Prehypertension and Cardiovascular Disease Risk in the Women’s Health Initiative

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Background—Prehypertension is common and is associated with increased vascular mortality. The extent to which it increases risk of nonfatal myocardial infarction, stroke, and congestive heart failure is less clear.

Methods and Results—We determined the prevalence of prehypertension, its association with other coronary risk factors, and the risk for incident cardiovascular disease events in 60 785 postmenopausal women during 7.7 years of follow-up using Cox regression models that included covariates as time-dependent variables. Prehypertension was present at baseline in 39.5%, 32.1%, 42.6%, 38.7%, and 40.3% of white, black, Hispanic, American Indian, and Asian women, respectively (P<0.0001 across ethnic groups). Age, body mass index, and prevalence of diabetes mellitus and hypercholesterolemia increased across blood pressure categories, whereas smoking decreased (all P<0.0001). Compared with normotensive women (referent), adjusted hazard ratios for women with prehypertension were 1.58 (95% confidence interval [CI], 1.12 to 2.21) for cardiovascular death, 1.76 (95% CI, 1.40 to 2.22) for myocardial infarction, 1.93 (95% CI, 1.49 to 2.50) for stroke, 1.36 (95% CI, 1.05 to 1.77) for hospitalized heart failure, and 1.66 (95% CI, 1.44 to 1.92) for any cardiovascular event. Hazard ratios for the composite outcome with prehypertension did not differ between ethnic groups (P=0.71 for interaction), although the numbers of events among Hispanic and Asian women were small.

Conclusions—Prehypertension is common and was associated with increased risk of myocardial infarction, stroke, heart failure, and cardiovascular death in white and nonwhite postmenopausal women. Risk factor clustering was conspicuous, emphasizing the need for trials evaluating the efficacy of global cardiovascular risk reduction through primordial prevention. (Circulation. 2007;115:855-860.)

Key Words: hypertension ■ myocardial infarction ■ risk factors ■ stroke ■ women

In observational studies including >1 million persons, blood pressure has been strongly related to heart disease and stroke mortality throughout middle and old age, without evidence of a threshold down to at least 115/75 mm Hg.1 Individuals with blood pressure close to the traditional threshold for the diagnosis of hypertension have a high likelihood of progression to blood pressure meeting the definition of hypertension over the ensuing 5 years.2 In 2003, the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) categorized individuals with systolic blood pressure between 120 and 139 mm Hg or diastolic pressure between 80 and 89 mm Hg as having prehypertension.3 Prevalence of prehypertension in the 1999 to 2000 National Health and Nutrition Examination Survey (NHANES) was 40% for men and 23% for women.4

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Estimates of cardiovascular risk with prehypertension have ranged from no increased cardiovascular mortality in NHANES5 to an 80% increase in cardiovascular disease risk among American Indians.6 In the Framingham study, the risk of a composite cardiovascular outcome, which included myocardial infarction, stroke, heart failure, or cardiovascular death, was greater among men (hazard ratio, 1.6; 95% confidence interval [CI], 1.1 to 2.2) and women (hazard ratio, 2.5; 95% CI, 1.6 to 4.1) with “high-normal” blood pressure (130 to 139 mm Hg systolic or 85 to 89 mm Hg diastolic) compared with individuals with blood pressure <120/80 mm Hg based on examinations in the original

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cohort (1956 to 1958, 1972 to 1974, 1984 to 1986) and in the offspring study (1978 to 1982). The predecessor to JNC7 was JNC6, which categorized optimal blood pressure as <120/80 mm Hg, normal as systolic pressure of 120 to 129 mm Hg or diastolic pressure of 80 to 84 mm Hg, and high normal as systolic pressure of 130 to 139 mm Hg or diastolic pressure of 85 to 89 mm Hg. Subsequently, JNC7 was mandated to simplify blood pressure classification, so the normal and high-normal categories were combined to define prehypertension. We assessed the risk of myocardial infarction, stroke, hospitalized heart failure, and cardiovascular death associated with prehypertension in the Women’s Health Initiative (WHI), a large, contemporary cohort that includes significant numbers of black, Hispanic, and Asian women.

Methods

Study Population

The WHI includes 161 808 postmenopausal women enrolled at 40 clinical sites in 4 randomized trials and an observational study. This analysis excludes women in the observational study, who did not have annual assessment of covariates used in the models, and women with prevalent myocardial infarction, stroke, or heart failure at baseline; thus, 60 785 women were included. The study population, recruitment methods, baseline data collection, and outcomes ascertainment procedures have been reported previously. The protocol and consent forms were approved by institutional review boards of the participating institutions; all trial participants provided written informed consent.

