Diet and Lifestyle Risk Factors Associated With Incident Hypertension in Women

John P. Forman, MD, MSc
Meir J. Stampfer, MD, DrPH
Gary C. Curhan, MD, ScD

Hypertension contributes to more excess deaths in women than any other preventable factor.1 Pharmacological treatment of established hypertension has proven benefits, yet these efforts are costly, require medical intervention, and have adverse effects. Furthermore, just 37% of individuals with hypertension in the United States have controlled blood pressure, a proportion that increases to 57% with pharmacological intervention.2 Primary prevention of hypertension, therefore, would have major positive public health ramifications.

Many modifiable risk factors for hypertension have been identified, including being overweight or obese,3,4 not participating in physical activity,5,7 and having a poor diet.8,9 In recent years, excessive alcohol intake and alcohol abstinence,10-12 use of nonnarcotic analgesics,13-15 and low folic acid intake16 have been identified as independent novel and modifiable risk factors for developing hypertension among women.

Although the effects of interventions to modify 1 or several of these factors have been documented,17-19 the proportion of new-onset hypertension cases that could conceivably be prevented by modification of a combination of lifestyle factors has not been evaluated. In this study, we examined the association between combinations of low-risk lifestyle factors and the risk of developing hypertension during 14 years of follow-up among women in the second Nurses’ Health Study.

See also pp 394 and 437.
METHODS

Source Population
The Nurses’ Health Study II is an ongoing prospective cohort study of 116,671 female registered nurses that began in 1989. Participants are followed up via biennial questionnaires that gather information on health-related behaviors (including diet) and medical events. Follow-up of participants was greater than 90% through 2005. The institutional review board at Brigham and Women’s Hospital reviewed and approved this study, including that participants provided implied consent by virtue of returning their questionnaires.

Study Population
Because diet was first assessed in the second Nurses’ Health Study in 1991, it was defined as the baseline year. Of the 116,630 women at the study start in 1989, this analysis was limited to 83,882 women aged 27 to 44 years for the following nonmutually exclusive reasons at baseline in 1991: (1) did not return the 1991 questionnaire or did not provide dietary information (n=16,415); (2) existing diagnosis of hypertension reported on 1989 or 1991 questionnaires (n=8,070); (3) use of antihypertensive medications (n=2962); (4) median reported systolic blood pressure was greater than 120 mm Hg or diastolic blood pressure was greater than 80 mm Hg (n=10,776); existing diagnosis of diabetes mellitus (n=489), myocardial infarction (n=42), angina (n=238), or stroke (n=100), elevated cholesterol level (n=8,697), or cancer diagnosis (n=6,242), except for non–melanoma skin cancer. Women whose median reported systolic blood pressure was higher than 120 mm Hg or diastolic blood pressure was higher than 80 mm Hg were excluded because prehypertension is one of the strongest risk factors for incident hypertension and many of the modifiable risk factors under study may be related to prehypertension. Excluding these women meant that the population under study had a normal blood pressure at baseline. The remaining 83,882 women were included in the analysis.

Ascertainment of Diet
To assess dietary intake, a semiquantitative food frequency questionnaire (FFQ) was used that asked about the usual intake of more than 130 foods and beverages during the previous year. Participants completed the baseline FFQ in 1991 and subsequent FFQs were completed every 4 years thereafter. Intake of individual dietary factors was computed from the reported frequency of consumption of each specified unit of food and from US Department of Agriculture data on the content of the relevant nutrient in specified portions. The intake of supplements (including folic acid) in multivitamins or in isolated form was determined by the brand, type, and frequency of reported use.

The reproducibility and validity of this FFQ has been documented in similar cohorts of health professionals, including nurses.21,22 Correlations between the intakes of individual food items as measured by the FFQ and intakes as assessed by dietary records were high. For example, correlations were 0.88 for skim milk, 0.86 for yogurt, 0.95 for bananas, 0.76 for oranges, 0.59 for green peppers, 0.71 for tomatoes, 0.77 for bacon, 0.63 for hamburger, and 0.84 for sugar-sweetened cola.23 The correlations were 0.77 for folic acid intake21 and 0.90 for alcohol intake.24

Based on the diet prescribed in the Dietary Approaches to Stop Hypertension (DASH) trial,17 a DASH score was constructed based on high intake of fruits, vegetables, nuts and legumes, low-fat dairy products, and whole grains, and low intake of sodium, sweetened beverages, and red and processed meats.25 The first 4 components were directly targeted in the DASH diet, which also included lower consumption of red and processed meats and greater consumption of whole grains.25

Each participant’s DASH score was calculated at baseline in 1991 using the FFQ, and then the DASH score was updated every 4 years (in 1995, 1999, and 2003) during the period of follow-up as participants completed subsequent FFQs. For each of the components, participants were classified into quintiles according to their intake. The component score for fruits, vegetables, nuts and legumes, low-fat dairy products, and whole grains was the participant’s quintile ranking (ie, quintile 1 was assigned 1 point and quintile 5 was assigned 5 points). For sodium, red and processed meats, and sugar-sweetened beverages, low intake was desired (the lowest quintile was assigned a score of 5 points and the highest quintile was assigned a score of 1 point). The component scores were then summed to obtain an overall DASH score ranging from 8 to 40.

