



Published in final edited form as:

*Am J Nephrol.* 2020 ; 51(6): 463–472. doi:10.1159/000507774.

## CKD Awareness and Longitudinal Health Outcomes: Results from the REGARDS Study

**Sri Lekha Tummalapalli<sup>(1),(2)</sup>, Eric Vittinghoff<sup>(3)</sup>, Deidra C. Crews<sup>(4),(5),(6)</sup>, Mary Cushman<sup>(7)</sup>, Orlando M. Gutiérrez<sup>(8),(9)</sup>, Suzanne E. Judd<sup>(10)</sup>, Holly J. Kramer<sup>(11),(12)</sup>, Carmen A. Peralta<sup>(1),(2),(13)</sup>, Delphine S. Tuot<sup>(1),(14),(15)</sup>, Michael G. Shlipak<sup>(2),(16)</sup>, Michelle M. Estrella<sup>(1),(2)</sup>**

<sup>1</sup>Division of Nephrology, Department of Medicine, University of California, San Francisco, CA, USA

<sup>2</sup>Kidney Health Research Collaborative, Department of Medicine, University of California, San Francisco, CA, USA and San Francisco Veterans Affairs Health Care System San Francisco, CA, USA

<sup>3</sup>Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, USA

<sup>4</sup>Welch Center for Prevention, Epidemiology, and Clinical Research, Johns Hopkins Medical Institutions, Baltimore, MD, USA

<sup>5</sup>Johns Hopkins Center for Health Equity, Johns Hopkins Medical Institutions, Baltimore, MD, USA

<sup>6</sup>Division of Nephrology, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA

<sup>7</sup>Departments of Medicine and Pathology and Laboratory Medicine, Larner College of Medicine, University of Vermont, Burlington, VT, USA

<sup>8</sup>Department of Epidemiology, Birmingham, AL, USA

<sup>9</sup>Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA

<sup>10</sup>Department of Biostatistics, University of Alabama at Birmingham, Birmingham, AL, USA

<sup>11</sup>Department of Public Health Sciences and Medicine, Loyola University, Chicago, IL

<sup>12</sup>Division of Nephrology and Hypertension, Loyola University, Chicago, IL

<sup>13</sup>Cricket Health, Inc., San Francisco, CA

---

**Corresponding Author:** Sri Lekha Tummalapalli, MD, MBA, Department of Medicine, Division of Nephrology, 533 Parnassus Avenue, U404, San Francisco, CA 94143-0532, Ph: (415) 476-1812, Fax: (415) 476-3381, srilekha.tummalapalli@ucsf.edu.

**Author Contributions:** research idea and study design: SLT, MME; data acquisition: MC, SEJ; data analysis/interpretation: SLT, EV, MGS, MME; statistical analysis: SLT; supervision or mentorship: MME. Each author contributed important intellectual content during manuscript drafting or revision, accepts personal accountability for the author's own contributions, and agrees to ensure that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

**Statement of Ethics:** This research was performed with the approval of the Institutional Review Board. Written informed consent to participate in the study was obtained from participants (or their parent/legal guardian where appropriate).

**Financial Disclosure:** Dr. Tummalapalli receives consulting fees from Bayer Pharmaceuticals, outside the proposed work.

<sup>14</sup>.Center for Innovation in Access and Quality at Zuckerberg San Francisco General Hospital, University of California San Francisco, CA, USA

<sup>15</sup>.Center for Vulnerable Populations at Zuckerberg San Francisco General Hospital, University of California, San Francisco, CA, USA

<sup>16</sup>.Department of Medicine, San Francisco Veterans Affairs Medical Center, San Francisco, California, USA

## Abstract

**Background**—The majority of people with chronic kidney disease (CKD) are unaware of their kidney disease. Assessing the clinical significance of increasing CKD awareness has critical public health and healthcare delivery implications. Whether CKD awareness among persons with CKD is associated with longitudinal health behaviors, disease management, and health outcomes is unknown.

**Methods**—We analyzed data from participants with CKD in the REasons for Geographic And Racial Differences in Stroke (REGARDS) study, a national, longitudinal, population-based cohort. Our predictor was participant CKD awareness. Outcomes were 1) Health behaviors (smoking avoidance, exercise, and nonsteroidal anti-inflammatory drug [NSAID] use); 2) CKD management indicators (angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use, statin use, systolic blood pressure, fasting blood glucose, and body mass index); 3) change in estimated glomerular filtration rate (eGFR) and urine albumin-to-creatinine ratio (UACR); and 4) health outcomes (incident end-stage kidney disease [ESKD], coronary heart disease, stroke, and death). Logistic and linear regression were used to examine the association of baseline CKD awareness with outcomes of interest, adjusted for CKD stage and participant demographic and clinical factors.

**Results**—Of 6,529 participants with baseline CKD, 285 (4.4%) were aware of their CKD. Among the 3,586 participants who survived until follow-up (median 9.5 years), baseline awareness was not associated with subsequent odds of health behaviors, CKD management indicators, or changes in eGFR and UACR in adjusted analyses.

Baseline CKD awareness was associated with increased risk of ESKD (HR=1.44; 95% CI: 1.08, 1.92) and death (HR=1.18; 95% CI: 1.00, 1.39), but not with subsequent coronary heart disease or stroke, in adjusted models.

**Conclusions**—Individuals aware of their CKD were more likely to experience ESKD and death, suggesting that CKD awareness reflects disease severity. Most persons with CKD, including those that are high-risk, remain unaware of their CKD. There was no evidence of associations between baseline CKD awareness and longitudinal health behaviors, CKD management indicators, or eGFR decline and albuminuria.

