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## Blood Pressure Components and End-stage Renal Disease in Persons With Chronic Kidney Disease:

### The Kidney Early Evaluation Program (KEEP)

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### Abstract

**Background**—Treatment of hypertension is difficult in chronic kidney disease (CKD), and blood pressure goals remain controversial. The association between each blood pressure component and end-stage renal disease (ESRD) risk is less well known.

**Methods**—We studied associations of systolic and diastolic blood pressure (SBP and DBP, respectively) and pulse pressure (PP) with ESRD risk among 16 129 Kidney Early Evaluation Program (KEEP) participants with an estimated glomerular filtration rate of 60 mL/min/1.73 m<sup>2</sup> using Cox proportional hazards. We estimated the prevalence and characteristics associated with uncontrolled hypertension (SBP ≥ 150 or DBP ≥ 90 mm Hg).

**Results**—The mean (SD) age of participants was 69 (12) years; 25% were black, 6% were Hispanic, and 43% had diabetes mellitus. Over 2.87 years, there were 320 ESRD events. Higher

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**Author Contributions:** Dr Peralta had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Peralta, Norris, Tamura, McCullough, and Shlipak. *Acquisition of data:* Li and Bakris. *Analysis and interpretation of data:* Peralta, Norris, Li, Chang, Jolly, McCullough, and Shlipak. *Drafting of the manuscript:* Peralta, Norris, Li, Bakris, and McCullough. *Critical revision of the manuscript for important intellectual content:* Peralta, Norris, Chang, Tamura, Jolly, McCullough, and Shlipak. *Statistical analysis:* Norris and Li. *Obtained funding:* Peralta. *Administrative, technical, and material support:* Norris, Tamura, McCullough, and Shlipak. *Study supervision:* Bakris and Shlipak.

SBP was associated with higher ESRD risk, starting at SBP of 140 mm Hg or higher. After sex and age adjustment, compared with SBP lower than 130 mm Hg, hazard ratios (HRs) were 1.08 (95% CI, 0.74–1.59) for SBP of 130 to 139 mm Hg, 1.72 (95% CI, 1.21–2.45) for SBP of 140 to 149 mm Hg, and 3.36 (95% CI, 2.51–4.49) for SBP of 150 mm Hg or greater. After full adjustment, HRs for ESRD were 1.27 (95% CI, 0.88–1.83) for SBP of 140 to 149 mm Hg and 1.36 (95% CI, 1.02–1.85) for SBP of 150 mm Hg or higher. Persons with DBP of 90 mm Hg or higher were at higher risk for ESRD compared with persons with DBP of 60 to 74 mm Hg (HR, 1.81; 95% CI, 1.33–2.45). Higher PP was also associated with higher ESRD risk (HR, 1.44 [95% CI, 1.00–2.07] for PP ≥ 80 mm Hg compared with PP < 50 mm Hg). Adjustment for SBP attenuated this association. More than 33% of participants had uncontrolled hypertension (SBP ≥ 150 mm Hg or DBP ≥ 90 mm Hg), mostly due to isolated systolic hypertension (54%).

**Conclusions**—In this large, diverse, community-based sample, we found that high SBP seemed to account for most of the risk of progression to ESRD. This risk started at SBP of 140 mm Hg rather than the currently recommended goal of less than 130 mm Hg, and it was highest among those with SBP of at least 150 mm Hg. Treatment strategies that preferentially lower SBP may be required to improve BP control in CKD.

Treatment of high blood pressure (BP) is one of the foundations of therapy to slow the progression from chronic kidney disease (CKD) to end-stage renal disease (ESRD).<sup>1</sup> A graded association between higher BP levels and ESRD risk has been shown in observational studies of persons with and without CKD.<sup>2,3</sup> Findings from some, but not all, clinical trials of persons with established CKD have suggested that lower BP levels are associated with slower progression of CKD among persons with proteinuria.<sup>4,5</sup> Based on these data, a BP goal of less than 130/80 mm Hg (rather than <140/90 mm Hg) is recommended for persons with CKD.<sup>1</sup> However, the most recent evidence in support of this lower target has been conflicting.<sup>6–8</sup> The association of BP levels and ESRD risk among persons with established CKD has not been well studied in recent large, national, diverse, community-based settings.

