

# Renal Disease Mortality in the U.S. General Population; Demographic, Socioeconomic, Behavioral, and Medical Risk Factors

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## Abstract

**Background:** Social, behavioral, and medical factors that predict specific causes of deaths may vary across countries.

**Objectives:** Current study aimed to determine social, behavioral, and medical characteristics that predict kidney disease mortality in general population in the United States.

**Methods:** Data came from the Americans' changing lives study (ACL), a nationally representative cohort, 1986 - 2011. The study followed 3,617 adults over age of 25 for up to 25 years. Main outcome was time to death due to kidney diseases, derived from death certificates and national death index. Cox proportional hazards models were used to determine the associations between baseline demographic (age, gender, and race), social (education, income, employment), behavioral (exercise, drinking, smoking), and medical (hypertension, diabetes, obesity, depression, and self-rated health) factors and renal disease mortality.

**Results:** In multivariable model, race, age, drinking, smoking, hypertension, and diabetes at baseline predicted deaths due to renal disease. Gender, education, income, employment, exercise, self-rated health, and depression did not predict the outcome.

**Conclusions:** Baseline characteristics can inform who is at higher risk of renal disease mortality over the next 25 years. Race, age, drinking, smoking, hypertension, and diabetes at baseline can all inform programs to reduce burden of kidney disease.

**Keywords:** Epidemiology, Longitudinal Cohort, Population, Deaths, Renal Diseases, Social Determinants, Hypertension, Cause of Death

## 1. Background

Cross-country studies have shown that demographic, social, behavioral, and medical correlates of health outcomes vary across countries (1-4). As a result, there is a need for local studies on demographic, social, behavioral, and medical risk factors of chronic kidney disease (CKD) and end stage renal disease (ESRD) that ultimately cause mortality due to renal diseases (5-7). Race (7), age (8, 9), gender (10), low socioeconomic status (11), life style (12), and medical risk factors (13) are all associated with morbidity and mortality due to CKD and ESRD. Although renal disease is a worldwide health problem (14), the epidemiological pattern and correlates of CKD and ESRD vastly differ in low income versus high income countries (15, 16), suggesting a need for demographic, social, behavioral, and medical risk factors of renal disease mortality in the U.S.

Demographic groups differ in epidemiology and course of CKD (17). In United States, race is a main determinant of mortality due to renal diseases (7, 18). Blacks have higher rate and burden of chronic kidney disease than Whites (7, 19). Compared to Whites, Blacks are 3-4 times more likely to develop kidney failure. While Blacks compose 13% of the US population, they account for one

third of incident kidney failures in the United States (18). Age is also a main determinant of CKD, as the condition is more common among elderly than adults (8, 9). Gender is also another demographic determinant of CKD (10, 20) with more men than women developing ESRD and requiring renal replacement therapy every year (21).

Low socioeconomic status is also another determinant of CKD (11). There is compelling body of evidence showing that economic and social disadvantage and low resources markedly increase the burden of CKD, particularly those unrecognized and untreated (14). Not only CKD is more common among the socially disadvantaged groups, poverty also bear a disproportionate burden of CKD as low SES individuals have worse CKD outcomes, suggesting that poverty may alter beyond the traditional risk factors and may be a vulnerability factor for CKD-associated complications (22).

Life style factors also influence increase risk of chronic kidney disease (12, 23). For instance, epidemiological studies have suggested that participating in vigorous physical activity may protect against kidney disease (24-26). Smoking also increases the risk of CKD, particularly those classified as hypertensive nephropathy and diabetic nephropathy.

thy. When compared to nonsmokers, current smokers have an increased risk of having CKD, while former smokers did not have a statistically significant difference (27).

Medical and clinical factors also increase risk of the conditions (13). For instance, the effects of hypertension (13), diabetes (28), and obesity (29, 30) on CKD are all well known. Self-rated health (SRH) also predicts all-cause (31), cardiovascular (32), cancer (33), and stroke (34), and renal (35) mortality. Not only SRH informs about risk of subsequent mortality (31), it also predicts outcomes associated with renal diseases (36). Finally, depression predicts renal disease and associated outcomes (6, 37).

