Physical Activity and Risk of Stroke in Women

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Background and Purpose—Physical activity has generally been inversely related to the risk of developing stroke, but details regarding the amount and kinds of activity required are unclear as are associations for specific stroke subtypes.

Methods—Eligible subjects were 39,315 healthy US women, ≥45 years of age, from the Women’s Health Study. Women reported physical activity at baseline (1992 to 1995) and at 36, 72, 96, 125, and 149 months’ follow-up. During an average follow-up of 11.9 years, 579 women developed incident stroke (473 ischemic, 102 hemorrhagic, and 4 of unknown type). Proportional hazards models related physical activity, updated over time, to the risk of incident stroke.

Results—The multivariable relative risks associated with <200, 200 to 599, 600 to 1499, and ≥1500 kcal/week of leisure-time physical activity were 1.00 (referent), 1.11 (95% CI, 0.87 to 1.41), 0.86 (95% CI, 0.67 to 1.10), and 0.83 (95% CI, 0.63 to 1.08), respectively (P_trend=0.06). Similar results were observed for ischemic stroke, whereas no associations were observed for hemorrhagic stroke. Vigorous physical activity was not related to stroke risk (P_trend=0.50); however, walking time and walking pace were inversely related, either significantly or with borderline significance, to total, ischemic, and hemorrhagic stroke risks (P_trend between 0.002 and 0.07).

Conclusions—This study shows a tendency for leisure-time physical activity to be associated with lower stroke risk in women. In particular, walking was generally associated with lower risks of total, ischemic, and hemorrhagic stroke. (Stroke. 2010;41:1243-1250.)

Key Words: brain ischemia ▪ exercise ▪ intracranial hemorrhage ▪ obesity ▪ physical activity ▪ stroke

Stroke is the third leading cause of death and the leading cause of adult disability in the United States.1 It is therefore important to identify modifiable risk factors for the primary prevention of stroke. Despite progress in identifying risk factors for stroke among women (eg, smoking, migraine with aura, postmenopausal hormone use, oral contraceptive use), continued research on other modifiable risk factors is required.2

A promising modifiable risk factor is physical activity, but cohort studies assessing the relation between physical activity and stroke risk, particularly early studies, have shown inconsistent results. Among more recently published reports, an inverse association between physical activity and risk of stroke has been identified in some3–9 but not all10–12 studies. Although recent reviews conclude that physical activity is associated with a 25% to 30% reduction in risk,13 there remains a need to clarify details of the physical activity required as well as the relation for specific stroke subtypes. Moreover, with 1 exception,5 no previous studies have incorporated repeated measures of physical activity, and many studies had limited power to assess potential associations, particularly with respect to hemorrhagic stroke subtypes.

We therefore conducted the present study to examine the association of physical activity with stroke risk in a large cohort of women, addressing details of the physical activity required and the association for specific stroke subtypes.

Methods

Study Population

Subjects were from the Women’s Health Study (WHS), a completed randomized trial of low-dose aspirin and vitamin E for primary prevention of cardiovascular disease and cancer. The methods and results of the WHS have previously been published in detail.14–16 In brief, between September 1992 and May 1995, female health professionals throughout the United States and Puerto Rico were asked to complete a mailed baseline questionnaire on sociodemographic characteristics, health habits, and medical history. A total of 39,876 eligible women free of heart disease, stroke, and cancer (other than nonmelanoma skin cancer) were randomized to receive either active drug or placebo.