## Keywords

Chronic kidney disease; Awareness; Patient education

## Introduction

The majority of people with chronic kidney disease (CKD) are unaware of their kidney disease, even among those with late stages of CKD.<sup>1</sup> Among those with CKD participating in the National Kidney Foundation's (NKF) Kidney Early Evaluation Program (KEEP) screenings from 2000 to 2007 and the National Health and Nutrition Examination Survey (NHANES) from 2005 to 2010, only 8.1% and 6.4% of participants, respectively, knew of their CKD.<sup>2,3</sup> Low CKD awareness and the predictors of awareness have been established in a variety of clinical settings.<sup>4</sup>

There have been calls for further research on the health implications of low CKD awareness, as studies examining the impact of CKD awareness on longitudinal health outcomes are scarce.<sup>1</sup> Prior analyses of CKD awareness were primarily cross-sectional; for example, an analysis of participants with CKD in the REasons for Geographic And Racial Differences in Stroke (REGARDS) Study did not find an association between CKD awareness and most health behaviors and chronic disease management indicators.<sup>5</sup> Although CKD awareness has been associated with incident end-stage kidney disease (ESKD) and mortality,<sup>6</sup> the associations of CKD awareness with longitudinal mediators of health outcomes, including health behaviors, chronic disease management, and CKD progression, have not been investigated.

Assessing the clinical significance of increasing CKD awareness has critical public health and healthcare delivery implications. We examined the association of baseline CKD awareness with health behaviors, chronic disease management indicators, CKD progression, and health outcomes including ESKD, coronary heart disease (CHD), stroke, and death during follow-up among participants with CKD in the REGARDS Study. We hypothesized that participants aware of their CKD would be more likely to adopt healthy behaviors and control risk factors related to kidney disease, in an effort to prevent disease progression. Understanding the relationship between CKD awareness and longitudinal health outcomes would further inform overall efforts to improve CKD management.

## Methods

### Study Population

We included participants from the REGARDS study, a longitudinal, population-based cohort designed to study reasons for disparities in stroke mortality by race and region. Between 2003 and 2007, 30,239 participants were recruited, with oversampling of black individuals and residents of the Southeastern United States (Alabama, Mississippi, Arkansas, Louisiana, Tennessee, Georgia, North Carolina, and South Carolina). At the baseline evaluation, participants completed computer-assisted telephone interviews and an in-home examination, consisting of anthropomorphic data measurements, medication inventory including prescription and over-the-counter medications, and fasting laboratory tests. After the baseline evaluation, participants were followed via telephone calls at 6-month intervals to assess symptoms, hospitalizations, and retrieval and adjudication of relevant medical records. A total of 14,685 participants consented for a follow-up visit between 2013 and 2016, which had similar procedures as the baseline evaluation. Written informed consent

was obtained at both visits and all participating institutional review boards approved the study methodology. The full methods of the REGARDS study have been previously described.<sup>7</sup>

Our analytic cohort included REGARDS participants with CKD at the baseline study visit, defined by an estimated glomerular filtration rate (eGFR) <60 mL/min and/or urine albumin-to-creatinine ratio (UACR) ≥ 30 mg/g (N = 6,686). The eGFR values were calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.<sup>8</sup> We excluded participants with missing kidney disease awareness variables at baseline (N = 54), persons who self-reported dialysis treatment at baseline (N = 103), leaving 6,529 participants in the analytic cohort as detailed in Supplemental Figure 1. A total of 3,586 participants in this analytic cohort who survived until the follow-up in-home visit was then used to examine health behaviors, chronic disease management indicators, and CKD progression ascertained at the follow-up visit. We included all surviving individuals to minimize selection bias due to loss to follow up, regardless of their second in-home visit completion (additional baseline characteristics in Supplemental Table 1).

### **Predictor**

Our predictor was an individual's CKD awareness at study entry, which was defined as a participant's affirmative answer to the question "Has a doctor or other health professional ever told you that you had kidney disease?"

### **Outcomes**

Outcomes were ascertained during follow-up and classified into four categories: 1) health behaviors, 2) chronic disease management indicators, 3) CKD progression, and 4) health outcomes. Health behaviors included smoking avoidance, exercise, and nonsteroidal anti-inflammatory drug (NSAID) avoidance at the follow-up visit. Smoking avoidance was defined as answering "no" to "Do you smoke cigarettes now, even occasionally?" Exercise was dichotomized as no exercise compared with one or more times per week. We used data from the medication inventory to identify prescription and over-the-counter NSAID use, as self-reported NSAID use was not collected at the follow-up visit. Chronic disease management indicators included use of angiotensin-converting enzyme inhibitor or angiotensin receptor blockers (ACEi/ARBs), statin use, systolic blood pressure, fasting blood glucose, and body mass index (BMI) at the follow-up visit. Use of ACEi/ARBs and statins was recorded from the medication inventory at both baseline and follow-up. Systolic blood pressure was the average of two measurements conducted during the in-home visits, and change in systolic blood pressure was calculated as the difference between the average values at baseline and follow-up. Changes in fasting blood glucose and BMI between baseline and follow-up visits were analyzed as continuous variables. In a sensitivity analysis, we dichotomized the variables of systolic blood pressure at <130 and ≥ 130 mm Hg, fasting blood glucose at <125 and ≥ 125 mg/dL, and BMI at >30 and ≤ 30 kg/m<sup>2</sup>. CKD progression outcomes included change in eGFR and UACR from the baseline visit to follow-up visit. Laboratory methods in the REGARDS study have been described elsewhere.<sup>9</sup>

