Published in final edited form as:

Am J Kidney Dis. 2019 April ; 73(4): 437–458. doi:10.1053/j.ajkd.2019.01.007.

KDOQI US Commentary on the 2017 ACC/AHA Hypertension Guideline

Holly J. Kramer, MD, MPH, **Raymond R. Townsend, MD**, **Karen Griffin, MD**, **Joseph T. Flynn, MD**, **Daniel E. Weiner, MD, MS**, **Michael V. Rocco, MD, MSCE**, **Michael J. Choi, MD**, **Matthew R. Weir, MD**, **Tara I. Chang, MD, MS**, **Rajiv Agarwal, MBBS**, **Srinivasan Beddhu, MD**

Departments of Public Health Sciences (HJK) and Medicine (HJK, KG), Loyola University Chicago Stritch School of Medicine, Maywood; Hines VA Medical Center, Hines, IL (HJK, KG); Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA (RRT); Department of Pediatrics, University of Washington School of Medicine, Seattle WA (JTF); Department of Medicine, Tufts Medical Center, Boston, MA (DEW); Department of Medicine, Wake Forest School of Medicine, Winston-Salem, NC (MVR); Department of Medicine, Johns Hopkins School of Medicine (MJC); Division of Nephrology, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD (MRW); Department of Medicine, Stanford Medical School, Palo Alto, CA (TIC); Department of Medicine, Indiana University School of Medicine, Indianapolis, IN (RA); and Department of Medicine, University of Utah, Salt Lake City, UT (SB).

Abstract

Hypertension is a modifiable risk factor for cardiovascular morbidity and mortality and reduction of elevated blood pressure (BP) remains an important intervention for slowing kidney disease progression. Over the past decade, the most appropriate BP target for initiation and titration of BP-lowering medications has been an area of intense research and debate within the clinical community. In 2017, the American College of Cardiology and the American Heart Association (ACC/AHA) in conjunction with several other professional societies released new hypertension guidelines based on data from a systematic review of clinical trials and observational data. While many of the recommendations in the ACC/AHA hypertension guideline are relevant to nephrology practice, BP targets and management strategies for patients receiving dialysis are not discussed. This Kidney Disease Outcomes Quality Initiative (KDOQI) commentary focuses largely on recommendations from the ACC/AHA hypertension guidelines that are pertinent to individuals at risk of chronic kidney disease or with non–dialysis-dependent chronic kidney disease. This KDOQI commentary also includes a brief discussion of the consensus statement regarding hypertension diagnosis and management for adults receiving maintenance dialysis published by the European Renal and Cardiovascular Medicine Working Group of the European Renal

Address for Correspondence: Holly J. Kramer, MD, MPH, Loyola University Chicago, Department of Public Health Sciences, 2160 S First Ave, Maywood, IL 60153. hkramer@lumc.edu.

Peer Review: Received on November 26, 2018, following review and approval of the NKF Scientific Advisory Board (kidney.org/about/sab; authors and individuals with *AJKD* editorial roles were recused). Accepted January 8, 2019, after editorial review by a Deputy Editor.

Other Disclosures: Dr Kramer is KDOQI Vice Chair (Commentaries) and President of the NKF. Dr Rocco is KDOQI Chair. Dr Choi is Past-President of the NKF and a member of the NKF Scientific Advisory Board.

Association–European Dialysis and Transplant Association (ERA-EDTA) and the Hypertension and the Kidney working group of the European Society of Hypertension. Overall, we support the vast majority of the ACC/AHA recommendations and highlight select areas in which best diagnosis and treatment options remain controversial.

Background

Clinical trials have established that lowering systolic blood pressure (SBP) significantly reduces risk for atherosclerotic cardiovascular disease (ASCVD) events such as myocardial infarction, stroke, and heart failure (HF) among adults with high CVD risk and may also reduce mortality.[1,2] Over the past decade, the most appropriate blood pressure (BP) target for initiation and titration of BP-lowering medications has been an area of intense research and debate within the clinical community. Prior to publication of the Systolic Blood Pressure Intervention Trial (SPRINT) in 2015, most existing guidelines, including the report from the panel members appointed to the Eighth Joint National Committee (JNC8) work group, recommended a target SBP < 140 mm Hg for the majority of adults and JNC8 recommended an SBP target < 150 mm Hg for adults 60 years or older.

When the JNC8 work group released their report in 2014, SPRINT was not yet completed. SPRINT evaluated adults with increased CVD risk in the absence of diabetes mellitus (DM), randomly assigning 9,361 adults, including many older individuals and individuals with chronic kidney disease (CKD) stages 3 to 4,[3] to an intensive SBP target of <120 mm Hg or a standard SBP target of <140 mm Hg. SPRINT was stopped early for efficacy in 2015, following an interim analysis that demonstrated a significantly lower risk of CVD events and all-cause mortality with intensive SBP lowering.

In 2017, a new clinical practice guideline was issued by the American College of Cardiology and the American Heart Association (ACC/AHA) in conjunction with several other professional societies, incorporating data from a systematic review of clinical trials and observational data, including more recent trials, such as SPRINT and the Heart Outcomes Prevention Evaluation (HOPE) 3 trial.[3,4] In addition to recommendations for hypertension management, the 2017 ACC/AHA hypertension guideline also describes best practices for BP measurement and presents algorithms for hypertension goals based on comorbid conditions and age. Most of the recommendations in the ACC/AHA hypertension guideline are pertinent to nephrology practice. However, BP targets and management strategies for patients receiving dialysis are not discussed in the ACC/AHA guideline. This National Kidney Foundation–Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) commentary focuses largely on individuals at risk of CKD or with non–dialysis-dependent CKD but includes a brief discussion of the consensus statement regarding hypertension diagnosis and management for adults receiving maintenance dialysis recently published by the European Renal and Cardiovascular Medicine working group of the European Renal Association–European Dialysis and Transplant Association (ERA-EDTA) and the Hypertension and the Kidney working group of the European Society of Hypertension (ESH).5

KDOQI Commentary Process

The NKF-KDOQI Steering Committee selected members of the KDOQI work group based on their clinical and research expertise, interest in the guideline process, and experience in taking care of adults with CKD, transplant recipients, and patients receiving dialysis. KDOQI work group members reviewed recent literature and provided commentary on 3 major focus areas within the ACC/AHA guideline: (1) BP measurement, diagnosis of hypertension, and white-coat and masked hypertension; (2) definition and management of hypertension in the setting of select comorbid conditions including non–dialysis-dependent and dialysis-dependent CKD, DM, and older age; and (3) medication choices and clinical monitoring in adults with CKD. The KDOQI work group discussed the guideline via teleconference, and then all work group members and KDOQI leadership reviewed and approved the commentary after reaching consensus.

The current commentary focuses on aspects of the 2017 ACC/AHA hypertension guideline most relevant for management of BP in patients with kidney diseases, including the applicability of the ACC/AHA guideline to individuals with CKD. We also discuss knowledge gaps, research needs, and potential barriers to implementation. The grading system used by the ACC/AHA work group, which comprised class of recommendation (COR) and level of evidence (LOE), is described in Table 1. The ACA/ AHA work group determined COR and LOE independent of each other. Thus, a COR may have a high level of recommendation based on the opinion of the work group even in the setting of poor LOE.

In the following commentary, numbered text within horizontal rules is quoted directly from the ACA/AHA guideline; however, the callouts to the guideline's tables or online data supplement are generally omitted. A numbering scheme, based on the organization of the original guideline document, has been added. In addition, the COR and LOE assigned by the ACC/AHA work group have been added in italics adjacent to each ACC/AHA guideline recommendation. All material is reproduced with permission of the AHA.

Guideline Statements and Commentary

Coexistence of Hypertension and Related Chronic Conditions

2.4-1. Screening for and management of other modifiable CVD risk factors are recommended in adults with hypertension *(COR I LOE B-NR)*

Commentary—The ACC/AHA guideline discusses the high prevalence of CVD risk factors including CKD among adults with hypertension. At the initial evaluation for hypertension, the ACC/AHA guideline recommends basic laboratory testing, including complete blood count, serum sodium potassium and calcium, fasting blood glucose, lipid profile, and thyroid-stimulating hormone, and an electrocardiogram to facilitate CVD risk factor profiling and establish baseline characteristics prior to treatment.[6] In addition, the guideline recommends measurement of serum creatinine to calculate estimated glomerular filtration rate (eGFR) and assessment of albuminuria with urine dipstick at the time of evaluation. Optional tests include echo-cardiogram, serum uric acid, and quantification of a urine albumin-creatinine ratio (UACR). We agree that modifiable CVD risk factors,

including CKD, should be screened for and managed in adults with hypertension. However, consistent with the KDIGO (Kidney Disease: Improving Global Outcomes) guideline for the evaluation and management of CKD and the KDOQI commentary on that guideline,[7,8] we recommend screening with a UACR measurement instead of urine dipstick, a less sensitive test.[7,9,10]

Clinical Utility—A moderately elevated UACR between 30 and 300 m g/g, an earlier marker of kidney disease, may indicate end-organ damage from hypertension. In addition, increased albuminuria, even at very low levels, indicates heightened CVD risk.[7,11–13] Screening for CKD, including assessing albuminuria, appears cost-effective in adults with hypertension.[14–16] In contrast, CKD screening in the general population has not been shown to be cost-effective based on limited data.[17] Because the use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) is associated with treatment benefits in adults with increased albuminuria in the setting of DM or CVD,17 screening for albuminuria may inform hypertension medication choices for some patients. Consistent with guidelines from KDIGO and the American Diabetes Association (ADA), assessment of urine albumin excretion should be performed using timed urine collections or via the UACR in a random urine specimen.[7,18]

Implementation and Challenges—Urine albumin measurements currently are not standardized by clinical laboratories, although progress is being made toward standardization.[18,19] While the American College of Physicians (ACP) has recommended against serial monitoring of urine albumin excretion due to low quality of evidence[17] temporal trends may help clinicians monitor response to treatment. More research is needed to determine whether serial monitoring of urine albumin excretion can improve hypertension management and slow CKD progression.

Definition of High BP

3.1-1. BP should be categorized as normal, elevated, or stage 1 or 2 hypertension to prevent and treat high BP. *(COR I, LOE B-NR)*

Commentary—The ACC/AHA guideline defines normal BP as <120/80 mm Hg. Stage 1 hypertension is defined by SBP of 130 to 139 mm Hg or diastolic BP (DBP) of 80 to 89 mm Hg, while stage 2 hypertension is defined by SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg (Table 2). These cutpoints differ from the definition of hypertension and prehypertension in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7; Table 2).[20] The rationale for lowering thresholds for the definition of hypertension in part reflects the continuous association between BP and CVD outcomes in meta-analyses of observational studies, including excess risk of stroke, myocardial infarction, HF, and cardiovascular death with SBP > 120 mm Hg, regardless of age group, sex, or race/ethnicity.[21–23]

Clinical Utility—BP is categorized to guide research, prognosis, and treatment. The KDOQI work group believes that the definition of hypertension is reasonable in this regard,

but the initiation, choice, and titration of BP-lowering medications should incorporate patients' comorbid conditions and treatment preferences.

Implementation and Challenges—The new definition of hypertension translates to a substantially higher prevalence of hypertension in the US population. Approximately 31 million additional US adults are classified as having hypertension based on the ACC/AHA guideline and 4.2 million more US adults will now have an indication for initiation of treatment with anti-hypertensive medication.[24,25] The prevalence of hypertension in the US population based on BP ≥ 140/90 mm Hg is 32% and increases to 46% based on the ACC/AHA hypertension definition of a BP ≥ 130/80 mm Hg. The largest change in hypertension prevalence with this new definition is among adults aged 20 to 44 years. In this age group, the prevalence of hypertension among men and women increases from 11% and 10% based on BP ≥ 140/ 90 mm Hg, respectively, to 30% and 19% based on BP ≥ 130/80 mm Hg, respectively. This prevalence increase is in large part a function of the lowering of the DBP threshold to 80 mm Hg, a change that is largely based on expert opinion. This lower BP threshold for defining hypertension may increase health care utilization for younger individuals who do not routinely receive preventive health care services, and the cost-effectiveness of lower BP goals in this population remains uncertain.

Mechanisms for screening for hypertension among younger adults who do not interact with health systems will be needed to ensure that they receive counseling on lifestyle modification for BP lowering and assessment of CVD risk (see below). Infrastructure for BP screening could be implemented into the work place or within retail shops such as drug stores and grocery stores, although these would require confirmation with more rigorous clinic-based or non–clinic-based assessment methods. Public health efforts will be needed to encourage young adults to check their BP annually. Another major challenge for implementation of the ACC/AHA hypertension guideline is the need for proper measurement of BP in clinical settings, as discussed next.

Measurement of BP

4.1-1. For diagnosis and management of high BP, proper methods are recommended for accurate measurement and documentation of BP. *(COR I, LOE C-EO)*

Commentary—The KDOQI work group strongly agrees with this recommendation. The ACC/AHA hypertension guideline provides a detailed discussion of best practices for BP measurement. Most clinicians rely on office BP readings with either auscultatory or semi-automated or automated oscillometric methods. BP often differs for many patients when measured in the clinic versus in nonclinic settings, and data on the clinical relevance of nonclinic BP measurements are accumulating.[26–28] Regardless of method, BP should be measured after the patient has been sitting quietly for 5 minutes with the back supported and both feet firmly on the ground. An appropriately sized cuff should be fitted on the unclothed upper arm, and this arm should be supported at the level of the right atrium.

Clinical Utility—This guideline emphasizes the importance of best practice methods for BP measurement.

Implementation and Challenges—BP measurement is performed incorrectly in most clinic settings, leading to inaccurate results that do not reflect a patient's BP at rest. Patients frequently have BP measured prior to a 5-minute rest period, and the cuff is often placed on top of clothing. Many times the patient will be talking while the BP measurement is made. Clinics often have sphygmomanometers mounted on the wall behind the examining table; BP is then measured with the patient sitting on an examination table without their back or arm supported and without feet firmly on the ground. An inappropriately sized BP cuff is also often used.[29–31] All these factors can lead to a falsely elevated BP, which increases the risk of over-treatment and adverse events. Use of automated oscillometric devices may lead to lower BP values than auscultatory techniques.[32] If health systems intend to address the management of hypertension to reduce the risk of ASCVD and kidney disease, systemic changes in clinic design and throughput are needed to ensure accurate clinic BP measurements.