Meeting BP targets among persons with CKD remains challenging, despite widespread dissemination of clinical guidelines. National data suggest that less than 45% of persons with CKD meet target BP goals, and adequate control often requires 3 to 4 medications.<sup>9–13</sup> One possibility to explain this difficulty in treating hypertension is the increased stiffness of the arteries seen in persons with CKD.<sup>14</sup> The use of multiple antihypertensive medications in this population may be associated with disproportionately lowering of diastolic BP (DBP), and thus a widening of pulse pressure.<sup>11</sup> Because of reports that higher pulse pressure (PP) and lower DBP<sup>15,16</sup> may be associated with adverse cardiovascular outcomes, clinicians face a dilemma when they attempt to control BP aggressively in patients with CKD. Few studies have investigated the association of each BP component with ESRD risk.<sup>17–19</sup>

Therefore, we designed this study to investigate the independent association of systolic BP (SBP) and DBP with ESRD risk among persons with CKD who participated in the Kidney Early Evaluation Program (KEEP). We also investigated whether calculation of the PP added important information to ESRD risk beyond that of each BP component. Finally, we explored the prevalence and characteristics of persons with CKD and uncontrolled hypertension in KEEP.

## METHODS

### PARTICIPANTS

The KEEP is a health screening program that attempts to raise awareness of CKD in the population. The KEEP targets enrollment of adults older than 18 years who have kidney disease, a history of diabetes mellitus (DM) or hypertension, or a family history of kidney disease, DM, or hypertension. Details on the KEEP database have been previously published.<sup>20</sup> Since August 2000, KEEP has screened more than 165 000 persons in 49 states and the District of Columbia. It was approved by the institutional review board of Hennepin County Medical Center.

For these analyses, we included persons who had established stage 3 CKD, defined as estimated glomerular filtration rate (eGFR) lower than 60 mL/min/1.73 m<sup>2</sup> and who had BP measurements, for a total sample size of 16 129. In KEEP, serum creatinine levels were measured by Satellite Laboratory Services (Redwood City, California) using the Olympus 5431 (Olympus Optical, Tokyo, Japan) and by Consolidated Laboratory Services (Van Nuys, California) using the Abbott Architect c8000 (Abbott Laboratories, Abbott Park, Illinois), and calibrated to the Cleveland Clinic (Cleveland, Ohio). The eGFR was estimated using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation.<sup>21</sup>

### PREDICTORS OF INTEREST

Blood pressure was measured following recommendations from the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure after a period of rest by a trained and certified volunteer. If the SBP was 140 mm Hg or higher or the DBP 90 mm Hg or higher, BP measurement was repeated, and the second measurement was averaged with the first for these analyses. Pulse pressure was calculated as the difference between SBP and DBP. Each of the BP components was used as a continuous linear predictor (per standard deviation [SD]) and categorized. Systolic BP was categorized based on clinically relevant cutpoints (<130, 130–139, 140–149, and ≥150 mm Hg).<sup>22</sup> Diastolic BP was categorized based on clinically relevant cut-points<sup>16,23</sup> and to approximate quartiles as DBP lower than 60, 60 to 74, 75 to 89, and 90 mm Hg or higher.

### OUTCOME

Incident ESRD was ascertained by linkage to the US Renal Data System (USRDS). The USRDS captures more than 90% of patients who undergo incident hemodialysis or kidney transplant. The last ESRD date in this analysis was September 30, 2009. We followed each person from the screening date until development of ESRD or September 30, 2009, or censored at death date.