## 2. Objectives

To extend the current knowledge on psychosocial and medical determinants of renal disease mortality, this study was aimed to determine social, behavioral, and medical characteristics that predict kidney disease mortality in general population in the United States. For this purpose we used Americans' changing lives (ACL) data with 25 years of follow up of a large nationally representative sample of adults in U.S.. As ACL has enrolled a nationally representative sample, our results are generalizable to the U.S. population.

## 3. Study Design

### 3.1. Design and Setting

The ACL is a nationally-representative cohort conducted from 1986 until 2011 in the U.S.. Detailed information on the study design is available elsewhere (38, 39).

### 3.2. Sampling and Participants

The ACL enrolled a stratified multistage probability sample of adults ages 25 or above who lived in the continental U.S. in 1986. The study included 3,617 non-institutionalized respondents (representing 70% of sampled households and 68% of sample individuals at baseline) with an oversampling of those age 60 and older, and African Americans. Wave 1 included 70% of sampled households and 68% of sampled individuals.

### 3.3. Measures

Data were collected on baseline demographic characteristics, socio-economic factors, health behaviors, and health via face to face interview in 1986. Mortality due to renal diseases was collected from 1986 to 2011.

### 3.3.1. Race

In this study, race was defined as non-Hispanic black or non-Hispanic white. Participant's race was defined based on self-reported race and ethnicity, collected at baseline in 1986 with several survey items. Respondents were asked an open-ended response to the question, "In addition to being American, what do you think of as your ethnic background or origins?" Respondents were then asked a multiple-choice question, "Are you white, black, American Indian, Asian, or another race?" and allowed to answer with multiple categories. Those who responded with more than one non-white group were asked to identify which "best described" their race. The survey also assessed the state or foreign country in which the respondent, respondent's mother, and respondent's father were born, and the respondent's father's last name. Finally, participants were asked "Are you of Spanish or Hispanic descent, that is, Mexican, Mexican American, Chicano, Puerto Rican, Cuban, or other Spanish?" Responses from above questions were used to construct race categories of "Non-Hispanic white", "Non-Hispanic black", "Non-Hispanic native American", "Non-Hispanic Asian", and "Hispanic". This analysis only included Non-Hispanic White and Non-Hispanic Black respondents. All Hispanic individuals were dropped from this analysis.

### 3.3.2. Demographic Factors

Demographic indicators included age (a continuous variable as number of years since birth) and gender (a dichotomous variable with male as the referent category).

### 3.3.3. Socio-Economic Characteristics

Socio-economic status was measured with education (less than 12 years of education, and 12 years or more) and household income (a continuous variable as total annual income in the household).

### 3.3.4. Self-Rated Health (SRH)

Respondents were asked to classify their self-rated health as excellent, very good, good, fair, or poor. As past literature has defined SRH in two distinct ways, (40, 41) we also operationalized as both a dichotomous measure and as a continuous score so that we could compare the robustness of findings across specifications. For the first approach we collapsed this five- category scale into two categories (fair/poor vs. excellent/very good/good), a cutpoint that is common in the literature. This measure has shown high test-retest reliability and validity, when considering its predictive power for mortality and other health outcomes (31). Continuous SRH was coded from 1 (excellent) to 5 (poor), with higher values indicative of worse SRH. We operationalized SRH as a dichotomized variable.

### 3.3.5. Hypertension and Diabetes

Hypertension and Diabetes and other medical conditions at baseline were measured using a self-reported measure on seven chronic medical conditions (38-40). All participants were asked whether a health care provider had ever told them they had each of seven focal conditions including hypertension, diabetes, heart disease, chronic lung disease, stroke, cancer, and arthritis.

Obesity. Obesity was defined based on the body mass index (BMI) of larger than 30 kg/m<sup>2</sup>. The BMI level was calculated based on self-reported weights and heights. Weight and height were originally collected in pounds (1 pound = 0.453 kg) and feet (1 foot = 0.3048 m)/inches (1 inch = 0.0254 m), respectively.

