

Hypertension and CKD: Kidney Early Evaluation Program (KEEP) and National Health and Nutrition Examination Survey (NHANES), 1999-2004

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Background: The prevalence and incidence of hypertension are increasing, and they correlate with the chronic kidney disease rate in the United States. Early identification and achievement of blood pressure goals may improve chronic kidney disease outcomes.

Methods: In this cross-sectional study, subjects were participants in the Kidney Early Evaluation Program (KEEP), a voluntary community-based health-screening program enrolling individuals 18 years and older with diabetes, hypertension, or family history of kidney disease, diabetes, or hypertension, administered by the National Kidney Foundation; and the National Health and Nutrition Examination Survey (NHANES), administered by the National Center for Health Statistics. All studied individuals in both databases were US residents aged 18 years or older. We evaluated multiple variables for participants in KEEP 2000-2006 and participants in NHANES 1999-2004 in this logistic analysis.

Results: Although distributions of hypertension were similar between databases, KEEP participants with cardiovascular risk factors, especially current smoking, have a greater prevalence of hypertension than similar NHANES participants. Of hypertensive participants, 35.8% were African American in KEEP data, and 13.2% in NHANES data. Associations with increased prevalence of hypertension were decreasing estimated glomerular filtration rate by increments of 10 mL/min/1.73 m², increasing age, obesity, African American race, and microalbuminuria. In both KEEP and NHANES data, study group participants younger than 46 years were more likely to have achieved goal blood pressure.

Conclusion: Several elements were identified by both registries as risk factors for linearly associated worsening of hypertension. In addition to the traditional risk factors of age, race, and geographic residence, such novel markers as microalbuminuria may also increase the risk.

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INDEX WORDS: Chronic kidney disease; hypertension; National Health and Nutrition Examination Survey (NHANES).

The incidence and prevalence of hypertension are increasing in the United States.¹ Hypertension is the most-often diagnosed disease in adults in the United States¹; approximately 72 million Americans have high blood pressure, and about 30% are undiagnosed.¹ The distribution of hypertension is heterogeneous among US regions, with historically greater rates in the South and Southeast.² Recent data estimate the cost of treating hypertension and its comorbid conditions at nearly \$55 billion annu-

ally.³ Some of this cost is attributed to more aggressive blood pressure management to achieve lower goals put forth by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), and some, to increased rates of obesity.^{4,5}

The diagnosis of chronic kidney disease (CKD) also has increased in the United States. According to a recent Centers for Disease Control and Prevention report, CKD prevalence was 16.8% in patients older than 20 years in National Health and Nutrition Examination Survey (NHANES) data from 1999 to 2004 and 14.5% in similar data from 1988 to 1994.⁶ The prevalence of CKD stages 1 to 4 increased from 10.0% in 1988 to 1994 to 13.1% in 1999 to 2004.⁷ Prevalence estimates of CKD stages in 1999 to 2004 were 1.8% for stage 1, 3.2% for stage 2, 7.7% for stage 3, and 0.35% for stage 4.⁷ This increase may be caused in part by greater awareness of CKD and more laboratories reporting estimated glomerular filtration rate (eGFR) as part of the chemistry panel. CKD is associated with increased cardiovascular risk, decreased quality of life, early

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death, and greater health care costs.⁸ One estimate indicated that patients with CKD required spending on average \$14,000 to \$22,000 greater per patient-year than age-matched controls without CKD.⁹

The Kidney Early Evaluation Program (KEEP) was developed by the National Kidney Foundation (NKF) as a voluntary CKD screening program to identify high-risk individuals. KEEP targets participants 18 years or older who have diabetes or hypertension or a first-order relative with diabetes, hypertension, or kidney disease. Hypertension is an early and common risk factor for CKD. In previous years, more than half the KEEP program respondents with an eGFR less than 60 mL/min/1.73 m² (<1.0 mL/s/1.73 m²) had self-reported hypertension.² In this analysis, we examined the effect of decreasing eGFR on hypertension prevalence.

Because neither hypertension nor CKD generally shows symptoms in the early stages, many people are unaware of their presence. Under the auspices of the NKF and the National Center for Health Statistics, the KEEP and NHANES registries are maintained to raise awareness of such issues. These programs focus primarily on maintaining epidemiological and outcomes data to monitor progress and help forge practice initiatives. The aim of this study is to compare and contrast data collected by KEEP and NHANES in an effort to disseminate the most recent information for hypertension, CKD, and the interplay between them.

