Time Trends in High Blood Pressure Control and the Use of Antihypertensive Medications in Older Adults

The Cardiovascular Health Study

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Background: Control of high blood pressure (BP) in older adults is an important part of public health efforts at prevention.

Objective: To assess recent time trends in the awareness, treatment, and control of high BP and in the use of medications to treat high BP.

Methods: In the Cardiovascular Health Study, 5888 adults 65 years and older were recruited from 4 US centers. At baseline, participants underwent an extensive examination that included the measurement of BP, use of medications, and other risk factors. Participants were followed up with annual visits that assessed BP and medication use from baseline in 1989-1990 through the examination in 1998-1999. The primary outcome measures were control of BP to levels lower than than 140/90 mm Hg and the prevalence of use of various classes of antihypertensive medications.

Results: The awareness, treatment, and control of high BP improved during the 1990s. The proportions aware and treated were higher among blacks than whites, though control prevalences were similar. For both groups combined, the control of high BP to lower than 140/90 mm Hg increased from 37% at baseline to 49% in 1999. The 51% whose BP was not controlled generally had isolated mild to moderate elevations in systolic BP. Among treated persons, the improvement in control was achieved in part by a mean increase of 0.2 antihypertensive medications per person over the course of 9 years. Improved control was also achieved by increasing the proportion of the entire Cardiovascular Health Study population that was treated for hypertension, from 34.5% in 1990 to 51.1% in 1999. Time trends in antihypertensive drug use were pronounced. Among those without coronary disease, the use of low-dose diuretics and β-blockers decreased, while the use of newer agents, such as calcium channel blockers, angiotensin-converting enzyme inhibitors, and α-blockers increased.

Conclusions: While control of high BP improved in the 1990s, about half the participants with hypertension had uncontrolled BP, primarily mild to moderate elevations in systolic BP. Low-dose diuretics and β-blockers—the preferred agents since 1993 according to the recommendations of the Joint National Committee on the Detection, Evaluation and Treatment of High Blood Pressure—remained underused. More widespread use of these agents will be an important intervention to prevent the devastating complications of hypertension, including stroke, myocardial infarction, and heart failure.

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declined from 18.5% in 1950 to 9.2% in 1989. Data from the National Health and Nutrition Examination Survey (NHANES) III, phase 1, in 1988-1991, suggested that among subjects with hypertension aged 18 to 74 years, the control of high BP to lower than 140/90 mm Hg was present in only 29%, 11,14 and in phase 2, conducted in 1991-1994, the proportion with controlled high BP declined slightly to 27%. 14 In a recent analysis of NHANES III data, Hyman and Pavlik13 have drawn attention to the importance of uncontrolled systolic BP.

Since 1993, the JNC guidelines have also recommended diuretics and β-blockers as first-line pharmacologic therapy for uncomplicated high BP. 14 The results of recent trials 15-17 and several meta-analyses 18,19 have drawn attention again to the importance of drug selection in defining appropriate care of high BP. Despite similar levels of BP lowering in the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), 15 doxazosin was associated with higher risk of heart failure, stroke, and angina than low-dose diuretics. In a trial in patients with diabetic nephropathy, 17 irbesartan was superior to both placebo and amloidipine in reducing the risk of major renal outcomes. In one meta-analysis of comparative clinical trials, calcium channel blockers were associated with higher risks of heart failure and myocardial infarction than other forms of antihypertensive therapy, 18,19 and in another, they were associated with higher risks of coronary disease and heart failure than angiotensin-converting enzyme (ACE) inhibitors. 19 In the present report, we use data from the Cardiovascular Health Study (CHS), 20 a cohort study of older adults, to trace control of high BP and treatment trends during the last decade of the 20th century.

