Effect of Age on the Efficacy of Blood Pressure Treatment Strategies

Michael J. Klag, Paul K. Whelton, and Lawrence J. Appel

To study whether the proportion of excess cardiovascular events attributable to various levels of systolic blood pressure varies with age, we calculated the population-attributable risk of all-cause mortality, fatal and nonfatal cardiovascular events (stroke, coronary heart disease, angina, congestive heart failure, and peripheral vascular disease), and stroke incidence due to systolic blood pressure in men and women 45 years of age or older in the United States during 1980. Our estimates are based on US census counts, blood pressure prevalence distributions from the second National Health and Nutrition Examination Survey, and the annual risk of cardiovascular complications during 18 years of follow-up in the Framingham cohort. We then determined the impact of age on the relative efficacy of mass treatment and case-finding strategies in preventing systolic blood pressure-related events. At 45-54 years of age, only 30-40% of systolic blood pressure-related excess events occur in hypertensive individuals (systolic blood pressure ≥160 mm Hg). With increasing age, however, the percentage of systolic blood pressure-related events that occur in hypertensive individuals rose substantially; in the oldest age group (≥75 years), 65-70% of fatal and nonfatal cardiovascular disease events occur in hypertensive persons. The pattern is similar for men and women. The potential impact of a mass treatment strategy designed to shift the distribution of blood pressure downward by a small amount is greater in younger than in older groups, whereas an opposite trend is seen for a high-risk, hypertensive case-finding and treatment approach. In every age, a combined mass and high-risk treatment strategy is superior to either strategy alone. Our analysis suggests that the age of the target population should be considered when designing interventions to prevent blood pressure-related cardiovascular disease (Hypertension 1990;16:700-705)

Population attributable risk (PAR) is the product of the absolute risk associated with a risk factor and the frequency of the risk factor in the community under study.1 Calculations of PAR provide an estimate of the excess burden of disease associated with a given level of a risk factor in a community; they also indicate for that population the potential health benefits of different therapeutic strategies aimed at amelioration of the risk factor profile. In the general population, most blood pressure-related cardiovascular disease occurs in those with normal or only minimally elevated levels of blood pressure.2-3 On this basis, mass treatment strategies have been recommended as an essential component of any meaningful attempt to decrease the community burden of blood pressure-related cardiovascular disease. However, average levels of systolic blood pressure and prevalence of hypertension rise with age; in fact, the prevalence of hypertension in persons aged 65 years and older is 40%.6,7 Because of the high prevalence of hypertension in older age groups, a hypertension case-finding and treatment strategy may be more effective than a community-wide mass treatment strategy that reduces blood pressure slightly in all persons. However, the effectiveness of a case-finding strategy is not merely dependent on a high prevalence of hypertension; it rests on demonstration that the majority of systolic blood pressure-related cardiovascular disease occurs in those with elevated blood pressure. We theorized that most of the cardiovascular disease attributable to systolic blood pressure in the elderly
would occur in hypertensive individuals (systolic blood pressure >160 mm Hg). Such a finding would stand in pronounced contrast to results from the general population and would have major implications regarding the relative value of case-finding versus mass treatment strategies in elderly persons.

