Healthy Lifestyle and the Risk of Stroke in Women

Tobias Kurth, MD, ScD; Steven C. Moore, MPH; J. Michael Gaziano, MD, MPH; Carlos S. Kase, MD; Meir J. Stampfer, MD, DrPH; Klaus Berger, MD, MPH, MSc; Julie E. Buring, ScD

Background: Healthy lifestyle has been associated with decreased risk of coronary heart disease. In contrast, little is known about its association with stroke risk.

Methods: This is a prospective cohort study among 37 636 women 45 years or older participating in the Women's Health Study. Stroke was self-reported and confirmed by means of medical record review. We considered the following self-reported lifestyle factors: smoking, alcohol consumption, exercise, body mass index, and diet. The health index was calculated from these variables by assigning scores from 0 to 4 to the respective variable categories, with a higher score indicating healthier behavior. Healthy behavior was defined as never smoking, alcohol consumption between 4 and 10.5 drinks per week, exercise 4 or more times per week, body mass index (calculated as weight in kilograms divided by the square of height in meters) less than 22, and a diet high in cereal fiber, folate, and omega-3 fatty acids, with a high ratio of polyunsaturated to saturated fat, and low in *trans* fat and glycemic load.

Results: During 10 years of follow-up, 450 strokes (356 ischemic, 90 hemorrhagic, and 4 undefined) were confirmed. Compared with participants with 0 to 4 health index points (4.3%), women with 17 to 20 health index points (4.7%) had multivariable-adjusted hazard ratios (95% confidence interval) of 0.45 (0.24-0.83; $P<.001$ for trend) for total stroke, 0.29 (0.14-0.63; $P<.001$ for trend) for ischemic stroke, and 1.27 (0.37-4.29; $P=.62$ for trend) for hemorrhagic stroke.

Conclusions: In this large prospective cohort of apparently healthy women, a healthy lifestyle consisting of abstinence from smoking, low body mass index, moderate alcohol consumption, regular exercise, and healthy diet was associated with a significantly reduced risk of total and ischemic stroke but not of hemorrhagic stroke. Our findings underscore the importance of healthy behaviors in the prevention of stroke.

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STROKE REMAINS A LEADING cause of morbidity and mortality worldwide. In the United States alone, approximately 700 000 strokes occur each year, of which approximately 23% are fatal; an equal number of people are left permanently disabled and in need of assistance with activities of daily living.[1] Effective therapies for the treatment of acute ischemic stroke are used uncommonly[2] and often do not completely reverse the impaired brain functions. Thus, identification of modifiable lifestyle factors remains critical for stroke prevention, particularly for women who, in the United States, have relatively more strokes than myocardial infarctions when compared with men.[1]

The association between many individual behavioral risk factors (including smoking,[3,4] alcohol consumption,[5] exercise,[6,7] body mass index [BMI],[8,9] and some dietary factors)[10,11] and stroke incidence has been studied. In contrast to findings for coronary heart disease[12] and diabetes mellitus,[13] however, the combined effects of health-related behaviors on the risk of stroke and stroke subtypes have not been studied. We thus aimed to evaluate whether a composite of healthy lifestyle factors reduces the risk of stroke and stroke subtypes in more than 37 000 apparently healthy women.

Author Affiliations are listed at the end of this article.

METHODS

PARTICIPANTS

Study subjects were all participants in the Women's Health Study (WHS), a completed randomized trial of low-dose aspirin and vitamin E in the primary prevention of cardiovascular disease and cancer. The methods and results of the WHS have been described in detail previously.[14-16] Briefly, 39 876 female health professionals in the United States who were 45 years or older at the beginning of 1993 and who did not have a history of cardiovascular disease, cancer, or other major illnesses were ran-

domly assigned to receive aspirin (100 mg on alternate days), vitamin E (600 IU on alternate days), both active agents, or both placebos. Baseline information on many lifestyle variables was collected by means of a mailed questionnaire. Twice in the first year and yearly thereafter, participants were sent follow-up questionnaires asking about study outcomes and other information during the study period. For this analysis, we included follow-up information from the time of randomization through March 31, 2004. As of this date, follow-up was 97.2% complete for morbidity and 99.4% for mortality.