Measurement of Blood Pressure and Covariates

At baseline and annual clinic visits, women sat quietly for 5 minutes before blood pressure was measured with a mercury manometer; 2 measurements, taken 30 seconds apart, were recorded. The average of the 2 measurements was used in these analyses. Appropriate cuff bladder size was determined at each visit based on arm circumference. For tables using JNC7 blood pressure categories and the Figure, normal blood pressure was defined as systolic pressure <120 mm Hg and diastolic <80 mm Hg, prehypertension as systolic pressure of 120 to 139 mm Hg or diastolic 80 to 89 mm Hg, and hypertension as systolic pressure ≥140 mm Hg or diastolic ≥90 mm Hg or self-reported hypertension with use of antihypertensive medication. For the table using JNC6 categories, blood pressure was defined as follows: optimal, <120/<80 mm Hg, normal, 120 to 129/80 to 84 mm Hg, high normal, 130 to 139/85 to 89 mm Hg, and hypertension as ≥140/≥90 mm Hg or self-reported hypertension with use of antihypertensive medication. Women with measured blood pressure in the prehypertension or high-normal range who were taking antihypertensive medication, either at baseline or during follow-up, were considered to have hypertension. If systolic and diastolic pressures fell into different categories, women were assigned to the higher category.

Height and weight, diabetes mellitus requiring dietary or pharmacological therapy, and medication inventory were updated at years 1, 3, 6, and 9. Hypercholesterolemia requiring drug treatment was determined by self-report at baseline and then by use of lipid-modulating medication. Smoking was assessed at baseline and years 1, 3, 6, and 9.

Outcomes Ascertainment

Participants reported emergency room visits, overnight hospital stays, and outpatient coronary revascularization procedures semiannually. Medical records for all overnight hospitalizations and outpatient coronary revascularization procedures were scrutinized for potential outcomes of interest. Centrally trained physician-adjudicators classified outcomes on the basis of medical record review. The composite cardiovascular outcome in this report is similar to that used in the Framingham study analysis5 and included cardiovascular death (excluding fatal pulmonary embolism), nonfatal myocardial infarction, stroke, and hospitalized heart failure.

Myocardial infarction was categorized using an algorithm that included symptoms, ECG findings, and cardiac enzymes. Stroke required rapid onset of a persistent neurological deficit not due to trauma, tumor, infection, or other cause. Hospitalized heart failure required overnight hospitalization with physician diagnosis of new or worsened heart failure and at least one of the following: medical treatment for heart failure, pulmonary congestion on chest roentgenogram, or imaging study documenting ventricular systolic or diastolic dysfunction.

