

**Mini Review**

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# A Review of Hypertension Treatment Disparities



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## Objectives

- Provide a review of current hypertension management best-practices.
- Assess and bridge any existing knowledge gap among providers regarding the understanding of current data related to the treatment of hypertension in specific populations.
- Understand strategies for individualizing the treatment of hypertension, given existing controversies and disparate treatment guidelines.
- Share recent clinical trial data on the use of angiotensin converting enzyme inhibitors/angiotensin receptor blockers as monotherapy and combination therapy in hypertensive African Americans.

## Introduction/Background

About 1 of 3 U.S. adults has high blood pressure. Only about half of these people have their high blood pressure under control [1]. Nearly 1 of 3 American adults has pre-hypertension, which is defined as higher than normal blood pressure values that are not yet in the high blood pressure range. Pre-hypertension is a critical threshold and an important risk factor for developing 'frank' hypertension. Hypertension increases the risk for heart disease and stroke, two of the leading causes of death for Americans. In terms of economic burden, hypertension costs the United States \$46 billion each year; these include the cost of health care services, medications to treat high blood pressure, and missed days of work. In 2013, there were over 360,000 American death cases (i.e., about 1,000 deaths per day), which included hypertension as a primary or contributing cause. Blacks develop high blood pressure more often, and at an earlier age than their white and Hispanic counterparts. However, black women are more affected by hypertension than black men [2].

The importance of early detection and control of hypertension in African-American patients cannot be over emphasized. Hypertension in Blacks has a more aggressive course, with more target organ damage and adverse cardiovascular outcomes [3]. Results of the SOLVD (Studies of Left Ventricular Dysfunction) registry show that hypertension often preceded the development of heart failure (HF) more often in African-American patients than in whites [4]. Adequate and timely administration of antihypertensive therapy has also been shown to be associated with over 50% decrease in HF, a 20%–25% decrease in MI, and a 35%–40% decrease in stroke [5]. Notwithstanding the undisputable evidence that shows that adequate BP control results in decreased cardiovascular morbidity and mortality, the prevalence of uncontrolled HTN is still significantly high. Between 1988 and 1991, less than 25% of hypertensive patients had their BP controlled compared to 31% of hypertensive patients in 2002 (NHANES data), demonstrating a modest improvement in BP control rate over a period of 11 years. A sub-group analysis of co-morbid patients receiving treatment showed that less than 50% of hypertensive-diabetic patients had their BP under control (<140/90mm Hg); however, only 4 quarter of these patients achieved the ideal BP goal of <130/85mm Hg [6].

Hypertension often occurs in association with other cardiovascular risk factors like dyslipidemia, diabetes mellitus, renal disease, and obesity. This association increases the risk of the occurrence of cardiovascular events. Mortality rate is increased by about 7.2 fold in hypertensive-diabetic patients and by 37-fold in the presence of nephropathy. The high prevalence of concomitant hypertension and diabetes in African Americans constitutes a high risk situation that predisposes this population to a disproportionate higher rate of cardiovascular-related complications. Adequate and timely control of BP. has been

shown to be associated with over 50% decrease in HF, a 20%-25% decrease in MI, and a 35%-40% decrease in stroke [3]. Nonetheless, the prevalence of uncontrolled HTN is still very high -33.5% (2013-2014, CDC's National Center for Health Statistics). A sub-group analysis of co-morbid patients receiving treatment showed that less than 50% of hypertensive-diabetic patients had their BP under control (<140/90mmHg); however, only a quarter of these patients achieved the ideal BP goal of <130/85mmHg [7].

### Disparities in the Treatment of Hypertension

Racial and ethnic disparities in healthcare persist despite guideline recommendations and attempts to improve treatment. In a study of post-MI patients, only 32.1% (N=13,681) of African Americans were treated with a beta-blocker at discharge compared to 34.7% (N=180,320) of their White counterparts [8].

