Cost-Related Non-adherence and Mortality in Patients with Diabetes and Cardiovascular Disease: A Multi-year Investigation Using the National Health Interview Survey

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I, Sarah Van Alsten, have neither given nor received any unauthorized assistance (as detailed in the Brown School student handbook) in the completion of this work. I certify that the work is authentically my own.

**INTRODUCTION**

Diabetes and cardiovascular disease (CVD) currently affect 15% and 13% of United States (U.S.) adults, respectively.1,2 These conditions are the seventh and first leading causes of death in the U.S.,3 and though progress has been made in reducing incidence and mortality of cardiovascular disease,4,5 diabetes incidence is increasing, particularly among younger age groups.1,6

Beyond the substantial human cost, diabetes and CVD are associated with significant economic burden. Together, diabetes and CVD accounted for nearly $200 billion in personal healthcare costs in the U.S. in 2013, a figure which increased to $283 billion when also accounting for treatment of hypertension, a common risk factor for heart disease.7 Moreover, expenditures are expected to grow in the coming decades, largely due to the aging of the population and increased number of years lived with disease.2,8–10 A substantial portion of these cost will come from prescription prices, which are continuing to grow at a rate of 5-6% annually.7

High medication costs primarily affect patients. Among persons with diabetes or hypertension, cost is the most common reason for medication nonadherence, with more than two-thirds of patients reporting skipping or delaying medication due to financial barriers.11 These behaviors are collectively referred to as ‘cost-related nonadherence’ (CRN).12

The prevalence of CRN among patients with chronic conditions is substantially higher than that of the general population.13 For instance, in comparison to the 6-7% of U.S. adults who reported at least one form of CRN in 2016,13 a 2018 survey of 627 U.S. adults with type 1 diabetes found that more than 25% had rationed insulin in the previous year to manage costs, with 3.2% of patients rationing insulin on a daily basis and 38.6% decreasing use of glucose testing equipment to manage costs.14(p1) A 2017 study including individuals with type 1 or type 2 diabetes seen at an outpatient clinic reported similar prevalence of CRN, finding that 40% of patients with non-adherence did not discuss underuse with their physician.14,15

Despite its high prevalence, few studies have investigated the medical implications of CRN. In general, non-adherence is associated with greater risk for hypertension, hypercholesterolemia, elevated HbA1c levels, and mortality in individuals with diabetes,15–17 and with greater risk for dyslipidemia, extended hospitalizations, and mortality in patients with hypertension or CVD.18–20 Yet, because previous studies documenting the adverse consequences of medication non-adherence have not specified reasons for non-adherence, it is unclear how CRN specifically contributes to these outcomes. The aims of this study were a) to assess the prevalence of CRN in a representative sample of U.S. adults with diabetes and CVD and b) to determine whether CRN is associated with higher risk of mortality in U.S. adults with diabetes and CVD.

**METHODS**

**Source Data**

This analysis used publicly available data from the National Health Interview Survey (NHIS).21 The NHIS is a cross-sectional, population-representative multi-stage probability sample of non-institutionalized U.S. adults administered annually by the National Center for Health Statistics.22 Briefly, all interviews were conducted using computer-assisted personal interviews by trained U.S. Census Bureau staff, and consisted of two parts: 1) the ‘core’ questionnaire and 2) supplemental questions. The core questionnaire \ assesses basic demographic information, health status, behaviors, and healthcare utilization. Supplemental questions vary from year to year to assess current health issues, and have included topics such as in-depth healthcare utilization and insurance information, cancer screening, and mental health.22 Questions relating to CRN were introduced into the survey in 2000, while 2014 is the most recent year for which mortality data are available, thus, in the current study I included data from the 2000 to 2014 waves only.

*Study Sample*

I restricted the study sample to individuals age 18 and over with diabetes, hypertension, and/or CVD for this secondary data analysis. Diabetes diagnosis was ascertained through a single item, asking whether participants had been told by a medical professional that they had “(Other than during pregnancy) diabetes?” (*N* = 39,571). I operationalized CVD as a diagnosis of one or more of the following: “a heart attack?” (*N* = 16,142), “angina pectoris?” (*N* = 11,064), “coronary heart disease ?” (*N* = 21,005), or “any kind of heart condition other than coronary heart disease, angina pectoris, or a heart attack?” (*N* = 35,016) or “any kind of stroke?” (*N* = 13,214). In total, there were 61,968 respondents with CVD. Additionally, I considered an expanded definition of CVD including diagnosis of hypertension (*N* = 133,967); under this expanded definition a total of 156,892 participants were considered to have CVD.

**Measures**

*Exposure*

The primary exposure of interest was CRN. Because CRN was assessed differently in the NHIS before and after 2010, I harmonized data to generate a single dichotomous variable representing whether a participant had experienced CRN in the previous year. From 2000 to 2009, I operationalized CRN as a positive response to the single item asking whether participants had needed, but could not afford, medication in the previous year. From 2010 to 2014, I coded CRN as any affirmative response to items asking participants whether, in order to save money, they had skipped medication doses, taken less medicine than prescribed, or delayed taking medicine in the last year.

*Outcome*

The two primary outcomes for this analysis were all-cause and disease-specific mortality. Vital status through December 2015 was determined through probabilistic linkage to the National Death Index. Respondents younger than age 18 and those providing insufficient identifying information were not eligible for linkage. Follow-up time was calculated as the span between date of interview and the last day in the quarter and year of death, when vital status was ascertained. For surviving individuals, follow-up time was censored at December 31, 2015. I excluded ten participants with diabetes (0.0007 %) and eight participants with heart conditions or CVD (0.0003 %) from analyses because recorded death dates occurred prior to interview dates. Figure 1 shows a conceptual model of the factors which contribute to CRN, and the proposed association between CRN and mortality.

*All-cause mortality*

I operationalized all-cause mortality as defined as any positive record of death in the National Death Index.

*Disease-specific mortality*

Probabilistic linkage between participant records and the National Death Index was used by staff at the National Center for Health Statistics to determine leading and contributing causes of death for all participants with recorded mortality events. I defined disease-specific deaths due to diabetes as those in which diabetes (ICD-10 codes E10 – E14) was listed as the primary cause of death. I included two definitions of disease-specific deaths for individuals with CVD, depending upon whether the definition of CVD was expanded to include hypertension. For the narrower definition, I operationalized disease-specific deaths due to CVD as those in which the leading cause of death was listed as heart (ICD-10 codes I00-I09, I11, I13, I20-I51) or cerebrovascular diseases (ICD-10 codes I60 – I69). For the expanded definition of CVD including hypertension, I operationalized disease-specific deaths as all causes in the narrow definition as well as essential hypertension and hypertensive renal disease (ICD-10 codes I10, I12, and I15). I defined disease-specific mortality separately by condition of interest such that individuals with a history of more than one condition (e.g. diabetes and hypertension) were only considered to have the outcome in analyses where the listed cause of death matched the primary disease of interest. For example, if an individual with both diabetes and CVD had diabetes listed as the primary cause of death, I considered them to have disease-specific morality in diabetes analyses but not in CVD analyses.

*Statistical Analyses*

I compared baseline demographic characteristics of participants with and without CRN using design-based Chi-squareand Wilcoxon signed rank tests for categorical and continuous variables, respectively. I used Cox proportional hazard regressions to assess the associations between CRN and all-cause and disease specific mortality among individuals with diabetes or CVD. Consistent with my operationalization of CVD, I modelled associations between CRN and mortality among two subsamples of participants with CVD: one, among those who met criteria for the narrow definition of stroke or any heart condition, excluding hypertension, and two, among those who met criteria under the expanded definition of stroke or any heart condition, including hypertension.