Out of Office and Self-Monitoring of BP

4.2-1. Out-of-office BP measurements are recommended to confirm the diagnosis of hypertension and for titration of BP-lowering medication, in conjunction with telehealth counseling or clinical interventions. *(COR I, LOE A^{SR})*

Commentary—The KDOQI work group supports this recommendation but acknowledges the need for more research in this area, expressing some hesitance with the assessment of the strength of the data to support the IA level of recommendation. The overwhelming majority of clinical trials that have rigorously assessed BP have relied on office BP measurement, rendering the relationship between home BP measurements and clinical outcomes less certain, especially in the setting of CKD. The greatest strength of ambulatory BP monitoring (ABPM) is its ability to assess BP during sleep and determine the presence or absence of nocturnal declines in BP, a strong predictor of cardiovascular outcomes.[33] The ability to measure BP during sleep is of particular relevance in individuals with CKD because they exhibit a higher prevalence of nondipping and reverse-dipping patterns (sleep to awake BP ratios > 1.0).[34] For example, in the African American Study of Kidney Disease and Hypertension (AASK), the prevalence of nondipping or reverse-dipping BP patterns was 80%.[34] Another study showed that out-of-office BP is better able to predict end-stage renal disease (ESRD) or death in patients with CKD and that elevated BP during sleep is associated with increased risk for all-cause mortality and a composite of ESRD or death, after adjustment for awake ambulatory BP.[35]

Properly performed home BP monitoring (HBPM) can accurately predict target-organ injury and holds several advantages over ABPM or office BP measurements.[27] First, HBPM can be conducted on multiple days. In addition, some automated HBPM machines can be programmed to measure BP during wake and sleep periods, assessing diurnal BP variations similar to ABPM.[36,37] Other studies suggest that HBPM may help overcome therapeutic inertia,[38] improve patient adherence,[39] reduce costs of care[40] and improve efficacy.[41] Advantages of either ABPM or HBPM over clinic BP measurements include avoidance of observer bias, digital preference, and detection of white-coat and masked hypertension.

Clinical Utility—Both ABPM and HBPM are effective tools to manage individuals with hypertension. With appropriate infrastructure, HBPM can be incorporated with telemonitoring to effectively manage hypertensive individuals,[42–45] with limited data suggesting lower risk of major cardiovascular events and all-cause mortality when used in this manner.[46] More studies are needed to determine whether HBPM helps prevent CKD progression.

Implementation and Challenges—In the United States, HBPM may be a more practical tool than ABPM to diagnose and manage hypertension, reflecting the current reimbursement structure, the availability of HBPM, increasing telemedicine infrastructure, and the ability of HBPM to provide data over a long period. An ongoing challenge is that most home BP monitors lack calibration and may give inaccurate results.[47] Devices instead are simply cleared for sale by the US Food and Drug Administration 5 10 (k) mechanism. Due to significant heterogeneity in previously conducted trials, additional studies are needed to substantiate the benefits of HBPM in clinical settings.[38,39,46]

Masked and White-Coat Hypertension

4.4-1. In adults with an untreated S B P greater than 130 mm Hg but less than 160 mm Hg or DBP greater than 80 mm Hg but less than 100 mm Hg, it is reasonable to screen for the presence of white coat hypertension by using either daytime ABPM or HBPM before diagnosis of hypertension. *(COR lla, LOE B-NR)*

4.2-2. In adults with white coat hypertension, periodic monitoring with either ABPM or HBPM is reasonable to detect transition to sustained hypertension. *(COR lla, LOE C-LD)*

4.4-3. In adults being treated for hypertension with office BP readings not at goal and HBPM readings suggestive of a significant white coat effect, confirmation by ABPM can be useful. *(COR lla, LOE C-LD)*

4.4-4. In adults with untreated office BPs that are consistently between 120 mm Hg and 129 mm Hg for SBP or between 75 mm Hg and 79 mm Hg for DBP, screening for masked hypertension with HBPM (or ABPM) is reasonable. *(COR lla, LOE B-NR)*

4.4-5. In adults on multiple-drug therapies for hypertension and office BPs within 10 mm Hg above goal, it may be reasonable to screen for white coat effect with HBPM (or ABPM). *(COR lib, LOE C-LD)*

4.4-6. It may be reasonable to screen for masked uncontrolled hypertension with HBPM in adults being treated for hypertension and office readings at goal, in the presence of target organ damage or increased overall CVD risk. *(COR lib, LOE C-EO)*

4.4-7. In adults being treated for hypertension with elevated HBPM readings suggestive of masked uncontrolled hypertension, confirmation of the

diagnosis by ABPM might be reasonable before intensification of antihypertensive drug treatment. *(COR lib, LOE C-EO)*

Commentary—While none of these recommendations are supported by well-designed clinical trials, accumulating evidence suggests that APBM and HBPM are useful for identifying both white-coat and masked hypertension, thereby improving hypertension management. An increase in BP that occurs in a clinic or office setting is called a white-coat effect. Not infrequently, clinic or office BP exceeds BP assessed in the home or with ABPM. If a person with this BP pattern is untreated for hypertension, the phenomenon is called white-coat hypertension. If they are treated for hypertension, then it is called white-coat uncontrolled hypertension. Agreement on this nomenclature is not universal, but it is sensible in our opinion. There is debate on whether CVD risk is increased in patients exhibiting white-coat effects, and recent large-scale general population studies suggest that the potential increase in CVD attributable to white-coat effects is driven by age.[48]

Masked hypertension is when clinic or office BP is lower while home or ambulatory BP is elevated. The presence of masked hypertension may indicate non-adherence to medication and is associated with higher risk of target-organ damage.[49] The prevalence of white-coat uncontrolled hypertension among 1,492 participants in the Chronic Renal Insufficiency Cohort (CRIC) was only 4%, while the prevalence of masked hypertension was more than 6-fold higher at 28%.[50] In A ASK, masked hypertension was present in 43% .[34]

To put white-coat and masked hypertension effects in perspective, the large Spanish ABPM registry reported that in untreated patients with white-coat hypertension, there was a 2-fold increase in death events during a 4.7-year follow-up compared with those normotensive both in the office and by ABPM.[51] In contrast, no statistically significant increase in mortality was noted with white-coat hypertension among adults with treated hypertension (white-coat uncontrolled hypertension). The most intriguing finding in this registry was that those with masked hypertension, whether on treatment or not, had the highest mortality rate, surpassing that of those with uncontrolled hypertension in the clinic or by ABPM.

Clinical Utility—Nephrologists should be aware that masked hypertension is common among adults with CKD and potentially that providers should not rely solely on clinic BP measurements for the diagnosis and/or management of hypertension in this population.[50,52] More studies are needed to apply these data clinically.

Implementation and Challenges—In the United States, Medicare and most insurance companies do not cover ABPM except for the diagnosis of white-coat hypertension. More studies are needed to determine optimal strategies for utilization of HBPM for adults with and without CKD, and payment policy changes are needed to increase ABPM utilization.

Secondary Forms of Hypertension

5.4-1. Screening for specific form(s) of secondary hypertension is recommended when the clinical indications and physical examination findings listed in Table 13 [in original guideline] are present or in adults with resistant hypertension. *(COR I, LOE C-EO)*

5.4-2. If an adult with sustained hypertension screens positive for a form of secondary hypertension, referral to a physician with expertise in that form of hypertension may be reasonable for diagnostic confirmation and treatment. *(COR lib, LOE C-EO)*

Primary Aldosteronism

5.4.2-1. In adults with hypertension, screening for primary aldosteronism is recommended in the presence of any of the following concurrent conditions: resistant hypertension, hypokalemia (spontaneous or substantial, if diuretic induced), incidentally discovered adrenal mass, family history of early-onset hypertension, or stroke at a young age. *(COR I, LOE C-EO)*

5.4.2-2. Use of the plasma aldosterone: renin ratio is recommended when adults are screened for primary aldosteronism. *(COR I, LOE C-LD)*

5.4.2-3. In adults with hypertension and a positive screening test for primary aldosteronism, referral to a hypertension specialist or endocrinologist is recommended for further evaluation and treatment. *(COR I, LOE C-EO)*

Renal Artery Stenosis

5.4.3-1. Medical therapy is recommended for adults with atherosclerotic renal artery stenosis. *(COR I, LOE A)*

5.4.3-2. In adults with renal artery stenosis for whom medical management has failed (refractory hypertension, worsening renal function, and/or intractable HF) and those with nonatherosclerotic disease, including fibromuscular dysplasia, it may be reasonable to refer the patient for consideration of revascularization (percutaneous renal artery angioplasty and/or stent placement). *(COR lib, LOE C-EO)*

Obstructive Sleep Apnea

5.4.4-1. In adults with hypertension and obstructive sleep apnea, the effectiveness of continuous positive airway pressure (CPAP) to reduce BP is not well established. *(COR lib, LOE B-R)*

Commentary—The ACC/AHA guideline includes an algorithm to help identify patients who should be screened for secondary hypertension. Overall, the work group agrees with these recommendations regarding evaluation and treatment of secondary causes of hypertension.

Clinical Utility—Primary aldosteronism is present in up to 20% of individuals with resistant hypertension and is frequently overlooked due to the misconception that primary aldosteronism does not occur in the absence of hypokalemia. The guideline discusses the utility of plasma aldosteronerenin ratio and suggests that a plasma aldosterone concentration should be as low as 10 ng/dL in order for a given ratio to be determined positive. However,

this aldosterone level is considered potentially indicative of hyperaldosteronism when collected with the patient in a supine position at the end of a 2-L saline suppression test.[53] Clinically, many clinicians do not apply the aldosteronerenin ratio unless a seated aldosterone level is >16 ng/dL without saline suppression. The aldosterone-renin ratio also must be evaluated in the setting of a normal serum potassium level and absence of aldosterone antagonist use. However, in the setting of hypokalemia, a plasma aldosterone level > 2 0 ng/dL and a renin level below detection basically confirm the diagnosis of hyperaldosteronism.

Although multiple trials have evaluated strategies for treating hypertension in individuals with renal arterial disease, optimal treatment strategies for atherosclerotic renal artery disease remain uncertain, reflecting the heterogeneous nature of renal artery stenosis (ostial vs non-ostial lesions, bilateral vs unilateral disease, and varying degrees of chronicity and severity). Both the Angioplasty and Stenting for Renal Artery Lesions (ASTRAL) and the Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) trials demonstrated no benefit of renal angioplasty over medical therapy.[54,55] The CORAL trial recruited adults with atherosclerotic renal artery disease defined as >60% stenosis and hypertension or CKD stages 3 to 4. Individuals with a serum creatinine level > 4 mg/dL, stenosis not treatable with a single stent, or fibromuscular dysplasia were excluded. Participants were then randomly assigned to medical therapy alone versus stenting combined with medical therapy. In the stenting with medical therapy group, each renal artery with >60% stenosis was stented. Annual eGFR decline was1.5 ± 7.0 mL/min /1.73 m^2 with stenting and 2.3 ± 6.3 m L/m in/ 1.73 m^2 without stenting (P = 0.18). Viewed in the context of other previously published studies, these results do not support routine use of stenting of unilateral renal artery stenosis due to atherosclerosis.

However, reflecting weak evidence, in individuals with significant atherosclerotic renal artery stenosis (>60%) and inability to control BP with medical management, stenting of the atherosclerotic renal artery could be considered, particularly in cases of bilateral renal artery stenosis, which were a priori excluded from the CORAL study. Other potential indications for renal artery stenting include flash pulmonary edema and the presence of nonatherosclerotic renal artery stenosis, such as that seen in fibromuscular dysplasia.

The guideline describes sleep apnea as a common cause of secondary hypertension. It should be noted that randomized clinical trials (RCTs) of continuous positive airway pressure for treatment of sleep apnea have not demonstrated consistent BP lowering in adults with hypertension.[56,57]

Implementation Issues—Primary care providers should refer patients with apparent treatment-resistant hypertension or with apparent secondary hypertension to hypertension specialists such as nephrologists, cardiologists, and endocrinologists. Treatment of obstructive sleep apnea will likely not substantially reduce BP, although it may have other beneficial effects for patients. Thus, treatment of hypertension should not be delayed until after initiation of treatment for sleep apnea. Larger studies with long-term follow-up are needed to further delineate the benefits of sleep apnea treatment for BP lowering and prevention of end-organ damage.[58]

Resistant Hypertension

Summary of Guideline Recommendations—In section 11.1, the ACC/AHA guideline defines resistant hypertension as BP ≥ 130/80 mm Hg in the setting of use of at least 3 antihypertensive medications with complementary mechanisms of action (a diuretic should be one of the medications) or when 4 or more medications are needed to achieve hypertension control. Previously, most studies defined treatment-resistant hypertension as BP ≥ 140/90 mm Hg despite use of at least 3 medications. In 2008, the AHA amended this definition by adding controlled hypertension (BP < 140/90 mm Hg) with at least 4 different medications as an additional criterion due to higher CVD risk observed in this group.[59]

The ACC/AHA guideline does not include specific recommendations regarding resistant hypertension but discusses the fact that nephrologists, endocrinologists, and hypertension specialists should be utilized in the management of resistant hypertension. The guideline provides an algorithm to delineate causes for resistant hypertension. This algorithm includes evaluating pseudo-resistance such as nonadherence or white-coat hypertension, identifying and reversing lifestyle factors, and discontinuing or minimizing interfering substances, such as use of nonsteroidal anti-inflammatory drugs or oral contraceptives. An evaluation of secondary causes of hypertension should then be completed. Critically, the term resistant hypertension may not be relevant for patients with CKD because kidney disease impairs sodium excretion and complicates hypertension management.

Commentary—The KDOQI work group suggests that treatment-resistant hypertension be termed “apparent treatment-resistant hypertension” because cases of treatment resistance may reflect poor medication adherence, improper measurement of BP, use of noncomplementary medications, or presence of undiagnosed secondary forms of hypertension. It is estimated that only 10% to 15% of patients with apparent treatment-resistant hypertension have true resistance to antihypertensive medications, with at least 50% of apparent treatment-resistant hypertension due to poor drug adherence and high-sodium diets and the remainder due to secondary causes including CKD.[60]

Apparent treatment-resistant hypertension is extremely common among individuals with CKD. In the CRIC Study, 40% had apparent treatment-resistant hypertension as defined by BP ≥ 140/90 mm Hg with 3 or more antihypertensive medications or BP < 140/90 mm Hg with use of 4 or more medications. Odds of apparent treatment-resistant hypertension increased with older age and greater body mass index, and prevalence was higher among men, African Americans, and those with DM. Apparent treatment-resistant hypertension was also associated with higher CVD risk and mortality.[61] The AHA/ACC guideline includes a short but excellent discussion regarding the importance of using antihypertensive medications with different mechanisms of action to address apparent treatment-resistant hypertension.

