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CKD Self-management: Phenotypes and Associations With Clinical Outcomes

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Abstract

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Article Information

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Background—To slow chronic kidney disease (CKD) progression and its complications, patients need to engage in self-management behaviors. The objective of this study was to classify CKD self-management behaviors into phenotypes, and assess the association of these phenotypes with clinical outcomes.

Study Design—Prospective cohort study

Setting & Participants—Adults with mild to moderate CKD enrolled in the Chronic Renal Insufficiency Cohort (CRIC) Study. The 3,939 participants in the CRIC Study recruited between 2003 and 2008 served as the derivation cohort and the 1,560 participants recruited between 2013 and 2015 served as the validation cohort.

Predictors—CKD self-management behavior phenotypes

Outcomes—CKD progression, atherosclerotic events, heart failure events, death from any cause

Measurements—Latent class analysis stratified by diabetes was used to identify CKD self-management phenotypes based on measures of: body mass index, diet, physical activity, blood pressure, smoking status, and hemoglobin A1c (if diabetic); Cox Proportional Hazards models.

Results—Three identified phenotypes varied according to the extent implementation of recommended CKD self-management behaviors: Phenotype I characterized study participants with the most recommended behaviors; Phenotype II, participants with a mixture of recommended and not recommended behaviors; and Phenotype III, participants with minimal recommended behaviors. In multivariable-adjusted models for those with and without diabetes, Phenotype III was strongly associated with CKD progression (HRs of 1.82 and 1.49), death (HRs of 1.95 and 4.14), and atherosclerotic events (HRs of 2.54 and 1.90) (each p-value <0.05). Phenotype II was associated with atherosclerotic events and death among those with diabetes and without diabetes.

Limitations—No consensus definition of CKD self-management; Limited to baseline behavior data

Conclusions—There are potentially three CKD self-management behavior phenotypes that distinguish risk for clinical outcomes. These phenotypes may inform the development of studies and guidelines regarding optimal self-management.

Keywords

chronic renal failure; self-care; self-management; chronic kidney disease (CKD); CKD progression; cardiovascular outcomes; all-cause death; atherosclerotic events; heart failure; healthy behaviors; modifiable risk factors; patient engagement; blood pressure control; smoking; diabetes

Management of chronic kidney disease (CKD) is challenging since it is a disease syndrome for which specific treatments are not known. Consequently, we rely on self-management, which requires patients to engage in behaviors, such as blood pressure monitoring, quitting smoking, and physical activity to reduce the risk of poor CKD outcomes.^{1–7} Self-management behaviors have been incorporated into current CKD guidelines, but little is known about the level of optimal engagement in behaviors among the CKD population.

Despite self-management's integral role in CKD care, there has been limited insight into its level of engagement or effectiveness in non-dialysis-dependent CKD, even though the earlier

stages of CKD are arguably the most critical to limit progression and prevent complications. Limited data exists on the association between self-management behaviors and clinical outcomes (such as end-stage renal disease (ESRD), cardiovascular disease (CVD), and death), and even though self-management behaviors modify CVD risk it is unclear if they slow CKD progression.^{8–15}

Many CKD patients engage only in certain self-management behaviors, and clustering of particular behaviors could disproportionately increase the risk of poor outcomes. Research is needed to identify how behaviors may cluster and explore the impact of self-management behaviors on outcomes. Increasingly, clustering statistical techniques have identified subgroups in complex clinical diseases, including behavioral patterns, to further understand the underlying heterogeneity of diseases.^{16,17} Identifying and analyzing clusters of CKD patients with similar self-management engagement could inform the relationship with important clinical outcomes. The primary goal of this study was to examine the clustering of subgroups of participants of the Chronic Renal Insufficiency Cohort (CRIC) Study by self-management behaviors, and to determine the association of the subgroups with clinical outcomes.

Methods

Data was utilized from the CRIC Study, a multi-center, prospective cohort study of 5,499 participants with CKD in the US.^{18,19} Participants were recruited in two phases: 1) Phase I, from 2003–2008 (3,939 participants), and 2) Phase III, from 2013–2015 (1,560 participants). Participants completed screening and baseline evaluations, and thereafter, annual in-person visits. At six-month intervals, telephone visits were performed. The study protocol was approved by the Institutional Review Boards of all participating centers and is in accordance with the Declaration of Helsinki. All participants provided informed consent. CRIC Study inclusion and exclusion criteria have been elsewhere.^{18,19} In brief, major eligibility criteria for the Phase I Cohort included adults 21–74 years with age-based estimated glomerular filtration rate (eGFR) 20–70 ml/min/1.73m². Entry into the Phase III Cohort required more preserved renal function (eGFR 45–70 ml/min/1.73m²) and older age (45–79 years). Exclusion criteria for both Phases included inability to consent, institutionalization, pregnancy, and certain severe conditions.^{18,19} All Phase I and III participants were included in the current study as they had baseline measures collected as described below.

The selection of self-management behavior measures was guided by previous literature and guidelines.^{4–6,20–22} Measures were collected at baseline. **Body Weight Maintenance:** A body mass index (BMI) served as a proxy of weight maintenance, dichotomized into “recommended” for a BMI of 20 to <25 kg/m², supported by CKD guidelines and the American Heart Association’s recommendations for cardiovascular health,^{20,23,24} and “not recommended” if otherwise. **Dietary Intake:** A diet score ranging from 0 to 4 constructed from the National Cancer Institute’s 12-month Diet History Questionnaire²⁵ based on fruit, vegetable, fish, grains and sweets/sweetened beverage intake.²⁴ A diet score of 3 or 4 was “recommended”, and <2 “not recommended”. **Physical Activity:** Participants reported weekly physical activity²⁶, categorized as “recommended” for moderate activity 150 minutes, vigorous 75 minutes, or moderate plus vigorous 150 minutes²⁴ and “not

recommended” if less. **Tobacco Use:** Past or never tobacco use was “recommended” and current use “not recommended”. **Blood Pressure Management:** A mean blood pressure measurement was a proxy for adherence to anti-hypertensive treatment, with 140/90 mmHg “recommended” and >140/90 mmHg “not recommended”.²³ **Glycemic Control:** Hemoglobin A1c (HbA1c) among those with diabetes was a proxy for blood glucose management, with 7.0% “recommended” and >7.0% “not recommended”.²⁰

Age, gender, race/ethnicity, education, and medical history were collected through self-report and health literacy, depressive symptoms, cognitive function, general health status, and self efficacy (only in Phase III Cohort) assessed through validated measures.^{27–33} Blood samples were used to measure HbA1c, serum fibroblast growth factor 23 (FGF-23), phosphate, creatinine, and cystatin C. A CRIC-specific equation was used to estimate GFR using creatinine and cystatin C.³⁴ A 24-hour urine collection assessed proteinuria. Genotyping was also done and two copies of high-risk alleles defined *APOL1* “high-risk” status.