HEALTH INDEX

To create a health index with components that have been previously proposed,[12,13] we considered self-reported lifestyle information from the baseline questionnaires, incorporating information about smoking, exercise, BMI, alcohol consumption, and dietary factors.

Smoking is a strong risk factor for ischemic[3] and hemorrhagic[4] stroke in women, and the risk increases with the number of cigarettes smoked. We categorized participants as never smokers, past smokers who smoked less than 20 pack-years, past smokers who smoked 20 or more pack-years, current smokers who smoke fewer than 15 cigarettes per day, and current smokers who smoke 15 or more cigarettes per day.

Physical activity has been associated inconsistently with risk of stroke. Findings from a recent meta-analysis[7] of observational studies showed that moderately intense physical activity compared with inactivity was protective for total stroke as well as for ischemic and hemorrhagic stroke. We categorized exercise on the basis of self-reported frequency of weekly strenuous exercise as rarely or never, less than once per week, once per week, 2 to 3 times per week, or 4 or more times per week.

Body mass index, calculated as weight in kilograms divided by the square of height in meters, has been associated consistently with a steady increase in risk of total and ischemic stroke.[8,9,17] Although the association between BMI and hemorrhagic stroke is less clear,[8,9,17] we decided to use the lowest category as the healthiest group, which is similar to previous approaches.[8,12,13,17] We categorized BMI as lower than 22.0, 22.0 to 24.9, 25.0 to 29.9, 30.0 to 34.9, and 35.0 or more.

The association between alcohol consumption and risk of stroke has been described as J-shaped, with the most benefit for light to moderate consumption of alcohol.[5,18] Study participants reported alcohol consumption as drinks per week or day. We categorized alcohol intake as never, less than 1, 1 to 3, 4 to less than 10.5, and 10.5 or more drinks per week. We assigned the health index points for alcohol consumption favoring moderate drinking habits and assigned a low health index score for women who rarely or never drank alcohol. Reassigning the low health index score to the highest alcohol consumption category did not substantially change the association between the health index and risk of stroke.

Women reported dietary intake on a 161-item standardized food frequency questionnaire.[19] Nutrient intake was calculated by multiplying the reported frequency by the nutritional content of the indicated portion sizes. We calculated glycemic load in a manner similar to previous approaches.[20] We adjusted each nutrient for total energy intake by using the residual method.[21] To incorporate diet into the health index, we considered 6 dietary factors as proposed by others[12,13] and the association of each with vascular disease[22-25]: cereal fiber, folate (including from supplement intake), the ratio of polyunsaturated to saturated fat, omega-3 fatty acids, *trans* fats, and glycemic load. Consumption of these dietary components was grouped into deciles and scored from 0 to 9 (inverse for *trans* fat and glycemic load), with 0 being least healthy consumption. The individual scores were then summed to a total diet score, which we categorized into quintiles.

The overall health index was calculated by assigning scores of 0 to 4 to each individual variable category, for which a higher point value indicates a healthier behavior. The health index ranged from 0 to 20. Healthiest behavior was defined as never smoking, consumption of between 4 and less than 10.5 alcoholic drinks per week, exercise 4 or more times weekly, a BMI lower than 22, and a healthy diet (ie, high in cereal fiber, folate, and omega-3 fatty acids, with a high ratio of polyunsaturated to saturated fat, and low in *trans* fat and glycemic load). The assigned point scheme per individual health behavior is summarized in **Table 1**. We a priori divided the health index into categories of 0 to 4, 5 to 8, 9 to 12, 13 to 16, and 17 to 20 points, reflecting the 4-point scheme that was used to create the index. We also evaluated the association between the health index as a continuous term and stroke risk.

