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Validation Study of Medicare Claims to Identify Older US Adults With CKD Using the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study

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Supplementary Material

Table S1: Sensitivity, specificity, PPV, and NPV of claims-based algorithm for identifying progressively lower levels of eGFR and higher ACRs using primary CKD definition in Medicare.

Table S2: Sensitivity, specificity, PPV, and NPV of claims-based algorithm for identifying progressively lower levels of eGFR and higher ACRs using secondary CKD definition in Medicare.

Table S3: Number and percentage of REGARDS participants with $CKD_{Medicare}$ in those with $CKD_{REGARDS}$ at their study visit.

Table S4: Rates and HRs for mortality and ESRD associated with $CKD_{Medicare}$ in participants with eGFR < 45 mL/min/1.73 m^2 or ACR >300 mg/g at REGARDS study visit.

Figure S1: Sensitivity, specificity, PPV, and NPV of $CKD_{Medicare}$ for identifying CKD defined as eGFR < 45 ml/min/1.73 m^2 or ACR >300 mg/g measured in REGARDS Study.

Item S1: Inpatient and outpatient ICD-9 codes in claims used to define $CKD_{Medicare}$ in primary analyses.

Item S2: Inpatient and outpatient ICD-9 codes in claims (inpatient and outpatient) used to define $CKD_{Medicare}$ in secondary analyses.

Note: The supplementary material accompanying this article (doi:_____) is available at www.ajkd.org

Abstract

Background—Healthcare claims data may provide a cost-efficient approach for studying chronic kidney disease (CKD).

Study Design—Prospective cohort study.

Setting & Participants—We compared characteristics and outcomes for individuals with CKD defined using laboratory measurements versus claims data from 6,982 Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study participants who had Medicare fee-for-service coverage.

Predictors—Presence of CKD as defined by both the REGARDS Study ($CKD_{REGARDS}$) and Medicare data ($CKD_{Medicare}$), absence of CKD as defined by both, presence of $CKD_{REGARDS}$ but not $CKD_{Medicare}$, and presence of $CKD_{Medicare}$ but not $CKD_{REGARDS}$.

Outcomes—Mortality and incident end-stage renal disease (ESRD).

Measurements—The research study definition of CKD ($CKD_{REGARDS}$) included estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73m^2 or albumin-creatinine ratio (ACR) > 30 mg/g at the REGARDS study visit. CKD in Medicare ($CKD_{Medicare}$) was identified during the two years before each participant's REGARDS visit using a claims-based algorithm.

Results—Overall, 32% of participants had $CKD_{REGARDS}$ and 6% had $CKD_{Medicare}$. The sensitivity, specificity, and positive and negative predictive values of $CKD_{Medicare}$ for identifying $CKD_{REGARDS}$ were 15.5% (95% CI, 14.0%–17.1%), 97.7% (95% CI, 97.2%–98.1%), 75.6% (95% CI, 71.4%–79.5%), and 71.5% (95% CI, 70.4%–72.6%), respectively. Mortality and ESRD incidence rates, expressed per 1,000 person-years, were higher for participants with versus without $CKD_{Medicare}$ (mortality: 72.5 [95% CI, 61.3–83.7] versus 33.3 [95% CI, 31.5–35.2]; ESRD: 16.4 [95% CI, 11.2–21.6] versus 1.3 [95% CI, 0.9–1.6]) and with versus without $CKD_{REGARDS}$ (mortality: 59.9 [95% CI, 55.4–64.4] versus 25.5 [95% CI, 23.6–27.4]; ESRD: 6.8 [95% CI, 5.4–8.3] versus 0.1 [95% CI, 0.0–0.3]). Among participants with $CKD_{REGARDS}$, those with abdominal obesity, diabetes, anemia, a lower eGFR, more outpatient visits, a hospitalization and a nephrologist visit in the two years before their REGARDS visit were more likely to have $CKD_{Medicare}$.

Limitations—$CKD_{REGARDS}$ relied on eGFR and albuminuria assessed at a single visit.

Conclusions—CKD, whether defined in claims or through research study measurements, was associated with increased mortality and ESRD. However, individuals with CKD identified in claims may represent a select high-risk population.

Index words

chronic kidney disease (CKD); health care claims data; sensitivity; specificity; predictive value; claims-based algorithm; albuminuria; estimated glomerular filtration rate (eGFR); end-stage renal disease (ESRD)

There has been substantial interest over the past few years in using healthcare claims data for conducting comparative effectiveness and safety research studies, quality improvement projects and public health surveillance.[1–4] Several prior studies have evaluated the ability of

claims data to identify individuals with chronic kidney disease (CKD). These studies have been summarized in two literature reviews that concluded claims data have low sensitivity and low negative predictive value (NPV) and high specificity for identifying CKD.[5, 6] The positive predictive value (PPV) varied widely (range, 29%–100%) in the studies identified for the literature review.

One potential source for studying CKD in claims is the US Medicare program. Medicare provides health insurance for eligible US adults aged 65 years or older, a population with a high prevalence of CKD. Given that over 95% of older US adults have health insurance through Medicare, it provides a large population with high generalizability to the US population of older adults.[7] One prior study evaluated the validity of Medicare claims for identifying individuals with CKD.[8] The study used data on Medicare beneficiaries presenting to a hospital with a myocardial infarction and several claims algorithms to identify CKD patients, yielding test characteristics ranging from 3% to 27% for sensitivity, 93% to 99% for specificity, 89% to 97% for PPV, and 32% to 37% for NPV. Given the high PPV and high specificity, the authors concluded that patients identified in Medicare as having CKD most likely have it, and cohorts of older adults with CKD can be assembled using Medicare claims.

As claims-based algorithms have generally demonstrated low sensitivity, they do not identify the majority of individuals with CKD. Studies using Medicare claims data to identify populations with CKD could produce biased results if the characteristics of individuals with CKD identified through Medicare claims are systematically different from those who are not identified. To better understand the strengths and limitations of using claims data to study CKD, we determined whether (1) correlates of having CKD, (2) the risk for all-cause mortality and end-stage renal disease (ESRD) associated with having CKD, and (3) risk factors for all-cause mortality and ESRD among individuals with CKD were similar when CKD was defined using Medicare claims versus estimated glomerular filtration rate (eGFR) and albuminuria measured in a research study. Additionally, among participants with CKD defined using eGFR and albuminuria, we determined whether (4) the presence of Medicare claims for CKD differed by participant characteristics and co-morbid conditions and (5) the risk for all-cause mortality and ESRD differed for those with versus without CKD claims in Medicare.

METHODS

Study Participants

We conducted an analysis of participants enrolled in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study linked to Medicare claims data. REGARDS is a population-based cohort study of 30,239 adults aged 45 years or older from across the continental United States.[9] Participants were enrolled from January 2003 through October 2007, and baseline data were collected during a telephone interview followed by an in-home study visit.