Every 6 months during the first year and annually thereafter, women completed follow-up surveys on treatment compliance, risk factors, and end points of interest. On scheduled completion of the trial in March 2004, women were invited to continue follow-up in an...
observational study, and 33 796 did (88.0% of those living). The
Institutional Review Board at Brigham and Women’s Hospital
approved this study.
For this study, we excluded women not reporting their physical
activity or weight (required to estimate energy expenditure) at
baseline (N = 554) or who, after randomization, reported a stroke or
heart disease occurring before randomization (N = 7), leaving 39 315
women.
Assessment of Physical Activity
On the baseline survey, women were asked to estimate the average
time (0, 1 to 19 minutes/week, 20 to 59 minutes/week, 1 hour/week,
1.5 hour/week, 2 to 3 hour/week, 4 to 6 hour/week, or ≥7
hour/week) spent on 8 groups of recreational activities during the
past year: walking or hiking; jogging (slower than 10-minute miles);
running (10-minute miles or faster); bicycling, including use of
stationary machines; aerobic exercise, aerobic dance, use of exercise
machines; tennis, squash, or racquetball; lap swimming; and lower-
intensity exercise, including yoga, stretching, or toning. They also
reported their usual walking pace (do not walk regularly, <3.2
km/hour [2 mph; casual pace], 3.2 to 4.7 km/hour [2 to 2.9 mph;
normal, average pace], 4.8 to 6.3 km/hour [3.0 to 3.9 mph; brisk
pace], or ≥6.4 km/hour [4.0 mph; very brisk/striding pace]) and the
number of flights of stairs climbed daily (0, 1 to 2, 3 to 4, 5 to 9, 10
to 14, or ≥15). Physical activity was updated at 36, 72, and 96
months during the trial; at trial conclusion (average follow-up, 125
months); and cycle 2 of observational follow-up (24 months after
trial conclusion). We refer to these times as the 36-, 72-, 96-, 125-,
and 149-month follow-up.
We assigned a multiple of resting metabolic rate (metabolic
equivalent score) to each group of activities and stair climbing based
on their energy costs23 and estimated the energy expended on each of
these activities.19 This assessment of physical activity has been
shown to be reliable and valid.19 We summed kilocalories per week
from the 8 groups of recreational activities and stair climbing to
estimate weekly energy expenditure and categorized women into
approximate quartiles of energy expenditure: <200, 200 to 599, 600
to 1499, or ≥1500 kcal/week, for analyses of physical activity.
We also conducted additional analyses with energy expenditure esti-
mated in metabolic equivalent-hours/week, a unit independent of
weight. The results were very similar and so we present results
in units of kcal/week, a more interpretable measure.
Assessment of Other Variables
We obtained information at baseline on potential confounders,
including age, weight, height, smoking, diet (including alcohol
use), parity, menopausal status, history of hypertension, history of
elevated cholesterol level, history of diabetes mellitus, use of
postmenopausal hormones, presence of migraine headaches, and
parental history of myocardial infarction before age 60 years.
Women were classified as being normal weight (body mass index
[BMI] <25 kg/m2), overweight (25 ≤BMI <30 kg/m2), or obese
(30 ≤BMI kg/m2) using World Health Organization criteria.20
Diet was assessed using a 131-item semiqualitative food
frequency questionnaire.21
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 medical record review by an End
Points Committee of physicians that included a neurologist. A
nonfatal stroke was defined as a focal neurological deficit of sudden
onset and vascular mechanism that lasted ≥24 hours. Cases of fatal
stroke were documented by evidence of a cerebrovascular mecha-
nism obtained from available sources, including death certificates
and hospital records. Stroke was classified according to the National
Survey of Stroke criteria22 as ischemic or hemorrhagic stroke or
unknown subtype. The interobserver agreement of the classification
of stroke and its major subtypes was excellent.24
Statistical Analysis
We used Cox proportional hazards regression to calculate hazard
ratios as estimates for the relative risks (RRs), and their associated
95% CIs, of stroke as a function of the different measures of physical
activity. Follow-up time was calculated from study entry to the
earliest of the following: stroke diagnosis, death, end of follow-up in
February 2007, or loss to follow-up (<3% of women).
We first estimated the RRs of total stroke associated with the 4
categories of energy expended on all leisure-time activities updated
over time to represent the most recent value available. When a
missing value of physical activity was encountered, the last known
value was carried forward. Initial models adjusted for age and
randomized treatment. A subsequent multivariable model additional-
ally adjusted for potential confounders: smoking status (never, past,
current), alcohol use (never, any), saturated fat intake (g/day;
quintiles), fiber intake (g/day; quintiles), fruit/vegetable intake (serv-
ings/day; quintiles) hormone therapy (never, past, current), meno-
pausal status (premenopausal, postmenopausal, unsure), migraine
(no migraine, prior migraine, active migraine without aura, active
migraine with aura), and parental history of myocardial infarction. A
second multivariable model further adjusted for variables that likely
are in the causal pathway relating physical activity to reduced stroke
occurrence: BMI, history of hypertension, history of diabetes, and
history of elevated cholesterol. We then separately examined the
relation between total leisure-time physical activity and the risks of
ischemic and hemorrhagic strokes.
To provide information on the kinds of activity required, we also
examined vigorous physical activity (requiring ≥6 metabolic-
equivalents)24 and risks of total, ischemic, and hemorrhagic stroke.
Women were categorized into those with no vigorous leisure-time
activity plus <200 kcal/week expended on other activities; no
vigorous leisure-time activity plus ≥200 kcal/week expended on
other activities; and >0 to 199, 200 to 499, or ≥500 kcal/week
expended on vigorous leisure-time activities based on previous
analyses.25 We further examined the relation among walking, a
moderate-intensity activity, and stroke risk. To prevent confounding
by vigorous activities, these analyses considered only women with
no vigorous activities. Women were classified according to the time
spent walking (no regular walking, 1 to 59 minutes/week, 1.0 to 1.5
hours/week, ≥2 hours/week) and their usual walking pace (no
regular walking, <3.2 km/hour [2 mph], 3.2 to 4.7 km/hour [2 to 2.9
mph], or ≥4.8 km/hour [3.0 mph]).
We also examined joint associations of physical activity and BMI
(World Health Organization categories) as well as age (≥60 years
at baseline) with stroke risk. Finally, we examined associations
between changes in the time spent walking between baseline and
36-month follow-up and risk of stroke occurring after 36 months.
Results
Table 1 shows the baseline characteristics of the 39 315
women by approximate quartiles of total leisure-time energy
expenditure. More active women generally had a healthier
profile. They also were more likely to be on postmenopausal
hormone therapy, be postmenopausal, and less likely to have
migraines.
During a mean follow-up of 11.9 years, 579 total strokes
occurred: 473 ischemic, 102 hemorrhagic, and 4 strokes of
unknown type. The associations between total leisure-time
physical activity and risks of total, ischemic, and hemorrhagic
stroke are provided in Table 2. For total stroke, there was an
inverse trend, of borderline significance after adjusting for
potential confounders (P trend=0.06). With additional ad-
justment for variables that likely are in the causal pathway,
the association was further attenuated (Table 2). With ische-
mic stroke, the associations were similar, because these
constituted the majority of strokes that women experienced.
For hemorrhagic stroke, there was no trend across categories of physical activity.

