Physical Activity and Ischemic Stroke Risk

The Atherosclerosis Risk in Communities Study

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Background and Purpose—The relationship between physical activity and stroke is inconclusive according to the 1996 US Surgeon General’s Report on Physical Activity and Health. Therefore, this study examined the relationship between physical activity and ischemic stroke risk among 14 575 Atherosclerosis Risk in Communities Study participants aged 45 to 64 years free of self-reported stroke and coronary heart disease at baseline.

Methods—Eligible potential stroke hospitalizations were identified from ongoing hospital surveillance and from hospitalizations reported by the cohort study participants. All strokes were validated by hospitalization records. Physical activity was measured as sport, leisure (nonsport), and work with the use of the Baecke questionnaire. Multivariable Poisson and Cox proportional hazards models were used to determine the association of differing levels of physical activity with ischemic stroke incidence.

Results—During an average of 7.2 years of follow-up, 189 incident ischemic strokes occurred. Ischemic stroke incidence rates were highest in the lowest quartile of sport, leisure, and work scores. The hazard rate ratios with 95% CIs for ischemic stroke for the highest quartile compared with the lowest quartile of activity adjusted for age, sex, race-center, education, and smoking, were sport 0.83 (0.52, 1.32), leisure 0.89 (0.57, 1.37), and work 0.69 (0.47, 1.00). Further adjustment for factors that likely were intermediate variables (hypertension, diabetes, fibrinogen, and body mass index) between physical activity and stroke attenuated the associations.

Conclusions—Our findings suggest that physical activity was weakly associated with a reduced risk of ischemic stroke among middle-aged adults. The association may be due to links between physical activity and other risk factors or due to chance. (Stroke. 1999;30:1333-1339.)

Key Words: epidemiology ■ leisure activities ■ stroke, ischemic ■ stroke prevention

Stroke is the third leading cause of mortality and the leading cause of neurological disability in the United States. The burden of stroke is heterogeneous, with blacks sustaining much higher death rates and incidence rates than whites. This difference persists even after controlling for several stroke risk factors, indicating that there may be other factors that account for the excess stroke burden.

While there is evidence relating physical activity to established stroke risk factors, such as hypertension, evidence relating physical activity to stroke incidence is inconclusive. Kohl and McKenzie concluded that “the currently available data are equivocal concerning the role that physical activity and physical fitness may play in the risk of stroke.” The American Heart Association 1996 Task Force on Prevention and Rehabilitation of Stroke recommended that researchers “clarify the relation between stroke risk and physical activity.” In the 1996 Surgeon General’s Report on Physical Activity and Health, reviewers concluded that “the existing data do not unequivocally support an association between physical activity and risk of stroke.” Therefore, the main objective of this study was to determine whether physical activity was related to ischemic stroke risk in a cohort of men and women aged 45 to 64 years at baseline.

Subjects and Methods

Study Population

The Atherosclerosis Risk in Communities (ARIC) Study is a prospective investigation into the etiology and natural history of atherosclerosis. The cohort comprised 15 792 individuals aged 45 to 64 years at recruitment in 1986–1989. Population samples were selected from 4 communities (Washington County, Maryland; northwest suburbs of Minneapolis, Minn; Jackson, Miss; and Forsyth County, North Carolina). Only blacks were enrolled from the Jackson site, while the remaining 3 samples approximately reflected the demographics of the communities from which they were chosen.

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Participation rates for the home interview and clinic examination were 46% at Jackson and 65% to 67% at the 3 remaining sites. ARIC participants attended a clinic visit triennially and received a follow-up telephone call yearly.

Ascertainment of Incident Stroke Events
Details of the identification and classification of stroke events are detailed elsewhere and are reviewed briefly here. Cohort members were contacted by telephone annually to record hospitalizations over the previous year. Eligible potential stroke hospitalizations were also identified from ongoing community-wide hospital surveillance in the study area and from hospitalizations reported by the study participants. Complete medical records of potential cases were obtained and abstracted.

Each potential case was assessed by a computerized diagnostic algorithm and a physician reviewer. The computer algorithm used information abstracted from the medical record, including the number, type, severity, and duration of neurological deficits as well as any angiographic, CT, MRI, spinal tap, or autopsy evidence. The algorithm was designed to simulate clinical judgment in distinguishing nonvascular from vascular events and helped to establish a standardized method for evaluating events over time at each field center. The physician reviewer made an independent stroke diagnosis after reviewing CT and MRI evidence, neurological consultation reports, discharge summary, and other detailed clinical findings based on a summary of the medical record. Final classification was established when the computer algorithm and the physician reviewer agreed. Disagreements on event classification were adjudicated by a second physician reviewer.