For all-cause mortality, I first fit an unadjusted model including only CRN, then adjusted for age, sex, insurance (private, public, Medicare, other, or none), race (white, Black or African American, Hispanic or Latino, Asian, or other), education (≤ high school, some college, college degree or greater), and diagnoses of other chronic conditions: cancer (all models), diabetes (CVD models only), hypertension (diabetes and CVD models not including hypertension) and CVD (diabetes models only). I selected adjustment variables using a directed acyclic graph as those with known or suspected confounding relationship between CRN and mortality (Supplementary Figure 1). Similarly, to estimate the unadjusted and adjusted association between CRN and disease-specific mortality, I fit a model including only CRN then adjusted for all confounders in all-cause mortality models except presence of additional chronic conditions (Supplementary Figure 2). Unless otherwise noted, hazard estimates for CRN represent the total, rather than the direct, effect of CRN on mortality, and I present coefficients for confounders as supplementary data because these estimates cannot typically be interpreted as either the direct or total effects of covariates on mortality.23

Additionally, I conducted a sensitivity analysis by stratifying at year of interview (≤ 2010, > 2010) to determine if the change in measurement of CRN in 2010 substantially impacted findings. I evaluated models for presence of influential observations and multicollinearity using standardized dfbeta values and variance inflation factors, respectively, tested for proportional hazards using scaled Schoenfeld residuals, and assessed log-linearity of by plotting Martingale residuals against continuous predictors. In instances where models did not meet assumptions, I performed further sensitivity analyses to assess the robustness of results against violations: for influential observations, I deleted suspected influential cases and then refit models, for log-linearity, I inspected plots for points at which the log-hazard deviated from linearity and refit models using natural splines at inflection points. All analyses were conducted in R, version 3.6.1,24 and RStudio, version 1.2.5019.25 Cox models were performed using the *survival* package,26 and, to account for the complex sampling methodology of the NHIS, all regressions and descriptive statistics were adjusted for survey design using the *survey* package.27

**Results**

*Descriptive Statistics*

The final analytic sample sizes were 34,839 for diabetes, 53,009 for CVD excluding hypertension, and 128,723 for CVD including hypertension. Twenty percent of participants with diabetes reported at least one form of CRN, as did 19.1% of participants with CVD and 17.2% of participants with CVD including hypertension. As depicted in Table 1, the most common form of nonadherence was needing but not being able to afford medication (86 - 88% for all three conditions), followed by delaying medication doses (68 – 70%), taking less medication than prescribed (56 – 58%), and skipping medication doses (53 – 56%). Among participants with information on specific forms of CRN, 37.8% reported all three CRN behaviors (delaying, taking less, and skipping medication), and 15.3% reported two CRN behaviors.

**All-cause Mortality**

Among individuals with diabetes, 8,909 (23.6%) died of any cause during the follow-up period, 1,086 (12.2%) of whom reported CRN. As shown in Table 2, the unadjusted hazard of all-cause mortality in individuals with CRN was 0.752 times (95% CI = 0.694 – 0.815) that of those without CRN. The direction of association between CRN and all-cause mortality was reversed after adjusting for potential confounders, such that CRN was associated with an 18.3% increase in the hazard of death (95% CI = 1.092 – 1.281) in individuals with diabetes relative to those without CRN. The unadjusted association between CRN and all-cause mortality was higher and the adjusted association lower for individuals interviewed prior to 2011 relative to those interviewed in and after 2011 (unadjusted *p*interaction= 0.006; adjusted *p*interaction= 0.004, Table 2). A complete list of hazard ratios for confounders is show in Supplementary Table 1.

*Cardiovascular Disease*

The median length of follow-up for individuals with CVD, excluding hypertension, was 304 weeks (IQR = 160 – 534). During that time, 16,345 (27.8%) of individuals categorized under the narrow definition of CVD died, 1,645 (10.1%) of whom reported CRN. CRN was associated with a 29.8% lower hazard of death (95% CI = 0.658 – 0.252) in the unadjusted model and a 14.8% increase in the hazard of death after adjustment (95% CI = 1.073 – 1.300) among individuals with CVD. The unadjusted hazard ratio of all-cause mortality for CRN was lower among those interviewed in and after 2011 compared to those interviewed before 2011 (*p*interaction < 0.001), while the adjusted hazard ratio did not significantly differ by interview period (*p*interaction = 0.149; Table 2). Findings were similar for the expanded definition of CVD (Table 2). Supplementary Tables 2 and 3 display the estimated hazard ratios for all confounders.

**Disease-Specific Mortality**

*Diabetes*

Among individuals with diabetes, 3,045 (8.74%) died of diabetes during the follow-up period and of these individuals, 392 (12.9%) had experienced CRN. As shown in Table 2, CRN was associated with a 24.3% lower hazard of diabetes-related deaths before adjustment for confounders (95% CI = 0.674 – 0.870). After adjustment, the direction of association changed such that CRN was associated with a 22.6% higher hazard of diabetes-related deaths (95% CI = 1.074 – 1.399). The strength of association between CRN and diabetes-related mortality did not differ between those interviewed prior to versus in and after 2011 in either unadjusted (*p*interaction = 0.211) or adjusted (*p*interaction *=* 0.272) models, although the association was significant only among those interviewed in earlier waves. Supplementary Table 4 shows the hazard ratios for confounding variables.

*Cardiovascular Disease*

During follow-up, 4,845 (9.14%) of individuals with CVD, excluding hypertension, died due to heart or cerebrovascular disease, 449 (9.3%) of whom had reported CRN. CRN was associated with a lower hazard of disease-specific mortality in the unadjusted model. After adjusting for confounders, individuals with CVD under the narrow and expanded definitions who reported CRN had 12.3% and 30% higher hazards of disease-specific mortality relative to individuals who did not report CRN, although the association was not significant for the narrow definition (narrow 95% CI = 0.993 – 1.271, expanded 95% CI = 1.196 - 1.434; Table 2). When stratified by year of interview, individuals interviewed prior to 2011 had significantly lower unadjusted hazard of disease-specific mortality than those interviewed in and after 2011 (narrow *p*interaction *=* 0.0179; expanded *p*interaction *=* 0.031), but the adjusted hazard ratios did not differ between strata (narrow *p*interaction *=* 0.139; expanded *p*interaction *=* 0.220). Hazard ratios for associated confounders are displayed in Supplementary Tables 5 and 6.

**Model Assumptions**

Deletion of cases with suspected influence did not substantially change estimates (Supplementary Table 7). Models did not show evidence of multicollinearity (all VIFs < 1.5). Age displayed log-linearity with estimated hazards from 18 – 75 years, after which there was a non-linear increase in the risks of both all-cause and disease specific deaths. Refitting models using natural splines at age 75 did not substantially change point estimates (Supplementary Table 8). Finally, while the assumption of proportional hazards was met for the CRN coefficient in all adjusted models, all models violated the proportional hazards assumption globally (all *p* < 0.001).

**Discussion**

In this secondary analysis, I found that one-fifth of persons with diabetes and CVD living in the United States experienced one or more forms of CRN in the previous year. Although CRN was associated with lower household income and lack of health insurance a substantial proportion of individuals unable to afford medication had insurance and incomes at or above the United States median. Moreover, CRN was associated with 15 – 30% higher risk of all-cause and disease-specific mortality among individuals with diabetes or CVD although significant associations were only observed among those interviewed prior to 2011. Associations were of similar magnitude irrespective of illness and ultimate cause of death.

In most cases, hazards of CRN were subject to strong qualitative confounding. Given that younger individuals are at greater risk for CRN and, in general, a lower risk for mortality, I speculate that this variable played the strongest role in the inverse associations observed for unadjusted estimates, particularly when considered in conjunction with insurance. Other confounders, such as education and higher household income were also significantly related to mortality but are expected to be positive confounders and would likely upwardly bias estimates.

The prevalence of CRN reported in this sample (~20%) remains largely consistent with assessments from other nationally representative data, such as the Behavioral Risk Factor Surveillance Survey (BRFSS).28 Similarly, while there is limited research on adverse outcomes associated with CRN, I note that the association between CRN and mortality in the present study is of similar magnitude to previous estimates for nonadherence generally,29,30 indicating that adverse effects of nonadherence may not vary according to reasons for nonadherence.

There most probable pathway through which CRN and mortality could be associated is increased risk of complications. Inconsistent adherence has been shown to increase adverse outcomes in patients with diabetes and CVD, including retinopathy, nephropathy, microvascular complications,31 uncontrolled hypertension and coronary revascularization.19 In addition to direct effects of complications on mortality, greater disease severity often necessitates additional treatment regimens and higher financial costs, thereby potentially reinforcing the likelihood of CRN and additional adverse consequences.