ASCERTAINMENT OF STROKE

Participants who reported a stroke on a follow-up questionnaire were asked for permission to review their medical records. A diagnosis of stroke was confirmed only after review of the medical records by an end-points committee of physicians. A nonfatal stroke was defined as a focal-neurological deficit of sudden onset and vascular mechanism that lasted more than 24 hours. Cases of fatal stroke were documented if they had evidence of cerebrovascular mechanism using information obtained from all available sources, including death certificates and hospital records. Clinical information and results from brain imaging were used to distinguish among ischemic, hemorrhagic, and unknown subtype. The interobserver agreement of the classification of stroke and its major subtypes in the WHS was excellent.[26]

STATISTICAL ANALYSES

Of the 39 876 participants, we excluded 2237 women with information missing on lifestyle factors and 3 women who reported a stroke before the baseline questionnaire, leaving 37 636 for this analysis. We used Cox proportional hazards models to evaluate the association between the health index and the risk of total, ischemic, and hemorrhagic stroke. We calculated age- and multivariable-adjusted hazard ratios (HRs) and their corresponding 95% confidence intervals (CIs), using the category conventionally believed to be least healthy as the reference group. We distinguished 2 multivariable models. Model 1 controlled for age (quadratic term), postmenopausal hormone use (never, past, or current), past and present use of oral contraceptives, family history of myocardial infarction before age 60 years, annual household income (<$50 000, $50 000 to <$100 000, or ≥$100 000), highest level of education (less than a bachelor's degree, bachelor's degree, or master's degree or doctorate), location of residence (Northeast, Southeast, Midwest, or West), marital status (single, married, or other), ethnicity (white, black, or other), and randomized treatment assignments. Model 2 additionally controlled for the potential consequences of an unhealthy lifestyle—history of hypertension (defined as systolic blood pressure of at least 140 mm Hg, diastolic blood pressure of at least 90 mm Hg, or self-reported physician-diagnosed hypertension), antihypertensive treatment, history of diabetes mellitus, and history of cholesterol of 240 mg/dL (6.21 mmol/L) or higher.

We evaluated whether the association between the health index and stroke was modified by age (<55, 55-64, or ≥65 years) and history of hypertension (defined as before). We tested age-

Table 1. Distribution of Modifiable Lifestyle Factors According to Health Index Categories* and Relative Hazard of Total Stroke in the Women's Health Study

Individual Component	Points†	Health Index 0-4 (n = 1615 [4.3%])	5-8 (n = 9891 [26.3%])	9-12 (n = 15 109 [40.1%])	13-16 (n = 9265 [24.6%])	17-20 (n = 1756 [4.7%])	Total (N = 37 636)	Hazard Ratio‡ (95% CI)
Smoking, %								
Current ≥15 cigarettes/d	0	54.3	13.9	4.6	1.0	0.0	8.1	1.00
Current <15 cigarettes/d	1	12.0	7.5	4.3	2.2	0.2	4.7	0.65 (0.43-0.98)
Past ≥20 pack-years	2	13.4	13.1	11.5	9.2	3.9	11.1	0.36 (0.25-0.50)
Past <20 pack-years	3	11.8	20.9	25.1	30.4	31.6	25.1	0.35 (0.25-0.46)
Never	4	8.5	44.7	54.5	57.2	64.2	51.0	0.29 (0.22-0.38)
Body mass index, %§								
≥35.0	0	31.5	12.1	3.2	0.4	0.0	5.9	1.00
30.0-34.9	1	25.4	22.0	10.9	3.6	0.3	12.2	0.67 (0.44-1.00)
25.0-29.9	2	24.2	36.5	34.5	24.6	6.7	30.9	0.57 (0.39-0.82)
22.0-24.9	3	13.8	20.7	32.7	38.5	35.7	30.3	0.53 (0.37-0.77)
<22.0	4	5.2	8.8	18.7	33.0	57.4	20.8	0.48 (0.32-0.71)
Exercise, %								
Rarely or never	0	85.8	65.5	35.9	11.4	0.0	38.1	1.00
<1 time/wk	1	12.1	23.9	23.7	14.3	1.7	19.9	1.13 (0.88-1.45)
1 time/wk	2	1.6	5.9	12.1	12.5	5.2	9.8	1.02 (0.72-1.43)
2-3 times/wk	3	0.5	4.2	21.4	39.7	43.1	21.5	0.89 (0.68-1.17)
≥4 times/wk	4	0.0	0.5	6.9	22.1	50.1	10.7	0.98 (0.70-1.37)
Alcohol consumption, %								
Never	0	86.2	70.7	44.8	17.6	0.0	44.6	1.00
<1 drink/wk	1	12.0	16.9	17.7	12.5	1.8	15.2	0.77 (0.57-1.04)
1-3 drinks/wk	3	0.9	5.6	16.4	24.9	21.6	15.2	0.95 (0.72-1.26)
4 to <10.5 drinks/wk	4	0.2	3.4	15.8	39.1	72.7	20.3	0.82 (0.63-1.06)
≥10.5 drinks/wk	2	0.7	3.5	5.3	5.9	3.9	4.7	0.84 (0.55-1.29)
Diet score quintile, %‖								
1st	0	65.3	37.1	15.8	4.5	0.0	20.0	1.00
2nd	1	25.8	33.6	26.3	14.2	1.8	24.1	1.20 (0.88-1.63)
3rd	2	6.8	15.2	20.5	18.0	9.0	17.4	1.13 (0.81-1.58)
4th	3	1.9	9.6	20.5	27.5	27.8	18.9	1.50 (1.10-2.04)
5th	4	0.3	4.6	16.9	35.8	61.4	19.7	1.63 (1.20-2.22)

