Residual Lifetime Risk for Developing Hypertension in Middle-aged Women and Men

The Framingham Heart Study

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HIGH BLOOD PRESSURE IS A KEY risk factor for cardiovascular disease events.1-3 The long-term risk for developing hypertension in an individual is best described by the lifetime risk statistic, ie, the probability that an individual will develop hypertension over the course of his or her remaining lifetime. Lifetime risk estimates for disease conditions are more easily understood by the general public compared with other measures of disease frequency, such as age-specific prevalence.4-6 For example, the American Cancer Society used the “1 in 9” statistic for the lifetime risk for breast cancer in the early 1990s to promote mammographic screening.5 Furthermore, lifetime risk estimates also may be used to assess temporal trends in long-term disease risk.4 Although lifetime risk estimates are available for several chronic disease conditions, including breast cancer, dementia, fractures, and coronary heart disease,3,8 the lifetime risk for developing hypertension has not been reported.

See also Patient Page.

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RISK FOR HYPERTENSION IN MIDDLE AGE

ience of hypertension in the community in the 1976-1991 period compared with surveys during the 1960-1974 period. A trend of decreasing blood pressure levels has been noted also in regional cross-sectional surveys of cardiovascular disease risk factors and in longitudinal cohort studies. Although these prevalence trends are encouraging, these data should not be interpreted to indicate that the risk for developing hypertension has decreased in recent times. It is possible that the lifetime risk for hypertension may have increased in recent years because of an increase in life expectancy and an increase in obesity in the United States. On the other hand, the lifetime risk for hypertension may have declined because of preventive efforts directed at patients with high-normal blood pressure. Accordingly, we estimated the residual lifetime risk for developing hypertension among Framingham Heart Study participants.

METHODS

Study Participants

The Framingham Heart Study is a prospective longitudinal cohort study that began in 1948 with the enrollment of 5209 men and women who were free of cardiovascular disease and between the ages of 28 and 62 years. These participants since have been examined every 2 years. Participants who were free of hypertension in 1975 and who attended subsequent biennial examinations were eligible for our investigation. We chose the period from 1976 onward up to 1998 so our estimates would reflect contemporary experience. We evaluated the residual lifetime risk for hypertension beginning at the baseline ages of 55 and 65 years because the risk for developing hypertension increases markedly during and after the sixth decade of life. Additionally, sufficient numbers of younger participants were not available in our cohort to estimate risks for those younger than 55 years.

Participants could contribute blood pressure information at more than 1 baseline age provided they reached the next baseline age free of hypertension. For example, a 55-year-old nonhypertensive subject attending a biennial examination in 1976 could contribute information over the next 10 years for this baseline age. If he or she was free of hypertension in 1986, the subject could provide additional information as a 65-year-old individual for the remainder of the time between 1986 and 1998.

Measurement of Blood Pressure

At each biennial examination, participants underwent a physical examination (with a medical history), laboratory assessment of cardiovascular disease risk factors, and routine electrocardiography. A physician measured the systolic and diastolic blood pressures of seated study participants using a mercury column sphygmomanometer and a standard protocol. The first and the fifth Korotkoff sounds were taken as indicative of systolic and diastolic blood pressure, respectively. The average of 2 such systolic and diastolic blood pressure readings was taken as the examination blood pressure. At each examination, participants were asked if they used antihypertensive medications for the purpose of lowering elevated blood pressure.

Blood Pressure on Follow Up

All eligible participants were followed up from the time of entry into the study until the end of the observation period, the development of hypertension, death (in the absence of hypertension), or the last follow-up examination. We examined separately the development of each of the following 5 blood pressure outcomes:

1. Hypertension defined according to the recommendations of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI) and the World Health Organization-International Society of Hypertension as a systolic blood pressure of 140 mm Hg or higher and/or a diastolic blood pressure of 90 mm Hg or higher or the use of medications for the purpose of treating high blood pressure at a qualifying examination;

2. Use of antihypertensive medication on follow-up for the treatment of hypertension;

3. Stage 1 high blood pressure or higher, defined as blood pressure of 140/90 mm Hg or higher regardless of the use of antihypertensive medications;

4. Stage 2 high blood pressure or higher, defined as blood pressure of 160/100 mm Hg or higher regardless of the use of antihypertensive medications;

5. Stage 2 high blood pressure or higher use of antihypertensive medication on follow-up.

Statistical Methods

Residual Lifetime Risk: Definitions. The term residual lifetime risk has been defined in 2 ways in the literature: (1) unadjusted lifetime cumulative incidence that indicates the cumulative risk over the remaining lifetime but does not consider the impact of mortality due to competing causes; and (2) mortality-adjusted lifetime cumulative incidence. We estimated both statistics in our study.

