Coffee Consumption and Risk of Stroke in Women

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Background—Data on the association between coffee consumption and risk of stroke are sparse. We assessed the association between coffee consumption and the risk of stroke among US women. To determine whether caffeine or other components in coffee may protect against type 2 diabetes,4–8 however, data on the relation between coffee consumption and stroke are sparse. Moreover, given that several studies have associated coffee consumption with increased risk of hypertension14 and hypercholesterolemia15,16 but reduced risk of type 2 diabetes,17 we examined whether the association between coffee consumption and stroke was modified by these vascular risk factors.

Methods and Results—We analyzed data from a prospective cohort of 83 076 women in the Nurses’ Health Study without history of stroke, coronary heart disease, diabetes, or cancer at baseline. Coffee consumption was assessed first in 1980 and then repeatedly every 2 to 4 years, with follow-up through 2004. We documented 2280 strokes, of which 426 were hemorrhagic, 1224 were ischemic, and 630 were undetermined. In multivariable Cox regression models with adjustment for age, smoking status, body mass index, physical activity, alcohol intake, menopausal status, hormone replacement therapy, aspirin use, and dietary factors, the relative risks (RRs) of stroke across categories of coffee consumption (<1 cup per month, 1 per month to 4 per week, 5 to 7 per week, 2 to 3 per day, and ≥4 per day) were 1, 0.98 (95% CI, 0.84 to 1.15), 0.88 (95% CI, 0.77 to 1.02), 0.81 (95% CI, 0.70 to 0.95), and 0.80 (95% CI, 0.64 to 0.98) (P for trend = 0.003). After further adjustment for high blood pressure, hypercholesterolemia, and type 2 diabetes, the inverse association remained significant. The association was stronger among never and past smokers (RR for ≥4 cups a day versus <1 cup a month, 0.57; 95% CI, 0.39 to 0.84) than among current smokers (RR for ≥4 cups a day versus <1 cup a month, 0.97; 95% CI, 0.63 to 1.48). Other drinks containing caffeine such as tea and caffeinated soft drinks were not associated with stroke. Decaffeinated coffee was associated with a trend toward lower risk of stroke after adjustment for caffeinated coffee consumption (RR for ≥2 cups a day versus <1 cup a month, 0.89; 95% CI, 0.73 to 1.08; P for trend = 0.05).

Conclusions—Long-term coffee consumption was not associated with an increased risk of stroke in women. In contrast, our data suggest that coffee consumption may modestly reduce risk of stroke. (Circulation. 2009;119:1116-1123.)

Key Words: coffee • nutrition • population • risk factors • stroke • women

Recent analyses support the hypothesis that coffee consumption does not increase the risk of coronary heart disease.1–3 In addition, increasing evidence suggests that coffee consumption may protect against type 2 diabetes.4–8 However, data on the relation between coffee consumption and stroke are sparse. No association has been found between coffee consumption and risk of total stroke among middle-aged healthy men9 and among patients with type 2 diabetes.10 By contrast, another study found that consumption of coffee was associated with an increased risk of ischemic stroke among hypertensive men.11 Finally, in a recent study of male smokers, an association between coffee and risk of stroke was observed.12 To the best of our knowledge, the association between coffee and stroke among women has not been examined previously.13

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In this study, we assessed the association between long-term coffee consumption and risk of stroke over 24 years of follow-up in US women. To determine whether caffeine or other components in coffee were responsible for the observed associations, decaffeinated coffee and other caffeinated beverages also were examined. Moreover, given that several studies have associated coffee consumption with increased risk of hypertension14 and hypercholesterolemia15,16 but reduced risk of type 2 diabetes,17 we examined whether the association between coffee consumption and stroke was modified by these vascular risk factors.