Methods

We calculated age-specific estimates of population-attributable risk of cardiovascular disease due to various levels of systolic blood pressure. PAR estimates of all-cause mortality, total cardiovascular disease (fatal and nonfatal stroke, coronary heart disease, angina, congestive heart failure, and peripheral vascular disease), and stroke due to various levels of systolic blood pressure for white people 45 years of age or older in the United States, by 10-year age groups, were calculated by applying the systolic blood pressure–related attributable risk to the corresponding prevalence of systolic blood pressure in the general population.7 Age, race, sex, and 10 mm Hg systolic blood pressure category–specific incidence rates for all three outcomes from the Framingham Study 18-year follow-up data were used to calculate systolic blood pressure–related attributable risk estimates.8 The prevalence of antihypertensive treatment in the community was low during this calendar time. Incidence of disease in the baseline blood pressure category (>110 mm Hg) was subtracted from disease incidence in higher blood pressure categories to define attributable risk, that is, the “excess” risk. Thus, associations between levels of blood pressure and cardiovascular disease incidence would not be confounded by treatment. For persons 75 years of age or older, Framingham 18-year incidence rates are unavailable; therefore, incidence data for 65–74-year-olds were used. Because the absolute risk of cardiovascular disease increases with age, use of data from younger groups should have minimized any differences in PAR between these age groups. The US population for each systolic blood pressure category was calculated by applying 1980 US census data9 to systolic blood pressure distribution estimates in the National Health and Nutrition Examination Survey II (NHANES II), which was conducted during 1976–1980.10 Because NHANES II only included persons up to 75 years of age, blood pressure distribution data for 75–79-year-olds from the National Health Examination Survey (NHES), collected in 1960–1962, were used for the age group 75 years or older.11 Each systolic blood pressure–related attributable risk estimate was multiplied by the prevalence of persons in the corresponding blood pressure category to calculate the number of systolic blood pressure–related excess events in that range of systolic blood pressure. Finally, events were summed across blood pressure categories to calculate the overall estimate of PAR.

The results of these analyses can be expressed in several ways. The PAR (i.e., total number of excess events) and the distribution of events by systolic blood pressure category for each age–sex group were calculated. A systolic blood pressure cutoff of 160 mm Hg or more was chosen as the definition of hypertension,12 and the percentage of events within each group that occurred in hypertensive individuals was calculated. To determine whether the results were heavily dependent on the age–sex distribution of the 1980 census and the corresponding NHANES II distributions of blood pressure, the calculations were repeated using prevalence estimates derived from national surveys performed during two earlier time periods. For 1960, data from the 1960 US census13 and the NHES, performed in 1960–1962, were used.11 For 1970, information from the 1970 US census14 and NHANES I, conducted in 1971–1974, was used.15

To compare the relative benefits of different therapeutic approaches, the percent reduction in the

### TABLE 1. Estimated Number (%) of Events Due to Systolic Blood Pressure Above 110 mm Hg in Men and Women in the United States in 1980, by Age

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Total deaths</th>
<th>Total CVD</th>
<th>Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men, 1980</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45–54</td>
<td>41,305 (18.2)</td>
<td>73,518 (20.9)</td>
<td>14,381 (18.0)</td>
</tr>
<tr>
<td>55–64</td>
<td>70,793 (31.2)</td>
<td>141,655 (40.3)</td>
<td>23,552 (29.4)</td>
</tr>
<tr>
<td>65–74</td>
<td>70,294 (31.0)</td>
<td>82,873 (23.6)</td>
<td>25,416 (31.8)</td>
</tr>
<tr>
<td>≥75</td>
<td>44,373 (19.6)</td>
<td>53,260 (15.2)</td>
<td>16,659 (20.8)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>226,765 (100.0)</td>
<td>351,306 (100.0)</td>
<td>80,008 (100.0)</td>
</tr>
<tr>
<td><strong>Women, 1980</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45–54</td>
<td>12,252 (6.6)</td>
<td>21,334 (7.1)</td>
<td>4,489 (4.6)</td>
</tr>
<tr>
<td>55–64</td>
<td>18,835 (10.2)</td>
<td>78,079 (25.9)</td>
<td>16,190 (16.5)</td>
</tr>
<tr>
<td>65–74</td>
<td>84,515 (45.9)</td>
<td>111,657 (37.0)</td>
<td>42,583 (43.3)</td>
</tr>
<tr>
<td>≥75</td>
<td>68,731 (37.3)</td>
<td>90,941 (30.1)</td>
<td>35,072 (35.7)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>184,333 (100.0)</td>
<td>302,011 (100.0)</td>
<td>98,334 (100.0)</td>
</tr>
</tbody>
</table>