METHODS

Use of KEEP and NHANES Databases for Screening Patients

For this report, its companion reports, and the reference tables reported in this supplement, we include only eligible KEEP participants screened from August 2000 through December 31, 2006, from 47 NKF affiliates and 1,608 screening programs in 49 states and the District of Columbia. After excluding individuals with missing hypertension values, the KEEP study cohort for this study includes 73,441 (of 73,460) eligible KEEP participants. To compare with KEEP data, all samples analyzed using NHANES 1999-2004 data were restricted to individuals 18 years or older ($n = 17,061$). We performed multivariate logistic analysis of participants included in both databases. For analyses related to smoking status, self-reported kidney disease, self-reported cardiovascular disease, and self-reported high cholesterol levels in NHANES, the study population is limited to participants aged 20 years or older ($n = 15,332$). The

KEEP program and the NHANES database are fully described elsewhere in this supplement.¹⁰

Definitions

To ensure consistent and unbiased comparisons between KEEP and NHANES participants, we applied common definitions of comorbid conditions used in the analyses. In KEEP, hypertension is defined as self-reported hypertension or increased blood pressure (JNC 7),⁴ defined as systolic blood pressure of 130 mm Hg or greater or diastolic blood pressure of 80 mm Hg or greater for persons with a history of diabetes or CKD and systolic blood pressure of 140 mm Hg or greater or diastolic blood pressure of 90 mm Hg or greater otherwise. In NHANES, hypertension is defined as self-reported hypertension or increased blood pressure (JNC 7).⁴

CKD is defined based on eGFR using the 4-variable Modification of Diet in Renal Disease Study equation and albumin-creatinine ratio (ACR): stage 1, eGFR greater than 90 mL/min/1.73 m² (>1.50 mL/s/1.73 m²) and ACR of 30 mg/g or greater; stage 2, eGFR of 60 to 89 mL/min/1.73 m² (1.00 to 1.48 mL/s/1.73 m²) and ACR of 30 mg/g or greater; stage 3, eGFR of 30 to 59 mL/min/1.73 m² (0.50 to 0.98 mL/s/1.73 m²); stage 4, eGFR of 15 to 29 mL/min/1.73 m² (0.25 to 0.48 mL/s/1.73 m²); and stage 5, eGFR less than 15 mL/min/1.73 m² (<0.25 mL/s/1.73 m²).

Statistical Analysis

We examined the prevalence of hypertension in KEEP and NHANES participants. Descriptive statistics are reported in counts and proportions in both KEEP and NHANES data sets. Logistic regression was used to analyze associations of risk factors with increased blood pressure in self-reported nonhypertensive KEEP participants and associations of risk factors with meeting target blood pressure with self-reported hypertension in KEEP and NHANES participants. The controlled risk factors in logistic regressions were age, sex, race, smoking status, self-reported diabetes, family history of diabetes, family history of hypertension, obesity, and CKD status. P less than 0.05 is considered statistically significant. To obtain national estimates of each statistic in NHANES, sampling weights and survey design were implemented by using SUDAAN (Research Triangle Institute, Research Triangle Park, NC).

RESULTS

The hypertension rate is greater for KEEP participants than for NHANES participants at all ages; however, rates are similar for older age groups (Table 1; Fig 1). KEEP participants with cardiovascular risk factors, especially current smoking, have a greater prevalence of hypertension than similar NHANES participants.

Although the distribution of participants with hypertension is similar in KEEP and NHANES, more NHANES men have hypertension than KEEP men. In hypertensive participants, 35.8%