Residual Lifetime Risk for Developing Hypertension and Other Blood Pressure Outcomes. The residual lifetime risk for developing the blood pressure-related outcomes was estimated for study participants who attained the ages of 55 and 65 years free of hypertension during the 1976-1998 period. Sex-specific analyses were performed separately for these 2 baseline ages. For 55-year-old participants, we estimated the risk for developing hypertension through age 80 years. For 65-year-old participants, we estimated the risk for developing hypertension through age 85 years. These follow-up time intervals (25 years for 55-year-olds and 20 years for 65-year-olds) correspond to the current mean residual life expectancies for white individuals at these 2 ages in the United States.

The residual lifetime risk for each blood pressure-related outcome (including hypertension) was calculated using the Practical Incidence Estimator macro detailed elsewhere. This method uses survival age as the time
scale, combines information on participants entering the observation periods at different ages, and accounts for varying durations of follow-up of individuals. Briefly, a modified Kaplan-Meier method was used with survival age as the time scale (FIGURE 1). For example, the remaining lifetime risk for hypertension for 55-year-old participants is simply the cumulative incidence of hypertension over 25 years (estimated residual life expectancy) thus:

Cumulative Incidence$_{55}=\sum_{i}(h_iS_{i-1})$

where $h_i$ is the conditional probability of developing hypertension at age $i$ years given survival beyond age $i-1$ years, $S_{i-1}$ is the probability of survival beyond age $i-1$ years free of hypertension, and $h_iS_{i-1}$ is the unconditional probability of developing hypertension at age $i$ years, where the summation is from $i=55$ to $i=80$. Thus, a person who attends an examination at age 61 years and is free of hypertension but who did not attend any examination at age 55 years (subject B in Figure 1) still can contribute to the es-
Table 1. Residual Lifetime Risk of Hypertension According to Baseline Age*  

<table>
<thead>
<tr>
<th>Time, y</th>
<th>Women, Age, y</th>
<th>Men, Age, y</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>55 (n = 709)</td>
<td>65 (n = 549)</td>
</tr>
<tr>
<td>10</td>
<td>52 (46-58)</td>
<td>64 (60-69)</td>
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<td>15</td>
<td>72 (68-76)</td>
<td>81 (77-84)</td>
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<td>20</td>
<td>83 (80-86)</td>
<td>89 (86-92)</td>
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<td>25</td>
<td>91 (89-93)</td>
<td>93 (91-96)</td>
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</table>

*For 55-year-old subjects, the risk for developing hypertension over 25 years represents their lifetime risk. For 65-year-old subjects, the risk for developing hypertension over 20 years indicates their lifetime risk. Ellipses indicate not applicable.

Temporal Trends in Residual Lifetime Risk for Developing Hypertension

We compared the residual lifetime risk for developing hypertension (and other blood pressure outcomes) in the 1976-1998 period with that in the 1952-1975 period. For this comparison, we focused on unadjusted lifetime cumulative incidence because this statistic is unaffected by changing rates of mortality due to other causes over time. Subjects in the Framingham Heart Study who were not hypertensive at their third biennial examination (earliest eligible baseline for that time) contributed to the estimation of lifetime risk for developing hypertension during the 1952-1975 period. We compared the sex- and age-specific risks of developing hypertension and other blood pressure outcomes for the 2 periods with z tests for lifetime risk estimates and with the Cox models with left truncation. For 65-year-old men, only 15-year risk estimates were compared because few individuals in this age group contributed information beyond this time interval in the 1952-1975 period. Two sets of analyses were performed: (1) models that included information from all eligible participants in each of the periods; participants who contributed to the 1952-1975 period could provide additional information in the later period (at a different age) provided they reached the later period free of hypertension and (2) models that compared incidence of blood pressure outcomes in participants who contributed to only the 1952-1975 period with that in participants who were eligible only in the 1976-1998 period.

Additionally, we compared sex-specific trends in body mass index (BMI), calculated as weight in kilograms divided by the square of height in meters, across the 2 periods for our study participants using repeated measures analysis of variance adjusting for age as a covariate. All P values reported are 2-sided, and a P value <.05 was considered statistically significant.

RESULTS

Residual Lifetime and Short-term Risks for Developing Hypertension

During the 1976-1998 period, 1298 participants (589 men and 709 women) provided 8469 person-years of observation. The residual lifetime risk for developing hypertension for study participants was 90% (TABLE 1). Lifetime risk for hypertension was similar for men and women and did not differ between participants aged 55 and 65 years (hazards ratio [HR] for women vs men aged 55 years, 0.91 [95% CI, 0.80-1.04]; for those aged 65 years, 0.88 [95% CI, 0.76-1.04]). More than half of the 55-year-old participants and about two thirds of the 65-year-old participants developed hypertension within 10 years.

