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Advances in CKD Detection and Determination of Prognosis: Executive Summary of the National Kidney Foundation–Kidney Early Evaluation Program (KEEP) 2012 Annual Data Report

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During 2012, the National Kidney Foundation (NKF)–Kidney Early Evaluation Program (KEEP) continued its efforts toward early detection of chronic kidney disease (CKD) in populations at high risk for kidney disease and in improving awareness of CKD across the globe. Through the completely volunteer participation of the nephrology community, including physicians and our allied health care partners, KEEP continues to screen volunteer participants as part of a national effort to detect and track CKD. In 2012, we observed some changes in the CKD landscape, including questions regarding the utility of CKD screening and detection strategies from the US Preventive Services Task Force.[1] Through the years, data derived from KEEP have provided important observations regarding detection and risk-stratification strategies using estimated glomerular filtration rate (eGFR) and proteinuria.[2–4] In this past year, KEEP provided new information on topics including blood pressure control, disorders of mineral metabolism, and awareness of CKD and access to health care as related to CKD outcomes.[5–11] In this supplement to AJKD, we focus on the variable nature of CKD progression. Interest is increasing in exploring factors that influence disease progression beyond traditional measures such as blood pressure and glycemic control, and in determining the contribution of socioeconomic factors.[12;13] We present three articles highlighting factors that influence disease progression in KEEP participants: 1) Chang *et al* describe risk factors for progression to end-stage renal disease (ESRD) among KEEP participants with preserved eGFR at screening, with and without albuminuria[14]; 2) Amin *et*

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al report on whether or not synergism in using eGFR and albuminuria enhances risk prediction for death and disease progression[15]; and 3) Jurkovitz *et al* report on insurance status as a risk factor for disease progression.[16]

Understanding Risk for Progression in Screened Participants With Preserved Estimated GFR

Current knowledge regarding disease progression has been defined by studies that explore factors such as hypertension, diabetes, and ethnicity, primarily among patients with already moderately reduced eGFR. However, there are few data on risk factors that influence progression in populations with preserved eGFR (i.e., > 60 mL/min/1.73 m^2). Available evidence in this rather unique population is limited due to the relatively large sample sizes and long follow-up time needed to accrue ESRD cases. KEEP provides a unique opportunity to explore risk factors for disease progression in a large screened cohort of participants at high risk for early-stage CKD. Chang *et al*[14] stratify participants by presence or not of albuminuria, and demonstrate that black race, diabetes mellitus, lower eGFR, and higher systolic blood pressure are associated with developing ESRD irrespective of albuminuria status (absolute magnitude of risk was higher among participants with albuminuria). Results from this study would suggest that screening for albuminuria in people with ESRD risk factors could aid in prognostication.

Does Use of Estimated GFR and albuminuria Enhance Risk Prediction?

An emerging subset of patients in population-based studies of CKD do not have proteinuria but exhibit progressively declining eGFR. Prior studies using KEEP and NHANES (National Health and Nutrition Examination Survey) data suggest that only a minority of participants experience both reduced eGFR and albuminuria (Figure 1),[17] including participants with diabetes. When considering detection of diabetic kidney disease, presence of proteinuria varies widely relative to eGFR decline and age; thus, KEEP data provide a unique opportunity to explore whether detecting CKD using both proteinuria and eGFR improves risk prediction in diabetic participants. Amin *et al*[15] observe that levels of albuminuria and eGFR may be discordant. In fact, 14% of participants with low eGFR had no albuminuria, while 12% of participants had albuminuria did not have decreased eGFR. Consistent with current knowledge regarding reduced eGFR and presence of albuminuria in CKD, both factors predicted mortality and progression to ESRD. A key novel observation was a highly significant interaction between lower eGFR and greater degree of albuminuria, such that presence of both factors amplified the risk for mortality and progression to ESRD beyond what would be expected by the simple combination of their independent effects. Interestingly, the authors also report that albuminuria was a stronger predictor of mortality and reduced eGFR was a stronger predictor of progression to ESRD. These data suggest that using both eGFR and albuminuria might improve risk prediction for CKD-related outcomes.

Insurance Status and Risk of Death and ESRD

Jurkovitz *et al*[16] explore whether or not health insurance status affects CKD-related outcomes. Studies in the general population suggest that lack of insurance is associated with higher mortality rates, and patients who have insurance are more likely to have controlled blood pressure and diabetes. Uninsured patients with CKD are less likely to receive appropriate risk factor interventions.[18] However, the impact of insurance status in a screened population as it relates to disease progression and mortality is unknown. Jurkovitz *et al* characterize the burden of disease in KEEP participants without insurance and report time to ESRD and mortality in participants with and without insurance. Interestingly, uninsured KEEP participants were 82% more likely to die and 72% more likely to progress to ESRD

than their insured counterparts, a significant finding that remained after clinical adjustments. Considering the morbidity and mortality and increasing costs associated with CKD, ensuring access to appropriate care and insurance coverage for CKD patients would seem essential for optimal outcomes. This study is particularly timely with regard to the controversial issues of health care reform, and the data support the view that expansion of health care coverage to more individuals may, at least in the case of early detection of progressive CKD, promote improved outcomes and reduced costs.

