Preventing heart disease by controlling hypertension: Impact of hypertensive subtype, stage, age, and sex

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Background Hypertension is related to significant morbidity and mortality rates from coronary heart disease (CHD). This report examines the relative and absolute impact on risk for CHD by controlling hypertension to high normal and optimal levels.

Methods Among all subjects with untreated or inadequately treated hypertension in the National Health and Nutrition Examination Survey (NHANES) III who were 30 to 74 years of age and without prior CHD, the 10-year risk of CHD was calculated. With the use of sampling weights, the number of CHD events by age group, hypertension subtype (isolated diastolic hypertension [IDH], systolic-diastolic hypertension [SDH], and isolated systolic hypertension [ISH]), and stage of hypertension was estimated. Risk was recalculated and the number of events reestimated, assuming a reduction in blood pressure (BP) to high normal and optimal levels. The number and proportion (population-attributable risk, or PAR%) of events that could be prevented were determined from the differences in events and risk between uncontrolled and controlled BP levels. Derived from this was the number of persons needing treatment per CHD event prevented.

Results Control of hypertension to high normal levels could prevent approximately one fifth (PAR = 19%) of CHD events in men and one third (PAR = 31%) of CHD events in women, whereas control to optimal levels may prevent 37% and 56% of CHD events, respectively (P < .01 for differences between men and women). Of CHD events that could be prevented, the greatest proportion occurred from controlling BP among older persons, men, and those with stage 1 hypertension (vs stages 2 and 3) or with ISH (vs IDH or SDH). The number of persons with hypertension needing treatment to prevent one CHD event ranged from 20.5 in men to 38.6 in women when controlled to high normal BP and 10.7 in men and 21.3 in women when controlled to optimal BP.

Conclusions The greatest impact from control of hypertension occurs in older persons, men, and those with ISH, whereas the greatest PAR% occurred in women. Optimal control of BP could prevent more than one third of CHD events in men and more than half of events in women. Greater efforts to control hypertension in these populations may have a substantial impact in preventing CHD events. (Am Heart J 2003;145:888-95.)
age, systolic and diastolic BP, total and HDL cholesterol, and the presence of diabetes and cigarette smoking. We applied the Framingham risk prediction algorithms\(^5\) to men and women with untreated or inadequately treated hypertension (>140 mm Hg systolic BP [SBP] or ≥90 mm Hg diastolic BP [DBP]) but without known CHD from the Third National Health and Nutrition Examination Survey (NHANES III), a United States population sample of noninstitutionalized adults examined with a variety of health measures performed between 1988 and 1994.\(^6\) BP was measured on 2 occasions, and those with CHD or who were <30 years of age or >74 years of age were not included because the Framingham algorithms used are not applicable to those groups.\(^7\) These algorithms provided an estimate of the 10-year probability of CHD for each individual, based on Cox proportional hazards regression equations, with \(\beta\) coefficients for each risk factor defined according to the risk factor category in which each subject was classified. In short, in this 10-year probability of CHD, \(P = 1 - (s[t])^B\), where the baseline survival function \(s[t]\) using total cholesterol categories (as we have done in our analysis) = 0.90015 for men and 0.96246 for women.\(^B\) = \(e^a\), where \(A = L - G\), G utilizing total cholesterol categories, is calculated as a linear function of the product of each risk factor \(\beta\) coefficient and the population mean value by using the equation below used to calculate \(L\) for individual values. \(\beta\) Coefficients, as shown below, were determined by the Framingham risk algorithms.\(^7\) \(G\) is calculated in our NHANES III study cohort to be 2.8932 for men and 10.55995 for women and is then subtracted from individual values of \(L\) for each subject, as calculated below, to obtain individualized values for \(A\).

