1-69

**Observed Benefits of Antihypertensive Treatment**
**Temporal Trends in Cardiovascular Disease**

**Increased Treatment of Hypertension Does Not Explain the Decline in Stroke Mortality in the United States, 1970–1980**

Ruth Bonita and Robert Beaglehole

The steady decline in mortality from stroke in the United States accelerated markedly in the 1970s. It has been widely assumed that an increase in the rate of treatment of hypertension is the most likely explanation for this major public health achievement. An analysis of available information, however, suggests that improvements in the community control of hypertension in the United States in the period 1970–1980 have contributed in only a minor way. There were 45,357 fewer deaths from stroke in 1980 among those aged 35–74 years than might have been expected if the death rates had stayed the same as in 1970. Data from the National Health and Nutrition Surveys indicate that six million more people received antihypertensive medication in 1980 than in 1970. Results from a pooled analysis of nine randomized controlled trials of the treatment of hypertension suggest that between 6% and 16% of the reduction in stroke mortality was due to the increased treatment of hypertension. Epidemiological observations indicate that between 16% and 25% of the overall decline in stroke mortality can be attributed to the treatment of hypertension, suggesting that clinical trials probably underestimate the community-wide benefits of treatment. These results also suggest that at least three quarters of the decline in stroke mortality in the United States in the period 1970–1980 is due to factors other than antihypertensive treatment. *(Hypertension 1989;13(suppl I):I-69–I-73)*

*Stroke mortality rates have been declining in the United States since the beginning of this century.*1 A similar decline has occurred in many other industrialized countries with the exception of the eastern European countries.2 Between 1970 and 1980, the decline in overall mortality in the United States was 42.5% in people aged 35–74 years. This is a real decline, most likely explained by a reduction in the incidence of stroke.1,3 In 1972, the National High Blood Pressure Education Program (NHBPEP), an ongoing national program to improve the detection, treatment, and control of hypertension through a wide range of public education campaigns, was implemented.4 Because hypertension is the most important modifiable risk factor for stroke, there has been a tendency to assume that the decline in stroke mortality is attributable to an increase in the proportion of hypertensive patients receiving treatment.1,4 It has been stated that "... the documented improvements in hypertension control since the beginning of the NHBPEP must be considered a major contribution ..." to the decline of cardiovascular disease mortality rates.5 Such an explanation has been strengthened by results of randomized controlled trials (RCT), which have demonstrated a major and consistent benefit of the treatment of hypertension for the prevention of fatal and nonfatal stroke events.6

This article uses data from two national surveys and a pooled analysis of the results of nine RCT, which include the Hypertension Detection and Follow-up Program (HDFP), to quantify the contribution of improvements in the control of hypertension to the stroke mortality decline observed in 1980. Because trials may underestimate the benefits of treatment, an upper limit for the effects of treatment in the period 1970–1980 is derived from the relation of blood pressure (BP) to stroke mortality observed in clinical trials and that expected from epidemiological studies, as well as estimates based on the population-attributable risk (PAR) of hypertension for stroke mortality.

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Subjects and Methods

National stroke mortality rates (8th and 9th revisions of the International Classification of Disease codes 430–438) for whites and blacks and for men and women in 10-year age groups (35–74 years) for 1970 were applied to the 1980 population to estimate the number of stroke deaths expected in 1980 had stroke mortality rates not declined. The observed number of deaths in 1980 was subtracted from the expected number of deaths to provide an estimate of the total number of stroke deaths prevented in 1980. The increase in the proportion of the population 35–74 years of age who were receiving pharmacological treatment for hypertension in the United States during the 1970–1980 period was derived from the results of the National Health and Nutrition Examination Survey conducted in 1971–1974 (NHANES I) and 1976–1980 (NHANES II). The additional people receiving treatment for hypertension in 1980 compared with those in 1970 was estimated by subtracting the NHANES II results from the NHANES I results.

The age-, sex-, and race-specific benefits of the treatment of hypertension (stroke deaths prevented/1,000 patients treated/yr) were determined initially from the results of the HDFP by subtracting the annual mortality rates for the stepped-care (SC) group from the annual mortality rates for the referred-care (RC) group. To estimate the number of stroke deaths prevented in 1980 as a rate of treatment of hypertension, the benefit rate as derived above was applied to the relevant age-, race-, and sex-specific groups of the additional people receiving treatment in 1980. Age groups in which there were no deaths or which appeared to have a negative benefit (i.e., RC outcome was better than that of SC) were assigned the benefit experienced by the total race or sex group, a conservative approach deliberately adopted to avoid underestimating the benefits of therapy.

A range of overall benefits was calculated for the upper and lower 95% confidence limits of benefit estimated from a pooled analysis of nine RCT of drug treatment for hypertension. A range of estimates (weighted according to the sex and race benefits demonstrated in the HDFP) of the proportion of the total stroke deaths prevented in 1980 as a result of treatment of hypertension was then calculated.

