Title

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Journal

The American Journal of Medicine, 125(7)

ISSN

0002-9343

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Publication Date

2012-07-01

DOI

10.1016/j.amjmed.2011.11.026

Peer reviewed

Published in final edited form as:
Am J Med. 2012 July ; 125(7): 661–669. doi:10.1016/j.amjmed.2011.11.026.

Awareness of Kidney Disease and Relationship to End-Stage Renal Disease and Mortality

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Abstract

Background—Patients with chronic kidney disease are often reported to be unaware. We prospectively evaluated the association between awareness of kidney disease to end-stage renal disease and mortality.

Methods—We utilized 2000–2009 data from the National Kidney Foundation-Kidney Early Evaluation Program (KEEP™). Mortality was determined by cross reference to the Social Security Administration Death Master File, and development of end-stage by cross reference with the United States Renal Data System.

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COI: The authors have no financial relationships to disclose

Verification Statement: All authors had access to the data and a role in writing.

Conflict of Interest: The authors have no conflicts.

Results—Of 109,285 participants, 28,244 (26%) had chronic kidney disease defined by albuminuria or eGFR <60ml/min/1.73m^2. Only 9% (n=2660) reported being aware of kidney disease. Compared to those who were not aware, participants aware of chronic kidney disease had lower eGFR (49 vs 62ml/min/1.73m^2) and a higher prevalence of albuminuria (52 vs 46%), diabetes (47 vs 42%), cardiovascular disease (43 vs 28%) and cancer (23 vs 14%). Over 8.5 years of follow-up, aware participants compared to those unaware had a lower rate of survival for end-stage (83% and 96%) and mortality (78 vs 81%), p<0.001 respectively. After adjustment for demographics, socioeconomic factors, comorbidity, and severity of kidney disease, aware participants continued to demonstrate an increased risk for end-stage renal disease [hazard ratio (95% CI) 1.37(1.07–1.75); p<0.0123] and mortality [1.27(1.07–1.52); p<0.0077] relative to unaware participants with chronic kidney disease.

Conclusions—Among persons identified as having chronic kidney disease at a health screening, only a small proportion had been made aware of their diagnosis previously by clinicians. This subgroup was at a disproportionately high risk for mortality and end-stage renal disease.

Keywords

KEEP; CKD; awareness; ESRD; mortality

Introduction

Chronic kidney disease is increasingly common among adults in the United States and increases risk for progression to end-stage renal disease and premature death (1,2). Detection of kidney disease in high risk populations has become a critical public health challenge, as evidence supports that late referral is associated with poor outcomes (3–5). In theory, detection of at an early stage would allow for timely intervention, potentially delay progression of disease, and decrease mortality (6,7). However, early stage kidney disease is typically asymptomatic, which in turn leads to low levels of awareness in at-risk individuals and in people with chronic kidney disease (7–9).

Low levels of awareness may reflect a poor understanding of kidney disease. Poor awareness may, in turn, reflect poor provider recognition and confusion regarding appropriate diagnosis and intervention, particularly at earlier stages of kidney disease, thereby leading to a lack of education of patients at risk for or with chronic kidney disease. In other disciplines, patient awareness and involvement in their care has been shown to be a critical part of the treatment plan and to improve treatment patterns (10,11). Education for patients with chronic kidney disease has been thought to improve patient awareness and nephrology referral. However, patient education and, potentially, awareness may reflect provider risk stratification for those at highest risk for progression or mortality. Yet, there is little data on awareness of kidney disease as it relates to patient outcomes such as progression to end-stage renal disease and mortality.

The National Kidney Foundation (NKF) implemented the Kidney Early Evaluation Program (KEEP) for the detection of kidney disease among high risk individuals, defined as presence of diabetes mellitus or hypertension, or having a first-order relative with diabetes, hypertension, or kidney disease (9). The NKF KEEP program is the only sustainable chronic disease screening program that has developed a strategy to assess awareness at the time of screening, to provide follow up with participants and providers on chronic kidney disease status and risk intervention, and to ascertain kidney disease-related morbidity and mortality. Thereby, we sought to compare prognosis on longitudinal follow up among persons identified as having chronic kidney disease according to their awareness of this diagnosis prior to screening.

Methods

Study Population

All protocols were IRB-approved with the University of Minnesota and in accordance with NIH guidelines. We included eligible KEEP participants screened from August 2000 through December 2009 aged at least 18 years and older. We excluded individuals receiving maintenance dialysis or with previous kidney transplant, or with missing values in chronic kidney disease and chronic kidney disease awareness (Figure 1). When assessing laboratory values of cholesterol, we only included individuals screened from 2005 to 2009.

