

# Risk of Recurrent Stroke and Death After First Stroke in Long-Distance Ski Race Participants

Ulf Hållmarker, MD; Signild Åsberg, MD, PhD; Karl Michaëlsson, MD, PhD; Johan Ärnlöv, MD, PhD; Dan Hellberg, MD, PhD; Johan Lindbäck, MSc; Per Wester, MD, PhD; Stefan James, MD, PhD

**Background**—Physical activity is of benefit for primary prevention of cardiovascular diseases, but it appears to increase the risk for atrial fibrillation. We aimed to study a cohort of patients following a first stroke in individuals with previous high physical activity, compare them to the general population with respect to recurrent stroke and death, and relate these to atrial fibrillation.

*Methods and Results*—From the participants of the Vasaloppet, the world's largest ski-race, and matched individuals from the general population (n=708 604), we identified 5964 patients hospitalized with a first-time stroke between 1994 and 2010. Individuals with severe diseases were excluded. One half percent of skiers and 1% of nonskiers were hospitalized due to stroke. The incidence rate was 8.3 per 100 person-years among skiers and 11.1 among nonskiers. The hazard ratio (HR) for recurrent stroke or death between the 2 groups was 0.76 (95% Cl 0.67 to 0.86). The result was consistent in subgroups. The HR for death was 0.66 (95% Cl 0.56 to 0.78) and for recurrent stroke 0.82 (95% Cl 0.70 to 0.96). After adjustment for smoking and socioeconomic factors, the HR for death was consistent at 0.70 (95% Cl 0.56 to 0.87) while the HR for recurrent stroke was not statistically significant. Outcomes for skiers with atrial fibrillation tended to show a lower risk than for nonskiers.

*Conclusions*—This large cohort study supports the hypothesis that patients with a stroke and with prior regular physical activity have a lower risk of death, while their risk for recurrent stroke is similar to that of nonskiers. The skiers had a higher incidence of atrial fibrillation, but still no increased risk of recurring stroke. (*J Am Heart Assoc.* 2015;4:e002469 doi: 10.1161/JAHA.115.002469)

Key Words: atrial fibrillation • cerebrovascular disease • cross-country skiing • epidemiology • lifestyle • physical activity • prevention • recurrent stroke • sports medicine • Sweden • Vasaloppet

H igher physical activity together with a healthy lifestyle have been shown to reduce the risk for cardiovascular diseases including stroke,<sup>1,2</sup> while recent studies report that long-term endurance sports practice is associated with an increased risk of atrial fibrillation (AF).<sup>3–5</sup> It is generally believed that embolic ischemic stroke associated with AF is

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more severe and more often fatal, and survivors are left more disabled than patients with other causes of stroke.<sup>6</sup>

The Vasaloppet is the largest cross-county ski race in the world. The race recruits both elite and recreational skiers. Among these skiers, a faster finishing time and a high number of completed races are associated with a future higher incidence of AF<sup>5</sup> that may theoretically increase the risk for embolic stroke. Yet, in contrast, the participants in the Vasaloppet have a substantially lower mortality rate compared with the general population.<sup>7</sup> There is a seemingly contradictory relationship between a high level off physical activity and risk of cardiovascular disease. Physically active and fit individuals appear to be protected against atherosclerotic artery disease<sup>8</sup> but at the same time have a higher risk of volume and pressure overload in their left atrium, leading to an increased risk for AF,<sup>3,4</sup> which may cause cardioembolic stroke.

We hypothesized that patients with a high level of physical activity prior to suffering stroke may have a lower risk of death, recurrent stroke, and myocardial infarction despite a higher incidence of AF. We also investigated

From the Departments of Medical Sciences (U.H., S.Å., J.Ä., S.J.), Surgical Sciences (K.M.), and Women's and Children's Health (D.H.) and Uppsala Clinical Research Center (S.Å., K.M., J.L., S.J.), Uppsala University, Uppsala, Sweden; Department of Internal Medicine, Mora Hospital, Mora, Sweden (U.H.); School of Health and Social Studies, Dalarna University, Falun, Sweden (J.Ä.); Department of Public Health and Medicine, Umeå University, Umeå, Sweden (P.W.).