The REGARDS participants were linked to Medicare enrollment and claims data by social security number, gender, and date of birth. Medicare Part A covers hospital care, skilled

nursing facility care, hospice, and home health services. Medicare Part B covers services or supplies that are needed to diagnose or treat medical conditions and preventive services such as to prevent illness or detect it at an early stage. Medicare Advantage plans include health plans offered by private companies that contract with Medicare to provide beneficiaries with coverage. Medicare Advantage plans include health maintenance organizations, preferred provider organizations, private fee-for-service plans, special needs plans, and Medicare medical savings account plans.

For this analysis, we included REGARDS participants who were aged 65 years or older at the beginning of a two-year look-back period (i.e., two years prior to the baseline REGARDS study visit) and provided a blood and urine sample during their in-home REGARDS study visit, had complete data for calculating eGFR and albumin-creatinine ratio (ACR), and had been living in the United States, continuously enrolled in Medicare parts A and B (fee-for-service hospital and outpatient coverage), but not in a Medicare Advantage plan for the two year look-back period.

We excluded participants enrolled in a Medicare Advantage plan as claims are not complete for these individuals. Additionally, we excluded participants who self-reported a history of ESRD at baseline or who had a record for ESRD in the US Renal Data System (USRDS) prior to their REGARDS baseline study visit.

A CONSORT diagram is provided in Figure 1. Overall, 6,982 participants met all of the inclusion criteria for this analysis. Institutional review boards of the collaborating institutions approved the REGARDS Study protocol and participants gave informed consent.

Determination of CKD in the REGARDS Study ($CKD_{REGARDS}$)

Serum creatinine assays, calibrated with an isotope dilution mass spectroscopic standard, were performed at the University of Vermont.[10] The CKD-EPI (CKD Epidemiology Collaboration) creatinine equation was used to calculate eGFR.[11] Results were similar using the Modification of Diet in Renal Disease (MDRD) Study equation and therefore not presented. Urinary albumin and creatinine were measured at the Department of Laboratory Medicine and Pathology at the University of Minnesota, using the BN ProSpec Nephelometer from Dade Behring (Marburg, Germany). The results were expressed for each participant as the ACR. For our primary analysis, CKD in the REGARDS study ($CKD_{REGARDS}$) was defined as an eGFR < 60 ml/min/1.73 m^2 or an ACR > 30 mg/g.[12] In secondary analyses, we defined $CKD_{REGARDS}$ as an eGFR < 45 ml/min/1.73 m^2 or an ACR > 300 mg/g. This definition of $CKD_{REGARDS}$ was used to capture a cohort of participants with more severe CKD.

Other Variables From the REGARDS Baseline Visit

Self-reported items determined in the REGARDS Study included age, race, gender, region of residence (West, Midwest, Northeast, and South), current smoking, family history of ESRD, history of coronary heart disease (CHD), history of diabetes, and use of antihypertensive, insulin or antidiabetes medications. During the REGARDS baseline study visit, blood pressure and anthropometric variables were measured. Blood pressure was measured two times and averaged for analysis. Hypertension was defined as systolic blood

pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, or current antihypertensive medication use. Waist circumference was measured mid-way between the lowest rib and the iliac crest using a tape measure with the participant standing; abdominal obesity was defined as levels > 88 cm for women and > 102 cm for men. Using blood collected during the baseline study visit, serum glucose and hemoglobin were measured. Anemia was defined as a hemoglobin level < 12 g/dL for women and < 13 g/dL for men. Diabetes mellitus was defined as fasting glucose level ≥ 126 mg/dL, non-fasting glucose ≥ 200 mg/dL, or self-report of a prior diagnosis of diabetes mellitus with current use of insulin or antidiabetes medication.

Medicare Claims

Medicare claims for the current analysis include those from the outpatient and inpatient settings. To identify CKD in Medicare claims ($CKD_{Medicare}$), we abstracted Medicare claims during the two years prior to each participant's REGARDS study visit (i.e., the look-back period). For the primary analysis, the algorithm for defining $CKD_{Medicare}$ follows that from the Centers for Medicare & Medicaid Services (CMS) chronic conditions warehouse (Item S1, available as online supplementary material).[13–15] This algorithm uses ICD-9 discharge diagnosis codes associated with a hospitalization or physician evaluation and management claims associated with outpatient physician visits. Coding in Medicare is a two-step process. Physicians provide diagnostic and procedures that were performed and administrative staff translate these into codes for billing purposes. Modifications to ICD-9 codes are used in Medicare claims. Therefore, some of the codes used in the current study may not be present in other settings. In secondary analyses, we evaluated the sensitivity, specificity, PPV and NPV using a more narrow set of claims to define $CKD_{Medicare}$ (Item S2). The claims used in the secondary analyses were chosen by authors to be more specific in identifying individuals with CKD as opposed to acute or transient kidney problems. For each participant, we also identified the number of outpatient visits, hospitalizations, and the occurrence of a nephrologist visit from Medicare claims during the two-year look-back period.

Outcomes

Participants were followed for all-cause mortality and incident ESRD. Mortality, subsequent to the REGARDS Study in-home examination and through March 2012 was assessed through contact with proxies provided by the participant upon recruitment or during follow-up. If a proxy reported a participant had died, an interview was conducted with their next of kin. The REGARDS Study confirmed dates of death through the Social Security Death Index, death certificates, or the National Death Index. ESRD subsequent to the in-home examination and through September 2011 was assessed via linkage with the USRDS. The USRDS is a registry of ESRD and captures the vast majority of incident cases in the United States.[16]

Statistical Analysis

The sensitivity, specificity, PPV, and NPV of $CKD_{Medicare}$ during the look-back period was calculated, with $CKD_{REGARDS}$ considered the "gold standard". Additionally, sensitivity, specificity, PPV and NPV for $CKD_{Medicare}$ was calculated for level of eGFR (<60, <45, and

<30 ml/min/1.73 m^2 and ACR > 30 and >300 mg/g). In a sensitivity analysis, we also calculated these test characteristics for $CKD_{Medicare}$ using Medicare claims from the one year before to one year after each participant's REGARDS Study visit. Participant characteristics were calculated by the cross-classification of $CKD_{Medicare}$ and $CKD_{REGARDS}$ with the statistical significance of differences calculated using ANOVA, a Kruskal-Wallis or chi-square test. Next, hazard ratios for all-cause mortality and ESRD were calculated using Cox proportional hazards models comparing individuals with versus without $CKD_{Medicare}$ and, separately, with versus without $CKD_{REGARDS}$. Hazard ratios for ESRD were calculated accounting for the competing risk of mortality using the method described by Fine and Gray.[17] Three levels of adjustment were performed. An initial model included adjustment for age, race, and gender. A second model included additional adjustment for number of outpatient visits, nephrologist visits, hospitalization and Medicaid eligibility during the look-back period as identified in Medicare. A third model also adjusted for smoking, abdominal obesity, hypertension, diabetes, and history of CHD from the REGARDS study. To evaluate whether risk factors for outcomes differ for individuals identified as having CKD in claims versus in a research study, we calculated the age, race, sex adjusted hazard ratios for all-cause mortality and ESRD among individuals with $CKD_{Medicare}$ (n=451) and, separately, among those with $CKD_{REGARDS}$ (n=2,203).

