NHLBI-INITIATED PROGRAM “INTERVENTIONS TO IMPROVE HYPERTENSION CONTROL RATES IN AFRICAN AMERICANS”: BACKGROUND AND IMPLEMENTATION

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Hypertension affects more than 70 million adults in the United States and nearly one billion globally.¹,² African Americans have been long recognized to have the highest prevalence and the earliest onset of hypertension. Hypertension is also a major contributor to the racial gap in cardiovascular mortality between Caucasians and African Americans – more than two-fold for ages 35–64, and for men this gap has increased since 1960.³

Background
National and Regional Surveillance

In 2002, Wong et al estimated cause-specific risks of death from the National Health Interview Survey conducted from 1986 through 1994 and from linked vital statistics (a national probability sample of over 600,000 individuals) according to education level and race.⁴ They identified hypertension as the single initiating cause of death independent of socioeconomic status that contributed the most to the racial disparity in potential life-years lost between African Americans and Caucasians.

At the same time, the National Health and Nutrition Examination Survey (NHANES) 1999–2000 data became available to NHLBI staff. These data revealed low rates of blood pressure (BP) control in treated African Americans, in addition to a long-recognized high prevalence of hypertension defined as BP>140/90 mmHg or treated. As shown in Figure 1, one out of five African American men age 30–39 had hypertension (compared with one out of eight Caucasian and Mexican American men the same age). Although the prevalence rates for women aged 30–39 were relatively low for all race/ethnic groups (6–9%), by age 40–49, nearly half of African American women had hypertension (compared with only 20% of Caucasian and Mexican American women). For the older age group 60–74 years, about three quarters of African American men and 81% of African American women had hypertension – numbers considerably higher than for either Caucasians or Mexican Americans.
Notably (Figure 2), in African Americans aged 40 and over, awareness of hypertension was high (71–83% across gender/age groups) and a large majority of those aware of their hypertension reported being treated (83–97% across gender/age groups), numbers similar to those in Caucasians and considerably higher than in Mexican Americans. However, the proportion of treated African American patients whose BP was controlled to below 140/90 mm Hg remained low (<50%), and in those aged 40–59 was more than one third lower than in Caucasians (49 versus 75% for men and 41 versus 72% for women).

These data were presented to the NHLBI Institute Director in February 2003 with a recommendation for research to evaluate strategies to increase the proportion of treated hypertensive African Americans with hypertension adequately controlled in diverse medical settings. This recommendation stemmed from a conclusion that given the importance of BP levels in determining future risk of cardiovascular events, intervention in this age group should lead to a decline in cardiovascular mortality and morbidity in African Americans, and thus decrease premature disability and associated economic burden.

In contrast, for Mexican Americans, the recommendation was for community-based interventions targeting awareness and access to care for multiple risk factors, given low levels of awareness and treatment, and lack of prominence of any of the components of the cardiometabolic syndrome.(5)

A recent publication from New York City HANES conducted in 2004 (modeled on national HANES) provides further evidence for the disparately low BP control rates among treated non-Hispanic Black individuals. After adjusting for socio-demographic variables, including insurance coverage and routine place of care, the OR (95% CI) for BP control among 20–64 years old African Americans with treated hypertension was 0.24 (0.06–0.92) compared with Caucasians.(6)

### Practice-based Clinical Trial

The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Trial (ALLHAT) was a randomized, double-blind, practice-based hypertension treatment trial in 42,418 men and women (46.8%) aged 55 years or older (mean 67 years) with hypertension and one or more additional cardiovascular risk factor. It compared four commonly used classes of antihypertensive agents (a thiazide-type diuretic, a calcium-channel blocker, an ACE-inhibitor, and an alpha-blocker) as initial therapy for hypertension for their effects on major cardiovascular outcomes.(7) The trial was conducted in diverse, mostly primary care, practice settings (623 centers in the United States, Canada, and the Caribbean) and by design included large representation of minority participants (15,094 were Black and 8,100 Hispanic).(8) ALLHAT participants were followed from 1994 to 2002 for an average of 4.9 years; 90% were on 1–2 medications prior to enrollment. After 5 years of follow-up, two-thirds of participants had their BP controlled to below target levels of 140/90 mm Hg. However, even in the clinical trial setting involving a large community-based research network, free medications, and education and feedback, BP control was lower in Black participants (60.9%) than in non-Black participants (68.2%), at year-5 clinic visit. This was despite the fact that more Black than non-Black participants were treated with 3 or more medications and that uptitration of drugs (increase in dose or addition of new drug) did not differ between non-Hispanic Blacks and non-Hispanic Whites (but did for Hispanics). The disparity between Black and non-Black participants was more pronounced in the ACE-inhibitor-based treatment arm, while first-step treatment with the diuretic clearly provided superior BP control overall, but especially in Black participants.(9,10)

