Antihypertensive Drug Therapy and Survival by Treatment Status in a National Survey

Richard J. Havlik, Andrea Z. LaCroix, Joel C. Kleinman, Deborah D. Ingram, Tamara Harris, and Joan Cornoni-Huntley

The National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-up Study, an investigation of a cohort originally examined during the period 1971-1975, provided an opportunity to assess the frequency of antihypertensive drug therapy in the United States during the period 1982-1984. For most age-sex-race subgroups, the frequency of medication use during 1982-1984 was higher than that observed during 1976-1980 based on the NHANES II. In the interval 1982-1984, diuretic agents were the most frequent medications prescribed (47% of drugs prescribed), and β-blockers were second (17%). At the time of the initial survey in 1971-1975, participants had their blood pressures measured and a history of diagnosis and treatment of hypertension ascertained. Follow-up for vital status was 93% complete by 1984 (average length of follow-up, 9 years). In white men and women aged 50 years and older, the relative risk of death increased steadily, from those with elevated blood pressure (systolic blood pressure >160 mm Hg or diastolic blood pressure >95 mm Hg) but no history of hypertension to those treated for hypertension but whose blood pressure was still elevated. Regardless of history or treatment, those with an elevated blood pressure had about a 25-30% excess risk of death. Evidence from these national studies shows a high frequency of antihypertensive drug therapy in 1982-1984 and suggests the importance of adequate blood pressure control for optimal survival. (Hypertension 1989;13(suppl I):I-28-I-32)

Repeated epidemiological studies in national and community samples have indicated that drug treatment of hypertension has increased substantially during the past 20 years. Comparison of the results from three national health surveys show that the age-adjusted proportion of white men taking antihypertensive medications doubled from 4% during the period 1960-1962 to 8% in 1976-1980. Similar increases were noted in the other major race-sex groups. The survey results indicate that most of these increases have occurred between the second survey in 1971-1974 and the third survey in 1976-1980. A report of two separate population samples in Minnesota surveyed during approximately the same time span as the national surveys had also shown a substantial increase in hypertension detection and control. The increases in therapy occurred during a period of intense education efforts by the National High Blood Pressure Education Program and the introduction of several new antihypertensive medications.

The findings of the Veterans Administration Cooperative Study and the Hypertension Detection and Follow-up Program in 1979 established the efficacy of antihypertensive therapy in reducing mortality associated with a diastolic blood pressure of 90 mm Hg and greater. As a result, in 1980, a Joint National Committee report recommended therapy for those with sustained diastolic blood pressures of 90 mm Hg and greater. Evidence from population-based and other descriptive studies suggests a relation between levels of baseline diastolic blood pressure in the range 90-95 mm Hg (mild hypertension) and subsequent mortality. However, some doubts have remained about the appropriateness of drug therapy in mild hypertension. Also, the effect of treating isolated systolic hypertension in the elderly is under study.

The National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-up Study (NHEFS) provided the opportunity to ascertain the frequency of antihypertensive treatment during the period 1982-1984 and to compare its results with those from a previous national survey (NHANES II, 1976-1980). In addition, information on the type of drug treatment was
available from NHEFS. Finally, because NHEFS is a follow-up study, it was possible to evaluate the effect of diagnosis, treatment, and control of hypertension on subsequent mortality. The purpose of this report is to present relevant trend and follow-up data from these national surveys.

Subjects and Methods

Study Population

The NHANES I, a probability sample of the US civilian noninstitutionalized population, was conducted in 1971–1975. As part of the examination, data were collected on blood pressure level, history of hypertension, and treatment status. The participation rate in the examination was approximately 70%. Blood pressures were measured on approximately 95% of those examined. The 14,407 NHANES I examinees who were 25–74 years of age became the base population for the NHANES I NHEFS. In 1982–1984, vital status was determined for 93% of the cohort, and interviews were conducted with 93% of traced survivors.

The second NHANES was conducted from 1976 to 1980. A probability sample of the US civilian noninstitutionalized population was studied at examination sites across the country. Response rates were comparable to those of NHANES I.

Medication and Hypertensive Status

In NHANES I, medication status was determined by current antihypertensive drug use or use during the past 6 months. In NHEFS, current use of antihypertensive medication was determined by the participants naming a blood pressure–lowering drug. In NHANES II, a report of taking antihypertensive medication "always," "often," or "sometimes" was accepted as indicating medication usage. The name of the drug was not obtained. In NHANES I, participants were asked if they had been told of elevated blood pressure or hypertension by a physician.