**Correspondence to:** Ulf Hållmarker, MD, Department of Medical Sciences, Uppsala University, Uppsala, Sweden and Department of Internal Medicine, Mora Hospital, 792 85 Mora, Sweden. E-mail: ulf.hallmarker@ltdalarna.se

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whether these patients with a high level of physical activity suffer a less severe stroke with more favorable outcomes after stroke recurrence. Among patients with a high level of physical activity, we wanted to investigate whether there is a dose–response relationship between fitness and outcomes.

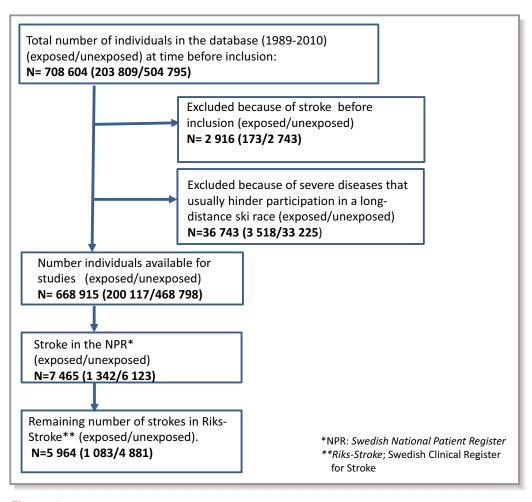
## **Methods**

# The Vasaloppet Register and the Swedish Stroke Register

The Vasaloppet is a long-distance cross-country ski race with various distances that takes place over 1 week annually in Sweden. From 1989 to 2010, 126 362 males (62%) and 77 447 females (38%) participated in at least 1 of the races. The majority (55%) of the skiers participated in the classic 90-km race and the rest in the 30- or 45-km races. The *Vasaloppet Register* has information about year and distance for each race, name, Swedish personal identification number,

address, number of races, and finish time, which is also presented as a percentage of the winner's time.

Participants in the Vasaloppet over the age of 19 were included in our cohort and were denoted as skiers (n=203 809 unique individuals). Each skier frequently participated in several races (on average 2.5 races per skier). Men and women from the general population in Sweden were randomly selected from the Total Population Register and frequency-matched to the skiers by age (5-year categories), sex, county of residence, and year of the ski race. They were denoted as nonskiers. Individuals with prior history of stroke were excluded from the cohort. We additionally excluded skiers and nonskiers with a history of severe disease<sup>8</sup> who therefore were unlikely to have been able to participate in the race. This exclusion list included chronic neurological, cardiovascular, psychiatric, and cancer diseases. The number of selected nonskiers was n=504 795. These nonskiers together with the skiers constitute the Vasaloppet cohort with a total number of 708 604 participants (Figure 1).



**Figure 1.** Flowchart describing the total number of individuals in Vasaloppet cohort before and after exclusions. From those availble for studies the number of first stroke is shown.

The *Swedish Stroke Register* is a national clinical quality register for stroke care and was initiated in 1994. Since 1994, it has retrieved data from all Swedish hospitals admitting patients with acute stroke.<sup>9</sup> The *Swedish Stroke Register* identifies the stroke hospitalizations and provides data on cardiovascular risk factors (such as AF, hypertension, diabetes, previous stroke, and smoking), level of consciousness on admission, living conditions, activities of daily living (ADL), and data on drug therapy both on admission and at discharge. The estimated coverage of acute stroke events in the *Swedish Stroke Register* varied during the study period between 80% and up to 96%.<sup>9</sup>

#### **Study Population**

We know from a published survey<sup>10</sup> and other studies published about the Vasaloppet cohort<sup>5,7,8,10,11</sup> that the long-distance skiers as a group have a healthier lifestyle, including less smoking, a diet of more fruits and vegetables, less obesity, and a higher level of physical activity compared with the general population. For example, 60% of skiers practice physical training more than 4 hours per week, while 17% of the general population were exercising for up to 1.5 hours per week. Information about all skiers between 1989 and 2010 was available in the *Vasaloppet Registry*.