Ascertainment of Nondietary Factors
In 1991 and every 2 years thereafter, body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) was ascertained; self-reported weight was highly reliable (r=0.97) among a subset of regionally residing participants who underwent direct measurement of their weight.26 Women also reported the amount of time they spent doing vigorous physical activity (either as days per week or minutes per week, depending on the questionnaire cycle), including jogging, running, swimming, racquet sports, bicycling, or other aerobic activity; questionnaire-derived information about these activities has been validated in comparison with physical activity diaries (r=0.79).27 Walking was not included because walking speed was not specified and reported walking did not correlate with vigorous exercise.

Use of nonnarcotic analgesics, including nonsteroidal anti-inflammatory drugs, acetaminophen, and aspirin, was reported on biennial questionnaires in 2 basic formats. Until 1995, women were asked whether they regularly used any of these medications, with regular use defined as 2 or more days per week. From 1995 onward, women were asked to report the frequency with which they took these medications in greater detail, allowing for categorization into none, 1 day per week, 2 to 3 days per
week, 4 to 5 days per week, or 6 to 7 days per week.\textsuperscript{13}

In addition to these factors, age, smoking status, and use of oral contraceptive pills were updated with each questionnaire cycle. Family history of hypertension was ascertained from the 1989 questionnaire. Race was included in the analysis because it is a risk factor for hypertension; participants self-classified their race in 1989 using the classification options southern European/Mediterranean, Scandinavian, other white, black, Hispanic, Asian, and other. Participants were permitted to select more than 1 race and indicator variables were used for white, black, Asian, and Hispanic (0 or 1). For example, if an individual was white and Hispanic, then that person received a 1 for white, 1 for Hispanic, 0 for black, and 0 for Asian.

**Definition of Low-Risk Groups**

A BMI of less than 25, which is the current cut point defined by the World Health Organization separating normal weight from overweight and obesity, was selected as the low-risk category for weight. Higher BMI is a strong risk factor for developing hypertension, and weight loss may reduce blood pressure.\textsuperscript{3,4,18,19}

Low-risk physical activity was defined as a mean of 30 minutes per day spent in vigorous exercise, in keeping with published guidelines.\textsuperscript{28,29} Physical activity lowers blood pressure and decreases hypertension risk.\textsuperscript{7,38}

The DASH diet has been shown in randomized controlled trials to lower blood pressure;\textsuperscript{17} and long-term observational data have shown that a DASH-style diet is associated with smaller 5-year increases in blood pressure.\textsuperscript{9} In keeping with these studies, women whose DASH scores were in the top quintile (20%) were classified as having a low-risk diet.

Previous observational studies have demonstrated a J-shaped relationship between alcohol use and risk of hypertension; specifically, modest alcohol use is associated with a lower risk of hypertension.\textsuperscript{10-12} Low-risk alcohol intake was defined as greater than zero but not exceeding 10 g/d (approximately 1 alcoholic beverage per day).

Because previous studies have documented increases in the risk of incident hypertension with even a low frequency of nonnarcotic analgesic use,\textsuperscript{13-15} the low-risk category was defined as use that was less frequent than once per week. In terms of supplemental folic acid use, previous data indicated that, among women with very low dietary intake of folate, higher intake of folic acid (principally from supplements) was inversely related to risk of incident hypertension, with a significant reduction in risk observed primarily in women whose intake exceeded 400 µg/d.\textsuperscript{16} Although in the prior analysis total folic acid intake (from both diet and supplements) also was inversely associated with hypertension, only supplemental folic acid was considered for the present analysis because the DASH score served as the assessment of diet. Therefore, women who took 400 µg/d or more of supplemental folic acid were defined as being in the low-risk group.

At 2-year intervals during the course of follow-up, information regarding BMI, diet, exercise, and other covariates were updated to reflect participants’ responses to the most recent questionnaire.

**Ascertainment of Hypertension**

The baseline and follow-up biennial questionnaires asked participants to report whether a clinician had made a new diagnosis of hypertension during the preceding 2 years. Self-reported hypertension was previously validated in this cohort.\textsuperscript{30} Among a randomly selected subset (n=147) of women who reported a new diagnosis of hypertension, 94% had the diagnosis confirmed by medical record review. Cases included individuals who first reported hypertension on questionnaires after 1991; new cases of hypertension were recorded as month and year of diagnosis.

**Statistical Analyses**

The person-time for each participant was calculated from the date of the return of the 1991 questionnaire to the date at which hypertension was first diagnosed, death, or June 2005, whichever came first.

The association between each of the 6 modifiable risk factors and the risk of developing incident hypertension was analyzed. Cox proportional hazards regression was used to compute the hazard ratio (HR) and 95% confidence intervals (CIs) for categories of each factor. This analysis adjusted simultaneously for all 6 of these modifiable risk factors, as well as for the a priori potential confounders of age (continuous), smoking status (current, past, never), oral contraceptive use (current user, nonuser), race, and family history of hypertension. As with the 6 low-risk factors, age, smoking status, and oral contraceptive use were updated as time-dependent variables with each questionnaire cycle to reflect the most recent information.

Next, each of these factors was dichotomized into low-risk vs non–low-risk categories, according to the description in the section above; specifically, BMI (<25 vs ≥25); vigorous physical activity (daily vs nondaily); DASH score (highest quintile vs lower 4 quintiles); alcohol intake (0.1 to 10 g/d vs other levels of intake); nonnarcotic analgesic use (<once/week vs ≥once/week); and supplemental folic acid use (≥400 µg/d vs <400 µg/d). The association between combinations of low-risk factors with incident hypertension was then analyzed using Cox proportional hazards regression.