### COVARIATES

The KEEP used standardized questionnaires to ascertain age, sex, and self-identified race/ethnicity, and smoking history. In this analysis, we categorized participants as a current smoker or not. Participants were also asked to identify their source of insurance (uninsured, or public, private or both) and whether they had health care access defined by the ability to visit a physician in the past 2 years. Diabetes mellitus was defined as a self-report of DM, using medication for DM, or glucose level of at least 126 mg/dL if fasting or at least 200 mg/dL if non-fasting. (To convert glucose to millimoles per liter, multiply by 0.0555.) Cardiovascular disease was self-reported and included history of myocardial infarction, heart angioplasty, bypass surgery, heart failure, abnormal heart rhythm, or stroke. Trained technicians recorded height and weight and body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared). Urine measures of albumin to creatinine ratio (ACR) were obtained using Bayer Healthcare's Clinitek (Bayer Diagnostics,

Tarrytown, New York). This method has been compared with direct measures of urine albumin and creatinine levels with good correlations.<sup>24,25</sup>

## STATISTICAL ANALYSIS

We described participant characteristics by SBP category using analysis of variance or  $\chi^2$  test where appropriate. We first estimated the rate of incident ESRD per 1000 person-years within each SBP, DBP, and PP category. We then studied the association of each BP component with development of ESRD using multivariate Cox models. We modeled each BP component as linear per SD and in categories as described in the previous subsection. For SBP, the referent category was SBP lower than 130 mm Hg because that is the current clinical recommendation. For DBP, the referent category was 60 to 74 mm Hg, based on published risk thresholds<sup>23</sup> and to investigate the potential importance of lower DBP. We used nested models to understand the relative contribution of potential confounders. Model 1 was age and sex adjusted. Model 2 was adjusted for age, sex, race/ethnicity, type of insurance, health care access, current smoking, DM, BMI, albuminuria (defined as an ACR>30 mg/g), baseline eGFR, and history of cardiovascular disease. We tested for interactions of BP with race/ethnicity, DM, and severity of CKD (eGFR<or 45 mL/min/1.73 m<sup>2</sup>) for the ESRD outcome.

We tested for interactions with albuminuria (defined as ACR 30 mg/g) and macroalbuminuria (defined as ACR 300 mg/g) because lower BP treatment goals have been most effective among persons with proteinuria.<sup>26</sup> We also conducted 2 sensitivity analyses: (1) including only persons with eGFR lower than 60 mL/min/1.73 m<sup>2</sup> and an ACR of at least 30 mg/g and (2) including only persons with eGFR lower than 60 mL/min/1.73 m<sup>2</sup> and an ACR of at least 300 mg/g.

In a second set of analyses, we examined the association of PP and incident ESRD. We were specifically interested in whether PP conveyed important information for ESRD risk beyond SBP. We modeled PP both as a linear predictor per SD and in categories based on prior reported risk thresholds and to approximate quartiles (<50, 50–64, 65–79, or 80 mm Hg). We adjusted for covariates as described herein, and built a third model adjusting for all covariates plus SBP.

Finally, after establishing the highest risk category (persons with SBP 150 or DBP 90 mm Hg), we determined the percentage of persons in this group who had isolated systolic or diastolic hypertension or both components elevated. To understand the clinical relevance of these categories, we estimated rates of ESRD per 1000 person-years for each of these groups. We studied characteristics associated with isolated systolic hypertension (SBP 150 and DBP<90) using multivariate logistic regression.

## RESULTS

Among KEEP participants with an eGFR lower than 60 mL/min/1.73 m<sup>2</sup>, the mean (SD) age was 69 (12) years, the mean SBP was 139 (21) mm Hg, and the mean DBP was 77 (12) mm Hg. Overall, 6936 (43%) had DM, and 14 971 (93%) had hypertension. Approximately 25% of participants in this study self-identified as non-Hispanic black, 6% as Hispanic, 4% as non-Hispanic Asian, and 5% as other.

Persons with an SBP level that was at least 150 mm Hg were older, were more likely to have a public source of insurance, were more likely to have DM, albuminuria (both ACR 30–300 mg/g and ACR>300 mg/g), and a lower eGFR at baseline (Table 1).