The associations between specific types of leisure-time physical activity and risks of total, ischemic, and hemorrhagic stroke are shown in Table 3. There was no overall linear trend of decreased risk for total stroke across categories of vigorous activity \((P_{\text{trend}} = 0.50\)). Findings for ischemic stroke again mirrored those for total stroke.

Associations of time spent walking and usual walking pace with stroke risk were next examined among women who engaged in no vigorous activity. There were inverse, dose–response relations with total stroke for both time spent walking and usual walking pace \((P_{\text{trend}} = 0.002\) and 0.007, respectively). Women who walked \(\geq 2\) hours per week had a 30% lower risk of any stroke than women who did not walk (multivariable-adjusted RR = 0.70; 95% CI, 0.52 to 0.94), whereas women whose usual walking pace was brisk (>4.8 km/hour) had a 37% lower risk (corresponding RR = 0.63; 95% CI, 0.44 to 0.91) compared with women who did not walk. Similar inverse dose–response trends were noted for ischemic stroke that were of borderline significance \((P_{\text{trend}} = 0.07\) for both time and pace of walking). For hemorrhagic stroke, these inverse associations were significant \((P_{\text{trend}} = 0.002\) and 0.04, respectively). Compared with women who did not walk, those walking \(\geq 2\) hours/week had a 57% lower risk of hemorrhagic stroke (multivariable-adjusted RR = 0.43; 95% CI, 0.20 to 0.89), whereas women whose usual walking pace was >4.8