Strokes were classified as ischemic, hemorrhagic, undetermined type, or fatal out-of-hospital stroke. We were unable to examine incident hemorrhagic stroke because of the small number of events (n = 26 for intracerebral and n = 17 for subarachnoid). Out-of-hospital fatal strokes (n = 2) and strokes of undetermined type (n = 9) were also excluded from these analyses.

Physical Activity Measurement
Physical activity was assessed at the baseline examination with the use of the Baecke questionnaire. The questionnaire was interviewer administered and yielded ordinal scores for sport, leisure, and work from 1 (low) to 5 (high). The number of possible values for each score was 17 for sport, 15 for leisure, and 32 for work. A few modifications to the original version of the Baecke questionnaire were made and are detailed elsewhere. The validity and reliability of the questionnaire were evaluated in several other populations and summarized elsewhere.

The sport score was derived from 3 questions regarding frequency of overall sport and exercise participation, frequency of sweating, and a subjective comparison of physical activity to others one’s own age. A fourth component on frequency, intensity, and duration of up to 4 activities also contributed to the sport score. The leisure score was designed to capture nonsport leisure activity and consisted of 4 questions on television viewing, biking, walking, and time spent walking and biking to and from work or shopping. The work score was calculated from 8 items. Individuals were asked how often while at work do they sit, stand, walk, lift heavy loads, sweat, and leave work physically tired. They were also asked to compare their work activity to others one’s own age. The last component of the work score consisted of a ranking (low, medium, or high) of activity based on occupational job title. Individuals classifying their primary occupation as homemaker were not asked their job title and therefore assigned a low-intensity job level for this component question. Individuals not reporting any occupational activity were assigned a work score of 1.

Other definitions for leisure activity were also used for these analyses. Vigorous activity was classified if participants reported at least 1 sport that was assigned as vigorous according to standard exercise intensities. Regular vigorous activity was defined as participation in a vigorous activity for at least 1 hour per week for ≥10 months per year. Arm exercise was defined as participation in any exercise or sport activity involving arm work (aerobics, swimming, weight lifting, gymnastics, martial arts, cross-country skiing, wrestling, canoeing, gardening, yard work, shoveling, or wood cutting) or work activity involving lifting heavy loads often or very often.

Cardiovascular and Demographic Measures
Participants were asked to fast 12 hours before clinic examination for an antecubital vein blood draw. Specimens were collected into vacuum tubes containing silicon for glucose, EDTA for lipid measurement, and sodium citrate for fibrinogen. Glucose was measured by a hexokinase/glucose-6-phosphate dehydrogenase method on a Coulter DACOS device. Diabetes mellitus was defined as a fasting glucose level ≥126 mg/dL, nonfasting glucose level ≥200 mg/dL, or history of and/or treatment for diabetes mellitus. Total and HDL cholesterol levels were measured by enzymatic procedures with reagents supplied by Boehringer Mannheim Biochemical, adapted for analysis in the Cobas-Bioanalyzer (Roche). LDL cholesterol was calculated by the Friedewald formula. Fibrinogen was analyzed at the ARIC Central Hemostasis Laboratory at the University of Texas Health Science Center in Houston with the use of a clotting time–based assay. Uric acid was assayed by the method of Haeckel. Hemoglobin (in percentage) and hematocrit (in grams per liter) were measured at local hematology laboratories.

Height and weight were measured with the participant in light clothing without shoes. After a 5-minute rest period, sitting blood pressure was measured 3 times with a standardized Hawksley random-zero sphygmanometer. The fifth phase of Korotkoff sounds was used to mark diastolic blood pressure. The average of the second and third measures, with 30 seconds of rest between measures, was used in this study. Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or antihypertensive medication use in the past 2 weeks.

Prevalent coronary heart disease was defined as history of any of the following: coronary artery bypass surgery, any balloon angioplasty, or myocardial infarction based on ECG or self-report. Prevalent stroke was self-reported at the baseline examination. Smoking and alcohol consumption were defined categorically as current, former, or never. Education was self-reported at the home interview and defined for these analyses categorically by years of education (less than high school, high school, or greater than high school).

