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RECOGNITION AND MANAGEMENT OF HYPERTENSION IN OLDER PERSONS: FOCUS ON AFRICAN AMERICANS

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Abstract

Hypertension is the most commonly diagnosed condition among persons 60 years and older and is the single most important risk factor for cardiovascular disease (e.g. ischemic heart disease, heart failure, stroke), kidney disease, and dementia. More than half of hypertensive patients in the US are over age 60. African Americans are disproportionately affected by hypertension, with all age groups, including the elderly, suffering a higher burden of hypertension-related complications compared to other U.S. populations. Multiple clinical trials have demonstrated the beneficial effects of BP reduction on cardiovascular morbidity and mortality with most of the evidence in patients age 60 years and older. Several guidelines have been recently published on the specific management of hypertension in patients age 60 years, including in high risk groups such as African Americans. Most recommend careful evaluation, the use of thiazide diuretics and calcium channel blockers for initial drug therapy in most African American patients, and angiotensin converting enzyme inhibitors and angiotensin receptor blockers in those with chronic kidney disease or heart failure. Among the areas of controversy is the recommended target blood pressure in African Americans age 60 years old. A recent U.S. guideline recommended raising the SBP target from < 140 mmHg to < 150 mmHg in this population. This paper will review the evidence and current guideline recommendations for hypertension treatment in older African Americans including the rationale for continuing to recommend a SBP target of < 140 in this population.

Keywords

Hypertension; African Americans; Management of hypertension; Clinical trials

The older population (persons 65 and over) in the United States is rapidly growing, accounting for 13.1% (40.2 million) of the U.S. population in 2010.[1] With increasing age, older adults are also at higher risk for developing chronic diseases, and 88% of individuals 65 years and older have at least one chronic disease.[1] To date, cardiovascular disease (CVD) continues to be the leading cause of morbidity and mortality in the elderly in the United States,[2, 3] and accounts for nearly one-third of all deaths annually (Table 1).[4] Hypertension is the single most important and major risk factor for CVD, including coronary heart disease (CHD), heart failure, stroke, chronic kidney disease (CKD) and dementia.[2, 5] It is also among the most commonly diagnosed chronic conditions in patients 60 years and older: men (54%) and women (57%),[6] and the majority of all hypertensives are 60 years old.[3, 7] In this paper, we review the evidence and current recommendations for the management of hypertension in older African Americans.

Epidemiology

In addition to hypertension prevalence being higher in older compared to younger populations, African Americans are disproportionately affected by hypertension with all age groups suffering a higher burden of hypertension-related complications (e.g., heart failure, stroke, and chronic kidney disease) compared to other U.S. populations.[4, 7, 8] African Americans have a higher prevalence of hypertension (40.4%) compared to whites (27.4%) and Hispanic persons (26.1%).[3] When compared to whites, African Americans are more aware of their hypertension status (87% vs. 81.4) and treated with antihypertensive (79.8% vs. 76.6%), yet have less controlled blood pressure (47.9% vs 56.3%).[3] The reasons for these differences are multifactorial including differences in access, quality, adherence to recommended medications and lifestyle modifications and greater number of co-morbidities. [8–10, 10, 11] Compared with whites, African Americans are 1.3 times more likely to have a nonfatal stroke, 1.8 times more likely to have a fatal stroke, 1.5 times more likely to die from heart disease, and are 4.2 times likely to develop end-stage kidney disease (ESKD).[4, 7]

U.S. mortality data over the past two decades reveals CHD mortality to be 35-fold higher in those over age 60 compared to those less than 60, and for stroke mortality the differential risk is 50-fold higher.[4, 7] At every age level, African American race is associated with incremental increase in risk.[7] Interestingly, over the same period, mortality from these disorders have been progressively declining, including in African Americans (though the rate of decline has been slower), and the mortality reduction has been greater in those over age 60.[4] While parallel reductions in other risk factors such as smoking and increased statin use has occurred, a recent analysis showed the reduction in mortality rate, especially the stroke mortality reduction is best associated with the reduction in blood pressure over this period.[12] From 2001–2008, mean SBP for treated hypertensive African Americans over age 60 was 144 mmHg, compared to 141 mmHg in whites of the same age group.[3, 13] Recently, the National Health and Nutrition Examination Survey reported that SBP has been decreasing over past several decades with corresponding increase in BP control rates in those over age 60 years, with over 80% under treatment.[3] However, the racial difference in event rates remains unchanged.

