



# Primary prevention of chronic kidney disease through population-based strategies for blood pressure control: The ARIC study

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While much of the chronic kidney disease (CKD) literature focuses on the role of blood pressure reduction in delaying CKD progression, little is known about the benefits of modest population-wide decrements in blood pressure on incident CKD. The authors used multivariable linear regression to characterize the impact on incident CKD of two approaches for blood pressure management: (1) a 1-mm Hg reduction in systolic BP across the entire study population; and (2) a 10% reduction in participants with unaware, untreated, and uncontrolled BP above goal as defined by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) thresholds. Over a mean of 20 years of follow-up (ARIC [Atherosclerosis Risk in Communities] study, n = 15 390), 3852 incident CKD events were ascertained. After adjustment, a 1-mm Hg decrement in systolic BP across the population was associated with an estimated 11.7 (95% confidence interval [CI], 6.2–17.3) and 13.4 (95% CI, 10.3–16.6) fewer CKD events per 100 000 person-years in blacks and whites, respectively. Among participants with BP above JNC 7 goal, a 10% decrease in unaware, untreated, or uncontrolled BP was associated with 3.2 (95% CI, 2.0–4.9), 2.8 (95% CI, 1.8–4.3), and 5.8 (95% CI, 3.6–8.8) fewer CKD events per 100 000 person-years in blacks and 3.1 (95% CI, 2.3–4.1), 0.7 (95% CI, 0.5–0.9), and 1.0 (95% CI, 1.3–2.4) fewer CKD events per 100 000 person-years in whites. Modest population-wide reductions in systolic BP hold potential for the primary prevention of CKD.

## 1 | INTRODUCTION

Chronic kidney disease (CKD) affects an estimated 14.8% (2011–2014) of US adults, with approximately 124 114 incident cases of hemodialysis being reported in 2015.<sup>1</sup> Despite increased screening and management of prevalent CKD, only 50% to 60% of patients who progress to requiring dialysis are alive 3 years after diagnosis of end-stage renal disease (ESRD), and dialysis patients experience adjusted all-cause mortality rates that are 6.5 to 7.9 times greater

than the general population.<sup>1</sup> The burden of hospitalization, disability, and increased risk of all-cause mortality associated with kidney disease and its severity<sup>2–6</sup> call for a better understanding of the potential benefits associated with preventive modification of risk factors associated with CKD.

Hypertension is a major modifiable risk factor for CKD and ESRD, and has been a target for intervention among patients with CKD.<sup>7–9</sup> The focus of these studies has traditionally been tertiary prevention, ie, the management of established kidney disease to prevent

progression, or to delay long-term complications.<sup>10</sup> Arguably, this approach has produced mixed results with respect to progression to ESRD.<sup>11</sup> Alternatively, strategies for the primary prevention of CKD seeks to reduce exposure to factors known to lead to kidney impairment. While this approach may provide a great opportunity to reduce the development of CKD, to our knowledge there are no studies on the predicted effects of blood pressure (BP) reductions applied to the general population. Here, we estimated the potential effects of modest population-wide BP decreases consistent with what could be achieved through lifestyle and pharmacologic management of BP to assess their possible impact on the population burden of incident CKD and kidney failure. We employed two hypothetical approaches: (1) achievement of a 1- or 2-mm Hg reduction in systolic BP across the entire study population; and (2) achievement of a 10% reduction in participants with unaware, untreated, or uncontrolled BP as defined separately by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC) 7 and Eighth Joint National Committee (JNC 8) thresholds.

## 2 | METHODS

### 2.1 | Study population

The ARIC (Atherosclerosis Risk in Communities) study is a prospective, population-based investigation of the etiology and natural history of CVD and its risk factors.<sup>5</sup> From 1987 to 1989, ARIC investigators sampled 15 792 predominately white and black participants between the ages of 45 and 64 years from four geographic regions in the United States: Washington County, Maryland; suburban Minneapolis, Minnesota; Forsyth County, North Carolina, and Jackson, Mississippi. The latter two communities contributed the majority of blacks to the cohort. Physical examinations and standardized questionnaires were administered by trained study personnel at baseline and during four follow-up examinations. Cohort follow-up for identification and classification of health outcomes is ongoing. The ARIC study obtained institutional review board approval from all participating institutions, and informed consent was obtained at each study visit.