According to recent NHANES data, 35% of patients with diabetes achieved their BP goals and less than 10% of diabetic patients had all vascular risk factors (HbA1c, BP, cholesterol) under control [6]. Although approximately 60% of both African Americans and whites were being treated for hypertension, only 45% of African Americans had their BP under control compared with 56% of whites, indicating that the BP control rates may have been overestimated in African Americans [9]. If we can achieve higher rates of BP control, we can significantly decrease disparities in cardiovascular outcomes. On the basis of these statistics, it is clear that physicians are not prescribing adequate therapy for African-American patients. To be more precise, the underutilization of cardio-protective therapy is profound. Although the rate of ACE inhibitors and beta-blockers prescription has somewhat increased, it is still generally at suboptimal levels, and more so in African-American patients.

Compared with whites, African Americans are at greater risk for developing a myriad of cardiovascular, metabolic, and renal complications of HTN. This mandates the need for regular BP measurement and CVD risk assessment in the primary care setting [8]. It is also important to take gene-environment interactions into account (i.e., it is more likely that multiple factors explain the excess hypertension-related morbidity and mortality in African Americans, including low SES, unhealthy lifestyle and diet, and limited access to quality health care) when deciding on therapy [10]. Additionally, emphasis should be placed on increasing awareness among African Americans regarding the important role that lifestyle choices play in cardiovascular and renal outcomes. Physicians should also screen for and treat comorbidities aggressively, as risk factors effects are multiplicative.

HTN is particularly significant in contributing to the black-white racial differences in health outcomes in the US. As such, in order to address these health disparities, practical clinical practice guidelines (CPGs) on how to treat HTN, specifically in blacks, are needed. It is the task of every physician to overcome the myth that it is more difficult to treat hypertension in African-American patients. It is paradoxical that the patients who would benefit the most from the use of certain antihypertensive agents

are the ones who do not receive them. The markedly inadequate use of these guideline-recommended, evidence-based therapies for the management of CVD in African-American patients strongly suggests the urgent need for newer strategies to increase their use. This situation must change, and it is the responsibility of every caring physician to ensure that this high-risk patient population receives proper and adequate medical treatment.

Clinical guidelines recommend using predicted atherosclerotic cardiovascular disease (ASCVD) risk to inform treatment decisions. Increases in systolic blood pressure and antihypertensive medication initiation are major contributors to the development of high 10-year predicted ASCVD risk in blacks, particularly among younger adults. Adverse cardiovascular outcomes have been shown to be associated with apparent treatment-resistant hypertension (aTRH), which is defined as uncontrolled blood pressure on three or more antihypertensive medication classes or, regardless of blood pressure, being on four or more antihypertensive medication classes. The prevalence of aTRH is higher among those with TIA, and much higher in those with a history of stroke than in those without a history of TIA/stroke. aTRH disproportionately affects African Americans, who tend to have relatively fewer sources of regular social network and support. Social network is independently associated with aTRH and warrants further investigation as a likely modifiable determinant of aTRH in African Americans.

Stroke increases the complexity of treating hypertension. Treatment and control of hypertension has been shown to be one of the most important goals in secondary stroke prevention. However, achieving adequate BP control following stroke is rather challenging. Outcomes of risk factor management in stroke survivors have described low prevalence of BP control (REGARDS study). Persistently elevated BP among black stroke survivors is especially concerning. Reasons for this are multifactorial and include compliance with medications, complexity of treatment regimen, poor healthy life style, low follow-up clinic attendance rates, and treatment resistant hypertension, among others.