## BP COMPONENTS AND INCIDENT ESRD

A total of 320 KEEP participants with eGFR lower than 60 mL/min/1.73 m<sup>2</sup> progressed to ESRD over a median follow-up time of 2.87 years. In unadjusted analyses, compared with persons with SBP lower than 130 mm Hg, rates of ESRD (per 1000 person-years) were higher among persons with SBP of 140 to 149 mm Hg and more than double among those with SBP of 150 mm Hg or higher. The ESRD rates among persons with SBP of 130 to 139 mm Hg were similar compared with those with SBP lower than 130 mm Hg (Figure). Compared with persons with DBP of 60 to 74 mm Hg, rates of ESRD were highest among persons with DBP of 90 mm Hg or higher in unadjusted analyses (Figure).

Each SD increase in SBP was associated with a hazard ratio (HR) for ESRD of 1.66 (95% CI 1.51–1.82) in age- and sex-adjusted models, and an HR of 1.23 (95% CI, 1.11–1.36) after full adjustment. The pattern of stepwise increase in ESRD risk starting at SBP higher than 140 mm Hg was also seen after sex and age adjustment (Table 2). After adjustment for all other sociodemographic variables and comorbidities, only persons with SBP of 150 mm Hg or higher remained at statistically significantly higher risk for ESRD compared with persons with SBP lower than 130 mm Hg (Table 2).

Each SD increase in DBP was associated with an HR for ESRD of 1.24 (95% CI, 1.11–1.38) after adjustment. Only persons with a DBP of 90 mm Hg or higher remained at significantly higher risk of ESRD compared with persons with DBP of 60 to 74 mm Hg (Table 2).

Tests of interactions by race, DM, and severity of CKD (eGFR < 45 mL/min/1.73 m<sup>2</sup>) showed no significant effect modification of the association of SBP and incident ESRD by these variables ( $P > .10$  for all comparisons). Tests of interaction by ACR of 30 mg/g or higher and ACR of 300 mg/g or higher were not statistically significant ( $P = .39$  and  $P = .83$ , respectively).

## SENSITIVITY ANALYSIS OF BP COMPONENTS AND ESRD AMONG PERSONS WITH ALBUMINURIA AND MACROALBUMINURIA

Among 3204 persons with eGFR lower than 60 mL/min/1.73 m<sup>2</sup> and albuminuria (ACR ≥ 30 mg/g), there were 281 ESRD events. Results were similar to those of the main analyses. In fully adjusted models, persons with SBP of 140 to 149 mm Hg and SBP of 150 mm Hg or higher had higher risk of ESRD (HR, 1.39 [95% CI, 0.94–2.06] and HR, 1.44 [95% CI, 1.03–2.01], respectively) compared with those with SBP lower than 130 mm Hg. The HR for SBP of 130 to 139 mm Hg was 0.63 (95% CI, 0.41–0.99). Results were also similar to those for DBP, in which only persons with DBP of 90 mm Hg or higher had significantly higher risk for ESRD (HR, 2.06 [95% CI, 1.49–2.86]), compared with persons with DBP of 60 to 74 mm Hg. The HRs for DBP lower than 60 mm Hg and DBP of 75 to 89 mm Hg, respectively, were 1.38 (95% CI, 0.78–2.47) and 0.98 (95% CI, 0.73–1.34).

Findings did not materially differ when limited to persons with eGFR lower than 60 mL/min/1.73 m<sup>2</sup> and macroalbuminuria (ACR ≥ 300 mg/g) (n=689). In fully adjusted models, the HRs for ESRD were 0.87 (95% CI, 0.45–1.69) for persons with SBP of 130 to 139 mm Hg, 1.71 (95% CI, 0.96–3.03) for those with SBP of 140 to 149 mm Hg, and 2.00 (95% CI, 1.21–3.30) for those with SBP of 150 mm Hg or higher, compared with those with SBP lower than 130 mm Hg.