Clinical Utility—Nephrologists are frequently consulted to assist with the care of apparent treatment-resistant hypertension. Selection of complementary medications and improving drug adherence often resolve treatment resistance. Thiazide and thiazide-like diuretics used in combination with ACE inhibitor/ARB or aldosterone antagonists can be very effective in

patients with apparent treatment-resistant hypertension.[62,63] The KDIGO guideline for hypertension management in CKD also discusses use of aldosterone antagonists as an adjunct to antihypertensive agents to treat apparent treatment-resistant hypertension.[64]

Implementation Issues—Unfortunately, nonmedical interventions such as renal sympathetic nerve ablation or carotid baroreceptor pacing have not shown sustained success,[65,66] and we continue to depend on modification of antihypertensive medication regimens complemented by diet and exercise to manage treatment-resistant hypertension.

Nonpharmacologic Interventions

6.2-1. Weight loss is recommended to reduce BP in adults with elevated BP or hypertension who are overweight or obese. *(COR I, LOE A)*

6.2-2. A heart-healthy diet, such as the DASH (Dietary Approaches to Stop Hypertension) diet, that facilitates achieving a desirable weight is recommended for adults with elevated BP or hypertension. *(COR I, LOE A)*

6.2-3. Sodium reduction is recommended for adults with elevated BP or hypertension. *(COR I, LOE A)*

6.2-4. Potassium supplementation, preferably in dietary modification, is recommended for adults with elevated BP or hypertension, unless contraindicated by the presence of CKD or use of drugs that reduce potassium excretion. *(COR I, L E A)*

6.2-5. Increased physical activity with a structured exercise program is recommended for adults with elevated BP or hypertension. *(COR I, LOE A)*

6.2-6. Adult men and women with elevated BP or hypertension who currently consume alcohol should be advised to drink no more than 2 and 1 standard drinks per day, respectively. *(COR I, LOE A)*

Commentary—The KDOQI work group strongly agrees with these recommendations.

Clinical Utility—Most patients do not receive adequate counseling for lifestyle changes such as improved patterns of diet, exercise, and alcohol consumption or smoking cessation. The Dietary Approaches to Stop Hypertension (DASH) diet, recommended for prevention and treatment of hypertension,[67] encourages high intake of fruits and vegetables and low-fat dairy products and low intake of fats and red meat. The PREMIER (Prevention of Myocardial Infarction Early Remodeling) clinical trial demonstrated substantial BP lowering with lifestyle changes including weight loss and exercise combined with the DASH diet.[68] The DASH diet has also been associated with lower risk of CKD.[69,70] Use of the DASH diet or other dietary modifications for hypertension management in the setting of CKD should utilize medical nutrition therapy services provided by a registered dietitian because individual patients may have specific dietary restrictions that require modification of the DASH diet. Of note, the DASH diet should not be used by people treated with dialysis and may need to be modified in people with advanced kidney disease.

Implementation Issues—Implementation of lifestyle modification for management of hypertension is extremely difficult in most clinical settings. The typical Western diet, in contrast to the DASH diet, is high in red meat and low in fruits and vegetables. Currently, <20% of US adults consume the recommended servings of fruits and vegetables.[71,72] A comprehensive team-based approach is essential for implementing lifestyle modification as an effective tool for lowering BP. Insurance coverage for dietician-led medical nutrition therapy is variable in the United States, focused on those with DM or advanced CKD rather than on controlling risk factors that lead to these severe chronic diseases. Insurance companies and health systems must create a health care system that is conducive to a broad team-based care approach as discussed in the ACC/AHA guideline.[6]

Treatment of High BP

8.1.2-1. Use of BP-lowering medications is recommended for secondary prevention of recurrent CVD events in patients with clinical CVD and an average SBP of 130 mm Hg or higher or an average DBP of 80 mm Hg or higher, and for primary prevention in adults with an estimated 10-year atherosclerotic cardiovascular disease (ASCVD) risk of 10% or higher and an average SBP 130 mm Hg or higher or an average DBP 80 mm Hg or higher. *(COR I, LOE: A for SBP; C-EO for DBP)*

8.1.2-2. Use of BP-lowering medication is recommended for primary prevention of CVD in adults with no history of CVD and with an estimated 10-year ASCVD risk <10% and an SBP of 140 mm Hg or higher or a DBP of 90 mm Hg or higher. *(COR I, LOE C-LD)*

Commentary—The KDOQI work group is generally supportive of the SBP thresholds. The current evidence supports an SBP goal of <130 mm Hg in CKD stages 1 to 3, particularly in those with elevated levels of urine albumin excretion.[73,75] Based on a lack of data evaluating DBP targets, the KDOQI work group deliberately focused on SBP targets in this commentary. In the view of the work group, the main exception to the 13 0–mm Hg target for SBP is for persons with a previous stroke; in these individuals, the work group recommends BP lowering for SBP values ≥ 140 mm Hg. In stage 4 CKD, limited data from existing trials support an SBP goal< 130 mm Hg, and more studies are needed to fully determine optimal BP goals in this group. There are no large definitive RCTs on SBP goals in dialysis-dependent or non–dialysis-dependent stage 5 CKD, and the ACC/AHA guideline thresholds do not apply to these patients.

Baseline ASCVD risk is important for determining the optimal BP targets for pharmacologic risk factor management. The ACC/AHA guideline recommends initiation of BP-lowering medications for adults with SBP > 130 mm Hg and DBP > 80 mm Hg if the 10-year ASCVD risk using the ACC/AHA Pooled Cohort Equations (http://tools.acc.org/ASCVD-Risk-Estimator/) is ≥10% or if the patient has clinical ASCVD. Both DM and CKD are considered high risk regardless of the 10-year calculated ASCVD risk.[76] While existing data generally favor this recommendation, not all meta-analyses support treatment of patients with SBP < 140 mm Hg to the ACC/AHA-recommended threshold SBP <130 mm Hg in the absence of prior CVD, stressing the need for optimal risk prediction.[24]

Implementation Challenges—Individuals with severely reduced eGFRs (<30 mL/min/1.73 m^2) are often excluded from clinical trials and notably were excluded from the ACCORD (Action to Control Cardiovascular Risk in Diabetes) BP trial, which assessed BP thresholds in adults with type 2 DM and hypertension.[77] Other trials that focused on adults with diabetic kidney disease have not evaluated lower SBP thresholds consistent with the ACC/AHA guideline recommendation. Although it is likely that most individuals with CKD have high CVD risk, research is needed to improve calibration and discrimination of risk instruments in CKD to allow optimal prognostication and risk stratification. This research should account for CKD stage and level of albuminuria. See also discussion of BP goals in the "Hypertension in Patients with Comorbidities: CKD" section.

Medication Choices

8.1.4-1. Simultaneous use of an ACE inhibitor, ARB, and/or renin inhibitor is potentially harmful and is not recommended to treat adults with hypertension. *(COR III: Harm, LOE A)*

8.1.6-1. For initiation of antihypertensive drug therapy, first- line agents include thiazide diuretics, CCB s, and ACE inhibitors or ARBs. *(COR I, LOE A^{SR})*

Commentary—Recommended first-line agents for BP reduction include thiazide diuretics, ACE inhibitors, ARBs, and calcium channel blockers (CCBs) due to their association with consistent reductions in CVD risk.[6] β-Blockers are not included in this list because these drugs are now considered significantly less effective for CVD prevention[78] and stroke protection than diuretics or CCBs in the absence of ischemic heart disease or HF.[79]

The KDIGO work group disagreed with the statement in the ACC/AHA guideline noting that thiazide diuretics should not be used in advanced CKD due to lack of efficacy. We agree with the recommendations that drug selection should be guided by age; concurrent medications; out-of-pocket costs; comorbid conditions such as gout, DM, and CKD; and history of drug tolerance. We also agree that providers should avoid using 2 or more drugs from the same class to treat hypertension with the exception of diuretics that have different mechanisms of action. The KDOQI work group specifically noted that although the combination of ACE inhibitors and ARBs could provide clinical benefits such as reducing urine protein excretion, this combination should be avoided to solely treat hyper-tension due to increased risks of hyperkalemia and acute kidney injury (AKI).[80,81]

Clinical Utility—In the setting of stages 1 to 3 CKD and severely increased urine albumin excretion, either ACE inhibitors or ARBs should be considered as first-line agents unless there are contraindications. In individuals with severely increased urine albumin excretion, ACE inhibitors and ARBs reduce the risk of kidney end points, such as rate of eGFR decline, 50% decline in eGFR, and incident kidney failure.[82]

Thiazide and thiazide-like diuretics are effective drugs for reducing BP but are often not utilized in advanced CKD due to the perceived absence of effectiveness.[83] Although no RCT to date has compared BP-lowering effects of thiazide diuretics with other drug classes in the setting of advanced CKD (eGFR < 30 mL/min/1.73 m^2), one study of 14 adults with a mean

eGFR of 26.8 ± 8.8 mL/min/1.73 m^2 showed that average 24- hour ambulatory BP levels declined by 10.5 ± 3 .1 mm Hg, with average reduction of 1.2 kg of body weight compared to baseline after 12 weeks of treatment with 25 mg of chlorthalidone.[84] Other previous studies demonstrated weight reductions and diuresis with chlorthalidone in the setting of advanced CKD. If specifically targeting diuresis rather than BP, maximal diuretic effects are seen when thiazide diuretics are combined with loop diuretics, but potassium levels should be monitored closely.[83,85–88] Meta-analyses of clinical trials comparing different drug classes have not demonstrated the superiority of any drug class compared to thiazide or thiazide-like diuretics for prevention of CVD.[79] Clinical trials have shown lower rates of kidney outcomes other than kidney failure with the use of ACE inhibitors versus thiazide diuretics, but differences are not statistically significant (Fig 1) .[79] Of note, chlorthalidone rather than hydrochlorothiazide has been used in many of the major BP trials, and specifically in more advanced CKD, chlorthalidone is likely a superior choice to hydrochlorothiazide.[89]

Implementation Issues—Clinicians may be hesitant to use thiazide diuretics for the management of hypertension.[90] A small body of evidence suggests that thiazide diuretics, especially chlorthalidone, may be effective for BP management in patients with advanced CKD. Thiazide diuretic treatment should not automatically be discontinued when eGFR decreases to <30 mL/min/1.73 m^2. Risks and benefits associated with thiazide diuretics should be assessed in each patient. Side effects include electrolyte level abnormalities and hyperuricemia; risks of hyponatremia in particular may be heightened among the elderly. However, these drugs may be effective for BP lowering, can be dosed once per day, and are associated with lower risk of incident HF.79 We recommend checking electrolyte levels and eGFRs within 4 weeks of initiation of treatment with a thiazide and following thiazide dose escalation.

Monitoring Strategies to Improve Control of BP in Patients on Drug Therapy for High BP

8.3.2-1. Follow-up and monitoring after initiation of drug therapy for hypertension control should include systematic strategies to help improve BP, including use of HBPM, team-based care, and telehealth strategies. *(COR I, LOE A)*

Commentary—Careful follow-up and monitoring are critical for safely achieving the SBP goal. During uptitration of medications to achieve the recommended SBP goal of <130 mm Hg, we recommend HBPM to avoid hypotension (SBP < 110 mm Hg); additionally, following the addition or titration of medications that may affect electrolyte levels or kidney function, it is reasonable to check a basic metabolic profile within 2 to 4 weeks. It is also important to monitor for changes in patient symptoms, including fatigue and light-headedness. Patients need to be trained and instructed to perform HBPM and be instructed to hold or reduce anti-hypertensive medication doses when oral intake is decreased or with vomiting or diarrhea, during which volume depletion and AKI could occur. We recommend clinic follow-up every 6 to 8 weeks until the BP goal is safely achieved. When the target BP is achieved, laboratory monitoring and clinic follow-up should occur every 3 to 6 months, depending on medications utilized and the stability of the patient.

Hypertension in Patients With Comorbidities: CKD

9.3-1. Adults with hypertension and CKD should be treated to a BP goal of less than 130/80 mm Hg. *(COR I, LOE B-R^{SR} for SBP, C EO for DBP)*

9.3-2. In adults with hypertension and CKD (stage 3 or higher or stage 1 or 2 with albuminuria [≥300 mg/d, or ≥300 mg/g albumin-to-creatinine ratio or the equivalent in the first morning void]), treatment with an ACE inhibitor is reasonable to slow kidney disease progression. *(COR lla, LOE B-R)*

9.3-3. In adults with hypertension and CKD (stage 3 or higher or stage 1 or 2 with albuminuria [≥300 mg/d or ≥300 mg/g albumin-to-creatinine ratio or the equivalent in the first morning void]), treatment with an ARB may be reasonable if an ACE inhibitor is not tolerated. *(COR lib, LOE C-EO)*

Commentary—The ACA/AHA guideline states that the "vast majority of patients with CKD have a 10-year ASCVD risk ≥ 10%, placing them in the high-risk category that requires initiation of antihypertensive drug therapy at BP ≥ 130/ 80 mm Hg."[6] The most recent nephrology-focused guideline and commentary published by KDIGO in 2012 was more nuanced, emphasizing the need for individualization of BP targets and hypertension management strategies based on comorbid conditions and age.[64,91] However, this guideline was published before completion of SPRINT. In the KDIGO 2012 guideline, a target BP < 130/80 mm Hg was suggested in persons with CKD in the presence of persistent albuminuria, defined as urine albumin excretion rate ≥ 30 mg/d or UACR ≥ 30 mg/g in a random specimen. This suggested BP goal for patients with CKD and moderate or severely increased albuminuria conflicted with recommendations by the JNC8 committee report published in 2014.[92] In contrast to previous guidelines,[20] the JNC8 work group recommended a target BP < 140/90 mm Hg for persons aged 18 to 69 years with eGFRs < 60 mL/min/1.73 m^2 or in people of any age with albuminuria. A more intensive BP target was not recommended in persons with non–dialysis-dependent CKD due to lack of evidence that a lower BP target reduces risk of stroke, heart disease, mortality, or kidney failure. Table 3 shows the differing BP targets for CKD by guideline group.

