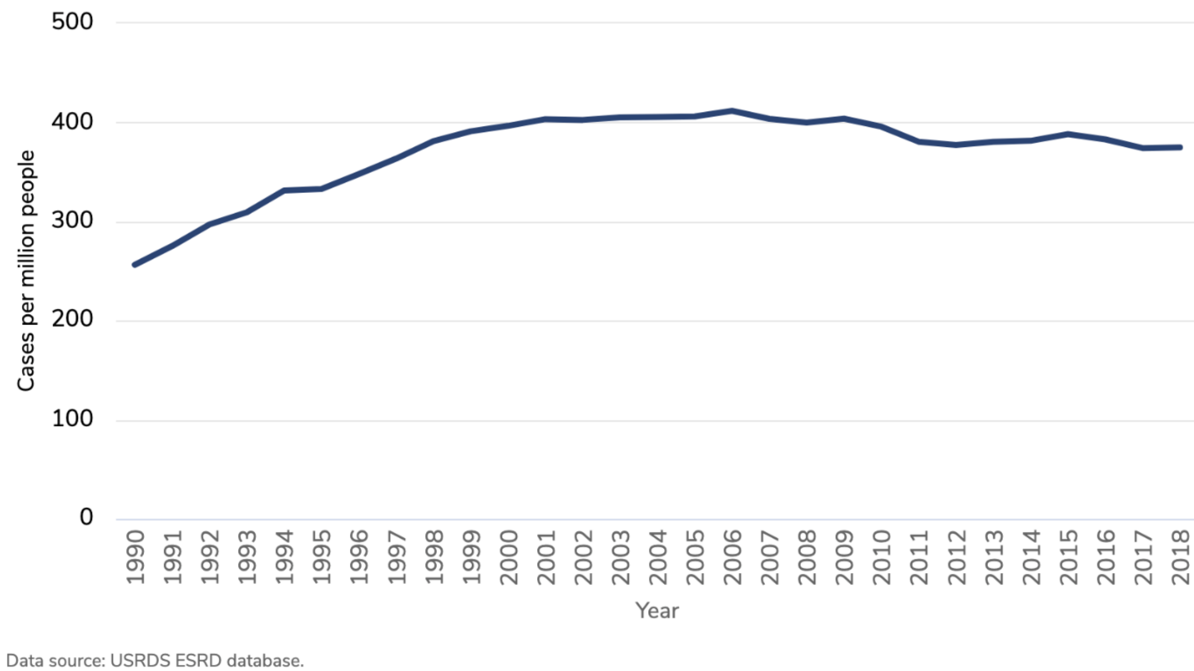

Figure 1. Trends in age, race, and sex adjusted end-stage kidney disease (ESKD) incidence, 1990-2018.[2]