On adjustment for competing causes of mortality, the mortality-adjusted lifetime risk remained unchanged in women (90% and 86%, respectively, for baseline ages 55 and 65 years) but decreased marginally in men (83% and 81%, respectively, for baseline ages 55 and 65 years).
Lifetime Probability of Using Antihypertensive Medications

Nearly 60% of men and women received blood pressure–lowering drugs on follow-up (Table 2). Estimates were similar for both sexes (HR for women vs men aged 55 years, 0.98 [95% CI, 0.83-1.16]; for those aged 65 years, 0.92 [95% CI, 0.76-1.11]), and for the 2 baseline ages. A third of 55-year-old and nearly half of 65-year-old participants were likely to receive antihypertensive medication within 15 years.

Residual Lifetime Risk for High Blood Pressure

The lifetime risk for high blood pressure in our study participants is shown in Table 3. Nearly 85% of our study participants developed stage 1 high blood pressure or higher (≥140 mm Hg systolic or ≥90 mm Hg diastolic) during a follow-up period of 20 to 25 years. Lifetime risk estimates did not vary for the 2 sexes (HR for women vs men aged 55 years, 0.91 [95% CI, 0.80-1.04]; for those aged 65 years 0.88 [95% CI, 0.76-1.04]) or between the 2 baseline ages.

The lifetime risk for experiencing stage 2 high blood pressure or higher (≥160 mm Hg systolic or ≥100 mm Hg diastolic) in the 1976-1998 period varied from 35% to 44% for different age-sex groups. The lifetime risk for developing stage 2 high blood pressure or higher or receiving antihypertensive medications was about 70% regardless of baseline age or sex.

Trends in Blood Pressure Outcomes Over Time

During the 1952-1975 period, 1740 participants (785 men, 955 women) contributed 12338 person-years of observation for the estimation of the residual lifetime risk for hypertension. In women, the residual lifetime risk for hypertension did not differ between the 2 periods; risk estimates for the 1952-1975 period were 92% vs 91% for the 1976-1998 periods for baseline age 55 years (P=.68); and 93% vs 89% for the baseline age 65 years, respectively (P=.51, Figure 2A). However, for 55-year-old men, the residual lifetime risk for hypertension was 93% in the 1976-1998 period vs 82% in the 1952-1975 period (P<.001). Similarly, the 15-year risk for hypertension in 65-year-old men increased from 65% in the 1952-1975 period to 85% in the 1976-1998 period (P<.001; Figure 2B). Cox regression analyses confirmed these observations (Table 4).

Women in the 1952-1975 period had a slightly higher risk for developing hypertension than men in that period (HR for women vs men aged 55 years, 1.15 [95% CI, 1.01-1.30]; for those aged 65 years, 1.23 [95% CI, 0.97-1.56]). As noted previously, point estimates of the HRs suggested a lower risk in women compared with men in the 1976-1998 period although this was not statistically significant.

The residual lifetime probability of being treated with antihypertensive medications ranged between 16% and 36% in different age-sex groups in the 1952-1975 period (data not shown), increasing 2- to 3-fold in both sexes in the 1976-1998 period (P<.001 for all comparisons). These findings were supported by the results of Cox models (Table 4). The risk for stage 1 high blood pressure or higher was 92% for women (for both baseline ages) but var-

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Table 2. Probability of Receiving Antihypertensive Treatment According to Baseline Age*

<table>
<thead>
<tr>
<th>Probability of Treatment for Hypertension, % (95% Confidence Interval)</th>
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<tr>
<td><strong>Women, Age, y</strong></td>
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<td>Time, y</td>
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*For 55-year-old subjects, the probability of treatment over 25 years represents their lifetime risk. For 65-year-old subjects, the probability of treatment over 20 years indicates their lifetime risk. Ellipses indicate not applicable.