The following outcomes were evaluated: 1) CKD progression, defined as a 50% decline in eGFR from baseline or incident ESRD (dialysis or kidney transplant)³⁵; 2) atherosclerotic cardiovascular events (myocardial infarction, stroke, or peripheral arterial disease); 3) death from any cause; 4) heart failure events. Cardiovascular events were adjudicated by review of hospital records.¹⁸ Deaths were ascertained from reports by next of kin, death certificates, obituaries, reviews of hospital records, and the Social Security Death Master File. Participants were followed until the occurrence of death, withdrawal from the study, or the end of follow up (mid-2014).

Statistical Analysis

We described the study population using mean and standard deviation, or median and interquartile range for continuous variables and frequency and proportion for categorical variables. The Pearson’s chi-square or Fisher’s exact test and ANOVA or Kruskal-Wallis test were used to compare categorical and continuous variables, respectively.

First, latent class analysis (LCA) was applied to the Phase I Cohort, which served as the derivation population for clusters of self-management engagement. LCA is a well-validated statistical technique that uses mixture modeling to identify unobserved clusters based on variables of interest without mandating consideration of the outcome.³⁶ The LCA was based on self-management behavior measures, stratified by diabetes given the observed differences of CKD progression within the CRIC population. To determine the optimal number of unobserved clusters (or phenotypes), latent class models with successive numbers of phenotypes were compared, and the best-fitting model chosen based on model fit indices (see Item S1). The best-fitting model estimated a predicted probability of membership to each phenotype, with the highest probability determining phenotype, and a probability of engaging in the recommended self-management behavior measure given phenotype. The latter probabilities were used to characterize the CKD self-management behavior phenotypes. Phase III Cohort participants (the validation population) were then assigned CKD self-management behavior phenotypes based on the predicted membership probabilities from the Phase I Cohort. The analytical steps are summarized in the figure in

Item S1. A sensitivity LCA, using only the Phase III Cohort was performed to determine if distinct phenotypes would be identified. To assess the influence of self-management behavior proxies (i.e. BMI, HbA1c, blood pressure), two separate LCAs were performed using only patient responses of behavior measures. First, we included validated self-report measures of tobacco use, physical activity, and diet history. Second, we performed an additional LCA with the inclusion of responses to: “do you currently take prescribed medication for your hypertension or high blood pressure?”, and for those with diabetes, “are you currently taking insulin” and “do you currently take diabetes pills to lower your blood sugar?”. Missing data in the LCA are assumed to be missed at random and are handled using the expectation-maximization (EM) algorithm (see Item S1).

We then investigated the construct validity of the CKD self-management behavior phenotypes by evaluating if clinical and demographic characteristics follow expected patterns across the phenotypes. To evaluate for potential predictors of self-management behavior phenotype membership, we analyzed the association of select variables in univariate multinomial regression models using the entire CRIC Cohort (N=5,499), with Phenotype I as the reference group and reported prevalence ratios (PRs).³⁷

Unadjusted survival curves were constructed using the cumulative incidence function by CKD self-management behavior phenotype and Cox proportional hazards models or cause-specific hazards models (in the presence of competing events) were used to generate crude and adjusted hazard ratios (HRs) using the Phase I Cohort only. Insufficient follow-up time precluded analyses using the Phase III Cohort. For each outcome, hierarchical modeling was performed. The assumptions of proportionality were tested in the fully adjusted model and if violated, the covariates were modified by an interaction with time, and for the CKD self-management phenotypes, HRs were reported in time intervals of hazard. Statistical analyses were conducted using STATA version 14.1, using the LCA Stata Plugin, Version 1.2 and the LCA Bootstrap, Version 1.0.^{38,39}

Results

Clustering of Self-management Behavior Phenotypes

Baseline characteristics of the Phase I and Phase III Cohorts are in Table 1. Three CKD self-management behavior phenotypes were identified (Table S1) and similarly characterized (Figure 1). Phenotype I consisted of clustering of nearly all recommended self-management behaviors, and characterized as the most engaged. Phenotype II clustered on controlled blood pressure, nonsmoking, obesity, poor diet, and physical inactivity, and characterized as moderately engaged. Lastly, Phenotype III clustered on nearly all the behaviors not recommended (smoking, poor diet, physical inactivity, uncontrolled blood pressure), but with a recommended BMI, and characterized as the least engaged. Further details are provided in Table S2. Nearly identical phenotypes were replicated using only the Phase III Cohort (Table S3).

Construct Validity of Phenotypes

Phenotype I was related to factors associated with increased self-management including higher education, adequate health literacy and lower depressive symptoms (Table 2). In contrast, Phenotypes II and III were associated with factors linked with reduced self-management, with Phenotype II to a lesser degree than Phenotype III. The Phase III Cohort replicated a majority of the Phase I Cohort findings (Table S4). Notable differences include the lack of association of the phenotypes with eGFR and proteinuria, which is likely due to the higher baseline values required for inclusion into the Phase III Cohort, which limited their variability. In both Cohorts, Phenotype II was associated with an older age, lower education, non-white race, greater CVD prevalence, lower eGFR, lower cognition, greater depressive symptoms, and lower reported health status, as compared to Phenotype I (Table 3). Phenotype III was associated with similar factors as Phenotype II.

Associations with Clinical Outcomes

During the follow up period, the following outcomes were observed (with reported median follow-up time): 1,284 CKD progression events (5.30 years), 612 atherosclerotic events (6.79 years), 693 heart failure events (6.72 years), and 1,000 deaths (8.45 years).