There are many controversies regarding treatment of hypertension, especially in African Americans, diabetics, and elderly individuals. For example, although the most recent U.S. CPG more explicitly emphasizes race into the algorithmic management of HTN, recent clinical research cautions that use of race as a proxy to determine therapeutic response to pharmaceutical agents may be erroneous. Also, the American College of Physicians (ACP) and the American Academy of Family Physicians (AAFP) support the JNC 8 guidelines for treating HTN in individuals  $\geq 60$  years old (systolic BP [SPB] target <150mmHg and <140mmHg with previous history of stroke or TIA), while the American College of Cardiologists (ACC), American Heart Association (AHA), and International Society of Hypertension in Blacks (ISHIB) advocate for a more aggressive SBP target. In addition, there has been a long standing misconception that the RAS system is less active in blacks versus whites because of the tendency towards suppressed

circulating renin activity in blacks and the lesser average BP response in blacks as compared to white hypertensive patients with ACE inhibitors when used as monotherapy. Conversely, circulating renin levels are not fully suppressed in the majority of blacks. Also, suppressed renin production and circulating renin levels from a high sodium intake have been associated with higher, rather than lower levels of vascular angiotensin II production. There are credible data suggesting greater activation of RAS system in healthy blacks as compared to whites.

Furthermore, results from the Systolic Blood Pressure Intervention Trial (SPRINT) that recruited 1,454 Blacks vs. 698 Whites (N=4,678) to the intensive BP treatment arm (SBP<120mmHg), and 1,493 Blacks vs. 2701 Whites (N=4,683) to the standard BP treatment arm (SBP<140mmHg) suggest that in patients at high risk for cardiovascular events but without diabetes, targeting a SBP of <120mmHg, as compared to <140mmHg, resulted in lower rates of fatal and non-fatal major cardiovascular events and death from any cause, although significantly higher rates of some adverse events (e.g. hypotension, syncope, AKI, and electrolyte abnormalities) were observed in the intensive-treatment group. The median systolic BP in the intensive-treatment group was just above 120mmHg, which indicates that more than half the participants had a systolic BP above the 120mmHg target. These observations suggest that achieving a SBP of <120mmHg in the overall population of patients with HTN would be more demanding and time-consuming for both providers and patients than achieving a goal of 140mmHg, and would necessitate increased medication costs and clinic visits. The study therefore raises important practical issues, given that the control of HTN to a BP of <140/90mmHg is achieved in only about 50% of the general population in the United States.

### Addressing the Hypertension Knowledge Gap

#### Evidence-based HTN management

**A quick review of HTN management in African Americans and other populations:** Management of HTN is a multi-faceted endeavor and includes non-pharmacologic management, pharmacologic management, or a combination of both. Accurate BP measurement (both clinic and ambulatory) is essential. Payers and providers need to be willing to invest in aggressive early care in such high-risk subgroups with the understanding that they could yield potential benefits downstream from long-term improved outcomes. Given that the control of HTN to a BP of <140/90mmHg is achieved in only about 50% of the general population in the United States, achieving a SBP of <120mmHg in the overall population of patients with HTN would be more demanding and time-consuming for both providers and patients than achieving a goal of 140mmHg, and would necessitate increased medication costs and clinic visits. Notwithstanding, as earlier mentioned, the management of HTN should be on a case-by-case basis.

#### Non-pharmacologic:

- a. Initially

- b. Life style modification - increased physical activity, weight loss, dietary changes (DASH diet)
- c. Patient education and help resources
- d. Cost-effective, little or no side effects
- e. Adherence to life style changes often difficult