Participants who reported a race other than black or white ( $n = 48$ ) and participants with prevalent CKD (estimated glomerular filtration rate [eGFR] < 60) or missing information to determine prevalent CKD at baseline ( $n = 354$ : 227 blacks, 127 whites) were excluded. After these exclusions, 15 390 participants were available for the evaluation of incident CKD. Follow-up time was calculated from study enrollment to the first identification of CKD, loss to follow-up, death, or December 31, 2011.

### 2.2 | Exposure and covariate assessment

Standardized seated BP measurements were taken after a 5-minute rest using a random-zero sphygmomanometer with participants fitted with the appropriate size cuff on the right arm according

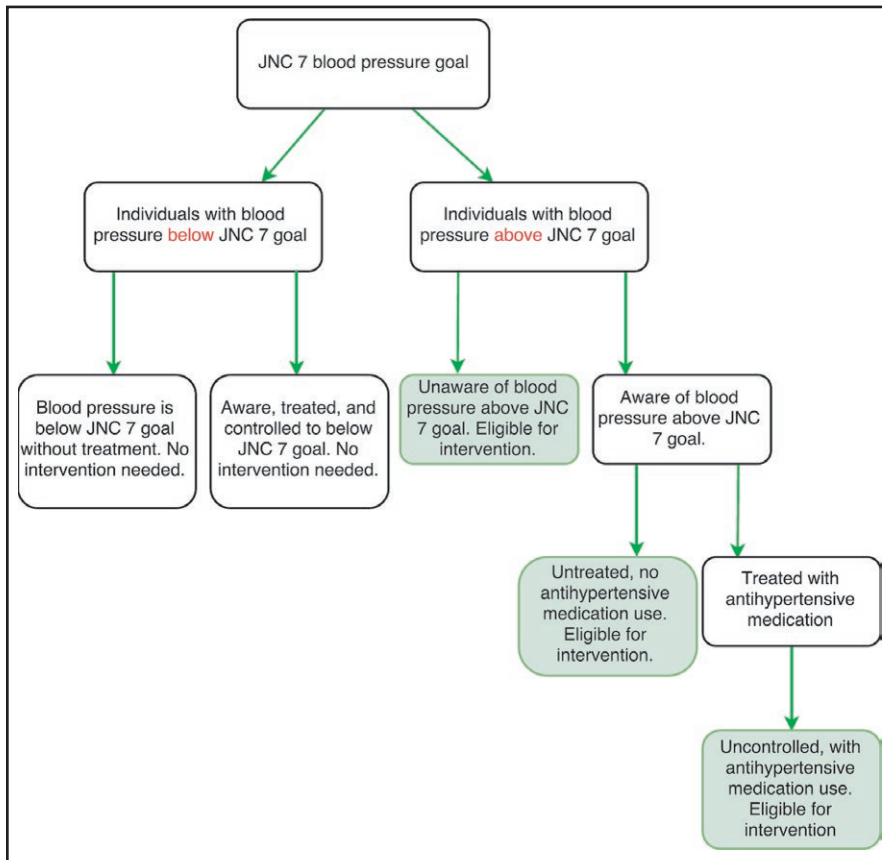
to study protocol ([http://www.csc.unc.edu/aric/visit/Sitting\\_Blood\\_Pressure\\_and\\_Postural\\_Changes\\_in\\_Blood\\_Pressure\\_and\\_Heart\\_Rate.1\\_11.pdf](http://www.csc.unc.edu/aric/visit/Sitting_Blood_Pressure_and_Postural_Changes_in_Blood_Pressure_and_Heart_Rate.1_11.pdf)). The mean of the second and third readings from the baseline examination was used for analysis. We used both JNC 8 and JNC 7 BP guidelines to identify participants with BP above goal. Using JNC 8, hypertension was classified by systolic BP (SBP)  $\geq 150$  mm Hg or diastolic BP  $\geq 90$  mm Hg for participants 60 years and older and systolic BP  $\geq 140$  mm Hg or diastolic BP  $\geq 90$  mm Hg for participants younger than 60 years.<sup>12</sup> Using JNC 7, hypertension was classified by a systolic BP  $\geq 140$  mm Hg or a diastolic BP  $\geq 90$  mm Hg for participants of all ages.<sup>13</sup> Participants with BP values below treatment goals, irrespective of medication usage or history of hypertension, were ineligible for reductions in BP targeted to populations with BP above goal (Figure). The term unaware BP above goal was used to describe participants with BP above treatment goals who were unaware of their high BP (Figure). Untreated BP above goal described participants with BP above goal who were aware of their high BP but were untreated with antihypertensive medication. Those with uncontrolled BP above goal were aware of their high BP, treated with antihypertensive medication but uncontrolled to below treatment thresholds. Antihypertensive medication use, race, age, diabetes mellitus, and sex were assessed at study baseline.