In general, there was an increased association for poor clinical outcomes for lesser engaged phenotypes (Phenotypes II and III), with generally a stronger association with Phenotype III and those with diabetes (Table 4, Figure 2). Phenotype III was associated with increased CKD progression in those with and without diabetes (HRs of 1.82 [95% CI, 1.32–2.52] and 1.49 [95% CI, 1.06–2.09], respectively). Phenotype II was not associated with CKD progression (Table 4). Using only ESRD as the definition of CKD progression, an increased risk was found among Phenotype III with diabetes but not without diabetes (Table S5).

Phenotype III was associated with an increased risk of death for those with diabetes (HR, 1.95; 95% CI, 1.35–2.81). For those without diabetes, the proportionality of hazards assumption was violated, with the hazard of death appearing to change after three years of follow up. Therefore, the HR is reported from baseline to 3 years, and thereafter. For those without diabetes, Phenotype III was associated with increased death in both time intervals (HRs of 4.14 [95% CI, 2.06–8.33] and 2.14 [95% CI, 1.44–3.19], respectively) and Phenotype II from baseline to three years (HR, 2.80; 95% CI, 1.60–4.89).

Phenotype III was associated with an increased risk of atherosclerotic events for those with and without diabetes (HRs of 2.54 [95% CI, 1.61–3.99] and 1.90 [95% CI, 1.18–3.06], respectively). Phenotype II was associated with atherosclerotic events among those with diabetes (HR, 1.40; 95% CI, 1.04–1.89). There was no statistically significant association with Phenotypes II or III and heart failure events.

In a sensitivity analysis utilizing only validated self-report behavior measures, we continued to find distinct phenotypes and significant associations with clinically important outcomes – namely, an increased risk of death among those with and without diabetes (Table S6–7). In a sensitivity analysis incorporating general questions of medication-taking behavior, we found different phenotypes and significant associations with outcomes, despite very uniform participant responses (Table S8–9).

DISCUSSION

Prior research investigating self-management in kidney disease has primarily focused on the ESRD population.^{40–42} The current study extends on this work to describe self-management among those with earlier stages of kidney disease through identification of self-management phenotypes, as well as to relate the phenotypes to important outcomes. We identified three distinct CKD self-management behavior phenotypes, which in turn distinguish risk for important outcomes in a large cohort of adults with CKD across the United States.

Phenotype I was characterized as the most engaged, Phenotype II as moderately engaged, and Phenotype III as the least engaged across diabetes strata. There was a graded increased risk for poor clinical outcomes for the lesser-engaged phenotypes, and generally a stronger association among those with diabetes than without.

There was good construct validity of the CKD self-management behavior phenotypes with factors known to be associated with chronic disease self-management.^{43–45} Phenotypes II and III were associated with factors related to reduced self-management and Phenotype I with increased self-management. For example, cognitive dysfunction^{46,47} and emotional problems have been shown to compromise self-management^{48,49}, and Phenotypes II and III had lower cognitive function scores and higher depressive symptom scores. Additionally, adequate health literacy has been highlighted as a key determinant of increased self-management engagement.^{45,50} In this study, adequate health literacy was associated with decreased membership to Phenotypes II and III, with a stronger negative relationship with Phenotype III, suggesting it may be protective from membership to the least engaged Phenotype.

There have been a number of studies examining the relationship of individual behaviors with CKD outcomes,^{51–54} but only a couple have assessed the association of the combination of behaviors with CKD outcomes.^{8,9} Muntner et al., found that with increasing numbers of ideal healthy behaviors, there was a trend to reduced all-cause mortality and lower ESRD risk, but the association was completely attenuated by eGFR and albuminuria.⁸ Similarly, Ricardo et al., found an association of a composite of four healthy behaviors with decreased all-cause mortality, but no association with CKD progression or atherosclerotic events.⁹ Therefore, both studies suggest that engaging in more behaviors has a protective effect, and also highlights that a large proportion of CKD participants have low levels of behavior engagement. However, these studies did not assess how engagement in specific behaviors informs the relationship with outcomes.

It is important to address particular behavior engagement as many CKD patients participate only in certain behaviors, and clustering of behaviors could disproportionately increase or decrease the risk of poor CKD outcomes. Consequently, this could impact the prioritization of self-management behaviors in CKD guidelines. In our study, there was a graded increased risk for poor clinical outcomes with clustering of fewer recommended behaviors (i.e., Phenotypes II and III). Phenotypes II and III were similar in that they both clustered poor diets and physical inactivity but differed in that Phenotype II had more obesity and Phenotype III, more smoking and uncontrolled blood pressure. Therefore, it suggests the addition of smoking and uncontrolled blood pressure confers the greater risk to adverse

outcomes, as demonstrated by the increased risk of CKD progression in Phenotype III, and not with Phenotype II.

Importantly, the relationship of the CKD self-management behavior phenotypes to outcomes differed across diabetes strata. In those with diabetes, the lesser-engaged phenotypes had a stronger relationship to CKD progression and atherosclerotic events than those without diabetes, even after adjusting for proteinuria, which suggests that engaging in self-management behaviors could be particularly protective among those with diabetes. Both Phenotypes II and III were associated with increased risk for death among those without diabetes, with attenuation of the risk over time, which is likely due to the lack of sustained effect of the behaviors that may change after baseline. An increased risk of death among those with diabetes was seen only with Phenotype III, which could suggest that with diabetes, the association with death emerges only in those with the fewest recommended behaviors. It is unclear why the phenotypes were not associated with heart failure events, but could be due to misclassification or under-reporting in medical records.

Overall, the results suggest that those who do not participate in recommended behaviors have worse outcomes, and therefore support guideline recommendations. The results also support that certain clustering of behaviors have worse outcomes (i.e. uncontrolled blood pressure and smoking despite a recommended BMI), as seen in Phenotype III. This particular finding supports the paradoxical association of BMI found in other CKD studies^{55–58} and highlights the need for a CKD-specific recommended BMI. This study also highlights that poor engagement in CKD self-management behaviors is highly prevalent. This lack of engagement, along with the high rate of poor outcomes underscores the importance to focus efforts on helping patients self-manage.