## PP AND INCIDENT ESRD

Among KEEP participants with CKD, the mean (SD) PP was 62 (18) mm Hg. Over 16% (2166) had a PP of 80 mm Hg or higher. In unadjusted analyses, the proportion of persons whose disease progressed to ESRD was highest among persons with a PP of 80 mm Hg or



higher compared with those with a PP lower than 50 mm Hg (Figure). In age- and sex-adjusted models, each SD increase in PP (18 mm Hg) was associated with an HR of 1.71 (95% CI, 1.55–1.89) for ESRD. Adjustment for co-morbidities attenuated this association to an HR of 1.12 (95% CI, 1.01–1.24). Only persons with a PP of 80 mm Hg or higher were at increased risk for ESRD after adjustment for age, sex, race/ethnicity, insurance status, health care access, current smoking, DM, BMI, eGFR, albuminuria, and history of cardiovascular disease (Table 3). To understand whether PP conveys important information on ESRD risk beyond SBP, we adjusted for SBP. The association of PP and ESRD risk was attenuated to non-significance after adjustment for SBP (Table 3).

Most of the high PP in KEEP was related to high SBP. Among 2666 persons with the highest PP ( $\geq 80$  mm Hg), only 69 persons (3%) had SBP lower than 140 mm Hg, 284 (13%) had SBP of 140 to 149 mm Hg, and 2313 (87%) had SBP of 150 mm Hg or higher.

### CHARACTERISTICS AND ESRD RISK AMONG PERSONS WITH UNCONTROLLED HYPERTENSION

More than 48% of persons in KEEP had SBP of 140 mm Hg or higher or DBP of 90 mm Hg or higher. In addition, more than 33% (5383) had SBP of 150 mm Hg or higher or DBP of 90 mm Hg or higher. Among persons with SBP of 150 mm Hg or higher or DBP of 90 mm Hg or higher, most of these persons (83%) could be identified by their high SBP. Over half of these persons (2908 [54%]) had isolated high SBP (SBP  $\geq 150$  mm Hg, but DBP  $< 90$  mm Hg), and another 29% (1555) had SBP of 150 mm Hg or higher and DBP of 90 mm Hg or higher. Only 17% (920) had isolated diastolic hypertension (SBP  $< 150$  mm Hg and DBP  $\geq 90$  mm Hg). Persons with *both* SBP of 150 mm Hg or higher and DBP of 90 mm Hg or higher had the highest rates of ESRD (18.3 per 1000 person-years), followed by persons with isolated systolic hypertension (SBP  $\geq 150$  mm Hg but DBP  $< 90$  mm Hg), 10.9 per 1000 person-years. Persons with isolated diastolic hypertension (SBP  $< 140$  mm Hg but DBP  $\geq 90$  mm Hg) had risks comparable with those of the rest of the KEEP cohort (7.3 per 1000 person-years). Persons with isolated SBP (SBP  $\geq 150$  mm Hg and DBP  $< 90$  mm Hg) were more likely to be older, non-Hispanic black, and have DM and albuminuria (Table 4).

### COMMENT

In these analyses, we found that higher SBP was independently associated with higher ESRD risk among persons with established CKD. This increased risk was observed at SBP higher than 140 mm Hg, but SBP of 150 mm Hg or higher conferred the highest risk compared with persons with SBP lower than 130 mm Hg. Persons with DBP of 90 mm Hg or higher were also at higher risk for ESRD. After accounting for SBP, PP was not independently associated with ESRD risk. Moreover, we found that over one-third of KEEP participants had uncontrolled BP levels in the highest risk group (those with SBP  $\geq 150$  mm Hg or DBP  $\geq 90$  mm Hg), and most of these persons had isolated systolic hypertension.