Though not necessarily motivated by net cost considerations, several states have begun to consider drug pricing policies that will make medication more affordable for individuals with diabetes. As of February 2020, two states (Colorado and Illinois) have instituted $100 monthly price caps on insulin co-payments,32,33 with several others considering similar legislation.34–38 Implicit in these policies is the assumption that lower prescription drug prices will have a positive impact on patients by decreasing financial burden, improving health, or both. The common counterargument is that price controls would have negative implications for pharmaceutical research and development,39 however, these considerations should be balanced against the necessity of the drug and availability of substitutes. In the case of insulin, a 100-year old drug that is essential for individuals with type 1 diabetes and requires little capital outlay on the production side,40 small reductions in innovation are likely justified by increasing prescription accessibility, especially for those in greatest financial need.41 Nonetheless, continued assessment is needed to monitor policy reach, effectiveness, and potential for translation to other chronic conditions.

The major strengths of this study were the use of a large and nationally representative sample, detailed adjustment for and identification of confounding variables, and thorough robustness checks for potential threats to internal validity. Given the nature of the sample, I was also able to investigate consequences of CRN in adults with all ranges of health insurance, including those covered through public and private sources. Previous analyses with comparable sample sizes to this study have been drawn limited to Medicare beneficiaries only,44–46 who are not representative of the younger population and may differ on other adherence dimensions, such as positive medication values and beliefs.45

Still, my findings should be interpreted in light of several limitations. First, because interviews were conducted cross-sectionally, I only had access to a single assessment of CRN, leading to probable immortal time bias in the measure of the exposure. Participants who did not report CRN at baseline may have experienced CRN later in the follow-up period and vice versa. Second, due to the change in survey questions about CRN behaviors beginning in 2011, observed differences in hazard ratios by year of interview should be interpreted with caution. Inconsistencies could be an artifact of measurement error, shorter follow-up times, or period effects such as the passage of the Affordable Care Act.46 Similarly, the measurement of CRN was non-specific and may not have captured variations in CRN behavior with consequences for mortality. For instance, respondents were also not asked about specific medications that they restricted or could not afford, so it is possible that individuals reporting CRN were adherent to crucial medications (e.g. insulin, statins) and non-adherent to others.47 However, lack of specificity in CRN measurement would likely bias results toward the null, as I expect that individuals with CRN to less critical medications would have better outcomes than those who were nonadherent to essential prescriptions. Third, although the number of individuals with improbable death dates was low and I excluded all such cases, the existence of cases with erroneous (negative) lengths of follow-up time in this study sample likely reduced the internal validity of mortality analyses. Nonetheless, the National Death Index is commonly used in studies of mortality and has been shown to have high sensitivity and validity when compared to other administrative records.48–50

Altogether, these results suggest that CRN is a substantial risk factor for mortality in persons with chronic illness and that efforts to address rising prescription drug costs may be valuable for increasing patient health and longevity. Future studies should identify other long-term health implications of CRN and potential strategies to increase adherence in patients with limited financial access to medication.

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**Figure 1.** Conceptual model of relationship between cost related nonadherence and mortality. Components depicted in grey are assumed to be determinants of healthcare access and utilization (Anderson, 1968) while components shown in black are the primary focus of the current study. Skipping medication means forgoing medication doses altogether as a result of cost, substitution of medication means taking cheaper alternative medications, and delaying medication means delaying taking doses or waiting to fill prescriptions to make medication last longer and save money.A screenshot of a cell phone

Description automatically generated

**Table 1.** Sociodemographic characteristics of 2000- 2014 National Health Interview Survey participants with diabetes, cardiovascular disease (CVD), and/or hypertension.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Diabetes | | CVD, excluding Hypertension | | CVD, including Hypertension | |
|  | CRN | No CRN | CRN | No CRN | CRN | No CRN |
| N (weighted) 2000 -2014 | 1872888.6 (19.9) | 7521527.8 (80.1) | 4311920.2 (19.1) | 18276849.2 (80.9) | 10364659.4 (17.2) | 49886713.8 (82.8) |
| Age Median (IQR) | **55.00 [46.00, 63.00]** | **64.00 [54.00, 73.00]** | **55.00 [45.00, 65.00]** | **67.00 [54.00, 77.00]** | **53.00 [42.00, 62.00]** | **62.00 [50.00, 74.00]** |
| Female | **779793.6 (61.2)** | **1071740.3 (52.2)** | **1178873.2 (62.2)** | **1535387.7 (50.7)** | **2653920.1 (62.9)** | **4260646.5 (53.5)** |
| BMI Median (IQR) | **31.10 [17.30, 54.50]** | **29.80 [16.10, 53.90]** | **28.20 [15.70, 54.50]** | **27.40 [14.80, 55.30]** | **29.00 [15.70, 54.50]** | **28.10 [14.80, 55.30]** |
| Region |  |  |  |  |  |  |
| Northeast | **153906.2 (12.1)** | **362749.5 (17.7)** | **233900.1 (12.3)** | **546129.7 (18.0)** | **515853.1 (12.2)** | **1421081.4 (17.8)** |
| Midwest | **299530.7 (23.5)** | **485259.3 (23.6)** | **471369.1 (24.9)** | **743503.1 (24.5)** | **990868.0 (23.5)** | **1935019.0 (24.3)** |
| South | **588225.5 (46.2)** | **819511.7 (39.9)** | **846689.4 (44.7)** | **1165676.9 (38.5)** | **1948269.3 (46.2)** | **3073716.8 (38.6)** |
| West | **232115.0 (18.2)** | **385883.1 (18.8)** | **343579.6 (18.1)** | **574697.3 (19.0)** | **764312.7 (18.1)** | **1532803.4 (19.2)** |
| Race/Ethnicity |  |  |  |  |  |  |
| White | **762645.3 (59.9)** | **1368077.9 (66.6)** | **1354773.1 (71.5)** | **2414174.9 (79.7)** | **2794604.7 (66.2)** | **5961428.7 (74.9)** |
| Black | **274570.6 (21.6)** | **319727.9 (15.6)** | **319393.8 (16.8)** | **314723.7 (10.4)** | **844987.7 (20.0)** | **1046326.7 (13.1)** |
| Hispanic/Latino | **196393.1 (15.4)** | **257571.8 (12.5)** | **171492.5 (9.0)** | **199751.8 (6.6)** | **463015.7 (11.0)** | **639574.3 (8.0)** |
| American Indian/Alaska Native | **15385.5 (1.2)** | **22876.9 (1.1)** | **25105.5 (1.3)** | **23328.1 (0.8)** | **44338.7 (1.1)** | **53119.3 (0.7)** |
| Asian | **21015.1 (1.6)** | **79854.6 (3.9)** | **20068.9 (1.1)** | **70387.3 (2.3)** | **60015.6 (1.4)** | **244833.0 (3.1)** |
| Other | **3767.9 (0.3)** | **5294.7 (0.3)** | **4704.3 (0.2)** | **7641.1 (0.3)** | **12340.8 (0.3)** | **17338.6 (0.2)** |
| Health Insurance Coverage |  |  |  |  |  |  |
| None | **321969.8 (25.3)** | **96992.3 (4.7)** | **475956.7 (25.2)** | **111246.1 (3.7)** | **1285644.8 (30.6)** | **410375.3 (5.2)** |
| Public Insurance (Medicaid/CHIP) | **243829.1 (19.2)** | **397405.6 (19.4)** | **382161.9 (20.2)** | **498622.5 (16.5)** | **728162.3 (17.3)** | **1138810.5 (14.3)** |
| Private | **466939.6 (36.7)** | **1041669.2 (50.8)** | **618065.9 (32.7)** | **1590471.4 (52.6)** | **1492673.9 (35.5)** | **4573969.1 (57.5)** |
| Military | **18252.2 (1.4)** | **125139.6 (6.1)** | **35798.0 (1.9)** | **206855.3 (6.8)** | **61814.6 (1.5)** | **451068.5 (5.7)** |
| Medicare | **216756.3 (17.1)** | **384122.1 (18.7)** | **372219.3 (19.7)** | **616005.1 (20.4)** | **627517.9 (14.9)** | **1364089.1 (17.2)** |
| Other | **2921.4 (0.2)** | **5098.1 (0.2)** | **5174.3 (0.3)** | **3378.5 (0.1)** | **10847.1 (0.3)** | **12089.2 (0.2)** |
| Education |  |  |  |  |  |  |
| High School or Less | **734748.8 (58.0)** | **1065573.4 (52.2)** | **1051034.3 (55.8)** | **1429955.7 (47.4)** | **2310737.6 (55.1)** | **3571093.8 (45.0)** |
| Some College | **386110.5 (30.5)** | **566380.7 (27.7)** | **608890.9 (32.4)** | **854274.1 (28.3)** | **1368270.2 (32.7)** | **2294780.0 (28.9)** |
| College Degree + | **145874.7 (11.5)** | **410085.9 (20.1)** | **222088.2 (11.8)** | **730832.0 (24.2)** | **511632.9 (12.2)** | **2063992.3 (26.0)** |
| Household Income |  |  |  |  |  |  |
| < $20,000 | **574066.5 (45.1)** | **576371.3 (28.1)** | **949730.5 (50.1)** | **823869.0 (27.2)** | **1939293.9 (46.0)** | **1830836.8 (23.0)** |
| $20,000 to < $45,000 | **323401.4 (25.4)** | **416123.4 (20.3)** | **459014.3 (24.2)** | **640813.9 (21.1)** | **1046478.0 (24.8)** | **1537042.2 (19.3)** |
| $45,000 to < $65,000 | **243470.7 (19.1)** | **467633.0 (22.8)** | **314766.9 (16.6)** | **643604.9 (21.2)** | **776030.1 (18.4)** | **1761969.1 (22.1)** |
| $65,000 to < $85,000 | **79488.3 (6.2)** | **224663.7 (10.9)** | **100902.7 (5.3)** | **314559.3 (10.4)** | **269453.2 (6.4)** | **939823.6 (11.8)** |
| $85,000 to < $100,000 | **24359.3 (1.9)** | **120192.7 (5.9)** | **34169.3 (1.8)** | **193219.8 (6.4)** | **87039.1 (2.1)** | **605169.0 (7.6)** |
| $100,000 or more | **28991.3 (2.3)** | **248419.7 (12.1)** | **36954.3 (1.9)** | **413940.1 (13.7)** | **101008.8 (2.4)** | **1287779.9 (16.2)** |
| Smoking Status |  |  |  |  |  |  |
| Never | **1248483.9 (45.3)** | **2267261.1 (52.4)** | **1449656.9 (37.6)** | **2796679.1 (46.0)** | **3761504.8 (42.7)** | **8691956.3 (52.3)** |
| Former | **786087.3 (28.5)** | **485042.3 (34.3)** | **1049201.6 (27.2)** | **2376857.2 (39.1)** | **2127650.7 (24.2)** | **5495561.7 (33.1)** |
| Current | **723574.5 (26.2)** | **571186.9 (13.2)** | **1355225.9 (35.2)** | **910527.1 (15.0)** | **2920187.5 (33.1)** | **2424061.0 (14.6)** |
| Cost-Related Nonadherence |  |  |  |  |  |  |
| Needed but couldn't afford medication | 2400453.7 (86.8) | 0 (0.0) | 3412747.5 (88.4) | 0 (0.0) | 7708209.7 (87.3) | 0 (0.0) |
| Skipped medication doses\* | 1874447.0 (56.2) | 0 (0.0) | 2222249.2 (52.9) | 0 (0.0) | 5371382.6 (53.6) | 0 (0.0) |
| Delayed medication doses\* | 2347292.6 (70.3) | 0 (0.0) | 2875838.6 (68.4) | 0 (0.0) | 6854083.4 (68.4) | 0 (0.0) |
| Took less medicine than prescribed\* | 1932055.2 (57.9) | 0 (0.0) | 2339466.4 (55.7) | 0 (0.0) | 5652058.2 (56.4) | 0 (0.0) |
| Note: All numbers displayed in table are survey-weighted N (%) unless otherwise indicated. Bold face denotes statistically | | | | |  |  |
| significant differences (p < 0.05) between CRN and no CRN within each disease category, as determined by t-tests or Rao-Scott Chi-Square tests. | | | | | |  |
| \*Indicates a survey item only included in 2010-2014 waves. | |  |  |  |  |  |