Because weight control, healthy eating, and exercise are the 3 lifestyle modifications with the strongest evidence base for blood pressure control (and are the 3 strongest lifestyle recommendations by the National Heart, Lung, and Blood Institute’s Joint National Committee [JNC] on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure),\textsuperscript{31} women with a combination of these 3 low-risk factors were compared with all...
other women adjusting for alcohol intake, nonnarcotic analgesic use, supplemental folic acid use, age, smoking, oral contraceptive use, race, and family history of hypertension. Women with a combination of the 4 low-risk factors of BMI, physical activity, diet, and alcohol intake were then analyzed because limiting alcohol intake also is supported by interventional studies and is recommended by the National Heart, Lung, and Blood Institute’s JNC on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Finally, women with the 5 low-risk factors of BMI, physical activity, diet, alcohol intake, and nonnarcotic analgesic use, and all 6 low-risk factors of BMI, physical activity, diet, alcohol intake, nonnarcotic analgesic use, and supplemental folic acid use were compared with all other women. Nonnarcotic analgesic use and folic acid use were compared on prior research, but were added to hypothetically prevent the development of normal BMI (≤25), daily vigorous exercise, 10% (95% CI, 8%-12%) for no or excessive alcohol consumption, and 4% (95% CI, 1%-7%) for supplemental folic acid use lower than 400 μg/d.

Results

At baseline in 1991, the mean (SD) age of the population was 36 (4.6) years and the mean (SD) BMI was 23.7 (4.3). During 14 years of follow-up, 12,319 women reported a new diagnosis of hypertension (approximately 15% of the population).

The multivariable-adjusted associations between the 6 individual modifiable risk factors and incident hypertension are shown in Table 1. The strongest risk factor was a higher BMI, with obese women having a HR for incident hypertension of 4.70 (95% CI, 4.45-4.96) compared with women whose BMI was less than 23.0. In this population, 40% (95% CI, 38%-41%) of new hypertension cases could hypothetically be attributed to overweight or obesity (defined as a BMI ≥25), and 50% (95% CI, 49%-52%) of new cases could hypothetically be attributed to a BMI of 23.0 or greater. The other 5 modifiable risk factors also were associated with incident hypertension after multivariable adjustment (Table 1). Individual hypothetical PARs for the other modifiable risk factors were much lower than overweight and obesity; ie, 17% (95% CI, 15%-19%) for routine nonnarcotic analgesic use, 14% (95% CI, 10%-17%) for not following a DASH style diet, 14% (95% CI, 9%-19%) for not engaging in daily vigorous exercise, 10% (95% CI, 8%-12%) for no or excessive alcohol consumption, and 4% (95% CI, 1%-7%) for supplemental folic acid use lower than 400 μg/d.

Specific groups of 3, 4, 5, and 6 low-risk factors were associated with progressively lower HRs of developing hypertension in multivariable models (Table 2). Women with a combination of normal BMI (<25), daily vigorous physical activity, and a DASH-style diet (in the highest quintile of DASH score) had a HR for incident hypertension of 0.46 (95% CI, 0.39-0.54). The hypothetical PAR was 53% (95% CI, 45%-60%), suggesting that 33% of new-onset hypertension in this population potentially might have been prevented if all women had these 3 low-risk factors. The corresponding hypothesized ARD was 6.02 cases per 1000 person-years and the hypothesized NNT over 10 years was 16.6 women. The hypothetical PAR increased to 58% (95% CI, 46%-67%; ARD, 6.28 cases per 1000 person-years; NNT over 10 years of 15.9 women) if the low-risk group also included modest alcohol intake (4 low-risk factors total) and to 72% (95% CI, 57%-82%; ARD, 7.76 cases per 1000 person-years).
years; NNT over 10 years of 12.9 women) if women also avoided routine nonnarcotic analgesic use (5 low-risk factors). Only 0.3% of the population had all 6 low-risk factors (including use of ≥400 µg/d of folic acid supplementation), but the analysis of hypothetical PAR suggested that if all women were at low risk for all 6 factors, then 78% (95% CI, 49%-90%; ARD, 8.37 cases per 1000 person-years; NNT over 10 years of 11.9 women) of new-onset hypertension cases might have been avoided.

The association between a parental family history of hypertension and the development of hypertension in the child may represent the effect of both genetic and nongenetic factors.\(^{34}\) To address whether a low-risk lifestyle would be similarly associated with lower hypertension risk among those with and without a familial predisposition to developing hypertension, the analyses were repeated after stratifying by family history of hypertension (TABLE 3). The hypothetical PAR associated with the 3 low-risk factors was 77% (95% CI, 50%-90%; ARD, 8.37 cases per 1000 person-years; NNT over 10 years of 12.9 women) among women with a family history of hypertension and 51% (95% CI, 40%-60%; ARD, 7.66 cases per 1000 person-years; NNT over 10 years of 13.1 women) among women without a family history of hypertension. Among women without a family history of hypertension, the hypothetical PAR was 90% (95% CI, 32%-99%; ARD, 6.82 cases per 1000 person-years; NNT over 10 years of 14.7 women) for the 6 low-risk factors; a similar analysis among women with a family history of hypertension yielded a hypothetical PAR of 69% (95% CI, 25%-87%; ARD, 8.37 cases per 1000 person-years; NNT over 10 years of 10.1 women). Tests for interaction were null regardless of how many low-risk factors were considered.

