Physical Activity and Functional Outcomes From Cerebral Vascular Events in Men

Pamela M. Rist, MSc; I-Min Lee, MBBS, ScD; Carlos S. Kase, MD; J. Michael Gaziano, MD, MPH; Tobias Kurth, MD, ScD

Background and Purpose—In studies enrolling patients with stroke, higher levels of prestroke physical activity are associated with better functional outcomes. However, prospective studies evaluating this association are sparse. Using a cohort of initially healthy men, we aimed to prospectively assess the association between physical activity and functional outcomes from cerebral vascular events.

Methods—We conducted a prospective cohort study among 21 794 men enrolled in the Physician’s Health Study who provided information on physical activity at baseline and who did not have a history of stroke or transient ischemic attack (TIA). Baseline levels of physical activity were categorized as: vigorous exercise <1, 1, 2 to 4, and ≥5 times/week. Possible functional outcomes included TIA and stroke with modified Rankin Scale score of 0 to 1, 2 to 3, or 5 to 6. Multinomial logistic regression was used to determine the association between physical activity and functional outcomes from cerebral vascular events.

Results—After a mean of 20.2 years of follow-up, 761 TIs, 1146 ischemic strokes, 221 hemorrhagic strokes, and 11 strokes of unknown type occurred. Compared with men who did not experience a stroke or TIA and who exercise vigorously <1 time/week, men who exercise vigorously ≥5 times/week had adjusted relative risk (95% CIs) of 0.67 (0.53–0.86) for TIA, 0.84 (0.61–1.14) for stroke with modified Rankin Scale score 0 to 1, 0.85 (0.67–1.08) for modified Rankin Scale score 2 to 3, and 1.12 (0.78–1.60) for modified Rankin Scale score 5 to 6 after total stroke. Other levels of physical activity did not have a significant impact on the risk of our outcomes.

Conclusions—Physical activity before TIA or stroke does not appear to influence functional outcomes after cerebral vascular events. (Stroke. 2011;42:3352-3356.)

Key Words: epidemiology ■ physical activity ■ stroke

A result of the large projected morbidity burden of stroke in the upcoming decades, identifying lifestyle factors that may reduce stroke morbidity and mortality has become increasingly important. One lifestyle factor that has been linked to a reduced risk of stroke is physical activity. Meta-analyses of the relationship between physical activity and stroke risk have shown that occupational or leisure-time physical activity reduces the risk of total, ischemic, and hemorrhagic stroke.1,2 A previous study performed using data from the Physician’s Health Study found that men who exercised vigorously once a week decreased their risk of stroke by 21% compared with men who exercised less than once per week.3

Although many studies have examined the association between physical activity and risk of stroke, only a few studies have explored whether physical activity is associated with functional outcome from stroke or stroke severity. These studies found that higher levels of prestroke physical activity were associated with initial reduced stroke severity and better long-term functional outcome.4–6 However, these studies only enrolled patients with stroke and assessed physical activity retrospectively. To address these limitations, we aimed to examine the association between physical activity and functional outcomes from stroke in a large prospective cohort study enrolling healthy men without a history of stroke at baseline. We hypothesized that increased levels of physical activity will be associated with a decreased risk of poor functional outcomes after incident cerebral vascular events.

Methods

The Physician’s Health Study was a randomized trial of the effect of low-dose aspirin and β-carotene in the primary prevention of cardiovascular disease and cancer. The design, methods, and results...
have been previously described.2–4 Briefly, in 1982, 22,071 US male physicians between the ages of 40 and 84 years were randomized to receive aspirin, β-carotene, both placebo, or both active agents. Participants were free of a history of stroke, transient ischemic attack (TIA), myocardial infarction, and other major diseases at baseline. All men provided written informed consent and this study has been approved by the Institutional Review Board at Brigham and Women’s Hospital. Since the completion of the trial,5–8 follow-up is ongoing.9 This analysis included data available as of March 2008 when morbidity and mortality follow-up was >99%.