Since clustering of behaviors have different relationships to important outcomes, the phenotypes of CKD self-management could be explored as different risk groups for outcomes or disease trajectories. Some factors associated with lesser engaged CKD self-management phenotypes are not modifiable, such as age, gender, and race, but they could be incorporated into the risk assessment of CKD patients. In complement, the more readily modifiable factors associated with self-management, such as education, health literacy, depression, and self-efficacy could be targeted in interventions to increase self-management. Targeting multiple modifiable factors has not had much success in the past, but is gaining favor since it is potentially cost-effective and may have a greater impact than other approaches.^{59,60}

A particular strength of this study is that it provides critical insights into the engagement of self-management in a large cohort of adults with CKD and the relationship to clinical outcomes. The CRIC Study and the wealth of data allowed for assessment of an array of psychosocial, clinical and sociodemographic factors that had not been previously studied in relation to self-management. Better understanding of self-management in this population will provide insights into potential interventions to help individuals optimally manage CKD. The Phenotypes could permit researchers to identify characteristics that distinguish CKD patients most likely to benefit from self-management support and guide the design of much needed support strategies.

There are notable limitations to discuss. A primary limitation is the lack of consensus on defining or measuring CKD self-management behaviors. In light of this limitation, we reviewed the literature and utilized the most cited and agreed upon parameters to define self-management behaviors, including three objective measures to serve as proxies for blood pressure medication adherence, glycemic control, and weight maintenance. We utilized these measures since there has been limited investigation into CKD self-management behaviors and to minimize recall bias of self-report. Unfortunately, the proxies could reflect the influence of the underlying disease process rather than the actual behavior. To address this concern, we performed sensitivity analyses utilizing validated self-report questions, and with the addition of self-report of medication-taking behaviors. The questions regarding medication-taking were not validated questions for this purpose, were very general, and may capture medication prescription rather than medication adherence. The variability in the responses was limited since nearly all participants reported medication-taking. As such, we think the most meaningful sensitivity analysis is that focused solely on the validated self-report measures, which largely support our primary analyses (Table S6).

Furthermore, CKD self-management behaviors and covariates were measured at baseline, which did not permit accounting for time varying confounders or changes in behaviors over time that might influence the relationship with outcomes. However, the goal of this study was to first demonstrate an association of self-management behavior measures at baseline with clinical outcomes, and future studies should address these and related questions with time updated measurements. Health literacy was not measured in all Phase I Cohort participants at baseline, and the lack of this integral factor in all participants is another limitation of the analyses. Moreover, as with any observational study, the presence of residual confounding is another limitation. Importantly, the Phase I and III Cohorts differed in some attributes at baseline. The Phase III Cohort was older with better renal function and more prevalent controlled blood pressure, which could represent selection bias of CKD trajectory and disease severity. However, other important parameters associated with disease progression were similar at baseline, including proteinuria, education, race/ethnicity, and CVD prevalence. The CKD self-management behavior phenotypes also differed at baseline. For example, Phenotypes II and III had a higher CVD prevalence and worse kidney function, which could reflect exposure to different disease processes and behaviors during the pre-study period, which might not be sufficiently accounted for with statistical adjustment. In an attempt to account for these differences, we adjusted for CVD history and kidney function, and stratified analyses by diabetes as those with and without diabetes in the CRIC Cohort have different disease trajectories. Since halving of eGFR is difficult to capture, we performed a sensitivity analysis assessing the outcome of ESRD only and found similar results.

In conclusion, this study conducted in a CKD cohort demonstrates that there are potentially three distinct phenotypes of CKD self-management engagement that vary with demographic, clinical, and psychosocial factors that also significantly associate with clinical outcomes. Given the increasing prevalence of CKD and its associated complications, this research focus is timely and could drive the development of future prospective studies and guidelines regarding appropriate management.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Levey A, Coresh J. Chronic Kidney Disease. *Lancet*. 2012; 379:165–180. [PubMed: 21840587]
2. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis*. 2002; 39(2 suppl 1):S1–266. [PubMed: 11904577]
3. MacGregor M, Taal M. Clinical Practice Guidelines: Detection, Monitoring and Care of Patients with CKD. 52011. 1–71. Available at: <http://www.renal.org/guidelines>
4. National Kidney Foundation. K/DOQI Clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease. *Am J Kidney Dis*. 2004; 43(5 Suppl 1):S1–S290. [PubMed: 15114537]
5. National Kidney Foundation. KDOQI Clinical Practice Guidelines for Diabetes and CKD: 2012 Update. *Am J Kidney Dis*. 2012; 60:850–886. [PubMed: 23067652]
6. National Kidney Foundation. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Diabetes and Chronic Kidney Disease. *Am J Kidney Dis*. 2007; 49(2 supplement 2):S12–S154. [PubMed: 17276798]
7. National Kidney Foundation. Kidney Disease Outcomes Quality Initiative: KDOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease. Secondary National Kidney Foundation Kidney Disease Outcomes Quality Initiative: KDOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease. 2014
8. Muntner P, Judd S, Gao L, et al. Cardiovascular Risk Factors in CKD Associate with Both ESRD and Mortality. *J Am Soc Nephrol*. 2013; 24:1159–1165. [PubMed: 23704285]
9. Ricardo A, Anderson C, Yang W, et al. Healthy Lifestyle and Risk of Kidney Disease Progression, Atherosclerotic Events, and Death in CKD: Findings From the Chronic Renal Insufficiency Cohort (CRIC) Study. *Am J Kidney Dis*. 2015; 65(3):412–424. [PubMed: 25458663]
10. Chagnac A, Weinstein T, Herman M, et al. The effects of weight loss on renal function in patients with severe obesity. *J Am Soc Nephrol*. 2003; 14:1480–1486. [PubMed: 12761248]
11. Morales E, Valero M, Leon M, et al. Beneficial effects of weight loss in overweight patients with chronic proteinuric nephropathies. *Am J Kidney Dis*. 2003; 41:319–327. [PubMed: 12552492]
12. Kriska AM, LaPorte RE, Patrick SL, et al. The association of physical activity and diabetic complications in individuals with insulin-dependent diabetes mellitus: the epidemiology of diabetes complications study-VII. *J Clin Epidemiol*. 1991; 44:1207–1214.
13. Krop JS, Coresh J, Chambless LE, et al. A community-based study of explanatory factors for the excess risk for early renal function decline in Blacks vs Whites with diabetes. The Atherosclerosis Risk in Communities Study. *Arch Intern Med*. 1999; 159:1777–1783. [PubMed: 10448782]