Oral contraceptive use at some point during follow-up was common (85.7% of women) and was independently associated with an increased risk of incident hypertension; oral contraceptive use may potentially have contributed to 15% (95% CI, 11%-20%) of all new cases of incident hypertension. Whether the association of various low-risk factors differed among those women who did vs did not use oral contraceptive pills was addressed (TABLE 4), with oral contraceptive use...
updated with each questionnaire cycle as a time-dependent variable. Among non–oral contraceptive users, the hypothetical PARs ranged from 59% (95% CI, 48%-69%) for 3 low-risk factors to 83% (95% CI, 30%-96%) for 6 low-risk factors. Among oral contraceptive users, the hypothetical PARs ranged from 48% (95% CI, 35%-57%) for 3

Table 2. Multivariable Relative and Hypothesized Population Attributable Risks (PARs) of Incident Hypertension Among 83 882 Young Women With Different Low-Risk Factors

<table>
<thead>
<tr>
<th>No. of low-risk factors</th>
<th>No. (%) of Participants</th>
<th>No. of Hypertension Cases</th>
<th>Multivariable HR (95% CI)</th>
<th>ARD, Cases per 1000 Person-Years&lt;sup&gt;a&lt;/sup&gt;</th>
<th>NNT for 10 y&lt;sup&gt;b&lt;/sup&gt;</th>
<th>PAR, % (95% CI)&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>3: highest DASH quintile, daily vigorous exercise, and BMI &lt; 25&lt;sup&gt;d&lt;/sup&gt;</td>
<td>2600 (3.1)</td>
<td>145</td>
<td>0.46 (0.39-0.54)</td>
<td>6.02</td>
<td>16.6</td>
<td>53 (45-60)</td>
</tr>
<tr>
<td>4: the 3 factors above plus alcohol intake 0.1-10.0 g/d&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1342 (1.6)</td>
<td>64</td>
<td>0.42 (0.33-0.54)</td>
<td>6.28</td>
<td>15.9</td>
<td>58 (46-67)</td>
</tr>
<tr>
<td>5: the 4 factors above plus nonnarcotic analgesic use &lt; 1 d/wk&lt;sup&gt;f&lt;/sup&gt;</td>
<td>671 (0.8)</td>
<td>21</td>
<td>0.28 (0.18-0.43)</td>
<td>7.76</td>
<td>12.9</td>
<td>72 (57-82)</td>
</tr>
<tr>
<td>6: the 5 factors above plus folic acid supplementation ≥ 400 µg/d&lt;sup&gt;g&lt;/sup&gt;</td>
<td>252 (0.3)</td>
<td>6</td>
<td>0.22 (0.10-0.51)</td>
<td>8.37</td>
<td>11.9</td>
<td>78 (49-90)</td>
</tr>
</tbody>
</table>

Abbreviations: ARD, absolute rate difference; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DASH, Dietary Approaches to Stop Hypertension; HR, hazard ratio; NNT, number needed to treat.
<sup>a</sup>Indicates the adjusted difference in hypertension incidence rate among the higher risk group minus the incidence rate among the lower risk group. <sup>b</sup>Indicates the number of higher risk women that would have to adopt the low-risk factors for a period of 10 years to prevent the occurrence of 1 hypertension case. <sup>c</sup>Indicates the percentage of new hypertension cases in the population that would hypothetically not have occurred if all women had been in the low-risk group. <sup>d</sup>Adjusted for age, race, family history of hypertension, use of oral contraceptive pills, smoking status, alcohol use, nonnarcotic analgesic use, and supplemental folic acid intake. The PAR for a BMI of less than 25 by itself was 40% (95% CI, 38%-41%).

Table 3. Multivariable Relative and Hypothesized Population Attributable Risks (PARs) of Incident Hypertension Among 83 882 Young Women With Multiple Low-Risk Factors and Stratified by Family History of Hypertension

<table>
<thead>
<tr>
<th>No. (%) of Participants&lt;sup&gt;a&lt;/sup&gt;</th>
<th>No. of Hypertension Cases</th>
<th>Multivariable HR (95% CI)</th>
<th>ARD, Cases per 1000 Person-Years&lt;sup&gt;b&lt;/sup&gt;</th>
<th>NNT for 10 y&lt;sup&gt;c&lt;/sup&gt;</th>
<th>PAR, % (95% CI)&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Family History of Hypertension</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>3: highest DASH quintile, daily vigorous exercise, and BMI &lt; 25&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1386 (3.2)</td>
<td>54</td>
<td>0.42 (0.32-0.56)</td>
<td>4.60</td>
<td>21.7</td>
</tr>
<tr>
<td>4: the 3 factors above plus alcohol intake 0.1-10.0 g/d&lt;sup&gt;f&lt;/sup&gt;</td>
<td>736 (1.7)</td>
<td>21</td>
<td>0.34 (0.23-0.53)</td>
<td>5.04</td>
<td>19.8</td>
</tr>
<tr>
<td>5: the 4 factors above plus nonnarcotic analgesic use &lt; 1 d/wk&lt;sup&gt;g&lt;/sup&gt;</td>
<td>390 (0.9)</td>
<td>7</td>
<td>0.23 (0.11-0.48)</td>
<td>5.86</td>
<td>17.1</td>
</tr>
<tr>
<td>6: the 5 factors above plus folic acid supplementation ≥ 400 µg/d&lt;sup&gt;h&lt;/sup&gt;</td>
<td>123 (0.3)</td>
<td>1</td>
<td>0.10 (0.01-0.68)</td>
<td>6.82</td>
<td>14.7</td>
</tr>
</tbody>
</table>