Assessment of Exposure

At baseline, all physicians filled out a questionnaire asking about health and lifestyle characteristics, including physical activity. Specifically, the men were asked, “How often do you exercise vigorously enough to work up a sweat?” Possible responses were rarely/never, 1 to 3 times/month, 1 time/week, 2 to 4 times/week, 5 to 6 times/week, or daily.1 Previous studies have shown that this method of assessing physical activity correlates well with physical fitness measures.11,12 To be consistent with a prior study,1 we combined the 2 lowest categories into <1 time/week and the 2 highest into ≥5 times/week. Physicians with missing information on physical activity at baseline were excluded (n = 247).

At the 36- and 108-month follow-up, the participants were asked “Do you engage in a regular program of exercise vigorous enough to work up a sweat?” If the participant responded affirmatively, he was asked “How many days per week?” The possible response categories were <1, 1 to 2, 3 to 4, or 5 to 7 days/week.3

Assessment of Outcome

Participants were asked on follow-up questionnaires whether they experienced any newly diagnosed medical conditions, including stroke and TIA. If a participant reported a trial outcome, we asked for permission to review his medical record. An end points committee of physicians confirmed all outcomes. A nonfatal stroke was defined as a focal neurological deficit with sudden or rapid onset attributable to a cerebrovascular event that lasted >24 hours. A TIA was defined as a focal neurological deficit with sudden or rapid onset attributable to a cerebrovascular event that lasted <24 hours. Participant deaths were usually reported by family members or postal authorities and all available medical records, death certificates, and eyewitness accounts were used to determine the cause of death. For confirmed stroke cases, the end points committee classified strokes as ischemic, hemorrhagic, or unknown type with high interobserver agreement.13

Using medical record information, the end points committee determined the functional outcome from confirmed strokes according to an amended version of the 7-point modified Rankin scale (mRS; 0 = no symptoms; 1 = no significant disability; 2 = slight disability; 3 = moderate disability; 4 = moderately severe disability; 5 = severe disability; 6 = death).14 At hospital discharge. Our amended version did not have the category of “4 = moderately severe disability.” We decided a priori to categorize the mRS score into 3 levels (0–1, 2–3, 5–6). If the participant experienced multiple strokes and/or TIAs, only the first event was used in our analysis. We excluded men from our analysis if they experienced a stroke or TIA before receiving the baseline questionnaire (n = 8) or if they experienced a confirmed stroke but were missing a mRS score (n = 22). After applying our exclusion criteria, 21,794 men were used in our analyses.

Statistical Analysis

We used Cox proportional hazards models to calculate the hazard ratios as a measure of the relative risk (RR) of incident TIA and total, ischemic, and hemorrhagic stroke for each level of physical activity. We graphically examined whether the assumption of proportional hazards was met and found no significant violation.

We used multinomial logistic regression to evaluate the relationship between levels of physical activity and functional outcomes from cerebral vascular events. Multinomial regression is an extension of binary regression in which the outcome can have >2 categories. The resulting ORs are used as a measure of the RR of each functional outcome according to level of physical activity. When examining the relationship between physical activity and functional outcome after hemorrhagic stroke, TIA was not included.

We distinguished 2 multivariable models: I (confounder model) included age (continuous), smoking status (never, past, or currently smoking <20 or ≥20 cigarettes daily), alcohol consumption (rarely, monthly, weekly, or daily), and parental history of myocardial infarction before age 60 years (yes/no). We also adjusted for randomized treatment assignments. II (intermediate model) additionally controlled for body mass index (continuous), history of hypertension (yes/no), history of high cholesterol (yes/no/missing), and history of diabetes (yes/no).

We examined whether age, randomized treatment assignment to aspirin, smoking status, history of hypertension, or obesity modified the association between physical activity at baseline and functional outcomes from total stroke by including an interaction term between physical activity and each variable in separate age-adjusted models.