Abbreviation: CI, confidence interval.
*Percentages may not add up to 100 because of rounding.
†Assigned point value to create the health index.
‡Adjusted for age and the components of the health index; the category conventionally believed to be least healthy serves as the reference group.
§Calculated as weight in kilograms divided by the square of height in meters.
‖The intakes of cereal fiber, folate (including from supplement intake), omega-3 fatty acids, the ratio of polyunsaturated to saturated fat, *trans* fat, and glycemic load were categorized in deciles. The decile values for each nutrient were summed (inverse for *trans* fat and glycemic load), and the sum was categorized into quintiles; a higher score indicates a healthier diet.

adjusted effect modification by using the likelihood ratio test. We calculated *P* for trend across the mean values of health index categories. All analyses were performed with SAS version 9.1 (SAS Institute Inc, Cary, NC); *P* values are 2-tailed, and we considered $P<.05$ statistically significant.

RESULTS

After a mean of 10 years of follow-up (374 658 person-years), 450 strokes (356 ischemic, 90 hemorrhagic, and 4 unknown) were confirmed among the 37 636 participating women. Table 1 summarizes the association between health index categories and the individual components of the index. In addition, we provide the association between individual components and risk of total stroke. As expected, women with 17 or more health index points (4.7% of the study population) were less likely to be current smokers, exercised more regularly, drank alcohol in moderation, had a lean BMI, and had a high diet score. We found strong associations between smoking, as well as BMI, and risk of stroke, whereas there was no apparent association between alcohol consumption and exercise with stroke risk. The diet score was inversely associated with stroke risk.

In **Table 2**, we summarize the association between various baseline characteristics and health index categories. As expected, the proportion of participants who reported history of hypertension, antihypertensive medication use, diabetes mellitus, or history of elevated cholesterol was higher in the lower health index categories. Current use of postmenopausal hormones was higher in the high health index categories, whereas the proportion of women with a family history of premature myocardial infarction was lower. Black women were more likely to be in the low health index category. Women in the low health index category reported lower annual household income, had lower levels of education, were

Table 2. Age-Adjusted Baseline Characteristics According to Health Index Categories*