METHODS

SETTING

The CHS is a prospective cohort study of risk factors for coronary heart disease and stroke in men and women 65 years and older. In June 1990, 4 Field Centers completed recruitment of 5201 participants. In June 1993, the recruitment of an additional 687 black subjects was completed using similar methods. Each community sample was obtained from random samples of the Medicare eligibility lists, and those eligible to participate included all persons who were living in the household of each individual sampled from the Health Care Financing Administration lists and who (1) were 65 years or older; (2) were not institutionalized; (3) expected to remain in the area for 3 years; and (4) gave informed consent and did not require a proxy respondent. Among those contacted and eligible, 57.3% were enrolled. The CHS design and recruitment experience are described in detail elsewhere. 20,21 Self-reported hypertension was about 7% higher among the eligible subjects who refused to participate than among those who were eligible and participated. 21

BASELINE EXAMINATION

The baseline examination consisted of a home interview and a clinic examination. Participants answered standard questionnaires assessing a variety of risk factors, including smoking status, physical activity, and history of cardiovascular conditions and procedures. 22 Self-reported cardiovascular conditions such as myocardial infarction, angina, and stroke were validated. 23 Medications were assessed by inventory at the home interview. 23

Participants were asked to come to a morning clinic examination after an 8- to 12-hour overnight fast. All examinations were scheduled in the morning. Seated BP measurements, electrocardiography, and venipuncture were all performed early in the examination. Blood pressure was measured in the right arm of seated participants after a 5-minute rest using an appropriately sized cuff and a Hawksley random-zero sphygmomanometer (model 7076; Hawksley and Sons Ltd, Sussex, England) in 1989-1990 and a standard mercury sphygmomanometer in 1992-1993. Duplicate measures of supine BP in the right arm and both posterior tibial arteries were assessed by an 8-MHz Doppler probe attached to a stethoscope, and the ratio of systolic BPs was used to calculate the ankle-arm index.

Anthropomorphic measures included weight and height. Blood samples from the fasting venipuncture were analyzed at the Central Blood Analysis Laboratory for glucose, total cholesterol, high-density lipoprotein cholesterol, and triglycerides, standardized according to the Centers for Disease Control and Prevention as previously described. 20,24 Low-density lipoprotein cholesterol was calculated according to the Friedewald equation. 25

FOLLOW-UP EXAMINATIONS

Participants were contacted every 6 months, and the contacts alternated between a telephone interview and a clinic examination. At all but 1 annual clinic examination when BP was not measured (1993-1996), BP was measured in the right arm of seated participants after a 5-minute rest using an appropriately sized cuff and a standard mercury sphygmomanometer. Time since last meal was recorded. Blood pressures were adjusted for fasting time to reduce the postprandial effects. 26,27 Participants were asked to bring their medications to the clinic, and use was assessed by medication inventory. 22 According to protocol, participants and their physicians were informed if their BPs were high, and the follow-up recommendations were based on the current JNC guidelines. At each contact, participants were asked about cardiovascular events and all hospitalizations. All deaths and cardiovascular events were reviewed and classified by an events committee. 28,29 Cumulative loss to follow-up through 1999 was 5.6%.

DEFINITION OF VARIABLES AND METHODS OF STATISTICAL ANALYSIS

Coronary heart disease was defined as a history of myocardial infarction or angina; coronary artery disease (CAD) was defined as coronary heart disease or a history of coronary bypass surgery or angioplasty; cerebrovascular disease was defined as a history of transient ischemic attack or stroke; and peripheral vascular disease was defined as a history of claudication, peripheral artery bypass grafting or angioplasty, or an ankle-arm index less than 0.9. During follow-up, when events occurred, the status of these event variables was updated to reflect its current status at each examination year. Left ventricular hypertrophy was defined by the baseline electrocardiogram by Minnesota code, 30 and body mass index was defined as weight in kilograms divided by the square of height in meters.

Medication use was defined according to major commonly used classes of antihypertensive medications, including diuretics (thiazide plus loop), β-blockers, calcium channel blockers, α-blockers, ACE inhibitors, and other miscellaneous vasodilators. The use of angiotensin receptor blockers was low during most of the study period, and these agents were included with the ACE inhibitors.

Definitions of awareness, treatment, and control were similar to those used in the NHANES. 31,32 Elevated BP was defined as...
as 140/90 mm Hg or higher. Treated hypertension at baseline was defined, regardless of BP, as a person who reported a history of high BP and who was using medications that are indicated for the treatment of hypertension. For the analyses of awareness, treatment, and control, the population with high BP included those with treated hypertension or elevated BP. Control was defined in several ways: BP lower than 140/90 mm Hg; diastolic BP lower than 90 mm Hg; or systolic BP lower than 140, 150, or 160 mm Hg. Stages of high BP were defined according to recommendations of the JNC.14 Systolic and diastolic BP criteria for types of hypertension were (1) isolated diastolic hypertension (<140 mm Hg systolic and ≥90 mm Hg diastolic); (2) isolated systolic hypertension (≥160 mm Hg systolic and <90 mm Hg diastolic); (3) borderline isolated systolic hypertension (140-159 mm Hg systolic and <90 mm Hg diastolic); and (4) combined hypertension (≥140 mm Hg systolic and ≥90 mm Hg diastolic). Several analyses were stratified by race as whites vs nonwhites. Since 96% of the nonwhites were blacks, for ease of reference we refer to this group as black.