In secondary analyses, we used updated physical activity information at 36 and 108 months to determine the relationship between physical activity and risk of our functional outcomes from stroke. Due to differences in the response categories, we a priori decided to dichotomize physical activity into <1 time/week and ≥1 time/week, consistent with a previous study.3

Participants with missing covariate information were assigned to the mean, reference, or past user category when the number of missing was <350. More than 350 men were missing information on history of high cholesterol so we used the missing indicator method. All statistical analyses were performed using SAS 9.2 (Cary, NC). All probability values are 2-tailed and P < 0.05 was considered statistically significant.

Results

Of the 21,974 who reported information on physical activity at baseline, 6048 (27.8%) exercised <1 time/week, 4007 (18.4%) exercised 1 time/week, 8187 (37.6%) exercised ≥2 to 4 times/week, and 3552 (16.3%) exercised ≥5 times/week. Table 1 shows the baseline characteristics of the participants according to their frequency of vigorous exercise. Men who exercised the most frequently were more likely to be never smokers and to not have a history of hypertension or high cholesterol than the men who exercised the least frequently.

After a mean of 20.2 years of follow-up, 761 TIA, 1146 ischemic strokes, 221 hemorrhagic strokes, and 11 strokes of unknown type occurred. Table 2 presents the multivariable adjusted RR of TIA, total stroke, ischemic stroke, and hemorrhagic stroke by frequency of physical activity. Men who exercised ≥5 times/week had a significantly reduced risk of TIA compared with those men who exercised <1 time/week (RR, 0.66; 95% CI, 0.52–0.84; P = 0.001). A significant reduced risk of total stroke was observed for those men who exercised 2 to 4 times/week compared with those men who exercised <1 time/week (RR, 0.86; 95% CI, 0.75–0.98; P = 0.02), but not for men in the other exercise categories. No level of exercise was associated with a significantly reduced risk of ischemic or hemorrhagic stroke.

For our functional outcomes from total stroke analysis, compared with men who did not experience a stroke or TIA and who exercised <1 time/week, men who exercised ≥5 times/week had adjusted RRs (95% CIs) of 0.67 (0.53–0.86) for TIA, 0.84 (0.61–1.14) for stroke with mRS 0 to 1, 0.85 (0.67–1.08) for mRS 2 to 3, and 1.12 (0.78–1.60) for mRS 5 to 6 after total stroke (Table 3). Men who exercised 2 to 4 times/week also had a reduced risk of TIA and more severe stroke (mRS 2–6) compared with men who exercised <1 time/week.
time/week and who did not experience a stroke or TIA, although this reduction in risk was not statistically significant. Adjusting for potential intermediates did not impact our results (data not shown). Results when examining only ischemic stroke outcomes were similar to those seen for total stroke outcomes (Table 3). When examining hemorrhagic stroke, there was some suggestion that exercising 2 to 4 times/week reduces one’s risk of any of our functional outcomes from stroke (Table 3).

We found no evidence of effect modification by age, history of hypertension, smoking status, randomized aspirin assignment, or obesity on the association between physical activity and functional outcome from total stroke (all $P_{interaction} > 0.16$).

When we dichotomized physical activity (<1 time/week versus ≥1 time/week) to perform analyses updated over time, results were essentially unchanged (Supplemental Tables; http://stroke.ahajournals.org).