Methods

Study Population

We used data from the Nurses’ Health Study (NHS), the full details of which have been published elsewhere.18 Briefly, this cohort was established in 1976, and information from the participants has been updated every 2 years. We used 1980 as the baseline because this was the first year in which information on diet was collected. For the present analysis, we excluded participants with a history of stroke, coronary heart disease, diabetes, or cancer at baseline and those with no information about coffee consumption at baseline (n = 879), leaving 83 076 women. The Harvard School of Public Health and Brigham and Women’s Hospital Human Subjects Committee Review boards approved the study protocol.
Assessment of Coffee Consumption

Food frequency questionnaires were sent to the NHS participants in 1980, 1984, 1986, 1990, 1994, 1998, and 2002. In each questionnaire, participants were asked how often on average during the previous year they had consumed coffee and tea. Decaffeinated coffee and different types of caffeinated soft drinks were first assessed in 1984. Using the US Department of Agriculture food composition data supplemented with other sources, we estimated that the caffeine content was 137 mg per cup of coffee, 47 mg per cup of tea, 46 mg per can or 12-ounce bottle of soft drink, and 7 mg per 1-ounce serving of chocolate candy. We assessed the total intake of caffeine by summing the caffeine content for a unit of each food during the previous year multiplied by a weight proportional to the frequency of its consumption. In our validation study, we obtained high correlations between consumption of coffee and other caffeinated beverages estimated from the food frequency questionnaire and consumption estimated from repeated 1-week diet records (coffee, \( r = 0.78 \); tea, \( r = 0.93 \); caffeinated soft drinks, \( r = 0.85 \)).

Ascertainment of Stroke

Incident stroke was defined as the first nonfatal stroke or stroke death occurring after the baseline questionnaire in 1980 but before June 1, 2004. Women who reported a stroke were asked for permission to contact medical records. Cases in which medical record release was not obtained were classified as probable stroke of undetermined type. In these analyses, 1909 cases of stroke were examined separately; therefore, confirmed strokes were examined jointly by age in months at start of follow-up and calendar year of the current questionnaire cycle. We used hazard ratios to estimate relative risks (RRs) in each category of coffee consumption compared with participants in the lowest category of coffee consumption. Multivariable models were adjusted for smoking, body mass index, physical activity, alcohol intake, menopausal status and use of postmenopausal hormone therapy, aspirin use, and dietary factors that have been associated with risk of hypertension and stroke.

Assessment of Medical History, Anthropometric Data, and Lifestyle Factors

In the baseline questionnaire, we requested information about age, weight and smoking, menopausal status and use of postmenopausal hormone therapy, aspirin use, and personal history of stroke, coronary heart disease, cancer, type 2 diabetes mellitus, hypertension, and hypercholesterolemia. This information has been updated in the biennial follow-up questionnaires. Height was ascertainment on the 1976 enroll-
In age-adjusted analyses, higher caffeinated coffee consumption was not associated with risk of total stroke (Table 2). However, after adjustment for smoking and other confounders, we found that women who consumed 2 to 3 cups of coffee per day had a 19% lower risk of stroke than women in the lowest category of consumption, whereas women consuming ≥4 cups of coffee per day had a 20% lower risk of stroke (P for trend=0.003). After adjustment for hypertension, hypercholesterolemia, and type 2 diabetes, the results were similar although the RR for consumption of ≥4 cups per day became nonsignificant. Moreover, when we analyzed types of strokes, we observed a suggestion of an inverse association for caffeinated coffee consumption and risk of ischemic stroke (P for trend=0.06) with similar attenuation after controlling for the potential biological mediators.