Health outcomes included incident ESKD, CHD, stroke, and death. Incident ESKD was determined via data linkage to the United States Renal Data System 2014 data, which monitors persons with ESKD requiring dialysis or transplant. Stroke symptoms were ascertained via telephone calls during follow-up at 6-month intervals, and medical records and neuroimaging were retrieved and reviewed. Stroke outcomes were adjudicated by two expert clinicians according to the World Health Organization definition, as described elsewhere.<sup>10,11</sup> Similarly, CHD events were monitored via telephone calls every 6-months, and events were adjudicated according to published guidelines, upon review of medical records and death certificates.<sup>12</sup> Deaths were reported by proxies through telephone or mail, and confirmed via death certificates or linkage to the National Death Index or Social Security Death Index.<sup>13,14</sup> CHD, stroke, and death outcomes were ascertained until 2016.

### Covariates

Covariates included in multivariable models were ascertained at baseline and included age, sex, race, education, income, insurance, marital status, urban residence, region, comorbidities (hypertension, diabetes, heart disease, and stroke), and family history of kidney disease. Race was self-reported and classified as black or white. Education and income were self-reported and grouped into four levels. Insurance status and marital status were self-reported. Hypertension was defined as a blood pressure  $\geq 140/90$  mm Hg or self-reported use of antihypertensive agents. Diabetes was defined as having a fasting blood glucose  $\geq 126$  mg/dL, non-fasting blood glucose  $\geq 200$  mg/dL, or taking pills or insulin for diabetes. Coronary artery disease (CAD) was defined as self-reported myocardial infarction, coronary artery bypass grafting, angioplasty, or stenting, or evidence of myocardial infarction on electrocardiogram. History of stroke and family history of kidney disease were self-reported.

### Statistical Analysis

We reported the baseline characteristics of REGARDS participants with CKD and compared those who were aware and not aware of their CKD using t-tests and chi-squared tests as appropriate. Missing baseline covariates and follow-up health behaviors, chronic disease management indicators, eGFR, and UACR were estimated using multiple imputation by chained equations using 50 imputations. Among participants with baseline CKD who survived until the follow-up in-home visit, we performed logistic regression to determine the association of baseline CKD awareness with health behaviors and chronic disease management indicators, in unadjusted and multivariable models. Model 1 adjusted for eGFR and UACR, as CKD stage has been shown to be a confounder in the association between CKD awareness and health behaviors and chronic disease management.<sup>4</sup> Model 2 additionally adjusted for participant demographic and clinical factors that were potential confounders due to their association with CKD awareness and health outcomes, including age, sex, race, education, income, insurance status, marital status, urban status, region, hypertension, diabetes, CAD, stroke, and family history of kidney disease. We performed linear regression to assess the association of baseline CKD awareness with 10-year changes in continuous chronic disease management indicators and CKD progression, adjusting for the baseline values of these outcomes. We applied the same staged multivariable adjustment for CKD stage, participant demographics, and clinical factors. We assessed residuals plotted

against fitted values which were consistent with linearity assumptions in linear regression models. As a sensitivity analysis, we examined the association of baseline CKD awareness with dichotomized outcomes of blood pressure control, fasting blood glucose control, and BMI control using logistic regression.

We then analyzed the association of baseline CKD awareness with longitudinal health outcomes using the full analytic cohort, including those that did not survive to the follow-up visit. We compared those who at baseline were aware versus unaware of their CKD and their risk of developing subsequent ESKD, CHD, stroke and death, using unadjusted and adjusted Cox proportional hazard models, using graphical analysis to check proportionality assumptions. We used Fine and Gray subdistribution hazard models to estimate the subhazard of ESKD, CHD, and stroke, accounting for the competing risk of death.<sup>15</sup>

## Results

### Participant Characteristics

Of the 6,529 REGARDS participants with baseline CKD in the analytic cohort, 285 (4.4%) were aware of their CKD. Individuals who were CKD aware were younger, more likely to be male (58% vs. 46%), have lower educational attainment and income, less likely to exercise, and more likely to have a family history of kidney disease (21 vs. 12%) (Table 1). Those who were CKD aware had higher levels of comorbidity, including a history of hypertension, diabetes, CAD, and stroke, and had higher CKD staging according to the Kidney Disease Improving Global Outcomes (KDIGO) heat map (49% vs. 10% with high-risk CKD).

Of the 3,586 participants who survived until the follow-up in-home visit (median time to follow-up visit 9.5 years), 106 (3.0%) were aware of CKD at baseline. Participants who were aware of their CKD at baseline were younger; were more likely to be male (54% vs. 41%), married (65% vs. 54%), have diabetes and CAD and use ACEi/ARBs; and had higher CKD stage at baseline (34% vs. 5% with KDIGO high-risk CKD, Table 1).

### Association of Baseline CKD Awareness with Health Behaviors and Chronic Disease Management at Follow-up

CKD awareness at baseline was associated with higher odds of NSAID avoidance (odds ratio [OR] 2.22; 95% confidence interval [CI]: 1.17, 4.23) and lower odds of ACEi/ARB use (OR 0.69; 95% CI: 0.51, 0.94) at follow-up in unadjusted analyses (Table 2). After adjustment for CKD stage, participant demographics, and clinical factors, there was no statistically significant association between baseline CKD awareness and follow-up NSAID use or ACEi/ARB use. Baseline CKD awareness was not significantly associated with subsequent odds of smoking avoidance, exercise, or statin use in unadjusted and adjusted analyses (Table 2).