**Table 2.** Associations of all-cause and disease-specific mortality with cost-related nonadherence among National Health Interview Survey (2000- 2014) participants with diabetes, cardiovascular disease, and/or hypertension.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | All-Cause Mortality | | |  | Disease Specific Mortality | | |
|  | Follow-Up Time, Weeks Median (IQR) | Died: N (%) | Model 1: HR (95% CI)1 | Model 2: HR (95% CI)2 |  | Died: N (%) | Model 1: HR (95% CI)1 | Model 2: HR (95% CI)3 |
| **Full Sample** |  |  |  |  |  |  |  |  |
| CRN for Diabetes | 291 (156 - 504) | 8909 (23.6) | **0.752 (0.694 - 0.815)** | **1.183 (1.092 - 1.281)** |  | 3045 (8.74) | **0.766 (0.674 - 0.870)** | **1.226 (1.074 - 1.399)** |
| CRN for CVD, narrow definition\* | 304 (160 - 534) | 16345 (27.8) | **0.702 (0.658 - 0.750)** | **1.148 (1.073 - 1.228)** |  | 4845 (9.14) | **0.618 (0.548 - 0.696)** | 1.123 (0.993 - 1.271) |
| CRN for CVD, expanded\*\* | 322 (169 - 552) | 28755 (19.5) | **0.771 (0.732 - 0.813)** | **1.230 (1.163 - 1.300)** |  | 10321 (7.44) | **0.728 (0.669 - 0.792)** | **1.310 (1.196 - 1.434)** |
| **2000-2010 Waves** | |  |  |  |  |  |  |  |
| CRN for Diabetes | 465 (360 - 652) | 7379 (34.1) | **0.799 (0.731 - 0.875)** | **1.222 (1.112 - 1.345)** |  | 2563 (13.0) | **0.809 (0.700 - 0.934)** | **1.289 (1.111 - 1.496)** |
| CRN for CVD, narrow definition\* | 474 (330 - 630) | 13771 (37.4) | **0.734 (0.685 - 0.786)** | **1.180 (1.100 - 1.271)** |  | 4282 (12.9) | **0.659 (0.582 - 0.747)** | **1.172 (1.028 - 1.334)** |
| CRN for CVD, expanded\*\* | 508 (360 - 652) | 24440 (27.1) | **0.805 (0.760 - 0.852)** | **1.265 (1.190 - 1.346)** |  | 9023 (10.7) | **0.758 (0.691 - 0.833)** | **1.326 (1.198 - 1.467)** |
| **2011 - 2014 Waves** | |  |  |  |  |  |  |  |
| CRN for Diabetes | 165 (104 - 230) | 1530 (9.50) | **0.681 (0.605 - 0.767)** | 0.967 (0.800 - 1.173) |  | 482 (3.20) | **0.779 (0.639 - 0.950)** | 1.055 (0.779 - 1.430) |
| CRN for CVD, narrow definition\* | 161 (100 - 230) | 2574 (11.77) | **0.620 (0.562 - 0.684)** | 1.019 (0.868 - 1.195) |  | 563 (2.84) | **0.768 (0.633 - 0.931)** | 1.054 (0.757 - 1.468) |
| CRN for CVD, expanded\*\* | 165 (104 - 234) | 4315 (7.53) | **0.695 (0.643 - 0.752)** | 1.083 (0.940 - 1.245) |  | 1298 (2.39) | **0.802 (0.700 - 0.918)** | **1.311 (1.051 - 1.634)** |

Note: All hazard ratios are weighted for survey design. Disease specific mortality is defined as having a listed cause of death of diabetes, heart or cerebrovascular disease, or heart, cerebrovascular disease or underlying hypertension for diabetes, CVD, and CVD with hypertension models, respectively. Bold face denotes statistical significance. \*The narrow definition of CVD includes heart attack, angina pectoris, coronary heart disease, other heart condition, or stroke. \*\* The expanded definition of CVD includes all conditions for the narrow definition or a diagnosis of hypertension. 1. Unadjusted Hazard Ratio. 2. Hazard Ratio adjusted for age, sex, insurance (private, public, Medicare, other, or none), race (white, Black or African American, Hispanic or Latino, Asian, or other), education (≤ high school, some college, college degree or greater), and diagnoses of other chronic conditions: cancer (all models), diabetes (CVD models only), hypertension (diabetes and CVD models not including hypertension) and CVD (diabetes models only). 3. Hazard ratio adjusted for age, sex, insurance (private, public, Medicare, other, or none), race (white, Black or African American, Hispanic or Latino, Asian, or other), and education (≤ high school, some college, college degree or greater). Abbreviations: CRN, cost-related nonadherence; CVD, cardiovascular disease; HR, Hazard Ratio.