Statistical Analysis

Hazard ratios with 95% CIs were calculated from Cox regression models stratified by age and randomization status in the hormone, calcium/vitamin D, and dietary modification trials. Cox models were adjusted for age as a continuous variable, body mass index, self-reported treated diabetes, high cholesterol, and current smoking. Some models also included alcohol use (number of servings per week) and physical activity (total energy expenditure in metabolic equivalents per week) as covariates. Coded values were used for tests of trend across blood pressure categories. Blood pressure category was updated with serial blood pressure measurement in a nonreversible fashion. For example, if a normotensive participant developed hypertension at year 3 of follow-up, she was shifted into the prehypertension category at that time and could not revert to the normal blood pressure category. During follow-up, 10 145 women...
were aware but untreated. Categories (all and hypercholesterolemia increased across the blood pressure
was identified in 39.5%, 32.1%, 42.6%, 38.7%, and 40.3% of
ethnicity was not known for 853 women. At baseline, 16,002
women were postmenopausal, with a mean age of
7.0 years. Although study participants were predomi-
antly white (n = 11,005), this analysis included 6222 black,
2599 Hispanic, 256 American Indian, and 1469 Asian women;
11/78 17/80 6 130 7/69
High cholesterol, n (%) 1320 (8.3) 2417 (10.2) 3622 (17.1)
Current smoker, n (%) 1599 (10.0) 1757 (7.4) 1342 (6.3)
Table 1. Cohort Characteristics by Blood Pressure Category at Baseline
<table>
<thead>
<tr>
<th>Age, y</th>
<th>Normal (n = 16,002)</th>
<th>Prehypertension (n = 23,596)</th>
<th>Hypertension (n = 21,187)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity, n (%)</td>
<td>White (13,747 (85.9))</td>
<td>19,483 (82.6)</td>
<td>16,156 (76.3) &lt;0.0001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Black (926 (5.8))</td>
<td>1,996 (8.5)</td>
<td>3,300 (15.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hispanic (752 (4.7))</td>
<td>1,108 (4.7)</td>
<td>739 (3.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>American Indian (53 (0.3))</td>
<td>99 (0.4)</td>
<td>104 (0.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Asian/Pacific Islander (325 (2.0))</td>
<td>592 (2.5)</td>
<td>552 (2.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unknown (199 (1.2))</td>
<td>318 (1.3)</td>
<td>336 (1.6)</td>
<td></td>
</tr>
<tr>
<td>History of hypertension, n (%)</td>
<td>Never (15,475 (96.7))</td>
<td>20,427 (86.6)</td>
<td>3196 (15.1) &lt;0.0001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treated (0 (0))</td>
<td>0 (0)</td>
<td>15,064 (71.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus, n (%)</td>
<td>296 (1.8)</td>
<td>707 (3.0)</td>
<td>1746 (8.2) &lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Current smoker, n (%)</td>
<td>1599 (10.0)</td>
<td>1757 (7.4)</td>
<td>1342 (6.3) &lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>High cholesterol, n (%)</td>
<td>1320 (8.3)</td>
<td>2417 (10.2)</td>
<td>3622 (17.1) &lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Blood pressure, mm Hg</td>
<td>109±7/69±6</td>
<td>130±11/78±7</td>
<td>141±17/80±10 &lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Body mass index, kg/m²</td>
<td>26.9±5.2</td>
<td>28.9±5.8</td>
<td>30.6±6.2 &lt;0.0001</td>
</tr>
</tbody>
</table>
Probability values from F test for continuous variables and from χ² for categorical variables. Percentages for ethnicity and history of hypertension indicate the column percent (not row percent) for each blood pressure category and may not add up to 100% because of missing data. History of untreated hypertension indicates that hypertension was previously diagnosed by a healthcare provider, but subject reports no current antihypertensive medication use at baseline.

Results
Women were postmenopausal, with a mean±SD age of
62.8±7.0 years. Although study participants were predomi-
nantly white (n = 49,386), this analysis included 6222 black,
2599 Hispanic, 256 American Indian, and 1469 Asian women;
ethnicity was not known for 853 women. At baseline, 16,002
(26%) were normotensive, 23,596 (39%) had prehypertension,
and 21,187 (35%) had hypertension (Table 1). Prehypertension
was identified in 39.5%, 32.1%, 42.6%, 38.7%, and 40.3% of
white, black, Hispanic, American Indian, and Asian women,
respectively. The distribution of blood pressure categories dif-
fined among ethnic groups (P < 0.0001).

Age, body mass index, and prevalence of diabetes mellitus and hypercholesterolemia increased across the blood pressure
categories (all P < 0.0001), whereas current smoking was more prevalent among normotensive women (10%) compared with
those with prehypertension (7.4%) or hypertension (6.3%; P < 0.0001 across the 3 categories). Among women with hyper-
tension, 15% were unaware of this condition, whereas 5.5% were aware but untreated.

The 10-year incidence of cardiovascular events was 3.63% for normotensive women, 7.11% for prehypertensive women, and
14.16% for hypertensive women. Compared with normotensive women (referent), hazard ratios after adjustment for age and
time-dependent adjustment for body mass index, diabetes mellitus, high cholesterol, and current smoking were higher for
cardiovascular death (1.58; 95% CI, 1.12 to 2.21), myocardial infarction (1.76; 95% CI, 1.40 to 2.22), stroke (1.93; 95% CI,
1.49 to 2.50), and heart failure (1.36; 95% CI, 1.05 to 1.77). Hazard ratios for cardiovascular events were even higher among
women with hypertension (Table 2). When alcohol use and
physical activity were added to the model, hazard ratios among
women with hypertension were attenuated (cardiovascular death: 1.31; 95% CI, 0.83 to 2.09; myocardial infarction: 1.61;
95% CI, 1.16 to 2.24; stroke: 1.79; 95% CI, 1.22 to 2.63; heart
failure: 1.54; 95% CI, 1.00 to 2.37), whereas hazard ratios among women with hypertension were higher (cardiovascular
death: 2.90; 95% CI, 1.87 to 4.51; myocardial infarction: 3.5;
95% CI, 2.37 to 4.47; stroke: 4.09; 95% CI, 2.83 to 5.91; heart
failure: 3.61; 95% CI, 2.38 to 5.47).