| Family History of Hypertension | | | | |
| 3: highest DASH quintile, daily vigorous exercise, and BMI < 25<sup>e</sup> | 1217 (3.0) | 91 | 0.48 (0.39-0.59) | 7.66 | 13.1 | 51 (40-60) |
| 4: the 3 factors above plus alcohol intake 0.1-10.0 g/d<sup>f</sup> | 649 (1.6) | 43 | 0.46 (0.34-0.63) | 7.75 | 12.9 | 53 (37-66) |
| 5: the 4 factors above plus nonnarcotic analgesic use < 1 d/wk<sup>g</sup> | 325 (0.8) | 14 | 0.31 (0.19-0.53) | 9.86 | 10.1 | 69 (47-81) |
| 6: the 5 factors above plus folic acid supplementation ≥ 400 µg/d<sup>h</sup> | 122 (0.3) | 5 | 0.31 (0.13-0.75) | 9.87 | 10.1 | 69 (25-87) |

Abbreviations: ARD, absolute rate difference; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DASH, Dietary Approaches to Stop Hypertension; HR, hazard ratio; NNT, number needed to treat.
<sup>a</sup>The percentage represents those within the given strata (i.e., among those with or without a family history of hypertension).
<sup>b</sup>Indicates the adjusted difference in hypertension incidence rate among the higher risk group minus the incidence rate among the lower risk group.
<sup>c</sup>Indicates the number of higher risk women that would have to adopt the low-risk factors for a period of 10 years to prevent the occurrence of 1 hypertension case.
<sup>d</sup>Indicates the percentage of new hypertension cases in the population that would hypothetically not have occurred if all women had been in the low-risk group.
<sup>e</sup>Adjusted for age, race, use of oral contraceptive pills, smoking status, alcohol use, nonnarcotic analgesic use, and supplemental folic acid intake. Adjusted for everything in footnote “e” except nonnarcotic analgesic and alcohol use.
<sup>f</sup>Adjusted for everything in footnote “d” except nonnarcotic analgesic and alcohol use.
<sup>g</sup>Adjusted for everything in footnote “d” except nonnarcotic analgesic and alcohol use and supplemental folic acid intake.
low-risk factors to 73% (95% CI, 28%-90%) for 6 low-risk factors. Again, no evidence for effect modification was found.

Because BMI was by far the strongest risk factor for incident hypertension, associations between low-risk factors and hypertension were stratified by BMI category (Table 5). Overall, low-risk factors were found to be inversely associated with hypertension among normal weight and overweight women, but not among obese women (P = .02 for interaction). Specifically, among normal weight women (BMI < 25), having 4 low-risk factors (DASH-type diet, daily exercise, modest alcohol intake, and avoidance of nonnarcotic analgesics) was associated with a HR for incident hypertension of 0.46 (95% CI, 0.30-0.71); the corresponding hypothetical PAR was 54% (95% CI, 29%-70%; ARD, 3.19 cases per 1000 person-years; NNT over 10 years of 31.3 years; NNT over 10 years of 31.3 women). The same 4 low-risk factors among overweight women (BMI, 25.0-29.9) yielded a hypothetical PAR of 47% (95% CI, 4%-71%; ARD, 6.83 cases per 1000 person-years; NNT over 10 years of 14.6 women); however, among obese women, the hypothetical PAR was a nonsignificant 5% (95% CI, 0%-51%) for 4 risk factors. When the 5 low-risk factors (DASH-type diet, daily exercise, modest alcohol intake, avoidance of nonnarcotic analgesics, and use of ≥ 400 µg/d of supplemental folic acid) were tested among normal, overweight, and obese women, the hypothetical PAR if women lacked these 5 low-risk factors was 62% (95% CI, 14%-83%; ARD, 3.65 cases per 1000 person-years; NNT over 10 years of 27.4 women) among normal weight women and was not statistically significant among overweight and obese women, although the sample sizes were very small (Table 5).

Baseline mean blood pressure, end-of-follow-up blood pressure, and antihypertensive medication use among all women (including those who did and did not develop hypertension during follow-up) are shown in Table 6. In 2005, women with 3 low-risk factors had a mean systolic blood pressure that was 4 mm Hg lower and a mean diastolic blood pressure that was 3 mm Hg lower compared with women without these 3 low-risk factors (P < .001). In women with all 6 low-risk factors in 2005, the mean systolic blood pressure was 6 mm Hg lower and the mean diastolic blood pressure was 4 mm Hg lower compared with women without these 6 low-risk factors (P < .001). Additionally, antihypertensive medication use was less frequent among those with low-risk factors. Of the women with 3 low-risk factors, antihypertensive medication use at the end of follow-up in 2005 was 5.8% compared to 13.5% among women who lacked these 3 risk factors (P < .001). The percentage represents those within the given strata who developed hypertension.