Table 1. Prevalence of Hypertension in Risk Groups

Characteristics	Hypertension			
	KEEP		NHANES	
	No. of Participants	%	No. of Participants	%
Age (y)				
18-30	1,747	29.4	439	11
31-45	8,014	48.7	875	23.9
46-60	18,391	71.2	1,452	48.1
61-75	16,429	86.1	2,244	73.0
>75	5,549	90.1	1,508	85.9
Sex				
Men	16,693	72.2	3,092	37.3
Women	33,391	66.5	3,426	38.4
Race				
White	23,358	69.8	3,393	38.5
African American	17,615	71.8	1,480	46.1
Other	8,207	59.4	1,645	29.8
Ethnicity				
Hispanic	5,172	57.2	1,493	28.5
Non-Hispanic	44,958	69.8	5,025	39.2
Education				
<High school	8,540	76.1	2,492	45.8
≥High school	40,814	66.8	4,000	35.8
Current smoker				
Yes	5,176	61.6	1,101	30.7
No	41,855	68.9	5,295	41.8
Obesity status (BMI ≥ 30 kg/m ²)				
Yes	25,067	78.6	2,389	52.0
No	24,274	60.3	3,455	30.8
Self-reported diabetes				
Yes	17,053	87.7	1,200	85.6
No	32,614	61.3	5,317	34.5
Self-reported cardiovascular disease				
Yes	11,957	82.1	1,416	77.0
No	38,173	64.8	4,930	35.2
Self-reported high cholesterol				
Yes	2,861	81.0	2,509	60.4
No	2,408	61.7	2,672	38.4
eGFR (mL/min/1.73 m ²)				
<30	605	95.6	113	97.5
30-<40	1,243	93.5	150	91.2
40-<50	2,897	90.6	338	89.6
50-<60	5,728	86.2	620	84.5
60-<70	7,685	72.4	815	49.6
70-<80	9,191	68.4	1,044	41.2
80-<90	7,209	63.7	968	34.8
90-<100	5,908	61.3	651	24.4
≥100	7,039	56.6	1,088	24.8
Microalbuminuria (mg/L)				
≤10	23,058	65.4	3,071	29.9
10-≤30	14,463	66.8	1,512	47.9
30-≤80	4,544	75.6	671	70.5
>80	4,362	89.7	663	88.1
All	50,130	68.3	6,518	37.9

Note: Values for NHANES are from 1999-2004 data. To convert GFR in mL/min to mL/s, multiply by 0.01667.

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; KEEP, Kidney Early Evaluation Program; NHANES, National Health and Nutrition Examination Surveys.

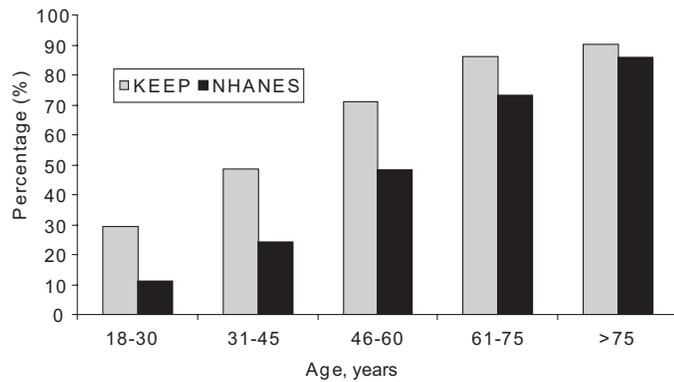


Figure 1. Percentage of participants with hypertension by age group, Kidney Early Evaluation Program (KEEP) and National Health and Examination Survey (NHANES) 1999-2004 data.

are African Americans in KEEP data, and 13.2%, in NHANES data (Table 2). Hypertension trends by age or CKD stage did not differ between databases (Table 3).

The probability of not reporting hypertension when present was significantly greater in participants aged 60 years and older, men, African Americans, and participants with diabetes, fam-

Table 2. Distribution of Characteristics by Hypertension Status

Characteristics	Hypertension			
	KEEP		NHANES	
	Yes	No	Yes	No
	(n = 50,130)	(n = 23,311)	(n = 6,518)	(n = 8,454)
Sex				
Men	33.3	27.7	47.1	48.3
Women	66.7	72.3	52.9	51.7
Race				
White	47.5	44.7	73.8	72
African American	35.8	30.6	13.2	9.4
Other	16.7	24.8	12.9	18.6
Ethnicity				
Hispanic	10.3	16.6	9.5	14.5
Non-Hispanic	89.7	83.4	90.5	85.5
Education				
<High school	17.3	11.7	25.1	18.1
≥High school	82.7	88.3	74.9	81.9
Current smoker				
Yes	11.0	14.6	19.3	27.9
No	89.0	85.4	80.7	72.1
Obesity status (BMI ≥ 30 kg/m ²)				
Yes	50.8	30.0	42.9	23.6
No	49.2	70.0	57.1	76.4
Self-reported diabetes				
Yes	34.3	10.4	14.7	1.5
No	65.7	89.6	85.3	98.5
Self-reported cardiovascular disease				
Yes	23.9	11.1	17.9	3.4
No	76.1	88.9	82.1	96.6
Self-reported high cholesterol				
Yes	54.3	30.9	49.9	28.9
No	45.7	69.1	50.1	71.1

Note: Categorical values are expressed in percent. Values for NHANES are from 1999-2004 data.