Definitions

As previously described (12), glomerular filtration rate (GFR) was estimated using the 4-variable Modification of Diet in Renal Disease (MDRD) Study equation (13). Serum creatinine values were calibrated to standardized serum creatinine at the Cleveland Clinic Research Laboratory (14). Chronic kidney disease was defined using estimated GFR (eGFR) and proteinuria: eGFR ≥60 mL/min/1.73 m^2 with proteinuria determined by an albumin/creatinine ratio (ACR) ≥30 mg/g or eGFR<60 mL/min/1.73 m^2. To assess early vs later stages of chronic kidney disease, we stratified eGFR>45 mL/min/1.73 m^2 and proteinuria or eGFR <45 mL/min/1.73 m^2 chronic kidney disease stages were defined as follows: stage 1, eGFR >90 mL/min/1.73m^2, ACR ≥30 mg/g; stage 2, eGFR 60–89 mL/min/1.73m^2, ACR ≥30 mg/g; stage 3, eGFR 30–59 mL/min/1.73m^2; stage 4, eGFR 15–29 mL/min/1.73m^2; and stage 5, eGFR <15 mL/min/1.73m^2 (12).

Chronic kidney disease awareness was defined as an affirmative answer to the question, “Have you ever been told by a doctor or healthcare professional you have kidney disease (do not include kidney stones, bladder infections or incontinence)?” Based on both chronic kidney disease and chronic kidney disease awareness definitions, we further categorized individuals into two study cohorts: chronic kidney disease but unaware; chronic kidney disease and aware.

Diabetes was defined as self-report, use of medications for diabetes, fasting glucose values ≥126 mg/dL, or non-fasting glucose values ≥200 mg/dL. All other covariates such as race, education, having health insurance, seeing a physician in the last year, smoking and alcohol use, and cancer history were self-reported. Cardiovascular disease was defined by heart angioplasty, heart bypass surgery, heart attack, heart failure, abnormal heart rhythm, stroke, or peripheral vascular disease (peripheral vascular disease information was collected only until May 2005).

Outcomes

Outcome variables included incident renal replacement therapy (dialysis) and all-cause mortality. KEEP obtains informed consent from individual KEEP participants to use social security number, first name, last name, and birth date in potential linkages for future research studies. All-cause mortality data in this study were ascertained by linking the KEEP study cohort to the first quarter 2010 Social Security Administration Death Master File. Data on end stage renal disease were obtained through linking the KEEP study cohort to the United States Renal Data System. All KEEP study participants were followed up through December 31, 2009 for mortality. All participants were followed up through September, 2009 for dialysis outcomes and censored at death date.

Statistical Analysis

Analyses were conducted using SAS v9.2. Patient baseline characteristics were compared between two participant categories: chronic kidney disease but unaware; chronic kidney

disease and aware. Chi-square tests were used for categorical variables and t-test for continuous variables. To compare incidences of end-stage renal disease and mortality, we performed Kaplan-Meier survival analyses for the two endpoints. We performed unadjusted (model 1) and adjusted Cox regression models. Model 2 adjusted for age, gender, race, education, seen a physician in last year, and health insurance. Model 3 adjusted for model 2 covariates plus eGFR and ACR. Model 4 adjusted for model 3 covariates plus the presence of cancer and cardiovascular disease. Analyses were peformed for the whole study cohort, by chronic kidney disease stage, as well as for those with an eGFR>45 ml/min/1.73m^2 and demonstrable albuminuria >30mg/g and <45 ml/min/1.73m^2.

Results

There were 124,277 eligible participants screened from August 2000 to December 2009, with 109,285 participants for the study excluding missing values in chronic kidney disease and chronic kidney disease awareness. Of 109,285 participants, 28,244 (26%) had chronic kidney disease defined by albuminuria or eGFR <60ml/min/1.73m^2. Among those with chronic kidney disease, only 9% (n=2660) reported having kidney disease across all stages; 4.9% in stage 1, 6.4% in stage 2, 9.2% in stage 3, and 43.6% in stages 4–5. Compared to those unaware of their kidney disease status, participants with chronic kidney disease and disease awareness had a lower eGFR (49 vs 62ml/min/1.73m^2) and had a higher prevalence of albuminuria (52 vs 46%), diabetes (47 vs 42%), cardiovascular disease (43 vs 28%), and cancer (23 vs 14%) (Table 1, all comparisons p<0.001). Participants who were aware of their chronic kidney disease also had higher iPTH and trigyclerides than those unaware (all comparisons p<0.001).

In a total of 109,117 participants with available longitudinal follow-up, there were 2991 deaths over a median of 3.3 years. Among 105,131 eligible participants, there were 471 incident cases of end-stage renal disease over a median of 3.2 years. Figure 2 presents results of Kaplan Meier survival analysis for time to renal replacement therapy and death over 8.5 years of follow-up for the entire cohort. Those who were aware had for a greater risk for end-stage renal disease and mortality compared to those unaware (78 vs 81% and 83% vs 97%, respectively) (log rank test, p<0.0001 for all analyses).

Similar to the survival analysis, on unadjusted analysis using Cox proportional hazard regression of persons with chronic kidney disease (Table 2), participants that were aware compared to those unaware were more likely to progress to end-stage and die. After adjusting for socioeconomic variables and family history of kidney disease in model 2, eGFR and ACR in model 3, and the presence of cardiovascular disease and cancer in model 4, the hazard ratios remained statistically significant, but were substantially attenuated for end-stage renal disease after adjustment for eGFR and ACR.