Three separate trials completed prior to 2014 suggested that a BP goal < 130/80 mm Hg led to slower rates of CKD progression in adults with eGFRs < 60 mL/min/1.73 m^2 in the presence of increased urine protein excretion compared to a BP goal < 140/90 mm Hg, but did not show a benefit on CVD, death, or kidney failure during the conduct of the trials.[74,75,93–95] Both AASK and the Modification of Diet in Renal Disease (MDRD) Study examined effects of a mean arterial pressure goal < 107 versus <92 mm Hg. During the trial phase, neither study noted a beneficial effect of a lower BP goal on CVD or kidney outcomes. In AASK, the trial was followed by a cohort phase with follow-up ranging from 8.8 to 12.2 years.75 In the entire AASK cohort, targeting the lower BP goal did not result in lower risk of the composite outcome of doubling of creatinine level, ESRD, or death during the trial phase (hazard ratio [HR], 0.88; 95% confidence interval [Cl], 0.71–1.09) and in the trial plus cohort phases (HR, 0.91; 95% Cl, 0.77–1.08). However, in the subgroup with baseline protein-creatinine ratio > 220 mg/g, the corresponding HRs of ESRD or doubling of serum creatinine level in the trial phase (HR, 0.76; 95% Cl, 0.55–1.04) and trial plus cohort

phases (HR, 0.76; 95% Cl, 0.58–0.99) reflected a risk reduction with the lower versus the standard BP goal, indicating a potential benefit of a lower BP goal in this subgroup (Table 4). The findings from long-term observational follow-up of the MDRD Study74 also support beneficial effects of lower BP goals in individuals with advanced CKD. In that study, the lower BP group as compared to the usual BP group had a lower risk for kidney failure (HR, 0.68; 95% Cl, 0.57–0.82) and the composite of kidney failure and death (HR, 0.77; 95% Cl, 0.65–0.91).

The potential CVD and mortality benefits of more intensive BP lowering in nondiabetic adults with eGFRs between 20 and 60 mL/min/1.73 m^2 were also investigated in a subset of 2,646 participants in SPRINT.3'73 There was a nonsignificant reduction in the composite CVD outcome with intensive SBP lowering in the CKD subgroup (HR, 0.81; 95% Cl, 0.63–1.05) that was consistent with the effect of lower SBP targets seen in SPRINT participants with higher eGFRs at baseline; overall mortality was significantly lower in those randomly assigned to intensive SBP lowering (HR, 0.72; 95% Cl, 0.53–0.99).[73] It should be noted that CKD was a predefined subgroup, but SPRINT was not powered to detect significant differences in the primary CVD outcome in the subgroup with low eGFRs.

Clinical Utility—Based on meta-analyses of well-designed clinical trials,[79] an SBP target <130 mm Hg seems reasonable for individuals with CKD stages 1, 2, 3a, and 3b, with stronger evidence for persons without DM or persons with moderate to severely increased urine albumin excretion; in contrast, although potentially reasonable, the DBP target remains opinion based. For individuals with CKD stages 4 and 5 not receiving dialysis, there are insufficient data because most trials, including SPRINT, excluded patients with advanced CKD. The recommendation for treatment with either an ACE inhibitor or an ARB is graded as Ha and lib, respectively, meaning that the strength of the recommendation is moderate for ACE-inhibitor use and weak for ARB use. Meta-analyses have shown that use of an ACE inhibitor compared to placebo significantly reduces the risk for kidney failure,[17,96] but this benefit appears driven by trials limited to persons with high levels of urine albumin excretion.[97–99] Kidney failure outcomes are uncommon in general population studies, in which few persons have severely increased urine albumin excretion or advanced CKD; lack of inclusion of persons with CKD markedly reduces the power of a trial to detect differences in kidney outcomes with a given intervention.

Clinical Utility—For individuals without moderate or severely increased urine albumin excretion, any first-line BP-lowering agent can be used, and among patients with CKD, often multiple medications will be required. Options for BP reduction, even at low eGFRs, may include thiazide diuretics, ACE inhibitors or ARBs, or CCBs.[6] In addition, volume control with the use of loop diuretics may be needed in patients with advanced CKD with signs of volume overload and in patients with nephrotic-range proteinuria. The initial selection of an antihypertensive agent should be based on an assessment of potential risks and benefits, particularly in patients with advanced CKD (Fig 1) .[79]

Implementation Issues—Lack of high-quality data impedes recommendations for specific BP targets in individuals with CKD stages 4, 5, and 5D. Although observational data in these populations report outcomes associated with BP levels, causal inferences for

BP targets should not be concluded as exemplified by prior observational reports contradicted by RCT data[100–102] The Blood Pressure Control for Renoprotection in Patients With Non-Diabetic Chronic Renal Disease (REIN-2) trial,[95] one of the few trials to include individuals with CKD stage 4, was stopped early for futility. In addition, the achieved BP separation between the intensive and standard BP-lowering groups in REIN-2 was small. In CKD stages 4 to 5, the risk of AKI is higher than in earlier CKD stages. In addition, among older individuals with CKD, DBP is often low, reflecting increased arterial stiffness. Thus, more intensive BP lowering in advanced CKD may accelerate the need for kidney replacement therapy in some patients.

Hypertension After Kidney Transplantation

9.3.1-1. After kidney transplantation, it is reasonable to treat patients with hypertension to a BP goal of less than 130/80 mm Hg. *(COR lla, LOE B-NR for SBP, C-EO for DBP)*

9.3.1-2. After kidney transplantation, it is reasonable to treat patients with hypertension with a calcium antagonist on the basis of improved GFR and kidney survival. *(COR lla, LOE B-R)*

Commentary—The work group agrees that these recommendations are likely reasonable but acknowledges the lack of strong evidence supporting either a lower BP target in this population or the preferential use of CCBs.

Clinical Utility—Evidence supporting optimal BP levels for maintaining allograft function or for prevention of CVD events in kidney transplant recipients remains scant and clinical trials are needed to identify best practices.[103] The KDIGO CKD guideline and the commentary from KDOQI provide recommendations and discussion of the diagnosis and treatment of hypertension in patients with CKD or kidney transplant recipients.[7,91] However, these recommendations are based on expert opinion, rather than high-level evidence from RCTs.

Implementation Issues—Achieving a BP goal in patients after kidney transplantation is often challenging due to the hypertensive effects of calcineurin inhibitors and steroids and the presence of reduced eGFR, diseased native kidneys, and weight gain. CCBs help counteract the arteriolar vasoconstriction of calcineurin inhibitors and are a first-line therapy[104]; however, they may need to be used with caution due to some drug-drug interactions with immunosuppression agents.[105] Other agents may also be effective. For example, Moes et al[106] performed a brief crossover trial and noted similar BP control for chlorthalidone and amlodipine, with slightly lower eGFRs but less proteinuria with chlorthalidone and more lower-extremity edema with amlodipine.

Diabetes Mellitus

9.6-1. In adults with DM and hypertension, antihypertensive drug treatment should be initiated at a BP of 130/80 mm Hg or higher with a treatment goal of less than 130/80 mm Hg. *(COR I, LOE B-R^{SR} for SBP, C-EO for DBP)*

9.6-2. In adults with DM and hypertension, all first-line classes of antihypertensive agents (i.e., diuretics, ACE inhibitors, ARBs, and CCBs) are useful and effective. *(COR I, LOE A^{SR})*

9.6-3. In adults with DM and hypertension, ACE inhibitors or ARBs may be considered in the presence of albumin-uria. *(COR lib, LOE B-NR)*

Commentary—Hypertension affects nearly all adults with both DM and CKD, and the combination of DM and hypertension is associated with a high risk of CVD, retinopathy, neuropathy, CKD, and mortality.[18] The ACC/AHA guideline recommends a BP target < 130/80 mm Hg for persons with DM. The issue of BP targets in adults with DM remains controversial because the primary results of the ACCORD BP trial, the largest BP goal study in type 2 DM, did not show evidence of beneficial effects of intensive SBP lowering. Briefly, the ACCORD BP trial randomly assigned 4,733 hypertensive adults with DM to either a target SBP <120 mm Hg or a target SBP < 140 mm Hg.[77] These participants were also randomly assigned to either standard glucose lowering (target hemoglobin A_{lc} of 7.0%–7.9%) or intensive glucose lowering (glycated hemoglobin A_{lc} < 6.0%).[107] The intensive glucose- lowering arm was discontinued after 3.5 years due to an increased risk of CVD death (HR, 1.22; 95% CI, 1.01–1.46) and all-cause death (HR, 1.35; 95% CI, 1.04–1.76).[107] The 2 BP arms were completed over 5 years and were not terminated prematurely. In the primary analysis that combined the intensive and standard glycemia arms, intensive SBP lowering was not associated with a significant change in the primary outcome of myocardial infarction, stroke, or CVD mortality (HR, 0.88; 95% CI, 0.73–1.06) or in all-cause mortality (HR, 1.07; 95% CI, 0.85–1.35) compared to standard SBP lowering.[7]

There is much debate about the reasons for the lack of significant effects of intensive SBP lowering in ACCORD BP given the highly significant findings observed in SPRINT.3 A participant-level pooled meta-analysis of SPRINT and ACCORD BP participants suggested that in the combined cohort, intensive SBP lowering decreased the risk of CVD events.[108] However, these results were primarily driven by the SPRINT data.[108] Differences in BP measurement techniques,[109] the achieved SBP separation,[110] and selection criteria[111] have also been proposed as potential explanations. However, the most widely cited reason for the discordant results is a lack of statistical power in ACCORD BP.[108,112] This is controversial because total numbers of CVD and death events were actually higher in ACCORD BP due to a higher event rate and longer duration of follow-up. Hence, a lack of statistical power in ACCORD BP compared to SPRINT does not appear to provide a sufficient explanation for the divergent results.

An alternative explanation is that there was an interaction between the intensive glycemia intervention and the intensive SBP-lowering intervention in ACCORD BP that may have masked the potential beneficial effects of the SBP intervention. This hypothesis is supported by a recent reanalysis of ACCORD BP and SPRINT data.[113] Intensive SBP lowering decreased the hazard of the composite CVD end point similarly in SPRINT (HR, 0.75; 95% CI, 0.64–0.89) and the ACCORD BP standard glycemia arm (HR, 0.77; 95% CI, 0.63–0.95; interaction P = 0.87). However, the effect of intensive SBP lowering on the composite CVD

end point in the ACCORD BP intensive glycemia arm (HR,1.04; 95% CI, 0.83–1.29) was significantly different from SPRINT (interaction P=0.02).

Clinical Utility—The ADA now recommends a BP < 130/80 mm Hg in adults with DM with high CVD risk if the goal can be achieved without "undue treatment burden."[114] In the ADA guideline, individuals with DM in the absence of high CVD risk (10-year risk < 10%) should be treated to a BP goal < 140/90 mm H g.[114] Due to limited evidence, the 2012 KDIGO guideline for BP management in CKD did not recommend but instead suggested that adults with DM and CKD with urine albumin excretion > 30 mg/d or an equivalent should have a target BP < 130/80 mm Hg. In contrast, strong evidence supported the recommendation that patients with DM with CKD without increased urine albumin excretion should have a BP target ≤ 140/90 mm Hg.[64] The AHA/ACC guideline does not delineate treatment goals or BP-lowering agents specifically for patients with DM who have moderate or severely increased urine albumin excretion and instead focus on CVD risk, assigning DM as a CVD risk equivalent and thereby designating all individuals with DM as high risk.

We agree that the AHA/ACC guideline recommendation of an SBP target <130 mm Hg for patients with DM and CKD is likely reasonable, although there is less certainty here than in non-DM populations. There are no data to support the DBP target, although isolated systolic hypertension is far more common than isolated diastolic hypertension in this population. Use of ACE inhibitors or ARBs in the setting of DM and severely increased urine albumin excretion has been shown to reduce progression of CKD.[18] Accordingly, the KDIGO guideline recommended that either an ACE inhibitor or an ARB be used in the setting of severely increased urine albumin excretion.[115] For patients with DM in the absence of CKD, individualized treatment strategies should be determined based on their comorbid conditions and overall CVD risk.

Implementation Issues—Risk of serious adverse events attributed to intensive SBP lowering was significantly higher in the intensive as compared to standard BP lowering in the ACCORD BP trial, a finding similar to SPRINT. Given these findings of the interactions between the intensive glycemia and intensive SBP-lowering interventions in the ACCORD BP trial,[113] intensive SBP lowering should not be combined with intensive glucose lowering (hemoglobin A_{lc} target < 7%).

Racial and Ethnic Differences in Treatment

10.1.1-1. In black adults with hypertension but without HF or CKD, including those with DM, initial antihypertensive treatment should include a thiazide-type diuretic or CCB. *(COR I, LOE B-R)*

10.1.1-2. Two or more antihypertensive medications are recommended to achieve a BP target of less than 130/80 mm Hg in most adults with hypertension, especially in black adults with hypertension. *(COR I, LOE B-R)*

Commentary—The work group believes that selection of BP-lowering medications should consider all aspects of the patient, including their comorbid conditions, age, and lifestyle

factors. Figure 2 shows the average number of medications needed to achieve a specific BP target by comorbidity. The KDOQI work group also stresses here that CKD in statement 10.1.1–1 refers not only to a low eGFR, but also to the presence of albuminuria and notes that with severely elevated urinary albumin excretion, an ACE inhibitor or an ARB would be first-line therapy.