Our finding that SBP of 140 mm Hg or higher and DBP of 90 mm Hg or higher, rather than the lower level of 130/80 mm Hg, was associated with increased risk of incident ESRD has important implications. Recent long-term follow-up from the AASK trial did not find significant attenuation of mortality or kidney disease progression among persons in the lower BP group, although there was a reduction in risk in the subgroup with an ACR of 300 mg/g or higher.<sup>6</sup> Data from the Modification of Diet in Renal Disease Study suggest improved renal survival in the lower BP group, but only for persons with proteinuria.<sup>7</sup> The association of a higher SBP level with ESRD risk starting at SBP higher than 140 mm Hg was recently reported in a single-center study of veterans.<sup>18</sup> Our findings in a large, community-based, diverse cohort of persons with CKD suggests that a BP goal that is lower

than 140/90 mm Hg, rather than the more aggressive target of lower than 130/80 mm Hg, may suffice for renal protection among persons with established CKD.

A more attainable BP goal among persons with CKD may ease some of the challenges faced by clinicians. First, target goals are difficult to achieve. Data from the National Health and Nutrition Survey show that a goal BP lower than 130/80 mm Hg is attained in less than 45% of persons with CKD.<sup>9</sup> Second, persons with CKD require 3 or 4 medicines, on average, to attain control,<sup>11,12</sup> and the appropriate combination therapy strategies remain controversial. Moreover, lower BP targets may be associated with increased number of adverse events.<sup>8</sup> Our findings, coupled with prior clinical trial data<sup>17,27</sup> that SBP, in particular, is associated with increased ESRD risk, suggest that education strategies on BP control should focus on lowering SBP.

The importance of SBP is also highlighted in our finding that wider PP was associated with higher ESRD risk, but that this association was primarily explained by high SBP. Although our findings suggest that, in the community, measuring of PP does not confer additional information to that provided by SBP, it does shed light on possible mechanisms to explain the remarkably high prevalence of uncontrolled hypertension in this cohort. Wide PP is a marker of arterial stiffness and is associated with increased risk of adverse outcomes.<sup>28</sup> In KEEP, most of the wide PP was a result of high SBP rather than low DBP. Moreover, older age, African American race, and the presence of albuminuria and DM were the most important predictors of uncontrolled isolated systolic hypertension. We have previously reported that use of more than 3 antihypertensive agents in persons with CKD is associated with lowering of the DBP more than SBP.<sup>11</sup> Together, these data suggest that further research is necessary to identify agents that lower arterial stiffness and that preferentially lower SBP to improve BP control among the highest-risk persons with CKD.

To our knowledge, our study comprises the largest national diverse CKD screening program in the United States. Our findings in a community-based sample add to recent clinical trial data in which the environment and selection may not be representative of the population at large. However, our study has important limitations. First, we rely on a 1-time BP measurement. However, 1-time BP measurements taken by trained personnel have been shown to correlate with average BP levels, which is an important predictor of adverse outcomes.<sup>29</sup> While personnel are certified and trained on obtaining BP measurements, we are unable to have 1 KEEP standard instrument for BP measurement. Our study does not include data on the use of inhibitors of the renin-angiotensin system or other classes of antihypertensive medications that may be important confounders of the reported associations. Moreover, our follow-up time is limited, and thus we are unable to investigate long-term associations of BP and ESRD risk. Given the observational nature of our study, residual confounding may be present. Finally, we did not study the association between BP components and risk for mortality or cardiovascular events. It is possible that lower BP targets reduce these risks even if they do not reduce the risk for ESRD.

In summary, we found that higher SBP and DBP was associated with increasing ESRD risk, and this risk is observed starting at an achieved SBP higher than 140 mm Hg and DBP higher than 90 mm Hg. Higher PP was also associated with higher ESRD risk, and this association was attenuated when accounting for SBP. Most interestingly, the prevalence of uncontrolled hypertension is very high among persons with CKD, and this is largely explained by isolated systolic hypertension. Future strategies, including new agents that reduce arterial stiffness, should be studied to control BP and assess clinical outcomes among persons with CKD. Our data suggest that a goal of BP lower than 140/90 mm Hg may be associated with renoprotection among persons with CKD. Whether lower targets may be beneficial for persons with proteinuria requires further study.