Figure 3 presents the results of survival analysis for time to end-stage and mortality by eGFR >45 ml/min/1.73m^2 with ACR >30 mg/g or <45 ml/min/1.73m^2. In those with an eGFR >45 ml/min/1.73m^2 and ACR >30 mg/g, those who were aware had a higher risk for both ESRD and mortality (98% and 67%) compared to unaware (99% and 85%; log rank test p=0.0296 and p=0.0025, respectively). In those with eGFR <45 ml/min/1.73m^2, those aware had a higher risk for both end-stage and mortality (63% and 67%) compared to unaware (87% and 64%, log rank test p=0.0227 and p=0.0296; respectively), but the separation of the curves was substantially smaller than for those with higher levels of GFR.

Similar to the survival analysis, on unadjusted analysis by an eGFR >45 ml/min/1.73m^2 with an ACR >30mg/g or <45 ml/min/1.73m^2 those aware were more likely to progress to end-stage and die compared to those unaware. After adjusting for socioeconomic variables

and family history of kidney disease, those aware were more likely to progress to end-stage with an eGFR <45 and die in those with an eGFR >45 ml/min/1.73m^2 with an ACR >30mg/g or <45 ml/min/1.73m^2 compared to those unaware. After further adjustment for eGFR and ACR in model 3 and for cardiovascular disease and cancer in model 4, hazard ratios were attenuated in those with an eGFR <45 ml/min/1.73m^2 and remained significant for mortality before adjustment for cardiovascular disease and cancer in model 4 in those with an eGFR >45 ml/min/1.73m^2.

Figure 4 presents the results of survival analysis for time to end-stage and mortality by chronic kidney disease stage 1 through 4. Participants in stages 1–4 and who were aware had a higher risk for progressing to end-stage compared to those unaware (96 vs 99%, 97 vs 99%, 95 vs 97%, and 18 vs 65%, respectively; log rank test, p=0.0041,=0.0224,=0.0001,<0.0001; respectively). Those who were aware had a higher risk for mortality in stages 1 and 3 compared to those who were unaware (86 vs 94% and 79 vs 80%; log rank test p<0.0001 and p=0.0001; respectively). For participants with chronic kidney disease stage 2 there was a trend in years 5 to 8 in those aware compared to unaware (86% and 94%, p=0.5605), which was reversed for participants with stage 4 with an improved trend in those aware in years 4 through 8 (60% vs 51%, p=0.2245).

Similar to the survival analysis, on unadjusted analysis persons that were aware compared to those unaware were more likely to progress to end-stage in stages 1 through 4 and more likely to die in stages 1 and 3 but not 2 and 4. However, after adjusting for socioeconomic variables and family history of kidney disease, those aware were more likely to progress to end-stage in stages 1, 3, and 4 but not 2 and more likely to die in stages 1 and 3 but not 2 and 4. After further adjustment for eGFR and ACR in model 3, those aware were likely to progress to end-stage in stages 1 and 4 but not 2 and 3 and likely to die in stages 1and 3 but not 2 and 4. After further adjustment for cardiovascular disease and cancer in model 4, those aware were likely to progress to end-stage in stages 1 and 4 but not 2 and 3 and likely to die in stages 1 and 3 but not 2 and 4.

Discussion

Our current study shows that chronic kidney disease awareness remains extremely poor despite efforts to raise community awareness. Additionally, this study suggests that awareness of chronic kidney disease does not necessarily translate to improved outcomes. Participants aware of their CKD status at baseline entry into the program demonstrated an increased risk for progression to end-stage and mortality. This increased risk was apparent across the range of eGFR including early stages of kidney disease with relatively preserved GFR. The risk for progression to end-stage and early mortality was attenuated significantly by adjustment for measured socioeconomic and clinical variables, and even more so by adjustments for the presence of cardiovascular disease and cancer, yet still remained significant in certain stages of chronic kidney disease.

Current estimates of awareness in early stages of chronic kidney disease (e.g. eGFR >60 ml/min per 1.73m2) indicate that both patient and provider level awareness remain low in early stages, roughly <5% across studies (7,8,15,18). Similar to previous work from the KEEP and other groups exploring awareness in the general population over time, our data corroborate this low level of awareness (9%) across the entire spectrum of eGFR. Awareness in the KEEP reflects an answer to a question on initial screening: “Have you ever been told by a doctor or healthcare professional you have kidney disease?” In contrast, the National Health and Nutrition Examination Survey (NHANES) determine awareness by the question, “Have you ever been told you have weak or failing kidneys (excluding kidney stones, bladder infections, or incontinence)?” The definitions differ slightly but in several

studies have shown similar rates of awareness (7,8,15,18). However, both studies have not explored the difference between awareness and knowledge of kidney disease.

Recent work suggest that individuals under the care of a nephrologist may not be aware of their chronic kidney disease status (19,20), supporting the notion then that patient-provider interaction may be a real unmeasured variable in assessing true knowledge of their chronic kidney disease status in our study. Additionally, participants unaware at study entry with chronic kidney disease were then made aware by the KEEP screening, suggesting the possibility that risk status is modified and this modification conveys some survival advantage during our observation period. While our study may not capture the difference between awareness and knowledge, which could be a function of health literacy, those aware at study entry represent a significant amount of patient-provider interaction that had to occur prior to screening. Hence, the finding that those aware had a long-term, poorer survival for progression to end-stage and mortality is of significance.