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; KEEP, Kidney Early Evaluation Program; NHANES, National Health and Nutrition Examination Surveys.

Table 3. Prevalence of Chronic Kidney Disease Stages in Persons With Hypertension

Characteristics	CKD Stages							
	KEEP				NHANES			
	No CKD	1	2	3-5	No CKD	1	2	3-5
Age (y)								
18-30	78.9	10.6	5.4	5.2	86.0	6.5	5.3	-
31-45	78.5	6.1	6.3	9.0	84.0	6.6	5.7	3.7
46-60	73.2	4.2	5.7	16.8	76.8	5.8	7.0	10.4
61-75	58.7	1.9	6.5	32.9	62.9	3.4	9.7	24.0
>75	41.7	0.9	7.2	50.2	34.7	1.9	10.8	52.6
Sex								
Men	67.9	3.3	6.7	22.2	71.9	5.1	8.2	14.7
Women	64.6	3.7	6.1	25.7	66.6	4.5	7.6	21.4
Race								
White	62.4	2.0	5.6	30.0	69.1	3.1	7.5	20.4
African American	70.2	5.0	6.5	18.3	70.9	8.4	8.0	12.7
Other	66.3	5.1	7.7	21.0	67.7	11.1	10.1	11.1
Ethnicity								
Hispanic	69.5	5.3	6.6	18.5	68.8	11.7	9.2	10.4
Non-Hispanic	65.3	3.3	6.2	25.2	69.2	4.1	7.8	19.0
Education								
<High school	59.0	4.0	7.6	29.3	59.7	7.1	10.0	23.2
≥High school	67.1	3.4	5.9	23.6	72.3	4.0	7.2	16.5
Current smoker								
Yes	69.4	5.6	7.2	17.9	71.6	8.6	8.3	11.5
No	65.3	3.3	6.2	25.3	68.4	3.8	7.9	19.9
Obesity status (BMI ≥ 30 kg/m ²)								
Yes	67.1	4.1	6.3	22.5	71.3	5.3	8.6	14.8
No	64.3	2.9	6.2	26.7	68.4	4.2	7.4	19.9
Self-reported diabetes								
Yes	60.6	4.7	7.9	26.7	51.5	9.1	14	25.3
No	68.4	2.9	5.3	23.4	72.1	4.0	6.9	17.0
Self-reported cardiovascular disease								
Yes	56.8	3.1	7.4	32.7	50.8	3.2	9.6	36.4
No	68.6	3.7	5.9	21.9	73.0	5.1	7.5	14.4
Self-reported high cholesterol								
Yes	66.5	2.7	6.5	24.2	67.8	4.1	7.9	20.2
No	73.0	4.0	7.1	15.9	69.2	4.4	8.2	18.2
Overall	65.7	3.5	6.3	24.5	69.1	4.8	7.9	18.2

Note: Categorical values are expressed in percent. Participants with missing estimated glomerular filtration rate values were excluded. Values for NHANES are from 1999-2004 data.

Abbreviations: CKD, chronic kidney disease; KEEP, Kidney Early Evaluation Program; NHANES, National Health and Nutrition Examination Surveys; BMI, body mass index.

ily history of hypertension, obesity (body mass index [BMI] ≥ 30 kg/m²), or CKD (Table 4). The greatest risk of not reporting hypertension when present was for participants with CKD.

The probability of reaching target blood pressure as defined by the JNC 7 (see⁴) was greatest for participants younger than 46 years (Table 5). Probability was lowest for participants aged 60 years or older, men, African Americans, and participants with self-reported diabetes, obesity, or CKD.