From the Vasaloppet cohort, we identified patients with an index of stroke and recurrent stroke events, both ischemic and hemorrhagic, in the *Swedish Stroke Register* from 1994 on. This resulted in a study population of 1083 skiers and 4881 nonskiers with a first-time stroke.

#### **Other Registers**

By using the individual personal identification numbers provided to all Swedish citizens, we were able to link information from the Vasaloppet cohort with information retrieved from several different nationwide registers. Beginning in 1964, the Swedish *National Patient Register* (NPR) has included dates of admission and discharge, as well as primary and secondary diagnoses. The registry has been complete since 1987.<sup>12</sup> The *Causes of Death Register* (CDR), established in 1961, contains the date and underlying cause of death as well as contributing causes. *Statistics Sweden* contains socioeconomic data for all Swedish citizens, including information about education, occupation, and civil status.

#### Variables and Outcome

Data on previous stroke, AF, hypertension, diabetes mellitus, and medications were retrieved from the *National Patient Register* and the *Swedish Stroke Register*. Information about activities of daily living (ADL), quality of life, and smoking were obtained from the *Swedish Stroke Register*, and all other comorbidities from the *National Patient Register*.

The Charlson comorbidity index was calculated to compare degree of comorbidity between the groups.<sup>13</sup> The main outcome was death and recurrent stroke. The secondary outcome was myocardial infarction and combinations of the outcome events (Table 1).

#### Statistical Analyses

The subjects were followed from the diagnosis of stroke either to the date of an event or end of follow-up (December 31, 2010), maximum 10 years with median 2.3 years. Incidence rates were estimated as the number of events divided by the total follow-up time. For the analysis of recurrent stroke, we also performed a competing risk analysis, with death as a competing risk, leading to materially unaltered results. We therefore decided to present the results from the simpler Coxregression model.

Table 1. Events (In	ncidence Rates) and	d Unadjusted and Adjusted	HR With Corresponding 95% Cl
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	Nonskiers Events (%/py*)	Skiers Events (%/py*)	HR [95% CI]	Adj HR <sup>†</sup> [95% CI]	Adj HR <sup>‡</sup> [95% CI]
Death	1089 (5.8)	163 (3.8)	0.66 [0.56, 0.78]	0.71 [0.57, 0.88]	0.70 [0.56, 0.87]
Death/re-stroke	1744 (11.1)	303 (8.3)	0.76 [0.67, 0.86]	0.86 [0.74, 1.00]	0.88 [0.75, 1.03]
Death/re-stroke/MI	1825 (11.9)	323 (9.0)	0.77 [0.69, 0.87]	0.88 [0.76, 1.02]	0.91 [0.78, 1.05]
Re-stroke	941 (6.0)	177 (4.8)	0.82 [0.70, 0.96]	0.96 [0.79, 1.17]	1.02 [0.84, 1.24]
MI	261 (1.4)	203 (1.0)	0.69 [0.50, 0.96]	0.74 [0.47, 1.15]	0.85 [0.54, 1.33]
Re-stroke/MI	1086 (7.1)	177 (5.6)	0.81 [0.70, 0.94]	0.95 [0.79, 1.14]	1.02 [0.85, 1.23]

Analysis is based on 4614 cases with nonmissing data. CI indicates confidence interval; HR, indicates hazard ratios; MI, myocardial infarction; nonskiers, population-based controls with the same age, sex, and same county of residence; Re-stroke, recurrent stroke; skiers, the participants in the Vasaloppet.

\*Incidence rate per 100 person-years.

<sup>‡</sup>Adjusted for age, sex, education, family and occupation status, smoking, hypertension, and diabetes.

<sup>&</sup>lt;sup>†</sup>Adjusted for age, sex, education, family and occupation status, and smoking.

Cox regression models were used to compare the eventfree survival probability between those exposed to the Vasaloppet (skiers), and those not exposed (nonskiers). The proportional hazard assumptions were confirmed graphically. We used the directed acyclic graph approach<sup>14</sup> to select suitable covariates for the multivariable model.