### 2.3 | Outcome ascertainment and definition

The eGFR for each participant was estimated from calibrated creatinine measurements using the CKD Epidemiology Collaboration equation.<sup>14</sup> Incident CKD was a composite outcome defined by at least one of the following conditions: (1) development of an eGFR < 60 mL/min/1.73 m<sup>2</sup> accompanied by 25% eGFR from baseline, using samples collected at ARIC visits 1, 2, 4, and 5; (2) death or hospitalization with CKD identified by *International Classification of Diseases Ninth Revision* or *International Classification of Diseases Tenth Revision* discharge code 585.X in any position; and (3) linkage to the United States Renal Data System national registry indicating ESRD treatment between baseline and the end of follow-up. Serum creatinine was measured using the modified kinetic Jaffé method and calibrated to the National Institute of Standards and Technology standard to account for variability among laboratories, assays, and methods.<sup>15</sup> ARIC study participants were interviewed annually by phone and all hospitalizations and deaths during the preceding year were identified, abstracted, and adjudicated according to study criteria. Active surveillance of the ARIC cohort through local hospital discharge records and vital records was also used to detect hospitalizations and deaths of cohort participants.

### 2.4 | Statistical analysis

Incidence rates, stratified by race were calculated by dividing the total number of CKD events by the person-years (PYs) at risk. A least squares linear regression approach<sup>16</sup> was used to estimate the number of incident CKD events per 100 000 PYs potentially



**FIGURE** Diagram defining categories of blood pressure above and below Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) treatment goals. Groups targeted by hypothetical interventions achieving 10% reductions in unaware, untreated, and uncontrolled blood pressure above the JNC 7 treatment goal are shaded in green [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

prevented after a population-wide 1- or 2-mm Hg systolic BP reduction adjusted for age, sex, diabetes mellitus, and antihypertensive medication use at baseline. These models provided estimates of the incidence rate difference (IRD) for CKD associated with a 1-mm Hg decrement in systolic BP at study baseline; estimates for a 2-mm Hg reduction were obtained by multiplying the systolic BP regression coefficient by 2. A modest reduction in systolic BP of 1- or 2-mm Hg represents a plausible decrement in systolic BP that could potentially be achievable, on average, population-wide after lifestyle modifications were fully implemented.<sup>17-21</sup>

To evaluate BP reduction strategies targeted to populations with BP above goal, we first estimated race-, sex-, diabetes mellitus-, and age- (in 5-year increments) specific IRDs using the least squares regression approach<sup>16</sup> for the association between BP above goal and incident CKD. Reduction on the incidence rate after a 10% reduction in unaware, untreated, or uncontrolled BP above goal at study baseline were then estimated in the ARIC study using the following equation:  $IRD_{ijk} \times (\text{proportion}_i - \text{proportion}_m)$ , where  $i$ ,  $j$ , and  $k$  index race, sex, and 5-year age categories,  $\text{proportion}_i$  is the race-specific proportion of BP above goal estimated in National Health and Nutrition Examination Survey (NHANES),<sup>22</sup> pre ( $i$  subscript) and post ( $m$  subscript) intervention that shifted 10% of the proportion of the population with unaware, untreated, or uncontrolled BP above goal to unexposed (ie, below goal BP). Results were estimated per 100 000 PYs and represent a special case of the population-attributable risk that considers a feasible partial (ie, 10% reduction in uncontrolled

BP) rather than an impractical complete elimination of the risk factor (ie, elimination of all uncontrolled BP above goal). Here, we considered partial elimination of BP above goal, achieved after fully implementing strategies that decreased the proportion of the population with unaware, untreated, or uncontrolled BP by 10%.<sup>23</sup> Age-, sex-, and diabetes mellitus-specific results were then collapsed by race using a case load-weighted summation method<sup>24,25</sup> and 95% confidence intervals (CIs) were obtained using bootstrapping.<sup>26</sup>

For sensitivity analyses, we estimated 5% to 20% proportional reductions in unaware, untreated, and uncontrolled BP above goal as well as 5% to 20% reductions in the total population with BP above goal. Contemporary race-specific population projections for the number of events potentially preventable following population-wide and targeted BP reductions were calculated by multiplying the race-specific IRD estimates by the race-specific total population aged 45 to 64 years from the 2010 US census population. All statistical analyses were performed with SAS 9.3 software (SAS Institute) and Stata12 (StataCorp).