DISCUSSION

Because cohort selection for KEEP and NHANES differs (KEEP is targeted and voluntary, and NHANES is a multiple-stage random selection of people who then volunteer to participate), the 2 databases differ regarding analyses performed for hypertension in patients with CKD, and direct comparison is not appropriate. African Americans are better represented in KEEP. We examine hypertension prevalence in the context

Table 4. Odds Ratio of Self-Reported Nonhypertension in Kidney Early Evaluation Program Participants With Increased Blood Pressure

Characteristics	Odds Ratio (95% confidence interval)	P
Age (y)		
18-30	0.40 (0.36-0.44)	<0.001
31-45	0.62 (0.58-0.67)	<0.001
46-60	1	
61-75	1.58 (1.45-1.72)	<0.001
>75	1.99 (1.71-2.31)	<0.001
Sex		
Women	1	
Men	1.77 (1.66-1.89)	<0.001
Race		
White	1	
African American	1.14 (1.06-1.22)	<0.001
Other	0.85 (0.79-0.92)	<0.001
Current smoker	0.96 (0.87-1.04)	0.3
Self-reported diabetes	3.29 (3.04-3.55)	<0.001
Family history of diabetes	1.01 (0.95-1.08)	0.8
Family history of hypertension	1.26 (1.17-1.37)	<0.001
Body mass index \geq 30 kg/m ²	2.27 (2.13-2.42)	<0.001
Chronic kidney disease	3.31 (3.06-3.57)	<0.001

Note: Increased blood pressure as defined by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.⁴ Number with self-reported nonhypertension and nonmissing value of first column = 24,089. Controlled risk factors in logistic regressions were age, sex, race, smoking status, self-reported diabetes, family history of diabetes, family history of hypertension, obesity, and chronic kidney disease status.

of eGFR as a continuous variable and confirm previous reports that as eGFR decreases, the probability of having hypertension increases.

We also confirm findings of an earlier KEEP database analysis using data through 2005, that participants most likely to have hypertension were least aware they had it. However, these same individuals, if aware and treated, were most likely to achieve blood pressure goals. This provides compelling evidence for the need to identify people who require treatment because they have the greatest cardiovascular risk and are more likely to successfully reach blood pressure goals.

Clinicians should be aware that more aggressive treatment of high blood pressure often is required in patients with advanced CKD to slow the need for renal replacement therapy. Recent

analyses of patients with diabetes with and without microalbuminuria showed the need for an average of 1 additional antihypertensive medication to achieve blood pressure goals for those with microalbuminuria than for those without microalbuminuria.¹¹

Level of microalbuminuria and frequency of hypertension increased almost linearly in the KEEP registry. More than 90% of patients with urinary ACR greater than 80 mg/g also had hypertension. Microalbuminuria has received much attention in regard to diabetes and cardiovascular risk¹²; however, recent data show that urinary albumin excretion in nondiabetic individuals represents a biomarker of essential hypertension development.¹³ The hypothesis behind this relation is that endothelial dysfunction is present in the vasculature, and this decrease in nitric oxide levels and changes in vascular permeability are manifest as microalbuminuria. This hypothesis was supported by studies by Wang et al¹⁴ showing that ACR greater than 6.67 mg/g in men and 15.24 mg/g in women resulted in doubling of the risk of development of hypertension when accounting for BMI, creatinine, and baseline blood pressure values.

Hypertension, CKD, and the combination have substantially affected African Americans, a premise supported by both the KEEP and NHANES registries. Hypertension prevalence in the KEEP African American cohort was 71.8% versus 46.1% in the NHANES African American cohort. The KEEP registry included a much larger sample of African Americans than the NHANES registry. In the KEEP registry, African Americans without self-reported hypertension had a 14% increased risk of having increased blood pressure than white counterparts. Furthermore, African Americans with hypertension had a nearly 21% greater rate of not meeting JNC 7 guidelines for blood pressure goals. This is important in light of evidence that hypertension-related end-stage renal disease is much more common in African Americans than whites, and in younger people (aged 20 to 44 years), the prevalence in African Americans is even greater.¹⁵

Obesity (defined as BMI \geq 30 kg/m²) has become a significant problem in the United States. It places people at greater risk of a number of other conditions, including hypertension and CKD. In both registries, a large proportion of