### Table 4. Multivariable Relative and Hypothesized Population Attributable Risks (PARs) of Incident Hypertension Among 83 882 Young Women With Multiple Low-Risk Factors and Stratified by Oral Contraceptive Use

<table>
<thead>
<tr>
<th>No. of low-risk factors</th>
<th>No. (%) of Participants&lt;sup&gt;a&lt;/sup&gt;</th>
<th>No. of Hypertension Cases</th>
<th>Multivariable HR (95% CI)</th>
<th>ARD, Cases per 1000 Person-Years&lt;sup&gt;b&lt;/sup&gt;</th>
<th>NNT for 10 yr&lt;sup&gt;c&lt;/sup&gt;</th>
<th>PAR, % (95% CI)&lt;sup&gt;d&lt;/sup&gt;</th>
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</thead>
<tbody>
<tr>
<td>No Oral Contraceptive Use</td>
<td></td>
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</tr>
<tr>
<td>3: highest DASH quintile, daily vigorous exercise, BMI &lt; 25&lt;sup&gt;e&lt;/sup&gt;</td>
<td>588 (4.3)</td>
<td>58</td>
<td>0.40 (0.30-0.51)</td>
<td>6.84</td>
<td>14.6</td>
<td>59 (48-69)</td>
</tr>
<tr>
<td>4: the 3 factors above plus alcohol intake 0.1-10.0 g/d&lt;sup&gt;f&lt;/sup&gt;</td>
<td>273 (2.0)</td>
<td>20</td>
<td>0.33 (0.21-0.51)</td>
<td>7.40</td>
<td>13.5</td>
<td>67 (48-79)</td>
</tr>
<tr>
<td>5: the 4 factors above plus nonnarcotic analgesic use &lt; 1 d/wk&lt;sup&gt;g&lt;/sup&gt;</td>
<td>150 (1.1)</td>
<td>6</td>
<td>0.20 (0.09-0.44)</td>
<td>8.78</td>
<td>11.4</td>
<td>80 (66-91)</td>
</tr>
<tr>
<td>6: the 5 factors above plus folic acid supplementation ≥ 400 µg/d&lt;sup&gt;h&lt;/sup&gt;</td>
<td>55 (0.4)</td>
<td>2</td>
<td>0.17 (0.04-0.70)</td>
<td>9.06</td>
<td>11.0</td>
<td>83 (30-96)</td>
</tr>
<tr>
<td>Oral Contraceptive Use</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>3: highest DASH quintile, daily vigorous exercise, BMI &lt; 25&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1755 (2.5)</td>
<td>87</td>
<td>0.51 (0.42-0.64)</td>
<td>5.4</td>
<td>18.5</td>
<td>48 (35-57)</td>
</tr>
<tr>
<td>4: the 3 factors above plus alcohol intake 0.1-10.0 g/d&lt;sup&gt;f&lt;/sup&gt;</td>
<td>983 (1.4)</td>
<td>44</td>
<td>0.48 (0.36-0.65)</td>
<td>5.57</td>
<td>18.0</td>
<td>52 (25-64)</td>
</tr>
<tr>
<td>5: the 4 factors above plus nonnarcotic analgesic use &lt; 1 d/wk&lt;sup&gt;g&lt;/sup&gt;</td>
<td>562 (0.8)</td>
<td>15</td>
<td>0.34 (0.20-0.56)</td>
<td>7.06</td>
<td>14.2</td>
<td>66 (44-80)</td>
</tr>
<tr>
<td>6: the 5 factors above plus folic acid supplementation ≥ 400 µg/d&lt;sup&gt;h&lt;/sup&gt;</td>
<td>140 (0.2)</td>
<td>4</td>
<td>0.27 (0.10-0.72)</td>
<td>7.77</td>
<td>12.9</td>
<td>73 (28-90)</td>
</tr>
</tbody>
</table>

*Abbreviations: ARD, absolute rate difference; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DASH, Dietary Approaches to Stop Hypertension; HR, hazard ratio; NNT, number needed to treat.*

<sup>a</sup>The percentage represents those within the given strata (i.e., among those who do and do not use oral contraceptives).

<sup>b</sup>Indicates the adjusted difference in hypertension incidence rate among the higher risk group minus the incidence rate among the lower risk group.

<sup>c</sup>Indicates the number of higher risk women that would have to adopt the low-risk factors for a period of 10 years to prevent the occurrence of 1 hypertension case.

<sup>d</sup>Indicates the percentage of new hypertension cases in the population that would hypothetically not have occurred if all women had been in the low-risk group.

<sup>e</sup>Adjusted for age, race, use of oral contraceptive pills, smoking status, alcohol use, nonnarcotic analgesic use, and supplemental folic acid intake.

<sup>f</sup>Adjusted for everything in footnote “e” except nonnarcotic analgesic use.

<sup>g</sup>Adjusted for everything in footnote “e” except nonnarcotic analgesic and alcohol use.

<sup>h</sup>Adjusted for everything in footnote “e” except nonnarcotic analgesic and alcohol use and supplemental folic acid intake.
with 11.9% among those who did not have these low-risk factors ($P < .001$). For 6 low-risk factors, this comparison was 3.9% vs 11.8% ($P < .001$).