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L \text{ (for men) } = (0.04826 \times \text{age}) - 0.65945 \text{ (if cholesterol <160) } + 0 \text{ (if cholesterol is 160-199) } + 0.17692 \text{ (if cholesterol is 200-239) } + 0.50539 \text{ (if cholesterol is 240-279) } + 0.65713 \text{ (if cholesterol is ≥280) } + 0.49744 \text{ (if HDL-C is <35) } + 0.24310 \text{ (if HDL-C is 35-44) } + 0.0 \text{ (if HDL-C is 45-49) } - 0.05107 \text{ (if HDL-C is 50-59) } - 0.48660 \text{ (if HDL-C is ≥60) } - 0.00226 \text{ (if BP is optimal) } + 0.0 \text{ (if BP is normal) } + 0.28320 \text{ (if BP is high normal) } + 0.52168 \text{ (if BP is stage I hypertension) } + 0.61859 \text{ (if BP is stage II or higher hypertension) } + 0.42839 \text{ (if diabetes is present) } + 0.0 \text{ (if diabetes is not present) } + 0.52337 \text{ (if smoker) } + 0.0 \text{ (if not smoker)}.
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\[
L \text{ (for women) } = (0.35766 \times \text{age}) - (0.00268 \times \text{Age})^2 - 0.26138 \text{ (if cholesterol is <160) } + 0 \text{ (if cholesterol is 160-199) } + 0.20771 \text{ (if cholesterol is 200-239) } + 0.24385 \text{ (if cholesterol is 240-279) } + 0.53513 \text{ (if cholesterol is ≥280) } + 0.84312 \text{ (if HDL-C is <35) } + 0.37796 \text{ (if HDL-C is 35-44) } + 0.19785 \text{ (if HDL-C is 45-49) } + 0 \text{ (if HDL-C is 50-59) } - 0.42951 \text{ (if HDL-C is ≥60) } - 0.53563 \text{ (if BP is optimal) } + 0.0 \text{ (if BP is normal) } + 0.06775 \text{ (if BP is high normal) } + 0.26288 \text{ (if BP is stage I hypertension) } + 0.46575 \text{ (if BP is stage II or higher hypertension) } + 0.59626 \text{ (if diabetes is present) } + 0.0 \text{ (if diabetes is not present) } + 0.29226 \text{ (if smoker) } + 0.0 \text{ (if not smoker)}.
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Analyses were stratified by age group (30-49, 50-74 years), based on our previous report using age 50 years as a useful cut point to stratify risk.\(^6\) JNC-VI stages of BP as used above included optimal (SBP <120 mm Hg and DBP <80 mm Hg), normal (SBP 120-129 mm Hg and DBP 80-84 mm Hg), high normal (SBP 130-139 mm Hg or DBP 85-89 mm Hg), stage I hypertension (SBP 140-149 mm Hg or DBP 90-99 mm Hg), stage II hypertension (SBP 160-179 mm Hg or higher or DBP 100-109 mm Hg or higher), or stage III hypertension (SBP 180 mm Hg or higher or DBP 110 mm Hg or higher). Individuals with hypertension were divided into subtypes: isolated diastolic hypertension (IDH) (SBP <140 mm Hg and DBP 90 mm Hg or higher), systolic-diastolic hypertension (SDH) (SBP 140 mm Hg or higher and DBP 90 mm Hg or higher), and isolated systolic hypertension (ISH) (SBP 140 mm Hg or higher and DBP under 90 mm Hg).

The 10-year calculated CHD risk for each group of subjects (age group, hypertension subtype, or JNC-VI stage, among men and women separately) was then multiplied by the NHANES III population size in each respective group. The NHANES III sample frequencies were weighted to the general population on the basis of their examination weights to yield the predicted number of CHD events over 10 years. Because of the stratified multistage probability design of NHANES III, in which certain subgroups were oversampled, weighting must be done according to the probability that one would have been selected from a random sample. This projects estimates to the national population distribution. The CHD risk was then recalculated by setting all hypertensive individuals to control at high normal BP levels. This involved resetting the \(\beta\) coefficients in all hypertensive individuals to the coefficients representing high normal as shown in the above equations for \(L\). These coefficients were obtained from the Framingham risk algorithms.\(^7\) This process was also repeated for control of hypertension to optimal levels. Both subjects with hypertension currently untreated and those inadequately treated and receiving therapy (where BPs were ≥140 mm Hg systolic or ≥90 mm Hg diastolic) were included because control to optimal or even high normal BP levels probably would result in further reduction of CHD risk. Of those with hypertension who fit the study selection criteria, 28% of men and 42% of women were currently reported to be taking medication. The difference between the number of CHD events calculated initially and after control of hypertension represents the number of CHD events that would be prevented. The proportion of the total, original number of CHD events was then defined as the PAR%.