The model included age (continuous), race year (1994-2000, 2001-2005, 2006-2010), sex, smoking habits (never, ex-smoker, current), education (primary school, high school, university), family (single), and occupational status (employed, unemployed, retired). Since hypertension and diabetes mellitus may be considered as confounding factors or in fact part of the lifestyle we are studying, we therefore reported the results in models with and without these factors (Table 1). We did not include type of discharge medication in the primary model as we regard these as a consequential part of the stroke. AF was registered on admission, which made it possible to perform stratified analyses by AF status. Finally, we included data on the ADL situation, health assessment, and discharge medication to attempt to estimate the severity of the stroke for skiers and nonskiers. All analyses were done using the R environment for statistical computing (version 3.0).15

The institutional Review Board (The Ethics Committees) at Uppsala University (Uppsala Dnr 2010/305, 2012/067 and Stockholm Dnr 2011/030) approved this Registry study under a waiver of informed consent. The approval included merging databases after anonymizing the data.

# Results

Baseline data for the first stroke in the study population of 1083 skiers and 4881 nonskiers is shown for both groups in Table 2. Age and sex were similar by design. Eighty-three percent were men and the median age at the time of the stroke was 64. Skiers had a higher educational level, reported less smoking, and had AF more often. Nonskiers had diabetes and hypertension more often. Drugs on admission to the hospital and at follow-up are shown in Tables 2 and 3. The discharge and follow-up frequencies are shown in Table 3. Nonskiers experienced worse health and more depression, had worse ADL functions, and were taking more pharmaceutical agents for the prevention of cardiovascular diseases. However, warfarin was prescribed more frequently to the skiers and this group also had more AF.

The total number of all-cause deaths or recurrent stroke rate was 2047. The incidence rate was 8.3 per 100 personyears among skiers and 11.1 among nonskiers. The unadjusted HR for recurrent stroke or death between skiers and nonskiers was 0.76 (95% CI: 0.67 to 0.86). The result was consistent in subgroups (Figure 2). After adjustment for smoking and socioeconomic factors, the HR for primary outcomes was 0.86 (95% CI: 0.74 to 1.00). The HR for death was 0.70 (95% CI: 0.56 to 0.87) while the HR for recurrent stroke was 0.96 (95% CI: 0.79 to 1.17) and not statistically significant (Table 1).

## Atrial Fibrillation (AF)

AF at the first stroke was more common among skiers compared with nonskiers, 20.4% and 14.7%, respectively (Table 2). However, skiers still had a lower incidence rate of recurrent stroke compared with the age-matched nonskiers, 4.8% and 6%, respectively (Table 1). The incidence rates for death or recurring stroke, as well as for a combination of these, were all higher for subjects with AF compared with those without AF. This was the case for both skiers and nonskiers (Figure 3).

#### **Dose–Response**

Among the skiers, we also studied the dose-response relationship with the finish time in relation to the winner's time, as a proxy measure of physical fitness and training intensity in a separate model shown in Figure 4. Overall there was an association showing a lower risk for death and recurrent stroke for skiers with better performance. However, there appeared to be a sex difference with a more obvious association between race time and outcome for women.

# Discussion

#### **Principal Findings**

The main finding is that stroke patients who had been physically active, as evidenced by their participation in a longdistance cross-country ski race, were associated after adjustment with a 29% relative risk reduction of all-cause death and no significant risk difference for recurrent stroke compared with less physically active stroke patients (nonskiers) despite a higher prevalence of AF. Skiers poststroke had better ADL functions, were less depressed, less help dependent, rated their health higher, and used fewer medications (Table 3). Skiers had AF more often and consequently used more warfarin. The effectiveness of anti-vitamin K treatment and compliance is generally very high in Sweden. There is likely no difference between skiers and nonskiers.<sup>16</sup> After adjustment for confounders such as socioeconomic data and smoking, the association remained essentially unchanged for death but the risk for recurrent stroke was similar for skiers and nonskiers. Interestingly, there appeared to be a dose-response relationship, suggesting that among individual