Next, to evaluate the selective coding of CKD in claims data, we restricted the sample to participants with $CKD_{REGARDS}$ and calculated the proportion of participants with $CKD_{Medicare}$ by demographic factors, co-morbid conditions and Medicare variables. The prevalence ratios for having $CKD_{Medicare}$ associated with participant characteristics were also calculated. Also, among those with the $CKD_{REGARDS}$, rates and hazard ratios for all-cause mortality and, separately, ESRD associated with having versus not having $CKD_{Medicare}$ were calculated. Prevalence ratios and hazard ratios were calculated with three levels of adjustment as described above. Additionally, we calculated the sensitivity, specificity, PPV and NPV for $CKD_{Medicare}$ using the secondary definition of $CKD_{REGARDS}$ (eGFR < 45 ml/min/1.73 m^2 or ACR > 300 mg/g). The rates and hazard ratios for all-cause mortality and ESRD associated with having versus not having $CKD_{Medicare}$ among those with $CKD_{REGARDS}$ were also calculated using this secondary definition. Multiple imputation was conducted using chained equations to account for missing data from the REGARDS Study. Data were missing for <1% of all variables except history of CHD (1.7% missing) and anemia (38.0% missing) and family history of ESRD (35.6% missing). The high percentage of participants missing anemia and family history of ESRD occurred because these variables were added to REGARDS data collection in May 2004 (about one third through recruitment of the cohort). Analyses were conducted using SAS V9.3 (SAS Institute Inc, Cary, NC) and Stata/MP 12.1 (Stata Corp, College Station, TX).

RESULTS

Test Characteristics of CKD Claims in Medicare

Overall, 2,203 of the 6,982 participants (32%) included in this analysis met the primary definition for $CKD_{REGARDS}$ (eGFR < 60 ml/min/1.73 m^2 or ACR > 30 mg/g) and 6% (n=451) met the primary definition for $CKD_{Medicare}$. Of participants with $CKD_{REGARDS}$,

15.5% (95% confidence interval [CI], 14.0%–17.1%) had $CKD_{Medicare}$ (sensitivity) and 97.7% (95% CI, 97.2%–98.1%) without $CKD_{REGARDS}$ did not have $CKD_{Medicare}$ (specificity, Figure 2 – left panel). Among participants with $CKD_{Medicare}$, 75.6% (95% CI, 71.4%–79.5%) had $CKD_{REGARDS}$ (PPV) and among participants without $CKD_{Medicare}$, 71.5% (95% CI, 70.4%–72.6%) did not have $CKD_{REGARDS}$ (NPV). Sensitivity was higher but specificity and PPV were lower for identifying lower levels of eGFR and higher levels of ACR (Table S1). Using Medicare claims from one year before to one year after the REGARDS study visit, the sensitivity, specificity, PPV, and NPV were 21.2% (95% CI, 19.5%–22.9%), 96.9% (95% CI, 96.3%–97.3%), 75.6% (95% CI, 72.1%–79.0%), and 72.7% (95% CI, 71.6%–73.8%), respectively.

Overall, 379 participants met the secondary definition for $CKD_{Medicare}$ (Figure 2 – right panel). The sensitivity was lower and the specificity and PPV were higher for this secondary definition. Sensitivity was higher but specificity and PPV were lower using the secondary definition of $CKD_{Medicare}$ to identify lower levels of eGFR and higher levels of ACR (Table S2). Due to the lower number of cases of $CKD_{Medicare}$ using this secondary definition, it was not investigated further.

Factors and Outcomes Associated With $CKD_{REGARDS}$ and $CKD_{Medicare}$

Characteristics of participants by the cross-classification of $CKD_{Medicare}$ and $CKD_{REGARDS}$ is provided in Table 1. $CKD_{Medicare}$ and $CKD_{REGARDS}$ were each associated with an increased risk for all-cause mortality and ESRD (Table 2). Although the mortality rate and incidence of ESRD were higher among participants with $CKD_{Medicare}$ compared to their counterparts with $CKD_{REGARDS}$, the hazard ratio for mortality was similar for $CKD_{Medicare}$ and $CKD_{REGARDS}$ and the hazard ratio for ESRD associated with $CKD_{REGARDS}$ was numerically larger than for $CKD_{Medicare}$.

Risk Factors for All-Cause Mortality and ESRD Among Participants With $CKD_{Medicare}$ and $CKD_{REGARDS}$

Among participants with $CKD_{Medicare}$ and those with $CKD_{REGARDS}$, older age, anemia, ACR > 30 mg/g, and being hospitalized during baseline were associated with an increased risk for all-cause mortality (Table 3). Among those with $CKD_{REGARDS}$, women were less likely to die than men but no association between gender and all-cause mortality was present among those with $CKD_{Medicare}$. Diabetes and history of CHD were associated with an increased risk for all-cause mortality among those with $CKD_{REGARDS}$ but not for those with $CKD_{Medicare}$ while eGFR<60 ml/min/1.73 m^2 was associated with an increased risk for all-cause mortality among those with $CKD_{Medicare}$ but not their counterparts with $CKD_{REGARDS}$. Older age was associated with a lower risk for ESRD among those with $CKD_{Medicare}$ and $CKD_{REGARDS}$. Being black versus white, having diabetes, anemia, eGFR<60 ml/min/1.73 m^2, ACR > 30 mg/g, and having a nephrologist visit were each associated with an increased risk for ESRD among those with $CKD_{Medicare}$ and $CKD_{REGARDS}$. A history of CHD was associated with an increased risk for ESRD among those with $CKD_{REGARDS}$ but not those with $CKD_{Medicare}$.

Factors and Outcomes Associated With $CKD_{Medicare}$ Among Individuals With $CKD_{REGARDS}$

Among participants with $CKD_{REGARDS}$, blacks, non-smokers, individuals with abdominal obesity, hypertension, diabetes, a history of CHD, anemia, eGFR < 60 ml/min/1.73 m^2, ACR > 30 mg/g were more likely to have $CKD_{Medicare}$ (Table S3). Additionally, having more outpatient visits, being hospitalized, having a nephrologist visit, and being Medicaid eligible during the look-back period were each associated with having $CKD_{Medicare}$. After multivariable adjustment, each of these factors except being black, not smoking, hypertension, history of CHD, ACR > 30 mg/g and being Medicaid eligible remained associated with an increased prevalence of $CKD_{Medicare}$ (Table 4).

Among participants with $CKD_{REGARDS}$, the crude mortality rate and age, race, gender adjusted hazard ratio for mortality was increased for those with versus without $CKD_{Medicare}$ (Table 5). The hazard ratio was 1.23 (95% CI, 0.99–1.53) after full multivariable adjustment. Among participants with $CKD_{REGARDS}$, the incidence of ESRD was 4.4 (95% CI, 3.2–5.7) and 22.1 (95% CI, 15.0–29.2) per 1,000 person-years among those without and with $CKD_{Medicare}$, respectively. The increased risk for ESRD associated with $CKD_{Medicare}$ remained present after multivariable adjustment.