We additionally found that participants who were aware of their chronic kidney disease status at study entry had higher rates of cardiovascular disease, cancer, and diabetes, which likely is responsible for the higher rates of progression to end-stage and mortality compared to those unaware. Thus, provider education and notification of patients about their chronic kidney disease status does seem targeted to patients at the highest risk for adverse kidney disease-related outcomes. However, the variability in our findings following adjustment for measured socioeconomic and clinical risk factors across stages and models for adverse chronic kidney disease outcomes suggest we can not fully account for the differences in risk between the aware and unaware subgroups. This would suggest there exist unmeasured factors such as provider-patient interactions, literacy, and or management variables that influence awareness's impact on outcomes.

Further work suggest that cardiovascular risk factors such as the presence of diabetes and or hypertension are possibly associated with chronic kidney disease awareness, (7,15). However, the presence of either diabetes or hypertension only modestly heighten awareness and it is unclear whether referral to a specialist improves awareness/knowledge as it relates to outcomes (4–7). Our limited understanding from one study suggests that provider recognition based on eGFR reporting may increase nephrology referrals but hard outcomes such as mortality and progression to end-stage were not determined (6). Thereby, our data are the first to support a relationship between awareness status of chronic kidney disease and outcomes.

We show that awareness in participants with chronic kidney disease predicted a higher risk for progression to end-stage renal disease and mortality compared to those unaware, a finding likely confounded by a lower eGFR and higher prevalence of albuminuria, cardiovascular disease and cancer at baseline. The aware participants in KEEP had an eGFR of approximately 49 ml/min/1.73m^2 with a higher level of albuminuria suggesting that the clinical detection system and the necessary provider-patient interactions to create awareness may have already been triggered by unmeasured factors in the KEEP or the presence of more advanced disease with a higher prevalence of cardiovascular disease and cancer.

The finding that higher mortality and incident end-stage renal disease remained significantly different between those aware compared to unaware on adjusted analysis despite controlling for socioeconomic factors, eGFR, and presence of cardiovascular disease and cancer suggests that awareness status may be a function of disease status in and may not denote a cause-effect relationship. After controlling for level of kidney function in our adjusted models in those with early stages of kidney disease (Model 3, Table 2) and then cardiovascular disease and cancer (Model 4, Table 2), awareness remained a significant risk

predictor for both mortality and progression. However, the discrepancy between end-stage renal disease and mortality on the survival analysis in those with early or advanced kidney disease (Figure 3) or by stages (Figure 4) was more pronounced, suggesting patient educated awareness may be targeted to patients at highest risk for chronic kidney disease progression. It is not clear in this analysis why significance was lost in stages 2 and 4 in our mortality analysis and whether this represents an unmeasured factor, is sample size-dependent with the relatively large N in Stage 3 or 4, or is due to our inability to determine cause of mortality.

While there are clear strengths to this study, there are also several limitations. We cannot determine causality or account for changes in chronic kidney disease status or risk factors over time. Our cohort is derived from a group of voluntary, screened participants that may be selected based on unawareness and of which more than 68% were women. We categorized participants according to their self-identified race/ethnicity status into one of five major racial/ethnic categories, however, the groups themselves are heterogeneous and we cannot account for differences in subgroups among them. There could also be an effect of misclassification of early chronic kidney disease as determination was made by a single urine sample and serum Cr determination. Our outcome is mortality and we do not have access to cause specific mortality or other relevant outcomes. Finally, it should be noted we have no data on the severity of co-morbidities and this may have biased provider decisions to reinforce chronic kidney disease awareness in our cohort through unmeasured factors.

With the recognition that prevalent and incident chronic kidney disease are increasing, the primary focus of current practice guidelines is to promote screening and detection of chronic kidney disease in early stages in order that appropriate interventions to prevent progression of kidney disease can be initiated (1,17). Our finding of higher end-stage renal disease and mortality in aware participants with chronic kidney disease highlights that awareness may be influenced by a high level of morbidity (e.g. the presence of cancer and cardiovascular disease as well as a more profound reduction in eGFR) with detection systems already in place. These results should not be interpreted as unawareness conveys a survival advantage, but rather that awareness on its own is not necessarily sufficient to reduce the poor outcomes associated with chronic kidney disease. Due to the observational nature of our current work, future data garnered from our longitudinal program of KEEP activities will help define the effect of informing and educating individuals with chronic kidney disease on risk intervention and overall outcomes.

Acknowledgments

The Kidney Early Evaluation Program (KEEP)™ is a program of the National Kidney Foundation, Inc., and is supported by Amgen, Abbott, Novartis, Siemens, Genentech, Genzyme, Nephroceuticals, Pfizer, LifeScan, and Suplena. The authors would like to thank Monica R. Gannon, KEEP director, for regulatory assistance. Dr Whaley-Connell is supported by the Dept of Veterans Affairs CDA-2, the NIH R03AG040638 and the ASN-ASP Development Grant in Geriatric Nephrology. Dr. Shlipak is supported in part by the American Heart Association Established Investigator Award, and R01 DK 066488 from NIDDK. Dr Inker is support by K23DK081017. Dr. Norris is supported in part by the NIH Grants U54 RR026138 and P20 MD00182.