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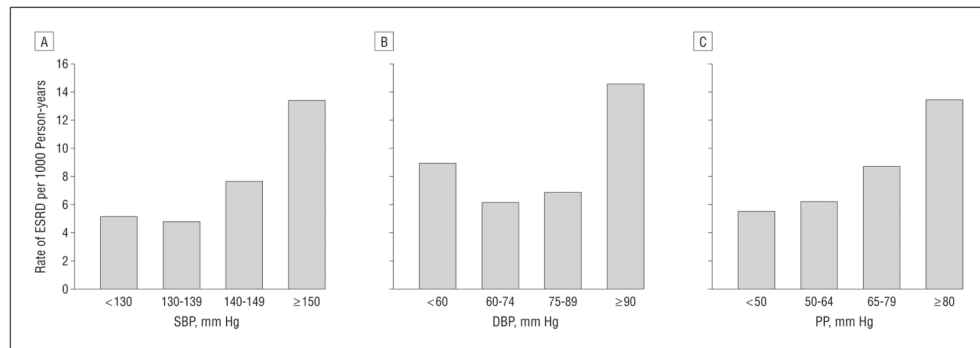
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**Figure.**  
Rates of end-stage renal disease per 1000 person-years. Rates according to systolic blood pressure (SBP) (A); diastolic blood pressure (DBP) (B); and pulse pressure (PP) levels (C).

**Table 1**  
 Characteristics of KEEP Participants With Chronic Kidney Disease by Systolic Blood Pressure (SBP) Level<sup>a</sup>

Characteristic	SBP Level				P Value
	<130 (n = 5266)	130–139 (n = 3421)	140–149 (n = 2956)	150 (n = 4486)	
Age, mean (SD), y	67 (13)	70 (11)	70 (11)	71 (11)	<.001
Sex					
Male	1645 (31)	1140 (33)	990 (32)	1407 (31)	.16
Female	3621 (69)	2281 (67)	1996 (68)	3079 (69)	
Race/ethnicity					
Non-Hispanic white	3318 (63)	2102 (61)	1770 (60)	2575 (57)	<.001
Non-Hispanic black	1118 (21)	804 (24)	787 (27)	1331 (30)	
Non-Hispanic Asian	224 (4)	136 (4)	101 (3)	130 (3)	
Non-Hispanic other	289 (5)	169 (5)	140 (5)	178 (4)	
Hispanic	317 (6)	210 (6)	158 (5)	272 (6)	
Family history of kidney disease	848 (17)	568 (17)	487 (17)	740 (17)	.90
Sources of insurance					
Public only	2363 (45)	1631 (48)	1438 (49)	2320 (52)	<.001
Private only	956 (18)	539 (16)	448 (15)	541 (12)	
Both public and private	685 (13)	486 (14)	426 (15)	636 (14)	
Uninsured	1212 (23)	738 (22)	616 (21)	951 (21)	
Had access to physician in past 2 y	5114 (98)	3315 (98)	2876 (99)	4349 (98)	.78
Smoking					
Current	387 (8)	182 (6)	171 (6)	203 (5)	<.001
Past or current	2186 (44)	1369 (42)	1159 (42)	1757 (42)	.18
Diabetes mellitus	2146 (41)	1453 (42)	1276 (43)	2061 (46)	<.001
Cardiovascular disease	1998 (38)	1281 (37)	1038 (35)	1712 (38)	.04
BMI, mean (SD)	29.4 (6)	30.1 (6)	30.3 (7)	30.3 (6)	<.001
eGFR, mean (SD)	48.2 (10)	48.1 (10)	47.8 (10)	46.8 (11)	<.001

Characteristic	SBP Level				P Value
	<130 (n = 5266)	130–139 (n = 3421)	140–149 (n = 2956)	150 (n = 4486)	
ACR, mg/g					
<30	4087 (83)	2573 (81)	2074 (77)	2617 (65)	<.001
30–300	716 (14)	515 (16)	507 (19)	1087 (27)	
>300	130 (3)	105 (3)	127 (5)	327 (8)	

Abbreviations: ACR, albumin-to-creatinine ratio; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); eGFR, estimated glomerular filtration rate.  
<sup>a</sup>Data are given as number (percentage) of patients except where noted.