### 3.3.6. Health Behaviors

The study also used ACL measures on exercise (physical activity), smoking (i.e., tobacco use), and drinking (i.e., alcohol consumption). The first measure, the physical activity index, asked respondents how often they engaged in the following activities: working in the garden or yard, participating in active sports or exercise, and taking walks. A 4-point Likert scale response ranged from "often" to "never." The index was scored by taking the mean of the three items (42). A high value scored by respondents indicated a high level of physical activity. To measure smoking behavior, we asked respondents whether they currently smoke. A dummy variable was created where 1 = current smoker and 0 = non-smoker. A similar dummy measure was used concerning alcohol use, that is, whether or not the respondent currently drinks (1 = current drinker and 0 = non-drinker) (43).

### 3.3.7. Depressive Symptoms

Depressive symptoms were measured with a brief version of the center for epidemiological studies-depression scale (CES-D) which included 11 items (44). Items measured the extent to which in the past week respondents felt depressed, happy, lonely, sad, restless sleep, that everything was an effort, that people were unfriendly, that they did not feel like eating, that people dislike them, that they could not get going, and that they enjoyed life. Item responses were 1 ("hardly ever") to 3 ("most of the time"). Positively worded items were reverse-coded, and a mean score was computed across all 11 items, resulting in a continuous measure of depressive symptoms for baseline, ranging from 1 to 3. Higher scores indicated more severe depressive symptoms.

### 3.3.8. Mortality Due to Renal Diseases

The main outcome in this study was time to death due to renal diseases, since 1986 over 25 years. Information

on mortality during the 25 follow up period was obtained via the national death index (NDI), death certificates, and also informants. In most cases, time and cause of death could be verified with death certificates. In a handful of cases where death could not be verified with death certificates, it was reviewed carefully. Actual death was certain in all cases. Only in a few cases, the date of death ascertained from the informants or the NDI report, rather than the death certificate (45, 46). Cause of death was coded as unknown when the death certificate or NDI report were unavailable.

The ICD 9 and 10 codes were used to determine cause of mortality, whichever was current at the time the death was recorded. For ICD -9 codes, we used codes 650 (acute glomerulonephritis and nephrotic syndrome), 660 (chronic glomerulonephritis, nephritis, and nephropathy, not specified as acute or chronic, and renal sclerosis, unspecified), 670 (renal failure, disorders resulting from impaired renal function, and small kidney of unknown causes), 680 (infections of kidney), and 690 (hyperplasia of prostate). For ICD-10 codes, we used the categorization of 113 selected causes of death provided by WHO, for which codes 97 (nephritis, nephrotic syndrome, and nephrosis), 98 (acute and rapidly progressive nephritic and nephrotic syndrome), 99 (chronic glomerulonephritis, nephritis, and nephropathy not specified as acute or chronic, and renal sclerosis unspecified), 100 (renal failure), 101 (other disorders of kidney), 102 (infections of kidney), 103 (hyperplasia of prostate), and 104 (inflammatory diseases of female pelvic organ) were used. Respondents who died due to other causes were censored at the time of death. Time of death was registered as number of months from time of enrollment to the study to time of death, based on the month of death and the month of the baseline interview.

### 3.4. Statistical Analysis

The ACL has used applied a complex sampling design (a multistage sample design involving clustering and stratification), which requires appropriate statistical techniques that account for the complex design. We applied weights based on strata, clusters and non-response in all our analyses. Sub-population analyses for surveys were also applied.

Standard error estimation accounted for the sampling weights (due to stratification, clustering, and non-response) using Taylor series linearization. For multivariable analysis, Cox proportional hazards models were used to determine factors associated with time to death due to renal diseases over the 25 year follow up. Sample sizes reflect the un-weighted sample distributions. Univariate, bivariate, and multivariable analyses were performed using Stata 13.0 (Stata Corporation, college station, TX, USA).

We used Cox proportional hazards models for multi-variable data analysis. These models require a dichotomous outcome (death due to renal diseases) and the time when that outcome occurred (time to death due to renal diseases). Renal death was coded zero if the respondent did not die, or died from any other causes. Time to the renal death event, or to censoring, was defined as the number of months from baseline to death, loss to follow up, or the end of the year 2011. In our model, main outcome was time to death due to kidney diseases, and baseline demographic (age, gender, and race), social (education, income, employment), behavioral (exercise, drinking, smoking), and medical (hypertension, diabetes, obesity, depression, self-rated health, and function) factors were independent variables. Hazard ratios with 95% confidence intervals (CI) are reported. A value of  $P < 0.05$  was considered to be statistically significant. Missing data was less than 5%.