Blood Pressure Measurement and Definition

At the time of the physical examination in NHANES I, which took place in a mobile examination center, the blood pressure was measured once by a physician with a standard sphygmomanometer with the bell of the stethoscope on the right arm of a seated subject. The measurement occurred at the beginning of the physical examination. Disappearance of sound was used for the determination of diastolic blood pressure.

For the purposes of this analysis, elevated blood pressure is defined as systolic blood pressure greater than or equal to 160 mm Hg or diastolic blood pressure greater than or equal to 95 mm Hg. Those with isolated systolic hypertension (systolic blood pressure ≥160 mm Hg and diastolic blood pressure <90 mm Hg) were included within the definition of definite hypertension. Other categories were not used in this analysis.

Statistical Analysis

The proportions of NHEFS and NHANES II participants receiving antihypertensive medication were determined by age, race, and sex. These were displayed graphically. The results from NHANES II were weighted to represent national estimates. Unweighted results from NHEFS are presented in Figures 1 and 2 (weighted estimates were very similar).

Cox proportional-hazards regression was used to evaluate the effect of diagnosis, treatment, and control of hypertension on all-cause mortality for white men and women 50–74 years of age who participated in NHEFS. The comparison group consisted of those white men and white women 50–74 years of age without elevated blood pressure or
without a history of being told of hypertension. Numbers were too small for analysis of mortality among younger ages or of black men and black women. Because age and smoking status (current, former, or never) at baseline were related to blood pressure and mortality, the former were included in the model. Relative-risk estimates were derived from the regression coefficients, and confidence limits were calculated from the standard errors. Adjustment for the differential sampling weights had little effect on the regression coefficients, so only unweighted results are shown. Results are based on 2,549 men (849 deaths) and 2,827 women (549 deaths).

Results

Frequency and Trends in Antihypertensive Therapy

The age-specific proportions of white men and white women receiving antihypertensive medication during the two study periods are shown in Figure 1. Treatment frequency was higher in women than in men, especially in the older age groups. For most age-sex groups, there were substantial increases over time in the proportions treated. However, the increase was somewhat higher for white men than white women.

Black women were treated at a high rate during both time periods. Although there is little difference between the proportions treated in the two periods, the small number of black women in the samples precludes a definitive assessment of change (Figure 2). For black men, a difference between the proportion treated in the earlier and later periods was evident. The proportions were about 10–20% in the earlier period compared with about 15–40% in the later period.

Type of Drug Treatment

Diuretic agents were the most frequent class of antihypertensive drug therapy in 1982–1984 (Table 1). The single-diuretic agents and the Aldactazide (Searle & Co., San Juan, Puerto Rico) or Dyazide (Smith Kline & French Laboratories, Philadelphia, Pennsylvania) diuretic drugs accounted for about 47% of the total number of prescribed antihypertensive drugs. β-Blockers were the next most frequent class of drugs prescribed, possibly because a number of different kinds of β-blockers were approved during this period. The proportions for diuretic drugs and β-blockers in Table 1 refer to prescribed drugs containing only one class of medication. Drug combinations of more than one class are included under "others." Because the 2,580 participants who reported taking antihypertensive medications mentioned 3,375 drugs, some individuals were taking more than one medication. In some cases, the self-specified drug was unlikely to have had a blood pressure–lowering function, but it was included in the tabulation.

Follow-up Data

The effect on survival of different combinations of blood pressure elevation, history of hypertension, and age was assessed using the Cox proportional hazards model (16). Differences in survival identified by the model were confirmed in analyses separately stratified by age range (35–44, 45–54, 55–64, and 65–74 years of age). Results are based on 2,380 participants. Results from the follow-up study are shown in Figure 2. Absolute differences in survival were small but consistent with the results from the NHANES I Epidemiologic Follow-up Study and the NHANES, National Health and Nutrition Examination Survey.
Discussion

Told, BP elevated,
Told, BP elevated,
Told, BP not elevated,
Told, BP not elevated,
Not told, BP not elevated*

<table>
<thead>
<tr>
<th>Hypertension diagnosis, blood pressure, and treatment status</th>
<th>White men (N=2,549)</th>
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</tr>
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<tbody>
<tr>
<td>No. of subjects</td>
<td>Relative risk</td>
<td>Confidence interval (95%)</td>
</tr>
<tr>
<td>Not told, BP elevated*</td>
<td>473</td>
<td>1.26</td>
</tr>
<tr>
<td>Told, BP not elevated, no medication</td>
<td>145</td>
<td>1.46</td>
</tr>
<tr>
<td>Told, BP not elevated, medication</td>
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BP, blood pressure and NHANES, National Health and Nutrition Examination Survey.
*Comparison subgroup.
Values were adjusted for age and smoking at baseline with a proportional-hazards regression model.