While BP control is a readily available marker of response to antihypertensive treatment, it is of great importance to recognize that the ultimate measure of the treatment success is its ability
to prevent major clinical outcomes. We treat hypertension to prevent stroke, heart failure, coronary heart disease, renal failure, and premature death. ALLHAT was designed to compare the effects on cardiovascular and renal outcomes of an established treatment based on a thiazide-type-diuretic (chlorthalidone; C) with three strategies based on newer medications with better biochemical profiles [an ACE-inhibitor (lisinopril; L), a calcium-channel blocker (amlodipine; A) and an alpha-blocker (doxazosin; D)]. After an average of 4.9 years of follow-up (3.2 for the terminated early doxazosin arm), the investigators reported no difference between randomized comparisons for the composite of myocardial infarction and fatal CHD (primary endpoint). However, chlorthalidone (average dose ~20 mg/day) was superior to all comparators in preventing new-onset heart failure (D/C RR=1.80, p<0.001; A/C RR=1.38, p<0.001; L/C RR=1.19, p<0.001). It was also superior to doxazosin and lisinopril groups in preventing a combined cardiovascular endpoint. An important race-specific finding was a higher rate of stroke in the lisinopril compared with chlorthalidone group in Black, but not in non-Black, participants [L/C RR(black)=1.40, p<0.001; RR(non-Black)=1.00; p=0.97; p for interaction=0.01]. These findings could not be explained by small differences in achieved BP levels in time-dependent analyses and the heart failure endpoint has been extensively validated (11–14). Except for stroke, the findings were consistent across pre-specified subgroups, including patients with diabetes (N=15,297), and were recently extended to those with metabolic syndrome, including Black individuals (N=23,077; 32% Black).(11–13,15)

**Initiative Development**

The above-described disparity in BP control between treated African Americans and Caucasians occurred despite availability of efficacious strategies for both lifestyle and pharmacological treatment of hypertension, including availability of several apparently well-tolerated generic medications.(16) ALLHAT results addressed two important barriers to effective treatment of hypertension in African Americans - lack of clinical trial data in African Americans on drugs other than diuretics and the cost of drugs.(10–15,17,18) This evidence and the release of JNC-7 guidelines provided opportune timing and the impetus for intervention studies targeted at improving quality of treatment of hypertension in African Americans.(16, 19)

At that time, intervention research in hypertensive African Americans had primarily focused on bringing individuals with elevated BP levels to medical attention and improving patient adherence to prescribed antihypertensive medications and clinic appointments.(20–26). Yet, observational studies were pointing to the importance of additional factors, such as patient experience with clinicians, clinicians’ acceptance of less than optimal blood pressure levels (clinical inertia), clinicians’ experience with a variety of antihypertensive medications, patients’ participation in treatment decisions, and commercial influences.(27–30) While many of these factors may be common across racial groups, it seemed reasonable to assume that intervention approaches may need to be tailored to race/ethnicity-specific cultural/social and clinical issues. Many hypertensive African American patients are younger than other demographic groups due to earlier onset of hypertension. In addition, long-standing hypertension and associated co-morbidities may make selection of treatment regimens more difficult and may affect adherence due to increased potential for side effects. Finally, there was evidence that African American patients reported less satisfaction with care and perceived racial bias, stereotyping, and prejudice appeared to continue affecting quality of care and treatment outcomes.(31) Researchers were consistently pointing to the need for more culturally acceptable and effective methods of delivering hypertension care.