We used SAS (version 8.2; SAS Institute Inc, Cary NC) and SPSS (version 10; SPSS Inc, Chicago, Ill) for Windows for data analysis. Techniques included analysis of variance for continuous variables and χ² tests for categorical variables.33 Comparision of means and proportions across time were analyzed using generalized estimating equations to adjust significance tests (for trend and for differences in proportions) for the nonindependence of the serial observations.34,35 All P values represent 2-sided tests. These analyses were based on the updated CHS database, which incorporated minor corrections through August 6, 2001.

(continued)
RESULTS

Of the 5888 CHS participants, 113 were excluded from the baseline analysis because of missing self-reported hypertension data (n=92), BP measurements (n=15), or medication data (n=6). The baseline characteristics of the remaining 5775 subjects are summarized in the Table according to race and self-reported hypertension status at baseline. At baseline, 44.0% of whites and 65.1% of blacks reported a history of hypertension. For both race groups, BP's were higher, and with the exception of smoking, other risk factors were generally more common in subjects with than in those without a self-reported history of hypertension. Among those with a history of high BP, mean levels were 139.8/70.3 mm Hg in whites and 144.2/75.6 mm Hg in blacks, and lack of control was typically characterized by isolated and borderline isolated systolic hypertension. Among whites and blacks, 78% and 84%, respectively, of those reporting a history of high BP were being treated with at least 1 antihypertensive medication. About 20% of those without a self-reported history of high BP were also taking at least 1 of these medications, typically for coronary disease or other indications.

At baseline in 1989-1990, 35.2% of the original cohort (1793/5098) had treated hypertension; at baseline for the new black cohort in 1992-1993, 57.2% (387/677) had treated hypertension; and by 1999, 51.1% of the surviving cohort (1623/3179) had treated hypertension. **Figure 1A** illustrates the time trends in awareness, treatment, and control among participants with high BP from the baseline examination through June 1999. During this period, awareness increased from 73% to 88%; treatment from 66% to 81%; and control, defined as BP less than 140/90 mm Hg, from 37% to 49% (P<.001 for trend). Figure 1B illustrates, according to several criteria, the control of high BP among those who were undergoing treatment. By the criterion of diastolic BP lower than 90 mm Hg, the BP of 94% to 98% of subjects was controlled throughout the study. For systolic BP, control to levels lower than 140 mm Hg improved from 56% to 61%; control to levels lower than 150 mm Hg improved from 71% to 77%; and control to levels lower than 160 mm Hg improved from 82% to 88%. Trends were significant (P<.01) for all 4 definitions of control in Figure 2. Among those who reported a history of hypertension by 1998-1999, the prevalences of diastolic, isolated systolic, and borderline isolated systolic hypertension (uncontrolled or untreated) were 2.5%, 11.7%, and 26.1%, respectively.

At baseline, subjects with treated hypertension were undergoing treatment with a mean of 1.5 antihypertensive medications. By 1999, the mean number of antihypertensive medications had increased to 1.7 per person (P<.001). **Figure 3** illustrates the proportions of subjects who were taking 1, 2, 3, or 4 or more medications. The proportion taking 1 medicine decreased from 55% at baseline to 48% in 1999 (P<.001 for trend), and the proportion taking 3 medications increased from 7% to 12% over the same period (P<.001 for trend). The number of medications in those controlled and noncontrolled to a BP of 140/90 mm Hg did not differ.
those with controlled BP in 1999, the proportions taking 1, 2, 3, and 4 or more antihypertensive medications were 46%, 40%, 12%, and 2%, respectively (mean, 1.7). Among those whose BP was not controlled in 1999, the proportions were 49%, 36%, 13%, and 2%, respectively (mean, 1.7).