Kaplan-Meier curves are shown for the composite outcome of
any cardiovascular event (cardiovascular death, myocardial in-
farction, stroke, or heart failure) in the 3 blood pressure catego-
ries (the Figure), adjusted for body mass index, diabetes, high
cholesterol, and current smoking as time-dependent variables.
Compared with normotensive women (referent), the hazard ratio
for the composite cardiovascular outcome was 1.66 (95% CI,
1.44 to 1.92) for women with prehypertension and 2.89 (95% CI,
2.52 to 3.32) for those with hypertension (P < 0.001 for trend
across blood pressure categories). When alcohol use and physi-
Risk factors other than blood pressure category that contributed significantly to cardiovascular risk in multivariable, time-dependent models included age at screening (hazard ratio, 1.09 per 1-year increment; 95% CI, 1.08 to 1.11), current smoking (hazard ratio, 1.34; 95% CI, 1.26 to 1.43), body mass index (hazard ratio, 1.02; 95% CI, 1.01 to 1.03), and especially treated diabetes (hazard ratio, 2.58; 95% CI, 2.32 to 2.86; all P<0.0001). Physical activity was inversely associated (hazard ratio, 0.99; 95% CI, 0.99 to 0.99; P<0.001), whereas self-reported hypercholesterolemia and alcohol use were not independent determinants of cardiovascular risk.

When blood pressure was categorized using the JNC6 categories of optimal, normal, high normal, and hypertension, the graded relationship between blood pressure and cardiovascular events persisted (Table 3). Compared with optimal blood pressure (referent), the hazard ratio for the composite cardiovascular outcome was 1.40 (95% CI, 1.18 to 1.67) for women with normal blood pressure, 1.77 (95% CI, 1.52 to 2.06) for high-normal blood pressure, and 2.86 (95% CI, 2.49 to 3.29) for hypertension.

Hazard ratios for the composite cardiovascular outcome are shown by JNC7 blood pressure category within ethnic groups (Table 4). Cardiovascular risk did not appear to differ among ethnic groups for either prehypertension (P=0.71 for interaction) or hypertension (P=0.19 for interaction), although the numbers of events among Hispanic and Asian women were small.

### Discussion

The prevalence of prehypertension was 39% among WHI participants at baseline. Risk factor clustering was conspicuous, with graded increases in age, body mass index, diabetes mellitus, and hypercholesterolemia across blood pressure categories and an inverse relationship with smoking. However, despite this clustering, adjustment for these risk factors had limited impact on the independent association of prehypertension with clinical cardiovascular events. After adjustment for multiple covariates as time-dependent variables, risks of myocardial infarction, stroke, heart failure, and cardiovascular death were higher among women with prehypertension compared with normotensive women and even higher among those with hypertension. Hazard ratios for cardiovascular events by blood pressure category were similar across ethnic groups, although the CIs were wide for Hispanic and Asian women.

For every 1000 women with prehypertension, ~7 had a first cardiovascular event each year compared with 14 events per year for women with hypertension and 4 events per year for normotensive women. Thus, the population-attributable risk to prehypertension was 3 excess cardiovascular events per year per 1000 women, whereas 8 excess events per year could be attributed to hypertension.

Our analysis provides estimates of cardiovascular risk with elevated blood pressure on a background of contemporary standard of care, with careful prospective outcome ascertainment, and uses the blood pressure categories as defined in the current JNC7 hypertension guideline.

### Table 2. Cardiovascular Risk by JNC7 Blood Pressure Category

<table>
<thead>
<tr>
<th></th>
<th>Normal, BP &lt;120/80 mm Hg (Referent)</th>
<th>Prehypertension, BP 120–139/80–89 mm Hg</th>
<th>Hypertension, BP &gt;140/&gt;90 mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (annualized %)</td>
<td>HR (95% CI)</td>
<td>n (annualized %)</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>83 (0.07)</td>
<td>1</td>
<td>219 (0.12)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>177 (0.14)</td>
<td>1</td>
<td>442 (0.24)</td>
</tr>
<tr>
<td>Stroke</td>
<td>137 (0.11)</td>
<td>1</td>
<td>407 (0.22)</td>
</tr>
<tr>
<td>Hospitalized heart failure</td>
<td>137 (0.11)</td>
<td>1</td>
<td>351 (0.19)</td>
</tr>
<tr>
<td>Any cardiovascular event</td>
<td>442 (0.35)</td>
<td>1</td>
<td>1196 (0.66)</td>
</tr>
</tbody>
</table>