Secondary Definition of $CKD_{REGARDS}$

Overall, 603 REGARDS participants (9%) had an eGFR < 45 ml/min/1.73 m^2 or ACR > 300 mg/g. Of participants meeting this secondary definition of $CKD_{REGARDS}$, 32.8% (95% CI, 29.1%–36.7%) had $CKD_{Medicare}$ (Figure S1). In contrast, 96.0% (95% CI, 95.5%–96.5%) of participants not meeting the secondary definition of $CKD_{REGARDS}$ did not have $CKD_{Medicare}$. Using the secondary definition of $CKD_{REGARDS}$, the PPV and NPV for $CKD_{Medicare}$ were 43.9% (95% CI, 39.3%–48.6%) and 93.8% (95% CI, 93.2%–94%), respectively. Among participants meeting the secondary definition of $CKD_{REGARDS}$, the risk for mortality was similar for participants with and without $CKD_{Medicare}$ (Table S4). The ESRD risk was higher for those with versus without $CKD_{Medicare}$. This association was attenuated and no longer present after adjustment for age, race, gender, and Medicare variables from the look-back period.

DISCUSSION

In this study, the majority of individuals with CKD in the REGARDS Study ($CKD_{REGARDS}$) as defined by eGFR < 60 ml/min/1.73 m^2 or ACR > 30 mg/g did not have Medicare claims for CKD ($CKD_{Medicare}$). This confirms prior studies showing claims data have low sensitivity for identifying CKD. The current study extends findings from prior studies by demonstrating the similarities and differences that exist when defining CKD using eGFR and ACR versus a claims data definition of CKD. With few exceptions, the same factors were associated with $CKD_{REGARDS}$ and $CKD_{Medicare}$, and $CKD_{REGARDS}$ and $CKD_{Medicare}$ were each associated with an increased risk for all-cause mortality and ESRD. However, some risk factors for all-cause mortality and ESRD differed for individuals with $CKD_{Medicare}$ and $CKD_{REGARDS}$, and among individuals with $CKD_{REGARDS}$, we identified differences among individuals with versus without $CKD_{Medicare}$. For example, among individuals with $CKD_{REGARDS}$, those with co-morbidities including diabetes, anemia and

more severe kidney disease at baseline were more likely to have $CKD_{Medicare}$. Individuals with $CKD_{Medicare}$ also had very high risk for ESRD.

The validity of Medicare claims to identify individuals with CKD has been evaluated previously.[8] The sensitivity, specificity, PPV and NPV for having CKD associated with Medicare claims was studied in 1,852 low income Medicare beneficiaries presenting to a hospital for myocardial infarction. The eGFR was calculated from the first in-hospital serum creatinine measurement and claims for CKD were identified over the 12 and 24 months prior to hospitalization. The prevalence of CKD was 67% (versus 32% in the present study) and the PPV ranged from 89% to 97% depending on the ICD-9 codes used to define CKD (versus 76% in the present study). Given the high PPV, the authors concluded claims data can be used to identify cohorts with "clinically relevant CKD". However, PPV is influenced by the prevalence of the outcome (e.g., CKD) with higher values present at higher disease prevalences. The lower prevalence of CKD in the REGARDS Study, when compared with prior studies of hospitalized patients, may explain the lower PPV we observed in the current study. A substantially higher sensitivity was present for more severe CKD (e.g., 36% and 56% for identifying eGFR <45 ml/min/1.73 m^2 and < 30 ml/min/1.73 m^2, respectively). Due to the low prevalence of these more severe reductions in eGFR, the PPV was substantially lower.

The current study extends prior investigations in several important ways. We included a population-based sample rather than patients presenting to the hospital with myocardial infarction and defined CKD using either reduced eGFR or elevated ACR. A number of recent studies and meta-analyses have demonstrated the prognostic importance of albuminuria for cardiovascular and kidney disease outcomes.[18–20] Additionally, the REGARDS Study had data on a broad range of objectively measured co-morbid conditions that allowed us to assess the generalizability of Medicare beneficiaries with CKD claims. Among those with $CKD_{REGARDS}$, determined by eGFR and ACR levels measured objectively in the REGARDS study, we found those with versus without $CKD_{Medicare}$ to have more co-morbid conditions including abdominal obesity, diabetes and an eGFR < 60 ml/min/1.73 m^2.

Traditional epidemiology studies are very expensive and take a long time to conduct. Therefore, claims data may provide an alternative approach to study CKD. In the current study, we found correlates of CKD and the risk for all-cause mortality to be similar when CKD was defined in claims data or in the REGARDS Study. However, the incidence of ESRD was substantially higher among individuals with $CKD_{Medicare}$ versus $CKD_{REGARDS}$. Additionally, in the current analysis, four risk factors (gender, diabetes, history of CHD and eGFR < 60 ml/min/1.73 m^2) for all-cause mortality and one risk factor (history of CHD) for ESRD were different when evaluated in two parallel cohorts of individuals with CKD, one defined using claims data and the other by measured eGFR and ACR. This suggests that assembling a cohort of individuals with CKD claims to study risk factors for outcomes may lead to different findings compared to studies that use measured eGFR and ACR to define CKD.

Although the current study found potential limitations in using claims data to study CKD in Medicare, algorithms for identifying several other diseases including diabetes, heart failure, and myocardial infarction have been validated in claims databases.[21–23] In general, these algorithms had substantially higher PPV than observed for CKD in the current study. For our primary analysis we used a broad set of claims to identify CKD. The narrower set of ICD-9 codes we used to define CKD in Medicare in secondary analyses resulted in a higher PPV but the sensitivity remained low. Future studies are needed to investigate whether other algorithms with higher sensitivity and PPV can be developed to identify CKD in Medicare claims.

The current study should be interpreted in the context of potential and known limitations. While the REGARDS Study measured both eGFR and ACR, they were obtained at a single time point. Some REGARDS participants identified as having CKD may not have had it if repeat eGFR or ACR measurements were performed.[24] The baseline visit in the REGARDS Study occurred in 2003–2007. ICD-9 diagnosis codes corresponding to CKD stage were introduced into Medicare claims in 2005. Too little look-back time was available in the current study to investigate the correlation of 585 sub-codes with CKD stage. Also, future studies with more contemporary data on CKD are needed to re-evaluate whether the differences between individuals with and without CKD claims in Medicare still remain present. Strengths of the current analysis include the large nationwide reach of the REGARDS Study. Participants were enrolled from across the continental United States. Broad data collection was conducted at baseline using a standardized protocol and participants have been prospectively followed for outcomes. This allowed us to evaluate correlates and outcomes associated with having CKD claims.