sion, and control with medication at baseline in NHEFS is shown in Table 2. A proportional-hazards regression model was used to compare survival for the six subgroups shown in the table (adjusting for age and smoking status). The subgroup sample sizes ranged from 115 to 1,386. The comparison group was the subgroup with neither elevated blood pressure nor history of hypertension. All relative risks were greater than one with a remarkable similarity for white men and white women. All but three of the 95% confidence intervals (CI) excluded unity, and the remaining three had lower limits around 0.9. Even for study participants with a single elevated blood pressure measurement but no history of hypertension, the excess risk of death was 26% for white men and 14% for white women. Those who had been diagnosed previously had a greater risk of death whether or not they were taking medication. In addition, blood pressure elevation in these groups (i.e., uncontrolled hypertension) further increased the risk of death.

There was reasonable consistency among the subgroups in terms of the multiplicative effect of each variable, thus allowing the five coefficients to be summarized by three coefficients. Those subjects with elevated blood pressure had a relative risk of 1.27 among men (CI: 1.10, 1.46) and 1.31 among women (CI: 1.10, 1.56) regardless of history or medication. Previously diagnosed hypertensive individuals had a relative risk of 1.37 for men (CI: 1.12, 1.70) and 1.29 for women (CI: 1.01, 1.64). Medication for hypertension was not associated with substantial excess risk (1.02 for men [CI: 0.81, 1.30] and 1.15 for women [CI: 0.90, 1.47]).

Discussion

Treatment Trends

In the 5-year period between approximately 1978 (the midpoint of NHANES II) and 1983 (the midpoint of NHEFS), the proportion of most age-sex-race specific subgroups taking antihypertensive medication increased in these national surveys. This was particularly evident for men. Change in the percent of those being treated in a sample of Connecticut residents at two comparable time points was similar to that found in this national study. Smaller community studies in Minnesota reported a similar increase in the percent detected and treated.

These studies are supportive of the conclusion that drug treatment for hypertension has continued to increase.

Various factors may have affected the recent increases in treatment. The first reports from the Hypertension Detection and Follow-up Program results appeared in 1979. These findings probably affected the conduct of practicing physicians. These effects were increased by the continued influence of the National High Blood Pressure Education Program and the recommendations of the Joint National Committee. In addition, demonstration projects were undertaken in certain states to enhance hypertension detection and treatment statewide.

Drug Type

Many drugs for antihypertensive therapy were reported by participants in NHEFS. Diuretic drugs represented the most frequently prescribed drugs. This finding was similar to those of the Minnesota community studies. Diuretic agents have been the represented the most frequently prescribed drugs. Some caution in interpreting the drug data is necessary. These data are based on self-response without a careful check

 chunk:“Table 2. Relative Risk of Death Among White Adults 50 Years of Age and Older Based on 9-Year Follow-up in the NHANES I Epidemiologic Follow-up Study”

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of bottles, prescriptions, or indications for the medications. It is likely that some of the reported drugs were not taken for hypertension treatment.

**Survival Data**

The mortality experience by age, race, and sex subgroups in NHEFS was quite similar to what was expected based on US life tables derived from vital statistics. Thus, the effects of baseline hypertension characteristics on mortality presented in Table 2 are particularly noteworthy, as the relations were derived from a nationally representative sample of the US population. Unfortunately, the number of blacks in the sample was too small to estimate the effect of hypertension status on mortality and blacks.

Those having elevated blood pressure on the single NHANES I measurement had about 25–30% excess risk of death, regardless of prior history or medication usage. Those previously told of high blood pressure presumably had elevated blood pressure in the past and experienced an additional 30–35% increased risk. Those receiving medication had a slightly higher risk than hypertensive individuals not on medication, but the medication group may have had more severe hypertension. Hypertensive subjects whose blood pressure remained high even with treatment must be considered to have poorly controlled hypertension.

**Conclusion**

The substantial and increasing proportion of the population receiving medication indicates progress in identification of hypertensive subjects. The survival experience of the NHEFS participants suggests that the major public health challenge is not only further identification of those with hypertension, but also more effective therapy. Certain questions remain about the efficacy of treatment of mild or borderline diastolic hypertension and isolated systolic hypertension in the elderly. The NHANES III, a new national sample study scheduled for initiation in 1988, will provide the opportunity to monitor future trends in the use and effects of antihypertensive drugs or other changes in the treatment of hypertension in the United States.

**Acknowledgment**

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**KEY WORDS** • blood pressure • surveys • epidemiology • race • sex differences
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