14. He J, Whelton P. Elevated systolic blood pressure and risk of cardiovascular and renal disease. Overview of evidence from observational epidemiological studies and randomized controlled trials. *Am Heart J*. 1999; 138:S211–S219.
15. Stengel B, Tarver-Carr M, Powe N, et al. Lifestyle factors, obesity, and the risk of chronic kidney disease. *Epidemiology*. 2003; 14:479–487. [PubMed: 12843775]
16. Fitzpatrick SL, Coughlin JW, Appel LJ, et al. Application of Latent Class Analysis to Identify Behavioral Patterns of Response to Behavioral Lifestyle Interventions in Overweight and Obese Adults. *Int J Behav Med*. 2015; 22(4):471–480. [PubMed: 25331853]
17. Reilly JP, Bellamy S, Shashaty MG, et al. Heterogeneous Phenotypes of Acute Respiratory Distress Syndrome After Major Trauma. *Ann Am Thorac Soc*. 2014; 11(5):728–736. [PubMed: 24712298]
18. Feldman HI, Appel LJ, Chertow GM, et al. The Chronic Renal Insufficiency Cohort (CRIC) Study: Design and methods. *J Am Soc Nephrol*. 2003; 14(Suppl 2):S148–S153. [PubMed: 12819321]
19. Lash JP, Go AS, Appel LJ, et al. Chronic Renal Insufficiency Cohort (CRIC) Study: baseline characteristics and associations with kidney function. *Clin J Am Soc Nephrol*. 2009; 4:1302–1311. [PubMed: 19541818]
20. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int*. 2013; 3(1)
21. Dunkler D, Kohl M, Teo KK, et al. Population-Attributable Fractions of Modifiable Lifestyle Factors for CKD and Mortality in Individuals with Type 2 Diabetes: A 23 Cohort Study. *Am J Kidney Dis*. 2016; 68(1):29–40. [PubMed: 26830448]
22. Toobert DJ, Hampson SE, REG. The summary of diabetes self-care activities measure: results from 7 studies and a revised scale. *Diabetes Care*. 2000; 23(7):943–950. [PubMed: 10895844]
23. KDIGO Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. *Kidney Int Supplements*. 2012; 2(5):341–342.
24. Lloyd-Jones D, Hong Y, Labarthe D, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's Strategic Impact Goal through 2020 and beyond. *Circulation*. 2010; 121:586–613. [PubMed: 20089546]
25. Diet History Questionnaire vB. MD: National Institutes of Health, Applied Research Program, National Cancer Institute; 2002.
26. Bertoni AG, Whitt-Glover MC, Chung H, et al. The association between physical activity and subclinical atherosclerosis: the Multi-Ethnic Study of Atherosclerosis. *Am J Epidemiol*. 2009; 169:444–454. [PubMed: 19075250]
27. Craven JL, Rodin GM, Littlefield C. The Beck Depression Inventory as a screening device for major depression in renal dialysis patients. *Int J Psychiatry Med*. 1988; 18:365–374. [PubMed: 3235282]
28. Teng EL, Chui HC. The Modified Mini-Mental State (3MS) examination. *J Clin Psychiatry*. 1987; 48(8):314–318. [PubMed: 3611032]
29. Ricardo AC, Hacker E, Lora CM, et al. Validation of the Kidney Disease Quality of Life Short Form 36 (KDQOL-36) US Spanish and English Versions in a Cohort of Hispanics with Chronic Kidney Disease. *Ethn Dis*. 2013; 23(2):202–209. [PubMed: 23530302]
30. Baker DW, Williams MV, Parker RM, Gazmararian JA, Nurss J. Development of a brief test to measure functional health literacy. *Patient Educ Couns*. 1999; 38:33–42. [PubMed: 14528569]
31. Ricardo AC, Yang W, Lora CM, et al. Limited health literacy is associated with low glomerular filtration in the Chronic Renal Insufficiency Cohort (CRIC) study. *Clin Nephrol*. 2014; 81:30–37. [PubMed: 24219913]
32. Maly RC, Frank JC, Marshall GN, DiMatteo MR, DBR. Perceived efficacy in patient-physician interactions (PEPPI): validation of an instrument in older persons. *J Am Geriatr Soc*. 1998; 46:889–894. [PubMed: 9670878]
33. Lorig K, Stewart A, Ritter P, González V, Laurent DJL. Outcome Measures for Health Education and other Health Care Interventions. Thousand Oaks, CA: Sage Publications; 1996.
34. Anderson A, Yang W, Hsu C, et al. Estimating GFR among participants in the Chronic Renal Insufficiency Cohort (CRIC) Study. *Am J Kidney Dis*. 2012; 60:250–261. [PubMed: 22658574]

