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ORIGINAL RESEARCH

Stroke Recurrence Following 28 Days After First Stroke in Men and Women 2012 to 2020: Observations From the Swedish Stroke Register

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BACKGROUND: Stroke incidence, care, and survival show continuous improvements in Sweden, including no or decreasing disparities between men and women. In this study, we aimed to estimate and compare the risk of stroke recurrence in men and women over time, accounting for the competing risk of death.

METHODS AND RESULTS: We included adult patients with first-time stroke (ischemic or intracerebral hemorrhage) registered in Riksstroke (the Swedish Stroke Register), 2012 to 2020, and followed until December 2020. Stroke recurrences included new events registered in Riksstroke from 28 days after stroke. To account for the competing risk of death, we used the cumulative incidence function to estimate crude incidences, and multivariable Cox regression to estimate cause-specific hazard ratios (HRs) adjusting for differences in patients' risk factor profiles. The study included 72 148 (53.5%) men and 62 689 (46.5%) women. We observed 10 925 stroke recurrences and 81 811 deaths following the initial 28 days after the first stroke. The cumulative incidence of stroke recurrence was 3.7% (95% CI, 3.6–3.8) after 1 year, 7.0 (95% CI, 6.8–7.1) after 3 years, and 9.1% (95% CI, 8.9–9.3) after 5 years. The incidence decreased substantially during the study period (HR, 2019–2020 versus 2012, 0.824 [95% CI, 0.759–0.894]). Overall, men had a lower risk of stroke recurrence. After adjustments for differences in patient characteristics, men had a slightly higher risk of recurrence (of any type) after an ischemic stroke (HR, 1.090 [95% CI, 1.045–1.138]) and a lower risk after hemorrhagic stroke (HR, 0.880 [95% CI, 0.781–0.991]) compared with women.

CONCLUSIONS: The risk of stroke recurrence has decreased in both men and women. Women's higher age and other differences in risk factors partly explain their higher risk of stroke recurrence compared with men.

Key Words: competing risk ■ sex differences ■ stroke ■ stroke recurrence

There have been major improvements in stroke incidence, care, and survival worldwide.[1,2] In Sweden, this also includes diminishing differences between men and women.[3] A meta-analysis from 2011 reported a temporal reduction in risk of stroke recurrence,[4] and results from more recent studies suggest further improvements.[4–7] However, studies of sex differences in stroke recurrence show different results.[6–9] This can be attributable to differences in demographics and health care but also in study population, design, or analysis that, for example, may not consider the competing risk of death.

The aim of this nationwide, register-based study was to estimate short- and long-term risk of stroke recurrence following the first 28 days after stroke, investigating differences between men and women, and follow longitudinal changes from 2012 to 2020, accounting for the competing risk of death.

METHODS

Because of the sensitive nature of the data collected for this study, requests to access the data set from

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CLINICAL PERSPECTIVE

What Is New?

- The incidence of stroke recurrence following the first 28 days after the initial stroke decreased by nearly 20% in both men and women between 2012 and 2020, a decrease that was significant after an ischemic stroke.
- After adjustments for differences in patient characteristics, men had a slightly higher risk of recurrence after an ischemic stroke and a lower risk after hemorrhagic stroke, compared with women.

What Are the Clinical Implications?

- The reduced incidence of stroke recurrence after ischemic stroke coincides with the improved secondary prevention that has been reported in previous studies.
- There is a need to consider sex-related differences to further improve secondary preventive treatment.

Nonstandard Abbreviations and Acronyms

Riksstroke	Swedish Stroke Register

qualified researchers trained in human subject confidentiality protocols may be sent to Riksstroke at riksstroke@regionvasterbotten.se.