The total number of expected CHD events was estimated for all persons with hypertension and then reestimated after control to high normal and optimal levels in separate analyses. This was repeated by age group, JNC-VI stage, and by hypertension subtype as defined above. This provided the absolute number of CHD events within each strata as well as the relative benefit in terms of PAR% associated with control of hypertension. To examine whether results would be similar among untreated persons with hypertension, results were reexamined, excluding those currently treated. Finally, to better understand potential reasons for any differences in benefit between hypertension subtype, means or prevalences of major risk factors were compared between hypertension subtypes. These risk factors included total cholesterol, HDL cholesterol, LDL cholesterol, body mass index (BMI), diabetes, and current cigarette smoking. SAS statistical software (SAS Institute, Cary, NC) was used for all these initial determinations. All calculations estimating CHD events were performed by using NHANES III sample weights. SUDAAN statistical software (Research Triangle Institute, Research Triangle Park, NC) was used to compute weighted variance estimates for...
Finally, the number of persons with hypertension needed to treat to high normal and to optimal levels to prevent one CHD event was determined by dividing the number of persons with hypertension in each age group, stage of hypertension, and hypertension subtype for men and women by the number of events that would be prevented if treated to either high normal or to optimal levels of BP.

### Results

Comparison of risk factor prevalence among men and women by age, hypertension subtypes, and JNC-VI stage of hypertension is shown in Table I. Women 50 to 74 years of age compared with those 30 to 49 years of age had significantly lower DBP \((P < .01)\) and BMI \((P < .001)\) but higher total and LDL cholesterol \((P < .001)\). Older men 50 to 74 years of age had significantly higher SBP \((P < .01)\) than men 30 to 49 years of age, and among both older men and women, more had diabetes but less were cigarette smokers \((P < .001)\). Those persons with ISH were significantly older than those with SDH or IDH, had higher total and LDL cholesterol levels (in women only), and had greater likelihood of having diabetes \((P < .001)\). Persons with SDH had the highest levels of SBP, and those with IDH had the lowest levels of SBP \((P < .001)\). Men with stage 3 hypertension were significantly older and had higher total cholesterol and more often had diabetes, whereas women with stage 3 hypertension had lower LDL cholesterol but more often had diabetes and smoked cigarettes \((P < .01)\) compared with their counterparts with less severe hypertension. Both men and women with stage 3 hypertension had the highest levels of SBP and DBP \((P < .001)\).

Table II shows the estimated population with hypertension, the 10-year CHD risk, total CHD events expected if levels of BP remain the same (uncontrolled), and number of CHD events that would be prevented by control to high normal and optimal levels of BP.
control to high normal BP and 1042 and 440, respectively, for control to optimal BP). A greater proportion (PAR%) of CHD events in women (31% for control to high normal and 56% for control to optimal BP) than in men (19% for control to high normal and 37% for control to optimal BP) (P < .01 between men and women) could be prevented. This proportion remains approximately the same regardless of age in both men and women.

Table III presents CHD risk, total events expected, events that could be prevented, and PAR% for men and women with hypertension controlled to high normal and to optimal, subclassified by JNC-VI stage of hypertension. The preponderance of CHD events, as well as the greatest absolute number of events (in thousands) that could be prevented by control of hypertension, occurred among persons with stage 1 hypertension (371 in men and 145 in women for control to high normal and 743 in men and 288 in women for control to optimal), despite PAR% being somewhat lower for those with stage 1 hypertension compared with stages 2 and 3 hypertension.