Table 3. Residual Lifetime Risk of High Blood Pressure According to Baseline Age

<table>
<thead>
<tr>
<th>Risk for High Blood Pressure, % (95% Confidence Interval)</th>
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<tbody>
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<td><strong>Women, Age, y</strong></td>
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<td>Time, y</td>
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<table>
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<tr>
<th>Stage 2 High Blood Pressure or Higher (≥160/100 mm Hg)</th>
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<tr>
<td>Time, y</td>
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<tr>
<th>Stage 2 High Blood Pressure or Higher (≥160/100 mm Hg) or Antihypertensive Medications Use</th>
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<td>Time, y</td>
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*For 55-year-old subjects, the risk for developing high blood pressure over 25 years represents their lifetime risk. For 66-year-old subjects, the risk for developing high blood pressure over 20 years indicates their lifetime risk. Ellipses indicates not applicable. High blood pressure stages are defined as systolic or diastolic measurements exceeding the specified threshold.
ied from 63% (age 65 years) to 82% (age 55 years) for men in the 1952-1975 period. The risk for stage 1 high blood pressure or higher did not change across the 2 periods for women but increased by about 25% in men (Table 4). The risk for stage 2 high blood pressure or higher was 57% for women (for both baseline ages) and varied from 35% (age 65 years) to 48% (age 55 years) for men in the 1952-1975 period. The risk for stage 2 high blood pressure or higher declined in the 1976-1998 period both in women and in men (Table 4).

There were 786 participants (344 men, 442 women) who contributed information to both periods although at different ages. Analyses were repeated after excluding these participants. Estimates of residual lifetime risk for hypertension in the 1976-1998 period were higher after these exclusions, in part because people who contributed to the 1952-1975 period and remained eligible in the 1976-1998 period (having reached this period free of hypertension) were likely participants with a lower risk for developing hypertension. A comparison of participants contributing to the 1952-1975 period only (n=954; 513 women, 441 men) with those providing information in the 1976-1998 period only (n=512; 267 women, 245 men) confirmed the increased risk for hypertension in men and the increased use of antihypertensive medications in both men and women in the 1976-1998 period. However, the increased risk for stage 1 high blood pressure or higher among men in the 1976-1998 period noted in earlier analyses did not achieve statistical significance, in part due to a decrease in sample size and statistical power.

The temporal trends we observed may be due, in part, to concomitant trends in obesity. In women, age-adjusted BMI decreased from 25.8 kg/m² in the 1952-1975 period to 25.3 kg/m² in the 1976-1998 period (P = .05). In contrast, age-adjusted BMI in men...
creased in men from 25.8 kg/m² in the 1952-1975 period to 26.3 kg/m² in the 1976-1998 period (P = .02).

**COMMENT**

**Principal Findings**

Our investigation provides estimates of the residual lifetime and the short-term risks for developing hypertension and examines trends in these risks over time. Whereas the short-term risk estimates are of more immediate value to individuals and, therefore, more likely to motivate behavioral changes, residual lifetime risk estimates permit a comparison of the likelihood of developing 1 or more disease conditions over a lifetime.

The residual lifetime risk for developing hypertension in our sample was about 90%. These risk estimates were similar for men and women and for participants aged 55 and 65 years. It is often assumed that the risk for hypertension increases with age because the incidence of hypertension increases with age. Although this is true of short-term age-conditional risk estimates, this may not be true for lifetime risk. The lack of increase in lifetime risk with increasing age is consistent with similar observations made for other chronic diseases such as dementia and may be because the rising age-specific incidence of hypertension is offset by a decreasing residual life expectancy. Using a higher threshold to define high blood pressure (stage 2 high blood pressure or higher or use of medications) yielded lifetime risk estimates of about 70% in both women and men.

A comparison of lifetime risk estimates over the 2 periods showed that the risk for developing hypertension was unchanged for women but increased for men. The increase in lifetime risk for hypertension in men may be related in part to the trend for an increase in BMI over this period among men (but not women) in our sample. Other investigators have also reported favorable secular trends in blood pressure of women but less encouraging trends in men. In contrast, in the 1976-1998 period, the lifetime probability of experiencing stage 2 high blood pressure or higher was considerably lower in both sexes, in tandem with and probably as a result of a 2- to 3-fold increased use of antihypertensive medications. These data are consistent with prior reports of a decrease in the prevalence of long-term sustained hypertension in our cohort and are likely the result of an increasing emphasis on pharmacological treatment of elevated blood pressure and the progressive lowering of blood pressure treatment thresholds in national guidelines for hypertension treatment (along with changing definitions of hypertension). However, the residual lifetime risk for experiencing stage 1 high blood pressure or higher is markedly high at about 85% in the 1976-1998 period.