**COMMENT**

In this large-scale prospective study of women, low-risk combinations of modifiable lifestyle factors such as maintenance of a normal BMI, eating a diet high in fruits, vegetables, low-fat dairy products and low in sodium, engaging in vigorous physical exer-

<table>
<thead>
<tr>
<th>Table 5. Multivariable Relative and Hypothesized Population Attributable Risks (PARs) of Incident Hypertension Among 83 882 Young Women With Multiple Low-Risk Factors and Stratified by Body Mass Index (BMI)$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of low-risk factors</td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td><strong>No. (% of Participants$^b$)</strong></td>
</tr>
<tr>
<td><strong>Normal Weight (BMI &lt; 25.0)</strong></td>
</tr>
<tr>
<td>4: highest DASH quintile, daily vigorous exercise, alcohol intake 0.1-10.0 g/d, nonnarcotic analgesic use &lt; 1 d/wk$^f$</td>
</tr>
<tr>
<td>5: the 4 factors above plus folie acid supplementation $\geq 400 \mu g/d$$g$</td>
</tr>
<tr>
<td><strong>Overweight (BMI, 25.0-29.9)</strong></td>
</tr>
<tr>
<td>4: highest DASH quintile, daily vigorous exercise, alcohol intake 0.1-10.0 g/d, nonnarcotic analgesic use &lt; 1 d/wk$^f$</td>
</tr>
<tr>
<td>5: the 4 factors above plus folie acid supplementation $\geq 400 \mu g/d$$g$</td>
</tr>
<tr>
<td><strong>Obese (BMI $\geq 30.0$)</strong></td>
</tr>
<tr>
<td>4: highest DASH quintile, daily vigorous exercise, alcohol intake 0.1-10.0 g/d, nonnarcotic analgesic use &lt; 1 d/wk$^f$</td>
</tr>
<tr>
<td>5: the 4 factors above plus folie acid supplementation $\geq 400 \mu g/d$$g$</td>
</tr>
</tbody>
</table>

Abbreviations: ARD, absolute rate difference; DASH, Dietary Approaches to Stop Hypertension; HR, hazard ratio; NA, data not computed due to nonsignificant results; NNT, number needed to treat.

$^a$Body mass index was calculated as weight in kilograms divided by height in meters squared.

$^b$The percentage represents those within the given strata of BMI.

$^c$Indicates the adjusted difference in hypertension incidence rate among the higher risk group minus the incidence rate among the lower risk group.

$^d$Indicates the number of higher risk women that would have to adopt the low-risk factors for a period of 10 years to prevent the occurrence of 1 hypertension case.

$^e$Indicates the percentage of new hypertension cases in the population that would hypothetically not have occurred if all women had been in the low-risk group.

$^f$Adjusted for age, race, family history of hypertension, use of oral contraceptive pills, smoking status, and supplemental folie acid intake.

$^g$Adjusted for everything in footnote "f" except supplemental folie acid intake.

<table>
<thead>
<tr>
<th>Table 6. Blood Pressure and Antihypertensive Medication Use at Baseline and at the End of Follow-up in All Study Participants, Including Those Who Developed Hypertension$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure, mean (SD), mm Hg</td>
</tr>
<tr>
<td>------------------------------------------</td>
</tr>
<tr>
<td>At Baseline</td>
</tr>
<tr>
<td>Present</td>
</tr>
<tr>
<td>Systolic</td>
</tr>
<tr>
<td>No. of low-risk factors</td>
</tr>
<tr>
<td>4: the 3 factors above plus alcohol intake 0.1-10.0 g/d</td>
</tr>
<tr>
<td>5: the 4 factors above plus nonnarcotic analgesic use $&lt; 1 d/wk$</td>
</tr>
<tr>
<td>6: the 5 factors above plus folie acid supplementation $\geq 400 \mu g/d$$g$</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DASH, Dietary Approaches to Stop Hypertension.

$^a$Present indicates the women who had the low-risk factors and absent indicates the women who did not. $P < .001$ for all comparisons. No women were taking antihypertensive medication at baseline. These data include women who did and did not develop hypertension during follow-up; approximately 15% of women developed hypertension during 14 years of follow-up.
exercise on a daily basis, drinking a modest amount of alcohol, avoiding non-narcotic analgesics, and taking supplemental folic acid were associated with dramatic reductions in the incidence of hypertension during follow-up. Although speculative, if these associations were causal and independent, then lifestyle modification could have the potential to prevent a large proportion of new-onset hypertension occurring among young women.

Each of these 6 modifiable lifestyle variables has been shown in various observational studies to be independently associated with risk for incident hypertension. Higher BMI or higher body weight has been well recognized for decades as a risk factor for developing hypertension among women.\(^4,33\) For example, the risk associated with a BMI of 31.0 or greater was 6-fold higher compared with a BMI of less than 20 in a large cohort of US women.\(^4\) Higher physical activity level also has been shown in multiple studies to be associated with a lower risk of incident hypertension.\(^3,7\) For example, the CARDIA (Coronary Artery Risk Development in Young Adults) study demonstrated a 15% reduction in risk Development in Young Adults) study demonstrated a decreased risk of incident hypertension with higher intake of folic acid. The risk for women whose total daily intake was 1000 µg/d or greater compared with those whose intake was less than 200 µg/d was 46% lower among younger women (second Nurses' Health Study) and 18% lower among older women (first Nurses' Health Study).\(^10\) When these analyses were restricted to women whose folic acid intake from food was negligible, higher daily intake from supplements also was associated with significantly lower risk of hypertension.\(^10\)

Interventional trials have confirmed the findings of these observational studies. Reductions in blood pressure resulted from weight loss,\(^18,19\) physical activity,\(^18\) DASH-type diets,\(^7,18,36\) alcohol reduction,\(^37\) and folic acid supplementation,\(^36,39\) while increases in blood pressure were noted with administration of acetaminophen, nonsteroidal anti-inflammatory drugs, and aspirin.\(^40-42\) The PREMIER study randomized individuals to receive an intervention combining weight loss, physical activity, and a DASH diet or to receive advice only.\(^18\) At 6 months, the change in systolic blood pressure was 4.5 mm Hg lower in the intervention group compared with the advice only group, and at 18 months, the odds of developing incident hypertension were 23% lower.\(^18\) These findings provide support for our assumptions that these associations might potentially be causal, and therefore estimates of the PAR may be appropriate.