Table IV presents CHD risk, total events expected, events that could be prevented, and PAR% for men and women with hypertension controlled to high normal and optimal, subclassified by subtype—IDH, SDH, and ISH. The greatest number of CHD events (in thousands) prevented by control of hypertension occurred...
in those with ISH (283 for men and 186 for women controlled to high normal levels and 553 for men and 342 for women controlled to optimal levels). More than half of the events in men that could be prevented by control of hypertension were in those with ISH, whereas three quarters of events that could be prevented in women by the control of hypertension were in those with ISH.

Table V shows a comparison of PAR% for treatment to high normal and optimal levels of blood pressure by age group, stage of hypertension, and hypertension subtype for men and for women between the entire cohort with hypertension and those with hypertension not reporting treatment with hypertension medication. Little difference is seen in PAR% for either age group, stage of hypertension, and hypertension subtype for both men and for women between the entire cohort with hypertension and those not reporting treatment with hypertension medication. Table VI presents the number of persons with hyper-
tension who need to be treated to either high normal or to optimal levels to prevent one CHD event by age group, stage of hypertension, and hypertension subtype for men and for women. The number of persons needing treatment (NNT) to high normal levels of BP to prevent one CHD event is 20.5 for men and 38.6 for women, whereas NNT to optimal levels of BP is 10.7 for men and 21.3 for women. NNT is substantially greater for younger versus older men (36.5 for 30-49 years of age and 21.3 for 50-74 years of age for control to high normal blood pressure and 19.2 and 8.3, respectively, for control to optimal BP) as well as for younger versus older women (102 for 30-49 years of age and 33 for 50-74 years of age for control to high normal blood pressure and 55.9 and 18.2, respectively, for control to optimal BP). The NNT is greatest for persons with stage I hypertension compared with those with stages II and III hypertension, as well as for persons with IDH compared with SDH or ISH, because those with stage I hypertension as well as those with IDH are at lower overall CHD risk than those with stages II and III hypertension or SDH or ISH.

### Discussion

Our data suggest that among those with hypertension, one fifth of CHD events in men and nearly one third of CHD events in women could be prevented by controlling hypertension to high normal levels, and more than one third of CHD events in men and one-half of CHD events in women could be prevented by controlling hypertension to optimal levels. With the increasing burden of CHD by age group in both men and women, the absolute number of preventable CHD events also increases with age. Whereas the absolute benefit could be greatest in men with stage 1 hypertension or ISH, the relative benefit of controlling hypertension to high normal levels, measured by PAR%, was greater among women.

### Clustering of risk factors

Risk of cardiovascular disease does not depend solely on BP but is markedly influenced by other cardiovascular risk factors that tend to cluster with hypertension. Less than 20% of persons with hypertension in the Framingham Heart Study had hypertension alone, whereas about 20% of CHD events in men and 48% in women showed clustering of ≥3 risk factors in a given individual. In our NHANES sample of persons with hypertension but without CHD, 25% of persons had at least 2 additional risk factors (dyslipidemia, diabetes, and/or obesity) in addition to hypertension or advanced age. It is possible that the relative benefit (eg, PAR%) of treatment of hypertension would be different, perhaps greater, in those with accompanying additional risk factors such as dyslipidemia, diabetes, smoking, or obesity; however, it was beyond the scope of the current report to examine this further.

### Sex differences in CHD risk

Although the Framingham Heart Study originally observed a consistently greater number of CHD events caused by hypertension in men compared with women at any age, others have noted the attributable risk percent to be as great or greater in women, which parallels our findings. In part, this was due to women having high ratios of total/HDL cholesterol, greater risk from diabetes, increased propensity for left ventricular hypertrophy, and an overall increased longevity compared with men. Risk ratios for CHD were 2-fold greater for women with diabetes than for the men without diabetes and almost 4-fold greater than for women without diabetes. Although left ventricu-
lar hypertrophy (LVH) and increased left ventricular mass were more common in men and may in part explain their greater absolute cardiac event rates. The Framingham Study has shown that women with LVH were at greater risk of cardiovascular events than were men with LVH. This could partially explain why hypertension control in women might result in a greater proportion of CHD events prevented.