Table 1. Baseline Characteristics According to Level of Physical Activity in the Physician’s Health Study (N=21 794)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Frequency of Vigorous Exercise</th>
<th>TIA</th>
<th>Total Stroke</th>
<th>Ischemic Stroke</th>
<th>Hemorrhagic Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (&lt;1 Time/Wk)</td>
<td>1 Time/Wk</td>
<td>2–4 Times/Wk</td>
<td>5 Times/Wk</td>
<td>No. (&lt;1 Time/Wk)</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>54.6</td>
<td>53.2</td>
<td>53.3</td>
<td>54.0</td>
<td>49.1</td>
</tr>
<tr>
<td>Mean body mass index, kg/m²</td>
<td>25.2</td>
<td>25.0</td>
<td>24.7</td>
<td>24.1</td>
<td>25.0</td>
</tr>
<tr>
<td>Cigarette use, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>47.1</td>
<td>49.4</td>
<td>50.6</td>
<td>50.8</td>
<td>49.4</td>
</tr>
<tr>
<td>Past</td>
<td>38.5</td>
<td>36.8</td>
<td>40.1</td>
<td>42.0</td>
<td>36.8</td>
</tr>
<tr>
<td>Current &lt;20 cigarettes/d</td>
<td>4.2</td>
<td>4.4</td>
<td>3.6</td>
<td>3.3</td>
<td>4.4</td>
</tr>
<tr>
<td>Current ≥20 cigarettes/d</td>
<td>10.0</td>
<td>9.1</td>
<td>5.5</td>
<td>3.7</td>
<td>9.1</td>
</tr>
<tr>
<td>Alcohol consumption, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rarely</td>
<td>17.1</td>
<td>13.2</td>
<td>13.0</td>
<td>16.4</td>
<td>13.2</td>
</tr>
<tr>
<td>Monthly</td>
<td>13.8</td>
<td>11.5</td>
<td>9.5</td>
<td>9.7</td>
<td>11.5</td>
</tr>
<tr>
<td>Weekly</td>
<td>44.5</td>
<td>50.3</td>
<td>51.7</td>
<td>47.8</td>
<td>50.3</td>
</tr>
<tr>
<td>Daily</td>
<td>24.0</td>
<td>24.4</td>
<td>25.2</td>
<td>25.5</td>
<td>24.4</td>
</tr>
<tr>
<td>History of diabetes, %</td>
<td>4.5</td>
<td>2.6</td>
<td>2.3</td>
<td>2.6</td>
<td>2.6</td>
</tr>
<tr>
<td>Mean blood pressure, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>127.2</td>
<td>127.3</td>
<td>125.6</td>
<td>124.5</td>
<td>127.2</td>
</tr>
<tr>
<td>Diastolic</td>
<td>79.5</td>
<td>79.4</td>
<td>78.6</td>
<td>77.5</td>
<td>79.4</td>
</tr>
<tr>
<td>History of hypertension, %*</td>
<td>26.4</td>
<td>25.0</td>
<td>22.0</td>
<td>21.0</td>
<td>25.0</td>
</tr>
<tr>
<td>History of high cholesterol, %†</td>
<td>11.0</td>
<td>10.5</td>
<td>10.6</td>
<td>9.5</td>
<td>10.5</td>
</tr>
<tr>
<td>Random assignment to aspirin group, %</td>
<td>49.5</td>
<td>49.9</td>
<td>50.7</td>
<td>49.2</td>
<td>49.9</td>
</tr>
</tbody>
</table>

Numbers may not add to 100% because of rounding or missing data.

*History of hypertension was defined as self-reported systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or treatment for hypertension.

†History of high cholesterol was defined as blood cholesterol ≥240 mg/100 mL or cholesterol medication use.

Table 2. Multivariable-Adjusted Relative Risk of Total Stroke, TIA, and Ischemic or Hemorrhagic Stroke According to Level of Physical Activity (N=21 794)*

<table>
<thead>
<tr>
<th>Frequency of Vigorous Exercise</th>
<th>TIA</th>
<th>Total Stroke</th>
<th>Ischemic Stroke</th>
<th>Hemorrhagic Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Relative Risk (95% CI)</td>
<td>No.</td>
<td>Relative Risk (95% CI)</td>
</tr>
<tr>
<td>1 time/wk</td>
<td>239</td>
<td>1.00</td>
<td>429</td>
<td>0.99 (0.81–1.22)</td>
</tr>
<tr>
<td>2–4 times/wk</td>
<td>150</td>
<td>0.99 (0.81–1.22)</td>
<td>249</td>
<td>0.94 (0.81–1.10)</td>
</tr>
<tr>
<td>≥5 times/wk</td>
<td>96</td>
<td>0.66 (0.52–0.84)</td>
<td>225</td>
<td>0.88 (0.75–1.03)</td>
</tr>
</tbody>
</table>

TIA indicates ischemic attack; CI, confidence interval.

*Men who exercised <1 time/wk and who did not experience a stroke or TIA, served as the reference category.