Age-Related Pathogenesis of Hypertension

Compared to younger populations, isolated systolic hypertension (ISH) is the predominant pattern of hypertension in older populations.[14, 15] Hypertension, predominantly isolated systolic hypertension (ISH), (SBP \geq 140 and DBP $<$ 90 mm Hg) is reported in more than 2/3rd of hypertensive patients 60 years and older, and SBP is more predictive of cardiovascular events than DBP in older patients.[7, 8] Age-related pathophysiologic changes associated with hypertension in the elderly include the loss of elasticity in the proximal aorta, increased systemic vascular resistance, and increased vascular stiffness, contributing to the higher prevalence of ISH and high pulse pressure.[14, 16] Other race/ethnic differences e.g. socioeconomic status, environmental factors, diet (i.e., high sodium and calorie intake, and low potassium), physical inactivity, health conditions (e.g., sleep apnea and obesity), and genetic susceptibility are also posited as significant contributors to

the excess burden of hypertension and its related morbidity in African Americans.[15, 17–20]

Hypertension is considered one of the clinical conditions in which population differences in prevalence, pathophysiology and outcome may, in part, be attributed to genetic differences. [21–23] However, research demonstrating the existence of genetic susceptibility variants for hypertension remains inconsistent due to the complexity of hypertension and other factors that may influence its occurrence. In spite of this, risk variants of the Apo-L1 gene have been shown to explain a substantial portion of the excess risk of ESKD and renal disease progression in hypertensive African Americans compared to whites.[21, 23]

Clinical Manifestations

Age-related pathophysiological changes may, in part, explain the increased prevalence of hypertension with increasing age, but the exact etiology of hypertension remains unclear. Regardless of age and race (though minorities are disproportionately affected), clinical manifestations of hypertension are related to the varying degrees of target organ damage (CHD, HF, CVA, CKD, and vascular damage to other vascular beds) that develop in those individuals with long-standing untreated or uncontrolled hypertension.[14, 24] There are some data that accelerated cognitive decline and dementia is also associated with BP elevation.[25] Sexual dysfunction (especially erectile dysfunction) often attributed to specific antihypertensive therapy is more often related to the vascular damage from cardiovascular factors including hypertension.[26] Specifically, orthostatic hypotension is more common in older hypertensive patients (compared to younger) due to the diminished baroreceptor responses to elevated arterial pressure and possibly associated with syncope, lightheadedness, and dizziness.[18]

Evidence Supporting Blood Pressure Treatment Targets in Older Hypertensive

Multiple randomized clinical trials (RCTs) have demonstrated that lowering BP substantially decreases the rates of cardiovascular morbidity and mortality in older hypertensive patients. The first VA Cooperative Trial and the Hypertensive Detection and Follow-up Program trial (HDFP) focused on testing DBP targets (DBP < 90 mmHg vs. placebo or usual care).[27, 28] They were conducted in a somewhat younger population (mean age ~51) but included approximately 40% African Americans. However, the majority of evidence documenting the value of BP reduction has focused on testing SBP targets and in hypertensive patients over age 60 years (Table 2). Only one of the trials (The Systolic Hypertension in the Elderly Program [SHEP],[29] had significant numbers of African Americans age 60 years and older; and another trial (The Systolic Blood Pressure Intervention Trial [SPRINT]),[30] scheduled to end in 2017 will also have significant numbers of African Americans age 60 years and older.