BP indicates blood pressure; HR, hazard ratio. Multivariable Cox regression model was stratified according to age (50 to 54, 55 to 59, 60 to 69, 70 to 79 years) and randomized trial participation and was adjusted for age (continuous) at baseline and the following time-dependent covariates: body mass index, diabetes mellitus, high cholesterol, and current smoking.

### Table 3. Cardiovascular Risk by JNC6 Blood Pressure Category

<table>
<thead>
<tr>
<th></th>
<th>Optimal BP, &lt;120/&lt;80 mm Hg (Referent)</th>
<th>Normal BP, 120–139/80–89 mm Hg</th>
<th>High-Normal BP, 130–139/85–89 mm Hg</th>
<th>Hypertension, BP &gt;140/&gt;90 mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (annualized %)</td>
<td>HR (95% CI)</td>
<td>n (annualized %)</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>83 (0.07)</td>
<td>1</td>
<td>115 (0.11)</td>
<td>1.56 (1.05–2.32)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>177 (0.14)</td>
<td>1</td>
<td>215 (0.21)</td>
<td>1.41 (1.07–1.87)</td>
</tr>
<tr>
<td>Stroke</td>
<td>137 (0.11)</td>
<td>1</td>
<td>204 (0.20)</td>
<td>1.38 (1.01–1.90)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>137 (0.11)</td>
<td>1</td>
<td>177 (0.17)</td>
<td>1.31 (0.96–1.79)</td>
</tr>
<tr>
<td>Any cardiovascular event</td>
<td>442 (0.35)</td>
<td>1</td>
<td>602 (0.59)</td>
<td>1.40 (1.18–1.67)</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 2. In the JNC6 blood pressure categories shown here, prehypertension (defined in JNC7 as BP 120 to 139/80 to 89 mm Hg) is subdivided into normal and high normal. Multivariable Cox regression model was stratified according to age (50 to 64, 55 to 59, 60 to 69, 70 to 79 years) and randomized trial participation and was adjusted for age (continuous) at baseline and the following time-dependent covariates: body mass index, diabetes mellitus, high cholesterol, and current smoking.
TABLE 4. Cardiovascular Risk by Ethnic Group With Prehypertension (as Defined in JNC7) and Hypertension

<table>
<thead>
<tr>
<th></th>
<th>Normal BP (Referent)</th>
<th>Prehypertension</th>
<th>Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events, n (annualized %)</td>
<td>HR</td>
<td>Events, n (annualized %)</td>
</tr>
<tr>
<td>White</td>
<td>395 (0.36)</td>
<td>1</td>
<td>1042 (0.69)</td>
</tr>
<tr>
<td>Black</td>
<td>23 (0.31)</td>
<td>1</td>
<td>86 (0.56)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>12 (0.22)</td>
<td>1</td>
<td>35 (0.43)</td>
</tr>
<tr>
<td>Asian</td>
<td>3 (0.12)</td>
<td>1</td>
<td>16 (0.35)</td>
</tr>
<tr>
<td>Combined*</td>
<td></td>
<td>1</td>
<td>1.56 (1.39–1.76)</td>
</tr>
<tr>
<td>P for interaction</td>
<td></td>
<td>0.71</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations as in Table 2. Multivariable Cox regression model for the composite cardiovascular outcome of cardiovascular death, myocardial infarction, stroke, or hospitalized heart failure was stratified according to age (50 to 54, 55 to 59, 60 to 69, 70 to 79 years) and randomized trial participation and was adjusted for age (continuous) at baseline and the following time-dependent covariates: body mass index, diabetes mellitus, high cholesterol, and current smoking.

*American Indians and women of unknown ethnicity were not included in this analysis.

Other strengths of our analysis are the cohort size and diversity. The Framingham analysis included 138 cardiovascular events in women compared with 3891 events in this report. The large size and long follow-up of the WHI cohort permit risk estimation for individual cardiovascular outcomes and the composite outcome. The geographic, socioeconomic, and ethnic diversity of the cohort also provides a broadly applicable estimate of the risk associated with prehypertension.