**Trends in Risk for Hypertension: Comparison With Prior Reports**

Our findings differ significantly from observations made in serial national cross-sectional surveys between 1960 and 1991, which suggest that the age-adjusted prevalence of hypertension in the United States declined from 36% in 1971 to 20% in 1988 through 1991, along with a downward shift in the average blood pressure of the population. A principal reason our results differ from data from national surveys is that we evaluated trends in the incidence of hypertension while the NHANES report assessed trends in the cross-sectional prevalence of hypertension. It is important to note that our study and the NHANES report evaluated slightly different periods; our investigation began earlier and extended into 1998. It has been reported that some of the “gains” noted in the initial phase of the NHANES III (1988-1991) had leveled off by the time of the second phase of the survey (1991-1994). Increases in the mean blood pressure of cohorts in Iowa and Minnesota in the late 1980s and 1990s, respectively, also have been reported. An additional explanation to be considered is that our sample was white and restricted in its age distribution while that of NHANES was ethnically more diverse and encompassed a wider age spectrum.

**Strengths and Limitations**

Our study is based on the longitudinal surveillance of the same community-based cohort over a period of 30 years. Over this time, blood pressure measurements were obtained every 2 years using a standardized protocol, and information regarding the use of antihypertensive medications was gathered consistently and routinely. Additionally, we examined trends in the lifetime risk for several blood pressure outcomes that yielded complementary information.

Nevertheless, we acknowledge certain limitations of our investigation. Our data indicate the residual lifetime risk of hypertension for 55- and 65-year-old participants who were free of hypertension at these baseline ages. It is important to note that a considerable proportion of individuals with hypertension have onset of the condition before this age. Therefore, the actual lifetime risk for hypertension for younger individuals may be different. Moreover, these lifetime risk data are average estimates for our study participants. The risk for hypertension for a given individual will vary depending on the presence or absence of risk factors for hypertension (such as obesity, family history of high blood pressure, dietary sodium and potassium intake, and alcohol consumption). We did not examine the impact of these covariates. Categorizing people as hypertensive based on a reading obtained on a single occasion may overestimate risk for hypertension. For this reason, we assessed risk for several blood pressure outcomes. The 90% lifetime risk estimate likely represents the upper estimate of true risk because it is based on a single occasion measurement and not on the average of multiple visits (required by the JNC VI). The lower bound of the residual lifetime risk for hypertension is 70%, a figure obtained using a composite definition of stage 2 high blood pressure or higher or the use of antihypertensive medications. We
may have underestimated the lifetime probability of experiencing stage 2 high blood pressure or higher because some participants experiencing this level of blood pressure on seeing a private physician between biennial Heart Study examinations may have had their blood pressure lowered with medications by the time of the next examination. Last, our lifetime risk estimates and trends may not be generalizable to other ethnic groups. Similar studies in other multiethnic cohorts are warranted to obtain information regarding risk for hypertension in different racial groups.

**Public Health Implications**

The finding that 9 out of 10 middle-aged and older adults are likely to develop elevated blood pressure over their remaining lifetime reemphasizes that hypertension poses a major public health burden. Furthermore, the lack of change in the lifetime risk over the 2 periods in women and the modest increase in risk in men is of concern. With the aging of the US population, the societal burden of hypertension will increase further if the lifetime risk for the condition remains unattenuated.

The marked decline in the lifetime risk for stage 2 high blood pressure or higher in men and women in our study sample represents a major public health achievement. In contrast, the risk for stage 1 high blood pressure or higher remained unaltered and represents the next frontier. Although hypertension is easily diagnosed and treated, prior data from Framingham and elsewhere suggest that stage 1 hypertension is inadequately controlled. This is of public health importance because a substantial proportion of cardiovascular diseases are attributable to stage 1 hypertension.

It is widely accepted that hypertension is preventable through lifestyle modification. Our estimates of the short-term risk for hypertension indicate that more than half of the residual lifetime risk for hypertension for 55- and 65-year-old participants is experienced over the initial 10 years of follow-up. The immediacy and the magnitude of this risk should encourage middle-aged nonhypertensive individuals to adopt lifestyle-related measures for maintaining optimal blood pressure and for preventing the development of hypertension. The approach of waiting for hypertension to develop and only then treating the elevated blood pressure is injudicious. As articulated by Stamler, such a strategy is “late, defensive, reactive, time consuming, associated with side effects, costly, only partially successful, and endless.”

**Author Contributions:** Study concept and design: Vasan, Beiser, Seshadri, Kannel, D’Agostino, Levy. Analysis and interpretation of data: Vasan, Beiser, Seshadri, Larson, Kannel, D’Agostino, Levy. Drafting of the manuscript: Vasan, Beiser, Seshadri, Levy.

Critical revision of the manuscript for important intellectual content: Vasan, Beiser, Seshadri, Larson, Kannel, D’Agostino, Levy.

Statistical expertise: Beiser, Larson, D’Agostino.

Study supervision: Vasan, Seshadri, Kannel, Levy.

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