There is overwhelming evidence that reducing BP to at least < 150/90 mmHg in patients 60 years and older reduces hypertensive morbidity and mortality (even in those over the age 80). Two large trials, Systolic Hypertension in the Elderly Program (SHEP) and

Hypertension in the Very Elderly Trial (HYVET), of patients in this age group showed that reducing SBP to 143 mmHg in SHEP and 144 mmHg in HYVET (in patients > 80 yrs) reduced cardiovascular events including mortality compared to those treated to 155–159 mmHg.[19, 29] Another large Chinese RCT, the Felodipine Event Reduction (FEVER) trial, compared the calcium channel blocker felodipine plus low dose hydrochlorothiazide to hydrochlorothiazide plus placebo and showed benefit in those treated to a mean SBP of 137 mmHg compared to those treated to a mean SBP of 143 mmHg.[31] A very small trial (Cardio-Sis), designed to compare the effect of treating to SBP < 130 mmHg vs <140 mmHg on incident ECG LVH in patients (mean age 67 years old) unexpectedly also showed benefit of the lower SBP target on composite cardiovascular clinical outcomes.[32]

Two additional trials of patients > 60 years of age conducted in Japan, Valsartan in Elderly Isolated Systolic Hypertension (VALISH) and Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients (JATOS), though negative were each underpowered to show a difference in clinical outcomes.[33, 34] However, with a combined total of more than 7,500 patients followed for more than two years, they nevertheless showed no increase in adverse effects in those treated to < 140 mmHg compared to those treated to less than 150–160 mmHg.[33, 34] Thus, there is substantial RCT evidence that treating to a SBP goal approximating 140 mmHg in non-frail, older hypertensive patients reduces clinical outcomes with little evidence of adverse risk (or suggestion of inconsistency in African Americans).[7, 35–37] While the above evidence is available in those over age 60, there are no randomized clinical outcome trials testing SBP targets in significant numbers of hypertensive patients < 60 years of age to justify a lower or different SBP goal in those less than age 60.

A concern often raised about antihypertensive treatment in those over age 60 is that excessive BP lowering would reduce blood flow to the brain, heart, and kidneys and precipitate ischemic events (e.g., stroke, CHD) causing further target organ damage.[2] There have been multiple attempts to ascertain the optimal BP target and level of blood pressure at which the cardiovascular risk increases (J-curve).[38–40] However, these types of analyses are fraught with pitfalls.[41]

In addition, there is concern that excessive BP lowering, coupled with safety and polypharmacy issues in older hypertensives may cause light-headedness and falls.[14] While data are limited in African Americans, RCT evidence from non-Black populations is available (Table 2). A trend towards more faintness and falls was seen in the lower SBP targets in the SHEP and ACCORD trials,[29] but were not associated with lower BP treatment targets in the JATOS, VALISH, Cardio-Sis, or FEVER trials,[31–34] or in the 80-year old participants in HYVET.[19] A recent report from the ACCORD trial,[42] observed in a cohort of diabetic hypertensives (mean age > 62 and 25% African Americans) a nonsignificantly lower risk of falls (Relative Risk [RR] = 0.84, 95 % CI 0.54–1.29, $p = 0.43$) and non-spine fracture risk (hazard ratio [HR], 0.79, 95 % CI 0.62–1.01, $p = 0.06$) in those treated to a SBP < 120 mmHg compared to those treated to SBP < 140 mmHg. Similar results were observed in another study, the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study,[43] which compared three age groups (55–64, 65–74, and >75 years) taking antihypertensive medications (without CVD history) and found no association

between SBP (120 to 139 vs >150 mmHg) and falls across all age groups.[43] The Secondary Prevention of Small Subcortical Strokes (SPS3) trial compared lower blood pressure targets (SBP < 130 mmHg vs 130–149 mmHg) in patients with recent lacunar stroke (mean age 63 years and 16% African Americans) reported a non-significant trend in total stroke reduction and significant reduction in hemorrhagic strokes.[44] Importantly, it also showed no increase in adverse side effects that was consistent across racial/ethnic groups, even in those with diabetes.[44] Risk/benefit of the < 120 mmHg SBP target is being tested in the NIH sponsored trial SPRINT, which is testing a strategy of treating SBP < 120 mmHg compared to treatment to < 140 mmHg on cardiovascular, renal, and stroke outcomes and cognitive decline.[30] Mean age in SPRINT is 67.9 years, and 28% of the 9,361 participants are age 75 years and older.[30]