In the Framingham study, the hazard ratio for any cardiovascular event in the JNC6 normal blood pressure category was 1.5 (95% CI, 0.9 to 2.5) compared with optimal blood pressure (referred) and 2.5 (95% CI, 1.6 to 4.1) for high-normal blood pressure. In our cohort, the hazard ratio was 1.40 (95% CI, 1.18 to 1.67) for normal blood pressure and 1.77 (95% CI, 1.52 to 2.06) for high-normal blood pressure. The somewhat lower hazard ratios in our report may reflect differences in underlying characteristics of current US residents because baseline visits for the Framingham study were conducted in the 1950s, as well as changes in standard of care for multiple risk factors.

Is the cardiovascular risk with blood pressures slightly above 120/80 mm Hg clinically important enough to justify the label of prehypertension? To some extent, the answer depends on the individual clinical outcome under consideration and the eye of the beholder. A 93% increase in stroke risk seems clinically relevant, whereas a 36% increase in hospitalized heart failure risk may be less compelling (Table 2). The increased cardiovascular risk with prehypertension is certainly smaller than the risk associated with having diabetes (hazard ratio, 2.58; 95% CI, 2.32 to 2.86) but is greater than that associated with smoking (hazard ratio, 1.34; 95% CI, 1.26 to 1.43). Smoking is pretty much unchallenged as a cardiovascular risk factor; perhaps prehypertension should be afforded the same acceptance.

Limitations of our analysis include the absence of men and younger adults. The latter is less of a handicap because younger individuals would contribute comparatively few cardiovascular events. WHI participants are not randomly selected but represent a broad ethnic, geographic, and socioeconomic swath of American adults and those with prehypertension.16 Our analysis also demonstrates increasing age, body mass index, and prevalence of diabetes mellitus and hypercholesterolemia across blood pressure categories. The clustering of conventional risk factors with prehypertension raises the possibility that the increased cardiovascular risk we observed was not due entirely to blood pressure but also to other risk characteristics that were not measured and for which we did not adjust in the multivariable analyses. These observations further underscore the importance of global cardiovascular risk assessment.

Both lifestyle19–22 and pharmacological interventions23 reduce progression from prehypertension to hypertension, but such intervention has not been shown to reduce cardiovascular events. These findings support the role of prudent lifestyle, which favorably affects other risk factors, including progression to diabetes mellitus24 and low-density lipoprotein cholesterol levels25. The differences in cardiovascular event rates between women with prehypertension and hypertension in our analysis and others1,6,7 provide support for recommendations aimed at reducing blood pressure at an earlier stage of this disease. Prospective trials are needed to evaluate the efficacy, feasibility, and cost-effectiveness of global primordial cardiovascular risk reduction.

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References


CLINICAL PERSPECTIVE

Prehypertension (ie, blood pressure between 120/80 and 140/90 mm Hg) is common; the extent to which it increases cardiovascular risk is unclear. We determined the risk of nonfatal myocardial infarction, stroke, and congestive heart failure with prehypertension in 60 785 postmenopausal women 50 to 79 years of age during 7.7 years of follow-up. At baseline, 38.8% of women had prehypertension and 34.9% had hypertension. Age, body mass index, and prevalence of diabetes and hypercholesterolemia increased across blood pressure categories, whereas smoking decreased (all P<0.0001). Compared with normotensive women (referent), adjusted hazard ratios for women with prehypertension were 1.58 (95% confidence interval [CI], 1.12 to 2.21) for cardiovascular death, 1.76 (95% CI, 1.40 to 2.22) for myocardial infarction, 1.93 (95% CI, 1.49 to 2.50) for stroke, 1.36 (95% CI, 1.05 to 1.77) for hospitalized heart failure, and 1.66 (95% CI, 1.44 to 1.92) for any cardiovascular event. Hazard ratios for the composite outcome with prehypertension did not differ between ethnic groups. Overall, prehypertension was common and associated with increased risk of myocardial infarction, stroke, heart failure, and cardiovascular death in white and nonwhite postmenopausal women. The differences in cardiovascular event rates between women with prehypertension and hypertension provide support for recommendations aimed at reducing blood pressure at an earlier stage of this disease. Risk factor clustering was conspicuous, emphasizing the importance of global cardiovascular risk assessment and management. Prospective trials are needed to evaluate the efficacy, feasibility, and cost-effectiveness of global primordial cardiovascular risk reduction.

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Prehypertension and Cardiovascular Disease Risk in the Women's Health Initiative
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