*Estimates were derived from 1980 US census data, National Health and Nutrition Examination Survey II, and Framingham 18-year incidence data. Total cardiovascular disease (CVD) includes fatal and nonfatal stroke, coronary heart disease, angina, congestive heart failure, peripheral vascular disease. Stroke includes fatal and nonfatal strokes.*
PAR was calculated for a mass treatment strategy, which would shift the systolic blood pressure distribution downward by 4 mm Hg; a case-finding ("high-risk") approach, which would reduce systolic blood pressure to 160 mm Hg among all hypertensive individuals; and a combined mass treatment/case-finding strategy. Separate calculations were performed by age and sex within each event category. A 4 mm Hg reduction in systolic blood pressure was chosen because this reduction represents the maximum average benefit achieved with nonpharmacological interventions. The benefit of a less effective mass treatment (i.e., a 2 mm Hg reduction) was also estimated.

Results

Table 1 shows estimates of the number of excess deaths, total cardiovascular disease events, and stroke events attributable to systolic blood pressure, by age, in white men and women in the United States during 1980. For men within each event category, greater than 60% of the estimated excess occurred in the 55–74-year-old group, with 15–21% in the group aged 75 years and older. In women, between two thirds and three quarters of systolic blood pressure-related fatal and nonfatal events occurred in the two oldest age categories, 65–75 years old and 75 or more years old, and roughly a third occurred in those 75 or more years old.

Figures 1 and 2 display the distribution of estimated excess deaths, total cardiovascular disease events, and strokes by systolic blood pressure categories in white men in the United States at the extremes of the age distributions studied (i.e., 45–54 years old and 75 or more years old). A comparison of these figures demonstrates that the distribution of excess events varied by age, with progressively more events occurring at high levels of blood pressure among those 75 years of age and older. The same pattern was seen for all three categories of events in both men and women but was most pronounced for women. Among women 75 years of age and older, 50% of the excess strokes occurred at blood pressure levels of 180 mm Hg and higher.

The proportion of excess disease attributable to hypertension (systolic blood pressure ≥160 mm Hg) showed a similar pattern as age increases (Figure 3). The percent of excess deaths, total cardiovascular disease events, and strokes attributable to systolic hypertension rose in a step-wise fashion with increasing age. At 45–54 years of age, 30–37% of excess events occurred among hypertensive individuals, whereas at 75 or more years of age, the corresponding estimates were 65–69%. A similar relation was seen for women (Figure 4). Lastly, analyses using data from 1960 and 1970 yielded similar results.
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mass treatment strategies. High-risk strategies seek to identify those at the extreme of the risk distribution (i.e., hypertensive individuals) and to reduce their risk and society’s burden of illness by application of a treatment that attempts to shift the risk factor from the extreme toward the middle part of the distribution. High-risk strategies frequently involve the administration of medications that have a powerful effect on the risk factor in question but also expose the individual to the possibility of adverse drug effects. Mass strategies, on the other hand, are designed to shift the risk distribution of the entire population. Often, the desired shift in risk distribution is relatively small and, therefore, the benefit to the individual of this shift is also quite small. However, this small decrease in risk is applied to almost everyone in the population and thus can result in substantial health benefits for the community. Mass strategies are usually nonpharmacological and, by necessity, must be extremely safe and acceptable to the population being treated.

PAR calculations provide an estimate of the maximum number of events that can theoretically be prevented by a completely effective intervention. By demonstrating where events occur in the blood pressure distribution, PAR calculations allow rational selection of the optimum therapeutic and preventive approach. For example, if only a minority of events within a community were to occur among hypertensive individuals, the high-risk approach could not appreciably reduce the burden of illness in that community.