Diagnostic Approach for Evaluating Older African Americans with Hypertension

National and international guidelines are available to guide the management of older hypertensives (Tables 3 and 4); most also discuss racial differences in management. As in other populations, general considerations for management and treatment begin with a thorough clinical assessment. This should include initial and periodic orthostatic BP measurements, particularly important in older African American patients because of greater risk of postural hypotension.[8, 18, 20] A detailed history and examination are important to rule out identifiable causes of hypertension (e.g., hyperaldosteronism, renal dysfunction, pheochromocytoma, and sleep apnea), other cardiovascular risk factor (e.g., diabetes), and target organ damage (e.g., heart failure, CKD, and stroke or dementia).[12, 17, 18, 20] Laboratory testing, in general, does not differ in older versus younger populations and should include complete blood count, serum potassium, creatinine, and calcium, fasting blood glucose, hemoglobin A1c, lipid panel, urinalysis and electrocardiogram.[18, 20, 24] While recent trials do not support the value of wide-spread screening for renovascular hypertension, screening may be appropriate in patients presenting with flash pulmonary edema, true resistant hypertension, or declining renal function.[45] It is important to ask elderly African Americans with hypertension about factors that might influence the prognosis and therapy, such as socioeconomic status (i.e., medication cost, health insurance coverage), psychosocial and environmental factors, and lifestyle behaviors (e.g., diet and exercise).[14, 18, 46, 47] Finally, factors that might adversely affect adherence to treatment should be reviewed such as social support, adverse events, polypharmacy issues, and cognition.[17, 18]

Primary, Secondary, and Tertiary Interventions

Blood Pressure Targets.

Adequate blood pressure control should be the focus of primary, secondary, and tertiary interventions, as evidence supports that reduction in blood pressure decreases morbidity and mortality from hypertension-related complications.[17, 18] There remains a critical void in the evidence base to document the optimal goal blood pressure in hypertensive patients of all ages including older patients, and a definitive answer still awaits a prospective clinical

outcome trial. However, all but one national and international hypertension guideline continue to recommend treating older patients up to age 80 years to a BP goal of < 140/90 mmHg; most recent guideline recommend a treatment target to at least < 150 mmHg systolic in those > age 80 (especially if frail) (Table 3).

One U.S. guideline panel has used the lack of benefit in the two underpowered trials (JATOS and VALISH) to recommend a more conservative management of hypertension (target SBP < 150 mmHg) in hypertensive patients 60 years and older,[2] without regard to factors such as black race (or other CVD risk factors) associated with increased risk. Though this panel began as a National, Heart, Lung, Blood, and Institute (NHLBI) supported by the Joint National Committee (JNC) guideline panel, the final publication was neither endorsed by National Institute of Health (NIH) NHLBI nor did it undergo the review process of previous JNC guidelines. The recommendation by this one panel to increase the SBP treatment target in hypertensives age 60 years and older, from 140 to 150 mmHg is not consistent with other guidelines (Table 3) and has met with substantial resistance especially with respect to treatment of hypertensive African Americans age 60 years and older, who are at substantially higher risk for complications of hypertension.[7, 35–37, 48] Because of the higher hypertension-related complication risk in African American patients, the less aggressive SBP target of < 150 in those > 60 is not supported by evidence in this patient population.[35, 37]

Lifestyle Modifications.

Lifestyle modifications are recommended as first line of treatment and adjunct therapy for management of hypertension, which has shown to substantially reduce BP or eliminate the need for antihypertensive medications in individuals with hypertension, including older African Americans.[2, 18, 36, 49] Lifestyle changes including weight reduction, dietary modification, and increased physical activity are particularly important in treatment of older African Americans as a primary and secondary interventions,[18, 47]given the higher prevalence of obesity (body mass index [BMI] ≥ 30) in this population.[50] Higher rates of obesity are observed among older African American women aged 65–74 (53.9%) and those women 75 years and older (49.4%) compared to elderly Hispanic (46.6% and 30.2%) and white (38.9% and 30.2%) women.[50] Several studies have shown that diets low in fat and high in vegetables, fruits, grains, protein, and fiber significantly lowers BP in hypertensive patients by as much as 10 mm Hg.[51, 52] The Trial of Nonpharmacologic Interventions in the Elderly (TONE) showed the benefit of salt reduction and weight loss on BP control (after withdrawal of antihypertensive medications) in hypertensive individuals (60–80 years of age).[52] In TONE 975 participants (47% women and 24% African Americans) were randomized to one of four groups, and showed that moderate reductions in weight loss (3.5 to 4.5 kg) and salt reduction (less than 920 mg per day) decreased the need for antihypertensives by 30%.[52]