### Table 1. Baseline Characteristics of Participants According to Total Leisure-Time Physical Activity,* WHS

<table>
<thead>
<tr>
<th>Baseline Physical Activity, kcal/week</th>
<th>&lt;200 (n=10 233)</th>
<th>200–599 (n=9855)</th>
<th>600–1499 (n=10 895)</th>
<th>(\geq 1500) (n=8332)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characteristics at baseline</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age, years</td>
<td>54.7 (7.1)</td>
<td>54.4 (7.0)</td>
<td>54.7 (7.1)</td>
<td>54.6 (7.0)</td>
</tr>
<tr>
<td>Mean BMI, kg/m²</td>
<td>27.0 (5.8)</td>
<td>26.0 (4.9)</td>
<td>25.5 (4.6)</td>
<td>25.6 (4.8)</td>
</tr>
<tr>
<td>Smoking status, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>48.6</td>
<td>52.6</td>
<td>53.0</td>
<td>49.7</td>
</tr>
<tr>
<td>Past</td>
<td>31.6</td>
<td>34.1</td>
<td>37.0</td>
<td>41.7</td>
</tr>
<tr>
<td>Current</td>
<td>19.7</td>
<td>13.4</td>
<td>10.0</td>
<td>8.6</td>
</tr>
<tr>
<td>Alcohol consumption, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rarely</td>
<td>52.9</td>
<td>45.5</td>
<td>41.6</td>
<td>39.3</td>
</tr>
<tr>
<td>1–3 drinks/month</td>
<td>12.5</td>
<td>13.6</td>
<td>13.4</td>
<td>13.3</td>
</tr>
<tr>
<td>1–6 drinks/week</td>
<td>25.4</td>
<td>30.7</td>
<td>34.4</td>
<td>36.3</td>
</tr>
<tr>
<td>(\geq 1) drinks/day</td>
<td>9.2</td>
<td>10.2</td>
<td>10.6</td>
<td>11.1</td>
</tr>
<tr>
<td>Saturated fat intake, mean (SD), g/day</td>
<td>20.5 (8.7)</td>
<td>20.1 (8.0)</td>
<td>19.4 (7.8)</td>
<td>18.8 (7.9)</td>
</tr>
<tr>
<td>Fiber intake, mean (SD), g/day</td>
<td>16.5 (7.3)</td>
<td>18.5 (7.7)</td>
<td>19.7 (8.1)</td>
<td>21.4 (9.1)</td>
</tr>
<tr>
<td>Fruit and vegetable consumption, mean (SD), servings/day</td>
<td>5.2 (3.5)</td>
<td>5.9 (3.2)</td>
<td>6.4 (3.5)</td>
<td>7.3 (4.0)</td>
</tr>
<tr>
<td>Postmenopausal hormone therapy, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>50.9</td>
<td>50.2</td>
<td>49.7</td>
<td>49.0</td>
</tr>
<tr>
<td>Past</td>
<td>10.4</td>
<td>8.8</td>
<td>8.3</td>
<td>8.8</td>
</tr>
<tr>
<td>Current</td>
<td>38.7</td>
<td>41.0</td>
<td>42.0</td>
<td>42.2</td>
</tr>
<tr>
<td>Menopausal status, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>26.3</td>
<td>28.4</td>
<td>28.0</td>
<td>27.6</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>55.0</td>
<td>53.8</td>
<td>54.4</td>
<td>54.7</td>
</tr>
<tr>
<td>Not Sure</td>
<td>18.7</td>
<td>17.9</td>
<td>17.7</td>
<td>17.6</td>
</tr>
<tr>
<td>Migraine, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No migraine</td>
<td>80.8</td>
<td>80.8</td>
<td>82.1</td>
<td>82.8</td>
</tr>
<tr>
<td>Prior migraine</td>
<td>5.7</td>
<td>5.6</td>
<td>5.3</td>
<td>5.1</td>
</tr>
<tr>
<td>Active migraine without aura</td>
<td>8.4</td>
<td>8.4</td>
<td>7.5</td>
<td>6.8</td>
</tr>
<tr>
<td>Active migraine with aura</td>
<td>5.2</td>
<td>5.2</td>
<td>5.0</td>
<td>5.3</td>
</tr>
<tr>
<td>Parental history of myocardial infarction &lt;60 years of age, %</td>
<td>13.8</td>
<td>12.5</td>
<td>12.7</td>
<td>12.8</td>
</tr>
<tr>
<td>History of hypertension, %</td>
<td>29.3</td>
<td>25.6</td>
<td>24.3</td>
<td>24.0</td>
</tr>
<tr>
<td>History of diabetes mellitus, %</td>
<td>3.4</td>
<td>2.3</td>
<td>2.4</td>
<td>2.1</td>
</tr>
<tr>
<td>History of elevated cholesterol, %</td>
<td>32.0</td>
<td>30.0</td>
<td>29.0</td>
<td>26.5</td>
</tr>
</tbody>
</table>

*Physical activity levels were estimated from assessment of leisure-time activities plus stair climbing.
km/hour had a 68% lower risk (corresponding RR=0.31; 95% CI, 0.12 to 0.77).

To examine the associations of change in physical activity with subsequent stroke risk, we investigated changes in walking, which was most consistently associated with lower stroke risk. We observed no clear associations, which may partly reflect the small numbers of cases, particularly for hemorrhagic stroke (Table 4).

Finally, we investigated whether age or BMI modified the physical activity–stroke relation; no significant interactions were observed (data not shown).

**Discussion**

The results of this large prospective cohort study of women with updated physical activity measurements over a mean follow-up of 11.9 years generally showed results congruent with the available body of evidence. We found an inverse association of borderline significance between total leisure-time physical activity and risks of total and ischemic stroke. No associations were observed between vigorous-intensity activity and stroke risk. However, there were significant inverse, dose–response relations of both time spent walking and usual walking pace with risks of total and hemorrhagic strokes and borderline significant relations with ischemic stroke.