The associations of baseline CKD awareness and change in systolic blood pressure, fasting blood glucose, and BMI were not statistically significant in unadjusted and adjusted models (Table 3). Sensitivity analysis of the association of baseline CKD awareness with blood pressure control, fasting blood glucose control, and BMI control also did not show statistically significant associations (Supplemental Table 2). Baseline CKD awareness was



also not statistically significantly associated with changes in eGFR or UACR, indicators of CKD progression (Table 3).

### Association of Baseline CKD Awareness with Longitudinal Health Outcomes

Of the 6,529 participants in the analytic cohort, 405 (6.2%) developed ESKD; 1,027 (16%) had a CVD event; 989 (15%) had a stroke; and 3,173 (49%) died. Median times to events were 6.4 years for ESKD, 6.8 years for CVD, 7.2 years for stroke, and 8.9 years for death. Participants who were CKD aware had a nearly 6-fold greater risk of ESKD (95% CI: 4.43, 7.53) which was attenuated but remained statistically significant after adjustment for baseline CKD stage, demographics, and clinical factors (adjusted hazard ratio [aHR] 1.44; 95% CI: 1.08, 1.92, Table 4). Those who were CKD aware also had nearly 2-fold risk of CHD in unadjusted models, but this association no longer reached statistical significance in the fully adjusted model (aHR 1.12; 95% CI: 0.85, 1.46). There were no statistically significant associations between CKD awareness and subsequent stroke. CKD awareness was associated with 64% increased risk of death in unadjusted models; this association was attenuated but remained statistically significant in the fully adjusted model (aHR 1.18; 95% CI: 1.00, 1.39).

When accounting for the competing risk of death, CKD awareness was associated with incident ESKD (subhazard ratio [sHR] 3.57; 95% CI: 1.99, 6.41), but the association did not reach statistical significance after adjustment for CKD stage (sHR 1.85; 95% CI: 0.98, 3.49). CKD awareness was not significantly associated with CHD or stroke after accounting for the competing risk of death.

## Discussion

In our analysis of a longitudinal cohort of REGARDS participants with CKD, those who were aware of their disease were more likely to have high-risk CKD, with more advanced CKD stages and higher prevalence of severely increased urine albumin excretion. Those aware of their CKD were more likely to develop incident ESKD and death, even after accounting for CKD stage, participant demographics, and clinical factors. We did not find evidence of an association between baseline CKD awareness and longitudinal health behaviors, chronic disease management indicators, or changes in eGFR or albuminuria.

Our study provides novel evidence in evaluating the relationship between CKD awareness and longitudinal health behaviors and chronic disease management indicators. Prior analyses have examined these associations cross-sectionally and found that CKD awareness was associated with higher tobacco avoidance, but not with other healthy behaviors or indicators of chronic disease management, including ACEi/ARB use, blood pressure control, and glycemic control, similar to our results.<sup>5</sup> Relatedly, others have hypothesized that patients who are aware of CKD may seek and advocate for better care, but prior cross-sectional analyses did not find an association between CKD awareness and guideline-concordant care in NHANES participants.<sup>16</sup> Taken together, findings from these and our longitudinal study suggest that awareness alone may not trigger better self-management or chronic disease management, and awareness efforts need to be combined with multimodal improvement interventions to achieve optimal CKD care.

Importantly, our study did not assess participant knowledge about CKD, which is a key element in translating CKD awareness into better health behaviors. CKD knowledge has been shown to be associated with self-care behaviors.<sup>17</sup> Moreover, CKD awareness and knowledge may more strongly influence health behaviors among those with a family history of kidney disease, as these individuals may have greater understanding of CKD progression and complications.<sup>18</sup> However, a study of patients with advanced CKD seen in a multidisciplinary clinic found that even in such a resource-intensive setting, patient knowledge about CKD was limited.<sup>19</sup> Future studies could assess the interplay of CKD awareness with knowledge in leading to patient activation and improving CKD self-management.<sup>20</sup>

Our evidence is concordant with a prior study that CKD awareness is associated with incident ESKD and death.<sup>6</sup> A longitudinal analysis of KEEP participants found that those aware of CKD at baseline were at increased risk of incident end-stage kidney disease (ESKD) and death independently of participant factors, suggesting that CKD awareness is a marker of disease severity and potential unmeasured participant factors that portend a higher risk of kidney failure.<sup>6</sup> For example, participants with electrolyte abnormalities, history of acute kidney injury, and other high-risk factors may be more likely to be educated about their kidney disease and/or referred to nephrology. In cross-sectional analyses of NHANES, those with more laboratory markers of kidney dysfunction were more likely to be aware of CKD, which supports the notion that CKD awareness is a marker of disease severity.<sup>21</sup> Thus, individuals with high-risk features, not captured by the measurements we adjusted for, may be more likely to be aware of their CKD and also at higher risk of kidney failure.