**Supplementary Table 1.** Hazard ratios and 95% confidence intervals for all coefficients in models of all-cause mortality risk among individuals with diabetes in the National Health Interview Survey, 2000 to 2014.

|  |  |  |  |
| --- | --- | --- | --- |
|  | All Waves | Waves ≤ 2010 | Waves > 2010 |
|  | HR (95% CI) | HR (95% CI) | HR (95% CI) |
| CRN | **1.182 (1.092 - 1.280)** | **1.223 (1.112 - 1.345)** | 0.967 (0.797 - 1.173) |
| Some College | 0.955 (0.902 - 1.011) | 0.940 (0.876 - 1.009) | 0.884 (0.754 - 1.035) |
| College Degree | **0.806 (0.745 - 0.872)** | **0.785 (0.712 - 0.866)** | **0.699 (0.559 - 0.874)** |
| Age | **1.061 (1.059 - 1.064)** | **1.062 (1.059 - 1.065)** | **1.064 (1.056 - 1.073)** |
| $20,000 to < $45,000 | **0.904 (0.848 - 0.962)** | **0.919 (0.854 - 0.989)** | 1.106 (0.937 - 1.306) |
| $45,000 to < $65,000 | **0.763 (0.710 - 0.820)** | **0.792 (0.725 - 0.865)** | **1.005 (0.841 - 1.202)** |
| $65,000 to < $85,000 | **0.646 (0.585 - 0.713)** | **0.662 (0.589 - 0.743)** | 0.987 (0.754 - 1.292) |
| $85,000 to < $100,000 | **0.446 (0.336 - 0.591)** | **0.446 (0.280 - 0.710)** | **0.633 (0.428 - 0.935)** |
| $100,000 or more | **0.611 (0.505 - 0.739)** | **0.549 (0.406 - 0.743)** | 0.859 (0.627 - 1.176) |
| Female Sex | **0.696 (0.663 - 0.729)** | **0.705 (0.665 - 0.747)** | **0.729 (0.645 - 0.825)** |
| Public Insurance | **1.434 (1.257 - 1.634)** | **1.512 (1.298 - 1.760)** | **1.529 (1.100 - 2.125)** |
| Private Insurance | 1.014 (0.897 - 1.147) | 1.019 (0.883 - 1.175) | 0.949 (0.683 - 1.320) |
| Military | **1.212 (1.031 - 1.425)** | **1.258 (1.034 - 1.530)** | 1.161 (0.774 - 1.743) |
| Medicare | **1.156 (1.014 - 1.317)** | **1.181 (1.016 - 1.372)** | 1.247 (0.881 - 1.766) |
| Other | 1.048 (0.740 - 1.485) | 1.257 (0.883 - 1.790) | 0.931 (0.116 - 7.456) |
| Black | **0.906 (0.851 - 0.965)** | **0.911 (0.845 - 0.981)** | 0.906 (0.777 - 1.055) |
| Hispanic | **0.673 (0.621 - 0.729)** | **0.673 (0.615 - 0.736)** | **0.708 (0.583 - 0.859)** |
| American Indian/Alaskan Native | 1.017 (0.807 - 1.282) | 0.873 (0.659 - 1.157) | 1.009 (0.565 - 1.801) |
| Asian | **0.537 (0.458 - 0.630)** | **0.522 (0.429 - 0.636)** | **0.585 (0.410 - 0.835)** |
| Other | 0.822 (0.478 - 1.411) | 0.721 (0.396 - 1.314) | 0.467 (0.131 - 1.670) |
| Cancer | **1.276 (1.200 - 1.357)** | **1.471 (1.361 - 1.589)** | **1.348 (1.164 - 1.560)** |
| CVD, including Hypertension | **1.406 (1.318 - 1.500)** | **1.266 (1.177 - 1.361)** | 1.164 (0.959 - 1.413) |

**Supplementary Table 2.** Hazard ratios and 95% confidence intervals for all coefficients in models of all-cause mortality risk among individuals with cardiovascular disease, not including hypertension, in the National Health Interview Survey, 2000 to 2014.

|  |  |  |  |
| --- | --- | --- | --- |
|  | All Waves | Waves ≤ 2010 | Waves > 2010 |
|  | HR (95% CI) | HR (95% CI) | HR (95% CI) |
| CRN | **1.148 (1.073 - 1.228)** | **1.180 (1.096 - 1.271)** | 1.019 (0.868 - 1.195) |
| Some College | **0.870 (0.831 - 0.911)** | **0.870 (0.828 - 0.914)** | 0.887 (0.784 - 1.003) |
| College Degree | **0.718 (0.677 - 0.762)** | **0.713 (0.668 - 0.761)** | **0.751 (0.646 - 0.873)** |
| Age | **1.074 (1.072 - 1.077)** | **1.075 (1.072 - 1.077)** | **1.071 (1.064 - 1.078)** |
| $20,000 to < $45,000 | **0.927 (0.882 - 0.975)** | **0.911 (0.865 - 0.960)** | 1.049 (0.919 - 1.198) |
| $45,000 to < $65,000 | **0.820 (0.773 - 0.870)** | **0.813 (0.761 - 0.867)** | 0.895 (0.773 - 1.036) |
| $65,000 to < $85,000 | **0.719 (0.664 - 0.779)** | **0.720 (0.663 - 0.782)** | **0.722 (0.571 - 0.912)** |
| $85,000 to < $100,000 | **0.613 (0.504 - 0.745)** | **0.584 (0.445 - 0.767)** | **0.700 (0.509 - 0.964)** |
| $100,000 or more | **0.663 (0.573 - 0.766)** | **0.586 (0.462 - 0.742)** | 0.797 (0.635 - 1.001) |
| Female Sex | **0.718 (0.692 - 0.746)** | **0.719 (0.690 - 0.750)** | **0.714 (0.649 - 0.786)** |
| Public Insurance | **1.369 (1.205 - 1.555)** | **1.352 (1.181 - 1.548)** | **1.465 (1.069 - 2.008)** |
| Private Insurance | 0.936 (0.828 - 1.059) | 0.955 (0.837 - 1.088) | 0.836 (0.607 - 1.152) |
| Military | 1.065 (0.910 - 1.246) | 1.084 (0.916 - 1.283) | 0.985 (0.682 - 1.422) |
| Medicare | 1.055 (0.929 - 1.199) | 1.050 (0.916 - 1.203) | 1.089 (0.790 - 1.500) |
| Other | 0.653 (0.395 - 1.079) | 0.672 (0.402 - 1.121) | 0.416 (0.056 - 3.068) |
| Black | 1.015 (0.954 - 1.079) | 1.023 (0.957 - 1.095) | 0.982 (0.848 - 1.138) |
| Hispanic | **0.718 (0.656 - 0.787)** | **0.711 (0.642 - 0.786)** | **0.762 (0.630 - 0.922)** |
| American Indian/Alaskan Native | 1.081 (0.833 - 1.403) | 1.128 (0.854 - 1.489) | 0.793 (0.401 - 1.568) |
| Asian | **0.644 (0.549 - 0.756)** | **0.645 (0.539 - 0.773)** | **0.637 (0.439 - 0.924)** |
| Other | 0.710 (0.418 - 1.207) | 0.612 (0.326 - 1.149) | 1.218 (0.437 - 3.394) |
| Diabetes | **1.466 (1.407 - 1.527)** | **1.510 (1.443 - 1.580)** | **1.273 (1.149 - 1.410)** |
| Cancer | **1.120 (1.076 - 1.165)** | **1.114 (1.068 - 1.163)** | **1.222 (1.095 - 1.364)** |
| Hypertension | **1.221 (1.167 - 1.278)** | **1.221 (1.162 - 1.284)** | **1.163 (1.036 - 1.305)** |