Table 1. Midpoint Characteristics (in 1990) by Levels of Caffeinated Coffee Consumption Among Participants in the NHS

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y</td>
<td>55</td>
<td>56</td>
<td>56</td>
<td>56</td>
<td>56</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.7</td>
<td>25.6</td>
<td>25.6</td>
<td>25.1</td>
<td>24.7</td>
</tr>
<tr>
<td>Physical activity,* h/wk</td>
<td>2.8</td>
<td>2.8</td>
<td>2.7</td>
<td>2.7</td>
<td>2.6</td>
</tr>
<tr>
<td>Alcohol intake, g/d</td>
<td>2.8</td>
<td>4.0</td>
<td>5.3</td>
<td>6.6</td>
<td>5.8</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>8</td>
<td>9</td>
<td>12</td>
<td>22</td>
<td>39</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>17</td>
<td>19</td>
<td>18</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>Hypercholesterolemia, %</td>
<td>26</td>
<td>30</td>
<td>30</td>
<td>26</td>
<td>21</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Aspirin use,† %</td>
<td>46</td>
<td>53</td>
<td>55</td>
<td>53</td>
<td>44</td>
</tr>
<tr>
<td>Postmenopausal hormone use, %</td>
<td>25</td>
<td>28</td>
<td>28</td>
<td>25</td>
<td>21</td>
</tr>
<tr>
<td>Antihypertensive medication, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuretics</td>
<td>11</td>
<td>14</td>
<td>13</td>
<td>10</td>
<td>6</td>
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<tr>
<td>β-Blockers</td>
<td>8</td>
<td>9</td>
<td>8</td>
<td>6</td>
<td>3</td>
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<tr>
<td>Calcium channel blockers</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Antihypercholesteremic medication, %</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Caffeinated coffee, cups/d</td>
<td>0</td>
<td>0.32</td>
<td>1.48</td>
<td>2.95</td>
<td>4.88</td>
</tr>
<tr>
<td>Decaffeinated coffee, cups/d</td>
<td>0</td>
<td>0.79</td>
<td>0.53</td>
<td>0.05</td>
<td>0</td>
</tr>
<tr>
<td>Tea, cups/d</td>
<td>0.66</td>
<td>0.50</td>
<td>0.38</td>
<td>0.25</td>
<td>0.09</td>
</tr>
<tr>
<td>Cola beverages, cans/d</td>
<td>0.07</td>
<td>0.07</td>
<td>0.10</td>
<td>0.14</td>
<td>0.12</td>
</tr>
<tr>
<td>Caffeine, mg/d</td>
<td>102</td>
<td>134</td>
<td>274</td>
<td>469</td>
<td>747</td>
</tr>
<tr>
<td>Calcium, mg/d</td>
<td>895</td>
<td>922</td>
<td>901</td>
<td>874</td>
<td>837</td>
</tr>
<tr>
<td>Potassium, mg/d</td>
<td>2651</td>
<td>2754</td>
<td>2850</td>
<td>2969</td>
<td>3161</td>
</tr>
<tr>
<td>Sodium, mg/d</td>
<td>1816</td>
<td>1856</td>
<td>1878</td>
<td>1864</td>
<td>1793</td>
</tr>
<tr>
<td>Folate, μg/d</td>
<td>404</td>
<td>420</td>
<td>397</td>
<td>372</td>
<td>345</td>
</tr>
<tr>
<td>Glycemic load</td>
<td>102</td>
<td>99</td>
<td>96</td>
<td>92</td>
<td>89</td>
</tr>
<tr>
<td>Cereal fiber, g/d</td>
<td>3.9</td>
<td>4.1</td>
<td>3.9</td>
<td>3.6</td>
<td>3.3</td>
</tr>
<tr>
<td>Whole grains, g/d</td>
<td>17.1</td>
<td>17.4</td>
<td>16.0</td>
<td>14.4</td>
<td>13.0</td>
</tr>
<tr>
<td>Fruits, serving/d</td>
<td>0.88</td>
<td>0.94</td>
<td>0.90</td>
<td>0.84</td>
<td>0.75</td>
</tr>
<tr>
<td>Vegetables, serving/d</td>
<td>1.73</td>
<td>1.78</td>
<td>1.76</td>
<td>1.71</td>
<td>1.67</td>
</tr>
<tr>
<td>Fish, serving/d</td>
<td>0.19</td>
<td>0.23</td>
<td>0.21</td>
<td>0.19</td>
<td>0.16</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; ACE, angiotensin-converting enzyme. Values are means unless otherwise indicated. Data, except age, were directly standardized to the age distributions of the entire cohort.