Although our findings show that some of the highest risk persons with CKD are being informed of their kidney disease, overall CKD awareness remains extremely low. Lack of symptoms contributes to low CKD awareness; similarly, awareness of nonalcoholic fatty liver disease, another asymptomatic condition, is only about 5%.<sup>22</sup> In contrast, the majority of persons with hypertension and diabetes are aware of their disease, indicating that a high level of awareness can be achieved for asymptomatic conditions.<sup>23,24</sup> In November 2019, the American Society of Nephrology, NKF, and Department of Health and Human Services announced a national public awareness initiative for kidney disease which was launched in March 2020.<sup>25</sup> Public health campaigns have been effective in increasing CKD awareness in international settings.<sup>26</sup> One study of 150 participants recruited from a nephrology clinic had a very high (88%) prevalence of CKD awareness, showing that in a select population receiving specialty care, a high level of awareness is attainable.<sup>27</sup> Furthermore, health literacy was not associated with CKD awareness in the nephrology clinic population and a population of discharged hospitalized patients, suggesting that the barrier of low health literacy (often cited as a potential reason for low awareness of CKD in the general population) can be overcome in making persons aware of their CKD.<sup>28</sup>

While patient-focused interventions, including increasing CKD awareness, remain important, our study additionally highlights the need for clinician-focused interventions. Clinician awareness of CKD is a crucial element in educating persons about their CKD, and there is evidence that clinician CKD awareness may improve chronic disease management such as blood pressure control.<sup>29</sup> Additionally, despite CKD awareness, approximately 40%



of those aware were not using ACEi/ARBs in our study, and half were not using of statin medications despite guideline recommendations, suggesting that clinician-directed interventions to improve medication management are needed to improve CKD care.<sup>30-32</sup>

Several limitations of our study should be noted. Ascertainment of CKD awareness varies according to how the question is worded. The question used in REGARDS, while specific, had a lower sensitivity compared with other questions, which may underestimate kidney disease awareness, resulting in misclassification of some participants.<sup>33</sup> CKD ascertainment at baseline was limited to a single measurement of eGFR and UACR, which may result in misclassification of baseline CKD status. Similarly, changes in outcomes such as systolic blood pressure, fasting blood glucose, eGFR, and UACR over a long period of time may be challenging to interpret without multiple values over time, as they are subject to measurement variability. Because of the low CKD awareness among REGARDS participants at baseline, our estimates of associations with outcomes were less precise. The REGARDS study oversampled from the southeastern United States, so our results may not be fully generalizable to other regions. Lastly, as our study is observational, our results are subject to residual confounding.

Our study finds that those aware of their CKD were more likely to experience ESKD and death, suggesting that CKD awareness is a marker of disease severity. However, most persons with CKD, including those that are high-risk, remain unaware of their CKD. Our results indicate that CKD awareness alone may be insufficient to improve kidney-related outcomes. Bundling interventions to increase CKD awareness with patient and clinician education may have greater impact on health behaviors and chronic disease indicators.<sup>34</sup> As the U.S. embarks on a public health initiative to improve kidney disease awareness, it is imperative to rigorously assess the impact on CKD awareness and the effect on health behaviors, chronic disease management, and CKD progression with the ultimate goal of improving care for the CKD population.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

**Support:** This research project is supported by cooperative agreement U01 NS041588 co-funded by the National Institute of Neurological Disorders and Stroke (NINDS) and the National Institute on Aging (NIA), National Institutes of Health, and Department of Health and Human Service. This work is also supported by grant R01 HL080477 funded by the National Heart, Lung, and Blood Institute (NHLBI) within the National Institutes of Health.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the NINDS or the NIA. Representatives of the NINDS were involved in the review of the manuscript but were not directly involved in the collection, management, analysis or interpretation of the data. The authors thank the other investigators, the staff, and the participants of the REGARDS study for their valuable contributions. A full list of participating REGARDS investigators and institutions can be found at: <https://www.uab.edu/soph/regardsstudy/>

Dr. Tummalapalli is supported by grant F32 DK122627 funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) within the National Institutes of Health and the Jonathan A. Showstack Career Advancement Award in Health Policy/Health Services Research at the UCSF Philip R. Lee Institute for Health Policy Studies.