Summary

NKF-KEEP remains the only sustained chronic disease screening, detection, and awareness program in the US. Its success should be attributed to the renal community and to a detection method that places a premium on patient care. Understanding of barriers to care and of factors that influence disease progression in early CKD stages is limited, but crucial to improving CKD-related morbidity and mortality. KEEP provides unique opportunities for the renal community to increase understanding of the role of detection on a large scale as related to variable CKD progression (Figure 2), related complications, and mortality. In 2012, data derived from KEEP continued to provide important information regarding CKD complications such as control of blood pressure and mineral metabolism, and regarding awareness and access issues.[5–11] In this supplement, we report factors that influence disease progression in high-risk participants with preserved eGFR,[14] whether combined use of eGFR and albuminuria enhances risk prediction,[15] and the role of insurance status.[16]

The KEEP steering committee continues to develop novel methods to reach patients and providers, expand understanding of barriers to care, and increase CKD awareness, and general measures to improve disease-related morbidity. We anticipate that future work will also improve the complex interface between disease detection, navigation of the health care system, and CKD-related outcomes. Of greatest importance will be movement toward enhanced scalability of KEEP to achieve even greater reach across the US and in partnership with our international colleagues around the world.

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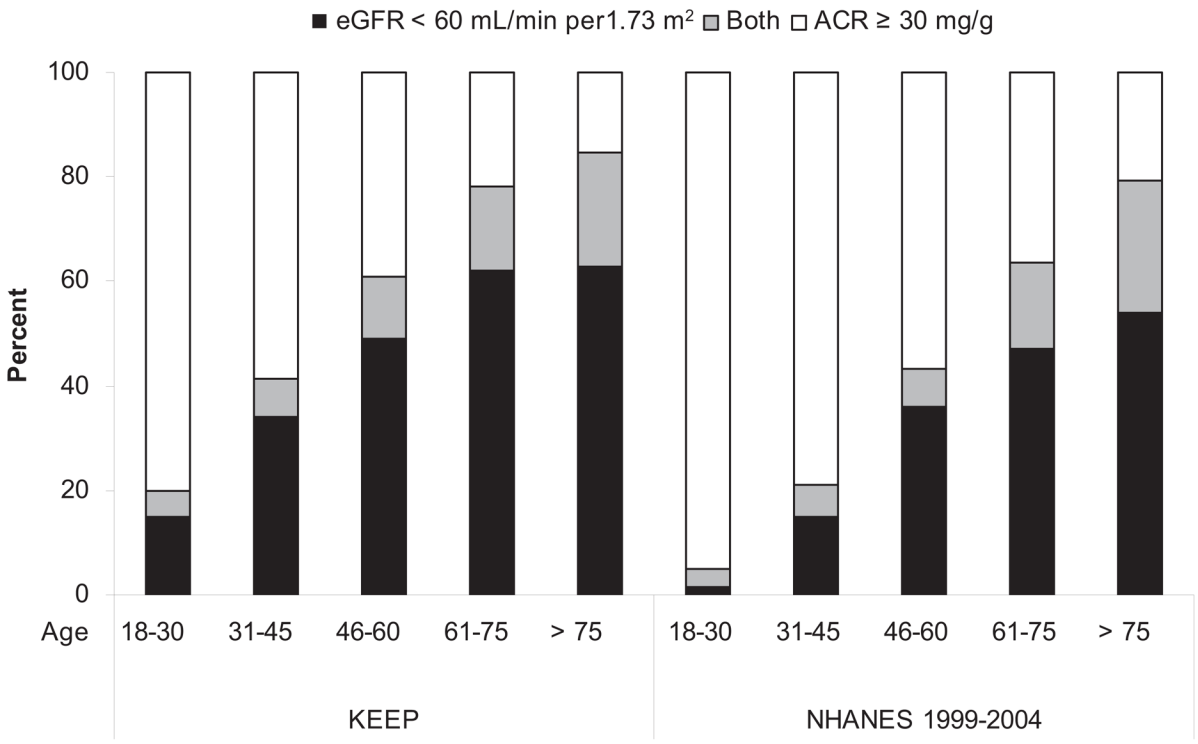

Figure 1.