For a variety of reasons, adoption of lifestyle recommendations may be a challenge for some older individuals, including African Americans due to barriers such as poor social support, lack of access to exercise and dietary resources, and financial considerations.[9] Furthermore, before recommending lifestyle changes to older African Americans, common

geriatric situations, such as cognitive impairment, mental health (e.g., depression), nutritional status, and physical limitation should be assessed as they may interfere with treatment compliance.[20, 46] One of the major problems facing older African Americans is that they tend to be of lower SES,[1] which impedes their basic living necessities,[46] including access to medical care and recommended food choices and the cost of medications.[9] Economic vulnerability further decreases the potential for medical compliance in a chronic disease like hypertension and should be explored.[46] Consideration must also be given to learning styles and preference, personal beliefs, values, and culture.[9, 18, 20]

Therapeutic Interventions for Older Hypertensive, including African Americans

Most large clinical trials have shown that thiazide (THZ) and thiazide-type diuretics (and/or calcium channel blockers) are more effective as monotherapy or as first-step in the regimen in lowering blood pressure and in reducing cardiovascular and cerebrovascular events in African Americans than renin angiotensin system inhibitors (RASI) drugs (i.e. ACE inhibitors, ARBs, renin inhibitors, and β -blockers) (Table 5).[53–55] For example, the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack ALLHAT) trial demonstrated that the thiazide-type diuretic (chlorthalidone) was unsurpassed in reducing blood pressure and in preventing cardiovascular events when compared to the calcium channel blocker (amlodipine), ACE inhibitor (lisinopril) and the alpha-adrenergic blocker (doxazosin).[55] For optimum endpoint protection, thiazide-type diuretic dose should be equivalent to chlorthalidone 12.5–25 mg/day or hydrochlorothiazide 25–50 mg/day as lower doses are either unproven or less effective in clinical outcome trials.[2, 55, 56] Calcium channel blockers are as effective as thiazide diuretics in reducing blood pressure and in reducing CVD and in meta-analyses slightly more effective in reducing stroke events though they are consistently less effective in preventing heart failure. Beta blockers have been shown to be significantly less effective in reducing blood pressure in African Americans unless they are combined with a diuretic or calcium channel blocker.[57] There are few hypertension clinical outcome trials containing significant numbers of African Americans, and most recent guidelines no longer recommend beta blockers as initial therapy (Table 4). Thus, in the absence of coronary artery disease or systolic heart failure, beta blockers are recommended only as add-on agents in older African American hypertensives.

When considering prescribing diuretics to older African Americans, clinicians should be conscious of adverse side effects such as hypokalemia, hyponatremia, and hypercalcemia (although the metabolic consequences of diuretics on CVD outcomes have been small) There is consensus that treatment of hypertension should begin with a diuretic (or calcium channel blocker) alone or in combination with another drug class in older hypertensive African Americans without compelling indications (Table 4). Most hypertensive patients, especially African Americans will require two or more antihypertensive medications to achieve adequate BP control. Some caution should be noted in treatment of older hypertensive patients; specifically, initial antihypertensive therapy should be initiated at the lowest dose and progressively increased to achieve the desired BP target based on side

effects profile. Electrolytes (i.e. sodium and potassium) should be measured after initiation and dosage escalation with diuretics, and potassium and renal function measured after initiation and significant dose escalation of ACEI's, and ARB's.[55]

Conclusions

It is well established that hypertension in African Americans occurs at an early age, is more severe, and more likely to be resistant to treatment than other populations.[3, 4, 17, 18] Poor BP control is an important factor in the disproportionately higher rates of hypertension-related complications in African Americans.[3, 4] Especially in the older African Americans, management should begin with appropriate evaluation, and treatment should include aggressive life-style change. Antihypertensive drug therapy should be initiated with a thiazide-type diuretic (or calcium channel blocker) and other agents added to achieve the BP target.[17, 18, 53, 55] The recommended SBP target for both the initiation of antihypertensive drug treatment and for blood pressure lowering in the older hypertensive patient remains somewhat consistent across various hypertension guidelines, with the exception of one recent U.S. guideline (Table 3).[2]