*Physical activity includes moderate and vigorous activity.
†Aspirin use ≥1 times per week.
Coffee may be short term, secondary analyses were performed to analyze for caffeinated coffee consumption. We observed a lower risk of stroke in women who drank moderate amounts of decaffeinated coffee after controlling the caffeine. We also assessed associations for decaffeinated coffee, which has a composition similar to that of caffeinated coffee except for caffeine. In the present large cohort of women, those who drank moderate to high amounts of coffee had a lower risk of stroke than those who did not consume coffee. This association was only partially mediated by potential biological mediators, including high blood pressure, hypercholesterolemia, and type 2 diabetes mellitus. Higher consumption of decaffeinated coffee, but not tea or decaffeinated soft drinks, also was associated with a generally lower stroke risk, supporting the hypothesis that components in coffee other than caffeine may lower risk of stroke.

**Discussion**

In the present large cohort of women, those who drank moderate to high amounts of coffee had a lower risk of stroke than those who did not consume coffee. This association was only partially mediated by potential biological mediators, including high blood pressure, hypercholesterolemia, and type 2 diabetes mellitus. Higher consumption of decaffeinated coffee, but not tea or decaffeinated soft drinks, also was associated with a generally lower stroke risk, supporting the hypothesis that components in coffee other than caffeine may lower risk of stroke.

**Table 2. RRs (95% CIs) of Types of Stroke According to Caffeinated Coffee Consumption in the NHS, 1980 to 2004**

<table>
<thead>
<tr>
<th>Total stroke</th>
<th>Caffeinated Coffee Consumption, cups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Person-years</td>
<td></td>
</tr>
<tr>
<td>Cases, n</td>
<td>329</td>
</tr>
<tr>
<td>Age adjusted</td>
<td>1.0</td>
</tr>
<tr>
<td>Age and smoking adjusted</td>
<td>1.0</td>
</tr>
<tr>
<td>Multivariable model 1*</td>
<td>1.0</td>
</tr>
<tr>
<td>Multivariable model 2†</td>
<td>1.0</td>
</tr>
</tbody>
</table>

**Hemorrhagic**

| Cases, n      | 57     | 51      | 141    | 124    | 53    |             |
| Age adjusted  | 1.0    | 0.98 (0.67–1.43) | 1.06 (0.78–1.45) | 1.14 (0.83–1.56) | 1.37 (0.94–1.99) | 0.05 |
| Age and smoking adjusted | 1.0    | 0.96 (0.66–1.41) | 1.00 (0.73–1.37) | 0.96 (0.70–1.32) | 0.95 (0.65–1.41) | 0.78 |
| Multivariable model 1* | 1.0    | 1.02 (0.89–1.52) | 1.03 (0.73–1.46) | 1.01 (0.70–1.47) | 0.79 (0.47–1.33) | 0.43 |
| Multivariable model 2† | 1.0    | 1.01 (0.68–1.51) | 1.03 (0.73–1.45) | 1.02 (0.70–1.48) | 0.81 (0.48–1.36) | 0.49 |

**Ischemic**

| Cases, n      | 171    | 182    | 449    | 308    | 114   |             |
| Age adjusted  | 1.0    | 0.99 (0.81–1.23) | 0.95 (0.80–1.14) | 0.91 (0.76–1.10) | 1.14 (0.90–1.45) | 0.65 |
| Age and smoking adjusted | 1.0    | 0.98 (0.80–1.21) | 0.91 (0.76–1.09) | 0.80 (0.66–0.97) | 0.85 (0.67–1.09) | 0.03 |
| Multivariable model 1* | 1.0    | 0.97 (0.78–1.20) | 0.90 (0.75–1.09) | 0.79 (0.64–0.97) | 0.86 (0.64–1.14) | 0.06 |
| Multivariable model 2† | 1.0    | 0.95 (0.77–1.17) | 0.90 (0.75–1.09) | 0.82 (0.67–1.01) | 0.94 (0.71–1.26) | 0.32 |