**Staging of hypertension by severity and subtype**

The greatest absolute benefit in terms of preventable CHD events would occur by control of persons with stage 1 hypertension to high normal BP, although more advanced stages (2 and 3) could yield a greater proportional benefit; for example, a greater PAR%. Because the greatest number of CHD events occur among persons with stage 1 ISH, the greatest number of preventable CHD events could occur from treating this population. However, persons with SDH have more advanced hypertension (stages 2 and 3) and could show the greatest relative benefit. Similarly, Ogden et al have shown that the NNT to prevent a cardiovascular event was smaller in persons with at least one additional major risk factor.

**Deficiencies in awareness, treatment, and control of hypertension**

To achieve control of hypertension in a greater percentage of individuals, intensified efforts must be made to identify persons with undetected hypertension, to treat those currently untreated, and to enhance treatment in those who are inadequately treated. A recent report indicated that nearly half of physicians had not heard of the JNC-VI guidelines and that those familiar with the guidelines tended to treat to lower thresholds. However, even physicians aware of these guidelines do not treat SBP aggressively, resulting in inadequate control of persons with stage 1 hypertension or ISH. These challenges will need to be surmounted before the year 2010 target goals for BP control rates of 50% to 55% can be reached. This will require intensified efforts at fully implementing the JNC-VI guidelines, which include initiating lifestyle modification and pharmacologic intervention as well as greater acceptance of SBP as the predominant standard on which to base the diagnosis and treatment of hypertension.

**Limitations**

There are several important considerations that may affect the validity of our findings. Persons with hypertension controlled to high normal or optimal were assumed to represent the same level of risk as those with these levels who were untreated. Those with hypertension may actually be at a higher risk, even when treated, which could underestimate the number of CHD events in this group. Therefore, the PAR% could be overestimated from our analyses.

We have examined the potential impact of controlling hypertension to both high normal levels as well as to optimal levels of BP as defined by the JNC-VI; the risk of CHD death begins to rise at SBP levels >120 mm Hg and levels of DBP >80 mm Hg. Whereas control to optimal levels represents an ideal situation that currently has not been achievable in the majority of persons with hypertension, control to high normal levels represents a more practical population target for BP control than the goal of achieving optimal BP levels. Furthermore, we have examined the potential impact of hypertension control in isolation of reducing other risk factors but realized that lifestyle measures normally undertaken in conjunction with pharmacologic therapy probably will benefit other risk factors as well, which could provide greater risk reduction than that accomplished solely by BP lowering.

Last, although the Framingham risk equations are applicable for stages of hypertension as determined by JNC-VI, projected risk reductions for each of these stages cannot differentiate hypertensive subtypes (ISH, IDH, and SDH) within the same stage, as the equations used did not use BPs as continuous variables; categoric indicators for JNC-VI stages were used instead. In addition, the Framingham equations may not be fully applicable across all ethnic groups included in our study, although a recent report demonstrates validation of the Framingham risk scores among major ethnic groups in several large, prospective studies.

**Conclusions**

The largest number of projected CHD events that could be prevented from control of hypertension to high normal or optimal levels of BP occurred in older persons, men, and those with ISH. Nearly double the number of CHD events could potentially be prevented by control of hypertension to optimal compared with high normal levels. Whereas more than twice as many CHD events could be prevented from hypertension control in men compared with women, a greater proportion of CHD events would be prevented in women (30.9% for control to high normal and 55.9% for control to optimal BP) compared with men (19.2% and 36.5%, respectively). The preponderance of CHD events that would be prevented from control of hypertension would be among those with stage I hypertension as well as those with isolated systolic hypertension, which comprise the majority of persons with hypertension. Intensified efforts to identify and more effectively treat these populations will be crucial to achieve year 2010 goals for hypertension control.
References