Detection of CKD as a function of age and measurement of eGFR and urine ACR in the same patients. Relative proportions of ACR ≥ 30 mg/g, eGFR < 60 mL/min/1.73 m^2, and both as positive screening tests for CKD in KEEP and NHANES 1999–2004. $P < 0.001$ for eGFR and ACR trend. ACR, albumin-creatinine ratio; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; KEEP, Kidney Early Evaluation Program; NHANES, National Health and Nutrition Examination Survey. Reproduced from McCullough et al[17] with permission of the National Kidney Foundation.

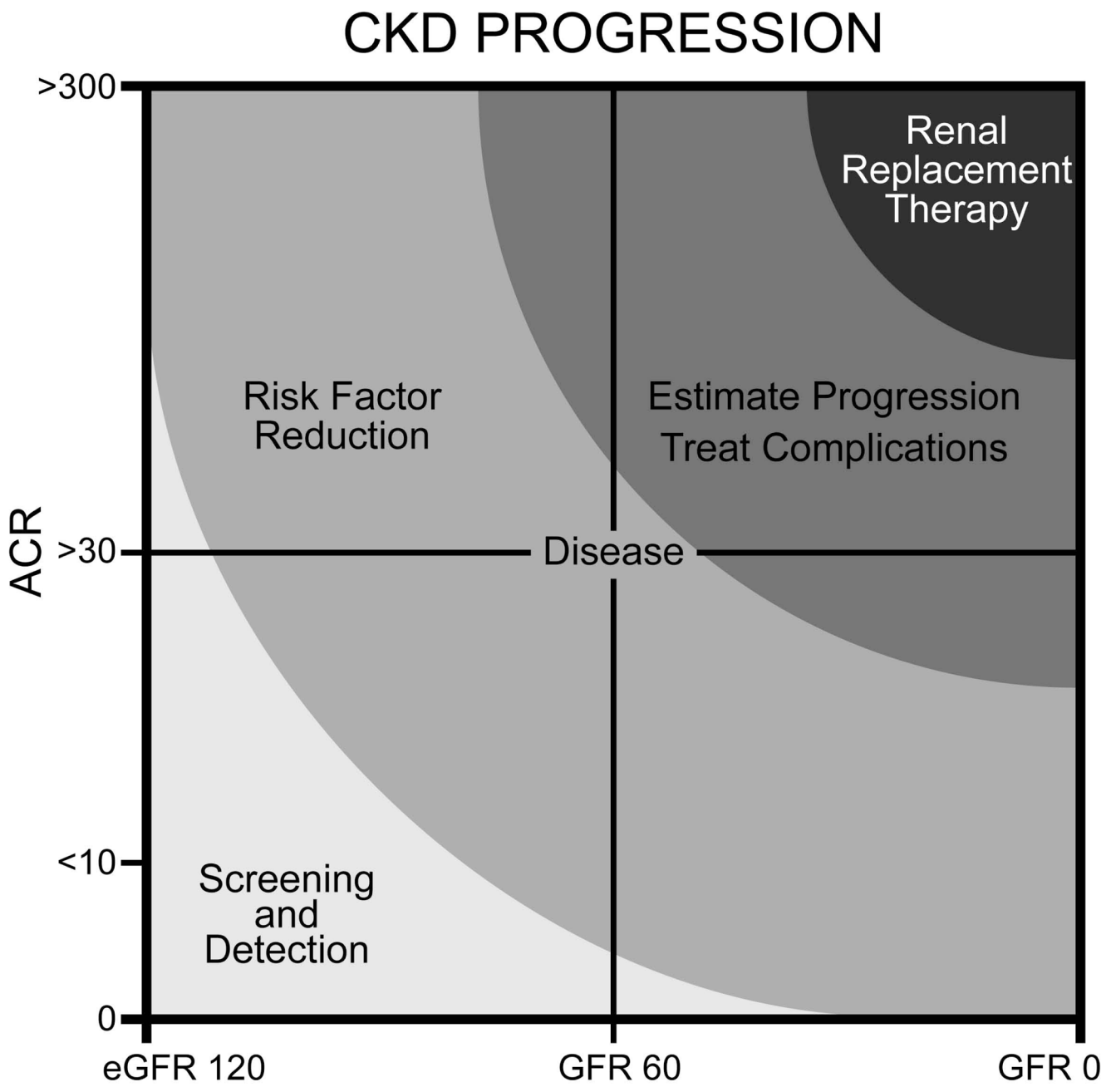

Figure 2.
The role for detection of CKD in earlier stages to allow sufficient time for risk factor reduction to reduce CKD-related complications and progression to renal replacement therapy. CKD, chronic kidney disease.