*Adjusted for the following: age (5-year categories); smoking status (never, past, and current 1 to 14, 15 to 24, and ≥25 cigarettes a day); body mass index (<23.0, 23.0 to 24.9, 25.0 to 27.9, 28.0 to 29.9, ≥30.0 kg/m²); physical activity (<1.0, 1.0 to 1.9, 2.0 to 3.9, 4.0 to 6.9, ≥7.0 h/wk); alcohol intake (never, 0.1 to 4.9, 5.0 to 9.9, 10.0 to 14.9, 15.0 to 29.9, ≥30.0 g/d); menopausal status and use of hormone replacement therapy (premenopausal women, postmenopausal without hormone therapy, postmenopausal with past hormone therapy, postmenopausal with current hormone therapy); aspirin use; total caloric intake; quintiles of calcium, potassium, sodium, and folate intake; glycemic load; whole grain intake; and tertiles of fruits, vegetables, and fish consumption.

†Additional adjustment for potential intermediates: high blood pressure, hypercholesterolemia, and type 2 diabetes mellitus.
increases blood pressure,33 regular exposure to caffeine can attenuate this effect. In addition, a study found that consumption of 3 cups of coffee per day increased the risk of stroke among hypertensive patients31 (RR, 2.1; 95% CI, 1.2 to 3.7). This study pointed to caffeine as potentially responsible for this association by increasing cardiovascular resistance and decreasing cerebral blood flow, which impair the already damaged vascular system in these patients.34 In our study, an inverse association between coffee consumption and risk of stroke was apparent only in women without hypertension, but no increase in risk of stroke was seen among hypertensive participants. More research is necessary to elucidate whether coffee may have a detrimental effect on these patients.

We also examined the effect of coffee on stroke separately in women with and without diabetes mellitus. Long-term studies have consistently found an association between higher coffee consumption and lower risk for type 2 diabetes.17 One study has suggested that the risk of stroke among diabetic patients, finding no association even with consumptions as high as 7 cups per day.10 Similarly, in our study, we did not find an association between coffee consumption and the incidence of antihypertensive drug use. They concluded that consumption of >2 cups of coffee per day increased the risk of antihypertensive drug treatment (RRs for consumption of 2 to 3, 4 to 5, 6 to 7, and >8 cups of coffee a day were 1.29 [95% CI, 1.09 to 1.54], 1.26 [95% CI, 1.06 to 1.49], 1.24 [95% CI, 1.04 to 1.48], and 1.14 [95% CI, 0.94 to 1.37] compared with 0 to 1 cup a day). Finally, Uiterwaal et al32 found that female abstainers and heavy consumers (>6 cups of coffee per day) had a lower risk of hypertension than moderate consumers (1 to 3 cups per day). Most of these studies suggest that although caffeine intake acutely increases blood pressure,33 regular exposure to caffeine can attenuate this effect. In addition, a study found that consumption of 3 cups of coffee per day increased the risk of stroke among hypertensive patients31 (RR, 2.1; 95% CI, 1.2 to 3.7). This study pointed to caffeine as potentially responsible for this association by increasing cardiovascular resistance and decreasing cerebral blood flow, which impair the already damaged vascular system in these patients.34 In our study, an inverse association between coffee consumption and risk of stroke was apparent only in women without hypertension, but no increase in risk of stroke was seen among hypertensive participants. More research is necessary to elucidate whether coffee may have a detrimental effect on these patients.