At the same time, results of two NHLBI-funded randomized clinical trials became available suggesting effectiveness of clinic-based programs in improving blood pressure control rates among treated hypertensive African Americans. (32,33) Notably, better hypertension control
(62% versus 41%) was achieved when the intervention included change in an institutional environment/culture, feedback to clinicians, and access to specialized care.(33) This control rate was similar to that achieved in ALLHAT (61%) using organizational-level approaches. (9) While representing substantial improvements, these rates were far from optimal. Thus, there was a need for further research into improving hypertension control in this population, especially in the area of interventions targeting clinical care delivery.

**Request for Applications**

To address this issue, NHLBI set aside $3 million in FY 04 and a total of $17.5 million over five years to fund 3–6 new grants. The objective of the request for applications (RFA) was to evaluate clinically feasible interventions to effect changes in medical care delivery leading to an increase in the proportion of treated hypertensive African American patients whose BP was controlled to levels specified by Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC) guidelines. The ultimate goal was to prevent complications of hypertension, and thus increase quality and years of healthy life in African Americans - a group with highest prevalence and earliest onset of hypertension, and disparately high premature cardiovascular mortality and morbidity. For the purpose of this initiative, components of medical care delivery consisted of patients, clinicians, interactions between patients and clinicians, and physical, social and administrative environments in which these interactions occur. A special requirement in the solicitation was inclusion of a cost-effectiveness analysis.

The RFA was published on September 2, 2003.(35) Following peer review by a specially appointed review panel, 5 top-ranked applications were awarded in September 2004. The five cluster-randomized, concurrently-controlled community-based projects in about 3,500 African-American patients, evaluate the following interventions: 1) a multi-component, multi-level intervention involving life-style and medications in 990 patients treated in 30+ health care centers; 2) a multi-component internet-based home automated tele-management system targeting both patients and providers (50 clinics, 550 patients); 3) a multi-component organization-level intervention in community pharmacies targeting both patients and physicians (28 pharmacy sites, 600 patients); 4) information, monitoring, and feedback for patients and physicians delivered by visiting nurses in home care settings (300 nurses, 850 patients); and 5) a diffusion of information theory-based intervention targeting provider treatment actions using uncertainty reduction tools, including 24-hour ambulatory BP monitoring, electronic bottle caps, and medication and life-style counseling (10 clinics, 700 patients).

**Establishing Collaboration**

The five grants were funded as independent research projects. However, the RFA contained a provision for collaboration amongst investigators to be encouraged and facilitated, as appropriate. There was also a provision for the grantees to meet annually to discuss project progress, share experiences and discuss overall progress of relevant scientific areas.

During the first year, the investigators had monthly conference calls and also met in person to learn about each other’s projects, share information and study materials, and identify possible areas for common data collection to allow pooled analyses and/or evaluation of results across two or more projects. Consideration was given to using the same BP measurement equipment across the trials. However, after careful review of individual study designs it turned out not to be feasible. The investigators engaged in extensive discussions about ways to promote and assess intervention fidelity, sharing experience and advice. Similarly, they explored patient adherence and physician engagement, including physician responsiveness to non-physician recommendations and/or prompts.
The investigators agreed on common core economic (CEA) and quality of life analyses. The analysis will be by intention-to-treat. Co-primary outcome measures for the CEAs will be reductions in systolic BP in mmHg and proportion of patients with BP controlled, defined according to JNC-7 criteria. Cost measurements were defined to include visit costs, intervention costs, and medication costs. All programs agreed to measure quality of life using the five-question Euroqol instrument plus Torrence’s transformation of the Visual Analog Scale (VAS), in addition to any project-specific measurements. (35)

When the investigators became busy implementing study protocols, conference calls were reduced to every 2–3 months. The calls and the annual in-person meetings served as forums to share progress, problems and solutions, and obtain advice and support from the group. As the projects enter close-out phase, the investigators are discussing and implementing strategies to minimize losses to follow-up. Their collective experience should make a valuable contribution to this important area of methodological and operational knowledge in community-based clinical trials.

Perspective

The RFA required that the applications include a plan for dissemination of research results and of the intervention – with the latter to be implemented only if the intervention is successful. The RFA also allowed for the dissemination implementation to continue for up to one year beyond the award period as a no-cost extension. The publication of the design papers constitutes the first step in the dissemination of these 5 projects’ results.

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References


Figure 1.
Prevalence of hypertension, NHANES 1999–2000
Figure 2.
Awareness, treatment, and control of hypertension, NHANES 1999–2000