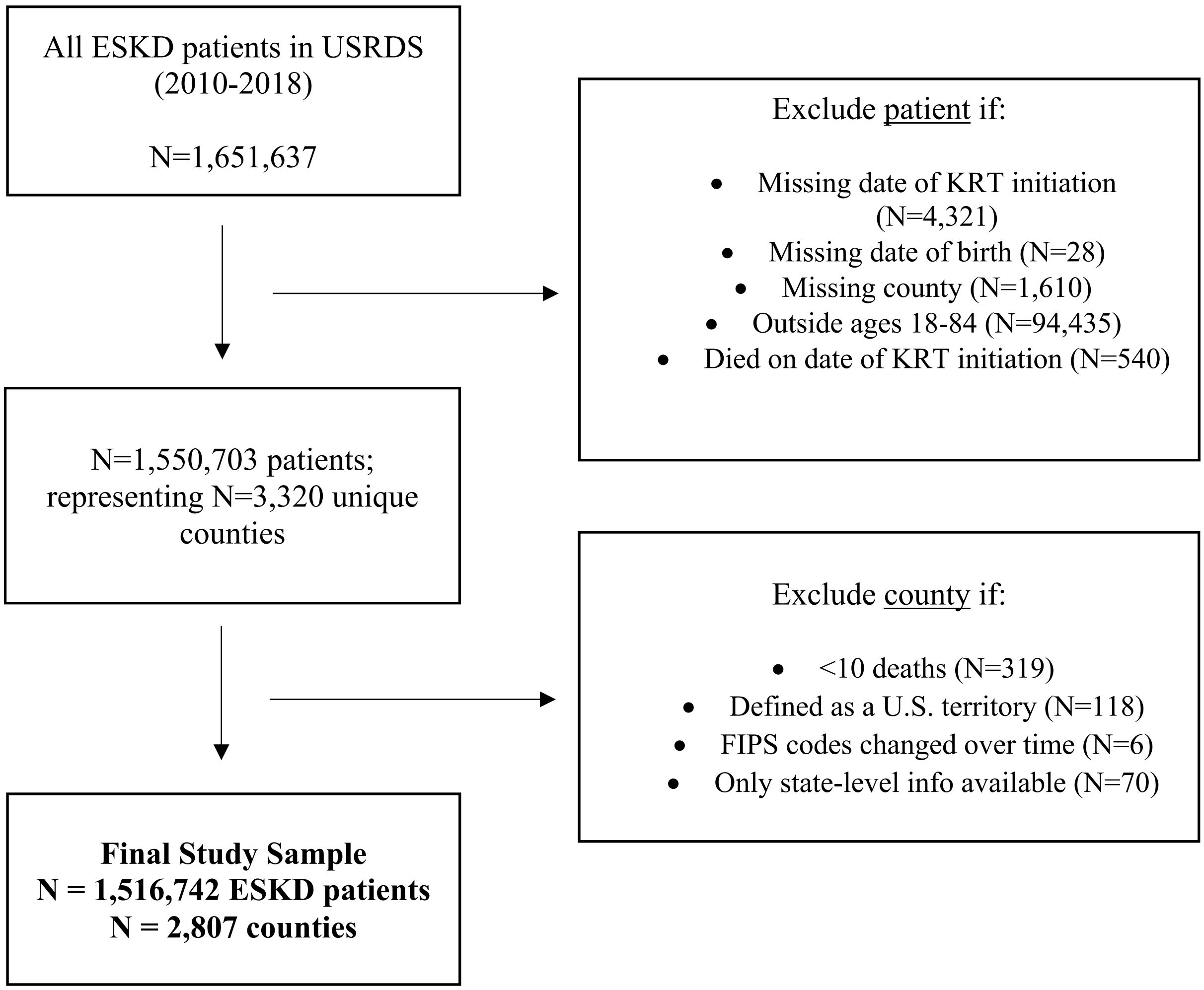

Figure 2. Flowchart of study cohort

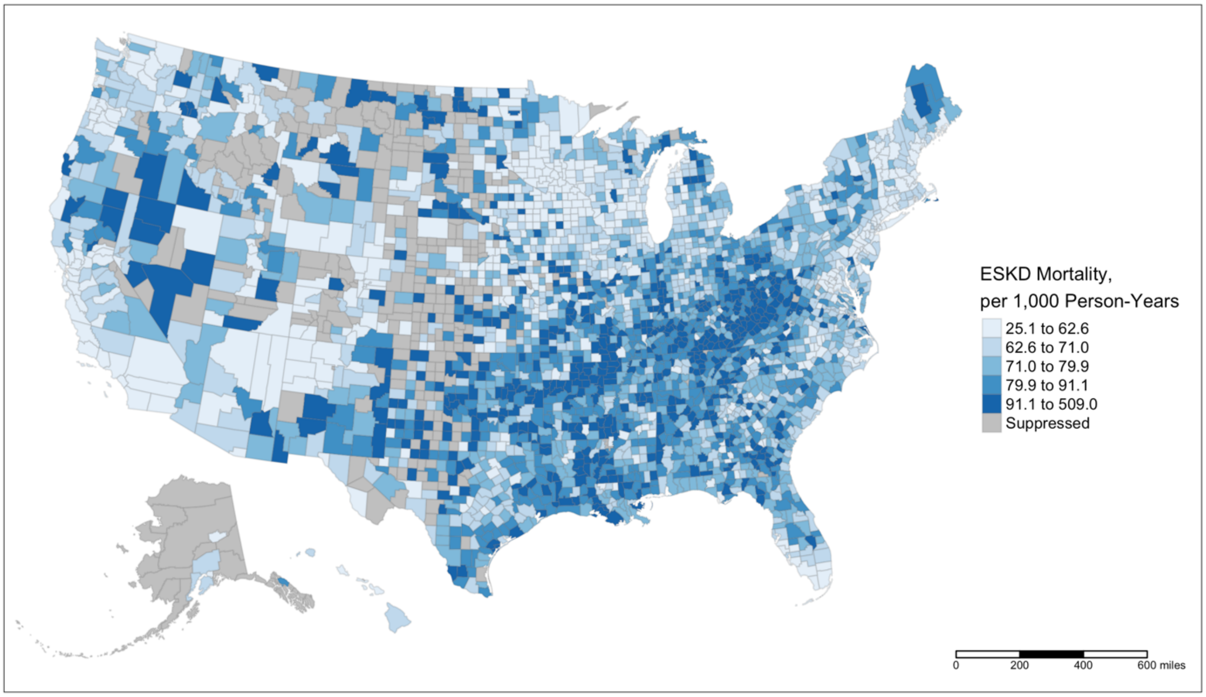

Figure 3. Age-standardized end-stage kidney disease (ESKD) mortality rates across 2,807 counties in the United States, 2010-2018. Mapped rates were obtained from the United States Renal Data System. Rates for counties with fewer than 10 deaths were suppressed. Alaska and Hawaii have been shifted and are not to scale.