In conclusion, the current analysis identified similarities and differences between older US adults with CKD identified in a research study versus in Medicare claims. Our data suggest that most individuals with claims for CKD in Medicare have reduced eGFR or albuminuria. Additionally, CKD, whether identified using a claims-based algorithm or through eGFR and ACR measurements, is associated with an increased risk for all-cause mortality and ESRD. However, regardless of the algorithm applied in the current study, Medicare claims algorithms had low sensitivity and identified a subset of individuals with CKD who had a high mortality and ESRD risk. Future studies are needed to assess whether the generalizability of individuals identified as having CKD in Medicare claims has improved since 2007 and to develop better approaches for identifying CKD in claims. In the interim, the inferences from studies of CKD defined using Medicare claims should be interpreted with caution.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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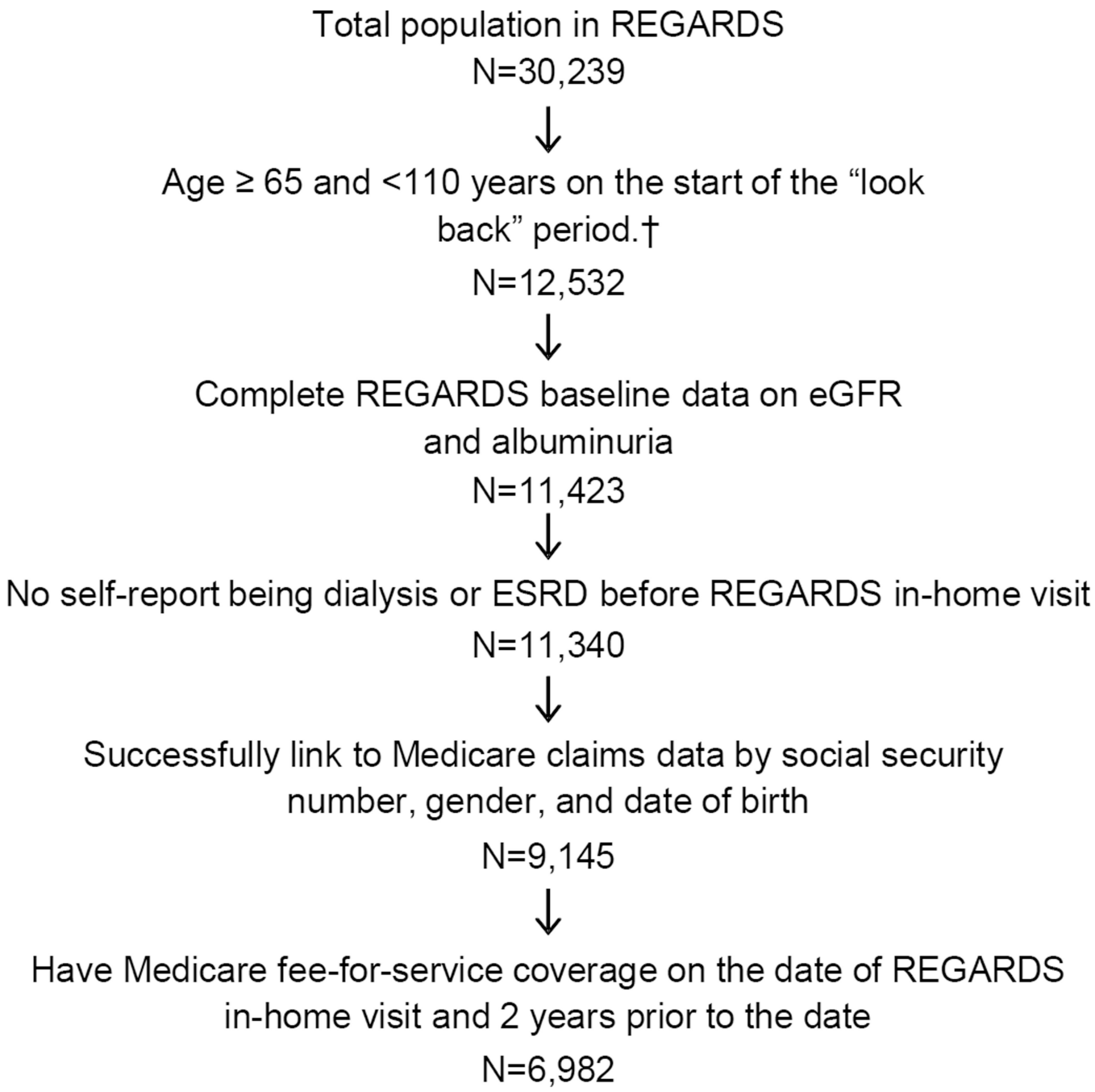

Figure 1.
Eligible cohort for identifying chronic kidney disease with claims data. †The look back period is the two years prior to each participant's REGARDS study visit