Characteristic	Health Index (N = 37 636)					Total (N = 37 636)
	0-4 (n = 1615 [4.3%])	5-8 (n = 9891 [26.3%])	9-12 (n = 15 109 [40.1%])	13-16 (n = 9265 [24.6%])	17-20 (n = 1756 [4.7%])	
Age, mean (SE), y	53.5 (0.18)	54.4 (0.07)	54.9 (0.06)	54.6 (0.07)	54.5 (0.17)	54.6 (0.04)
Systolic blood pressure, mean (SE), mm Hg	129.9 (0.33)	126.8 (0.13)	123.8 (0.11)	121.2 (0.14)	119.2 (0.31)	124.0 (0.07)
History of hypertension, %†	38.1	32.6	25.0	19.3	14.6	25.7
Antihypertensive medication use, %	18.7	17.9	13.2	10.4	6.9	13.7
History of diabetes mellitus, %	5.7	4.0	2.2	1.2	0.8	2.5
History of elevated cholesterol (≥240 mg/dL [≥6.21 mmol/L]), %	34.7	31.7	30.1	25.7	23.0	29.3
Postmenopausal hormone use, %						
Never	55.2	52.9	49.6	47.1	44.3	49.8
Past	14.2	10.7	8.6	7.5	6.0	9.0
Current	30.4	36.2	41.6	45.3	49.6	41.0
Ever used oral contraceptives, %	68.0	67.4	68.7	72.0	75.0	69.4
Family history of MI before age 60 years, %	15.2	13.6	12.7	12.1	12.2	12.9
Ethnicity, %						
White	94.5	93.5	94.0	95.5	96.9	94.4
Black	3.3	2.7	2.3	1.4	0.9	2.1
Other	2.2	3.8	3.8	3.1	2.2	3.5
Annual household income, %						
<$50 000	66.7	56.5	46.1	36.1	28.6	46.4
$50 000-$100 000	30.1	36.9	42.5	44.5	41.7	41.0
≥$100 000	3.2	6.6	11.4	19.4	29.7	12.6
Highest level of education, %						
Less than bachelor's degree	79.0	67.2	56.5	46.1	38.7	56.9
Bachelor's degree	13.6	19.4	23.9	26.8	28.6	23.2
Master's degree or doctorate	7.4	13.4	19.6	27.2	32.7	19.9
Marital status, %						
Single	7.0	6.4	6.0	4.9	4.5	5.8
Married	61.7	70.6	74.6	76.8	77.8	73.7
Other	31.3	23.0	19.4	18.4	17.7	20.5
Geographic location, %‡						
Northeast	20.3	19.3	19.1	20.2	17.9	19.4
Southeast	24.3	23.8	23.7	21.5	20.9	23.1
Midwest	41.2	40.1	36.1	31.6	27.2	35.8
West	14.2	16.8	21.1	26.7	34.0	21.6

Abbreviations: MI, myocardial infarction.
*Percentages may not add up to 100 because of rounding or missing values.
†Defined as systolic blood pressure of at least 140 mm Hg, diastolic blood pressure of at least 90 mm Hg, or self-reported physician-diagnosed hypertension.
‡Northeast: Maine, New Hampshire, Vermont, Massachusetts, Connecticut, Rhode Island, New York, New Jersey, Pennsylvania.
Southeast: Delaware, Maryland, Washington, DC, Virginia, West Virginia, Kentucky, Tennessee, North Carolina, South Carolina, Georgia, Florida, Alabama, Mississippi.
Midwest: Ohio, Michigan, Indiana, Illinois, Wisconsin, Minnesota, North Dakota, South Dakota, Nebraska, Kansas, Iowa, Missouri, Oklahoma, Arkansas, Louisiana, Texas.
West: Montana, Idaho, Wyoming, Colorado, New Mexico, Arizona, Utah, Nevada, Washington, Oregon, California, Alaska, Hawaii.

less likely to be married, and were more likely to live in the Southeast or Midwest.