Statistical Methods
Among the 15,792 individuals attending the initial examination, we excluded participants not identifying themselves as black or white (n = 48) and blacks from Minneapolis (n = 22) or Washington County (n = 33) to adjust for race and center simultaneously. Participants with missing information on physical activity (n = 75), education (n = 26), or follow-up (n = 2) and individuals with a positive or unknown history of stroke (n = 317) or positive history of coronary heart disease at baseline (n = 694) were also excluded, leaving 14,575 ARIC participants for these analyses.

With the use of multivariable linear and unconditional logistic regression, sex-specific baseline adjusted means or percentages of potential risk factors were compared across quartiles of the Baecke scores. A corresponding P value for linear trend was calculated. Similar calculations were performed to compare adjusted means and percentages of Baecke scores between those who did and did not develop an ischemic stroke over the follow-up period. For all quartile analyses, the Baecke scores were divided as follows: sport 1.75/2.25/3.36, leisure 2.25/2.5/2.75, and work 1.25/2.25/2.875. Because of the semicontinuous nature of the Baecke scores, these cut points approximated quartile categories.

Multivariable Poisson regression was used to estimate adjusted incident ischemic stroke incidence rates and corresponding rate ratios. Multivariable Cox proportional hazards models were used to determine the association of differing levels of physical activity with ischemic stroke incidence. For participants with an ischemic stroke event, follow-up time was defined as the number of days from the first examination visit to the hospital admission date of the first stroke. For participants without an ischemic stroke, follow-up time was defined as the number of days from the first examination visit to
TABLE 1. Sex-Specific Means or Percentiles of Baseline Risk Factors According to Cohort-Specific Quartiles* of the Baecke Sports Score, Adjusted for Age, Race-Center, and Education

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Women (n=8296)</th>
<th>Men (n=6279)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Quartile 1 (n=2683)</td>
<td>Quartile 2 (n=2095)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>28.2</td>
<td>27.8</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>219.6</td>
<td>220.3</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>56.6</td>
<td>57.4</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td>137.5</td>
<td>138.0</td>
</tr>
<tr>
<td>Fibrinogen, mg/dL</td>
<td>314.3</td>
<td>308.1</td>
</tr>
<tr>
<td>Uric acid, mg/dL</td>
<td>5.5</td>
<td>5.5</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>39.7</td>
<td>39.6</td>
</tr>
<tr>
<td>Hemoglobin, g/L</td>
<td>13.2</td>
<td>13.2</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>38.4</td>
<td>35.2</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>12.9</td>
<td>11.4</td>
</tr>
<tr>
<td>Current drinker, %</td>
<td>48.5</td>
<td>50.2</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>26.6</td>
<td>24.5</td>
</tr>
</tbody>
</table>

*Sport quartiles are divided at 1.75, 2.25, and 3.
†Value for linear trend.

Results

Over an average of 7.2 years of follow-up, 189 incident ischemic stroke events occurred among the cohort at risk. Ninety-six incident ischemic strokes occurred among women, and 93 occurred among men. Furthermore, 87 incident ischemic strokes occurred among black participants, and 102 occurred among white participants.

Risk Factors by Physical Activity and Ischemic Stroke Status

Table 1 displays sex-specific risk factor means or percentiles according to quartiles of the sport score, adjusted for age, race-center, and education. Body mass index, fibrinogen, hematocrit, hypertension, and prevalence of current smoking decreased as sport quartiles increased for both men and women. HDL cholesterol increased across sport quartiles for both men and women. Uric acid and prevalence of diabetes declined across sport quartiles for women. When we examined the percentage of participants with less than a high school education across sport quartiles, adjusting for age and race-center, the results from lowest to highest quartiles were 24.0%, 26.8%, 19.1%, and 16.4% for women (P=0.0001) and 31.3%, 31.5%, 20.3%, and 14.1% for men (P=0.0001).

Sex-specific risk factor means or percentiles by incident ischemic stroke status were also calculated, with adjustment for age, race-center, and education (data not shown). For men and women, ischemic stroke incidence was significantly related to higher baseline fibrinogen, systolic blood pressure, diastolic blood pressure, hypertension, and diabetes. Among women, ischemic stroke was also significantly related to elevated uric acid, hematocrit, hemoglobin, and total and LDL cholesterol and to lower HDL cholesterol. Among men, ischemic stroke was also significantly related to a higher prevalence of current smoking at baseline.