†Values have also been adjusted for age, smoking status, alcohol consumption, parental history of myocardial infarction before age 60 y, and randomized treatment assignments.
### Discussion

Our updated analysis on the risk of stroke and TIA in the Physician’s Health Study showed a decreased risk of TIA and total, ischemic, and hemorrhagic stroke for men who exercise vigorously at least twice per week. The results of the evaluation of the association between physical activity and TIA or functional outcome from stroke suggested decreased risk of TIA and milder strokes (mRS 0–3) among those who exercise 2–4 times/week, although this decrease was only statistically significant for TIA.

Although we did observe a protective association of physical activity on the risk of stroke, the magnitude of our results is attenuated with those observed in an earlier study using data from the Physician’s Health Study. Despite the lack of effect modification by age in our study, physical activity may exert a stronger protective effect at younger ages.

A few studies have examined the association among prestroke physical activity, stroke severity, and functional outcomes after stroke and found that higher levels of physical activity were associated with better functional outcomes. One study in patients with ischemic stroke found that moderate physical activity and leisure-time physical activity were associated with increased odds of having National Institutes of Health Stroke Scale score of 0 to 5 at admission, mRS score of 0 to 1 at Day 8, and Barthel Index score of 95 to 100 at Day 8. Another study found that moderate or heavy levels of physical activity were more likely to present with a less severe stroke as measured by the Scandinavian Stroke Scale and to have decreased odds of having a higher mRS score 2 years after stroke.

In contrast, our results do not show a strong association between higher levels of physical activity and better functional outcomes after stroke. One possible explanation for these discrepancies may be the different populations studied and study designs. Previous studies enrolled only patients with stroke and retrospectively assessed physical activity through self-report. This implies that the most severely affected patients (those who died or who could not communicate) are excluded from these studies. As a result, these studies are exploring the association between physical activity and stroke severity in stroke survivors only. In contrast, our study is exploring whether physical activity influences functional outcome from stroke in an initially healthy population.

Although we did not have information on prestroke disability levels, men were most likely able-bodied at baseline because they had to be free of many major disabling diseases at baseline to be enrolled in the cohort. Additionally, an advantage to using the mRS as our measure of functional outcome from stroke is that it takes into account prestroke ability,16 and does not seem to demonstrate a “ceiling effect” like the Barthel Index. Finally, it can be assessed retrospectively through self-report. This implies that the most severely affected patients (those who died or who could not communicate) are excluded from these studies.

### Table 3. Multivariable-Adjusted ORs of Functional Outcomes According to Level of Physical Activity (N=21 794)*

<table>
<thead>
<tr>
<th>No TIA/stroke</th>
<th>TIA</th>
<th>mRS 0–1</th>
<th>mRS 2–3</th>
<th>mRS 5–6</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>Percent</td>
<td>No.</td>
<td>Percent</td>
<td>RR (95% CI)†</td>
</tr>
<tr>
<td>Total stroke</td>
<td>(n=761)</td>
<td>(n=429)</td>
<td>(n=708)</td>
<td>(n=241)</td>
</tr>
<tr>
<td>&lt;1 time/wk</td>
<td>5380</td>
<td>27.4</td>
<td>239</td>
<td>31.4</td>
</tr>
<tr>
<td>1 time/wk</td>
<td>3608</td>
<td>18.4</td>
<td>150</td>
<td>19.7</td>
</tr>
<tr>
<td>2–4 times/wk</td>
<td>7436</td>
<td>37.8</td>
<td>276</td>
<td>36.3</td>
</tr>
<tr>
<td>≥5 times/wk</td>
<td>3231</td>
<td>16.4</td>
<td>96</td>
<td>12.6</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>(n=761)</td>
<td>(n=386)</td>
<td>(n=634)</td>
<td>(n=116)</td>
</tr>
<tr>
<td>&lt;1 time/wk</td>
<td>5380</td>
<td>27.4</td>
<td>239</td>
<td>31.4</td>
</tr>
<tr>
<td>1 time/wk</td>
<td>3608</td>
<td>18.4</td>
<td>150</td>
<td>19.7</td>
</tr>
<tr>
<td>2–4 times/wk</td>
<td>7436</td>
<td>37.8</td>
<td>276</td>
<td>36.3</td>
</tr>
<tr>
<td>≥5 times/wk</td>
<td>3231</td>
<td>16.4</td>
<td>96</td>
<td>12.6</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>(n=761)</td>
<td>(n=30)</td>
<td>(n=73)</td>
<td>(n=118)</td>
</tr>
<tr>
<td>&lt;1 time/wk</td>
<td>5380</td>
<td>27.4</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>1 time/wk</td>
<td>3608</td>
<td>18.4</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>2–4 times/wk</td>
<td>7436</td>
<td>37.8</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>≥5 times/wk</td>
<td>3231</td>
<td>16.4</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