In African Americans, it is clear that the evidence is insufficient to raise the threshold for SBP goal from its current level of less than 140 mmHg, particularly in those with CVD or with multiple cardiovascular risk factors.[35, 37] The recent “*2014 U.S. Evidence-base Guideline for Management of High Blood Pressure in Adults*” published in JAMA is the only guideline recommending raising the SBP target to < 150 mmHg in patients as young as age 60 years, including African Americans.[2] Other national and international guidelines recommend a goal of < 140 mmHg for patients less than age 80 years, and some members of the U.S. guideline panel and others have published their dissent with the recommendation to raise the SBP target to >150 mmHg in this population.[35, 37]

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Table 1.

Leading Causes of Death Among Older Adults in U.S. by Age and Race in 2010

Cause of Death	>65 years and over		>85 years	
	White	Black	White	Black
	Death Ranked (%)			
Diseases of heart (heart disease)	1 (26.5)	1 (27.2)	1 (30.0)	1 (29.6)
Malignant neoplasms (cancer)	2 (21.9)	2 (23.4)	2 (12.3)	2 (13.8)
Chronic lower respiratory diseases	3 (6.9)	5 (3.8)	5 (5.1)	7 (3.2)
Cerebrovascular diseases (stroke)	4 (6.0)	3 (6.6)	4 (7.1)	3 (7.2)
Accidents (unintentional injuries)	7 (2.4)	----	7 (2.4)	8 (2.8)
Alzheimer's disease	5 (4.6)	7 (3.2)	3 (7.2)	4 (6.0)
Diabetes mellitus (diabetes)	6 (2.7)	4 (4.6)	9 (1.9)	6 (3.6)
Nephritis, nephrotic syndrome and nephrosis (kidney disease)	8 (2.3)	6 (3.7)	8 (2.3)	5 (3.6)
Influenza and pneumonia	7 (2.4)	9 (2.2)	6 (3.0)	----
Septicemia	10 (1.5)	8 (2.4)	----	10 (2.2)
Essential hypertension and hypertensive renal disease (hypertension)	----	10 (2.1)	10 (1.4)	9 (2.7)

Note. Adapted from “Deaths: Leading Causes for 2010. National Vital Statistics Reports,” by M Heron, 2013. Copyright 2013 National Center for Health Statistics.[4]

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Table 2.

Clinical Outcome Trials Comparing Blood Pressure Targets

Trials Comparing SBP Target < 150 mmHg					
Trial Name	Age Range	Race/Ethnic #	BP Entry Criteria	Intervention	Findings
SHEP[29]	>60 years (mean age 72)	Blacks 657 Whites 4,079	SBP: 160–219 DBP: <100	THZD ± BB vs placebo	Achieved SBP: 143 vs. 155 mmHg CVD death ↓ 14%, $p=0.026$ Total CVA ↓ 36%
Sys-Eur [58]	> 60 (mean age 70.3)	Europeans 4,695	SBP: 160–219 DBP: <95	CCB ± ACEI ± THZ vs placebo	Achieved SBP: 151 vs. 161 mmHg CVA ↓ 42% ($p=0.003$) Fatal and nonfatal CVD ↓ 26% ($p=0.03$)
HYVET[19]	80–105 years (mean age 83.6)	W. Europeans 86 E. Europeans 2,144 Chinese 1,526 Australasian 19 Tunisian 70	SBP: > 160	THZ ± ACEI vs placebo	Achieved SBP: 143.5 vs. 158.0 mmHg Fatal and nonfatal CVA ↓ 30% ($p=0.06$) Fatal stroke ↓ 39% ($p=0.05$) HF ↓ 64% CVD mortality ↓ 23% ($p<0.001$), Total death ↓ 21% ($p=0.02$)
Trials Comparing SBP Target < 140 mmHg					
JATOS[34]	65 to 85 years (mean age 73.6)	Japanese 4,418	SBP: >160 DBP: <120	SBP <140 vs. SBP >140 to <160 mmHg	Achieved SBP: 135.9 vs. 145.6 mmHg No difference CVD No difference in AEs
VALISH[33]	70 and < 85 (mean age 76)	Japanese 3,260	SBP: >160 DBP: <90	SBP <140 vs. SBP >140 to <150 mmHg	Achieved SBP: 136.6 vs. 142.0 mmHg No differences in CVD No difference in AEs
Cardio-Sis[32]	> 55 (mean age 67.7)	Italians 1,111	SBP: >150	SBP <130 vs. SBP (<140 mm Hg	Achieved SBP: 131.6 vs. 135.6 mmHg LVH ↓ 39% ($p=0.0008$) CVD ↓ 50% ($p=0.003$)
Trials Comparing SBP Target < 140 mmHg compare to SBP target < 120 mmHg					
ACCORD[59]	> 40 to 79 years (mean age 62.2)	Blacks 1,142 Whites 2,864 Hispanic 330	SBP: 130–180	Antihypertensive drug treatment to either: SBP <120 mmHg (Intensive) vs. SBP <140 mm Hg (Standard)	Achieved SBP: 119 mmHg vs. 134 mmHg No differences in primary composite outcomes or CVD death
SPRINT[30]	> 50 (mea age 67.9)	Blacks 2,802 Whites 5,399 Hispanic 984 Other 176	SBP: 130–180	Open-label, various antihypertensive use in two SBP treatment arms: Intensive arm (<120 mm Hg) or Standard arm (<140 mm Hg)	Trial in progress.