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We also examined the effect of coffee on stroke separately in women with and without diabetes mellitus. Long-term studies have consistently found an association between higher coffee consumption and lower risk for type 2 diabetes.17 One study has suggested that the risk of stroke among diabetic patients, finding no association even with consumptions as high as 7 cups per day.10 Similarly, in our study, we did not find an association between coffee consumption and stroke in the subsample of diabetic patients. Although coffee has been shown to have a beneficial effect on glucose metabolism,37 the null association between coffee and stroke found in these patients may reflect the important effect of diabetes on atherosclerosis and hypercoagulability, among other vascular alterations,38 which neutralizes any beneficial effect of coffee in this population.

Hypercholesterolemia is another important risk factor for stroke. Although short-term clinical trials have confirmed the cholesterol-raising effect of diterpenes present in boiled coffee,15 no long-term studies have assessed this association.
In a previous cross-sectional study, we did not find increased levels of total, low-density lipoprotein, and high-density lipoprotein cholesterol among individuals consuming non-paper-filtered coffee compared with nonconsumers. In the present study, we found an inverse association between coffee and stroke among participants without hypercholesterolemia but not among those with the risk factor. We can only speculate that the effect of coffee might be of a lower relevance for patients with a higher degree of atheromatosis. Finally, smoking is a strong confounder in the study association because it is a potent risk factor for stroke and because smoking is more frequent among coffee drinkers. Therefore, stratified analyses were performed to more thoroughly eliminate residual confounding. Coffee consumption was associated with a substantially lower risk of stroke among nonsmokers but not among current smokers. We hypothesize that the potential benefit of coffee reducing the risk of stroke cannot counterbalance the detrimental effect of smoking on health.

Several mechanisms might help to explain the reduced incidence of stroke that we observed among individuals who consumed coffee. Some substances in coffee may have beneficial effects on glucose metabolism, inflammation, and endothelial dysfunction. For example, habitual coffee consumption has been associated with higher insulin sensitivity. In addition, we previously reported an inverse association of caffeinated coffee consumption with surface leukocyte adhesion molecules (E-selectin) and with C-reactive protein, an inflammatory marker, in diabetic women, as well as an inverse association of decaffeinated coffee consumption with C-reactive protein in healthy women. Furthermore, the phenolic compounds of coffee (chlorogenic acid, ferulic acid, and p-coumaric acid) have a strong antioxidant capacity, which may improve endothelial function. The modest inverse association between decaffeinated coffee consumption and risk of stroke in our study supports the hypothesis that components in coffee other than caffeine may be responsible for the potential beneficial effect of coffee on stroke risk.

The present study had several strengths for the examination of the association between coffee consumption and risk of stroke. First, the study included multiple repeated measures of coffee consumption, limiting misclassification. Some measurement error in the assessment of coffee consumption may still have occurred because data on consumption were self-reported. However, results from our validation study indicate that coffee was among the most accurately reported foods in the dietary questionnaire. Second, we were able to control for potential confounders in more detail than in earlier studies because information on risk factors has been updated every 2 years; however, residual confounding by other factors associated with coffee consumption cannot be excluded. Third, data collection on incident strokes was thorough, and a high percentage of events were confirmed by imaging studies. On the other hand, the possibility that reverse causation may have biased our results