#### Pharmacologic:

- a. Accurate BP measurement before starting or changing treatment
- b. Given the many controversies around a consensus management protocol for HTN treatment in African Americans and older patients ( $\geq 60$  years old), treatment of HTN should be individualized using the clinician's best judgment, especially in patients with co-morbid conditions, on multiple medications, or with resistant HTN. Clinical practice guidelines are only "guides" and may not apply to all patients and to all clinical situations.
- c. Start with monotherapy and begin combination therapy if BP remains persistently elevated.
- d. In patients requiring more than one medication, consider lessening the treatment burden (i.e. avoid multiple single medications, lean more towards combination pills), and bear in mind the likelihood of drug interaction, especially for older patients on multiple treatment regimens.
- e. Use generic drugs when possible-cheaper, hence better adherence; efficacy often comparable to brand medications.
- f. In the general black population, including women and those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic or CCB.
- g. If goal BP is not reached within a month of treatment, increase the dose of the initial drug or add a second drug from one of the following classes-thiazide-type diuretic, CCB, and ACEI or ARB. The clinician should continue to assess BP and adjust the treatment regimen until goal BP is reached. If goal BP cannot be reached with 2 drugs, add and titrate a third drug from the list provided. Do not use an ACEI and an ARB together in the same patient. If goal BP cannot be reached using the suggested classes of drugs because of a contraindication or the need to use more than 3 drugs to reach goal BP, antihypertensive drugs from other classes can be explored.
- h. There is a need for physicians and other healthcare personnel to be aware of upcoming new clinical trials information related to the use of ACEIs and ARBs (RAAS blockers) in the treatment of HTN in African-Americans. For example, chlorthalidone has been shown to be effective in many hypertensive populations and has been found to be particularly effective when given in combination with a RAAS blocker (antagonist). Race and or ethnicity should not always

be used as a sole determinant of whether or not to use a RAAS antagonist, especially when used synergistically with other classes of medications like chlorthalidone.

i. Care providers should avoid treatment inertia toward the use of certain medication for treating HTN in African Americans (especially in those with other co-morbid conditions like CKD, MI, and HF), including the use of ACEI, ARBS and B-blockers, when necessary.

j. Referral to a hypertension specialist may be indicated for patients in whom goal BP cannot be attained using the above strategy, or for the management of complicated patients for whom additional clinical consultation is needed.

### Education knowledge gap

While the disproportionate impact of CVD on African Americans may in part be due to genetic factors, it is undeniable that environmental risks and treatment differences exist. The African-American population is treated less aggressively for CVD, and it was shown in one study that revascularization procedures are less likely to be performed in African-American than in white patients [11]. Physicians may require both educational tools and specific guidelines for providing care to African-American patients, and they may need to have a heightened awareness of the risk factors for hypertension and the early markers of target-organ disease. They also need clear, evidence-based clinical guidelines for specific interventions, used singly and in combination, to achieve optimal outcomes. New guidelines for screening and treating BP should be applied to all patients, including African Americans. In addition, physicians need guidelines to screen for other potentially critical clinical markers such as impaired glucose tolerance, micro-albuminuria, and central obesity. There are a number of barriers to achieving adequate BP goals in African-American patients, but it is possible to overcome these barriers by refuting the misconceptions that BP goals are not achievable in this population, that medications are not tolerated, and that certain medications do not work in African-American patients.

### A new treatment paradigm

It is imperative to acknowledge that more research is needed to better understand the context of race in medicine. Race per se is neither physiologic nor scientific, but rather refers to a grouping of individuals with similar inherited traits and shared environmental stresses. The physiologic determinants of the excess in CVD burden and/or the important psychosocial and socioeconomic factors that contribute to this disease burden need further clarification. Nevertheless, a new paradigm for the treatment of the African-American patient at risk for CVD is necessary since it has become clear that physicians still have a lot to do in properly and adequately treating this high-risk population. This new paradigm needs to encompass a comprehensive patient assessment for treatment that includes race, family history, and concomitant conditions in addition to

earlier treatment with appropriate agents. Physicians should be familiar with antihypertensive agents and should employ them more frequently.

### Future directions in HTN research

It is very important to consider including more individuals from special populations in future HTN trials. Many clinical trials on life-saving cardiac interventions [9] and hypertension [12-15] have enrolled a disproportionately smaller number of African-Americans and other special populations; therefore, making conclusions based on sub-group analyses difficult to interpret. In future HTN studies, researchers should endeavor to work towards a better representation of under-represented populations, and assess whether or not race and ethnicity should or should not impact the development of clinical practice guidelines. Designing more hypertension studies, and ensuring better representation of African-Americans in these studies would provide more evidence-based insights for formulating race-based clinical practice guidelines. Additional research is also needed to assess specific treatment needs of hypertensive patients with other concomitant chronic conditions as well as the utility of targeting treatment according to diastolic BP.

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