A strength of the present study is that our blood pressure prevalence estimates are drawn from national surveys that are representative of the US population. This approach allows us to estimate the number of deaths and events prevented by mass treatment, case finding, and combined strategies in the US population. Table 2 displays the percent reductions in excess total deaths, total cardiovascular disease events, and strokes from mass treatment, case-finding, and combined strategies, according to age group. Among men 45–54 years old, the percent reduction in total deaths from a 4 mm Hg mass treatment strategy was similar to a case-finding (≥160 mm Hg) and treatment approach (i.e., 14% and 13%, respectively). For men, as age increases, the percent reduction in excess total deaths from mass treatment dropped from 14% to 8%; conversely, the percent reduction from case finding increased from 13% to 26%. The combination of mass treatment with case finding and treatment reduced excess total deaths by nearly 25% in each age group except the oldest one in which the reduction was 31%. The pattern for total cardiovascular disease and strokes among men was similar to that of total deaths. Likewise, the pattern for all three categories of events among women was similar to that of men. When a 2 mm Hg drop in blood pressure from a mass strategy was used, similar trends across age groups were observed.

Discussion

Approaches to reducing society’s burden of blood pressure–related cardiovascular disease can be broadly grouped under two headings: high-risk and mass treatment strategies. High-risk strategies seek to identify those at the extreme of the risk distribution (i.e., hypertensive individuals) and to reduce their risk and society’s burden of illness by application of a treatment that attempts to shift the risk factor from the extreme toward the middle part of the distribution.
population. In addition, the definition of systolic hypertension (≥160 mm Hg) represents a consensus that is widely accepted. The similarity of the results when data from alternative time periods and a less effective (2 mm Hg reduction) mass strategy are used also strengthens our conclusion.

A potential weakness is that the risk estimates are based on observational studies. Such data may not accurately reflect the benefits that can be derived from either a mass or high-risk case-finding and treatment intervention. For example, antihypertensive drug therapy reduces stroke morbidity and mortality but does not significantly decrease coronary heart disease incidence. Thus, inferences from observational studies, such as the Framingham Heart Study, may overestimate the effect of hypertension treatment interventions. An additional consideration is that Framingham risk information was generated in a select sample of predominantly white men and women residing in one geographic area. In theory, Framingham risk estimates might not reflect those being experienced by the general population.

Leaverton et al have shown, however, that Framingham coronary heart disease risk information is applicable to the entire population of the United States. Risk estimates of blood pressure–related cardiovascular disease from more recent studies may differ from Framingham 18-year rates used in this analysis, but any difference would probably be primarily due to the increased prevalence of antihypertensive treatment. The ramifications of this confounding on estimates of PAR would depend on a number of factors, including the time at which treatment is initiated (i.e., before or after measurement of blood pressure).

Another concern regarding the present study might be that risk factor distribution and cardiovascular disease incidence data are not available for the oldest age group (≥75 years old). However, our approach of using information from younger age groups as a surrogate measure should serve only to minimize differences in PAR between the older and younger age groups because average systolic blood pressure and cardiovascular disease incidence progressively increase with aging. Thus, our analyses may actually underestimate the differences between younger and older persons in the contribution of hypertension to blood pressure–related cardiovascular diseases. A final concern is that the approach we used to calculate PAR assumes equal risk of cardiovascular disease within each systolic blood pressure category and ignores the effect of other risk factors for cardiovascular disease such as cigarette smoking and hyperlipidemia. Because of these concerns, the calculations presented here can only serve as an approximation of the true value of detecting and treating hypertension at different ages.

Despite the above limitations, these PAR estimates provide important information that strongly suggests that the distribution of excess events due to systolic blood pressure varies substantially with age and that a sizeable portion of such events occurs in the elderly, particularly in women 65 years of age and older. In older persons, the majority of systolic blood pressure–related cardiovascular disease can be attributed to those with a blood pressure in the hypertensive range. In contrast, most such disease in younger age groups can be attributed to those with a normal or high-normal level of blood pressure. As a consequence of these differences, the societal benefits of case-finding and mass treatment approaches also vary by age. In an elderly population, a case-finding strategy is more efficacious than a mass treatment approach. However, a combined approach using both interventions would produce the greatest reduction in the number of events at every age. The relative ability to implement these two types of strategies may vary with age; older persons visit physicians more frequently than younger and may differ in their ability to change their behavior. Such possible age-related differences in the efficacies of these strategies need to be studied in future research.

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References


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