Recommendations for Treatment of Hypertension in Older Persons

10.3.1-1. Treatment of hypertension with a SBP treatment goal of less than 130 mm Hg is recommended for noninstitutionalized ambulatory community-dwelling adults (≥65 years of age) with an average SBP of 130 mm Hg or higher. *(COR I, LOE A)*

10.3.1-2. For older adults (≥65 years of age) with hypertension and a high burden of comorbidity and limited life expectancy, clinical judgment, patient preference, and a team-based approach to assess risk/benefit is reasonable for decisions regarding intensity of BP lowering and choice of antihypertensive drugs. *(COR I la, LOE C-EO)*

Commentary—The ACC/AHA guideline recommends a targeted SBP <130 mm Hg (but no DBP goal) for noninstitutionalized adults 65 years or older regardless of non-dialysis-dependent CKD status and regardless of other risk factors. In part this recommendation reflects the characteristics of the ASCVD risk equation: most men older than 65 years and women older than 70 years with SBP > 130 mm Hg or higher, regardless of other risk factors, will reach the 10% risk threshold using the ASCVD risk calculator. Accordingly, based on the ACC/AHA guideline, almost all community-dwelling older adults should receive BP-lowering medications for both primary and secondary prevention targeting an SBP <130 mm Hg threshold. Some questions have been raised about performance of the ASCVD risk calculator. For example, in the large insured population of Kaiser Permanente of Northern California, the ASCVD risk calculator substantially overestimated actual 5-year risk.[116] The ASCVD risk calculator may work better in research cohorts than in clinical practice, suggesting a need for recalibration.

SPRINT included adults 75 years and older with no age ceiling for recruitment.[3] Among this older group (n = 2,636; mean baseline age, 79.9 years), treatment to an intensive SBP goal was associated with a 34% (95% CI, 15%–49%) lower risk of the primary composite outcome (nonfatal myocardial infarction, acute coronary syndrome, nonfatal stroke, cardiovascular death, or hospitalized HF) relative to a standard SBP target.[117] Of note, ~44% of these older SPRINT participants had baseline eGFRs <60 mL/min/1.73 m^2, and the presence of a low eGFR did not modify the effects of intensive SBP lowering on the primary outcome (adjusted P for interaction = 0.18).[73,117] The benefits of intensive SBP lowering did not differ substantially by baseline frailty status, and participants who were the frailest at baseline had the greatest reduction in risk of the primary composite outcome with the intensive SBP target. Frailty also did not modify the benefits of BP lowering in the Hypertension in the Very Elderly Trial (HYVET).[118] Of note, not all adults 65 years or older without DM would have qualified for SPRINT. Hence, BP goal in the low-risk elderly is not well established.

Clinical Utility—Even in the subgroup of elderly frail individuals, intensive SBP lowering appeared to have beneficial effects on CVD outcomes and all-cause mortality in SPRINT. The incidence of serious adverse events (HR, 0.99; 95% CI, 0.89–1.11) and injurious falls (HR, 0.91; 95% CI, 0.65–1.29) in the intensive and standard SBP groups were similar in the older SPRINT subgroup. Rates of AKI were higher among older SPRINT participants in the intensive SBP target group (5.5%) compared with the standard SBP target group (4.2%; HR, 1.39; 95% CI, 0.97–1.99). In the entire SPRINT population, the vast majority of AKI events resolved, with creatinine levels returning nearly to baseline creatinine values.[119] Similarly, rates of syncope, hypotension, and electrolyte level abnormalities were all higher among older SPRINT participants in the intensive SBP target group, but these differences were not statistically significant. It should be noted that adults with a standing SBP <110 mm Hg at screening were excluded from SPRINT; accordingly, caution is warranted when determining BP targets and treatment strategies for these individuals, with careful consideration of undue risks of hypotension and syncope.

We agree with the ACC/AHA guideline that caution should be used when initiating BP lowering medications in older adults regardless of CKD status. Due to comorbid conditions and increased risk of adverse events, the ACC/AHA guideline suggests using a stepped-care approach instead of starting with 2-drug therapy when initiating BP-lowering therapy in an elderly patient with SBP ≥150 mm Hg. Elderly patients also need to be monitored closely for adverse effects from BP lowering, especially AKI, the most common adverse effect with intensive SBP lowering.

Implementation and Challenges—Older patients are disproportionately affected by CKD and hypertension, and they are also a subgroup for which there is considerable controversy regarding optimal BP targets (Table 3). The ACC/AHA guideline recommended an SBP target of <130 mm Hg, largely based on results from SPRINT. In contrast, the ACP/American Academy of Family Physicians (AAFP) 2017 guideline recommended an SBP goal < 140 mm Hg only for older adults with similar characteristics to the SPRINT population, while continuing to endorse an SBP target <150 mm Hg for most patients older than 60 years; the ACP/AAFP guideline refrains from providing a DBP target due to lack of evidence. The Hypertension Canada 2017 guidelines “split the difference,” recommending a target BP <140 / 90 mm Hg for most older patients and a more intensive SBP target of <120 mm Hg only for patients with characteristics similar to the SPRINT population.

We agree with the ACC/AHA guideline that an SBP goal of <130 mm Hg may be reasonable for many older individuals with non–dialysis-dependent CKD. However, management must be individualized based on the patient’s tolerance to BP lowering and should account for informed patient-stated goals. For some patients with advanced CKD, intensive SBP lowering could lead to further reductions in eGFR and hasten the need for kidney replacement therapy. Close monitoring of patient symptoms, electrolyte levels, and kidney function is needed in older patients who are treated to an SBP <130 mm Hg.

BP Management in Patients Receiving Maintenance Dialysis

The 2012 KDIGO BP guideline[64] and the ACC/AHA guideline do not recommend BP goals in patients receiving maintenance dialysis due to lack of evidence. In 2010, KDIGO convened a controversies conference on BP in patients receiving dialysis.[120] Areas of research need highlighted by this conference included optimal assessment of BP, with discussion of the accumulating evidence supporting HBPM or ABPM. KDIGO did not make any recommendations regarding the diagnosis or treatment of hypertension in patients receiving dialysis and cited problems associated with a standard BP target for patients receiving dialysis, including the effects of cardiomyopathy and other common comorbid conditions in this population. The absence of a recommendation from the controversies conferences was congruent with the subsequent 2012 KDIGO BP in CKD guideline, which elected to not address hyper-tension diagnosis or management in the setting of dialysis due to lack of sufficient evidence.

Due to lack of evidence supporting a diagnosis and treatment algorithm, optimal BP values for patients receiving maintenance dialysis remain a contentious but important question. Most observational data from the dialysis population show a “U” - or “J ”-shaped relationship between BP and mortality.[1,121–123] The 2005 K/DOQI guideline for CVD in dialysis patients made a grade C recommendation for a predialysis BP target of < 140/90 mm Hg and a postdialysis BP target of <130/80 mm Hg, but acknowledged the lack of evidence supporting any specific BP threshold for initiating and titrating antihypertensive medications or reductions in dry weight.[124] This recommendation was based largely on expert opinion.

Optimal assessment of BP in dialysis patients also remains controversial. Several studies document a poor correlation between dialysis clinic BP measurements and mean inter-dialytic BP assessed using 44-hour ABPM.[125–127] Limitations to BP assessment in the hemodialysis facility include improper measurement techniques, fluid overload at dialysis therapy initiation, hemodialysis vascular access, and fluid shifts during the immediate postdialysis period.[5] An average of ABPM measurements over the 44-hour interdialytic period shows stronger correlations with left ventricular mass,[128] and higher average BP assessed using ABPM is also associated with increased mortality.[129,130] However, implementing ABPM for patients receiving dialysis may not be feasible due to lack of reimbursement in the United States and patient burden.[131] HBPM is an alternative to ABPM, but again, data for home BP measurements and clinical outcomes among patients receiving dialysis remain extremely limited.

The Medicine working group of the ERA-EDTA and the Hypertension and the Kidney working group of the ESH5 published a consensus document on the diagnosis and management of hypertension among dialysis patients in 2017, and their recommendations are summarized in Table 5. This document recommends ABPM for the diagnosis of hypertension in both hemodialysis and peritoneal dialysis, and if ABPM is not available, HBPM or use of clinic BP measures is recommended. These recommendations are opinion based and not a function of a rigorous guideline process. Regardless of the use of ABPM, HBPM, or clinic measurements, the ERA-EDTA/ESH consensus statement suggests that BP be measured using best practices and suggested thresholds for defining hypertension (Table

5). Given the lack of clinical trial evidence supporting a given BP target, we can only highlight the existing gaps in research and not support any specific suggestion from any group. Research is urgently needed to help identify optimal methods for diagnosing hypertension and optimal BP targets for treatment.

Patients Undergoing Surgical Procedures

11.5-1. In patients with hypertension undergoing major surgery who have been on beta blockers chronically, beta blockers should be continued. *(COR I, LOE B-NR)*

11.5-2. In patients with hypertension undergoing planned elective major surgery, it is reasonable to continue medical therapy for hypertension until surgery. *(COR I la, LOE C-EO)*

11.5-3. In patients with hypertension undergoing major surgery, discontinuation of ACE inhibitors or ARBs perioperatively may be considered. *(COR lib, LOE B-NR)*

11.5-4. In patients with planned elective major surgery and SBP of 180 mm Hg or higher or DBP of 110 mm Hg or higher, deferring surgery may be considered. *(COR lib, LOE C-LD)*

11.5-5. For patients undergoing surgery, abrupt preoperative discontinuation of beta blockers or clonidine is potentially harmful. *(COR III: Harm, LOE B-NR)*

11.5-6. Beta blockers should not be started on the day of surgery in beta blocker-naive patients. *(COR III: Harm, LOE B-NR)*

Commentary—Nephrologists and hypertension specialists are frequently consulted for management of patients prior to surgery and for assessment of preoperative risk. The work group agrees with these recommendations.

Clinical Utility—The ACC/AHA guideline provides recommendations for the selection and management of BP-lowering agents prior to surgery. Specifically, it is recommended to not initiate β-blocker treatment immediately prior to surgery. However, β-blocker treatment should be continued if they were being taken routinely prior to surgery. Discontinuation of treatment with ACE inhibitors or ARBs is suggested prior to surgery based on the mechanism of action for these agents and the known increased risk of AKI with hemodynamic challenges in the setting of ACE-inhibitor or ARB use, but this recommendation is not supported by level 1 evidence.

Antihypertensive Medication Adherence Strategies

12.1.1-1. In adults with hypertension, dosing of antihypertensive medications once daily rather than multiple times daily is beneficial to improve adherence. *(COR I, LOE B-R)*

12.1.1-2. Use of combination pills rather than free individual components can be useful to improve adherence to antihypertensive therapy. *(COR I la, LOE B-NR)*

Commentary—The work group agrees with these recommendations. Both ACCORD and SPRINT utilized once-a-day long-acting medications when possible. The average number of medications needed to achieve an SBP goal <120 mm Hg was about 3 in both trials and frequently exceeded 3 in individuals with CKD. Figure 2 shows the average number of BP-lowering medications by comorbid conditions and BP targets across different trials.

Clinical Utility—Use of once-daily medications should improve medication adherence.

Conclusion

Nephrologists are frequently at the front line of care for patients with hypertension in the context of multiple comorbid conditions. Guidelines cannot address every ambiguity that clinicians encounter on a daily basis. As is the case with other clinical practice guidelines, the ACC/AHA 2017 hypertension guideline is intended to serve as a tool to facilitate clinical decision making and should only be used in conjunction with the clinician's best clinical judgment to deliver high-quality care for each individual patient. Nonetheless, these guidelines dramatically alter the landscape of hypertension diagnosis and treatment and many recommendations are based on high-quality evidence. More research is needed to determine optimal methods for implementing many of the recommendations, especially in settings with limited resources.

Acknowledgements:

We thank Laura Brereton and the NKF staff for assistance with this commentary.

Support: No financial support was required for the development of this commentary.

Financial Disclosure: Dr Kramer was a site principal investigator (PI) in SPRINT and reports payments from Fresenius and NxStage. Dr Townsend was a SPRINT site PI and reports payments from Relypsa and Medtronic Vascular. Dr Griffin reports payments from EMD Serono and NxStage. Dr Flynn is a consultant to Ultragenyx, Inc and Silvergate Pharmaceuticals and reports payments from Alexion, Mallinckrodt, Vertex, Pfizer, and Genentech. Dr Weiner has received research funding from Boston Scientific paid to his institution for clinical trial conduct. Dr Weiner was a site PI in SPRINT, as well as a site PI for trials by Ardelyx, AstraZeneca, and Janssen Biotech, and has consulted for Tricida; all funding has been paid to his institution. Dr Weiner has received payments from Keryx, Merck, and Relypsa. Dr Rocco was a site PI and network consortium PI for SPRINT, has received funding paid to his institution from Bayer for clinical trial conduct, and has received payments from AbbVie. Dr Choi has received honoraria from AstraZeneca for running the Mid-Atlantic Young Investigator's Forum in 2016–2018 and has received payments from GlaxoSmithKline. Dr Weir has received payments from Vifor, Merck, Janssen, Relypsa, AbbVie, Ablative Solutions, Novo Nordisk, Sanofi-Aventis, Boston Scientific, Keryx, AstraZeneca, NxStage, Opko, Boehringer Ingelheim, Lilly, Genzyme, Vifor Fresenius, Hexal, Bayer, and Novartis. Dr Chang was a site investigator in SPRINT and has received consulting fees from Janssen and Novo Nordisk and payments from Fresenius and Amgen. Dr Agarwal has received payments from Boehringer Ingelheim, Janssen, Bayer, Sanofi-Aventis, AstraZeneca, Ironwood, Lilly, Fresenius, Relypsa, Otsuka, Opko, ER Squibb, GlaxoSmithKline, Celgene, Takeda, Daiichi Sankyo, and Gilead. Dr Beddhu was a site PI and Utah network consortium co-PI for SPRINT and has received research funding from Bayer and AbbVie, consultation fees from Reata, payments from Amgen, royalties from UpToDate, and other grants from the National Institutes of Health.