35. Yang W, Xie D, Anderson AH, et al. Association of Kidney Disease Outcomes with Risk Factors for CKD: findings from the Chronic Renal Insufficiency Cohort (CRIC) Study. *Am J Kidney Dis*. 2014; 63(2):236–243. [PubMed: 24182662]
36. Lanza ST, Bray BC, LMC. An Introduction to Latent Class and Latent Transition Analysis. In: IBW, editor *Handbook of Psychology*. 2. Vol. 2. Hoboken, NJ: John Wiley & Sons, Inc; 2013. 691–716.
37. Behrens T, Taeger D, Wellmann J, UK. Different methods to calculate effect estimates in cross-sectional studies. A comparison between prevalence odds ratio and prevalence ratio. *Methods Inf Med*. 2004; 43:505–509. [PubMed: 15702210]
38. Lanza S, Dziak JJ, Huang L, Wagner AT, LMC. LCA Stata plugin users' guide (Version 1.2). University Park: The Methodology Center, Penn State; 2015. Available from methodology.psu.edu
39. Huang L, Dziak JJ, Wagner AT, STL. LCA Bootstrap Stata function users' guide (Version 1.0). University Park: The Methodology Center, Penn State; 2016. Retrieved from <http://methodology.psu.edu>
40. Bonner A, Havas K, Douglas C, Thepha T, Bennett P, RC. Self-management programmes in stages 1–4 chronic kidney disease: a literature review. *J Ren Care*. 2014; 40(3):194–204. [PubMed: 24628848]
41. Constantini L, Beanlands H, McCay E, Catran D, Hladunewich M, Francis D. The self-management experience of people with mild to moderate chronic kidney disease. *Nephrol Nurs J*. 2008; 35(2):147–155. [PubMed: 18472683]
42. Curtin RB, Mapes D, Schatell D, SB-H. Self-management in patients with end stage renal disease: exploring domains and dimensions. *Nephrol Nurs J*. 2005; 32:389–398. [PubMed: 16180780]
43. Cameron J, Worrall-Carter L, Riegel B, Lo SK, SS. Testing a model of patient characteristics, psychological status, and cognitive function as predictors of self-care in persons with chronic heart failure. *Heart Lung*. 2009; 38(5):410–418. [PubMed: 19755191]
44. Rockwell JM, BR. Predictors of self-care in persons with heart failure. *Heart Lung*. 2001; 30:18–25. [PubMed: 11174364]
45. Disler RT, Gallagher RD, PMD. Factors influencing self-management in chronic obstructive pulmonary disease: an integrative review. *Int J Nurs Stud*. 2012; 49:230–242. [PubMed: 22154095]
46. Harkness K, Heckman GA, Akhtar-Danesh N, Demers C, Gunn E, RSM. Cognitive function and self-care management in older patients with heart failure. *Eur J Cardiovasc Nurs*. 2014; 13(3):277–284. [PubMed: 23733350]
47. Sinclair AJ, Girling AJ, AJB. Cognitive dysfunction in older subjects with diabetes mellitus: impact of diabetes self-management and use of care services. *Diabetes Res Clin Pract*. 2000; 50:203–212. [PubMed: 11106835]
48. Cicutto L, Brooks D, KH. Self-care issues from the perspective of individuals with chronic obstructive pulmonary disease. *Patient Educ Couns*. 2004; 55:168–176. [PubMed: 15530751]
49. Smith K, Coston M, Glock K, et al. Patient perspectives on fluid management in chronic hemodialysis. *J Ren Nutr*. 2010; 20(5):334–341. [PubMed: 19913443]
50. Powell CK, Hill EG, DEC. The relationship between health literacy and diabetes knowledge and readiness to take health actions. *Diabetes Educ*. 2007; 33(1):144–151. [PubMed: 17272800]
51. Hallan SI, SRO. Smoking is a risk factor in the progression of kidney failure. *Kidney Int*. 2011; 80:516–523. [PubMed: 21677635]
52. Haroun MK, Jaar BG, Hoffman SC, Comstock GW, Klag MJ, JC. Risk factors for chronic kidney disease: A prospective study of 23,534 men and women in Washington county, Maryland. *J Am Soc Nephrol*. 2003; 14:2934–2941. [PubMed: 14569104]
53. Beddhu S, Baird BC, Zitteroph J, Neilson J, TG. Physical activity and mortality in chronic kidney disease (NHANES III). *Clin J Am Soc Nephrol*. 2009; 4:1901–1906. [PubMed: 19820134]
54. Shlipak MG, Fried LF, Cushman M, et al. Cardiovascular mortality risk in chronic kidney disease: comparison of traditional and novel risk factors. *JAMA*. 2005; 293:1737–1745. [PubMed: 15827312]
55. Khedr A, Khedr E, House A. Body mass index and the risk of progression of chronic kidney disease. *J Ren Nutr*. 2011; 21:455–461. [PubMed: 21454093]

56. de Boer I, Katz R, Fried L, et al. Obesity and change in estimated GFR among older adults. *Am J Kidney Dis.* 2009; 54:1043–1051. [PubMed: 19782454]
57. Hsu C, McCulloch C, Iribarren C, Darbinian J, Go A. Body mass index and risk for end-stage renal disease. *Ann intern Med.* 2006; 144:21–28. [PubMed: 16389251]
58. Iseki K, Ikemiya Y, Kinjo K, Inoue T, Iseki C, Takishita S. Body mass index and the risk of development of end-stage renal disease in a screened cohort. *Kidney Int.* 2004; 65:1870–1876. [PubMed: 15086929]
59. Goldstein MG, Whitlock EP, JD. Multiple behavioral risk factor interventions in primary care. Summary of research evidence. *Am J Prev Med.* 2004; 27(2 Suppl):61–79. [PubMed: 15275675]
60. Prochaska JJ, Spring B, CRN. Multiple health behavior change research: An introduction and overview. *Prev Med.* 2008; 46(3):181–188. [PubMed: 18319098]
61. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care.* 1992; 30(6):473–483. [PubMed: 1593914]

Figure 1.

Response probabilities of the recommended CKD self-management behavior measures given membership to a particular CKD self-management behavior phenotype, among those with diabetes (top panel), and without diabetes (bottom panel).

Figure 2.

Forest Plot of hazard ratios (HR; 95% confidence intervals) of clinical outcomes by CKD self-management phenotype for those with diabetes (DM) (gray rows) and those without diabetes (ND) (white rows). Reference group is Phenotype I for both DM and ND. *HR is reported from baseline to 3 years, and thereafter since the proportionality of hazards assumption was violated, with the hazard of death appearing to change after three years of follow up.