Table 5. Odds Ratios of Meeting Target Blood Pressure

Characteristics	KEEP		NHANES	
	Odds Ratio (95% confidence interval)	P	Odds Ratio (95% confidence interval)	P
Age (y)				
18-30	1.98 (1.69-2.32)	<0.001	4.25 (2.47-7.30)	<0.01
31-45	1.33 (1.22-1.44)	<0.001	2.10 (1.62-2.73)	<0.01
46-60	1		1	
61-75	0.85 (0.80-0.91)	0.002	0.77 (0.60-0.99)	0.04
>75	0.75 (0.68-0.82)	<0.001	0.28 (0.19-0.39)	<0.01
Sex				
Women	1		1	
Men	0.83 (0.78-0.88)	<0.001	1.09 (0.88-1.36)	0.4
Race				
White	1		1	
African American	0.79 (0.74-0.84)	<0.001	0.61 (0.47-0.79)	<0.01
Other	1.10 (1.02-1.19)	0.01	0.60 (0.46-0.79)	<0.01
Current smoker	1.04 (0.96-1.14)	0.3	1.05 (0.80-1.37)	0.7
Self-reported diabetes	0.48 (0.45-0.51)	<0.001	0.42 (0.29-0.61)	<0.01
Family history of diabetes	1.01 (0.95-1.07)	0.8	0.85 (0.69-1.05)	0.1
Family history of hypertension	0.97 (0.90-1.04)	0.4	0.91 (0.74-1.11)	0.3
Body mass index \geq 30 kg/m ²	0.69 (0.65-0.73)	<0.001	0.84 (0.68-1.03)	0.09
Chronic kidney disease	0.41 (0.38-0.43)	<0.001	0.20 (0.14-0.28)	<0.01

Note: Target blood pressure as defined by The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.⁴ Controlled risk factors in the logistic regressions were age, sex, race, smoking status, self-reported diabetes, family history of diabetes, family history of hypertension, obesity, and chronic kidney disease status. KEEP participants with self-reported hypertension (number with self-reported hypertension and nonmissing value of the first column = 27,704) and NHANES 1999-2004 participants aged 20 years and older (n = 3,363).

Abbreviations: KEEP, Kidney Early Evaluation Program; NHANES, National Health and Nutrition Examination Survey.

obese participants had hypertension compared with nonobese participants (KEEP, 78.6% for obese participants, 60.3% for nonobese participants; NHANES, 52% for obese participants, 30.8% for nonobese participants). Obese participants who reported no hypertension were at greatest risk of having hypertension at the time of screening. In addition, results for hypertension, CKD, and obesity show an interesting pattern. In patients with early stages of CKD (stages 1 and 2), greater rates of hypertension were seen for obese participants than for nonobese participants in both databases. This pattern reverses for CKD stages 3 to 5, in which nonobese participants have more hypertension. Possibly, the effects of uremia leading to weight loss have a role in this trend.

Gelber et al¹⁶ studied 11,104 healthy men who took part in the Physicians' Health Survey and showed that increased BMI was an independent risk factor for CKD, defined as eGFR less than 60 mL/min/1.73 m² (<1.0 mL/s/1.73 m²). Trends we note in KEEP and NHANES data further support

evidence that the epidemic of obesity raises the risk of CKD, as well as cardiovascular disease.

Limitations of this study include its cross-sectional nature involving 2 national registries. Both registries rely on voluntary screening history and physical examination, and both rely on the volunteers to self-report such diseases as hypertension or provide the information through their physicians' offices. A known limitation of the NHANES database is the low percentage of patients with eGFR less than 30 mL/min/1.73 m² (<0.5 mL/s/1.73 m²); comparison with the more robust data of the KEEP registry would not be appropriate. Finally, because the presence of hypertension is a KEEP eligibility criterion, KEEP subjects may have greater awareness of hypertension than their NHANES counterparts.

In conclusion, this analysis of KEEP and NHANES data helps illustrate the magnitude and complexity of hypertension in the United States. These databases point out the effect of hypertension on kidney disease and vice versa. We show that eGFR assessed as a continuous variable has a

linear relationship to hypertension prevalence, and there are limitations to doing such analyses by stages of CKD as outlined by the NKF-Kidney Disease Outcomes Quality Initiatives guidelines. Our results indicate that awareness of the disease is critical to achieving the recommended guideline goals. This is evident because participants at greatest risk of having hypertension who were unaware of its presence were the same participants most likely to achieve guideline goals when treated. Our findings further support the use of screening programs to improve public kidney and cardiovascular health.

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