#### Table 2. Baseline Characteristics

	N*	Nonskiers N=4881	Skiers N=1083	₽ Value <sup>†</sup>
Male	5964	4062 (83.2)	888 (82.0	0.33 <sup>1</sup>
Age	5964	64.0 (24.0 to 99.0)	64.0 (25.0 to 96.0)	0.20 <sup>2</sup>
Smokers	4689	1066 (27.8)	61 (7.2)	<0.0011 <sup>1</sup>
Education level	5911			<0.001 <sup>1</sup>
Primary school		1962 (40.6)	249 (23.0)	
High school		2019 (41.8)	429 (39.7)	
University		849 (17.6)	403 (37.3)	
Occupation level	5962			<0.001 <sup>1</sup>
Unemployed		1102 (22.6)	102 (9.4)	
Employed		2209 (45.3)	591 (54.6)	
Retired		1568 (32.1)	390 (36.0)	
Family status: single	6964	2033 (41.7)	325 (30.0)	< 0.001 <sup>1</sup>
Living alone	5912	1522 (31.4)	228 (21.3)	<0.001 <sup>1</sup>
Mobility without assistance	5930	4705 (97.0)	1057 (98.1)	0.092 <sup>1</sup>
Dressing: need help	5922	125 (2.6)	137 (2.3)	0.004 <sup>1</sup>
Level of consciousness	5903			0.21 <sup>1</sup>
RLS 1		4218 (87.2)	952 (89.3)	
RLS 2 to 3		383 (7.9)	68 (6.4)	
RLS 4 to 8		150 (3.1)	26 (2.4)	
Charlson index: 1+	5964	1477 (30.3)	267 (24.7)	< 0.001 <sup>1</sup>
Atrial fibrillation <sup>‡</sup>	5658	679 (14.7)	212 (20.4)	< 0.0011 <sup>1</sup>
Race time p%		· · · ·		· · ·
100 to 150; m age 63 (33 to 92)			22 (20.2)	
151 to 200; m age 65 (30 to 93)			88 (24.9)	
>200; m age 63 (25 to 96)			65 (15.2)	
Diabetes <sup>‡</sup>	5274	947 (21.9)	63 (6.7)	<0.0011 <sup>1</sup>
Hypertension <sup>‡</sup>	5357	3633 (60.0)	446 (45.9)	< 0.0011 <sup>1</sup>
Admission treatments				· ·
Aspirin	5117	1014 (24.2)	203 (21.8)	0.111 <sup>1</sup>
Clopidogrel	4219	72 (2.1)	12 (1.5)	0.281 <sup>1</sup>
Aspirin+clopidogrel	4222	31 (0.9)	6 (0.8)	0.681 <sup>1</sup>
Dipyridamole	4221	35 (1.0)	13 (1.6)	0.141 <sup>1</sup>
Warfarin	5113	171 (4.1)	34 (3.7)	0.541 <sup>1</sup>
Calcium antagonists	4205	467 (13.7)	68 (8.6)	< 0.0011 <sup>1</sup>
ACE-inhibitors	2844	427 (18.5)	84 (18.8)	0.151 <sup>1</sup>
Angiotensin II-blockers	2843	232 (10.0)	37 (7.0)	0.0281 <sup>1</sup>
Diuretics	4206	533 (15.6)	72 (9.1)	< 0.001 <sup>1</sup>
Statins	4206	676 (19.8)	119 (15.0)	0.0021 <sup>1</sup>

Numbers represent frequencies with percentages in parentheses (age represents the median and range). Note that the denominator is different between variables due to partial missing of data. ACE indicates angiotensin-converting enzyme; m age, median age and range in parentheses; Nonskiers, population-based controls with the same age, sex, and same county of residence; Race time p%, race time as a percentage of the winner's time; RLS, reaction-level scale; Skiers, the participants in the Vasaloppet.

\*Number of nonmissing observations.

<sup>†</sup>Pearson  $\chi^2$  test<sup>1</sup> or Wilcoxon-Mann–Whitney test<sup>2</sup>.

<sup>‡</sup>Information from the Swedish Stroke Register and from Swedish National Patient Register (NPR).