The overall health index showed strong associations between total and ischemic stroke but not hemorrhagic stroke (**Table 3**). Compared with women with 0 to 4 health index points, women with 17 to 20 points had multivariable-adjusted (model 1) HRs of 0.45 (95% CI, 0.24-0.83) for total, 0.29 (95% CI, 0.14-0.63) for ischemic, and 1.27 (95% CI, 0.37-4.29) for hemorrhagic stroke. There was a significant trend across the mean values of health index categories for total and ischemic stroke ($P<.001$ for both) but not for hemorrhagic stroke ($P=.62$). Additional adjustment for the potential consequences of an unhealthy lifestyle—indicators of hypertension, diabetes mellitus, and elevated cholesterol—attenuated these associations; however, there remained a statistically significant reduction of risk for total and ischemic stroke.

When we evaluated the association between health index as a continuous term and stroke, a 1-unit increase was associated with a 5% reduction (95% CI, –2% to –7%) for total stroke, a 6% reduction (95% CI, –3% to –9%) for ischemic stroke, and 0% (95% CI, –6% to 6%) for hemorrhagic stroke. We found no statistically significant deviation from linearity ($P>.27$ for total, ischemic, and hemorrhagic stroke).

The beneficial effect of healthy lifestyle was apparent in all age groups, although the trend was not statistically significant among women 65 years or older. Overall, however, the association between healthy lifestyle and risk of total stroke was not statistically significantly modified by

Table 3. Relative Hazards of Total, Ischemic, and Hemorrhagic Stroke According to Health Index Categories

Health Index Category and Points	No. of Subjects With Stroke	Age-Adjusted HR (95% CI)	Model 1* HR (95% CI)	Model 2† HR (95% CI)
Total Stroke	**450**	. . .	. . .	. . .
0-4 (n = 1615)	31	1.00	1.00	1.00
5-8 (n = 9891)	131	0.59 (0.40-0.88)	0.63 (0.42-0.93)	0.65 (0.44-0.97)
9-12 (n = 15 109)	190	0.53 (0.36-0.77)	0.58 (0.40-0.86)	0.65 (0.44-0.95)
13-16 (n = 9265)	82	0.38 (0.25-0.58)	0.43 (0.28-0.65)	0.51 (0.33-0.78)
17-20 (n = 1756)	16	0.40 (0.22-0.73)	0.45 (0.24-0.83)	0.56 (0.30-1.05)
P for trend		<.001	<.001	.01
Ischemic Stroke	**356**	. . .	. . .	. . .
0-4 (n = 1615)	26	1.00	1.00	1.00
5-8 (n = 9891)	106	0.57 (0.37-0.87)	0.59 (0.39-0.91)	0.62 (0.40-0.96)
9-12 (n = 15 109)	156	0.51 (0.34-0.77)	0.55 (0.36-0.84)	0.63 (0.41-0.96)
13-16 (n = 9265)	59	0.32 (0.20-0.51)	0.35 (0.22-0.57)	0.43 (0.27-0.70)
17-20 (n = 1756)	9	0.27 (0.12-0.57)	0.29 (0.14-0.63)	0.38 (0.18-0.82)
P for trend		<.001	<.001	.001
Hemorrhagic Stroke	**90**	. . .	. . .	. . .
0-4 (n = 1615)	5	1.00	1.00	1.00
5-8 (n = 9891)	24	0.71 (0.27-1.85)	0.77 (0.29-2.03)	0.79 (0.30-2.08)
9-12 (n = 15 109)	33	0.61 (0.24-1.56)	0.72 (0.28-1.87)	0.73 (0.28-1.91)
13-16 (n = 9265)	22	0.67 (0.26-1.78)	0.85 (0.32-2.30)	0.92 (0.34-2.49)
17-20 (n = 1756)	6	0.98 (0.30-3.22)	1.27 (0.37-4.29)	1.38 (0.41-4.71)
P for trend		.94	.62	.49

Abbreviations: CI, confidence interval; HR, hazard ratio.

*Model 1 adjusted for age, postmenopausal hormone use, oral contraceptive use, family history of myocardial infarction, income, geographic location of home, level of education, ethnicity, marital status, and randomized treatment assignments.