Table 1

Baseline characteristics of the Derivation and Validation CRIC Populations

	CRIC Phase I Cohort (n=3,939)		CRIC Phase III Cohort (n=1,560)	
Characteristic	With Diabetes (n=1,908)	Without Diabetes (n=2,031)	With Diabetes (n=908)	Without Diabetes (n=652)
Demographics				
Age, year	60 (53–66)	59 (49–65)	65 (59–70)	65 (58–71)
Male Sex	55.8%	54.0%	65.2%	53.2%
Education				
Less than high school	27.4%	15.0%	16.4%	12.6%
High school/some college	48.6%	47.2%	51.1%	42.9%
College graduate	24.0%	37.7%	32.5%	44.6%
Race/Ethnicity				
Non-Hispanic White	34.0%	48.7%	36.1%	47.6%
Non-Hispanic Black	44.4%	39.5%	52.0%	46.0%
Hispanic	17.6%	8.0%	8.5%	4.5%
Other	4%	3.8%	3.4%	2.0%
Clinical Site Location *				
Midwest	53.5%	45.4%	42.3%	39.9%
West Coast	9.6%	18.1%	10.9%	19.5%
South	9.8%	10.8%	18.1%	13.7%
East Coast	27.2%	25.7%	28.7%	27.0%
Clinical Measures				
eGFR, ml/min/1.73m ²	41.1 (14.8)	48.5 (17.9)	57 (12.3)	59.2 (12)
Proteinuria, g/24 h	1.6 (2.9)	0.59 (1.3)	1.2 (2.0)	0.54 (1.2)
Any CVD	42.8%	24.6%	41.4%	25.2%
CKD Self Management Measures				
BMI	33.9 (8.0)	30.3 (7.1)	34.3 (7.1)	31.3 (7.2)
BMI 20 to <25, kg/m ²	9.1%	18.4%	7.0%	14.6%
Non-smoker	88.3%	85.6%	88.6%	88.3%
Systolic BP, mm Hg	133.6 (22.8)	123.7 (20.4)	130.6 (19.8)	124.4 (17.3)
Diastolic BP, mm Hg	69.8 (12.8)	73.2 (12.6)	68.5 (11.7)	71.6 (11.9)
Controlled BP (< 140/90 mm Hg)	63.1%	77.9%	69.4%	80.2%
Diet Score				
0	7.9%	11.2%	12.9%	15.6%
1	26.2%	26.1%	33%	27.5%
2	28.0%	30.4%	26.5%	31.2%
3	27.8%	24.3%	20.4%	20.1%
4	10.1%	8.0%	7.3%	5.6%

	CRIC Phase I Cohort (n=3,939)		CRIC Phase III Cohort (n=1,560)	
Characteristic	With Diabetes (n=1,908)	Without Diabetes (n=2,031)	With Diabetes (n=908)	Without Diabetes (n=652)
Diet Score >2	37.9%	32.3%	27.7%	25.7%
Met Recommended Physical Activity	38.8%	43.0%	40.3%	44.8%
Vigorous/moderate activity, min	282.4 (489.1)	389.1 (619.7)	284.2 (463)	409.4 (692.7)
HbA1c	7.7 (1.7)	n/a	7.6 (1.6)	n/a
HbA1c ≥ 7	41.4%	n/a	44.3%	n/a

Values for continuous data given as median [IQR] or mean $\pm$ SD; values for categorical data given as percentage.

* Clinical site location: Midwest region comprised of participants recruited at sites located in Chicago, IL, Ann Arbor and Detroit, MI, and Cleveland, OH. West Coast region recruited at sites located in San Francisco, CA. South region recruited at a site located in New Orleans, LA. East Coast region recruited from sites located in Philadelphia, PA and Baltimore, MD.

Abbreviations: IQR - interquartile range, SD - standard deviation, eGFR - estimated glomerular filtration rate, CVD - cardiovascular disease, BMI - body mass index, BP- blood pressure, HbA1c - hemoglobin A1c

Clinical and demographic characteristics of latent class-defined phenotypes of CKD Self-management in the CRIC Phase I Cohort

Table 2

	With Diabetes (n=1,908)				p-value*	Without Diabetes (n=2,031)			p-value
	Phenotype I (n=362; 19%)	Phenotype II (n=1,434; 75.2%)	Phenotype III (n=112; 5.9%)			Phenotype I (n=1,033; 50.9%)	Phenotype II (n=825; 40.6%)	Phenotype III (n=173; 8.5%)	
Age, year	57.8 (10.1)	59.4 (9.6)	56.3 (10.8)		0.001	55.7 (12.3)	57.7 (11.5)	55.5 (10.6)	0.001
Male Sex	61.1%	54.7%	52.7%		0.07	57.0%	49.7%	56.7%	0.005
Race/Ethnicity					<0.001				<0.001
Non-Hispanic White	41.7%	32.5%	28.6%			53.5%	46.3%	31.2%	
Non-Hispanic Black	43.1%	44.9%	42.9%			34.9%	40.0%	64.7%	
Hispanic	9.4%	19.4%	20.5%			6.7%	10.7%	2.9%	
Other	5.8%	3.2%	8.0%			4.9%	3.0%	1.2%	
Education					<0.001				<0.001
Less than high school	16.9%	29.2%	38.4%			10.7%	18.8%	23.1%	
High school/some college	47.2%	49.2%	45.5%			41.9%	50.3%	64.7%	
College graduate	35.9%	21.6%	16.1%			47.5%	30.9%	12.1%	
Clinical Measures									
eGFR, ml/min/1.73m ²	45.5 (16.7)	40.2 (14.1)	38.2 (14)		<0.001	52.2 (18.4)	45 (16.3)	42.7 (17.3)	0.001
Proteinuria, g/24 h	1.3 (2.3)	1.6 (3)	2.6 (3.6)		<0.001	0.53 (1.2)	0.61 (1.4)	0.86 (1.6)	<0.001
Any CVD	37.0%	44.1%	43.8%		0.05	21.4%	26.6%	34.7%	<0.001
Adequate Health Literacy	83.7%	75.5%	69.1%		0.01	91.6%	89.3%	77.6%	<0.001
Cognition score	91.5 (9.4)	89.2 (9.8)	87.9 (11.1)		0.001	93.9 (6.6)	91.9 (8.2)	89.9 (9.5)	<0.001
Depressive symptom score	7.0 (7)	9.4 (8.6)	10.6 (7.8)		0.001	5.6 (6.0)	8.4 (8.2)	10.6 (9)	<0.001
Reported Good-Excellent Health Status**	59.5%	44.8%	41.1%		<0.001	80.9%	60.2%	59.2%	<0.001

* p-value: Testing the differences across phenotype values.