Contemporary race-specific weighted proportions of unaware, untreated, and uncontrolled BP above JNC 7 goal for ages 45 to 64 years were estimated from NHANES 2009-2012 with whites having 15.8% of the population with BP above goal (42% unaware; 17% untreated; 41% uncontrolled) and blacks having 26.4% of the population with BP above goal (25% unaware; 20% untreated; 55% uncontrolled). Individuals with hypertension who were aware and treated to JNC 8 or JNC 7 treatment goals were not included in the targeted group for the respective analyses.

**TABLE 1** Baseline characteristics of the ARIC study cohort (N = 15 390) by race, 1987–1989

Baseline characteristics	Blacks (n = 4039)	Whites (n = 11 351)
Mean follow-up in y, (SD)	18.7 (7.2)	20.0 (6.4)
Mean age in y, (SD)	53.5 (5.8)	54.3 (5.7)
Diabetes mellitus	750 (18.6)	1016 (9.0)
Mean body mass index, (SD)	29.6 (6.1)	27.0 (4.9)
Women, No. (%)	2488 (61.6)	5990 (52.8)
Reported antihypertensive use, No. (%)	1597 (50.6)	2201 (22.2)
Mean systolic BP, mm Hg (SD)	128.5 (21.1)	118.4 (17.0)
Mean diastolic BP, mm Hg (SD)	76.7 (12.2)	71.5 (10.1)
BP categories <sup>a</sup>		
BP below JNC 8 goal, No. (%)	2892 (71.6)	10 182 (89.7)
BP above JNC 8 goal, No. (%)	1146 (28.4)	1164 (10.3)
BP below JNC 7 goal, No. (%)	2807 (69.5)	9922 (87.5)
BP above JNC 7 goal, No. (%)	1231 (30.5)	1424 (12.6)

ARIC, Atherosclerosis Risk in Communities study; SD, standard deviation.  
<sup>a</sup>Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7): blood pressure (BP) values that are above or below thresholds for management of BP defined by JNC 7; Eighth Joint National Committee (JNC 8): BP values that are above or below thresholds for management of BP defined by JNC 8.

### 3 | RESULTS

At study baseline, 15 390 (26% black, 55% women) eligible ARIC cohort members were available for analysis (Table 1). On average, blacks were twice as likely to have BP above goal, to report the use of antihypertensive medications, or to have diabetes mellitus. As expected, 2% more blacks and whites were defined as having BP above goal using JNC 7 BP guidelines compared with JNC 8. Over a mean 19.7 years of follow-up, 3852 incident CKD events (24% among those with BP above JNC 7 goal; 29% among blacks) were identified with an incident rate of 1476/100 000 PYs for blacks and 1203/100 000 PYs for whites.

After a population-wide hypothetical BP reduction that achieved an overall 1-mm Hg decrement in systolic BP at study baseline, a reduction of 13.4 (95% CI, 7.8–19.0) and 11.7 (95% CI, 6.2–17.3) incident CKD events per 100 000 PYs in whites and blacks was estimated, respectively (Table 2). A 2-mm Hg population-wide decrement in BP was associated with two times the reductions in the incidence of CKD for both racial groups compared with a

**TABLE 2** Estimated incident CKD events reduced from hypothetical population-wide or targeted interventions that achieve a 1- to 2-mm Hg decrement in BP or a 10% reduction of unaware, untreated, or uncontrolled BP above goals, by race (N = 15 390)—ARIC study: 1987–2011,