Plausible biological pathways support an inverse association between physical activity and risk of stroke, both ischemic and hemorrhagic. Physical activity modifies risk factors for stroke such as hypertension, cardiovascular disease, Type 2 diabetes, and obesity by reducing blood pressure, improving lipid profile, decelerating atherosclerosis, ameliorating endothelial dysfunction, reducing systemic inflammation, and improving insulin sensitivity. Potential effects on ischemic stroke risk may be mediated through mechanisms common to coronary heart disease (eg, factors that modify atherosclerotic progression, especially risk of acute clot rupture), whereas potential effects on hemorrhagic stroke risk may be mediated through blood pressure and related mechanisms.

Previous cohort studies that have assessed the potential relation between physical activity and risk of stroke have varied in terms of physical activity assessment, stroke outcomes, study base (eg, gender, age), control for confounding, and sample size and have shown inconsistent results. Although many studies have found an inverse relation between physical activity and stroke risk, a number of studies have observed no association. Recent reviews conclude that overall, evidence support a 25% to 30% reduction in stroke risk with physical activity, although there remains ambiguous evidence for an added reduction in risk when moving from moderate to high levels of activity. Among studies that have included ≥3 categories of physical activity, varying dose–response relations have been observed, including inverse monotonic, similar risk reductions for any nonreference activity level, U-shaped, null less the most active, and null.

Our results are similar to those of recent studies and in general agree with a recent expert review in that we observed some inverse associations between physical activity and risk of stroke. However, unlike female cohorts from

| Table 2. RRs of Stroke According to Total Leisure-Time Physical Activity* |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Kcal/week                  | <200            | 200–599         | 600–1499        | ≥1500           | P§              |
| No. of women at baseline   |                 |                 |                 |                 |                 |
| Total stroke               |                 |                 |                 |                 |                 |
| No. of cases               | 181             | 138             | 147             | 113             |                 |
| Age- and treatment-adjusted RR (95% CI) |   |   |   |   | <0.0001 |
| Multivariable-adjusted RR1† (95% CI) |   |   |   |   | 0.06 |
| Multivariable-adjusted RR2‡ (95% CI) |   |   |   |   | 0.21 |
| Ischemic stroke            |                 |                 |                 |                 |                 |
| No. of cases               | 155             | 106             | 123             | 89              |                 |
| Age- and treatment-adjusted RR (95% CI) |   |   |   |   | <0.0001 |
| Multivariable-adjusted RR1† (95% CI) |   |   |   |   | 0.06 |
| Multivariable-adjusted RR2‡ (95% CI) |   |   |   |   | 0.22 |
| Hemorrhagic stroke         |                 |                 |                 |                 |                 |
| No. of cases               | 24              | 32              | 22              | 24              |                 |
| Age- and treatment-adjusted RR (95% CI) |   |   |   |   | 0.64 |
| Multivariable-adjusted RR1† (95% CI) |   |   |   |   | 0.84 |
| Multivariable-adjusted RR2‡ (95% CI) |   |   |   |   | 0.98 |

*Updated over time.
†Adjusted for age, randomized treatment assignment, plus smoking; alcohol; saturated fat, fruit and vegetable, and fiber intake; postmenopausal hormone therapy; menopausal status, parental history of myocardial infarction, and migraine aura.
‡Adjusted for the previously mentioned variables plus BMI, history of diabetes, history of elevated cholesterol, and history of hypertension.
§P value for linear trend across categories of physical activity.
Table 3. RRs of Stroke According to Types of Physical Activity*

| Kcal/week Range | 0 + <200§ | 0 + ≥200§ | >0–199 | 200–499 | ≥500 | P|| |
|-----------------|-----------|-----------|--------|--------|------|------|
| No. of women at baseline | 9326 | 13 536 | 4100 | 4119 | 8234 |

**Total stroke**

- **No. of cases**: 167, 211, 45, 57, 99
- **Age- and treatment-adjusted RR (95% CI)**: 1.00, 0.79 (0.64–0.96), 0.91 (0.73–1.37), 0.91 (0.67–1.23), 0.63 (0.49, 0.83)
- **Multivariable-adjusted RR1† (95% CI)**: 1.00, 0.98 (0.78–1.24), 1.41 (1.01–1.97), 1.08 (0.76–1.52), 0.83 (0.61, 1.12)
- **Multivariable-adjusted RR2‡ (95% CI)**: 1.00, 1.04 (0.82–1.31), 1.51 (1.07–2.12), 1.21 (0.86–1.72), 0.90 (0.66, 1.23)