Figure 4 illustrates the time trends in the use of major classes of antihypertensive drugs stratified on the presence or absence of CAD. Among those free of CAD, the use of thiazide diuretics dropped markedly from 60% in 1990 to 38% in 1999; β-blocker use declined until 1994 and then increased slightly; use of ACE inhibitors doubled gradu- ally from 17% to 37%; use of calcium channel blockers increased from 14% to 35% in 1995 and remained about the same until 1999 (36%; \( P = .58 \) for 1995–1999 trend); α-blockers increased from 6% to 9%; and loop diuretics doubled from 8% to 16% (\( P < .01 \) for all 1990–1999 trends except β-blockers). The patterns differed for those with CAD (Figure 4B). While the use of thiazide diuretics declined from 36% to 19%, the use of loop diuretics increased from 19% to 30% (\( P < .001 \) for trend). Calcium channel blocker use increased to a peak of 57% in 1994 and then declined to 43% in 1999 (\( P < .001 \) for 1995–1999 trend). The course of β-blocker use was a mirror image—first declining to 32% in 1993 and then increasing to 41% in 1999 (\( P < .003 \) for 1995–1999 trend). Use of ACE inhibitors increased almost linearly from 18% in 1990 to 40% in 1999. 

**COMMENT**

Despite the expected increases in systolic BP with the advancing age of the CHS cohort, the awareness, treatment, and control of high BP improved steadily during the 1990s. The proportions of subjects aware and treated were higher among blacks than whites, though control was similar. For both groups combined, the control of high BP to lower than 140/90 mm Hg increased from 37% in 1990 to 49% in 1999. The proportion with controlled hypertension depended importantly on the systolic BP criterion. The 51% whose BP was not optimally controlled often had isolated mild to moderate elevations in systolic BP. The improvement in control may have been achieved in part by a greater use of multidrug therapy in those who were treated—a mean increase of 0.2 antihypertensive medications per person over the course of 9 years. Improved control in the cohort was also achieved by increasing the proportion of CHS participants who were treated from 34.5% in 1990 to 51.1% in 1999. Time trends in antihypertensive drug use were pronounced. Among those without CAD, the use of low-dose diuretics and β-blockers—the preferred agents since 1993 according to the JNC V \( ^{10} \) and JNC VI \( ^{11} \) recommendations—decreased, while the use of newer agents, such as calcium channel blockers, ACE inhibitors, and α-blockers all increased, sometimes markedly.

In the present study, the time trends represent findings in a cohort observed over time, and as the cohort ages, the characteristics may become unrepresentative of a random sample of adults 65 years or older. In this observational study, participants and their physicians were also informed of the study BP levels, and the protocol included appropriate “alerts” defined by the level of the increased BP. These “observational interventions” probably affected levels of awareness, treatment, and control over time. In Figure 1B, for instance, the 687 new members of the black cohort entered the study in 1993; their control level was
significantly lower than that of whites, who had been in the study for several years; and by the next year, after they and their physicians would have received feedback on their baseline BP levels, the proportion of black subjects with controlled BP had improved. Of course, feedback to participants and physicians is not a powerful intervention; if it were, levels of control, for instance, would have improved over the course of 9 years far above the 49% seen in 1999. Other studies have suggested little or no improvement in awareness, treatment, and control of high BP in the late 1980s and early 1990s.10,13,14

While the national guidelines define a treatable level of high BP as equal to or greater than 140/90 mm Hg, it is clear that physicians do not uniformly agree with this criterion for older adults. In a survey of primary care physicians, Hyman and Pavlik38 report that, for patients with a systolic BP between 140 and 160 mm Hg, 52% of physicians would not start antihypertensive treatment for middle-aged adults, and 76% would not start treatment for patients 70 years or older. Similarly, for a persistent BP of 158/88 mm Hg in a patient with treated hypertension, 33% of physicians would not intensify therapy in middle-aged adults and 48% would not intensify therapy in patients 70 years and older. In a survey of physicians conducted by Oliveria and colleagues,37 the average systolic BP thought to require treatment in patients without comorbidities was 150.4 mm Hg.