An independent upper estimate of the benefits of treatment for the period 1970–1980 was calculated from data on the decline in stroke mortality expected from a reduction in population mean BP levels. This estimate was based on the observed effects of RCT and on the predicted effect derived from epidemiological studies. Trends in population BP levels are derived from the Multiple Risk Factor Intervention Trial (MRFIT) screeners, and a PAR was selected that was intermediate to those of the two studies.

Results

In 1980, there were 55,689 stroke deaths in the US adult population aged 35–74 years. This represents 45,357 fewer deaths than expected had the stroke mortality rates remained the same as in 1970 (Table 1). The proportion of stroke deaths prevented in men and women was equal although there were marked age and race differences: 38.5% of the decline occurred among blacks. One fifth of these declines occurred among blacks.

### Table 2. Proportion of the US Adult Population Taking Antihypertensive Medication*

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>White</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td>35–44</td>
<td>2.2</td>
<td>3.4</td>
</tr>
<tr>
<td>45–54</td>
<td>5.9</td>
<td>11.6</td>
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<tr>
<td>55–64</td>
<td>14.4</td>
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<tr>
<td>65–74</td>
<td>14.7</td>
<td>22.4</td>
</tr>
<tr>
<td>Total</td>
<td>8.2</td>
<td>12.3</td>
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</table>

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</thead>
<tbody>
<tr>
<td>35–44</td>
<td>3.2</td>
<td>4.3</td>
</tr>
<tr>
<td>45–54</td>
<td>7.8</td>
<td>15.0</td>
</tr>
<tr>
<td>55–64</td>
<td>16.6</td>
<td>23.6</td>
</tr>
<tr>
<td>65–74</td>
<td>25.7</td>
<td>34.9</td>
</tr>
<tr>
<td>Total</td>
<td>11.9</td>
<td>18.2</td>
</tr>
</tbody>
</table>


### Table 1. Magnitude of Stroke Mortality Decline in the United States*

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>Black</td>
<td>White</td>
<td>Black</td>
</tr>
<tr>
<td>35–44</td>
<td>775</td>
<td>378</td>
<td>720</td>
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<tr>
<td>45–54</td>
<td>1,268</td>
<td>554</td>
<td>1,115</td>
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<tr>
<td>55–64</td>
<td>5,301</td>
<td>1,384</td>
<td>3,173</td>
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<tr>
<td>65–74</td>
<td>12,309</td>
<td>1,765</td>
<td>11,178</td>
</tr>
<tr>
<td>35–74</td>
<td>19,653</td>
<td>4,081</td>
<td>16,186</td>
</tr>
</tbody>
</table>

*Magnitude is reported as the expected (based on 1970 rates) minus the observed number of deaths from stroke in 1980 by age, sex, and race.
An increase in the proportion of the population taking antihypertensive medication between the two NHANES surveys was observed for all age, sex, and race categories except for black men aged 45–54 years (Table 2). The proportion of black women aged 45–54 years taking antihypertensive medication doubled in this period. The most striking changes occurred in the older age categories (65–74 years) and in women, especially black women. Overall, the proportion of the population aged 35–74 years taking antihypertensive medication increased from 10.9% to 16.4%. It was estimated from these two data sets that an additional six million people 35–74 years of age were treated for hypertension in 1980 compared with 1970; two thirds were women, almost one half were aged 65–74 years, and one sixth were black.

The HDFP investigated the effects of treatment of hypertension by comparing patients with diastolic BP of the population would explain approximately 6 mm Hg. A 1-mm-Hg decline in mean population diastolic BP of the population aged 35–74 years declined by only 1 mm Hg, with no change in white men, a 1-mm-Hg decline in white women, and a 3-mm-Hg decline in blacks. A 1-mm-Hg decline in mean population diastolic BP of the population would explain approx-
Estimates of the PAR of hypertension for stroke vary depending on the definitions used and the populations studied. From the mortality follow-up data of MRFIT screeners aged 35–59 years, it was calculated that if all those with diastolic BP greater than or equal to 95 mm Hg experienced the same death rate as those with a diastolic BP less than 95 mm Hg, then 29% of all stroke deaths in that age group would be prevented. These results are consistent with Framingham data, where 31% and 37% of all stroke events in men and women 35–64 years of age, respectively, could be attributed to a diastolic BP greater than or equal to 95 mm Hg. To be conservative, we have assumed a PAR of hypertension for stroke mortality of one third (33%); this implies that, if all hypertensive persons had their diastolic BP reduced to less than 95 mm Hg, the burden of stroke mortality in the community would be reduced by one third. However, we know that, in the late 1970s, only 55% of hypertensive persons were receiving treatment. If it is assumed that all treatment was initiated between 1970 and 1980 and was directed at those with the highest risk, then, at most, antihypertensive treatment would account for an 18% decline in mortality (54.5%×33% PAR), and this 18% decline is 42% of the observed decline (18%/÷42.5%) in stroke mortality in the age range 35–74 years. Finally, because only 60% of hypertensive patients receiving treatment achieved an adequately controlled BP, a more realistic estimate of the observed decline would be 25% (42%×60%).