**Ischemic stroke**

- **No. of cases**: 143, 166, 38, 45, 81
- **Age- and treatment-adjusted RR (95% CI)**: 1.00, 0.75 (0.60–0.94), 0.77 (0.55–1.10), 0.85 (0.55–1.10), 0.60 (0.45, 0.81)
- **Multivariable-adjusted RR1† (95% CI)**: 1.00, 0.95 (0.74–1.23), 0.91 (0.61–1.37), 0.81 (0.58, 1.14), 0.49 (0.30–0.81)
- **Multivariable-adjusted RR2‡ (95% CI)**: 1.00, 1.01 (0.76–1.31), 1.61 (1.12–2.33), 1.05 (0.69–1.58), 0.90 (0.64, 1.27)

**Hemorrhagic stroke**

- **No. of cases**: 22, 44, 7, 12, 17
- **Age- and treatment-adjusted RR (95% CI)**: 1.00, 1.06 (0.63–1.78), 1.83 (0.96–3.48), 0.85 (0.44, 1.64), 0.86
- **Multivariable-adjusted RR1† (95% CI)**: 1.00, 1.27 (0.73–2.22), 2.04 (1.01–4.12), 0.94 (0.45, 1.97), 0.38
- **Multivariable-adjusted RR2‡ (95% CI)**: 1.00, 1.34 (0.76–2.37), 2.16 (1.06–4.41), 0.90 (0.64, 2.12), 0.84

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**Km/hour Range**

| 1–59 Minutes | 60–90 Minutes | ≥2 Hours | P|| |
|---------------|---------------|----------|------|
| No. of women at baseline | 5817 | 6036 | 4410 | 6599 |

**Total stroke**

- **No. of cases**: 119, 93, 65, 101
- **Age- and treatment-adjusted RR (95% CI)**: 1.00, 0.83 (0.64–1.07), 0.75 (0.55–1.01), 0.85 (0.55–1.07), 0.61 (0.47–0.80)
- **Multivariable-adjusted RR1† (95% CI)**: 1.00, 0.86 (0.65–1.14), 0.87 (0.62–1.20), 0.70 (0.52–0.94), 0.53 (0.40–0.71)
- **Multivariable-adjusted RR2‡ (95% CI)**: 1.00, 0.91 (0.68–1.21), 0.96 (0.69–1.34), 0.78 (0.58–1.06), 0.01

**Ischemic stroke**

- **No. of cases**: 101, 77, 50, 81
- **Age- and treatment-adjusted RR (95% CI)**: 1.00, 1.27 (0.73–2.22), 1.34 (0.58–3.09), 2.04 (1.01–4.12), 0.94 (0.45, 1.97)
- **Multivariable-adjusted RR1† (95% CI)**: 1.00, 0.97 (0.71–1.33), 0.81 (0.55–1.19), 0.79 (0.57–1.10), 0.72 (0.53–1.01)
- **Multivariable-adjusted RR2‡ (95% CI)**: 1.00, 1.04 (0.76–1.43), 0.92 (0.63–1.36), 0.91 (0.66–1.27), 0.27

**Hemorrhagic stroke**

- **No. of cases**: 17, 15, 15, 19
- **Age- and treatment-adjusted RR (95% CI)**: 1.00, 0.57 (0.30–1.10), 1.06 (0.56–2.01), 0.42 (0.21–0.84), 0.0005
- **Multivariable-adjusted RR1† (95% CI)**: 1.00, 0.48 (0.24–0.99), 1.06 (0.56–2.01), 0.42 (0.20–0.87), 0.002
- **Multivariable-adjusted RR2‡ (95% CI)**: 1.00, 0.50 (0.24–1.02), 1.09 (0.57–2.08), 0.43 (0.20–0.89), 0.002

---

**Usual Walking Pace, km/hour¶**

| 3.2 | 3.2–4.7 | ≥4.8 | P|| |
| No. of women at baseline | 3347 | 3135 | 10 526 | 5854 |

**Total stroke**

- **No. of cases**: 85, 68, 149, 76
- **Age- and treatment-adjusted RR (95% CI)**: 1.00, 0.75 (0.55–1.03), 0.63 (0.49–0.82), 0.51 (0.37–0.71), 0.53 (0.37–0.71)
- **Multivariable-adjusted RR1† (95% CI)**: 1.00, 0.82 (0.58–1.16), 0.72 (0.54–0.96), 0.63 (0.44–0.91), 0.63 (0.44–0.91)
- **Multivariable-adjusted RR2‡ (95% CI)**: 1.00, 0.82 (0.58–1.17), 0.77 (0.57–1.04), 0.75 (0.52–1.08), 0.52