Ischemic Stroke Incidence Rates by Physical Activity

Ischemic stroke incident rates were calculated for the study population overall and stratified by sex, with adjustment for age, race-center, and education. When the lowest (less active) to the highest (more active) quartiles of Baecke scores were compared, incidence rates per 1000 person-years were as follows: sport 2.00 (95% CI, 1.52, 2.62) versus 1.65 (95% CI, 1.13, 2.40), leisure 2.09 (95% CI, 1.63, 2.68) versus 1.75 (95% CI, 1.21, 2.54), and work 2.45 (95% CI, 1.90, 3.16) versus 1.82 (95% CI, 1.33, 2.47). The highest ischemic stroke incidence rates occurred in the lowest quartile for sport, leisure, and work scores. For men the highest incidence rates occurred in the lowest quartile for sport, leisure, and work scores, with a decline in incidence with increasing quartiles for sport and leisure scores. Among women, incidence rates were highest in the lowest quartile of work activity. However, for women consistent patterns were not identified across sport or leisure scores.

Physical Activity and Ischemic Stroke Risk

Mean Baecke scores were calculated according to incident ischemic stroke status by sex, with adjustment for age, race-center, and education (Table 2). Mean baseline sport and work scores were lower, implying less activity, among participants who had an ischemic stroke over the follow-up period than among those who did not. However, when the sample was reduced to include only those working, work scores among those who subsequently had an ischemic stroke...
were higher than for those not having an ischemic stroke over the follow-up period. The pattern for leisure scores was not consistent across sex.

The hazard rate ratios of ischemic stroke for a 1-unit change in physical activity scores are reported in Table 3. The basic model adjusted for demographic factors and smoking, while the full model adjusted further for factors that likely were intermediate variables. From the basic model, age, sex, education, and smoking were not significant effect modifiers. Alcohol, height, total cholesterol, HDL cholesterol, LDL cholesterol, uric acid, hematocrit, and hemoglobin were dropped from the full models since they did not confound or modify the relationship between physical activity and ischemic stroke. Among the vascular factors that were retained (hypertension, fibrinogen, body mass index, and diabetes), none of these were significant effect modifiers.

For the basic models, hazard ratios for sport, leisure, and work scores overall were <1 for ischemic stroke incidence. However, the pattern of risk was not consistent across all strata. Among women, the hazard ratio for the work score was significantly <1 for ischemic stroke incidence. When the total cohort was stratified by ethnicity, ischemic stroke incidence declined with increasing Baecke scores for blacks, while among whites the pattern was less consistent. When the cohort was reduced to workers only, the hazard ratio for the work scores was above the null except among blacks.

Our full models adjusted for factors that were likely intermediate variables in the “causeway” between physical activity and stroke risk. Accordingly, hazard ratios were attenuated when adjusted further for hypertension, diabetes, fibrinogen, and body mass index. Whether continuous sport, leisure, or work indices were examined, quadratic terms and quadratic splines (1 knot at median or 2 knots evenly spaced) did not significantly add to the Cox proportional hazard models according to likelihood ratio tests.

The risk of ischemic stroke was further examined by quartiles of the Baecke score, with adjustment for age, race-center, sex, education, and smoking (Figure). A consis-

### TABLE 2. Sex-Specific Baecke Scores According to Incident Ischemic Stroke With 95% CIs, Adjusted for Age, Race-Center, and Education

<table>
<thead>
<tr>
<th>Baecke Score</th>
<th>Women Ischemic Stroke</th>
<th>Men Ischemic Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n=86)</td>
<td>No (n=8200)</td>
</tr>
<tr>
<td>Sport</td>
<td>2.32 (2.17, 2.46)</td>
<td>2.34 (2.32, 2.35)</td>
</tr>
<tr>
<td>Leisure</td>
<td>2.44 (2.33, 2.55)</td>
<td>2.39 (2.38, 2.40)</td>
</tr>
<tr>
<td>Work</td>
<td>1.76 (1.58, 1.95)</td>
<td>2.02 (2.00, 2.04)</td>
</tr>
<tr>
<td>(n=39)</td>
<td></td>
<td>(n=5224)</td>
</tr>
<tr>
<td>Work among workers</td>
<td>2.71 (2.51, 2.91)</td>
<td>2.65 (2.63, 2.67)</td>
</tr>
</tbody>
</table>