†Model 2 adjusted for all variables in model 1 plus history of hypertension, antihypertensive treatment, diabetes mellitus, and elevated cholesterol (≥240 mg/dL [≥6.21 mmol/L]).

age (*P*=.67). Healthy lifestyle consistently reduced the risk of total stroke among women with hypertension (*P*=.007 for trend) and among women with no history of hypertension (*P*=.03 for trend); hypertensive state was not a statistically significant effect modifier (*P*=.59 for interaction). Furthermore, there was no effect modification according to randomized aspirin (*P*=.95 for interaction) or vitamin E (*P*=.23 for interaction) assignment.

Because some may consider an increased relative body weight (ie, BMI) to be a consequence rather than a component of an unhealthy lifestyle, we also created another health index incorporating all lifestyle variables except BMI. This score ranged from 0 to 16 points. The association between this health index and stroke showed similar but weaker associations compared with the health index including BMI. Compared with women with 0 to 4 points, women with 13 to 16 points (healthiest category) had multivariable-adjusted HRs of 0.58 (95% CI, 0.37-0.92; *P*=.03 for trend) for total, 0.54 (95% CI, 0.31-0.92; *P*=.04 for trend) for ischemic, and 0.36 (95% CI, 0.27-1.60; *P*=.35 for trend) for hemorrhagic stroke. Additional adjustments for BMI categories reduced the effect estimates and led to nonsignificant trends across health index categories for all outcomes. The association between the health index that excluded BMI and total stroke was not statistically significantly modified by BMI categories.

COMMENT

In this large prospective cohort of women, a composite healthy lifestyle involving abstinence from smoking, low BMI, moderate alcohol consumption, regular exercise, and a healthy diet was associated with a substantial reduction in risk of total and ischemic stroke. These associations were apparent even after controlling for the potential biological mediators hypertension, diabetes mellitus, and elevated cholesterol. The association was not significantly modified by age or history of hypertension. The association between healthy lifestyle and hemorrhagic stroke was less clear, and the results suggested a U-shaped association. However, the number of hemorrhagic stroke cases was small, so the effect estimates were imprecise.

With regard to the individual components of the health index, we found substantial reduction of stroke risk for women who never smoked or were past smokers and for women who had lower BMI. Alcohol consumption and physical activity were only weakly associated with risk of total stroke. Surprisingly, the diet index was inversely related to stroke risk. The increased risk of stroke among those with the healthier diet was apparent for ischemic and hemorrhagic stroke (data not shown). Excluding diet from the health index did not change the association between the remaining health index with total and ischemic stroke (*P*<.001 for trend) and showed no significant beneficial association with hemorrhagic stroke (*P*=.30 for trend).

Our finding for smoking is in agreement with results from previous studies that established smoking as an independent risk factor for ischemic[3,27] and hemorrhagic[4,28,29] stroke. The risk of stroke from smoking is dose related, and there is good evidence that smoking cessa-

tion can reduce the risk of stroke,[3] which is supported by our results.

Overweight and obesity have been associated consistently with increased risk of total and ischemic stroke.[8,9] However, the association between BMI and hemorrhagic stroke is less clear, with a generally positive association in men[17] but inconsistent associations in women,[8,9] which may explain in part the lack of association between our health index and risk of hemorrhagic stroke. When we evaluated a healthy lifestyle excluding BMI, we found similar but weaker associations with stroke risk compared with the health index incorporating BMI.

With regard to physical activity and alcohol consumption, meta-analyses of observational studies indicate a protective effect of moderately intense physical activity on total stroke,[7] a J-shaped association between alcohol consumption and the risks of total and ischemic stroke,[18] and a linear association between alcohol consumption and the risk of hemorrhagic stroke. Heavy alcohol consumption was associated with an increased relative risk of total, ischemic, and hemorrhagic stroke.[18] In our data, moderate alcohol consumption and vigorous physical activity were not strongly associated with stroke risk.