#### 4. Results

Table 1 shows descriptive statistics for the overall sample. Most participants were women. Only 37 individuals died due to renal diseases (0.5%).

According to our Cox regression model, race (HR = 2.25), age (HR = 1.07), drinking (HR = 0.16), smoking (HR = 3.22), hypertension (HR = 2.39), and diabetes (HR = 5.21) at baseline predicted deaths due to renal disease. Gender, education, income, employment, exercise, self-rated health, and depression did not predict the outcome ( $P > 0.05$  for all) (Table 2)

#### 5. Discussion

Current study investigated multiplicative risk factors that influence kidney disease mortality over 25 years in U.S.. According to our findings, race, age, drinking, smoking, hypertension, and diabetes at baseline predicted deaths due to renal disease. Findings are unique as we used a nationally-representative sample of U.S. adults.

In line with previous research that has shown demographic groups may differ in epidemiology and course of CKD (17), we showed that age and race influences which Americans die from renal disease. In United States, race is a main determinant of mortality due to renal diseases (7, 18). Blacks have highest rates and burden of CKD compared to any other racial group (7, 19). Compared to Whites, Blacks are 3-4 times more likely to develop kidney failure (18).

In our study, Blacks were at higher risk of renal disease mortality. Ironically, there are previous studies that have documented better survival and lower psychological distress among Blacks with CKD when compared to Whites,

despite their higher number of medical comorbidities as well as more severe CKD (47).

Similar to our finding, age is also shown as a main determinant of CKD, as CKD is more common among elderly (8, 9). In our study, however, gender did not show an independent effect on outcome. Gender is shown to be another major determinant of CKD (10, 20). More men than women develop ESRD every year, requiring renal replacement therapy (21). In United States, from 96,295 patients who initiated ESRD therapy in 2001, 54% were men and 46% were women (21).

In our study, education, income and employment did not stay as independent predictors of renal disease mortality, while all other risk factors are considered. Although low socioeconomic status is a determinant of CKD (11), their effects may be due to medical and behavioral risk factors (7). Economic and social disadvantage and low resources operate as a distal determinant and increase the burden of CKD (14, 22) possibly through increasing risk of diabetes, hypertension, and obesity, smoking, and lack of exercise.

In our study, drinking and smoking were predictive of renal disease mortality, however, exercise did not independently predict the same outcome. Role of life style as a modifiable determinant of CKD is known (12, 23). In line with our findings, smoking also increases the risk of CKD, particularly those classified as hypertensive nephropathy (OR = 2.85) and diabetic nephropathy (OR = 2.24). When compared to nonsmokers, current smokers have an increased risk of having CKD (OR = 1.63), while former smokers did not have a statistically significant difference. The CKD risk associated with smoking is dosage dependent and OR for smokers with  $> 30$  pack-years reaches 2.6. (27). Although not supported by our study, exercise may protect against CKD (23-26).

We could also replicate the literature on medical and clinical factors of CKD (13). Similar to our study, hypertension (13) and diabetes (28) are shown to shape risk of CKD. We could not however, replicate the effect of obesity, as its effect may not be independent but via hypertension and diabetes (29, 30). We also did not find role of depression as a predictor of renal disease mortality, however, depression is shown to have a role previously (6, 37).

We also did not show that SRH predicts renal disease mortality, while diabetes, hypertension, and other risk factors are controlled. SRH is shown to predict all-cause (31), cardiovascular (32), cancer (33), and stroke (34), and renal (35) mortality. Although SRH predicts outcomes associated with renal diseases (36), this effect may be due to other risk factors that we controlled for.