Material

This study included patients aged ≥18 years, registered in Riksstroke (the Swedish Stroke Register) 2012 to 2020 with a first-ever stroke (intracerebral hemorrhage [*International Classification of Diseases, Tenth Revision* (*ICD-10*)]: [I61], ischemic stroke [I63], or an unspecified stroke [I64]). Subarachnoid hemorrhage (I60) and other nontraumatic intracranial hemorrhage (I62) were excluded. Since Riksstroke does not fully capture recurrent strokes within the first 28 days, the start of follow-up was day 28. Patients who died during the first 28 days (7949 men and 10 103 women) or had a shorter follow-up time than 28 days (540 men and 428 women) were excluded.

Riksstroke is a national Swedish quality register for stroke care and has been described in detail in previous publications.[10,11] In short, all 72 Swedish hospitals admitting patients with acute stroke participate, and the coverage is estimated to be 90% of all patients with acute stroke treated in a hospital. The register includes information on demography, living situation, cardiovascular risk factors, stroke diagnosis, stroke severity (alert, drowsy, or unconscious at hospital admission), acute treatment, and secondary prevention. The forms are available at Riksstroke's web page (https://www.riksstroke.org/forms/). Date of death was retrieved by individual linkage with the cause-of-death register, a register with almost 100% coverage, managed by the National Board of Health and Welfare.

Statistical Analysis

Pearson's χ^2-test was used to assess whether background characteristics differed between men and women. Patients were followed until the time of the first stroke recurrence (ischemic, hemorrhagic, or unspecified), death, or end of study (December 31, 2020). Patients were censored if they had not experienced an event before the end of the study. Death was considered a competing risk because it precludes stroke recurrence. To account for the competing risk of death, the crude incidence (probability) of stroke recurrence with 95% CI was estimated by the cumulative incidence function.

As has been suggested for epidemiological questions of etiology, we used Cox proportional hazard regression to estimate cause-specific hazard ratios (HRs) of stroke recurrence.[12] The cause-specific HR for sex, for example, represents the relative difference between men and women regarding the rate of stroke recurrences at a certain point in time in patients who are still event free. Major deviations from the proportional hazard assumption in risk of stroke recurrence were assessed from the cumulative incidence function plots. For minor deviations from the assumption, the estimated HR can be interpreted as a (weighted) average of the true time-varying HRs.[13] A multivariable model was used to adjust for potential confounding factors, including age group (18–54, 55–64, 65–74, 75–84, and ≥85 years), year of stroke (2012, 2013, 2014, 2015–2016, 2017–2018, and 2019–2020), stroke type (ischemic, hemorrhagic, and unspecified), level of consciousness at hospital admission (alert, drowsy, and unconscious), living alone, dependence in activities of daily living (including mobility and ability to manage dressing and toileting without assistance) before stroke, and cardiovascular risk factors (previously known or newly detected atrial fibrillation, diabetes, hypertensive medication before stroke, smoking), and hospital. An initial model also included the sex-by-period–, sex-by-age–, and sex-by-stroke–type interactions. Sex-by-stroke type was significant (P=0.019), and the multivariable analyses were subsequently stratified by stroke type. The confounding factors were selected on the basis of preexisting knowledge and availability in the register. The relation between the log hazard and the continuous variables (age and year) were not linear and were therefore included as categorical variables. Information

on smoking was missing for 9.7% of patients; these were included in the analysis with smoking as a separate category ("Unknown"). Other variables contained <2% missing (Table 1), and patients missing variables other than smoking were excluded from relevant analysis (complete case analysis).

Table 1. Patient Characteristics in Men and Women Who Were Event Free 28 Days After Stroke 2012 to 2020