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Appendix

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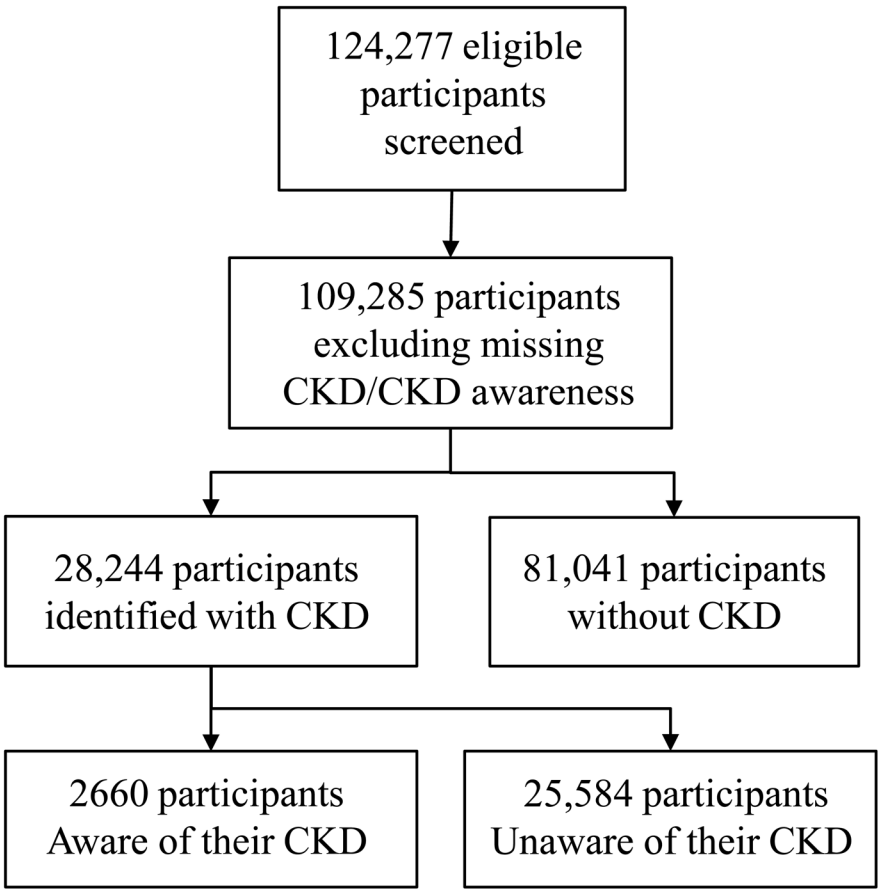