**Supplementary Table 3.** Hazard ratios and 95% confidence intervals for all coefficients in models of all-cause mortality risk among individuals with cardiovascular disease, including hypertension, in the National Health Interview Survey, 2000 to 2014.

|  |  |  |  |
| --- | --- | --- | --- |
|  | All Waves | Waves ≤ 2010 | Waves > 2010 |
|  | HR (95% CI) | HR (95% CI) | HR (95% CI) |
| CRN | **1.230 (1.163 - 1.300)** | **1.265 (1.190 - 1.346)** | 1.083 (0.940 - 1.248) |
| Some College | **0.887 (0.856 - 0.918)** | **0.897 (0.864 - 0.932)** | **0.834 (0.756 - 0.919)** |
| College Degree | **0.752 (0.718 - 0.787)** | **0.759 (0.722 - 0.798)** | **0.718 (0.634 - 0.813)** |
| Age | **1.077 (1.076 - 1.079)** | **1.078 (1.076 - 1.080)** | **1.075 (1.069 - 1.080)** |
| $20,000 to < $45,000 | **0.886 (0.854 - 0.919)** | **0.874 (0.841 - 0.907)** | 0.989 (0.893 - 1.095) |
| $45,000 to < $65,000 | **0.795 (0.760 - 0.832)** | **0.782 (0.745 - 0.820)** | 0.904 (0.802 - 1.017) |
| $65,000 to < $85,000 | **0.662 (0.623 - 0.702)** | **0.656 (0.616 - 0.698)** | **0.706 (0.592 - 0.841)** |
| $85,000 to < $100,000 | **0.588 (0.509 - 0.678)** | **0.558 (0.456 - 0.682)** | **0.686 (0.541 - 0.870)** |
| $100,000 or more | **0.621 (0.562 - 0.687)** | **0.600 (0.516 - 0.697)** | **0.707 (0.586 - 0.851)** |
| Female Sex | **0.663 (0.644 - 0.682)** | **0.663 (0.642 - 0.684)** | **0.661 (0.614 - 0.711)** |
| Public Insurance | **1.299 (1.197 - 1.411)** | **1.303 (1.192 - 1.423)** | **1.297 (1.056 - 1.594)** |
| Private Insurance | **0.852 (0.788 - 0.920)** | **0.871 (0.803 - 0.946)** | **0.745 (0.607 - 0.913)** |
| Military | 1.036 (0.935 - 1.149) | 1.047 (0.936 - 1.170) | 0.975 (0.762 - 1.248) |
| Medicare | 0.956 (0.882 - 1.036) | 0.960 (0.880 - 1.046) | 0.939 (0.760 - 1.160) |
| Other | 0.821 (0.603 - 1.118) | 0.839 (0.610 - 1.154) | 0.595 (0.154 - 2.304) |
| Black | 0.971 (0.930 - 1.014) | 0.981 (0.936 - 1.029) | 0.914 (0.816 - 1.024) |
| Hispanic | **0.705 (0.662 - 0.751)** | **0.700 (0.654 - 0.749)** | **0.737 (0.637 - 0.853)** |
| American Indian/Alaskan Native | 1.189 (0.975 - 1.450) | **1.230 (1.006 - 1.505)** | **0.955 (0.584 - 1.562)** |
| Asian | **0.659 (0.582 - 0.747)** | **0.666 (0.578 - 0.768)** | **0.639 (0.506 - 0.808)** |
| Other | 0.766 (0.503 - 1.166) | 0.743 (0.463 - 1.192) | 0.937 (0.398 - 2.206) |
| Diabetes | **1.482 (1.434 - 1.531)** | **1.514 (1.461 - 1.568)** | **1.328 (1.225 - 1.439)** |
| Cancer | **1.306 (1.261 - 1.351)** | **1.299 (1.251 - 1.349)** | **1.346 (1.233 - 1.469)** |

**Supplementary Table 4.** Hazard ratios and 95% confidence intervals for all coefficients in models of diabetes-specific mortality risk among individuals with diabetes in the National Health Interview Survey, 2000 to 2014.

|  |  |  |  |
| --- | --- | --- | --- |
|  | All Waves | Waves ≤ 2010 | Waves > 2010 |
|  | HR (95% CI) | HR (95% CI) | HR (95% CI) |
| CRN | **1.226 (1.074 - 1.399)** | **1.289 (1.111 - 1.496)** | 1.055 (0.779 - 1.430) |
| Some College | 0.956 (0.856 - 1.069) | 0.972 (0.860 - 1.100) | 0.911 (0.691 - 1.201) |
| College Degree | **0.819 (0.702 - 0.956)** | **0.835 (0.707 - 0.987)** | 0.780 (0.525 - 1.158) |
| Age | **1.068 (1.063 - 1.073)** | **1.070 (1.064 - 1.075)** | **1.061 (1.048 - 1.075)** |
| $20,000 to < $45,000 | 0.910 (0.810 - 1.022) | 0.902 (0.794 - 1.025) | 1.066 (0.795 - 1.429) |
| $45,000 to < $65,000 | **0.765 (0.671 - 0.872)** | **0.746 (0.644 - 0.865)** | 1.003 (0.719 - 1.400) |
| $65,000 to < $85,000 | **0.685 (0.576 - 0.815)** | **0.639 (0.531 - 0.770)** | 1.186 (0.728 - 1.932) |
| $85,000 to < $100,000 | **0.423 (0.250 - 0.714)** | **0.339 (0.149 - 0.773)** | 0.697 (0.346 - 1.402) |
| $100,000 or more | **0.473 (0.322 - 0.696)** | **0.465 (0.260 - 0.832)** | 0.627 (0.349 - 1.128) |
| Female Sex | **0.689 (0.631 - 0.752)** | **0.687 (0.623 - 0.756)** | **0.690 (0.565 - 0.843)** |
| Public Insurance | **1.671 (1.318 - 2.119)** | **1.625 (1.256 - 2.102)** | **2.245 (1.254 - 4.022)** |
| Private Insurance | 1.098 (0.882 - 1.367) | 1.043 (0.823 - 1.321) | 1.491 (0.829 - 2.684) |
| Military | **1.417 (1.052 - 1.907)** | **1.380 (1.003 - 1.899)** | 1.856 (0.923 - 3.734) |
| Medicare | 1.243 (0.982 - 1.572) | 1.171 (0.909 - 1.508) | 1.817 (0.981 - 3.364) |
| Other | **1.895 (1.059 - 3.392)** | **1.904 (1.059 - 3.423)** | 0.240 (0.026 - 2.221) |
| Black | 0.975 (0.865 - 1.099) | 0.972 (0.856 - 1.104) | 0.972 (0.712 - 1.328) |
| Hispanic | **0.662 (0.577 - 0.760)** | **0.621 (0.531 - 0.727)** | 0.891 (0.649 - 1.224) |
| American Indian/Alaskan Native | 0.840 (0.539 - 1.307) | 0.802 (0.495 - 1.299) | 1.125 (0.456 - 2.778) |
| Asian | **0.523 (0.377 - 0.724)** | **0.494 (0.343 - 0.712)** | 0.669 (0.340 - 1.316) |
| Other | 0.315 (0.099 - 1.003) | 0.375 (0.115 - 1.223) | 0.957 (0.443 - 2.070) |

**Supplementary Table 5.** Hazard ratios and 95% confidence intervals for all coefficients in models of cardiovascular disease-specific mortality risk among individuals with cardiovascular disease in the National Health Interview Survey, 2000 to 2014.