## References:

1. Plantinga LC, Tuot DS, Powe NR. Awareness of chronic kidney disease among patients and providers. *Adv Chronic Kidney Dis* 2010;17:225–36. [PubMed: 20439091]
2. Vassalotti JA, Li S, McCullough PA, Bakris GL. Kidney early evaluation program: a community-based screening approach to address disparities in chronic kidney disease. *Semin Nephrol* 2010;30:66–73. [PubMed: 20116650]
3. Shirazian S, Diep R, Jacobson AM, Grant CD, Mattana J, Calixte R. Awareness of Chronic Kidney Disease and Depressive Symptoms: National Health and Nutrition Examination Surveys 2005–2010. *Am J Nephrol* 2016;44:1–10. [PubMed: 27322107]
4. Plantinga LC, Boulware LE, Coresh J, et al. Patient awareness of chronic kidney disease: trends and predictors. *Arch Intern Med* 2008;168:2268–75. [PubMed: 19001205]
5. Tuot DS, Plantinga LC, Judd SE, et al. Healthy behaviors, risk factor control and awareness of chronic kidney disease. *American journal of nephrology* 2013;37:135–43. [PubMed: 23392070]
6. Whaley-Connell A, Shlipak MG, Inker LA, et al. Awareness of kidney disease and relationship to end-stage renal disease and mortality. *Am J Med* 2012;125:661–9. [PubMed: 22626510]
7. Howard VJ, Cushman M, Pulley L, et al. The reasons for geographic and racial differences in stroke study: objectives and design. *Neuroepidemiology* 2005;25:135–43. [PubMed: 15990444]
8. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009;150:604–12. [PubMed: 19414839]
9. Gillett SR, Boyle RH, Zakai NA, McClure LA, Jenny NS, Cushman M Validating laboratory results in a national observational cohort study without field centers: the Reasons for Geographic and Racial Differences in Stroke cohort. *Clin Biochem* 2014;47:243–6. [PubMed: 25130959]
10. Stroke--1989. Recommendations on stroke prevention, diagnosis, and therapy. Report of the WHO Task Force on Stroke and other Cerebrovascular Disorders. *Stroke* 1989;20:1407–31. [PubMed: 2799873]
11. Howard G, Cushman M, Kissela BM, et al. Traditional risk factors as the underlying cause of racial disparities in stroke: lessons from the half-full (empty?) glass. *Stroke* 2011;42:3369–75. [PubMed: 21960581]
12. Safford MM, Brown TM, Muntner PM, et al. Association of race and sex with risk of incident acute coronary heart disease events. *Jama* 2012;308:1768–74. [PubMed: 23117777]
13. Halanych JH, Shuaib F, Parmar G, et al. Agreement on cause of death between proxies, death certificates, and clinician adjudicators in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study. *Am J Epidemiol* 2011;173:1319–26. [PubMed: 21540327]
14. Olubowale OT, Safford MM, Brown TM, et al. Comparison of Expert Adjudicated Coronary Heart Disease and Cardiovascular Disease Mortality With the National Death Index: Results From the REasons for Geographic And Racial Differences in Stroke (REGARDS) Study. *J Am Heart Assoc* 2017;6.
15. Fine JP, Gray RJ. A Proportional Hazards Model for the Subdistribution of a Competing Risk. *Journal of the American Statistical Association* 1999;94:496–509.
16. Tuot DS, Plantinga LC, Hsu CY, Powe NR. Is awareness of chronic kidney disease associated with evidence-based guideline-concordant outcomes? *Am J Nephrol* 2012;35:191–7. [PubMed: 22286715]
17. Schrauben SJ, Cavanaugh KL, Fagerlin A, et al. The Relationship of Disease-Specific Knowledge and Health Literacy With the Uptake of Self-Care Behaviors in CKD. *Kidney Int Rep* 2020;5:48–57. [PubMed: 31922060]
18. Gheewala PA, Peterson GM, Zaidi STR, Jose MD, Castelino RL. Public knowledge of chronic kidney disease evaluated using a validated questionnaire: a cross-sectional study. *BMC Public Health* 2018;18:371. [PubMed: 29554891]
19. Molnar AO, Akbari A, Brimble KS. Perceived and Objective Kidney Disease Knowledge in Patients With Advanced CKD Followed in a Multidisciplinary CKD Clinic. *Can J Kidney Health Dis* 2020;7:2054358120903156. [PubMed: 32110417]

20. Narva AS, Norton JM, Boulware LE. Educating Patients about CKD: The Path to Self-Management and Patient-Centered Care. *Clin J Am Soc Nephrol* 2016;11:694–703. [PubMed: 26536899]
21. Tuot DS, Plantinga LC, Hsu CY, et al. Chronic kidney disease awareness among individuals with clinical markers of kidney dysfunction. *Clin J Am Soc Nephrol* 2011;6:1838–44. [PubMed: 21784832]
22. Le MH, Yeo YH, Cheung R, Wong VW, Nguyen MH. Ethnic influence on nonalcoholic fatty liver disease prevalence and lack of disease awareness in the United States, 2011–2016. *J Intern Med* 2020.
23. Zhang Y, Moran AE. Trends in the Prevalence, Awareness, Treatment, and Control of Hypertension Among Young Adults in the United States, 1999 to 2014. *Hypertension* 2017;70:736–42. [PubMed: 28847890]
24. Russell E, Oh KM, Zhao X. Undiagnosed diabetes among Hispanic and white adults with elevated haemoglobin A1c levels. *Diabetes Metab Res Rev* 2019;35:e3153. [PubMed: 30884138]
25. Executive Order on Advancing American Kidney Health. <https://www.whitehouse.gov/presidential-actions/executive-order-advancing-american-kidney-health/>. Accessed September 1, 2019.
26. Chin HJ, Ahn JM, Na KY, et al. The effect of the World Kidney Day campaign on the awareness of chronic kidney disease and the status of risk factors for cardiovascular disease and renal progression. *Nephrol Dial Transplant* 2010;25:413–9. [PubMed: 19783595]
27. Devraj R, Borrego ME, Vilay AM, Pailden J, Horowitz B. Awareness, self-management behaviors, health literacy and kidney function relationships in specialty practice. *World J Nephrol* 2018;7:41–50. [PubMed: 29359119]
28. Saunders MR, Snyder A, Chin MH, Meltzer DO, Arora VM, Press VG. Health Literacy Not Associated with Chronic Kidney Disease Awareness. *Health Lit Res Pract* 2017;1:e117–e27. [PubMed: 31294258]
29. Ravera M, Noberasco G, Weiss U, et al. CKD awareness and blood pressure control in the primary care hypertensive population. *Am J Kidney Dis* 2011;57:71–7. [PubMed: 21087817]
30. Group. KDIGOKCW. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney inter., Suppl* 2013; 3: 1–150.
31. Group. KDIGOKBPW. KDIGO Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. *Kidney inter., Suppl* 2012; 2: 337–414.
32. Wanner C, Tonelli M. KDIGO Clinical Practice Guideline for Lipid Management in CKD: summary of recommendation statements and clinical approach to the patient. *Kidney international* 2014;85:1303–9. [PubMed: 24552851]
33. Tuot DS, Zhu Y, Velasquez A, et al. Variation in Patients' Awareness of CKD according to How They Are Asked. *Clin J Am Soc Nephrol* 2016;11:1566–73. [PubMed: 27340288]
34. Leek RB, Park JM, Koerschner C, et al. Novel educational and goal-setting tool to improve knowledge of chronic kidney disease among liver transplant recipients: A pilot study. *PLoS One* 2019;14:e0219856. [PubMed: 31344043]

**Table 1.**

Baseline participant characteristics among the analytic cohort (N = 6,529) and in the cohort that survived until the follow-up in-home visit (N = 3,586), by CKD awareness status at baseline.