BP intervention	Incident CKD events reduced per 100 000 PYs (95% CI) by hypothetical interventions achieving reductions in BP	
	Blacks	Whites
Hypothetical population-wide intervention to decrease systolic BP		
1-mm Hg Decrease	11.7 (6.2–17.3)	13.4 (10.3–16.6)
2-mm Hg Decrease	23.5 (12.3–34.6)	26.8 (20.6–33.1)
Hypothetical intervention to reduce BP (above JNC 8 treatment threshold)		
10% Decrease in unaware BP	2.7 (1.6–4.2)	2.5 (1.8–3.3)
10% Decrease in untreated BP	2.4 (1.4–3.7)	0.5 (0.4–0.7)
10% Decrease in uncontrolled BP	4.9 (2.9–7.6)	1.5 (1.0–1.9)
10% Decrease in all BP above goal	13.6 (8.0–21.1)	6.2 (4.4–8.2)
Hypothetical intervention to reduce BP (above JNC 7 treatment threshold)		
10% Decrease in unaware BP	3.2 (2.0–4.9)	3.1 (2.3–4.1)
10% Decrease in untreated BP	2.8 (1.8–4.3)	0.7 (0.5–0.9)
10% Decrease in uncontrolled BP	5.8 (3.6–8.8)	1.9 (1.3–2.4)
10% Decrease in all BP above goal	16.1 (10.0–24.3)	7.8 (5.6–10.2)

ARIC, Atherosclerosis Risk in Communities study; CI, confidence interval; CKD, chronic kidney disease; JNC 7, Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; JNC 8, Eighth Joint National Committee.

1-mm Hg reduction (Table 2). The estimated preventable incident CKD events following a 1-mm Hg reduction in systolic BP were fairly comparable by race, with preventable events estimated to be slightly greater for whites. If applied nationwide, a hypothetical 1-mm Hg shift in systolic BP among black and white US populations aged 45 to 64 years was estimated to prevent approximately 9996 incident CKD events annually (Table 3).

As a contrast to hypothetical systolic BP reductions population-wide, we estimated the effect of BP management strategies targeted to populations with BP above goal that achieved a 10% proportional reduction in unaware, untreated, or uncontrolled BP. These targeted BP above goal strategies were applied to the corresponding (smaller) subset of the total population. For example, using JNC 7 guidelines for BP, before targeted reductions, 28.3% of blacks and 15.8% of whites aged 45 to 64 years were classified as having BP above goal

BP intervention	Incident CKD events reduced <sup>a</sup> per 100 000 PYs (95% CI) by hypothetical interventions achieving reductions in BP	
	Black US population (n = 9 042 518)	White US population (n = 57 864 260)
Hypothetical population-wide intervention to decrease systolic BP		
1-mm Hg Decrease	1351	8645
2-mm Hg Decrease	2702	17 290
Hypothetical intervention to reduce BP (above JNC 8 treatment threshold)		
10% Decrease in unaware BP	245	1425
10% Decrease in untreated BP	216	229
10% Decrease in uncontrolled BP	444	846
10% Decrease in all BP above goal	1227	3563
Hypothetical intervention to reduce BP (above JNC 7 treatment threshold)		
10% Decrease in unaware BP	291	1807
10% Decrease in untreated BP	256	380
10% Decrease in uncontrolled BP	526	1072
10% Decrease in all BP above goal	1454	4518

CI, confidence interval; CKD, chronic kidney disease; JNC 7, Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; JNC 8, Eighth Joint National Committee; PYs, patient-years.

<sup>a</sup>Total 2010 US census race-specific populations aged 45 to 64 years (blacks n = 9 042 518, whites n = 57 864 260) were used to calculate the above goal blood pressure (BP).

(NHANES 2009–2012; Table 4). We therefore evaluated a targeted BP reduction strategy that achieved a 10% proportional decrease in unaware BP above goal (ie, 25% to 23% among blacks and 42% to 38% among whites, respectively), resulting in a postreduction proportion of BP above goal of 27.6% for blacks and 15.1% for whites (Table 4). In contrast to results from the population-wide systolic BP reduction, a 10% proportional reduction in unaware, untreated, or uncontrolled BP above JNC 7 goal produced the largest reduction in events for blacks particularly for untreated and uncontrolled BP above goal (Table 2). Specifically, a 10% proportional reduction in unaware, untreated, or uncontrolled BP above goal at ARIC study baseline resulted in approximately 3.2 (95% CI, 2.0–4.9), 2.8 (95% CI, 1.8–4.3), and 5.8 (95% CI, 3.6–8.8) fewer incident CKD events per 100 000 PYs, respectively, in blacks and 3.1 (95% CI, 2.3–4.1), 0.7 (95% CI, 0.5–0.9), and 1.9 (95% CI, 1.3–2.4) fewer CKD events per 100 000 PYs, respectively, in whites (Table 2).