|  |  |  |  |
| --- | --- | --- | --- |
|  | All Waves | Waves ≤ 2010 | Waves > 2010 |
|  | HR (95% CI) | HR (95% CI) | HR (95% CI) |
| CRN | 1.123 (0.993 - 1.271) | **1.172 (1.028 - 1.337)** | 1.054 (0.757 - 1.468) |
| Some College | **0.866 (0.797 - 0.940)** | **0.870 (0.796 - 0.950)** | 0.910 (0.720 - 1.150) |
| College Degree | **0.649 (0.580 - 0.726)** | **0.645 (0.570 - 0.729)** | **0.699 (0.509 - 0.961)** |
| Age | **1.094 (1.090 - 1.098)** | **1.095 (1.091 - 1.100)** | **1.090 (1.078 - 1.102)** |
| $20,000 to < $45,000 | **0.888 (0.813 - 0.971)** | **0.876 (0.798 - 0.963)** | 1.217 (0.943 - 1.570) |
| $45,000 to < $65,000 | **0.806 (0.728 - 0.892)** | **0.818 (0.734 - 0.913)** | 1.003 (0.749 - 1.345) |
| $65,000 to < $85,000 | **0.700 (0.610 - 0.803)** | **0.710 (0.613 - 0.823)** | 0.725 (0.472 - 1.113) |
| $85,000 to < $100,000 | **0.560 (0.392 - 0.802)** | **0.540 (0.339 - 0.862)** | 0.943 (0.526 - 1.691) |
| $100,000 or more | **0.432 (0.310 - 0.601)** | **0.356 (0.219 - 0.578)** | 0.829 (0.524 - 1.311) |
| Female Sex | **0.625 (0.582 - 0.670)** | **0.631 (0.586 - 0.681)** | **0.583 (0.476 - 0.715)** |
| Public Insurance | 1.058 (0.849 - 1.318) | 1.040 (0.820 - 1.318) | 1.145 (0.614 - 2.135) |
| Private Insurance | **0.799 (0.644 - 0.990)** | **0.791 (0.631 - 0.992)** | 0.675 (0.354 - 1.289) |
| Military | 0.805 (0.610 - 1.063) | 0.858 (0.643 - 1.145) | 0.571 (0.246 - 1.326) |
| Medicare | 0.834 (0.668 - 1.042) | 0.837 (0.660 - 1.060) | 0.770 (0.400 - 1.481) |
| Other | 1.205 (0.603 - 2.408) | 1.173 (0.574 - 2.397) | 1.443 (0.173 - 12.037) |
| Black | **1.225 (1.095 - 1.371)** | **1.253 (1.109 - 1.416)** | 1.093 (0.794 - 1.505) |
| Hispanic | **0.789 (0.677 - 0.919)** | **0.788 (0.666 - 0.931)** | 0.814 (0.571 - 1.159) |
| American Indian/Alaskan Native | 1.386 (0.799 - 2.402) | 1.477 (0.824 - 2.646) | 0.817 (0.180 - 3.711) |
| Asian | **0.667 (0.505 - 0.880)** | **0.734 (0.545 - 0.989)** | 0.443 (0.181 - 1.083) |
| Other | 0.962 (0.372 - 2.491) | 0.610 (0.229 - 1.622) | 3.306 (0.703 - 15.545) |

**Supplementary Table 6.** Hazard ratios and 95% confidence intervals for all coefficients in models of cardiovascular disease or hypertension mortality risk among individuals with cardiovascular disease or hypertension in the National Health Interview Survey, 2000 to 2014.

|  |  |  |  |
| --- | --- | --- | --- |
|  | All Waves | Waves ≤ 2010 | Waves > 2010 |
|  | HR (95% CI) | HR (95% CI) | HR (95% CI) |
| CRN | **1.300 (1.187 - 1.424)** | **1.326 (1.198 - 1.467)** | **1.311 (1.051 - 1.634)** |
| Some College | **0.910 (0.859 - 0.964)** | **0.926 (0.870 - 0.985)** | 0.852 (0.717 - 1.011) |
| College Degree | **0.738 (0.683 - 0.797)** | **0.758 (0.696 - 0.826)** | **0.643 (0.521 - 0.794)** |
| Age | **1.097 (1.094 - 1.100)** | **1.098 (1.094 - 1.101)** | **1.096 (1.088 - 1.105)** |
| $20,000 to < $45,000 | **0.850 (0.798 - 0.905)** | **0.840 (0.786 - 0.898)** | 1.039 (0.883 - 1.224) |
| $45,000 to < $65,000 | **0.790 (0.735 - 0.849)** | **0.783 (0.726 - 0.845)** | 0.998 (0.824 - 1.209) |
| $65,000 to < $85,000 | **0.614 (0.555 - 0.679)** | **0.610 (0.548 - 0.679)** | 0.700 (0.520 - 0.942) |
| $85,000 to < $100,000 | **0.469 (0.359 - 0.613)** | **0.426 (0.304 - 0.598)** | 0.753 (0.490 - 1.158) |
| $100,000 or more | **0.438 (0.355 - 0.539)** | **0.383 (0.287 - 0.511)** | 0.732 (0.523 - 1.024) |
| Female Sex | **0.601 (0.572 - 0.631)** | **0.606 (0.575 - 0.639)** | **0.567 (0.494 - 0.650)** |
| Public Insurance | **1.188 (1.028 - 1.373)** | 1.165 (0.995 - 1.364) | 1.358 (0.948 - 1.947) |
| Private Insurance | **0.788 (0.686 - 0.905)** | **0.769 (0.661 - 0.893)** | 0.809 (0.572 - 1.143) |
| Military | 0.960 (0.798 - 1.153) | 0.960 (0.790 - 1.168) | 0.984 (0.624 - 1.554) |
| Medicare | **0.843 (0.730 - 0.974)** | **0.832 (0.712 - 0.973)** | 0.882 (0.602 - 1.294) |
| Other | 0.783 (0.486 - 1.261) | 0.751 (0.460 - 1.226) | 0.911 (0.201 - 4.124) |
| Black | **1.155 (1.078 - 1.237)** | **1.164 (1.083 - 1.252)** | 1.108 (0.916 - 1.341) |
| Hispanic | **0.777 (0.707 - 0.854)** | **0.754 (0.679 - 0.836)** | 0.955 (0.768 - 1.188) |
| American Indian/Alaskan Native | 1.331 (0.910 - 1.947) | 1.417 (0.967 - 2.076) | 0.737 (0.281 - 1.934) |
| Asian | **0.720 (0.605 - 0.857)** | **0.742 (0.609 - 0.903)** | **0.676 (0.456 - 1.000)** |
| Other | 0.675 (0.369 - 1.235) | **0.416 (0.203 - 0.851)** | 2.593 (0.996 - 6.751) |

**Supplementary Table 7.** Association of CRN and all-cause and disease-specific mortality among National Health Interview Survey (2000- 2014) participants with diabetes, cardiovascular disease, and/or hypertension after excluding potentially influential cases.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | All-Cause Mortality | | |  | Disease Specific Mortality | | | |
|  | Follow-Up Time, Weeks Median (IQR) | Died: N (%) | Model 1: HR (95% CI)1 | Model 2: HR (95% CI)2 |  | Died: N (%) | Model 1: HR (95% CI)1 | | Model 2: HR (95% CI)3 |
| **Full Sample** |  |  |  |  |  |  |  | |  |
| CRN for Diabetes | 295 (161 - 504) | 8737 (23.5) | **0.748 (0.686 - 0.815)** | **1.182 (1.091 - 1.280)** |  | 2882 (8.4) | **0.750 (0.669 - 0.840)** | | **1.180 (1.045 - 1.331)** |
| CRN for CVD, narrow definition\* | 313 (165 - 539) | 15979 (27.6) | **0.646 (0.600 - 0.694)** | **1.133 (1.066 - 1.205)** |  | 4692 (8.9) | **0.602 (0.542 - 0.668)** | | 1.080 (0.968 - 1.206) |
| CRN for CVD, expanded definition\*\* | 326 (178 - 561) | 28340 (19.4) | **0.705 (0.667 - 0.746)** | **1.232 (1.172 - 1.296)** |  | 10028 (7.39) | | **0.695 (0.643 - 0.752)** | **1.265 (1.162 - 1.378)** |
| **2000-2010 Waves** |  |  |  |  |  |  | |  |  |
| CRN for Diabetes | 456 (321 - 613) | 7650 (31.9) | **0.799 (0.240 - 0.862)** | **1.225 (1.125 - 1.334)** |  | 2258 (10.39) | | **0.765 (0.676 - 0.867)** | **1.210 (1.061 - 1.380)** |
| CRN for CVD, narrow definition\* | 478 (322 - 635) | 14146 (35.4) | **0.706 (0.664 - 0.750)** | **1.151 (1.079 - 1.228)** |  | 4692 (12.0) | | **0.631 (0.656 - 0.704)** | **1.125 (1.003 - 1.262)** |
| CRN for CVD, expanded definition\*\* | 500 (339 - 648) | 25180 (25.5) | **0.774 (0.737 - 0.813)** | **1.244 (1.180 - 1.310)** |  | 9143 (9.9) | | **0.724 (0.667 - 0.786)** | **1.309 (1.197 - 1.432)** |
|  |  |  |  |  |  |  | |  |  |
| **2011 - 2014 Waves** |  |  |  |  |  |  | |  |  |
| CRN for Diabetes | 152 (100 - 204) | 1092 (8.2) | **0.610 (0.505 - 0.737)** | 1.000 (0.818 - 1.225) |  | 324 (2.6) | | **0.706 (0.521 - 0.958)** | 1.103 (0.795 - 1.532) |
| CRN for CVD, narrow definition\* | 156 (100 - 208) | 1833 (10.2) | **0.554 (0.473 - 0.647)** | 1.031 (0.877 - 1.211) |  | 380 (2.3) | | **0.494 (0.359 - 0.679)** | 0.993 (0.701 - 1.406) |
| CRN for CVD, expanded definition\*\* | 156 (104 - 208) | 3043 (6.5) | **0.584 (0.511 - 0.670)** | 1.061 (0.927 - 1.214) |  | 885 (2.0) | | **0.569 (0.457 - 0.709)** | 1.096 (0.864 - 1.390) |