TIA indicates ischemic attack; mRS, modified Rankin Scale; RR, relative risk; CI, confidence interval; OR, odds ratio; NA, not applicable.

*Men who exercised <1 time/wk and who did not experience a stroke or TIA, served as the reference category.

†Values have also been adjusted for age, smoking status, alcohol consumption, parental history of myocardial infarction before age 60 y, and randomized treatment assignments.
Several limitations should be considered when interpreting our results. Although we have updated information on physical activity during follow-up, we only could dichotomize activity levels, which may lead to some misclassification. Additionally, we did not have information on the types and intensities of physical activity. Because this is an observational study, residual confounding may be present. Finally, although the homogeneity of the cohort improves our internal validity, it may limit the generalizability of our results to other male populations or women.

In conclusion, results of this large prospective study in men suggest that physical activity may help to reduce the risk of incident stroke, but there is little evidence that prestroke physical activity influences functional outcomes after stroke. Future research is warranted to explore whether specific types of physical activity or other lifestyle factors influence functional outcomes from stroke.

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Disclosures
None.

References
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Online Table. Multivariable-adjusted odds ratios of functional outcomes after cerebral vascular events according to baseline level of physical activity (N=21,794).*

<table>
<thead>
<tr>
<th></th>
<th>No TIA or stroke</th>
<th>TIA</th>
<th>MRS 0-1</th>
<th>MRS 2-3</th>
<th>MRS 5-6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td><strong>Total Stroke</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 time/wk</td>
<td>5380</td>
<td>27.4</td>
<td>127</td>
<td>29.6</td>
<td>1.00</td>
</tr>
<tr>
<td>≥1 time/wk</td>
<td>14275</td>
<td>72.6</td>
<td>302</td>
<td>70.4</td>
<td>0.88 (0.75, 1.04)</td>
</tr>
<tr>
<td><strong>Ischemic Stroke</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 time/wk</td>
<td>5380</td>
<td>27.4</td>
<td>115</td>
<td>29.0</td>
<td>1.00</td>
</tr>
<tr>
<td>≥1 time/wk</td>
<td>14275</td>
<td>72.6</td>
<td>281</td>
<td>71.0</td>
<td>0.88 (0.75, 1.04)</td>
</tr>
<tr>
<td><strong>Hemorrhagic Stroke</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 time/wk</td>
<td>5380</td>
<td>27.4</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>≥1 time/wk</td>
<td>14275</td>
<td>72.6</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

* CI denotes confidence interval. Men who exercised less than one time per week served as the reference category.
† Values have also been adjusted for age, smoking status, alcohol consumption, parental history of myocardial infarction before age 60, and randomized treatment assignment to aspirin and/or beta-carotene.
Online Table. Multivariable-adjusted odds ratios of functional outcomes after cerebral vascular events according to 36 month level of physical activity (N=20,997).*