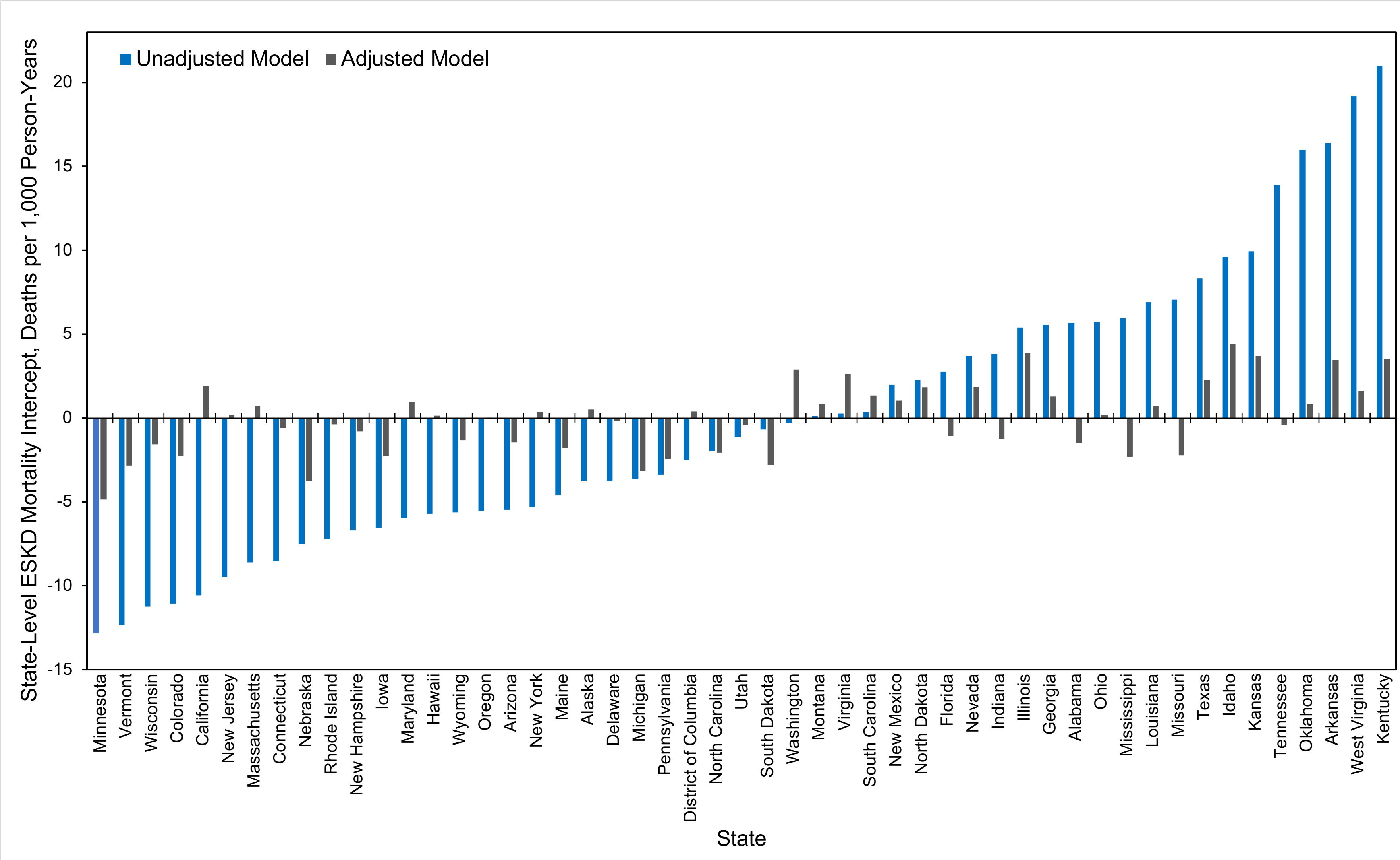

Figure 4. State-level intercepts for age-standardized end-stage kidney disease (ESKD) mortality rates before and after adjustment for county-level characteristics in 2,807 counties in the United States, 2010-2018. The plot shows model intercepts in the unadjusted model (null model) and in the adjusted model (adjusted for all county-level characteristics). Mortality rates were obtained from the United States Renal Data System.