**Table 2**

Association of Each Blood Pressure (BP) Component With Incident ESRD Among KEEP Participants With Chronic Kidney Disease

BP, mm Hg	Patients, No.	Age- and Sex-Adjusted HR (95% CI)	Adjusted <sup>a</sup> HR (95% CI)
Systolic			
<130	4556	1 [Reference]	1 [Reference]
130–139	2932	1.08 (0.74–1.59)	0.71 (0.48–1.05)
140–149	2481	1.72 (1.21–2.45)	1.27 (0.88–1.83)
150	3685	3.36 (2.51–4.49)	1.36 (1.02–1.85)
Diastolic			
<60	692	1.40 (0.81–2.41)	1.12 (0.65–1.95)
60–74	5207	1 [Reference]	1 [Reference]
75–89	5716	0.90 (0.69–1.17)	0.91 (0.69–1.19)
90	2039	1.67 (1.25–2.23)	1.81 (1.33–2.45)

Abbreviations: ESRD, end-stage renal disease; HR, hazard ratio; KEEP, Kidney Early Evaluation Program.

<sup>a</sup>Adjusted for age, sex, race/ethnicity, insurance, access to a physician, current smoking, diabetes mellitus, body mass index, baseline estimated glomerular filtration rate, albuminuria, and prevalent cardiovascular disease.



**Table 3**

The Association of Pulse Pressure (PP) With Incident ESRD Among KEEP Participants With Chronic Kidney Disease

PP, mm Hg	Patients, No.	Age- and Sex-Adjusted HR (95% CI)	Adjusted <sup>a</sup> HR (95% CI)	SBP-Adjusted <sup>b</sup> HR (95% CI)
<50	3458	1 [Reference]	1 [Reference]	1 [Reference]
50–64	4973	1.39 (1.00–1.93)	0.95 (0.67–1.33)	0.79 (0.55–1.13)
65–79	3357	2.26 (1.58–3.23)	1.03 (0.71–1.48)	0.71 (0.45–1.10)
80	2166	4.80 (3.40–6.80)	1.44 (1.00–2.07)	0.76 (0.44–1.32)

Abbreviations: ESRD, end-stage renal disease; HR, hazard ratio; KEEP, Kidney Early Evaluation Program; SBP, systolic blood pressure.

<sup>a</sup> Adjusted for age, sex, race/ethnicity, insurance, access to physician, current smoking, diabetes mellitus, body mass index, baseline estimated glomerular filtration rate, albuminuria, and prevalent cardiovascular disease.

<sup>b</sup> Further adjusted for SBP.

**Table 4**

Characteristics Associated With Isolated Systolic Hypertension Among KEEP Participants With Chronic Kidney Disease<sup>a</sup>

Characteristic	OR (95% CI)
Age, y	
<60	1 [Reference]
60–75	2.24 (1.91–2.63)
>75	3.69 (3.13–4.37)
Sex	
Male	0.81 (0.74–0.90)
Race/ethnicity	
White	1 [Reference]
African American	1.13 (1.02–1.26)
Asian	0.76 (0.58–0.99)
Hispanic	1.12 (0.92–1.36)
Other	0.87 (0.69–1.09)
Diabetes mellitus	1.31 (1.19–1.43)
ACR > 30 mg/g	1.72 (1.56–1.90)
Insurance status	
Both private and public	1 [Reference]
Private only	0.74 (0.64–0.87)
Public only	0.97 (0.86–1.10)
Neither	0.92 (0.80–1.04)
Saw physician in last 2 y	1.07 (0.70–1.64)

Abbreviations: ACR, albumin-to-creatinine ratio; OR, odds ratio.

<sup>a</sup>Systolic blood pressure 150 mm Hg or higher and diastolic blood pressure lower than 90 mm Hg.