References

1. Bundy JD, Li C, Stuchlik P, et al. Systolic blood pressure reduction and risk of cardiovascular disease and mortality: a systematic review and network meta-analysis. JAMA Cardiol. 2017;2(7): 775–781. [PubMed: 28564682]
2. Ettehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Lancet. 2016;387(10022): 957–967. [PubMed: 26724178]
3. The SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med. 2016;373(22):2103–2116.
4. Lonn EM, Bosch J, Lopez-Jaramillo P, et al. Blood-pressure lowering in intermediate-risk persons without cardiovascular disease. N Engl J Med. 2016;374(21):2009–2020. [PubMed: 27041480]
5. Sarafidis PA, Persu A, Agarwal R, et al. Hypertension in dialysis patients: a consensus document by the European Renal and Cardiovascular Medicine (EURECA-m) Working Group of the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) and the Hypertension and the Kidney Working Group of the European Society of Hypertension (ESH). Nephrol Dial Transplant. 2017;32(4):620–640. [PubMed: 28340239]
6. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/ APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/ American Heart Association task force on clinical practice guidelines. J Am Coll Cardiol. 2018;71 (19):e127–e248. [PubMed: 29146535]
7. Kidney Disease: Improving Global Outcomes (KDIGO). KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013;3(1) :1–150.
8. Inker LA, Astor BC, Fox CH, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. Am J Kidney Dis. 2014;63(5):713–735. [PubMed: 24647050]
9. Jl Park, Baek H, Kim BR, Jung HH. Comparison of urine dipstick and albumin:creatinine ratiofor chronic kidney disease screening: a population-based study. PLoS One. 2017;12(2): e0171106. [PubMed: 28151999]
10. Nagrebetsky A, Jin J, Stevens R, et al. Diagnostic accuracy of urine dipstick testing in screening for microalbuminuria in type 2 diabetes: a cohort study in primary care. Fam Pract. 2013;30(2): 142–152. [PubMed: 22990027]
11. Gerstein HC, Mann JF, Yi Q, et al. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. JAMA. 2001 ;286(4):421–426. [PubMed: 11466120]
12. Wachtell K, Olsen MH, Dahlof B, et al. Microalbuminuria in hypertensive patients with electrocardiographic left ventricular hypertrophy: the LIFE study. J Hypertens. 2002;20(3):405–412. [PubMed: 11875307]
13. Herzog CA, Asinger RW, Berger AK, et al. Cardiovascular disease in chronic kidney disease. A clinical update from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int. 2011 ; 80(6):572–586. [PubMed: 21750584]
14. Komenda P, Ferguson TW, Macdonald K, et al. Cost-effectiveness of primary screening for CKD: a systematic review. Am J Kidney Dis. 2014;63(5):789–797. [PubMed: 24529536]
15. Boulware LE, Jaar BG, Tarver-Carr ME, Brancati FL, Powe NR. Screening for proteinuria in US adults: a cost-effectiveness analysis. JAMA. 2003;290(23):3101–3114. [PubMed: 14679273]
16. Hoerger TJ, Wittenborn JS, Segel JE, et al. A health policy model of CKD: 2. The cost-effectiveness of microalbuminuria screening. Am J Kidney Dis. 2010;55(3):463–473. [PubMed: 20116910]
17. Fink HA, Ishani A, Taylor BC, et al. Screening for, monitoring, and treatment of chronic kidney disease stages 1 to 3: a systematic review for the U.S. Preventive Services Task Force and for an American College of Physicians clinical practice guideline. Ann Intern Med. 2012;156(8):570–581. [PubMed: 22508734]

18. Tuttle KR, Bakris GL, Bilous RW, et al. Diabetic kidney disease: a report from an ADA consensus conference. Am J Kidney Dis. 2014;64(4):510–533. [PubMed: 25257325]
19. Miller WG, Seegmiller JC, Lieske JC, Narva AS, Bachman LM. Standardization of urine albumin measurements: status and performance goals. J Appl Lab Med. 2017.
20. Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA. 2003;289(19):2560–2572. [PubMed: 12748199]
21. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002;360(9349):1903–1913. [PubMed: 12493255]
22. Guo X, Zhang X, Guo L, et al. Association between prehypertension and cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. Curr Hypertens Rep. 2013;15(6): 703–716. [PubMed: 24234576]
23. Shen L, Ma H, Xiang MX, Wang JA. Meta-analysis of cohort studies of baseline prehypertension and risk of coronary heart disease. Am J Cardiol. 2013;112(2):266–271. [PubMed: 23608614]
24. Bell KJL, Doust J, Glasziou P. Incremental benefits and harms of the 2017 American College of Cardiology/American Heart Association high blood pressure guideline. JAMA Intern Med. 2018; 178(6):755–757. [PubMed: 29710197]
25. Muntner P, Carey RM, Gidding S, et al. Potential U.S. population impact of the 2017 ACC/AHA high blood pressure guideline. J Am Coll Cardiol. 2018;71 (2):109–118. [PubMed: 29146532]
26. [No author listed]. Screening for high blood pressure in adults: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2015;163(10):l–32.
27. Peacock J, Diaz KM, Viera AJ, Schwartz JE, Shimbo D. Unmasking masked hypertension: prevalence, clinical implications, diagnosis, correlates and future directions. J Hum Hypertens. 2014;28(9):521–528. [PubMed: 24573133]
28. Shimbo D, Pickering TG, Spruill TM, Abraham D, Schwartz JE, Gerin W. Relative utility of home, ambulatory, and office blood pressures in the prediction of end-organ damage. Am J Hypertens. 2007;20(5):476–482. [PubMed: 17485006]
29. Maxwell MH, Waks AU, Schroth PC, Karam M, Dornfeld LP. Error in blood-pressure measurement due to incorrect cuff size in obese patients. Lancet. 1982;2(8288):33–36. [PubMed: 6123760]
30. Marks LA, Groch A. Optimizing cuff width for noninvasive measurement of blood pressure. Blood Press Monit. 2000;5(3):153–158. [PubMed: 10915227]
31. Fonseca-Reyes S, de Alba-Garcia JG, Parra-Carrillo JZ, Paczka-Zapata JA. Effect of standard cuff on blood pressure readings in patients with obese arms. How frequent are arms of a ‘large circumference’? Blood Press Monit. 2003;8(3):101–106. [PubMed: 12900586]
32. Landgraf J, Wishner SH, Kloner RA. Comparison of automated oscillometric versus auscultatory blood pressure measurement. Am J Cardiol. 2010;106(3):386–388. [PubMed: 20643251]
33. Hermida RC, Ayala DE, Mojon A, Fernandez JR. Sleep-time blood pressure and the prognostic value of isolated-office and masked hypertension. Am J Hypertens. 2012;25(3):297–305. [PubMed: 22089106]
34. Pogue V, Rahman M, Lipkowitz M, et al. Disparate estimates of hypertension control from ambulatory and clinic blood pressure measurements in hypertensive kidney disease. Hypertension. 2009;53(1):20–27. [PubMed: 19047584]
35. Agarwal R, Andersen MJ. Prognostic importance of ambulatory blood pressure recordings in patients with chronic kidney disease. Kidney Int. 2006;69(7):1175–1180. [PubMed: 16467785]
36. Drawz PE, Abdalla M, Rahman M. Blood pressure measurement: clinic, home, ambulatory, and beyond. Am J Kidney Dis. 2012;60(3):449–462. [PubMed: 22521624]
37. Lindroos AS, Johansson JK, Puukka PJ, et al. The association between home vs. ambulatory night-time blood pressure and end-organ damage in the general population. J Hypertens. 2016;34(9): 1730–1737. [PubMed: 27348519]

38. Agarwal R, Bills JE, Hecht TJ, Light RP. Role of home blood pressure monitoring in overcoming therapeutic inertia and improving hypertension control: a systematic review and meta-analysis. Hypertension. 2011 ;57(1):29–38. [PubMed: 21115879]
39. Bosworth HB, Powers BJ, Olsen MK, et al. Home blood pressure management and improved blood pressure control: results from a randomized controlled trial. Arch Intern Med. 2011 ;171 (13): 1173–1180. [PubMed: 21747013]
40. McManus RJ, Mant J, Roalfe A, et al. Targets and self-monitoring in hypertension: randomised controlled trial and cost effectiveness analysis. BMJ. 2005;331 (7515):493. [PubMed: 16115830]
41. Cappucciof P, Kerry SM, Forbes L, Donald A. Blood pressure control by home monitoring: meta-analysis of randomised trials. BMJ. 2004;329(7458):145. [PubMed: 15194600]
42. McManus RJ, Mant J, Bray EP, et al. Telemonitoring and self-management in the control of hypertension (TASMINH2): a randomised controlled trial. Lancet. 2010;376(9736):163–172. [PubMed: 20619448]
43. Godwin M, Lam M, Birtwhistle R, et al. A primary care pragmatic cluster randomized trial of the use of home blood pressure monitoring on blood pressure levels in hypertensive patients with above target blood pressure. Fam Pract. 2010;27(2):135–142. [PubMed: 20032170]
44. Bennett H, Laird K, Margolius D, Ngo V, Thom DH, Bodenheimer T. The effectiveness of health coaching, home blood pressure monitoring, and home-titration in controlling hypertension among low-income patients: protocol for a randomized controlled trial. BM C Public Health. 2009;9:456.
45. Agarwal R, Andersen MJ. Prognostic importance of clinic and home blood pressure recordings in patients with chronic kidney disease. Kidney Int. 2006;69(2):406–411. [PubMed: 16408134]
46. Omboni S, Guarda A. Impact of home blood pressure tele-monitoring and blood pressure control: a meta-analysis of randomized controlled studies. Am J Hypertens. 2011;24(9): 989–998. [PubMed: 21654858]
47. Ruzicka M, Akbari A, Bruketa E, Kayibanda JF, Baril C, Hiremath S. How accurate are home blood pressure devices in use? A cross-sectional study. PLoS One. 2016;11 (6):e0155677. [PubMed: 27249056]
48. Franklin SS, Thijs L, Asayama K, et al. The cardiovascular risk of white-coat hypertension. J Am Coll Cardiol. 2016;68(19): 2033–2043. [PubMed: 27810041]
49. Fagard RH, Cornelissen VA. Incidence of cardiovascular events in white-coat, masked and sustained hypertension versus true normotension: a meta-analysis. J Hypertens. 2007;25(11): 2193–2198. [PubMed: 17921809]
50. Drawz PE, Alper AB, Anderson AH, et al. Masked hypertension and elevated nighttime blood pressure in CKD: prevalence and association with target organ damage. Clin J Am Soc Nephrol. 2016;11 (4):642–652. [PubMed: 26912547]
51. Banegas JR, Ruilope LM, de la Sierra A, et al. Relationship between clinic and ambulatory blood-pressure measurements and mortality. N Engl J Med. 2018;378(16):1509–1520. [PubMed: 29669232]
52. Bangash F, Agarwal R. Masked hypertension and white-coat hypertension in chronic kidney disease: a meta-analysis. Clin J Am Soc Nephrol. 2009;4(3):656–664. [PubMed: 19261815]
53. Funder JW, Carey RM, Manterof, et al. The management of primary aldosteronism: case detection, diagnosis, and treatment: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2016;101 (5):1889–1916. [PubMed: 26934393]
54. Tuttle KR, Dworkin LD, Henrich W, et al. Effects of stenting for atherosclerotic renal artery stenosis on eGFR and predictors of clinical events in the CORAL trial. Clin J Am Soc Nephrol. 2016;11(7):1180–1188. [PubMed: 27225988]
55. The ASTRAL Trial Investigators. Revascularization versus medical therapy for renal-artery stenosis. N Engl J Med. 2009;361:1953–1962. [PubMed: 19907042]
56. Huang Z, Liu Z, Luo Q, et al. Long-term effects of continuous positive airway pressure on blood pressure and prognosis in hypertensive patients with coronary heart disease and obstructive sleep apnea: a randomized controlled trial. Am J Hypertens. 2015;28(3):300–306. [PubMed: 25125635]
57. Feldstein CA. Blood pressure effects of CPAP in nonresistant and resistant hypertension associated with OSA: a systematic review of randomized clinical trials. Clin Exp Hypertens. 2016;38(4):337–346. [PubMed: 27159803]

58. Sapina-Beltran E, Torres G, Martinez-Alonso M, et al. Rationale and methodology of the SARAH trial: long-term cardiovascular outcomes in patients with resistant hyper-tension and obstructive sleep apnea. Arch Bronconeumol. 2018.
59. Calhoun DA, Jones D, Textor S, et al. Resistant hypertension: diagnosis, evaluation, and treatment. A scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. Hypertension. 2008;51 (6):1403–1419. [PubMed: 18391085]
60. Burchell AE, Chan K, Ratcliffe LE, et al. Controversies surrounding renal denervation: lessons learned from real-world experience in two United Kingdom centers. J Clin Hypertens (Greenwich). 2016;18(6):585–592. [PubMed: 26857092]
61. Thomas G, Xie D, Chen HY, et al. Prevalence and prognostic significance of apparent treatment resistant hypertension in chronic kidney disease: report from the Chronic Renal Insufficiency Cohort Study. Hypertension. 2016;67(2):387–396. [PubMed: 26711738]
62. Liu G, Zheng XX, Xu YL, Lu J, Hui RT, Huang XH. Effect of aldosterone antagonists on blood pressure in patients with resistant hypertension: a meta-analysis. J Hum Hypertens. 2015;29(3): 159–166. [PubMed: 25078487]
63. Williams B, MacDonald TM, Morant S, et al. Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial. Lancet. 2015;386(10008):2059–2068. [PubMed: 26414968]
64. KDIGO. KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease. Kidney Int Suppl. 2012;2(5).
65. Townsend RR, Mahfoud F, Kandzari DE, et al. Catheter-based renal denervation in patients with uncontrolled hypertension in the absence of antihypertensive medications (SPYRAL HTNOFF MED): a randomised, sham-controlled, proof-of-concept trial. Lancet. 2017;390(10108):2160–2170. [PubMed: 28859944]
66. Azizi M, Schmieder RE, Mahfoud F, et al. Endovascular ultra-sound renal denervation to treat hypertension (RADIANCE-HTN SOLO): a multicentre, international, single-blind, randomised, sham-controlled trial. Lancet. 2018;391 (10137):2335–2345. [PubMed: 29803590]
67. Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH collaborative research group. N Engl J Med. 1997;336(16): 1117–1124. [PubMed: 9099655]
68. Appel LJ, Champagne CM, Harsha DW, et al. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial. JAMA. 2003;289(16):2083–2093. [PubMed: 12709466]
69. Rebholz CM, Crews DC, Grams ME, et al. DASH (Dietary Approaches to Stop Hypertension) diet and risk of subsequent kidney disease. Am J Kidney Dis. 2016;68(6):853–861. [PubMed: 27519166]
70. Jacobs DR Jr, Gross MD, Steffen L, et al. The effects of dietary patterns on urinary albumin excretion: results of the Dietary Approaches to Stop Hypertension (DASH) trial. Am J Kidney Dis. 2009;53(4):638–646. [PubMed: 19167797]
71. Centers for Disease Control and Prevention (CDC). State-specific trends in fruit and vegetable consumption among adults - United States, 2000–2009. MMWR Morbid Mort Wkly Rep. 2010;59(35):1125–1130.
72. Lee-Kwan SH, Moore LV, Blanck HM, Harris DM, Galuska D. Disparities in state-specific adult fruit and vegetable consumption - United States, 2015. MMW R Morb Mortal Wkly Rep. 2017;66(45):1241–1247.
73. Cheung AK, Rahman M, Reboussin DM, et al. Effects of intensive BP control in CKD. J Am Soc Nephrol. 2017;28(9): 2812–2823. [PubMed: 28642330]
74. Sarnak MJ, Greene T, Wang X, et al. The effect of a lower target blood pressure on the progression of kidney disease: long-term follow-up of the Modification of Diet in Renal Disease Study. Ann Intern Med. 2005;142(5):342–351. [PubMed: 15738453]
75. Appel LJ, Wright JT Jr, Greene T, et al. Intensive blood-pressure control in hypertensive chronic kidney disease. N Engl J Med. 2010;363(10):918–929. [PubMed: 20818902]

76. Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association task force on practice guidelines. J Am Coll Cardiol. 2014;63(25, pt B):2935–2959. [PubMed: 24239921]
77. ACCORD Study Group; Cushman WC, Evans GW, Bylington RP, et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. N Engl J Med. 2010;362(17): 1575–1585. [PubMed: 20228401]
78. Zhang Y, Sun N, Jiang X, Xi Y. Comparative efficacy of (3-blockers on mortality and cardiovascular outcomes in patients with hypertension: a systematic review and network meta-analysis. J Am Soc Hypertens. 2017;11 (7):394–401. [PubMed: 28760243]
79. Reboussin DM, Allen NB, Griswold ME, et al. Systematic review for the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/ American Heart Association Task Force on clinical practice guidelines. Hypertension. 2018;71 (6):e116–e135. [PubMed: 29133355]
80. Fried LF, Emanuele N, Zhang JH, et al. Combined angiotensin inhibition for the treatment of diabetic nephropathy. N Engl J Med. 2013;369(20):1892–1903. [PubMed: 24206457]
81. Yusuf S, Lonn E, Pais P, et al. Blood-pressure and cholesterol lowering in persons without cardiovascular disease. N Engl J Med. 2016;374(21):2032–2043. [PubMed: 27039945]
82. Wright JT Jr, Dunn JK, Cutler JA, et al. Outcomes in hypertensive black and nonblack patients treated with chlorthalidone, amlodipine, and lisinopril. JAMA. 2005;293(13):1595–1608. [PubMed: 15811979]
83. Sinha AD, Agarwal R. Thiazide diuretics in chronic kidney disease. Curr Hypertens Rep. 2015;17(3):13. [PubMed: 25749608]
84. Agarwal R, Sinha AD, Pappas Mk, Ammous F. Chlorthali-done for poorly controlled hypertension in chronic kidney disease: an interventional pilot study. Am J Nephrol. 2014;4: 171–182.
85. Fliser D, Schroter M, Neubeck M, Ritz E. Coadministration of thiazides increases the efficacy of loop diuretics even in patients with advanced renal failure. Kidney Int. 1994;46:482–488. [PubMed: 7967362]
86. Knauf H, Mutschler E. Diuretic effectiveness of hydrochlorothiazide and furosemide alone and in combination in chronic renal failure. J Cardiovasc Pharmacol. 1995;26:394–400. [PubMed: 8583780]
87. Dussol B, Moussi-Frances J, Morange S, Somma-Delpero C, Mundler O, Berland Y. A randomized trial of furosemide vs. hydrochlorothiazide in patients with chronic renal failure and hypertension. Nephrol Dial Transplant. 2005;20:349–353. [PubMed: 15615808]
88. Dussol B, Moussi-Frances J, Morange S, Soma-Delpero C, Mundler O, Berland Y. A pilot study comparing furosemide and hydrochlorothiazide in patients with hypertension and stage 4 or 5 chronic kidney disease. J Clin Hypertens. 2012;14:32–37.
89. Roush GC, Holford TR, Guddati AK. Chlorthalidone compared with hydrochlorothiazide in reducing cardiovascular events: systematic review and network meta-analyses. Hypertension. 2012;59(6):1110–1117. [PubMed: 22526259]
90. Kramer H, Han C, Post W, et al. Racial/ethnic differences in hypertension and hypertension treatment and control in the Multi-Ethnic Study of Atherosclerosis (MESA). Am J Hyper-tens. 2004;17(10):963–970.
91. Taler SJ, Agarwal R, Bakris GL, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for management of blood pressure in CKD. Am J Kidney Dis. 2013;62(2):201–213. [PubMed: 23684145]
92. James PA, Oparil S, Carter BL, et al. 2014 Evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014;311(5):507–520. [PubMed: 24352797]
93. Appel LJ, Wright JT Jr, Greene T, et al. Long-term effects of renin-angiotensin system-blocking therapy and a low blood pressure goal on progression of hypertensive chronic kidney disease in African Americans. Arch Intern Med. 2008;168(8): 832–839. [PubMed: 18443258]

94. Klahr S, Levey AS, Beck GJ, et al. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. Modification of Diet in Renal Disease Study Group. N Engl J Med. 1994;330(13):877–884. [PubMed: 8114857]
95. Ruggenenti P, Perna A, Loriga G, et al. Blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease (REIN-2): Multicentre, randomised controlled trial. Lancet. 2005;365(9463):939–946. [PubMed: 15766995]
96. Xie X, Atkins E, Lv J, et al. Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis. Lancet. 2016;387(10017): 435–443. [PubMed: 26559744]
97. Lewis EJ, Hunsicker LG, Bain RP, Rohde RD. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. the Collaborative Study Group. N Engl J Med. 1993;329(20): 1456–1462. [PubMed: 8413456]
98. Ruggenenti P, Perna A, Gherardi G, et al. Renoprotective properties of ACE-inhibition in non-diabetic nephropathies with non-nephrotic proteinuria. Lancet. 1999;354(9176):359–364. [PubMed: 10437863]
99. The GISEN Group (Gruppo Italiano di Studi Epidemiologici in Nefrologia). Randomized placebo controlled trial of effect of ramipril on decline in glomerular filtration rate and risk of terminal renal failure in proteinuric, non-diabetic nephropathy. Lancet. 1997;349:1857–1863. [PubMed: 9217756]
100. Bansal N, McCulloch CE, Rahman M, et al. Blood pressure and risk of all-cause mortality in advanced chronic kidney disease and hemodialysis: the Chronic Renal Insufficiency Cohort Study. Hypertension. 2015;65(1):93–100. [PubMed: 25287404]
101. Sumida K, Molnar MZ, Potukuchi PK, et al. Blood pressure before initiation of maintenance dialysis and subsequent mortality. Am J Kidney Dis. 2017;70(2):207–217. [PubMed: 28291617]
102. Kovesdy CP, Bleyer AJ, Molnar MZ, et al. Blood pressure and mortality in U.S. veterans with chronic kidney disease: a cohort study. Ann Intern Med. 2013;159(4):233–242. [PubMed: 24026256]
103. Weir MR, Burgess ED, Cooper JE, et al. Assessment and management of hypertension in transplant patients. J Am Soc Nephrol. 2015;26(6):1248–1260. [PubMed: 25653099]
104. Mangray M, Vella JP. Hypertension after kidney transplant. Am J Kidney Dis. 2011 ;57(2):331–341. [PubMed: 21251543]
105. Divac N, Naumovic R, Stojanovic R, Prostran M. The role of immunosuppressive medications in the pathogenesis of hypertension and efficacy and safety of antihypertensive agents in kidney transplant recipients. Curr Med Chem. 2016;23(19): 1941–1952. [PubMed: 26687832]
106. Moes AD, Hesselink DA, van den Meiracker AH, Zietse R, Hoorn EJ. Chlorthalidone versus amlodipine for hypertension in kidney transplant recipients treated with tacrolimus: a randomized crossover trial. Am J Kidney Dis. 2017;69(6):796–804. [PubMed: 28259499]
107. ACCORD Study Group; Gerstein HC, Miller ME, Genuth S, et al. Long-term effects of intensive glucose lowering on cardiovascular outcomes. N Engl J Med. 2011;364(9): 818–828. [PubMed: 21366473]
108. Brouwer TF, Vehmeijer JT, Kalkman DN, et al. Intensive blood pressure lowering in patients with and patients without type 2 diabetes: a pooled analysis from two randomized trials. Diabetes Care. 2018;41 (6):1142–1148. [PubMed: 29212825]
109. Kjeldsen SE, Julius S, Dahlof B, Weber MA. Physician (investigator) inertia in apparent treatment-resistant hypertension -insights from large randomized clinical trials. Lennart Hansson memorial lecture. Blood Press. 2015;24(1):1–6. [PubMed: 25162203]
110. Huang C, Dhruva SS, Coppi AC, et al. Systolic blood pressure response in SPRINT (Systolic Blood Pressure Intervention Trial) and ACCORD (Action to Control Cardiovascular Risk in Diabetes): a possible explanation for discordant trial results. J Am Heart Assoc. 2017;6(11)
111. Buckley LF, Dixon DL, Wohlford GF 4th, Wijesinghe DS, Baker WL, Van Tassell BW. Intensive versus standard blood pressure control in SPRINT-eligible participants of ACCORD- BP. Diabetes Care. 2017;40(12):1733–1738. [PubMed: 28947569]
112. Perkovic V, Rodgers A. Redefining blood-pressure targets-SPRINT starts the marathon. N Engl J Med. 2015;373(22):2175–2178. [PubMed: 26551394]

113. Beddhu S, Chertow GM, Greene T, et al. Effects of intensive systolic blood pressure lowering on cardiovascular events and mortality in persons with type 2 diabetes on standard glycemic control and in persons without diabetes: reconciling results from ACCORD BP and SPRINT. J Am Heart Assoc. 2018.
114. de Boer IH, Bangalore S, Benetos A, et al. Diabetes and hypertension: a position statement by the American Diabetes Association. Diabetes Care. 2017;40(9):1273–1284. [PubMed: 28830958]
115. Kidney Disease: Improving Global Outcomes (KDIGO) Work Group. KDIGO clinical practice guideline for lipid management in chronic kidney disease. Kidney Int Suppl. 2013;3:259–305.
116. Rana JS, Tabada GH, Solomon MD, et al. Accuracy of the atherosclerotic cardiovascular risk equation in a large contemporary, multiethnic population. J Am Coll Cardiol. 2016;67(18):2118–2130. [PubMed: 27151343]
117. Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs standard blood pressure control and cardiovascular disease outcomes in adults aged >/= 75 years: a randomized clinical trial. JAMA. 2016;315(24):2673–2682. [PubMed: 27195814]
118. Warwick J, Falaschetti E, Rockwood K, et al. No evidence that frailty modifies the positive impact of antihypertensive treatment in very elderly people: an investigation of the impact of frailty upon treatment effect in the HYpertension in the Very Elderly Trial (HYVET) study, a double-blind, placebo-controlled study of antihypertensives in people with hypertension aged 80 and over. BMC Med. 2015;13:78. [PubMed: 25880068]
119. Rocco MV, Sink KM, Lovato LC, et al. Effects of intensive blood pressure treatment on acute kidney injury events in the Systolic Blood Pressure Intervention Trial (SPRINT). Am J Kidney Dis. 2018;71 (3):352–361. [PubMed: 29162340]
120. Levin NW, Kotanko P, Eckardt KU, et al. Blood pressure in chronic kidney disease stage 5D-report from a Kidney Disease: Improving Global Outcomes controversies conference. Kidney Int. 2010;77(4):273–284. [PubMed: 20016467]
121. Robinson BM, Tong L, Zhang J, et al. Blood pressure levels and mortality risk among hemodialysis patients in the Dialysis Outcomes and Practice Patterns Study. Kidney Int. 2012;82(5): 570–580. [PubMed: 22718187]
122. Zager PG, Nikolic J, Brown RH, et al. "U" curve association of blood pressure and mortality in hemodialysis patients. Medical Directors of Dialysis Clinic, Inc. Kidney Int. 1998;54(2):561–569. [PubMed: 9690224]
123. Port FK, Hulbert-Shearon TE, Wolfe RA, et al. Predialysis blood pressure and mortality risk in a national sample of maintenance hemodialysis patients. Am J Kidney Dis. 1999;33(3):507–517. [PubMed: 10070915]
124. K/DOQI Workgroup. K/DOQI clinical practice guidelines for cardiovascular disease in dialysis patients. Am J Kidney Dis. 2005;45(4)(suppl 3):S1–S153.
125. Agarwal R, Peixoto AJ, Santos SF, Zoccali C. Pre- and postdialysis blood pressures are imprecise estimates of interdialytic ambulatory blood pressure. Clin J Am Soc Nephrol. 2006;1 (3):389–398. [PubMed: 17699236]
126. Agarwal R, Nissenson AR, Batlle D, Coyne DW, Trout JR, Warnock DG. Prevalence, treatment, and control of hypertension in chronic hemodialysis patients in the United States. Am J Med. 2003;115(4):291–297. [PubMed: 12967694]
127. Alborzi P, Patel N, Agarwal R. Home blood pressures are of greater prognostic value than hemodialysis unit recordings. Clin J Am Soc Nephrol. 2007;2(6):1228–1234. [PubMed: 17942773]
128. Agarwal R, Brim NJ, Mahenthiran J, Andersen MJ, Saha C. Outof-hemodialysis-unit blood pressure is a superior determinant of left ventricular hypertrophy. Hypertension. 2006;47(1):62–68. [PubMed: 16344376]
129. Agarwal R Blood pressure and mortality among hemodialysis patients. Hypertension. 2010;55(3): 762–768. [PubMed: 20083728]
130. Amar J, Vernier I, Rossignol E, et al. Nocturnal blood pressure and 24-hour pulse pressure are potent indicators of mortality in hemodialysis patients. Kidney Int. 2000;57(6): 2485–2491. [PubMed: 10844617]

131. Miskulin DC, Gassman J, Schrader R, et al. BP in dialysis: results of a pilot study. J Am Soc Nephrol. 2018;29(1):307–316. [PubMed: 29212839]

132. Lewis EJ, Hunsicker LG, Clarke WR, et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med. 2001 ; 345(12):851–860. [PubMed: 11565517]

133. Brenner BM, Cooper ME, de Zeeuw D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med. 2001 ;345(12): 861–869. [PubMed: 11565518]

134. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ. 1998;317(7160): 703–713. [PubMed: 9732337]

135. Qaseem A, Wilt TJ, Rich R, et al. Pharmacologic treatment of hypertension in adults aged 60 years or older to higher versus lower blood pressure targets: a clinical practice guideline from the American College of Physicians and the American Academy of Family Physicians. Ann Intern Med. 2017;166(6):430–437. [PubMed: 28135725]

136. Leung AA, Nerenberg K, Daskalopoulou SS, et al. Hypertension Canada's 2016 Canadian hypertension education program guidelines for blood pressure measurement, diagnosis, assessment of risk, prevention, and treatment of hypertension. Can J Cardiol. 2016;32(5):569–588. [PubMed: 27118291]

137. Hiddo J, Heerspink L, Ninomiya T, Huxley R, Perkovic V. Kidney Health Australia-caring for Australians with renal impairment. Cardiovascular effects of blood pressure lowering in patients with chronic kidney disease. 2013 http://www.cari.org.au/CKD/CKD%20cardiovascular%20disease/Blood_pressure_May_2013_final.pdf. Accessed May 15, 2018.