Compared with the association between diet and coronary heart disease, the association between dietary factors and stroke risk is less well studied. In this study, we considered the main components of a previously proposed diet index that mostly related to coronary heart disease.[12,13,22-25] Although results from previous studies did not indicate strong associations with components of the diet index and risk of stroke, such as consumption of polyunsaturated fatty acids,[30] glycemic load among obese women,[31] or even inverse associations with hemorrhagic stroke,[32] our diet results were still unexpected. Future study should address the association between dietary factors and risk of stroke and stroke subtypes. A Western dietary pattern may increase stroke risk, but a diet rich in fruits, vegetables, whole grains, and fish may protect against stroke.[11]

Despite the numerous studies on individual lifestyle factors and risk of stroke, evaluations of combined effects of these factors are sparse. For coronary heart disease, analyses from the Nurses' Health Study showed a substantial reduction in risk of coronary heart disease for women who lived healthy lifestyles.[12] Women who never smoked, had low BMI, exercised regularly, consumed alcohol moderately, and ate a healthy diet had an adjusted relative risk of coronary heart disease of 0.17 (95% CI, 0.07-0.41) compared with the other women in the study. In secondary analyses, the authors also included total stroke in the outcome, yielding a relative risk of 0.25 (95% CI, 0.14-0.44) for the healthy lifestyle group compared with the other women. The number of stroke cases was too small, however, to provide separate estimates for stroke.

Strengths of our study include the large number of outcome events and participants, long follow-up and high participation rate, detailed standardized information on many lifestyle factors, confirmed stroke cases with high interobserver agreement,[26] and the homogeneity of the cohort, which reduces confounding by access to medical care.

Several limitations should be considered when interpreting our findings. First, information on all lifestyle factors was self-reported, so misclassification is possible. However, in a prospective study, misclassification is typically considered nondifferential and therefore is expected to lead to an underestimation of risk. In addition, health professionals are known to report their health status and lifestyle factors with reasonable accuracy.[33] Second, women who participated in the WHS were health professionals and mostly white. Thus, generalizability to other populations may be limited; blacks and Hispanics have a higher incidence of stroke,[34] and lifestyle factors may be part of the reason for this observation. Our data support the contention that blacks and those with lower socioeconomic status have less healthy lifestyles. Third, despite adjustments for potential confounding factors, residual confounding remains plausible because our study design is observational. Fourth, we did not update information on lifestyle factors during follow-up because such updated information was not ascertained for all factors that were included in the health index. Fifth, the relationship between the health index and stroke is influenced by the weight given to each component of the index. Because we did not aim to maximize the likelihood of observing a significant effect, we chose to give equal weight to each health-behavior component. However, because the use of equal weight is an imperfect approximation of the underlying biological relationships between the different health behaviors and stroke, future analyses should examine the issue of weighting.

In conclusion, in this large prospective cohort of apparently healthy women, a healthy lifestyle was associated with a substantial and statistically significant reduction in the risk of total and ischemic stroke with no apparent benefit in the incidence of hemorrhagic stroke. Our findings show the importance of healthy behaviors in the prevention of total and ischemic stroke.

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Author Affiliations: Divisions of Preventive Medicine (Drs Kurth, Gaziano, and Buring) and Aging (Drs Kurth, Gaziano, and Buring), Channing Laboratories (Dr Stampfer), Department of Medicine, Brigham and Women's Hospital, Harvard Medical School; Department of Epidemiology, Harvard School of Public Health (Drs Kurth, Stampfer, and Buring); Department of Ambulatory Care and Prevention, Harvard Medical School (Dr Buring); Massachusetts Veterans Epidemiology Research and Information Center, Boston Veterans Affairs Healthcare System (Dr Gaziano); Department of Neurology, Boston University School of Medicine (Dr Kase), Boston, Mass; Department of Epidemiology, Yale School of Public Health, New Haven, Conn (Mr Moore); and Institute of Epidemiology and Social Medicine, University of Muenster, Muenster, Germany (Dr Berger).
Correspondence: Tobias Kurth, MD, ScD, Division of Preventive Medicine, Brigham and Women's Hospital, 900 Commonwealth Ave E, Boston, MA 02215 (tkurth@rics.bwh.harvard.edu).
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