**Ischemic stroke**

- **No. of cases**: 71, 55, 117, 66
- **Age- and treatment-adjusted RR (95% CI)**: 1.00, 0.76 (0.54–1.07), 0.62 (0.47–0.83), 0.55 (0.39–0.78), 0.55 (0.39–0.78)
- **Multivariable-adjusted RR1† (95% CI)**: 1.00, 0.90 (0.61–1.33), 0.74 (0.53–1.03), 0.75 (0.50–1.12), 0.75 (0.50–1.12)
- **Multivariable-adjusted RR2‡ (95% CI)**: 1.00, 0.92 (0.62–1.36), 0.82 (0.59–1.16), 0.94 (0.62–1.42), 0.54

(Continued)
Finland, Norway, and the United States where significant inverse relations were observed, our results are more similar to those from a Japanese cohort that found a nonsignificant inverse association among females. In terms of the magnitude of the inverse association, our results again are similar to the Japanese cohort in that we found that the most active women were 17% less likely to have any stroke than the least active compared with analogous risk reductions of 17% in the Japanese women (fatal stroke only) but larger risk reductions of 25% in US, 34% in Finnish, and 53% in Norwegian women (fatal stroke only).

The present findings for vigorous physical activity provide little evidence for any relation with stroke risk; no inverse trend was observed, and although women in the highest category of vigorous activity were at 17% lower risk of total stroke, this was not significant. These findings are similar to those from several male or mixed-gender American cohorts but differ from those of other female cohorts, which observed a significant reduction in stroke risk among women in the highest category of vigorous-intensity physical activity.

When we examined walking, we observed consistent inverse dose–response relations between walking time or walking pace and total stroke risk that are comparable to findings from another study of US women but differ from those of the Japanese cohort discussed, which did not find an association between walking and stroke risk among women.

It is not entirely clear why we observed an association between walking, a moderate-intensity activity, and stroke risk, but no association with vigorous-intensity activity.

Participation in vigorous activities was far lower than moderate activities such as walking in the present cohort, which may reduce our ability to observe an effect.

---

**Table 3. Continued**

<table>
<thead>
<tr>
<th>Hemorrhagic stroke</th>
<th>No. of cases</th>
<th>Age- and treatment-adjusted RR (95% CI)</th>
<th>Multivariable-adjusted RR1† (95% CI)</th>
<th>Multivariable-adjusted RR2‡ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>0.68 (0.31–1.49)</td>
<td>0.51 (0.22–1.19)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12</td>
<td>0.71 (0.39–1.30)</td>
<td>0.70 (0.38–1.30)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>31</td>
<td>0.39 (0.17–0.89)</td>
<td>0.32 (0.13–0.79)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10</td>
<td>0.31 (0.12–0.77)</td>
<td>0.31 (0.12–0.77)</td>
</tr>
</tbody>
</table>

*Updated over time.
†Adjusted for age, randomized treatment assignment, plus smoking; alcohol; saturated fat, fruit and vegetable, and fiber intake; postmenopausal hormone therapy; menopausal status, parental history of myocardial infarction, and migraine aura.
‡Adjusted for the previously mentioned variables plus BMI, history of diabetes, history of elevated cholesterol, and history of hypertension.
§Total leisure time physical activity.
¶P value for linear trend across categories of physical activity.
*Analyses are restricted to women without any vigorous leisure-time activities.