SRH has previously shown to predict renal and all-cause mortality across diverse populations (48). While

**Table 1.** Descriptive Statistics in the Pooled Sample and Also Based on Race

	Mean (SE)	95 % CI	Mean (SE)
<b>Age</b>	47.79 (0.53)	46.72 - 48.86	47.98 (0.60)
<b>Chronic Medical Conditions</b>	0.80 (0.03)	0.74 - 0.85	0.78 (0.03)
<b>Self-Rated Health</b>	2.30 (0.024)	2.25 - 2.35	2.28 (0.026)
<b>Education</b>	12.53 (0.096)	12.34 - 12.73	12.69 (0.105)
<b>Income</b>	5.41 (0.093)	5.22 - 5.60	5.57 (0.101)
	% (SE)	95 % CI	% (SE)
<b>Gender</b>			
Men	47.26 (0.01)	44.86 - 49.68	47.82 (0.01)
Women	52.74 (0.01)	50.32 - 55.14	52.18 (0.01)
<b>Education &gt; 12</b>			
No	23.93 (0.01)	21.37 - 26.70	21.71 (0.01)
Yes	76.07 (0.01)	73.30 - 78.63	78.29 (0.01)
<b>Renal death</b>			
No	99.48 (0.00)	98.97 - 99.74	99.56 (0.00)
Yes	0.52 (0.00)	0.26 - 1.03	0.44 (0.00)
<b>Self-Rated Health</b>			
Good-Excellent	85.06 (0.008)	83.33 - 86.64	85.97 (0.009)
Poor-Fair	14.94 (0.008)	13.36 - 16.67	14.03 (0.009)

some studies suggest that contextual factors such as race and ethnicity alter the effect of SRH on mortality (49, 50), some other studies have suggested that SRH universally predicts mortality across populations, irrespective of population and geographic region (51, 52).

### 5.1. Limitations

This study has a few limitations. First and foremost, we did not have any measure of baseline kidney disease, and only used a limited number of medical risk factors at baseline. We relied on self-reported data to measure hypertension and diabetes that may be subjected to recall bias (53). Future research should also validate self-reported chronic medical conditions using medical record data. Future research should specifically measure baseline and progression of kidney disease as well as biological measures of kidney function. In addition, while all risk factors are subject to change over time, their change was not modeled in this study. This approach was taken because we were interested in the long term effects of demographic, social, behavioral, and medical risk factors of renal disease mortality in the U.S..Despite these limitations, the results extend our current understanding regarding in predictors of mortality due to renal disease (54-56). Main strengths of this study include using a nationally representative sample, large sam-

ple size, and long term- follow up all needed to study rare outcomes such as death due to renal diseases.

### 5.2. Conclusions

A number of baseline factors such as race, age, drinking, smoking, hypertension, and diabetes predict death due to renal disease over a 25-year period in United States. These findings can be used for programming as well as planning to reduce death due to renal diseases particularly among socially disadvantaged populations in the U.S.

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**Table 2.** Results of Cox Proportional Hazards Models Predicting Death Due to Renal Disease Over 25 Years in United States

	HR	SE	95% CI		P
<b>Race</b>					
Whites	ref				
Non-Hispanic Black	2.25	0.89	1.01	4.98	0.046
Non-Hispanic Other	1.03	1.24	0.09	11.55	0.981
Hispanic	0.54	0.43	0.11	2.66	0.441
Age (Years)	1.07	0.02	1.03	1.11	0.000
<b>Gender</b>					
Men	ref				
Women	0.43	0.25	0.13	1.39	0.153
<b>Education</b>					
High	ref				
Low	0.59	0.27	0.23	1.49	0.254
<b>Income</b>					
High	ref				
Low	0.94	0.47	0.35	2.57	0.907
<b>Employment</b>					
Employed	ref				
Unemployed	2.73	1.70	0.77	9.59	0.115
<b>Smoking</b>					
Negative	ref				
Positive	3.22	1.64	1.15	8.98	0.027
<b>Drinking</b>					
Negative	ref				
Positive	0.16	0.07	0.06	0.39	0.000
Exercise	0.75	0.17	0.48	1.19	0.218
<b>Obese</b>					
Negative	ref				
Positive	1.29	0.52	0.58	2.88	0.529
<b>Hypertension</b>					
Negative	ref				
Positive	2.39	1.04	1.00	5.75	0.051
<b>Diabetes</b>					
Negative	ref				
Positive	5.21	2.23	2.20	12.35	0.000
<b>Depressive Symptoms</b>					
Low (< = M + SD)	ref				
High (> M + SD)	1.77	0.99	0.57	5.46	0.316
<b>Self-Rated Health</b>					
Excellent-Good	ref				
Poor-Fair	1.68	0.71	0.72	3.94	0.226

## Footnote

**Informed Consent:** All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from all participants included in the study.

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