#### Table 3. Discharge/Follow-Up Characteristics

	N*	Nonskiers N=4881	Skiers N=1083	P Value <sup>†</sup>
Severity of stroke	I			I
Mobility	5231			<0.001
Deceased		351 (8.3)	73 (7.5)	
No assistance		3271 (76.9)	819 (83.8)	
With assistance indoors		310 (7.3)	44 (4.5)	
With assistance $\ddagger$		322 (7.6)	41 (4.2)	
Need assistance for toilet visits	4812	385 (9.9)	51 (5.6)	<0.001
Dressing with assistance	4809	470 (12.0)	67 (7.4)	<0.001
Dependent	4066			0.001
Partially		1132 (34.3)	229 (29.9)	
Totally		292 (8.9)	49 (6.4)	
Speaking problems	2356	512 (27.1)	111 (23.8)	0.15
Depressive mode	4028			<0.001
Almost never		1438 (44.1)	418 (54.4)	
Sometimes		1477 (43.3)	306 (39.8)	
General health	3983			<0.001
Poor		67 (2.1)	9 (1.2)	
Bad		427 (13.2)	48 (6.3)	
Good		2181 (67.6)	499 (65.8)	
Very good		550 (17.1)	202 (26.6)	
Smoking 3474		398 (14.2)	24 (3.5)	<0.001
Discharge/follow-up treatments				
Hypertension treatment	3394	1989 (72.8)	383 (57.9)	<0.001
Warfarin	5003	411 (10.0)	132 (14.5)	<0.001
Thrombolysis	5137	192 (4.6)	60 (6.4)	0.017
Calcium antagonists	4127	467 (23.2)	130 (16.8)	<0.001
ACE-inhibitors	2767	931 (41.3)	182 (35.4)	<0.014
Angiotensin II-blockers	2766	263 (11.7)	42 (8.2)	<0.022
Diuretics	4127	740 (22.1)	118 (15.2)	<0.001
Statins	4127	1958 (58.4)	438 (56.5)	0.33
Aspirin	5015	2611 (63.6)	554 (60.9)	0.13
Clopidogrel	4128	213 (6.4)	48 (6.2)	0.87
Aspirin+clopidogrel	4131	136 (4.1)	36 (4.6)	0.46
Dipyridamole	4138	491 (14.6)	103 (13.3)	0.33

Numbers represent frequencies with percentages in parentheses. Note that the denominator is different between variables due to partial missing of data. ACE indicates angiotensinconverting enzyme; Nonskiers, population-based controls with the same age, sex, and same county of residence; Skiers, the participants in the Vasaloppet. \*Number of nonmissing observations.

<sup>†</sup>Pearson  $\chi^2$  test.

<sup>‡</sup>From 2001.

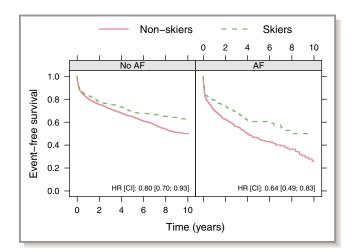
skiers those with shorter race times had a lower risk for death and recurrent stroke compared with skiers with longer race times. This relationship was more pronounced in women (Figure 4).

# Comparison With the Literature

This study supports the results of previous studies suggesting that physically fit or active people have a lower incidence of