---

**Table 4. RRs of Stroke According to Changes in Time Spent Walking**

<table>
<thead>
<tr>
<th>Time spent walking at baseline/at 3 years, hours/week</th>
<th>&lt;2/≤2</th>
<th>&gt;2/≤2</th>
<th>&gt;2/2</th>
<th>&gt;2/2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of women at baseline</td>
<td>8235</td>
<td>2365</td>
<td>1999</td>
<td>2829</td>
</tr>
<tr>
<td>Total stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>117</td>
<td>29</td>
<td>26</td>
<td>31</td>
</tr>
<tr>
<td>Age- and treatment-adjusted RR (95% CI)</td>
<td>0.85 (0.57–1.27)</td>
<td>0.87 (0.57–1.33)</td>
<td>0.65 (0.44–0.97)</td>
<td></td>
</tr>
<tr>
<td>Multivariable-adjusted RR1† (95% CI)</td>
<td>0.86 (0.55–1.34)</td>
<td>0.84 (0.52–1.37)</td>
<td>0.78 (0.51–1.19)</td>
<td></td>
</tr>
<tr>
<td>Multivariable-adjusted RR2‡ (95% CI)</td>
<td>0.89 (0.57–1.38)</td>
<td>0.85 (0.53–1.39)</td>
<td>0.82 (0.54–1.27)</td>
<td></td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>98</td>
<td>28</td>
<td>19</td>
<td>26</td>
</tr>
<tr>
<td>Age- and treatment-adjusted RR (95% CI)</td>
<td>0.98 (0.64–1.49)</td>
<td>0.76 (0.46–1.24)</td>
<td>0.64 (0.42–0.99)</td>
<td></td>
</tr>
<tr>
<td>Multivariable-adjusted RR1† (95% CI)</td>
<td>1.00 (0.63–1.58)</td>
<td>0.66 (0.37–1.18)</td>
<td>0.77 (0.48–1.23)</td>
<td></td>
</tr>
<tr>
<td>Multivariable-adjusted RR2‡ (95% CI)</td>
<td>1.04 (0.66–1.65)</td>
<td>0.68 (0.38–1.22)</td>
<td>0.85 (0.53–1.36)</td>
<td></td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>19</td>
<td>1</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Age- and treatment-adjusted RR (95% CI)</td>
<td>0.18 (0.02–1.35)</td>
<td>1.48 (0.62–3.51)</td>
<td>0.70 (0.26–1.88)</td>
<td></td>
</tr>
<tr>
<td>Multivariable-adjusted RR1† (95% CI)</td>
<td>0.20 (0.03–1.48)</td>
<td>1.70 (0.70–4.12)</td>
<td>0.79 (0.28–2.21)</td>
<td></td>
</tr>
<tr>
<td>Multivariable-adjusted RR2‡ (95% CI)</td>
<td>0.20 (0.03–1.47)</td>
<td>1.62 (0.66–3.94)</td>
<td>0.74 (0.26–2.07)</td>
<td></td>
</tr>
</tbody>
</table>

*Analyses are restricted to women without any vigorous leisure-time activities.
†Adjusted for age, randomized treatment assignment, plus smoking; alcohol; saturated fat, fruit and vegetable, and fiber intake; postmenopausal hormone therapy; menopausal status, parental history of myocardial infarction, and migraine aura.
‡Adjusted for the previously mentioned variables plus BMI, history of diabetes, history of elevated cholesterol, and history of hypertension.
misclassification of vigorous activity is an explanation, because vigorous-intensity physical activity tends to be better reported than moderate-intensity activity.\(^{17}\) Another possible explanation is that moderate-intensity physical activity may be more effective at lowering blood pressure, a strong risk factor for stroke, compared with vigorous-intensity activity as suggested by some\(^{27}\) but not all\(^{28}\) randomized controlled trials.

With regard to the associations of physical activity with stroke subtypes, our results do not indicate a substantial difference similar to other studies,\(^{5,6,12}\) but the low number of hemorrhagic strokes limits the power of these analyses.

Obesity is a strong risk factor for total and ischemic stroke,\(^{29}\) and no interaction was previously reported between obesity and baseline physical activity in relation to stroke risk in the WHS.\(^{29}\) In the present analysis, using updated measures of physical activity, we continued to observe no effect of physical activity to be associated with lower stroke risk in white women, in particular black women in whom stroke rates are almost twice that of white women. In particular, walking was generally associated with physical activity measures to be associated with lower stroke risk in the WHS.\(^{29}\) In the present analysis, using updated measures of physical activity collected using a validated instrument\(^{19}\) on repeated occasions. Stroke outcomes were confirmed with medical records, and ischemic and hemorrhagic subtypes were differentiated. We also controlled for many potential confounders in analyses.

Our study was limited by its observational design; thus, the potential for residual confounding remains. Physical activity was self-reported, allowing for potential misclassification. However, because activity was prospectively ascertained, this bias is likely to be nondifferential causing a bias toward the null (no association). The associations among measures of physical activity and stroke risk that we observed are thus likely to underrepresent the true associations. Potential confounders, including dietary intake from food frequency questionnaires, were also self-reported. Physical activity measures were restricted to leisure-time activity; no household or occupational activity, or sedentary behaviors, was assessed. The numbers of ischemic and hemorrhagic stroke subtypes were too small to conduct further analyses. We had limited power to assess potential associations with hemorrhagic stroke. Finally, the WHS comprises predominantly white US female health professionals, which may limit the generalizability of findings to other populations.

In conclusion, this study shows a tendency for leisure-time physical activity to be associated with lower stroke risk in women. In particular, walking was generally associated with lower risks of total, ischemic, and hemorrhagic stroke. Future studies with larger numbers of hemorrhagic strokes will be useful. Also, studies among racial/ethnic minorities, particularly black women in whom stroke rates are almost twice that in white women, are needed.\(^{30}\)

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References


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