Clinical Trial Acronyms: 1) ACCORD= The Action to Control Cardiovascular Risk in Diabetes (ACCORD) blood pressure trial (ACCORD BP); 2) Cardio-Sis = Italian Study on the Cardiovascular Effects of Systolic Blood Pressure Control; 3) HYVET = Hypertension in the Very Elderly Trial; 4) JATOS = Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly; 5) SHEP = The Systolic Hypertension in the Elderly Program; 6) Sys-Eur = The Systolic Hypertension in Europe; 7) VALISH = Valsartan in Elderly Isolated Systolic Hypertension Study; 8) SPRINT = The Systolic Blood Pressure Intervention Trial. Thiazide-type diuretic (THZD), beta blocker (BB), calcium channel blocker (CCB), angiotensin converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB).

Table 3.

Hypertension Guideline Recommendations for Blood Pressure Targets

Guideline	Evidence Review Methodology	BP Target in General Adult Population	BP Target in CKD and DM
ISHIB (2010)[18]	Consensus	<135/85	<130/80
ACCF/AHA (2011) [15]	Consensus	Age < 80: 140/90 Age <u>80</u> : 140–145/90	<130/80
NICE (2011)[60]	Systematic Review	Age < 80: <140/90 Age <u>80</u> : <150/90	<140/90
NKF-KDOQI (2012)[61]	Consensus (Graded)	<140/90	<140/90
ESH/ESC (2013)[5]	Consensus (Graded)	Age < 80: <140/90 Age <u>80</u> : <150/90	<140/90
ADA (2013)[62]	Consensus		<140/80
ASH/ISH (2014)[36]	Consensus	Age < 80: <140/90 Age <u>80</u> : <150/90	<140/90
CHEP (2014)[63]	Consensus	Age < 80: <140/90 Age <u>80</u> : <150/90	<140/90 (CKD) < 130/80 (Diabetes)
JAMA 2014 HTN Guideline[2]	Systematic Review	Age <60: <140/90 Age <u>60</u> : <150/90	<140/90

Acronyms: 1) ADA = American Diabetes Association; 2) ACCF/AHA = American College of Cardiology Foundation; 3)ASH/ISH = American Society of Hypertension and the International Society of Hypertension; 4) CHEP = Canadian Hypertension Education Program; 5) ESH/ESC = European Society of Hypertension/European Society of Cardiology; 6) ISHIB = International Society on Hypertension in Blacks; 7) JAMA = The Journal of American Medical Association; 8) NICE = National Institute for Health and Clinical; 10) NKF-KDOQI = The National Kidney Foundation Kidney Disease Outcomes Quality Initiative.

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Table 4.