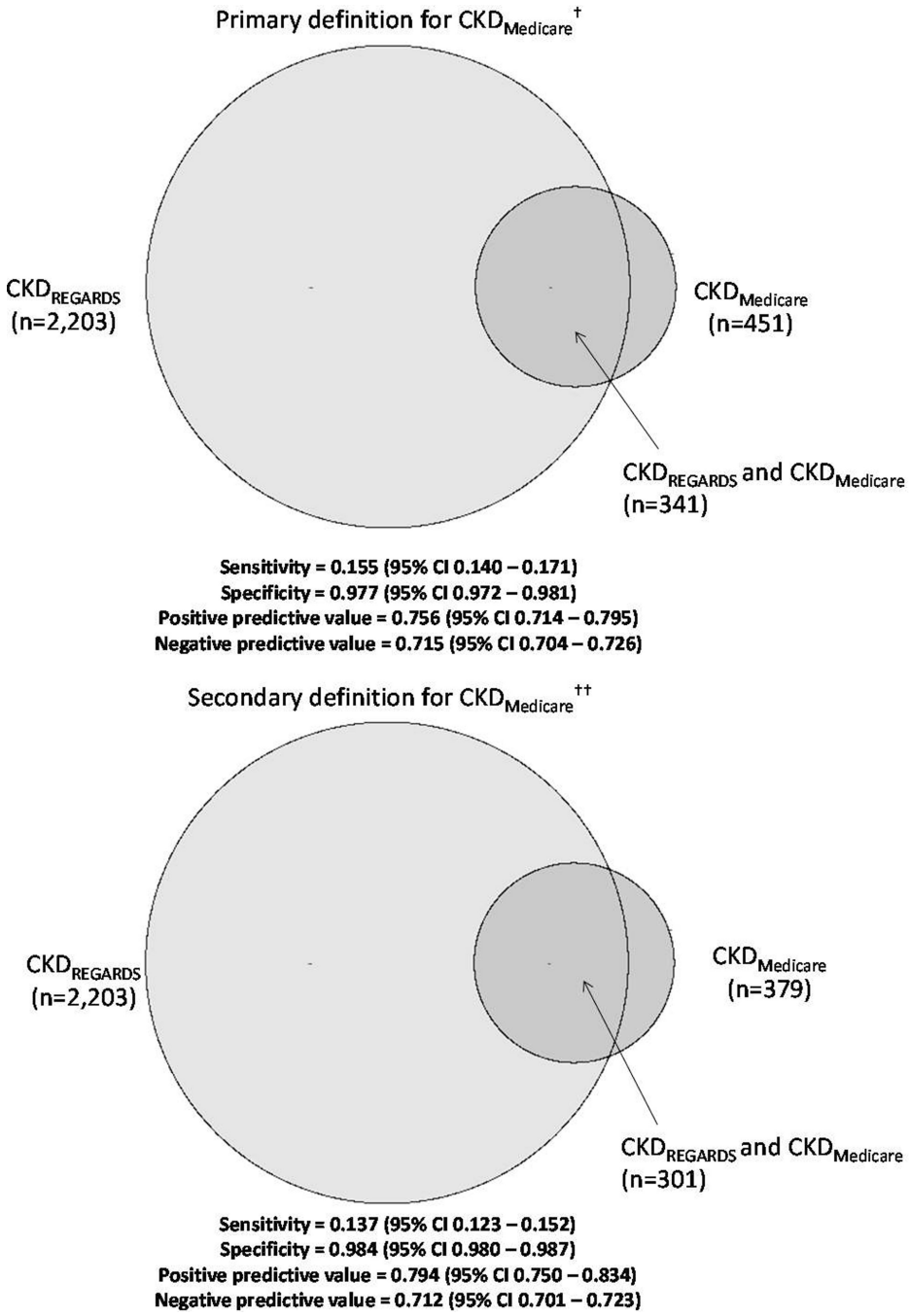

Figure 2.

Sensitivity, specificity, positive and negative predictive values of a Medicare claims-based algorithm ($CKD_{Medicare}$) for identifying chronic kidney disease with estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m^2 or albumin-creatinine ratio > 30 mg/g measured in a research study ($CKD_{REGARDS}$) serving as the gold standard. $CKD_{REGARDS}$ defined as eGFR < 60 mL/min/1.73 m2 or albumin-creatinine ratio > 30 mg/g. †Primary definition for

$CKD_{Medicare}$ provided in Item S1. ††Secondary definition for $CKD_{Medicare}$ is provided in Item S2.

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Table 1

Characteristics of REGARDS study participants with and without $CKD_{Medicare}$ and $CKD_{REGARDS}$.

	No $CKD_{Medicare}$ No $CKD_{REGARDS}$ (n=4669)	**No $CKD_{Medicare}$ Yes $CKD_{REGARDS}$ (n=1862)**	**Yes $CKD_{Medicare}$ No $CKD_{REGARDS}$ (n=110)**	**Yes $CKD_{Medicare}$ Yes $CKD_{REGARDS}$ (n=341)**	**p-value**
REGARDS Variables, Collected at Baseline					
Age category					<0.001
<75 y	2924 (62.6)	865 (46.5)	80 (72.7)	166 (48.7)	
75 – 84 y	1604 (34.4)	855 (45.9)	N<11	146 (42.8)	
≥ 85 y	141 (3.0)	142 (7.6)	N<11	29 (8.5)	
Black race	1325 (28.4)	603 (32.4)	47 (42.7)	133 (39.0)	<0.001
Female sex	2334 (50.0)	920 (49.4)	45 (40.9)	163 (47.8)	0.3
Region of residence					0.8
West	299 (6.4)	119 (6.4)	N<11	18 (5.3)	
Midwest	701 (15.0)	303 (16.3)	18 (16.4)	60 (17.6)	
Northeast	262 (5.6)	96 (5.2)	N<11	21 (6.2)	
South	3407 (73.0)	1344 (72.2)	77 (70.0)	242 (71.0)	
Current smoker	358 (7.7)	199 (10.7)	N<11	24 (7.1)	<0.001
Abdominal obesity	1986 (42.8)	910 (49.2)	55 (50.9)	206 (60.4)	<0.001
Hypertension	2774 (59.6)	1449 (78.0)	75 (68.2)	280 (82.8)	<0.001
Diabetes	780 (16.8)	540 (29.1)	35 (31.8)	158 (46.5)	<0.001
History of CHD	1037 (22.5)	578 (31.7)	42 (40.4)	149 (44.6)	<0.001
Anemia	336 (11.4)	259 (23.8)	25 (32.1)	109 (48.0)	<0.001
Family history of ESRD	262 (8.6)	131 (11.6)	11 (13.1)	31 (13.7)	0.003
eGFR <60 ml/min/1.73 m^2	0 (0)	1108 (59.5)	0 (0)	288 (84.5)	<0.001
eGFR (ml/min/1.73 m^2)	82.3 ±11.8	62.3 ±19.1	79.4 ±13.2	45.8 ±17.1	<0.001
ACR >30 mg/g	0 (0)	1056 (56.7)	0 (0)	214 (62.8)	<0.001
ACR (mg/g)	7.2 [4.9–12.0]	34.8 [9.4–77.4]	9.4 [5.7–14.3]	56.1 [13.3–175.9]	<0.001
Antihypertensive medication use	2351 (52.0)	1277 (70.5)	68 (64.2)	269 (80.8)	<0.001
Statin use	1652 (35.4)	792 (42.5)	48 (43.6)	165 (48.4)	<0.001

	No $CKD_{Medicare}$ No $CKD_{REGARDS}$ (n=4669)	No $CKD_{Medicare}$ Yes $CKD_{REGARDS}$ (n=1862)	Yes $CKD_{Medicare}$ No $CKD_{REGARDS}$ (n=110)	Yes $CKD_{Medicare}$ Yes $CKD_{REGARDS}$ (n=341)	p-value
BMI category					<0.001
<25 kg/m^2	1415 (30.4)	544 (29.4)	24 (21.8)	72 (21.4)	
25-<30 kg/m^2	1921 (41.3)	720 (38.9)	45 (40.9)	126 (37.4)	
≥30 kg/m^2	1317 (28.3)	588 (31.7)	41 (37.3)	139 (41.2)	
SBP ≥140 mm Hg	1075 (23.1)	621 (33.5)	24 (21.8)	106 (31.1)	<0.001
Medicare Variables, During Look-Back Period					
No. of outpatient visits					<0.001
<10	1617 (34.6)	505 (27.1)	14 (12.7)	18 (5.3)	
10–19	1641 (35.1)	633 (34.0)	24 (21.8)	79 (23.2)	
≥ 20	1411 (30.2)	724 (38.9)	72 (65.5)	244 (71.6)	
Hospitalization	1179 (25.3)	657 (35.3)	59 (53.6)	220 (64.5)	<0.001
Nephrology visit	134 (2.9)	68 (3.7)	23 (20.9)	138 (40.5)	<0.001
Medicaid eligible	319 (6.8)	173 (9.3)	16 (14.5)	50 (14.7)	<0.001

Note: Values for categorical variables are given as number (percentage); values for continuous variables are given as mean ± standard deviation or median [interquartile range].