	Analytic cohort, Aware of CKD at Baseline (n = 285)	Analytic cohort, Not aware of CKD at Baseline (n = 6,244)	p-values	Surviving cohort, Aware of CKD at Baseline (n = 106)	Surviving cohort, Not aware of CKD at Baseline (n = 3,480)	p-values
<b>Sociodemographics</b>						
Age						
45-59	23	18	<0.001	34	26	0.042
60-69	41	32		42	39	
70-79	26	35		23	29	
80	10	15		2	7	
Sex						
Male	58	46	<0.001	54	41	0.010
Female	42	54		46	59	
Race						
Black	50	47	0.409	53	49	0.403
White	50	53		47	51	
Education						
Less than high school	23	18	0.025	20	14	0.295
High school graduate	31	27		30	27	
Some college	21	26		24	27	
College graduate and above	24	28		26	32	
Income (per year)						
Less than \$20k	31	24	0.048	21	21	0.219
\$20k – 34k	29	28		34	26	
\$35k – 74k	23	25		28	28	
\$75k and above	6	9		7	13	
Refused	11	14		10	13	
Insurance status						
Yes	95	95	0.694	93	93	0.878
No	5	5		7	7	
Marital status						
Married	56	52	0.101	65	54	0.031
Not married	44	48		35	46	
Urban group*						
Urban ( 75% urban)	78	81	0.331	80	80	0.997
Mixed (25-75% urban)	12	9		10	10	
Rural ( 25% urban)	10	9		11	11	

	Analytic cohort, Aware of CKD at Baseline (n = 285)	Analytic cohort, Not aware of CKD at Baseline (n = 6,244)	p-values	Surviving cohort, Aware of CKD at Baseline (n = 106)	Surviving cohort, Not aware of CKD at Baseline (n = 3,480)	p-values
Region						
Belt Region	36	33	0.683	38	34	0.627
Buckle Region	20	21		19	21	
Non-belt Region	44	46		43	45	
<b>Clinical Characteristics</b>						
Hypertension	87	76	<0.001	81	74	0.105
Diabetes *	56	37	<0.001	48	33	0.001
CAD *	42	28	<0.001	33	19	<0.001
Stroke	20	11	<0.001	8	7	0.676
Family history of kidney disease *	21	12	<0.001	20	13	0.058
Current Smoking Avoidance	88	84	0.095	88	86	0.591
Exercise						
None	50	43	0.006	38	37	0.771
1 to 3 times per week	32	32		38	35	
4 or more times per week	18	26		25	28	
ACEi/ARB use	62	52	0.001	65	49	0.001
Statin use	50	40	0.001	46	39	0.116
SBP (mm Hg)	133 [18.9]	133 [18.8]	0.998	131 [16.6]	132 [17.9]	0.786
DBP (mm Hg)	75 [10.6]	77 [10.9]	0.0019	77 [10.2]	78 [10.7]	0.216
BMI (kg/m <sup>2</sup> )	31 [6.9]	30 [6.6]	0.0017	32 [7.7]	31 [6.6]	0.025
<b>Laboratory Results</b>						
UACR (mg/g) *						
<30	25	31	<0.001	27	32	<0.001
30 – 299.9	41	57		49	60	
300	35	12		24	8	
CKD Stage (eGFR mL/min/1.73m <sup>2</sup> )						
Stage 1 ( > 90)	6	23	<0.001	12	30	<0.001
Stage 2 (60 – 89.9)	13	27		20	27	
Stage 3a (45 – 59.9)	25	34		26	34	
Stage 3b (30 – 44.9)	25	12		28	8	
Stage 4 (15 – 29.9)	24	3		13	1	
Stage 5 (<15)	8	0.3		2	0.1	

\* Among participants without missing values.

Values are percentages for categorical variables and mean [standard deviation] for continuous variables. Percentages may not add to 100% due to rounding.

The belt region includes Alabama, Arkansas, Georgia, Indiana, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, and Virginia. The buckle region includes areas of North Carolina, South Carolina and Georgia.

CKD – chronic kidney disease; CAD – coronary artery disease; ACEi/ARB - angiotensin-converting enzyme inhibitor or angiotensin receptor blocker; SBP – systolic blood pressure; DBP – diastolic blood pressure; BMI – body mass index; UACR – urine albumin-to-creatinine-ratio; eGFR – estimated glomerular filtration rate.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript



**Table 2.**

Association of baseline CKD awareness with health behaviors and chronic disease management at follow-up (N = 3,586).

	Prevalence of Behavior or Medication at Follow-up if CKD Aware (%)	OR (95% CI) Unadjusted	p-value	aOR (95% CI) Model 1	p-value	aOR (95% CI) Model 2	p-value
<b>Health Behaviors</b>							
Smoking Avoidance	93.9	1.77 (0.88, 3.54)	0.108	1.16 (0.59, 2.30)	0.665	1.33 (0.50, 3.57)	0.563
Exercise	33.6	0.75 (0.53 to 1.06)	0.103	1.00 (0.69, 1.43)	0.977	0.89 (0.60, 1.33)	0.574
NSAID Avoidance	92.0	2.22 (1.17, 4.23)	0.015	1.55 (0.80, 2.99)	0.189	1.41 (0.72, 2.78)	0.317
<b>Chronic Disease Management Indicators</b>							
ACEi/ARB Use	45.3	0.69 (0.51, 0.94)	0.017	0.82 (0.60, 1.13)	0.223	0.72 (0.50, 1.03)	0.075
Statin Use	61.1	1.19 (0.85, 1.69)	0.312	1.06 (0.75, 1.48)	0.744	0.79 (0.53, 1.18)	0.255

Model 1: Adjusted for eGFR and UACR.