### TABLE 3. Multivariable* Hazard Rate Ratios of Incident Ischemic Stroke per 1-Unit Increase in Baecke Scores With 95% CIs

<table>
<thead>
<tr>
<th></th>
<th>Sport</th>
<th>Leisure</th>
<th>Work</th>
<th>Work Among Workers†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (n=14 575)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic</td>
<td>0.94</td>
<td>0.92</td>
<td>0.86</td>
<td>1.22 (0.90, 1.66)</td>
</tr>
<tr>
<td>Full</td>
<td>1.03</td>
<td>0.99</td>
<td>0.94</td>
<td>1.26 (0.92, 1.71)</td>
</tr>
<tr>
<td>Women (n=8296)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic</td>
<td>0.98</td>
<td>1.20</td>
<td>0.76</td>
<td>1.19 (0.72, 1.97)</td>
</tr>
<tr>
<td>Full</td>
<td>1.11</td>
<td>1.29</td>
<td>0.88</td>
<td>1.13 (0.68, 1.90)</td>
</tr>
<tr>
<td>Men (n=6279)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic</td>
<td>0.89</td>
<td>0.70</td>
<td>0.98</td>
<td>1.27 (0.87, 1.87)</td>
</tr>
<tr>
<td>Full</td>
<td>0.95</td>
<td>0.74</td>
<td>1.02</td>
<td>1.33 (0.91, 1.96)</td>
</tr>
<tr>
<td>Black (n=3885)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic</td>
<td>0.76</td>
<td>0.70</td>
<td>0.90</td>
<td>0.93 (0.60, 1.44)</td>
</tr>
<tr>
<td>Full</td>
<td>0.85</td>
<td>0.73</td>
<td>1.06</td>
<td>0.97 (0.63, 1.50)</td>
</tr>
<tr>
<td>White (n=10 690)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic</td>
<td>1.03</td>
<td>1.20</td>
<td>0.80</td>
<td>1.53 (1.01, 2.32)</td>
</tr>
<tr>
<td>Full</td>
<td>1.12</td>
<td>1.27</td>
<td>0.84</td>
<td>1.58 (1.04, 2.41)</td>
</tr>
</tbody>
</table>

*Basic models are adjusted for age, race-center, sex, education, and smoking (former, current, never) except where stratified by the factor. Full models are adjusted for age, race-center, sex, education, smoking (former, current, never), hypertension, fibrinogen, body mass index, and diabetes except where stratified by the factor.

†Sample sizes and events are reduced among workers.
tent monotonic trend was not evident when sport, leisure, or work scores were examined, although hazard ratios remained <1 across quartiles of activity. Further adjustment for hypertension, diabetes, fibrinogen, and body mass index attenuated the results (data not shown).

We also examined other components of physical activity to understand its association with stroke risk, adjusting for age, race-center, sex, education, and smoking. Both participation in any leisure activity (0.87; 95% CI, 0.64, 1.18) and walking often or very often during leisure (0.87; 95% CI, 0.60, 1.26) were inversely but not significantly associated with ischemic stroke risk. However, vigorous activity (1.11; 95% CI, 0.67, 1.84) and regular vigorous activity (1.21; 95% CI, 0.56, 2.59) were not. Arm exercise or lifting heavy loads often or very often was inversely related to ischemic stroke risk for women (0.79; 95% CI, 0.45, 1.39) but not for men (1.07; 95% CI, 0.68, 1.67). Among workers, lifting heavy loads often or very often was also inversely related to ischemic stroke risk for women (0.53; 95% CI, 0.16, 1.74) but not for men (1.43; 95% CI, 0.74, 2.76).

Discussion

We found that among 14,575 individuals followed for an average of 7.2 years, physical activity was weakly associated with a lower ischemic stroke risk. Although associations between physical activity and ischemic stroke incidence were typically inverse, most did not reach statistical significance. When the relative risk of an ischemic stroke was examined by quartiles of physical activity, the lowest quartile of activity generally conferred the highest risk for an ischemic stroke. This finding is consistent with previous work in the ARIC cohort, which reported an inverse association between intimal-medial carotid wall thickness and both sport and work scores.24 Work scores were also inversely related to transient ischemic attacks or stroke symptomology in ARIC at the cross-sectional level.25

We attempted to examine the amount of physical activity required for optimum stroke benefit but failed to detect significant departures from linearity for any of the physical activity scores. Although several studies have identified a linear reduction in stroke risk with increasing intensity or duration of physical activity,26–33 others have reported U-shaped or no association between physical activity and stroke.34–47 The differences across studies may be due to imprecision in measurement of physical activity, confounding, study variation, or low statistical power or may represent evidence for only a weak association.