In our study, BMI was the most powerful predictor of incident hypertension and the largest single contributor to the hypothetical PAR. We therefore tested whether individuals who were overweight, but otherwise followed a healthy lifestyle, had a lower likelihood of developing hypertension. Although we found that multiple low-risk factors were significantly associated with lower risk among normal weight and overweight women, there was no association among obese women; these findings imply that, in the context of hypertension risk, obese women might not benefit from other low-risk behaviors unless weight loss also is addressed. Because obesity is common (approximately one-third of the US population), this finding has important consequences, particularly because, in the absence of calorie restriction and additional physical activity, adherence to the other 5 low-risk factors may not reduce weight.

In contrast to the BMI-stratified models, our data indicate that adherence to a combination of low-risk lifestyle factors could have the potential to prevent the majority of new-onset hypertension in young women irrespective of family history of hypertension and irrespective of oral contraceptive use. The former conclusion is particularly poignant given that some women may mistakenly believe that their parental history signifies that their own development of hypertension may be unavoidable; rather, these women may conceivably at least delay onset of hypertension by reducing their risk factors.

**Limitations**

Our study has some limitations. First, we dichotomized lifestyle factors into low risk vs not low risk for the purposes of calculating PAR; the associations between these factors and hypertension risk are continuous, not dichotomous. However, increasing the number of categories for each of the 6 risk factors would have exponentially increased the number of possible low-risk factors and thereby make calculation and presentation of the data overly complex and underpowered. Second, we did not include oral contraceptive use in our analyses as a seventh modifiable factor even though it does contribute to risk. We did so because a woman's decision to use oral contraceptives is multidimensional, with both risks as well as proven benefits. Third, we did not have information in the whole cohort on other potentially important modifiable risk factors, such as plasma 25-hydroxyvitamin D levels, which recently have been demonstrated to be inversely related to hy-
HYPERTENSION RISK IN WOMEN BASED ON LIFESTYLE, DIET

pertension risk as well as waist circumference.

Fourth, follow-up for hypertension incidence was 14 years; it is possible that low-risk factors delay rather than entirely prevent hypertension at the rates calculated by the PAR. Fifth, it is possible that because of measurement error inherent in the questionnaires, some women may have had their BMI, level of physical activity, and nonnarcotic analgesic use misclassified; however, the questionnaires have been demonstrated previously to reliably ascertain this information. Misclassification of diet is particularly relevant because, although most foods and nutrients are reliably measured, dietary sodium intake is not measured well with the FFQ. Nevertheless, this type of misclassification would likely be random, and therefore our calculations of risk may in fact be underestimated of true risk; indeed, others have estimated that a population-based prevalence of misclassification would likely be random. Sixth, because hypertension was self-reported, some women may have had their hypertension status misclassified. Nonetheless, hypertension reporting in these nurses has been shown to be reliable. Similarly, we did not have information about whether hypertension was primary or secondary.

Seventh, the findings in this population may not necessarily be generalizable to the population as a whole; not only was our population mostly white, and entirely female, but all of the participants were nurses and thus presumably similar in socioeconomic status and health consciousness. On the other hand, the risk factors that we studied (BMI, diet, physical activity, alcohol intake, nonnarcotic analgesic use, and folate intake) have all been associated with hypertension status in other cohort studies, including those with more broadly based populations. Eighth, the proportion of women with all 6 low-risk factors (0.3%) was very low, and it is unrealistic to believe that all of these low-risk factors could be achieved in the other 99.7%. However, because of the staggering morbidity and mortality associated with hypertension, achieving risk factor modification in a fraction of these women could potentially have substantial positive health benefits. Finally, our study was not randomized; however, the impact of these modifiable factors on blood pressure has been documented in randomized trials, and a large-scale long-term randomized trial of 6 interventions may not be feasible.

Conclusion

In conclusion, adherence to low-risk dietary and lifestyle factors was associated with significant reductions in the incidence of self-reported hypertension and could have the potential to prevent a large proportion of new-onset hypertension occurring among young women. Prevention of hypertension would, in turn, have major public health benefits.

Author Contributions: Dr Forman had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Forman, Stamper, Curhan.

Acquisition of data: Forman, Stamper, Curhan.

Analysis and interpretation of data: Forman, Stamper, Curhan.

Drafting of the manuscript: Forman.

Critical revision of the manuscript for important intellectual content: Forman, Stamper, Curhan.

Statistical analysis: Forman.

Obtained funding: Forman, Stamper, Curhan.

Administrative, technical, or material support: Forman, Stamper, Curhan.

Study supervision: Curhan.

Financial Disclosures: None reported.

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Role of the Sponsor: The American Heart Association and the National Institutes of Health had no role in the collection, management, analysis, or interpretation of the data and had no role in the preparation, review, or approval of the manuscript.

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