Supplementary Files

Table S1. Variance inflation factors for county characteristics

County Characteristic	Variance Inflation Factor
Population size (N, in thousands)	1.53
Female (%)	1.31
Aged ≥ 65 years (%)	2.28
Hispanic (%)	3.42
Asian-American (%)	2.90
Black (%)	2.05
Native American/Alaskan Native (%)	1.85
Foreign born (%)	11.83
Not proficient in English (%)	9.71
Rural (%)	3.18
Income level (median, $ in thousands)	5.40
Unemployed (%)	1.82
Without high school education (%)	4.33
In poverty (%)	5.89
Primary care physicians (N, per 100,000)	2.43
Internal medicine subspecialists (N, per 100,000)	2.08
Without health insurance (%)	2.19
Health-care expenditures ($ in thousands)	1.29
Access to exercise opportunities (%)	2.05
Food environment index	3.04
Current smoking (%)	3.62
Excessive drinking (%)	2.13

Table S2. Correlation matrix for county characteristics

		V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14	V15	V16	V17	V18	V19	V20	V21	V22
V1	Population size (N, in thousands)	1.00																					
V2	Female (%)	.11	1.00																				
V3	Aged ≥ 65 years (%)	-.22	.08	1.00																			
V4	Hispanic (%)	.21	-.15	-.26	1.00																		
V5	Asian-American (%)	.50	.08	-.29	.18	1.00																	
V6	Black (%)	.06	.14	-.16	-.11	.01	1.00																
V7	Native American/Alaskan Native (%)	-.04	-.03	-.11	.02	-.05	-.11	1.00															
V8	Foreign born (%)	.51	-.03	-.34	.68	.64	-.02	-.06	1.00														
V9	Not proficient in English (%)	.32	-.10	-.31	.82	.34	-.04	-.01	.87	1.00													
V10	Rural (%)	-.40	-.17	.45	-.32	-.47	-.06	.10	-.53	-.35	1.00												
V11	Income level (median, $ in thousands)	.29	.06	-.28	.05	.51	-.26	-.13	.39	.12	-.44	1.00											
V12	Unemployed (%)	-.05	.00	.14	.06	-.16	.26	.13	-.08	.04	.15	-.45	1.00										
V13	Without high school education (%)	-.07	-.14	-.10	.40	-.18	.31	.03	.17	.43	.24	-.57	.41	1.00									
V14	In poverty (%)	-.12	-.10	-.02	.08	-.22	.48	.24	-.13	.04	.24	-.78	.55	.68	1.00								
V15	Primary care physicians (N, per 100,000)	.23	.21	-.08	-.02	.36	-.06	-.06	.23	.04	-.48	.36	-.20	-.39	-.26	1.00							
V16	Internal medicine subspecialists (N, per 100,000)	.28	.19	-.18	.02	.36	.08	-.06	.28	.10	-.41	.28	-.12	-.21	-.13	.69	1.00						
V17	Without health insurance (%)	-.06	-.07	-.05	.43	-.15	.19	.23	.21	.38	.14	-.36	.03	.57	.38	-.25	-.16	1.00					
V18	Health-care expenditures ($ in thousands)	.03	-.03	-.15	.03	-.16	.17	-.02	-.08	.01	.11	-.29	.18	.39	.34	-.26	-.11	.29	1.00				
V19	Access to exercise opportunities (%)	.31	.14	-.13	.12	.38	-.20	-.11	.36	.17	-.63	.47	-.19	-.42	-.40	.47	.34	-.30	-.28	1.00			
V20	Food environment index	.10	-.03	.02	-.01	.17	-.54	-.29	.15	.04	-.08	.61	-.46	-.41	-.73	.17	.08	-.38	-.23	.31	1.00		
V21	Current smoking (%)	-.23	-.01	-.05	-.29	-.36	.28	.29	-.42	-.27	.32	-.64	.39	.46	.66	-.30	-.17	.13	.39	-.41	-.51	1.00	
V22	Excessive drinking (%)	.14	-.18	-.20	.03	.22	-.38	-.03	.16	.04	-.29	.54	-.36	-.52	-.55	.27	.17	-.39	-.28	.41	.49	-.47	1.00