If 10% proportional reductions in unaware, untreated, or uncontrolled BP above JNC 7 goal were achieved nationwide in black and white populations aged 45 to 64 years, approximately 2098, 636, and 1598 fewer incident CKD events, respectively, could be prevented annually (Table 3). Notably, BP management strategies

**TABLE 3** Estimated incident CKD events reduced from hypothetical population-wide and targeted BP reduction interventions, by race, 2010 US census population aged 45 to 64 years

targeted at the population with BP above JNC 7 goal could produce greater estimated reductions in incident CKD than strategies targeted at reductions in BP above JNC 8 goal. Additional analyses examining 5% to 20% proportional reductions in the total population with BP above goal target a larger segment of the population with BP above goal and demonstrated considerably larger reductions in incident CKD events than targeting 10% decreases in the population with unaware, untreated, or uncontrolled BP above JNC 7 goals (Table S1).

## 4 | DISCUSSION

Predicted benefits from BP reductions estimated in a biracial, population-based cohort showed that a modest population-wide 1 or 2-mm Hg decrement in systolic BP could potentially prevent more CKD events per 100 000 PYs than a 10% proportional reduction in unaware, untreated, or uncontrolled BP above goal. Although the population-wide approach estimated a similar number of CKD event reductions by race, the estimated benefits of lowering the proportion of the population with BP above goal on CKD events

**TABLE 4** Proportion of black and white NHANES participants aged 45 to 64 years with BP above JNC 8 and JNC 7 goal before and after targeted hypothetical interventions improving unaware, untreated, and uncontrolled BP by 10%, 2009–2012

BP guidelines	Race	Proportion of participants with BP above goal			
		Before hypothetical intervention	After 10% reduction in proportion of unaware BP above goal	After 10% reduction in proportion of untreated BP above goal	After 10% reduction in proportion of uncontrolled BP above goal
JNC 8	Blacks	26.36	25.84	25.78	24.82
	Whites	11.88	11.41	11.71	11.33
JNC 7	Blacks	28.31	27.60	27.74	26.75
	Whites	15.79	15.12	15.53	15.14

BP, blood pressure; JNC 7, Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; JNC 8, Eighth Joint National Committee; NHANES, National Health and Nutrition Examination Survey.

were greater for blacks, particularly in regard to 10% reductions in untreated and uncontrolled BP above goal.

Healthy People 2020 goals aimed for a 10% reduction in the proportion of the US population with CKD a goal that focuses research on prevention of CKD however, little evidence is available on population-based interventions to prevent the initial development of CKD.<sup>27–29</sup> A number of observational studies identified elevated BP as a risk factor for development of CKD<sup>30–33</sup> and support the notion of a benefit from BP reduction on the risk of CKD. Despite a strong association between elevated BP and CKD, randomized controlled trials of antihypertensive therapy on CKD progression have failed to provide sufficient evidence of efficacy, particularly for intensive control of BP, stressing the importance of prevention.<sup>10,11,34</sup> Primordial prevention of CKD provides the greatest opportunity for reducing the incidence of CKD and kidney failure, and will likely shape future public health initiatives for CKD as the focus shifts from halting progression of CKD to preventing its development.

An exclusive focus on BP treatment goals as opposed to reducing the risk of developing CKD as BP shifts to higher values constrains the opportunity to examine high-impact, population-wide approaches to blood pressure management. Given the monotonic (graded) relationship between BP level and disease risk, a population-based strategy is posited to achieve the largest benefit in reducing the burden of BP-related outcomes in the overall at risk population.<sup>35,36</sup> Although small reductions in BP across the population resulted in modest IRD estimates when applied to the population as a whole, the impact of a 1-mm Hg decrement in BP population-wide is pronounced with approximately 10 000 annual incident CKD events theoretically prevented among US black and white populations aged 45 years or older. Prevention-oriented lifestyle modifications are expected to have a positive impact on disease incidence and progression across race groups if implemented population-wide or reinforced during medical encounters among high-risk groups, yet these are often undervalued or unsupported as public health strategies for CKD prevention.<sup>37–40</sup> A better understanding of the potential benefits associated with modification of risk factors for CKD at the population level as well as among high-risk groups is needed to reduce the population burden of disease attributable to CKD.