These physician-survey findings are consistent with the levels and types of control seen in the CHS. Diastolic BP has been a traditional target and, even in older adults, is directly related to the risk of cardiovascular events.39 While diastolic hypertension was all but eliminated from the population of older adults in the CHS, mild to moderate elevations in systolic BP were common. Despite annual BP measurements and feedback on elevated levels, about 40% of the treated patients with hypertension had systolic blood pressures of 140 mm Hg or higher. Based on epidemiologic evidence and extrapolations from clinical trial experience, the expected public health benefit of more aggressive treatment of systolic hypertension is likely to be large.39,40 Data from the CHS38 suggest that the undertreatment of a systolic BP of 140 mm Hg or higher may be responsible for 22% of myocardial infarctions and 34% of strokes in older adults.

High BP is a common condition among older adults.37,42 The attention to systolic rather than diastolic BP is itself relatively recent. Treatment trials, moreover, have not been conducted specifically in patients with mild elevations of systolic BP. Borderline isolated systolic hypertension is the only hypertension condition for which a placebo-controlled major-disease end point trial would not be clearly unethical. Perhaps the results of clinical trials that are currently under way will help persuade physicians of the importance of aggressive treatment of mild to moderate elevations of systolic blood pressure.93

Importantly, 46% of the 979 treated patients with hypertension who had a BP lower than 140/90 mm Hg in 1999 had their BP well controlled with 1 medication. The idea of starting combination therapy for all patients with hypertension, advocated by some,4 is unnecessary for half the hypertension population, would subject these patients to the unnecessary costs and risks of a second medication, and remains untested as an approach to reduce the cardiovascular morbidity and mortality associated with hypertension.

Calcium channel blockers and ACE inhibitors were available and began to increase in use from the early 1980s. A number of studies have noted the trends in antihypertensive drug therapy during the late 1980s and early 1990s.43-50 In subjects with hypertension and CAD, the trend toward higher use of calcium channel blockers seems to have abated with a greater emphasis on the use of β-blockers. This finding in the CHS is consistent with a number of US and European consensus recommendations that identify β-blockers as the preferred first-line agent for subjects with ischemic heart disease.51-55

In hypertensive patients without CAD, the use of diuretics has declined precipitously even though clinical trials, several published in 1991 and 1992,6,56 have shown that low-dose diuretics are safe and effective in preventing stroke, myocardial infarction, heart failure, and total mortality.57 The trend away from proven drugs coincided with the increased use of ACE inhibitors and calcium channel blockers. The first and only trial to suggest a benefit from the calcium channel blocker nifedipine, a placebo-controlled trial in isolated systolic hypertension, was published only in 1997.58 The time trends in drug use are consistent with advertising trends. Between 1985 and 1996,59 for instance, the proportion of all advertising pages of the New England Journal of Medicine devoted to advertisements for calcium channel blockers increased from 4.6% in 1985 to 26.9% in 1996. Advertisements for diuretics, on the other hand, were uncommon (4.2% to 0%).

In 1986, Wayne Ray and colleagues60 called for “prospective clinical trials . . . to ascertain if the increased cost of the newly developed drugs is justified by the potential benefit.” Some results are just now in. Evidence from more recent trials has tended to extend the indications for ACE inhibitors61 and limit or reduce the indications for calcium channel blockers16 and α-blockers.12 In the meta-analysis by Pahor et al,19 compared with other antihypertensive agents in head-to-head trials, calcium channel blockers were associated with higher risks of myocardial infarction and heart failure. In another meta-analysis,10 ACE inhibitors were associated with lower risks of coronary disease or heart failure than calcium channel blockers. Many commentators now regard calcium channel blockers as second- or third-line agents,44 although they are still commonly used.

In recommending specific classes of drugs as first-line pharmacologic treatments for high BP, the JNC guidelines focused on health benefits demonstrated in large, long-term clinical trials.14 Since the JNC guidelines recommend low-dose diuretics and β-blockers as first-line agents in patients with uncomplicated hypertension, and since comparative clinical trials have demonstrated important differences between antihypertensive drugs in their effects on major disease end points,15,18 the use of specific, proven antihypertensive agents is an important component of tracking the appropriate care of high BP.

For older adults, undertreatment of hypertension was common. In the late 1990s, lack of control was primarily characterized by mild to moderate elevations in systolic
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BP. More widespread use of low-dose diuretics is likely to be an important public health intervention to prevent the devastating complications of hypertension, including stroke, myocardial infarction, and heart failure.

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