	Exp.	Unexp.			
	x/n	x/n	HR	95 % C.I.	
Gender					
Women	225/819	41/195	0.74	[0.53; 1.04]	
Men	1519/4062	262/888	0.77	[0.67; 0.87]	<b>_+</b> _
Age					
[20,50]	121/498	30/147	0.84	[0.56; 1.25]	
(50,60]	434/1376	61/258	0.71	[0.55; 0.93]	
(60,70]	616/1872	89/377	0.67	[0.54; 0.84]	
(70,100]	573/1135	123/301	0.77	[0.63; 0.93]	<b>_</b>
Year					
[1994–2000]	366/610	48/132	0.51	[0.38; 0.69]	
[2001-2005]	675/1487	114/315	0.78	[0.64; 0.96]	
[2006–2010]	703/2784	141/636	0.87	[0.73; 1.04]	
Charlson index					
0	1040/3404	188/816	0.73	[0.63; 0.86]	
1+	704/1477	115/267	0.92	[0.75; 1.11]	
Education level					
Primary school	835/1962	83/249	0.75	[0.60; 0.94]	
High school	652/2019	124/429	0.88	[0.73; 1.06]	
University	226/849	95/403	0.88	[0.69; 1.12]	
Occupation level					
Unemployed	392/1102	34/102	0.88	[0.62; 1.26]	
Employed	540/2209	113/591	0.77	[0.63; 0.94]	
Retired	812/1568	156/390	0.74	[0.62; 0.87]	
Family status					
Cohabitor	958/2848	197/758	0.75	[0.65; 0.88]	
Single	786/2033	106/325	0.82	[0.67; 1.00]	
Atrial fibrillation					
No AF	1272/3942	217/825	0.80	[0.70; 0.93]	
AF	319/679	72/212		[0.49; 0.83]	
					0.2 0.5 0.7 1.0 1.5 2
					0.2 0.3 0.7 1.0 1.5 2 Hazard ratio

**Figure 2.** Relative hazard of stroke or all-cause mortality with corresponding 95% CI for skiers compared with nonskiers in different subgroups. The vertical dashed line indicates the unadjusted HR (0.76). AF indicates atrial fibrillation; CI, confidence interval; Exp, Eexposed; HR, hazard ratio; Unexp, Unexposed; x/n actual number out of the cohort.

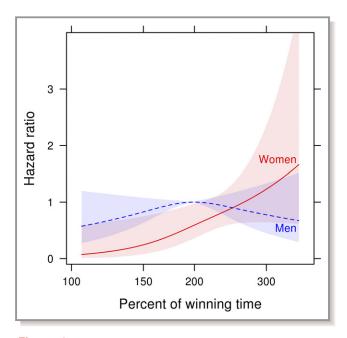


**Figure 3.** Stroke-free survival with unadjusted hazard ratios (HR) and corresponding 95% CI for subjects (skiers and nonskiers) with and without atrial fibrillation (AF). Skiers: Participants in the Vasaloppet. Nonskiers: population-based controls with the same age, sex, and same county of residence. CI indicate confidence interval.

first stroke and all-cause of death.<sup>2,7</sup> We found no prior reports regarding the benefits of physical activity prior to a stroke in relation to the risk of suffering a recurrent stroke, nor are we aware of studies reporting that individuals with a high level of physical activity suffer a less severe stroke than those less physically active. Our finding that 15% of stroke events are due to AF is similar to the estimates from a previous study.<sup>17</sup>

#### **Potential Mechanisms**

A healthy lifestyle including physical activity has recently been shown to reduce stroke.<sup>18</sup> Thus, in the present study, it is difficult to discern the individual contribution of physical activity and physical fitness on these associations. It has previously been shown that physical fitness has a stronger relationship to a reduced risk for cerebrovascular disease than physical activity,<sup>19</sup> but both physical fitness and physical activity are independent risk factors for cardiovascular



**Figure 4.** Estimated risk of death or stroke vs race time adjusted for age. The overall median relative race time (197%) and male sex is set as the reference. Comparison of skiers with different performance levels (finish times) is shown. Note the log scale.