Figure 1.
Description of study population

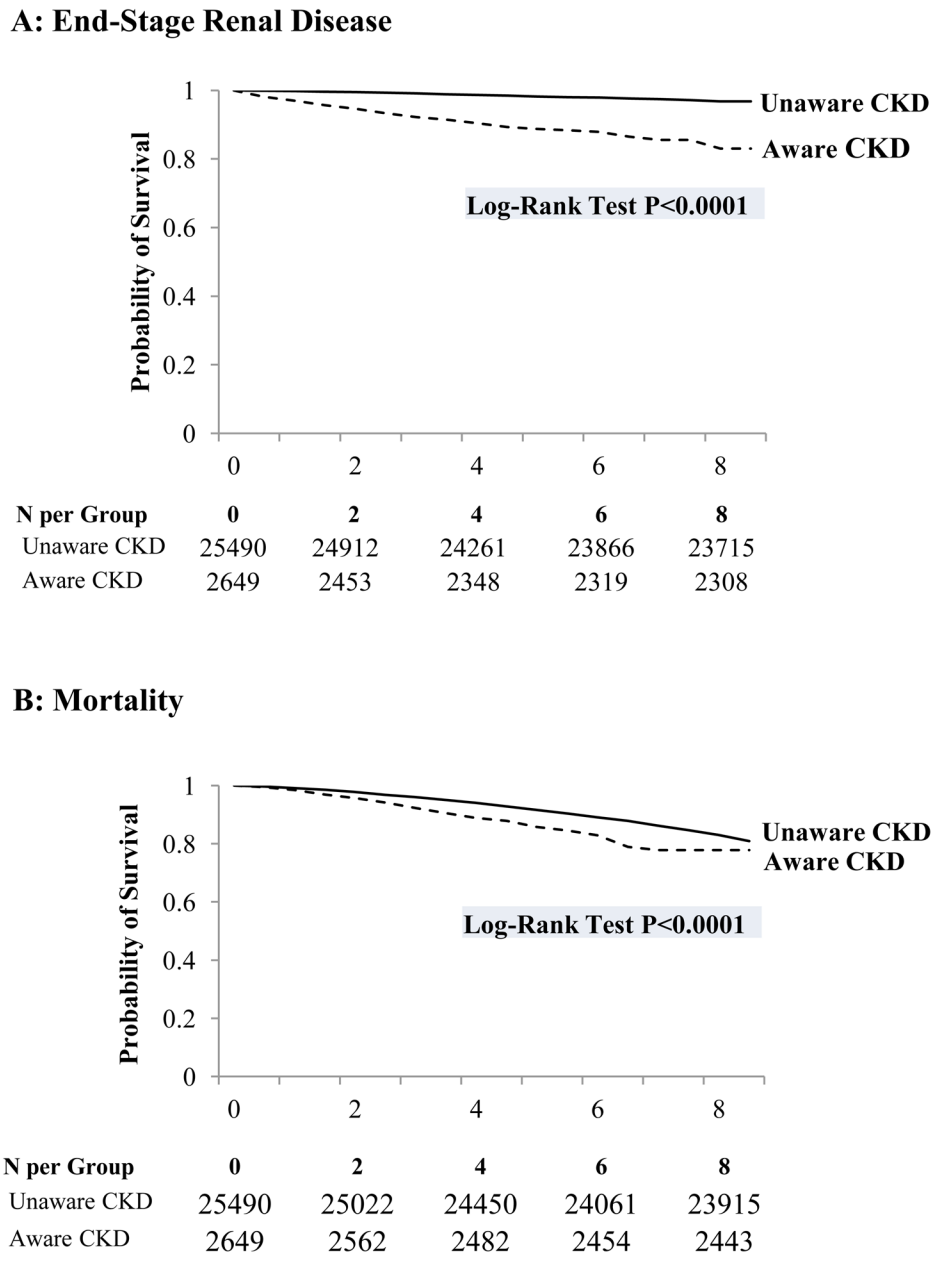

Figure 2.

Kaplan-Meier analysis for end-stage renal disease and mortality by study group. Probability of Survival on 8.5 years of follow up. Log-Rank Test P<0.0001 for interaction between groups

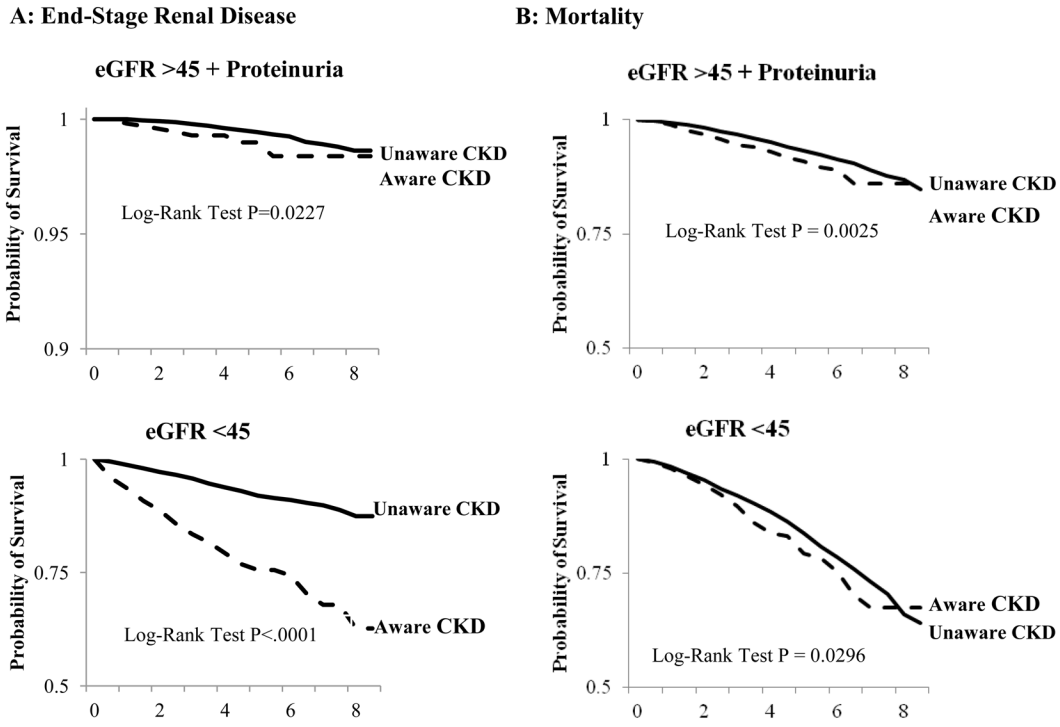

Figure 3.