**Discussion**

This article has evaluated the premise that the temporal association between recent increased rates of detection and treatment of hypertension and a decline in stroke mortality are related as cause and effect. Our calculations show that improvements in the treatment of hypertension could account for a proportionate reduction in stroke mortality in 1980, ranging from a low of 12% (based on data from two national surveys and RTC), to 16.7% based on observations on the relations between BP reduction and stroke mortality from clinical trials and epidemiological studies, and to a high of 25% based on the PAR of hypertension for stroke mortality.

Several assumptions were made in reaching these conclusions. The major limitation in extrapolating from a clinical trial like the HDFP relates to the fact that the RC participants did not face any deterrent to seeking treatment. Because the patients in this group most likely to receive active treatment would be those most likely to be at highest risk, a favorable effect of treatment in the RC group would dilute the observed net benefit. On the other hand, benefits obtained in a clinical trial are unlikely to be achieved in the general population in the absence of the close medical supervision and free therapy that characterized the trial.

However, use of the HDFP data has the advantage that, unlike other clinical trials, there were few exclusions for disease among the subjects before the trial began; the data are reported for both sexes, for the young (<55 years), and for the elderly (>60 years); and a high proportion of blacks (45%) is included. Furthermore, it is this study more than any other that has been used to justify the widespread treatment of hypertension, especially in people closer to the middle-of-the-population distribution of blood pressures. The overall improvements in stroke mortality in the HDFP (44%) are consistent with the results of the pooled analysis of nine long-term RCT that suggest that the treatment of mild-to-moderate hypertension reduced stroke mortality by 38% (95% confidence limits: 19%, 55%) during a 5-year period. Although the benefits of treatment of hypertension are greater in severely hypertensive people, they comprise only a small proportion of the population: the major emphasis in the period 1970–1980 was on improving the treatment of people in the mild-to-moderate range of hypertension.

The NHANES studies included only noninstitutionalized civilians to estimate community improvements in the treatment of hypertension. This limitation was not considered a problem in this analysis because most of those allocated to the institutionalized category were in older age groups that were not examined in this study. Because the data for the two surveys were collected for a number of years (1971–1974 and 1976–1980), it is possible that the estimated proportion of people receiving treatment in 1970 is an overestimate, and that those receiving treatment in 1980 is an underestimate. To examine this possibility, a similar analysis was undertaken for the midpoints (1972 and 1978) of the respective NHANES study years. The overall contribution rose to 14.7% for this shorter period, confirming the hypothesis that the widespread use of antihypertensive medication has had a disappointingly small effect on the absolute decline in stroke mortality despite the apparent "striking" relative improvements.

The small reductions in the mean population BP that have occurred appear to explain only about one sixth of the stroke mortality decline. This is likely to be an underestimate because an assumption was made that the reductions occurred at all levels of blood pressure. The decline in BP levels among hypertensive subjects would probably be greater than among normotensive people. The absence of a significant decline in levels between the two NHANES studies is perhaps surprising. Because the data in our analyses were based on the first blood pressure determination, it may have been slightly elevated due to examinee anxiety. However, the degree of elevation would have been similar in each survey, and it is unlikely that comparisons between race-sex groups would have been affected. Small reductions in mean diastolic BP levels of the order of 2 mm Hg have been noted in...
some but not all community-based BP education programs in the period under consideration. Although many studies have documented a decline in the prevalence of hypertension, no community-wide reduction in diastolic BP large enough to explain more than a relatively small proportion of the mortality decline has been reported.

The estimates based on PAR provide the maximum likely effect of improvements in the treatment of hypertension. They are, of course, dependent on the definitions used. We chose to define hypertension as diastolic BP greater than or equal to 95 mm Hg, since it was not until after a review of the HDFP results that the second Joint National Committee report (published in 1980) recommended treatment of persons with diastolic BP greater than or equal to 90 mm Hg.

The influence of secular trends on other risk factors for stroke, in particular cigarette smoking, has not been investigated. Factors responsible for the decline in mortality that occurred long before the widespread use of antihypertensive medication may also continue to be important. Finally, whatever caused the recent acceleration in the decline in stroke mortality in all age groups, in both sexes, and in blacks and whites were affected with equal force and at the same time. A satisfactory explanation for the decline in stroke mortality in the United States would also need to consider the reasons for the increase in mortality rates that have occurred in the same period in the eastern European countries. In conclusion, this article suggests that most of the recent decline in stroke mortality is due to factors other than antihypertensive treatment. It is important that the reasons for the decline in stroke mortality are elucidated because this information is highly pertinent to the ongoing debate about the costs and benefits of treatment of mild hypertension.

References

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Key Words • stroke mortality decline • clinical trials • antihypertensive agents • risk factors • statistical studies • epidemiology • hypertension detection and control
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