disease. Regarding fitness, the maximum oxygen uptake (VO<sub>2</sub>max) for the skiing population is between 45 and 80 mL·kg<sup>-1</sup>·min<sup>-1</sup> compared with the general population's  $VO_2$ -max of 35 mL·kg<sup>-1</sup>·min<sup>-1</sup>.<sup>20</sup> Besides this higher fitness level, the Vasaloppet skiers are also physically more active than the general population. From questionnaires we know that a large part of them (60%) exercise for at least 4 hours weekly.<sup>10</sup> This corresponds approximately to a mean value of about 20 MET-h·week<sup>-1</sup> (metabolic equivalent hours per week). The skiers have a healthy lifestyle in common; they have a higher education and are likely motivated to be physically active. The level of physical activity, for the majority at least 20 MET-h weekly, may lead to a protective effect against developing atherosclerosis. It has been shown that cardiorespiratory fitness and physical activity have significantly different relationships to cardiovascular risk. The risks of coronary heart disease or cardiovascular disease decrease linearly in association with increasing physical activity but the risk reduction is significantly greater for fitness than physical activity.<sup>19</sup> No such dose-response associations were seen for the risk of recurrent myocardial infarction in a previous report based on the Vasaloppet cohort.<sup>8</sup> In this stroke study, however, individuals with better fitness had the lowest risk of recurrent stroke or death. We know that various cardiovascular risk factors have a different impact on the various cardiovascular outcomes, and it is likely that the benefits of physical activity are also different. The potential mediating mechanisms for physical activity and lower risk for cardiovascular events have been studied in a large cohort study.<sup>21</sup> Inflammatory, hemostatic biomarkers made the largest contribution to lower risk followed by blood pressure, lipids, body mass index, and hemoglobin A1c in diabetes.

One alternative explanation for the results is that the Vasaloppet skiers may have a genetic predisposition (ie, an inherited lower risk for cerebrovascular diseases).<sup>22</sup> Our study was not designed to investigate potential explanations for these relationships.

In our cohort, the nonskiers had a 15% incidence of AF. The prevalence of AF as a risk factor for stroke has been highlighted in a study in which AF increased the risk of stroke 5-fold and caused 15% of all strokes.<sup>23</sup> There was a strong relationship between age and AF in stroke as shown in the Swedish Stroke Register, ranging from 10% in stroke patients below the age of 65 to 40% in those above 80 years of age.<sup>24</sup>

There is evidence from other publications that people who practice strenuous sports<sup>25</sup> have a higher proportion of AF, just like our cohort. Thus, physically active people appear to suffer fewer strokes despite more AF. The explanation for this finding can only be speculated. There might be a lower incidence of concomitant diseases or structural cardiac changes, factors that reduce their risk for thromboembolic stroke. People with a high level of physical activity are likely to have a low CHADS<sub>2</sub> (Congestive heart failure, Hypertension, age  $\geq$ 75 years, Diabetes, previous Stroke)/CHA<sub>2</sub>DS<sub>2</sub>-VASc (Vascular disease, age 65 to 74 years, sex category) score, with a low stroke risk. CHA2DS2-VASc grade 0 in AF is associated with <1% annual risk for stroke.26 This background, in addition to a generally lower risk of cardiovascular events, may explain the trend in our study (Figure 3), namely, that skiers have fewer strokes than nonskiers, even if they have a higher frequency of AF.

#### Strengths and Limitations

Our study included a larger population of physically active people than most previous studies and a matched population not exposed to the long-distance ski race, the Vasaloppet. This study was possible thanks to the individual personal identification number of each participant and the unique national registers in Sweden.

When comparing 2 different cohorts, there is an inherent risk of selection bias. To avoid this we excluded all patients in the cohort with known severe diseases. We thereby tried to compare the skiers with a "healthy" population.

We have defined stroke as 1 group: ischemic, hemorrhagic, and nonspecific stroke. The consequences for ischemic strokes may therefore be diluted.

We are unaware of the physical activity of each study participant among the skiers and nonskiers. Previous studies of the Vasaloppet skiers show that in addition to being active, cross-country skiers are physically active and have a generally healthy lifestyle.<sup>10</sup> We therefore cannot isolate the physical activity factor and sedentary time from factors related to a healthy lifestyle.

#### Conclusions

Among patients with a history of stroke, those with high physical activity and a healthy lifestyle have a lower incidence of all-cause death but a similar incidence of recurrent stroke. The skiers had a higher frequency of atrial fibrillation, but despite this they seemed to suffer less severe stroke and had no increased risk of recurrent stroke. Our data suggest that a lifestyle with a higher level of physical activity may work as a protection against recurrent cardiovascular events and death, and may reduce the severity of such events. The underlying mechanisms of these observations remain to be established.

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#### **Disclosures**

None.

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