138. ESH/ESC Task Force for the Management of Arterial Hyper-tension. 2013 Practice guidelines for the management of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC): ESH/ ESC task force for the management of arterial hypertension. J Hypertens. 2013;31 (10):1925–1938. [PubMed: 24107724]

139. Department of Veterans Affairs/Department of Defense. VA/DoD Clinical practice guideline for the diagnosis and management of hypertension. Version 3.0. 2014. Washington, DC https://www.healthquality.va.gov/guidelines/CD/htn/VADoDCPGHTN2014.pdf. Accessed May 1, 2018.

As they are designed to reflect the views and recommendations of the responsible KDOQI Commentary work group and because they are reviewed and approved by KDOQI and NKF leadership, KDOQI Commentaries are not peer reviewed by AJKD. This article was prepared by a KDOQI Commentary work group comprising the authors and co-chaired by Drs Holly Kramer and Srinivasan Beddhu. It was reviewed and approved by the NKF Scientific Advisory Board.

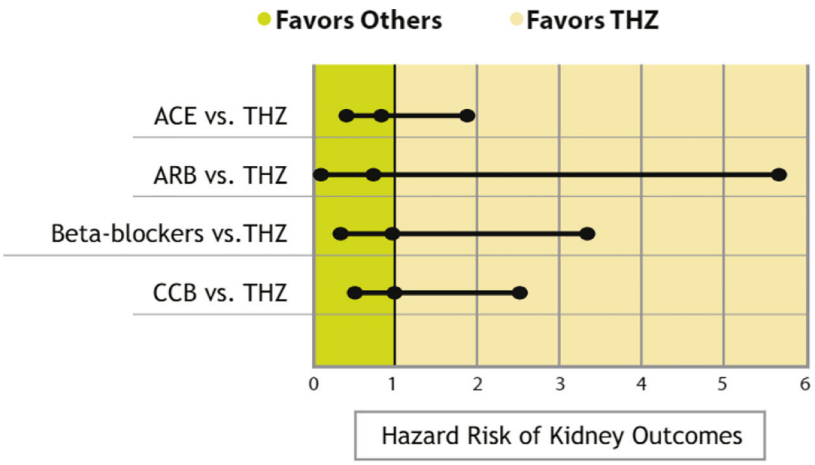

Figure 1.

Hazard ratios of kidney outcomes by use of nonthiazide blood pressure-lowering medications versus thiazide diuretic (THZ) medications. Abbreviations: ACE, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CC B, calcium channel blockers. Data obtained from Reboussin et al.[79]

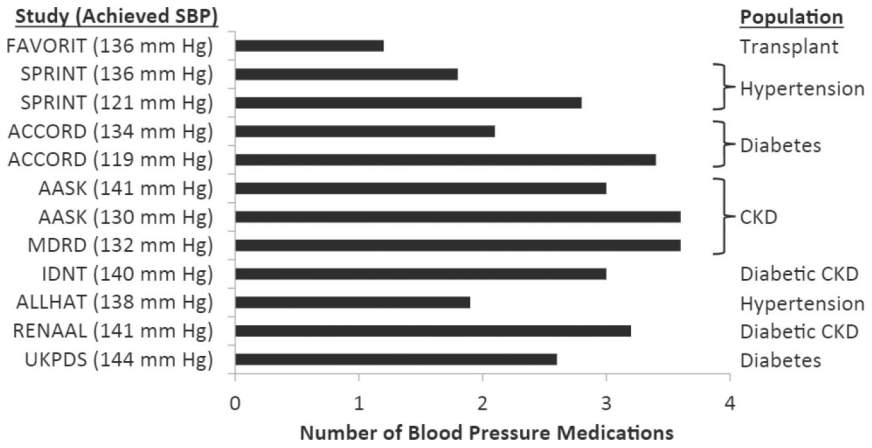

Figure 2.

Average number of blood pressure (BP) medications needed to achieve a BP goal in clinical trials. Abbreviations: AASK, African American Study of Kidney Disease and Hypertension[93]; ACCORD, Action to Control Cardiovascular Disease in Diabetes[77]; ALLHAT, Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; CKD, chronic kidney disease; IDNT, Irbesartan Diabetic Nephropathy Trial[132]; MDRD, Modification of Diet in Renal Disease[94]; RENAAL, Reduction of Endpoints in NIDDM With the Angiotensin II Antagonist Losartan[133,134] SBP, systolic blood pressure; SPRINT, Systolic Blood Pressure Intervention Trial[3]; UKPKDS, United Kingdom Prospective Kidney Disease Study.[134]

Table 1.

Description for COR and LOE

COR	Strength of Recommendation	Suggested Phrase for Recommendation
I	Strong	Is recommended
IIa	Moderate	Is reasonable
IIb	Weak	May/might be reasonable or considered
III: No benefit	Moderate	Is not recommended
III: Harm	Strong	Potentially harmful

LOE[a]	Quality of Evidence
A	Strong; high-quality evidence (≥2 RCTs)
B-R	Moderate-quality evidence (≥1 RCT)
B-NR	Moderate-quality evidence (observational or registry studies)
C-LD	Limited data (observational or registry studies, physiologic or mechanistic studies)
C-EO	Expert opinion (opinion based on clinical experience only)

Note: The COR and LOE are mutually exclusive.

Abbreviations: COR, class of recommendation; LOE, level of evidence; NR, nonrandomized; R, randomized; RCT, randomized controlled trial.

Table adapted from the 2017 ACC/AHA hypertension guideline[6] with permission of the American Heart Association, Inc.

[a]When added, a superscript “SR” indicates evidence includes a systematic review.

Table 2.

Definitions of Hypertension in the ACC/AH A and JNC7 publications

Hypertension Classification	ACC/AHA 2017[6]	JNC7 2003[20]
Normal	SBP < 120 mm Hg and DBP < 80 mm Hg	SBP < 120 mm Hg and DBP < 80 mm Hg
Elevated BP	SBP 120–129 mm Hg and DBP < 80 mm Hg	SBP 120–139 mm Hg or DBP 80–89 mm Hg
Stage 1 hypertension	SBP 130–139 mm Hg or DBP 80–89 mm Hg	SBP 140–159 mm Hg or DBP 90–99 mm Hg
Stage 2 hypertension	SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg	SBP > 160 mm Hg or DBP ≥ 100 mm Hg

Abbreviations: ACC/AHA, CC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines; BP, blood pressure; DBP, diastolic blood pressure; JNC7, Seventh Report From the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure; SBP, systolic blood pressure.

Table 3.

Summary of Recommended Blood Pressure Targets by Comorbid Conditions and Age and by Guideline Group

	ADA[114] (2018)	ACC/AHA[6] (2017)	ACP/AAFP[135] (2017)	Hypertension Canada[136] (2017)	KHA-CARI[137] (2013)	ESH/ESC[138] (2013)	KDIGO[64] (2012)	JNC8[92] (2014)	VA/DoD[139] (2014)
Most adults	-	<130/80	<140/90	<140/90	-	-	-	<140/90	<140/90
CKD, no DM									
No proteinuria	-	<130/80	-	<140/90; SBP < 120 if high CV risk	<140/90	<140/90	<140/90	<140/90	<140/90
Proteinuria	-	<130/80	-	<140/90; SBP < 120 if high CV risk	<130/80	<140/90	<130/80	<140/90	<140/90
CKD and DM									
No proteinuria	<140/90; <130/80 or <120/80 if high CV risk & tolerated	<130/80	-	<130/80	<140/90	<140/85	<140/90	<140/90	<140/85
Proteinuria	<140/90; <130/80 or <120/80 if tolerated	<130/80	-	<130/80	<130/80	<140/85	<130/80	<140/90	<140/85
Kidney transplant recipients	-	<130/80	-	-	<130/80 <125/75 if proteinuria[a]	-	<130/80	-	-
Older population	-	<130/80	SBP < 150; <140 if h/o stroke or high CV risk[a]	<140/90; SBP < 120 if age ≥ 50 y & high CV risk or if age ≥ 75 y		<150/90	Individualize	<150/90	Unable to determine

Abbreviations: ACC/AHA, ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines; ACP/AAFP, American College of Physicians/American Academy of Family Physicians; ADA, American Diabetes Association; CKD, chronic kidney disease; CV, cardiovascular; DM, diabetes mellitus; ESH/ESC, European Society of Hypertension and the European Society of Cardiology; h/o, history of; JNC8, Report from the Panel Members Appointed to the Eighth Joint National Committee workgroup; KDIGO, Kidney Disease: Improving Global Outcomes; KHA-CARI, Kidney Health Australia-Caring for Australians With Renal Impairment; SBP, systolic blood pressure; VA/DOD, Veterans Affairs/Department of Defense.

[a]No recommendations regarding diastolic blood pressure.

Table 4.

BP Target Studies in Populations With CKD

Study	Description	BP Groups	Mean f/u, y	Kidney End Point
SPRINT subgroup with CKD[73] (N = 2,646)	Aged ≥50 y, high CVD risk, UPCR < 1 g/g; eGFR > 20 mL/min/1.73 m^2, no DM	SBP < 120 vs <140 mm Hg	3.3	HR, 0.90 (95% Cl, 0.44, 1.83) for composite of ≥50% decline in eGFR oi ESRD
REIN-2[95] (N = 338)	Aged 18–70 y, urine protein excretion 1 −3 g/d with CL_{cr} < 45 mL/min or ≥3 g/d with CL_{cr} < 70 mL/min	SBP/DBP < 130/80 mm Hg vs DBP < 90 mm Hg	1.6	HR, 1.00 (95% Cl, 0.61–1.64) for ESRD
AASK[75] trial phase (N = 1,094)	18–70 y, African Americans with clinically attributed hypertensive CKD, GFR 20–65 mL/min/1.73 m^2, UPCR < 2.5 g/g, no DM	MAP ≤ 92 vs 102–107 mm Hg	4.1	HR, 1.06 (95% Cl, 0.89–1.27) for ESRD
AASK trial phase with UPCR > 0.22 g/g[75] (N = 357)			4.1	HR, 0.76 (95% Cl, 0.55–1.04) for doubling of Scr or ESRD
AASK trial & cohort phases[75] (N = 691)			9.1	HR, 0.95 (95% Cl, 0.78–1.15) for ESRD
AASK trial & cohort phases[75] with UPCR > 0.22 g/g (N = 357)			9.1	HR, 0.76 (95% Cl, 0.58–0.99) for doubling of Scr or ESRD
MDRD Study trial phase[88] (N = 840)	Aged 18–70 y with GFR 13–55 mL/min/1.73 m^2	MAP < 92 mm Hg if age ≤ 60 y & MAP < 98 mm Hg if age ≤ 61 y vs 107 mm Hg if age < 60 y & <113 mm Hg if age ≥ 61 y	2.2	HR, 0.78 (95% Cl, 0.66–0.93) for kidney failure
MDRD Study trial & cohort phases[73] (N = 840)			9.2	HR, 0.68 (95% Cl, 0.57–0.82) for ESRD

Abbreviations: AASK, African American Study of Kidney Disease and Hypertension; BP, blood pressure; CI, confidence interval; CKD, chronic kidney disease; CL_{cr} creatinine clearance; CVD, cardiovascular disease; DBP, diastolic blood pressure; DM, diabetes mellitus; (e)GFR, (estimated) glomerular filtration rate; ESRD, end-stage renal disease; HR, hazard ratio; MAP, mean arterial pressure; MDRD, Modification of Diet in Renal Disease; REIN-2, Blood Pressure Control for Renoprotection in Patients With Non-Diabetic Chronic Renal Disease; SBP, systolic blood pressure; Scr, serum creatinine; SPRINT, Systolic Blood Pressure Intervention Trial; UPCR, urinary protein-creatinine ratio.

Table 5.

EURECA-m Working Group Recommendations for Diagnosis and Treatment of Hypertension for Patients Receiving Maintenance Dialysis

		Hypertension	
BP Measurement[a]	**Method**	**Hemodialysis**	**Peritoneal Dialysis**
ABPM	Minimum of 24-h monitoring without dialysis; when feasible, 44-h monitoring over midweek interdialytic period for patients on hemodialysis	≥130/80 mm Hg	≥130/80 mm Hg
Home	Average of readings from both morning and evening over 6 nondialysis days for patients receiving hemodialysis and over 7 consecutive days for patients receiving peritoneal dialysis	≥135/85 mm Hg	≥135/85 mm Hg
Office	Midweek on a nondialysis day, average of 3 readings	≥140/90 mm Hg	≥140/90 mm Hg

Abbreviations: ABPM, ambulatory blood pressure monitoring; BP, blood pressure; EURECA-m, European Renal and Cardiovascular Medicine Working Group of the European Renal Association-European Dialysis and Transplant Association and the Hypertension and the Kidney working group of the European Society of Hypertension.

[a]AII measurements should be taken after a 5-minute rest with patient sitting and back and arm supported.

Source: EURECA-m Consensus Statement.[5]

Am J Kidney Dis. Author manuscript; available in PMC 2020 April 01.