Hypertension affects more than 70 million adults in the United States and nearly one billion globally.\textsuperscript{1,2} Blacks 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 whites and blacks—more than 2-fold for ages 35 to 64, and for men this gap has increased since 1960.\textsuperscript{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 more than 600,000 individuals) according to education level and race.\textsuperscript{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 blacks and whites.

At the same time, the National Health and Nutrition Examination Survey (NHANES) 1999 to 2000 data became available to National Heart, Lung, and Blood Institute (NHLBI) staff. These data revealed low rates of blood pressure (BP) control in treated non-Hispanic blacks, in addition to a long-recognized high prevalence of hypertension defined as BP $\geq$ 140/90 mm Hg or treated. As shown in Figure 1, 1 of 5 black men age 30 to 39 had hypertension (compared with 1 of 8 white and Hispanic men the same age). Although the prevalence rates for women aged 30 to 39 were relatively low for all race/ethnic groups (6% to 9%), by age 40 to 49, nearly half of black women had hypertension (compared with only 20% of white and Hispanic women). For the older age group 60 to 74 years, about three quarters of black men and 81% of black women had hypertension—numbers considerably higher than for either whites or Hispanics.

Notably (Figure 2), in blacks aged 40 and over, awareness of hypertension was high (71% to 83% across gender/age groups) and a large majority of those aware of their hypertension reported being treated (83% to 97% across gender/age groups), numbers similar to those in whites and considerably higher than in Hispanics. However, the proportion of treated black patients whose BP was controlled to below 140/90 mm Hg remained low (<50%), and in those aged 40 to 59 was more than one third lower than in whites (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 blacks with BP 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 blacks, and thus decrease premature disability and associated economic burden.

In contrast, for Hispanics, 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 cardio-metabolic syndrome.\textsuperscript{5}

A recent publication from New York City HANES conducted in 2004 (modeled on NHANES) 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 odds ratio (95% CI) for BP control among 20 to 64 years old blacks with treated hypertension was 0.24 (0.06 to 0.92) compared with whites.\textsuperscript{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 1 or more additional cardiovascular risk factor. It compared 4 commonly used classes of antihypertensive agents (a thiazide-type diuretic, a calcium-channel
blocker, an angiotensin-converting enzyme 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 to 2 medications before 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 nonblack participants (68.2%), at year-5 clinic visit. This was despite the fact that more black than nonblack 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 nonblack participants was more pronounced in the angiotensin-converting enzyme inhibitor-based treatment arm, whereas first-step treatment with the diuretic clearly provided superior BP control overall, but especially in black participants.\(^9,10\)

Although 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 3 strategies based on newer medications with better biochemical profiles (an angiotensin-converting enzyme 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 end point). However, chlorthalidone (average dose \( \approx 20 \) mg/d) was superior to all comparators in preventing new-onset heart failure (D/C relative risk [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 end point. An important race-specific finding was a higher rate of stroke in the lisinopril compared with chlorthalidone group in black, but not in nonblack, participants (L/C RR [black] = 1.40, \( P < 0.001 \); RR [nonblack] = 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 end point has been extensively validated.\(^11-14\) Except for stroke, the findings were consistent across prespecified 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 blacks and whites 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 ad-
dressed 2 important barriers to effective treatment of hypertension in blacks—lack of clinical trial data in blacks on drugs other than diuretics and the cost of drugs.10–15,17,18 This evidence and the release of Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC)-7 guidelines provided opportune timing and the impetus for intervention studies targeted at improving quality of treatment of hypertension in blacks.16,19

At that time, intervention research in hypertensive blacks 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 Although 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 black patients are younger than other demographic groups because of earlier onset of hypertension. In addition, long-standing hypertension and associated comorbidities may make selection of treatment regimens more difficult and may affect adherence because of increased potential for side effects. Finally, there was evidence that black 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 2 NHLBI-funded randomized clinical trials became available suggesting effectiveness of clinic-based programs in improving blood pressure control rates among treated hypertensive blacks.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 Although 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 fiscal year 2004 and a total of $17.5 million over 5 years to fund 3 to 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 black patients whose BP was controlled to levels specified by JNC guidelines. The ultimate goal was to prevent complications of hypertension, and thus increase quality and years of healthy life in blacks—a group with highest prevalence and earliest onset of hypertension, and disproportionately 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, 2003.34 Following peer review by a specially appointed review panel, 5 top-ranked applications were awarded in September 2004. The 5 cluster-randomized, concurrently-controlled community-based projects in ~3500 black patients, evaluate the following interventions: (1) a multicomponent multi-level intervention involving lifestyle and medications in 990 patients treated in 30+ health care centers; (2) a multicomponent internet-based home automated telemanagement 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 lifestyle counseling (10 clinics, 700 patients).

**Establishing Collaboration**

The 5 grants were funded as independent research projects. However, the RFA contained a provision for collaboration among 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 or evaluation of results across 2 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 nonphysician recommendations or prompts.

The investigators agreed on common core economic and quality of life analyses. The analysis will be by intention-to-treat. Co-primary outcome measures for the core economic analyses will be reductions in systolic BP in mm Hg 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 5-question Euroqol instrument plus Torrence transformation...
of the Visual Analog Scale, in addition to any project-specific measurements.  

When the investigators became busy implementing study protocols, conference calls were reduced to every 2 to 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 1 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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Disclosures

None.

References


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