<table>
<thead>
<tr>
<th></th>
<th>No TIA or stroke</th>
<th>TIA</th>
<th>MRS 0-1</th>
<th>MRS 2-3</th>
<th>MRS 5-6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
<td>RR (95% CI)†</td>
</tr>
<tr>
<td><strong>Total Stroke</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 time/wk</td>
<td>8149</td>
<td>42.7</td>
<td>329</td>
<td>48.8</td>
<td>1.00</td>
</tr>
<tr>
<td>≥1 time/wk</td>
<td>10933</td>
<td>57.3</td>
<td>345</td>
<td>51.2</td>
<td>0.86 (0.73, 1.00)</td>
</tr>
<tr>
<td><strong>Ischemic Stroke</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 time/wk</td>
<td>8149</td>
<td>42.7</td>
<td>329</td>
<td>48.8</td>
<td>1.00</td>
</tr>
<tr>
<td>≥1 time/wk</td>
<td>10933</td>
<td>57.3</td>
<td>345</td>
<td>51.2</td>
<td>0.86 (0.73, 1.00)</td>
</tr>
<tr>
<td><strong>Hemorrhagic Stroke</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 time/wk</td>
<td>8149</td>
<td>42.7</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>≥1 time/wk</td>
<td>10933</td>
<td>57.3</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

* CI denotes confidence interval. Men who exercised less than one time per week served as the reference category.
† Values have also been adjusted for age, smoking status, alcohol consumption, parental history of myocardial infarction before age 60, and randomized treatment assignment to aspirin and/or beta-carotene.
Online Table. Multivariable-adjusted odds ratios of functional outcomes after cerebral vascular events according to 108 month level of physical activity (N=19735). *

<table>
<thead>
<tr>
<th></th>
<th>No TIA or stroke</th>
<th>TIA</th>
<th>MRS 0-1</th>
<th>MRS 2-3</th>
<th>MRS 5-6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Total Stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 time/wk</td>
<td>7510</td>
<td>41.1</td>
<td>252</td>
<td>46.5</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>(n=542)</td>
<td></td>
<td></td>
<td></td>
<td>(95% CI)†</td>
</tr>
<tr>
<td>≥1 time/wk</td>
<td>10755</td>
<td>58.9</td>
<td>290</td>
<td>53.5</td>
<td>0.90</td>
</tr>
<tr>
<td></td>
<td>(n=239)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 time/wk</td>
<td>7510</td>
<td>41.1</td>
<td>252</td>
<td>46.5</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>(n=542)</td>
<td></td>
<td></td>
<td></td>
<td>(95% CI)†</td>
</tr>
<tr>
<td>≥1 time/wk</td>
<td>10755</td>
<td>58.9</td>
<td>290</td>
<td>53.5</td>
<td>0.90</td>
</tr>
<tr>
<td></td>
<td>(n=227)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| * CI denotes confidence interval. Men who exercised less than one time per week served as the reference category.  
† Values have also been adjusted for age, smoking status, alcohol consumption, parental history of myocardial infarction before age 60, and randomized treatment assignment to aspirin and/or beta-carotene.  
Due to the limited number of hemorrhagic stroke cases, we could not perform an analysis at 108 months.
Online Table. Multivariable-adjusted odds ratios of functional outcomes after stroke and stroke subtypes according to level of physical activity at baseline, 36 months and 108 months (N=11,497).*

<table>
<thead>
<tr>
<th></th>
<th>Total Stroke</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>MRS 0-1</td>
<td>MRS 2-3</td>
<td>MRS 5-6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(n=294)</td>
<td>(n=138)</td>
<td>(n=320)</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>No TIA or stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Always &lt;1 time/wk</td>
<td>2919</td>
<td>27.4</td>
<td>101</td>
<td>34.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Always ≥1 time/wk</td>
<td>7740</td>
<td>72.6</td>
<td>193</td>
<td>65.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Always &lt;1 time/wk</td>
<td>2919</td>
<td>27.4</td>
<td>101</td>
<td>34.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Always ≥1 time/wk</td>
<td>7740</td>
<td>72.6</td>
<td>193</td>
<td>65.6</td>
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</tr>
</tbody>
</table>

* CI denotes confidence interval. Men who exercised less than one time per week served as the reference category.
† Values have also been adjusted for age, smoking status, alcohol consumption, parental history of myocardial infarction before age 60, and randomized treatment assignment to aspirin and/or beta-carotene.

Due to the limited number of hemorrhagic stroke cases, we could not perform this analysis for hemorrhagic stroke.