Hypertension Guidelines and Recommendations: Initial Drug Selection

Guideline	Evidence Review Methodology	General Adult Population	General Black Adult Population	Diabetes Mellitus	Chronic Kidney Disease
JAMA 2014 HTN Guideline[2]	Systematic Review	ACEI/ARB/CCB/THZ	THZ/CCB/	ACEI/ARB/BB/CCB/THZ	ACEI/ARB
ISHIB (2010)[18]	Consensus	NA	Diuretic or CCB RAS/CCB over RAS/THZ unless edema or ↑ volume	ACEI/ARB	ACEI/ARB
ACCF/ANA (2011)[15]	Consensus	ACEI/ARB/CCB/THZ	THZ or CCB	ACEI/ARB/BB/CCB/THZ	ACEI/ARB
NICE (2011)[60]	Systematic Review	CCB/THZ (Age: > 55) ACEI/ARB/BB (Age: < 55)	THZ or CCB	ACEI/ARB	ACEI/ARB
NKF-KDOQI (2012)[61]	Consensus (Graded)	NR	NR	NR	ACEI or ARB with albuminuria >30 mg/day
ESH/ESC (2013)[5]	Consensus (Graded)	ACEI/ARB/BB/CCB/THZ	THZ or CCB	ACEI/ARB	ACEI/ARB
ASH/ISH (2014)[36]	Consensus	ACEI/ARB (Age: < 60) CCB/THZ (Age: > 60)	THZ or CCB	ACEI/ARB (non-Blacks) CCB/THZ (Blacks)	ACEI/ARB
CHEP[63]	Consensus	ACEI/ARB/BB*/CCB/THZ *in pts < age 60	ACEI/ARB/BB*/CCB/THZ *in pts < age 60	ACEI/ARB/BB*/CCB/THZ *in pts < age 60	

Acronyms: 1) ACCF/AHA = American College of Cardiology Foundation; 2) ASH/ISH = American Society of Hypertension and the International Society of Hypertension; 3) CHEP = Canadian Hypertension Education Program; 4) ESH/ESC = European Society of Hypertension/European Society of Cardiology; 5) ISHIB = International Society on Hypertension in Blacks; 6) JAMA = The Journal of American Medical Association; 7) NICE = National Institute for Health and Clinical; 8) NKF-KDOQI = The National Kidney Foundation Kidney Disease Outcomes Quality Initiative.

Table 5.

Trials Comparing Drug Classes in Older Black Hypertensive Patients

Trial Name (n)	Age Range	Race/Ethnic NO. (%)	Intervention	Findings
LIFE[53]	55–80 years (mean age 66.9)	Blacks 533 (6) Whites 8503 (92) Asian 43 (0.5) Hispanic 100 (1) Other 14 (0.2)	Losartan vs Atenolol	Interaction of race & treatment on CVD events ($p = 0.005$) CVD ↑ 55% in Blacks in the Losartan group
VALUE[54]	> 50 years (mean age 67.3)	Blacks 658 (4.3) Whites 13,643 (89.1) Asian 535 (3.5) Other 474 (3.1)	Valsartan vs Amlodipine	CVD† ~20% (ns) in Blacks in Valsartan group
ALLHAT[55]	> 50 years	Blacks 15,085 (35.5) Whites 19,977 (47.0) Hispanic 5,299 (12.5)	Chlorthalidone vs Doxazosin, Amlodipine, or Lisinopril	Chlorthalidone was superior in reducing BP by 4/1 mm Hg and CVD events (stroke and cardiovascular disease) compared to lisinopril in blacks
ACCOMPLISH[56]	65 years (mean age 68.4)	Blacks 1,416 (11.6) Whites 9,612 (79.0) Hispanic 623 (5.0) Other 477 (3.9)	Benazepril-Amlodipine vs Benazepril-HCTZ (only 12.5–25 mg/day HCTZ)	CVD ↓ 20% in Benazepril-amlodipine group $p < 0.001$

Clinical Trial Acronyms: 1) ACCOMPLISH = Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension; 2) ALLHAT = The Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial; 3) LIFE = Losartan Intervention For Endpoint Reduction Trial; 4) VALUE = Valsartan Antihypertensive Long-term Use Evaluation.