Abbreviations and definitions: $CKD_{Medicare}$, chronic kidney disease defined using the claims-based algorithm outlined in Item S1;$CKD_{REGARDS}$, chronic kidney disease defined as eGFR < 60 ml/min/1.73 m^2 or ACR > 30 mg/g at the REGARDS study visit; CKD – chronic kidney disease; CHD – coronary heart disease; ESRD – end-stage renal disease; eGFR – estimated glomerular filtration rate; ACR – albumin-creatinine ratio. BMI, body mass index; SBP, systolic blood pressure; N<11 – cells with less than 11 Medicare beneficiaries are suppressed per the Center for Medicare & Medicaid Services data agreement; REGARDS, Reasons for Geographic and Racial Differences in Stroke

Table 2

Rates and hazard ratios for mortality and ESRD associated with $CKD_{Medicare}$ and $CKD_{REGARDS}$

	No $CKD_{Medicare}$ (n=6531)	$CKD_{Medicare}$ (n=451)	No $CKD_{REGARDS}$ (n=4779)	$CKD_{REGARDS}$ (n=2203)
Mortality				
No. of cases (%)	1242 (19.0)	160 (35.5)	713 (14.9)	689 (31.3)
Incidence rate (95% CI)†	33.3 (31.5–35.2)	72.5 (61.3–83.7)	25.5 (23.6–27.4)	59.9 (55.4–64.4)
Hazard ratio (95% CI)				
Model 1	1.00 (reference)	2.10 (1.78–2.48)	1.00 (reference)	1.90 (1.71–2.12)
Model 2	1.00 (reference)	1.54 (1.29–1.85)	1.00 (reference)	1.75 (1.56–1.95)
Model 3	1.00 (reference)	1.47 (1.22–1.77)	1.00 (reference)	1.63 (1.45–1.83)
ESRD				
No. of cases (%)	50 (0.8)	38 (8.4)	N<11	N<11*
Incidence rate (95% CI)†	1.3 (0.9–1.6)	16.4 (11.2–21.6)	0.1 (0.0–0.3)	6.8 (5.4–8.3)
Hazard ratio (95% CI)				
Model 1	1.00 (reference)	11.6 (7.55–17.7)	1.00 (reference)	48.1 (17.6–131)
Model 2	1.00 (reference)	5.80 (3.49–9.7)	1.00 (reference)	37.8 (13.8–104)
Model 3	1.00 (reference)	4.62 (2.72–7.84)	1.00 (reference)	30.9 (11.2–85.5)

Note: Model 1 is adjusted for age, race, and gender; model 2 is adjusted for age, race, gender and Medicare variables during the look-back period (outpatient visits, nephrologist visits, hospitalization during baseline and Medicaid eligible); model 3 is adjusted for variables in model 2 and smoking, abdominal obesity, hypertension, diabetes, and history of coronary heart disease from the REGARDS study.

Abbreviations and definitions: $CKD_{Medicare}$, chronic kidney disease defined using the claims-based algorithm outlined in Item S1; $CKD_{REGARDS}$, chronic kidney disease defined as eGFR < 60 ml/min/1.73 m^2 or albumin-creatinine ratio > 30 mg/g at the REGARDS study visit. CI – confidence interval; CKD – chronic kidney disease; ESRD, end-stage renal disease; REGARDS, Reasons for Geographic and Racial Differences in Stroke; N<11: cells with less than 11 Medicare beneficiaries are suppressed per the Center for Medicare & Medicaid Services data agreement.

† Incidence rate per 1,000 person-years (95% CI).

* Although the number of ESRD cases with $CKD_{REGARDS}$ is >11, this cell is suppressed to prevent calculation of the cell size for ESRD cases with no $CKD_{REGARDS}$.

Table 3

Hazard ratios for all-cause mortality and ESRD among study participants with $CKD_{Medicare}$ and $CKD_{REGARDS}$

	All-Cause Mortality		ESRD	
	$CKD_{Medicare}$ (n=451)	**$CKD_{REGARDS}$ (n=2,203)**	**$CKD_{Medicare}$ (n=451)**	**$CKD_{REGARDS}$ (n=2,203)**
Risk Factors From REGARDS Study				
Age category				
<75 y	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
75–84 y	1.75 (1.25 – 2.47)	1.89 (1.61 – 2.22)	0.56 (0.28 – 1.11)	0.57 (0.37 – 0.90)
≥ 85 y	3.89 (2.37 – 6.37)	3.18 (2.51 – 4.03)	NA*	0.11 (0.02 – 0.81)
Black vs. white	1.19 (0.85 – 1.68)	0.86 (0.73 – 1.01)	3.03 (1.57 – 5.86)	3.69 (2.32 – 5.85)
Women vs. men	0.85 (0.61 – 1.18)	0.60 (0.52 – 0.70)	0.79 (0.42 – 1.48)	0.77 (0.50 – 1.18)
Hypertension	0.76 (0.52 – 1.11)	0.85 (0.72 – 1.00)	NA*	2.14 (1.01 – 4.52)
Diabetes	1.16 (0.83 – 1.6)	1.52 (1.31 – 1.77)	3.06 (1.52 – 6.16)	1.77 (1.14 – 2.73)
History of CHD	1.09 (0.78 – 1.51)	1.45 (1.25 – 1.69)	0.96 (0.52 – 1.79)	1.60 (1.03 – 2.48)
Anemia	1.53 (0.97 – 2.41)	1.40 (1.07 – 1.84)	3.07 (1.25 – 7.55)	2.51 (1.57 – 4.01)
eGFR < 60 ml/min/1.73 m^2	1.68 (1.14 – 2.47)	0.94 (0.80 – 1.09)	5.29 (1.94 – 14.4)	5.17 (2.65 – 10.1)
ACR > 30 mg/g	1.55 (1.12 – 2.14)	1.46 (1.25 – 1.69)	4.11 (1.91 – 8.84)	3.98 (2.16 – 7.32)
Risk Factors From Medicare Claims				
No. of outpatient visits				
<10	1.00 (reference)	1 (reference)	1 (reference)	1 (reference)
10–19	1.50 (0.61 – 3.71)	0.91 (0.74 – 1.13)	0.96 (0.22 – 4.22)	0.82 (0.44 – 1.53)
≥ 20	2.03 (0.86 – 4.78)	1.24 (1.02 – 1.51)	1.13 (0.28 – 4.47)	1.07 (0.61 – 1.89)
Hospitalization during baseline	2.08 (1.43 – 3.03)	1.79 (1.54 – 2.08)	1.57 (0.83 – 2.96)	1.19 (0.77 – 1.84)
Nephrologist visit	1.00 (0.72 – 1.40)	0.83 (0.64 – 1.08)	5.05 (2.58 – 9.87)	4.57 (2.91 – 7.18)
Medicaid eligible	0.65 (0.38 – 1.10)	1.09 (0.84 – 1.41)	0.81 (0.37 – 1.79)	1.18 (0.68 – 2.05)

Note: Values are given as hazard ratio (95% confidence interval). Models include adjustment for age, race, gender.