	Overall		Women		Men	
	No.	Percentage	No.	Percentage	No.	Percentage
Sex	134 837	100	62 689	46.5	72 148	53.5
Median follow-up, quartile 1; quartile 3, y	2.8	1.1; 5.2	2.7	1.0; 5.1	2.9	1.1; 5.3
Median age, quartile 1; quartile 3, y	75	66; 83	78	69; 85	73	64; 81
Age, y						
18–54	11 365	8.4	4190	6.7	7175	9.9
55–64	17 298	12.8	5804	9.3	11 494	15.9
65–74	35 781	26.5	14 185	22.6	21 596	29.9
75–84	42 153	31.3	20 657	33.0	21 496	29.8
85+	28 240	20.9	17 853	28.5	10 387	14.4
Stroke type						
Hemorrhagic	14 046	10.4	6215	9.9	7831	10.9
Ischemic	119 701	88.8	55 944	89.2	63 757	88.4
Unspecified	1090	0.8	530	0.8	560	0.8
Consciousness at hospital admission						
Alert	120 712	89.5	55 325	88.3	65 387	90.6
Drowsy	10 550	7.8	5734	9.1	4816	6.7
Unconscious	1927	1.4	917	1.5	1010	1.4
Missing	1648	1.2	713	1.1	935	1.3
Living alone before stroke						
Yes	7174	5.3	4520	7.2	2654	3.7
No	127 257	94.4	57 988	92.5	69 269	96.0
Missing	406	0.3	181	0.3	225	0.3
Dependent in personal activities of daily living before stroke						
Yes	9366	6.9	5780	9.2	3586	5.0
No	122 947	91.2	55 429	88.4	67 518	93.6
Missing	2524	1.9	1480	2.4	1044	1.4
Atrial fibrillation						
Yes	33 578	24.9	16 309	26.0	17 269	23.9
No	100 731	74.7	46 140	73.6	54 591	75.7
Missing	528	0.4	240	0.4	288	0.4
Diabetes						
Yes	27 340	20.3	11 263	18.0	16 077	22.3
No	107 378	79.6	51 362	81.9	56 016	77.6
Missing	119	0.1	64	0.1	55	0.1
Hypertensive medication before stroke						
Yes	78 746	58.4	38 400	61.3	40 346	55.9
No	55 749	41.3	24 150	38.5	31 599	43.8
Missing	342	0.3	139	0.2	203	0.3
Smoker						
Yes	18 874	14.0	7976	12.7	10 898	15.1
No	102 833	76.3	48 390	77.2	54 443	75.5
Unknown	13 130	9.7	6323	10.1	6807	9.4

Number of patients (n) and frequency (%), median follow-up time, and age with quartiles 1 and 3.

We analyzed the data using SAS software version 9.4 for Windows (SAS Institute Inc., Cary, NC).

Ethical Considerations

The study was approved by the Swedish Ethical Review Authority (reference no. 2019–02777). Data were pseudo-anonymized by the quality register (removing all personal identifications) before they were submitted for research. All patients are informed about registration in the quality register Riksstroke, that the aim of the register is to support high and consistent quality of care for patients with stroke throughout Sweden, and those data may be used for developing and ensuring the quality of stroke treatment, for compiling statistics, and for health care research purposes. They are informed of their rights to deny participation (opt-out consent). In accordance with the Personal Data Act (Swedish law No. SFS 1998:204), no informed consent is needed to collect data from medical charts or inpatient records for quality registers.

RESULTS

Patient Characteristics

The study included 134837 patients with first-stroke (14046 hemorrhagic, 119701 ischemic, and 1090 unspecified strokes) who survived the initial 28 days after stroke between 2012 and 2020. Of these, 72148 (53.5%) were men and 62689 (46.5%) were women. Women were older, more often drowsy at hospital admission, dependent in activities of daily living, living alone, and more likely to have atrial fibrillation or hypertension before stroke than men (all $P<0.001$). Men were more likely to have hemorrhagic stroke or diabetes or to smoke (all $P<0.001$; Table 1).

Recurrence

During a total follow-up time of 442899 years, we observed 10925 stroke recurrences, and 42101 deaths following the initial 28 days after the first stroke. Of the recurrent strokes, 9364 (85.7%) were ischemic and 1446 (13.2%) were hemorrhagic.