Note: All hazard ratios are weighted for survey design. Disease specific mortality is defined as having a listed cause of death of diabetes, heart or cerebrovascular disease, or heart, cerebrovascular disease or underlying hypertension for diabetes, CVD, and CVD with hypertension models, respectively. Bold face denotes statistical significance. \*The narrow definition of CVD includes heart attack, angina pectoris, coronary heart disease, other heart condition, or stroke. \*\* The expanded definition of CVD includes all conditions for the narrow definition or a diagnosis of hypertension. 1. Unadjusted Hazard Ratio. 2. Hazard Ratio adjusted for age, sex, insurance (private, public, Medicare, other, or none), race (white, Black or African American, Hispanic or Latino, Asian, or other), education (≤ high school, some college, college degree or greater), and diagnoses of other chronic conditions: cancer (all models), diabetes (CVD models only), hypertension (diabetes and CVD models not including hypertension) and CVD (diabetes models only). 3. Hazard ratio adjusted for age, sex, insurance (private, public, Medicare, other, or none), race (white, Black or African American, Hispanic or Latino, Asian, or other), and education (≤ high school, some college, college degree or greater). Abbreviations: CRN, cost-related nonadherence; CVD, cardiovascular disease; HR, Hazard Ratio.

**Supplementary Table 8.** Association of CRN and all-cause and disease-specific mortality among National Health Interview Survey (2000- 2014) participants with diabetes, cardiovascular disease, and/or hypertension after adjusting for age using natural splines at age 75.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | All-Cause Mortality | | |  | Disease-Specific Mortality | | | |
|  | Follow-Up Time, Weeks Median (IQR) | Died: N(%) | Model 1: HR (95% CI) | Model 2: HR (95% CI) |  | Died: N(%) | Model 1: HR (95% CI) | | Model 2: HR (95% CI) | |
| **Full Sample** |  |  |  |  |  |  |  | |  | |
| CRN for Diabetes | 291 (156 - 504) | 8909 (23.6) | **0.752 (0.694 - 0.815)** | **1.158 (1.063 - 1.261)** |  | 3045 (8.7) | **0.766 (0.674 - 0.870)** | | **1.228 (1.076 - 1.402)** | |
| CRN for CVD, narrow definition\* | 304 (160 - 534) | 16345 (27.8) | **0.702 (0.658 - 0.750)** | **1.147 (1.072 - 1.228)** |  | 4845 (9.1) | **0.618 (0.548 - 0.696)** | | 1.119 (0.989 - 1.267) | |
| CRN for CVD, expanded definition\*\* | 322 (169 - 552) | 28755 (19.5) | **0.771 (0.732 - 0.813)** | **1.229 (1.162 - 1.300)** |  | 10321 (7.4) | **0.728 (0.669 - 0.792)** | | **1.300 (1.183 - 1.421)** | |
|  |  |  |  |  |  |  |  | |  | |
| **2000-2010 Waves** |  |  |  |  |  |  |  | |  | |
| CRN for Diabetes | 465 (360 - 652) | 7379 (34.1) | **0.799 (0.731 - 0.875)** | **1.220 (1.109 - 1.343)** |  | 2563 (13.0) | **0.809 (0.700 - 0.934)** | | **1.288 (1.111 - 1.496)** | |
| CRN for CVD, narrow definition\* | 474 (330 - 630) | 13771 (37.4) | **0.734 (0.685 - 0.786)** | **1.180 (1.095 - 1.271)** |  | 4282 (12.9) | **0.659 (0.582 - 0.747)** | | **1.170 (1.025 - 1.335)** | |
| CRN for CVD, expanded definition\*\* | 508 (360 - 652) | 24440 (27.1) | **0.805 (0.760 - 0.852)** | **1.264 (1.188 - 1.344)** |  | 9023 (10.7) | **0.758 (0.691 - 0.833)** | | **1.322 (1.194 - 1.464)** | |
|  |  |  |  |  |  |  |  | |  | |
| **2011 - 2014 Waves** |  |  |  |  |  |  |  | |  | |
| CRN for Diabetes | 165 (104 - 230) | 1530 (9.5) | **0.681 (0.605 - 0.767)** | 0.960 (0.790 - 1.166) |  | 482 (3.2) | **0.779 (0.639 - 0.950)** | | 1.055 (0.777 - 1.434) | |
| CRN for CVD, narrow definition\* | 161 (100 - 230) | 2574 (11.8) | **0.620 (0.562 - 0.684)** | 1.007 (0.856 - 1.183) |  | 563 (2.8) | **0.768 (0.633 - 0.931)** | | 1.042 (0.747 - 1.453) | |
| CRN for CVD, expanded definition\*\* | 165 (104 - 234) | 4315 (7.5) | **0.695 (0.643 - 0.752)** | 1.076 (0.932 - 1.241) |  | 1298 (2.4) | **0.802 (0.700 - 0.918)** | | **1.201 (1.042 - 1.623)** | |
|  |  |  |  |  |  |  |  |  | |

Note: All hazard ratios are weighted for survey design. Disease specific mortality is defined as having a listed cause of death of diabetes, heart or cerebrovascular disease, or heart, cerebrovascular disease or underlying hypertension for diabetes, CVD, and CVD with hypertension models, respectively. Bold face denotes statistical significance. \*The narrow definition of CVD includes heart attack, angina pectoris, coronary heart disease, other heart condition, or stroke. \*\* The expanded definition of CVD includes all conditions for the narrow definition or a diagnosis of hypertension. 1. Unadjusted Hazard Ratio. 2. Hazard Ratio adjusted for age, sex, insurance (private, public, Medicare, other, or none), race (white, Black or African American, Hispanic or Latino, Asian, or other), education (≤ high school, some college, college degree or greater), and diagnoses of other chronic conditions: cancer (all models), diabetes (CVD models only), hypertension (diabetes and CVD models not including hypertension) and CVD (diabetes models only). 3. Hazard ratio adjusted for age, sex, insurance (private, public, Medicare, other, or none), race (white, Black or African American, Hispanic or Latino, Asian, or other), and education (≤ high school, some college, college degree or greater). Abbreviations: CRN, cost-related nonadherence; CVD, cardiovascular disease; HR, Hazard Ratio.

A close up of a logo

Description automatically generated**Supplementary Figure 1.** Directed acyclic graph depicting hypothesized causal interrelations between CRN, sociodemographic characteristics, and all-cause mortality.

**Supplementary Figure 2.** Directed acyclic graph depicting hypothesized causal interrelations between CRN, sociodemographic characteristics, and disease-specific mortality.