** determined using the general health perception question (SF-1) in the short-form health survey (SF-36).⁶¹

Abbreviations: SD- standard deviation, eGFR- estimated glomerular filtration rate; CVD- cardiovascular disease

Potential Predictors of less-engaged CKD self-management behavior Phenotypes among 5,499 CRIC Cohort participants

Table 3

	Phenotype II			Phenotype III		
	With Diabetes (n=2,170)	Without Diabetes (n=1,091)	With Diabetes (n=151)	Without Diabetes (n=217)	PR	95% CI
	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)		
Age (per 1-SD greater)	1.18 (1.07–1.30)	1.13	0.84	0.71–0.99	0.89	0.77–1.02
Education						
Less than high school	1.00 (reference)	1.00	1.00 (reference)	1.00 (reference)	1.00	(reference)
High school/some college	0.66	0.50–0.87	0.67	0.52–0.86	0.45	0.45–0.95
College degree or more	0.44	0.33–0.59	0.35	0.28–0.46	0.20	0.12–0.35
Female sex	1.26	1.03–1.55	1.35	1.15–1.59	1.51	1.05–2.19
Race/Ethnicity						
Non-Hispanic White	1.00 (reference)	1.00	1.00 (reference)	1.00 (reference)	1.00	(reference)
Non-Hispanic Black	1.25	1.01–1.54	1.42	1.19–1.68	1.64	1.07–2.52
Hispanic	2.38	1.66–3.42	1.82	1.34–2.49	3.55	1.97–6.41
Other	0.76	0.47–1.21	0.8	0.51–1.26	1.95	0.87–4.36
Clinical Measures						
Adequate Health Literacy	0.84	0.62–1.12	0.75	0.56–1.01	0.55	0.32–0.95
Cognition score (per 1-SD greater)	0.83	0.74–0.92	0.77	0.71–0.84	0.73	0.61–0.87
Depressive symptom score (per 1-SD greater)	1.40	1.24–1.58	1.49	1.36–1.63	1.58	1.32–1.90
Good-Excellent Reported General Health Status	0.59	0.49–0.73	0.34	0.28–0.41	0.50	0.34–0.72
eGFR (per 1-SD greater)	0.82	0.75–0.91	0.69	0.64–0.75	0.71	0.59–0.85
Proteinuria, (per 1-SD greater)	1.10	0.98–1.24	1.03	0.95–1.13	1.36	1.16–1.59
Any CVD	1.32	1.08–1.61	1.30	1.08–1.56	1.45	1.0–2.09
Clinical Site Location *						
Midwest	1.00 (reference)	1.00	1.00 (reference)	1.00 (reference)	1.00	(reference)
West Coast	0.57	0.42–0.78	0.56	0.45–0.70	0.23	0.10–0.55
South	1.06	0.77–1.48	1.1	0.84–1.43	0.72	0.37–1.37
East Coast	0.71	0.56–0.89	0.87	0.72–1.06	0.85	0.56–1.27
					0.71	0.50–1.01

	Phenotype II			Phenotype III		
	With Diabetes (n=2,170)		Without Diabetes (n=1,091)	With Diabetes (n=151)		Without Diabetes (n=217)
	PR (95% CI)		95% CI	PR	95% CI	PR
	0.66	0.53–0.82	0.67–0.93	0.61	0.42–0.88	0.65
Disease Self-efficacy score (per 1-SD greater)	***					0.49–0.86

Phenotype I (the most engaged in self-management) used as the referent group.

* Clinical site location: Midwest region comprised of participants recruited in Chicago, IL, Ann Arbor and Detroit, MI and Cleveland, OH. West Coast region recruited at sites located in San Francisco, CA. South region recruited at a site in New Orleans, LA. East Coast region recruited from Philadelphia, PA and Baltimore, MD.

*** Assessed only in the Phase III Cohort.

Abbreviations: PR – prevalence ratio, SD- standard deviation, eGFR- estimated glomerular filtration rate; CVD- cardiovascular disease

Table 4

Associations of CKD self-management behavior phenotypes with adverse events among 3,939 CRIC Phase I participants, stratified by diabetes

	With Diabetes		Without Diabetes	
	Model 1	Model 2	Model 1	Model 2
	HR (95%CI)	HR (95%CI)	HR (95%CI)	HR (95%CI)
CKD Progression				
Phenotype II vs. I	1.12 (0.92–1.36)	1.11 (0.91–1.35)	1.02 (0.83–1.26)	1.01 (0.82–1.25)
Phenotype III vs. I	1.91 (1.40–2.62)	1.82 (1.32–2.52)	1.43 (1.02–2.00)	1.49 (1.06–2.09)
Death				
Phenotype II vs. I	1.23 (0.97–1.55)	1.22 (0.97–1.55)	1.43 (1.12–1.82)	<3 y: 2.80 (1.60–4.89) [*] >3 y: 1.11 (0.83–1.47)
Phenotype III vs. I	2.02 (1.41–2.89)	1.95 (1.35–2.81)	2.56 (1.82–3.59)	<3 y: 4.14 (2.06–8.33) >3 y: 2.14 (1.44–3.19)
Atherosclerotic Events				
Phenotype II vs. I	1.38 (1.03–1.85)	1.40 (1.04–1.89)	1.27 (0.92–1.74)	1.15 (0.83–1.60)
Phenotype III vs. I	2.44 (1.56–3.83)	2.54 (1.61–3.99)	2.07 (1.30–3.29)	1.90 (1.18–3.06)
Heart Failure Events				
Phenotype II vs. I	1.07 (0.83–1.38)	1.08 (0.84–1.40)	1.43 (1.04–1.96)	1.35 (0.97–1.86)
Phenotype III vs. I	0.98 (0.62–1.55)	0.90 (0.56–1.45)	1.15 (0.68–1.94)	1.12 (0.66–1.92)

Model 1: age, sex, race/ethnicity +APOL risk, education level, recruitment geographical region + baseline eGFR, 24 hour urine protein, any cardiovascular disease

Model 2: Model 2 + serum FGF23, serum phosphate

^{*} Model 2 for Death: HR reported in 3 year intervals as the hazard changed before and after 3 years.

Abbreviations: HR – hazard ratio, CI, confidence interval