Kaplan-Meier analysis for end-stage renal disease and mortality by study group and estimated GFR >45 ml/min/1.73m^2 with ACR >30 mg/g or <45 ml/min/1.73m^2

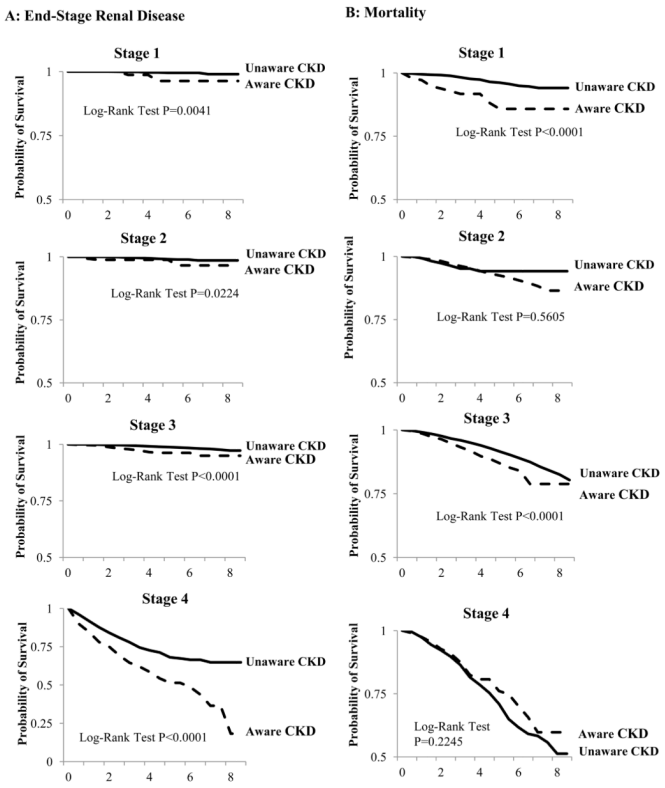

Figure 4.
Kaplan-Meier analysis for end-stage renal disease and mortality by study group and stage of chronic kidney disease.

Table 1

Patient population/demographics

	Unaware N= 25584	Aware N = 2660	P value
Age (mean ± s.d)	62.9 ± 14.6	63.8 ± 14.4	0.0020
Male (%)	30.1%	36.0%	<0.0001
Race (%)			<0.0001
White	56.8%	63.0%	
Black	27.8%	19.1%	
Other	15.4%	17.9%	
Smoker (%)			0.0006
Never	58.0%	54.4%	
Quit	32.8%	36.6%	
Current	9.2%	9.0%	
Alcohol use (%)			0.0327
Never	45.0%	48.0%	
Rare	32.4%	30.5%	
Often	16.6%	15.1%	
Daily	6.0%	6.4%	
High school education (%)	82.3%	80.2%	0.0068
Seen physician in last year (%)	71.4%	63.3%	<0.0001
Health insurance (%)	85.5%	81.2%	<0.0001
Co-morbid conditions			
Diabetes (%)	42.0%	47.4%	<0.0001
Cardiovascular disease (%)	28.4%	42.6%	<0.0001
Cancer (%)	13.9%	22.6%	<0.0001
Autoimmune disease (%)	4.1%	6.9%	<0.0001
Physical examination measurements			
Systolic BP (mmHg) (mean ± sd)	138.1 ± 21.5	138.2 ± 21.5	0.8168
BMI (kg/m^2) (mean ± sd)	30.5 ± 6.9	30.5 ± 7.1	0.5780
Laboratory measurements			
eGFR ($ml/min/1.73m^2$) (mean ± sd)	61.7 ± 22.7	49.3 ± 23.3	<0.0001
Calcium (mg/dl)^ (mean ± sd)	9.65 ± 0.47	9.58 ± 0.52	<0.0001
Phosphorus (mg/dl)^ (mean ± sd)	3.71 ± 0.62	3.77 ± 0.68	0.0018
iPTH (ng/ml)^ (median IQR)	65 (45–96)	79 (49–123)	<0.0001
Cholesterol (mg/dl)^^ (mean ± sd)	196.2 ± 44.6	192.3 ± 47.2	0.0001
Triglycerides (mg/dL)^^ (mean ± sd)	176.1 ± 130.9	184.3 ± 182.3	0.0105

Plus-minus values are means ± SD except for intact parathyroid (iPTH) which is median IQR. BP=blood pressure, BMI=body mass index.

^ for participants with eGFR<60

^^ for participants screened from 2005 to 2009

Table 2

Risk for End-Stage Renal Disease and Mortality in those Aware

A: ESRD	HR (95% CI)		B: Total Mortality	HR (95% CI)	
Model 1 (N=105131)	7.91 (6.54–9.57)	P<0.0001	Model 1 (N=109117)	1.76 (1.52–2.04)	P<0.0001
Model 2 (N=95218)	7.82 (6.37–9.58)	P<0.0001	Model 2 (N=98634)	1.69 (1.45–1.97)	P<0.0001
Model 3 (N=93843)	1.36 (1.07–1.73)	P<0.0123	Model 3 (N=97247)	1.37 (1.15–1.63)	P<0.0003
Model 4 (N=89840)	1.37 (1.07–1.75)	P<0.0123	Model 4 (N=93158)	1.27 (1.07–1.52)	P<0.0077

Unaware as referrant

Model 1 = Unadjusted

Model 2 = Adjusted for age, race, gender, high school education (yes/no), seen physician in last year (yes/no), health insurance (yes/no), and Family history of kidney disease

Model 3 = + estimated GFR and albumin-creatinine ratio

Model 4 = + cardiovascular disease and cancer

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Table 3

Risk for End-Stage Renal Disease and Mortality in those Aware with an eGFR > 45 and ACR >30 mg/dl or eGFR <45