Differences in stroke risk reduction may exist according to type of activity. For example, in the Oslo Study a consistent trend was identified for leisure activity but not for occupational activity.48 We generally did not find major differences across Baecke scores, although there were some differences for work scores when the sample was reduced to only workers. Additionally, upper body exercise may have a different effect on the cerebral circulation, affecting the vertebral and carotid arteries differently than lower body exercise such as in subclavian steal syndrome.49,50 We found that arm exercise during leisure or work was inversely related to stroke incidence among women but not among men.

Physical activity may affect stroke differently, depending on the event type. Physical activity may play direct and indirect roles in atherosclerosis formation, thereby reducing ischemic stroke risk, and hemorrhagic stroke risk may be reduced through the long-term effect of physical activity on blood pressure.51,52 Differences in the association between physical activity and stroke type were examined in several studies and are generally consistent with a protective effect of physical activity for both ischemic33,41,42 and hemorrhagic stroke.33,41 However, in our study we were only able to examine relationships with ischemic stroke, since not enough hemorrhagic stroke cases had accrued. According to recent results from the ARIC Study,13 the 30-day case-fatality rate for ischemic strokes was ≈7%. Therefore, because of the small absolute number of stroke events and corresponding low statistical power, we were also unable to address whether survival from ischemic stroke was related to physical activity.

Several prospective cohort studies identified differences in the relationship between physical activity and stroke risk based on smoking status. In the Honolulu Heart Study,41 the Copenhagen City Heart Study,53,54 and the National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study (among white men),42 smokers did not attain the same benefit of activity as nonsmokers, indicating that the inverse association of physical activity with stroke risk may be diminished for those who smoke. In contrast, a case-control study reported that physical activity was inversely associated with stroke risk regardless of smoking status, with the strongest benefit among former smokers.55 In the Physicians’ Health Study, no difference in risk was found according to smoking status.53 Our data also did not support differing risks between stroke and physical activity by smoking status, whether sport, leisure, or work scores were examined, although the role of chance cannot be ruled out. Differences across published studies may be due to differing statistical power or some mismeasurement in smoking exposure between studies.

Our full statistical models containing vascular risk factors may be subject to overadjustment bias.56–58 Since physical activity is known to favorably influence body mass index, blood pressure, diabetes, and fibrinogen,10 these factors not only may confound the results but may also lie in the causal
pathway between physical activity and stroke risk. Indeed, we found that many of these vascular risk factors were related to physical activity (Table 1). Adjustment for these factors attenuated the hazard ratios, suggesting that any role of physical activity may likely operate through these factors, although both the basic and full models were generally nonsignificant. If physical activity acts both independently and through other factors to mediate stroke risk, then with current methodology it remains challenging to obtain an unbiased estimate of both effects. Regardless of the pathways, the public health view would argue for recommending a physically active lifestyle if a reduction in stroke risk resulted.

The ARIC cohort represents 4 US communities and includes a substantial number of black participants. This study used a clinically defined, validated diagnosis of stroke, which represents an improvement over previous work relying solely on self-report or discharge codes from hospital or death certificate records. A validated physical activity questionnaire was also used. Nevertheless, since physical activity was assessed only at the beginning of the study in these analyses, we must assume that this measure was a valid proxy for activity over the follow-up period. Most likely measurement error was nondifferential, and the impact would likely bias results toward the null value. There may also be other unmeasured confounders that we did not consider, such as self-perception of health. Additionally, there may be uncontrolled confounding of socioeconomic status, since education and self-perception of health. Additionally, there may be unmeasured confounders that we did not consider, such as self-perception of health. Furthermore, the "healthy worker effect" may have influenced our results when the analyses were reduced to workers only.

The number of Americans who sustain a stroke is likely to increase in the next 30 years because of a rise in older and minority populations. Prevention is a key factor in offsetting the anticipated rise in the number of stroke-related deaths. While the totality of our findings points to physical activity as being weakly associated with a reduction in ischemic stroke incidence among middle-aged adults, the role of associated risk factors or chance cannot be ruled out.

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