Model 2: Adjusted for eGFR and UACR + age, sex, race, education, income, insurance status, marital status, urban status, region, hypertension, diabetes, coronary artery disease, stroke, family history of kidney disease, and baseline health behaviors and chronic disease management indicators.

Imputed data used for those who did not complete the follow-up in-home visit.

CKD – chronic kidney disease, OR – odds ratio; CI – confidence interval, aOR – adjusted odds ratio; NSAID – nonsteroidal anti-inflammatory drug; ACEi/ARB – angiotensin-converting enzyme inhibitor or angiotensin receptor blocker.

**Table 3.**

Association of baseline CKD awareness with changes in chronic disease management indicators and CKD progression at follow-up (N = 3,586).

	Mean Change at Follow-up if CKD Aware	Coefficient (95% CI) Unadjusted	p-value	Coefficient (95% CI) Model 1	p-value	Coefficient (95% CI) Model 2	p-value
<b>Chronic Disease Management Indicators</b>							
Systolic BP (mm Hg)	-7.2	-2.25 (-5.75, 1.25)	0.206	0.19 (-3.20, 3.58)	0.910	-0.47 (-3.82, 2.88)	0.783
Fasting blood glucose (mg/dL)	-1.7	-3.48 (-10.9, 3.94)	0.357	2.03 (-5.38, 9.44)	0.590	-0.16 (-7.90, 7.57)	0.967
BMI (kg/m <sup>2</sup> )	-0.5	-1.46 (-22.0, 19.1)	0.888	-0.23 (-19.6, 19.1)	0.981	-1.04 (-20.4, 18.3)	0.915
<b>CKD Progression</b>							
eGFR (mL/min/1.73m <sup>2</sup> )	-17.1	0.17 (-3.27, 3.60)	0.924	-2.08 (-5.05, 0.88)	0.168	-2.79 (-5.72, 0.13)	0.061
UACR (mg/g)	-7.7	-54.0 (-1293, 1186)	0.931	153 (-957, 1263)	0.785	67.8 (-1018, 1153)	0.902

Model 1: Adjusted for eGFR and UACR.

Model 2: Adjusted for eGFR and UACR + age, sex, race, education, income, insurance status, marital status, urban status, region, hypertension, diabetes, coronary artery disease, stroke, family history of kidney disease, and baseline values of chronic disease management indicators.

Imputed data used for those who did not complete the follow-up in-home visit.

CKD – chronic kidney disease; CI – confidence interval; BP – blood pressure; BMI – body mass index; eGFR – estimated glomerular filtration rate; UACR – urine albumin-to-creatinine ratio.

Coefficients are the 10-year change in outcome associated with baseline CKD awareness.

**Table 4.**

Association of baseline CKD awareness with incident ESKD, CHD, stroke, and death, using Cox proportional hazard models and accounting for the competing risk of death (N = 6,529).

	IR per 1000 person-years (95% CI)	HR (95% CI) Unadjusted	p-value	aHR (95% CI) Model 1	p-value	aHR (95% CI) Model 2	p-value
<b>ESKD</b>							
<b>Cox Model</b>	4.74 (4.29, 5.23)	5.78 (4.43, 7.53)	<0.001	2.11 (1.60, 2.80)	<0.001	1.44 (1.08, 1.92)	0.013
<b>Competing Risk Model</b>	--	3.57 (1.99, 6.41)	<0.001	1.85 (0.98, 3.49)	0.059	1.23 (0.63, 2.42)	0.550
<b>CHD</b>							
<b>Cox Model</b>	16.2 (15.2, 17.2)	1.88 (1.46, 2.42)	<0.001	1.31 (1.00, 1.70)	0.046	1.12 (0.85, 1.46)	0.424
<b>Competing Risk Model</b>	--	0.77 (0.36, 1.64)	0.503	0.87 (0.40, 1.89)	0.728	0.69 (0.31, 1.52)	0.357
<b>Stroke</b>							
<b>Cox Model</b>	9.04 (8.44, 9.69)	1.17 (0.85, 1.60)	0.342	1.04 (0.75, 1.44)	0.808	1.04 (0.75, 1.45)	0.811
<b>Competing Risk Model</b>	--	0.67 (0.35, 1.31)	0.242	0.93 (0.47, 1.82)	0.826	--	
<b>Death</b>							
<b>Cox Model</b>	45.0 (47.2, 50.8)	1.64 (1.40, 1.91)	<0.001	1.08 (0.92, 1.26)	0.360	1.18 (1.00, 1.39)	0.047

Competing risk models report subhazard ratios obtained from Fine and Gray subdistribution hazard models.

Model 1: Adjusted for eGFR and UACR.

Model 2: Adjusted for eGFR and UACR + age, sex, race, education, income, insurance status, marital status, urban status, region, hypertension, diabetes, coronary artery disease, stroke, and family history of kidney disease.

CKD – chronic kidney disease; ESKD – end-stage kidney disease; CHD – coronary heart disease; IR – incidence rate; HR – hazard ratio; CI – confidence interval; aHR – adjusted hazard ratio.