| Table 4. RRs (95% CIs) of Total Stroke According to Caffeine Intake and Consumption of Tea, Cola Beverages, and Decaffeinated Coffee in the NHS, 1980 to 2004 |
|-----------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|
| Beverage Consumption, cups | Caffeine intake (quintiles) | Person-years | Cases, n | Age adjusted | Multivariable* | Person-years | Cases, n | Age adjusted | Multivariable† | Person-years | Cases, n | Age adjusted | Multivariable‡ |
|-----------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|
| 71 | 191 | 318 | 423 | 687 | | 377 854 | 377 540 | 377 194 | 378 933 | 378 664 | | | 493 | 483 | 482 | 432 | 390 | | 0.96 |
| 0.93 (0.82–1.06) | 0.94 (0.83–1.07) | 0.94 (0.82–1.07) | 0.98 (0.86–1.12) | 0.96 |
| 0.90 (0.79–1.02) | 0.87 (0.76–1.00) | 0.84 (0.72–0.96) | 0.73 (0.62–0.85) | <0.001 |
| 1.0 | 0.92 (0.83–1.03) | 0.91 (0.81–1.03) | 0.84 (0.69–1.02) | 0.98 (0.67–1.42) | 0.10 |
| 1.07 (0.95–1.20) | 1.05 (0.92–1.20) | 0.92 (0.74–1.14) | 0.79 (0.49–1.29) | 0.19 |
| 1.0 | 0.97 (0.88–1.07) | 1.06 (0.90–1.26) | 1.26 (0.88–1.82) | 0.15 |
| 1.04 (0.94–1.16) | 1.04 (0.87–1.24) | 1.08 (0.74–1.57) | 0.66 |
| 1.0 | 0.86 (0.77–0.96) | 0.77 (0.69–0.87) | 0.84 (0.70–1.01) | 0.002 |
| 1.0 | 0.98 (0.87–1.10) | 0.86 (0.76–0.98) | 0.89 (0.73–1.08) | 0.05 |
| *Model adjusted for the same covariates as in model 1 (Table 2). |
| †Models adjusted for the same covariates as in model 1 (Table 2), plus caffeinated coffee consumption. |
| ‡Follow-up from 1984. |
should be considered. For example, women who were diagnosed with hypertension may have lowered their consumption of caffeinated coffee as a result of the diagnosis. We addressed this issue by examining the association between coffee and risk of stroke among nonhypertensive women only, as well as performing additional analyses that stopped updating consumption when hypertension was diagnosed. The associations between coffee and risk of stroke were similar to those in the main analysis.

**Conclusions**

In the present long-term follow-up study, coffee consumption was not associated with an increased risk of stroke. In contrast, we observed that women who regularly consumed coffee had a modestly lower risk of stroke than nonconsumers. Our data support the hypothesis that components in coffee other than caffeine may lower the risk of stroke, although the association was modest and the biological mechanism is unclear. These results should be supported by further research before the possible implications for public health and clinical practice are considered.

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**Disclosures**

None.

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<table>
<thead>
<tr>
<th>Table 5. Cohort Studies Addressing the Association Between Caffeinated Coffee Consumption and Risk of Stroke*</th>
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<td><strong>Author, Country</strong></td>
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<td>Grobbee et al,9 US</td>
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<td>Bidel et al,10 Finland</td>
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<td>Hakim et al,11 US Hypertensive and nonsmoking men</td>
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<td>Larsson et al,12 Finland Male smokers</td>
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</tbody>
</table>

SMK indicates smoking; BMI, body mass index; MI, myocardial infarction; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high-density lipoprotein; and CHD, coronary heart disease.

*Obtained from a MEDLINE search through June 2008 using the key words “coffee” and “caffeine” in combination with “stroke.”
References


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**CLINICAL PERSPECTIVE**

Data on the relation between coffee consumption and stroke are sparse. We followed up a large population of US women during 24 years, assessing coffee intake repeatedly. For consumption of ≥2 cups of coffee per day, a 20% reduction in the risk of stroke was observed. After additional adjustment for potential mediators of the relation between coffee consumption and stroke such as high blood pressure, hypercholesterolemia, and type 2 diabetes mellitus, the inverse association was slightly attenuated. The association was stronger among nonsmokers than among current smokers. Decaffeinated coffee also was associated with lower risk of stroke. By contrast, other drinks containing caffeine were not associated with stroke. Our results provide evidence that coffee consumption does not increase the risk of stroke in women. In contrast, our data suggest that coffee consumption may modestly reduce the risk of stroke.
Coffee Consumption and Risk of Stroke in Women
Esther Lopez-Garcia, Fernando Rodriguez-Artalejo, Kathryn M. Rexrode, Giancarlo Logroscino, Frank B. Hu and Rob M. van Dam

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