A: eGFR > 45 ml/min/1.73m^2 and ACR >30 mg/dl					
ESRD	**HR (95% CI)**		**Mortality**	**HR (95% CI)**	
Model 1 (N=21884)	2.28 (1.10–4.73)	P<0.0267	Model 1 (N=22699)	1.43 (1.13–1.81)	P<0.0026
Model 2 (N=19487)	1.90 (0.82–4.40)	P=0.1356	Model 2 (N=20188)	1.49 (1.16–1.91)	P<0.0017
Model 3 (N=18483)	1.70 (0.72–4.01)	P=0.2301	Model 3 (N=19183)	1.43 (1.10–1.87)	P<0.0078
Model 4 (N=17647)	1.60 (0.68–3.81)	P=0.2852	Model 4 (N=18330)	1.26 (0.96–1.66)	P=0.0962
B: GFR ≤45 ml/min/1.73m^2					
ESRD	**HR (95% CI)**	**P-value**	**Total Mortality**	**HR (95% CI)**	**P-value**
Model 1 (N=5227)	3.87 (3.15–4.76)	<.0001	Model 1 (N=5440)	1.24 (1.02–1.50)	0.0299
Model 2 (N=4543)	3.22 (2.58–4.02)	<.0001	Model 2 (N=4714)	1.43 (1.16–1.76)	0.0007
Model 3 (N=4172)	1.13 (0.88–1.46)	0.3425	Model 3 (N=4332)	0.94 (0.74–1.19)	0.5889
Model 4 (N=3966)	1.15 (0.89–1.49)	0.2867	Model 4 (N=4122)	0.92 (0.71–1.18)	0.4995

Unaware as referrant

Model 1 = Unadjusted

Model 2 = Adjusted for age, race, gender, high school education (yes/no), seen physician in last year (yes/no), health insurance (yes/no), and Family history of kidney disease.

Model 3 = + estimated GFR and albumin-creatinine ratio (ACR)

Model 4 = + cardiovascular disease and cancer

Am J Med. Author manuscript; available in PMC 2013 July 01.

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Table 4

Risk for End-Stage Renal Disease and Mortality in those Aware by CKD Stage

ESRD	HR (95%CI)	P-value	Mortality	HR (95% CI)	P-value
A: Stage 1					
Model 1 (N=3125)	7.18 (1.49–34.70)	0.0141	Model 1 (N=3213)	3.69 (2.05–6.63)	<.0001
Model 2 (N=2815)	6.72 (1.37–32.98)	0.0189	Model 2 (N=2893)	4.09 (2.17–7.71)	<.0001
Model 3 (N=2815)	6.45 (1.29–32.34)	0.0233	Model 3 (N=2893)	3.98 (2.11–7.51)	<.0001
Model 4 (N=2685)	6.07 (1.21–30.56)	0.0288	Model 4 (N=2762)	3.41 (1.79–6.50)	0.0002
B. Stage 2					
Model 1 (N=5217)	3.22 (1.11–9.32)	0.0309	Model 1 (N=5406)	0.84 (0.47–1.50)	0.5611
Model 2 (N=4651)	2.79 (0.80–9.70)	0.1068	Model 2 (N=4820)	1.08 (0.60–1.95)	0.7865
Model 3 (N=4651)	2.58 (0.74–9.04)	0.1374	Model 3 (N=4820)	1.07 (0.60–1.92)	0.821
Model 4 (N=4456)	2.65 (0.75–9.35)	0.1308	Model 4 (N=4623)	0.87 (0.47–1.61)	0.6587
C: Stage 3					
Model 1 (N=17781)	3.65 (2.45–5.43)	<.0001	Model 1 (N=18487)	1.55 (1.28–1.88)	<.0001
Model 2 (N=15689)	3.12 (2.00–4.88)	<.0001	Model 2 (N=16277)	1.55 (1.26–1.90)	<.0001
Model 3 (N=15689)	1.34 (0.84–2.13)	0.2149	Model 3 (N=16277)	1.35 (1.10–1.66)	0.0048
Model 4 (N=14992)	1.31 (0.82–2.10)	0.2596	Model 4 (N=15562)	1.25 (1.01–1.55)	0.039
D: Stage 4					
Model 1 (N=988)	1.83 (1.44–2.34)	<.0001	Model 1 (N=1033)	0.83 (0.62–1.12)	0.2252
Model 2 (N=875)	1.72 (1.33–2.23)	<.0001	Model 2 (N=912)	0.94 (0.68–1.29)	0.6982
Model 3 (N=875)	1.72 (1.32–2.23)	<.0001	Model 3 (N=912)	0.84 (0.61–1.16)	0.2895
Model 4 (N=843)	1.71 (1.31–2.23)	<.0001	Model 4 (N=880)	0.78 (0.56–1.09)	0.1522

Unaware as referrant

Model 1 = Unadjusted

Model 2 = Adjusted for age, race, gender, high school education (yes/no), seen physician in last year (yes/no), health insurance (yes/no), and Family history of kidney disease.

Model 3 = + estimated GFR and albumin-creatinine ratio

Model 4 = + cardiovascular disease and cancer