Contrasting population-wide BP management strategies with high-risk approaches relies on assumptions and is inherently dependent on the thresholds used to define the high-risk populations, and thus the size of the population targeted for intensive reductions. Controversially, the 2014 JNC 8 BP guidelines raised the treatment thresholds for adults 60 years or older to systolic BP  $\geq$  150 mm Hg as opposed to the more proactive systolic BP threshold of 140 mm Hg used to identify hypertension and treatment initiation under JNC 7.<sup>13,41</sup> As a result of these differences in thresholds, 10% improvements in uncontrolled BP above goal as defined by JNC 7 are expected to prevent 300 more events in the US black and white populations aged 45 years or older annually compared with a 10% reduction in BP above goal defined by JNC 8. Evidence from randomized controlled trials of the benefit

of treatment thresholds lower than JNC 7 for CKD prevention remains unclear. SPRINT (Systolic Blood Pressure Intervention Trial) demonstrated the value of controlling BP to or below the level recommended by treatment guidelines for cardiovascular outcomes with or without CKD, suggesting that proper management of patients with elevated BP could reduce cardiovascular disease in the US population.<sup>34</sup> However, the group treated most intensively for BP control also experienced higher risk of CKD, or a decrease in eGFR of  $\geq 30\%$  to a value of  $< 60$  mL/min per  $1.73$  m<sup>2</sup>, than the standard group, suggesting that pharmacologic treatment of BP to lower levels potentially harms levels of kidney function.<sup>34</sup> As future trials decipher antihypertensive medication effects on incident CKD from the effect of lower BP, estimates of preventable events from control of BP to lower treatment threshold can be estimated, appropriately interpreted, and compared with the preventable burden of CKD caused by BP reductions under previous guidelines.

Among the clinical management approaches considered, improvements in uncontrolled BP offered the greatest opportunity to prevent incident CKD. In the general population, only approximately half of the population with elevated BP is effectively controlled to the recommended goals, leaving much room for improvement in the management strategy used to prescribe, dose, and monitor the regimen used to achieve BP targets. Recent clinical trial evidence demonstrates that proper management of patients with elevated BP can improve the suboptimal levels of BP control currently documented in the US population.<sup>34</sup> As CKD progresses, so does the difficulty in controlling BP, accentuating the importance of BP management before the development of CKD. Providing estimates of CKD events potentially preventable through reductions in uncontrolled BP above goal invites a review of current BP management practices, although a greater convergence among trial findings supporting the use of antihypertensive therapy for CKD prevention is needed.

## 5 | STUDY STRENGTHS AND LIMITATIONS

The strengths of this study include the use of a large, biracial cohort with high retention and quality-assurance protocols over an average of 20 years of follow-up. There also are several limitations that deserve consideration. The ARIC cohort was sampled from four geographically defined locales and results may not be fully generalizable to the US population, particularly for blacks who were primarily recruited from Jackson, Mississippi, and Forsyth County, North Carolina. Other US minority groups were not represented in this study. The ARIC study was restricted to participants aged 45 to 64 years at study baseline. Further, we assumed the same incidence rate reduction when calculating the number of events that could be prevented from targeted decreases in the proportion of the population with unaware, untreated, and uncontrolled BP above goal. We also estimated separate effects for unaware, untreated, and uncontrolled BP above goal. In practice, these targets would likely be promoted in combination and

associated with target-specific IRDs. Lastly, our analysis only evaluated the JNC 7 and JNC 8 BP guidelines. While the 2017 American Heart Association/American College of Cardiology BP guidelines changed the criteria for defining hypertension, compared with the JNC 7 guidelines, the 2017 guidelines only resulted in a small increase in the proportion of black and white Americans recommended for antihypertensive medication as opposed to lifestyle modifications, and thus would only result in modest improvement in the number of potential events prevented by reductions in untreated, and uncontrolled BP above goal.<sup>42</sup>

## 6 | CONCLUSIONS

As the focus of CKD research shifts from studying disease progression to disease prevention, modest BP reductions population-wide and among the high-risk population with BP above goal both provide an opportunity to substantially reduce the burden of CKD. BP thresholds used to define and treat the high-risk group are evolving, making the estimation of preventable CKD events under each guideline particularly timely as an intuitive means of expressing the potential implications of BP treatment thresholds on the development of disease. While lowering the threshold for BP treatment could increase the impact of high-risk strategies on CKD prevention, small decrements in the population level of systolic BP offer an effective method to prevent the largest number of CKD events and could be developed as an integral component of CKD prevention strategies.

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## DISCLOSURES

None.

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#### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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