Abbreviations and definitions: $CKD_{Medicare}$, chronic kidney disease defined using the claims-based algorithm outlined in Item S1; $CKD_{REGARDS}$, chronic kidney disease defined as eGFR < 60 ml/min/1.73 m^2 or ACR > 30 mg/g at the REGARDS study visit; CI – confidence interval, eGFR – estimated glomerular filtration rate, ESRD, end-stage renal disease; ACR – albumin-creatinine ratio, CHD – coronary heart disease. NA, not available; REGARDS, Reasons for Geographic and Racial Differences in Stroke

*All participants with $CKD_{Medicare}$ developing ESRD had hypertension and none were ≥ 85 years of age; therefore, a hazard ratio could not be calculated.

Table 4

Prevalence ratios for $CKD_{Medicare}$ among participants with $CKD_{REGARDS}$

	Model 1	Model 2	Model 3
REGARDS Variables, Collected at Baseline			
Age category			
< 75 y	1.00 (reference)	1.00 (reference)	1.00 (reference)
75–84 y	0.92 (0.75 – 1.13)	0.95 (0.79–1.15)	0.99 (0.82 – 1.20)
≥ 85 y	1.07 (0.75 – 1.54)	1.08 (0.81–1.44)	1.16 (0.86 – 1.57)
Black race	1.29 (1.05 – 1.57)	1.12 (0.93–1.34)	1.09 (0.91 – 1.30)
Female sex	0.91 (0.75 – 1.11)	0.84 (0.71–1.00)	0.83 (0.69 – 1.00)
Region of residence			
West	1.00 (reference)	1.00 (reference)	1.00 (reference)
Midwest	1.18 (0.72 – 1.93)	1.18 (0.76 – 1.82)	1.18 (0.69 – 2.01)
Northeast	1.32 (0.74 – 2.36)	1.38 (0.81 – 2.35)	1.18 (0.68 – 2.03)
South	1.14 (0.73 – 1.78)	1.12 (0.76 – 1.65)	1.18 (0.68 – 2.05)
Current smoker	0.66 (0.45 – 0.98)	0.83 (0.58 – 1.18)	0.87 (0.60 – 1.25)
Abdominal obesity	1.50 (1.22 – 1.84)	1.27 (1.06 – 1.52)	1.21 (1.01 – 1.46)
Hypertension	1.27 (0.97 – 1.65)	1.10 (0.87 – 1.39)	1.06 (0.84 – 1.34)
Diabetes	1.83 (1.50 – 2.23)	1.31 (1.09 – 1.56)	1.24 (1.03 – 1.49)
History of CHD	1.64 (1.33 – 2.01)	1.20 (1.01 – 1.44)	1.18 (0.99 – 1.41)
Anemia	2.50 (1.93 – 3.24)	1.61 (1.28 – 2.01)	1.54 (1.22 – 1.94)
Family history of ESRD	1.09 (0.73 – 1.62)	0.84 (0.62 – 1.14)	0.82 (0.60 – 1.12)
eGFR < 60 ml/min/1.73 m^2	3.32 (2.51 – 4.40)	2.24 (1.71 – 2.95)	2.29 (1.74 – 3.01)
ACR > 30 mg/g	1.20 (0.98 – 1.48)	1.15 (0.96 – 1.39)	1.11 (0.92 – 1.34)
Medicare Variables, During Look-Back Period			
No. of outpatient visits			
< 10	1.00 (reference)	1.00 (reference)	1 (reference)
10–19	3.32 (2.02 – 5.48)	2.56 (1.57 – 4.19)	2.50 (1.53 – 4.09)
≥ 20	7.58 (4.75 – 12.1)	4.03 (2.49 – 6.52)	3.71 (2.31 – 5.97)
Hospitalization	2.79 (2.27 – 3.42)	1.79 (1.47 – 2.17)	1.74 (1.43 – 2.11)
Nephrology visit	6.59 (5.58 – 7.77)	4.77 (4.01 – 5.69)	4.62 (3.88 – 5.51)
Medicaid eligible	1.47 (1.11 – 1.96)	1.04 (0.83 – 1.32)	0.99 (0.79 – 1.24)

Note: Values are given as prevalence ratio (95% confidence interval). Model 1 includes adjustment for age, race, gender; model 2 includes adjustment for age, race, gender, outpatient visits, nephrologist visits, hospitalization during baseline and Medicaid eligible; model 3 is adjusted for variables in model 2 and smoking, abdominal obesity, hypertension, diabetes, and history of CHD from the REGARDS study.

Abbreviations and definitions: CKD – chronic kidney disease, eGFR – estimated glomerular filtration rate, ACR – albumin-creatinine ratio, CHD – coronary heart disease; REGARDS, Reasons for Geographic and Racial Differences in Stroke; $CKD_{Medicare}$, chronic kidney disease defined using the claims-based algorithm outlined in Item S1; $CKD_{REGARDS}$, chronic kidney disease defined as eGFR < 60 ml/min/1.73 m^2 or ACR > 30 mg/g at the REGARDS study visit.

Table 5

Rates and hazard ratios for mortality and ESRD associated with $CKD_{Medicare}$ among participants with $CKD_{REGARDS}$

	Mortality		ESRD	
	No $CKD_{Medicare}$ (n=1862)	**$CKD_{Medicare}$ (n=341)**	**No $CKD_{Medicare}$ (n=1862)**	**$CKD_{Medicare}$ (n=341)**
No. of cases (%)	551 (29.6)	138 (40.5)	47 (2.5)	37 (10.9)
Incidence rate (95% CI)†	55.7 (51.0 – 60.3)	85.9 (71.6 – 100.0)	4.4 (3.2 – 5.7)	22.1 (15.0 – 29.2)
Hazard ratio (95% CI)				
Model 1	1.00 (reference)	1.59 (1.32 – 1.91)	1.00 (reference)	4.32 (2.80 – 6.67)
Model 2	1.00 (reference)	1.27 (1.03 – 1.57)	1.00 (reference)	2.49 (1.45 – 4.27)
Model 3	1.00 (reference)	1.23 (0.99 – 1.53)	1.00 (reference)	2.19 (1.26 – 3.83)

†Incidence rate per 1,000 person-years.

Abbreviations and definitions: CI – confidence interval; CKD – chronic kidney disease; ESRD, end-stage renal disease; $CKD_{Medicare}$, chronic kidney disease defined using the claims-based algorithm outlined in Item S1; $CKD_{REGARDS}$, chronic kidney disease defined as estimated glomerular filtration rate < 60 ml/min/1.73 m^2 or albumin-creatinine ratio > 30 mg/g at the REGARDS study visit; REGARDS, Reasons for Geographic and Racial Differences in Stroke

Note: Model 1 is adjusted for age, race, and gender; model 2 is adjusted for age, race, gender and Medicare variables during the look-back period (outpatient visits, nephrologist visits, hospitalization during baseline and Medicaid eligible); model 3 is adjusted for variables in model 2 and smoking, abdominal obesity, hypertension, diabetes, and history of coronary heart disease from the REGARDS study.