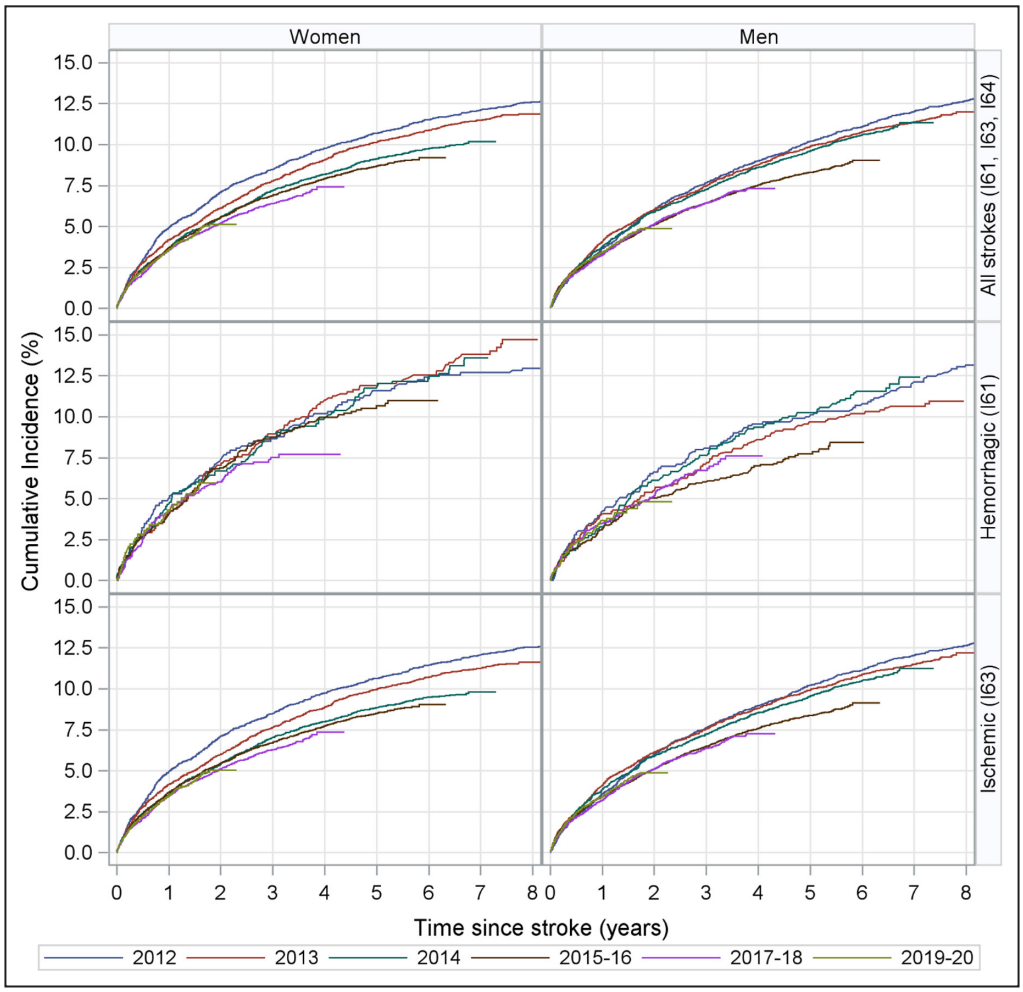

Figure 1. Estimated crude cumulative incidence of stroke recurrence (of any type) following 28 days after stroke, in men and women after any stroke (I61, I63, or I64), after intracerebral hemorrhage (I61), or after ischemic stroke (I63) during different time periods 2012 to 2020.

Table 2. Stroke Recurrence Following 28 Days After Hemorrhagic or Ischemic Stroke. Univariable (Crude) and Multivariable Models (Including and Adjusting for Hospital and All Other Variables) on the Basis of Cause-Specific Hazards

	Recurrence after hemorrhagic stroke (I61)		Recurrence after ischemic stroke (I63)	
	Univariable HR (95% CI)	Multivariable HR (95% CI)	Univariable HR (95% CI)	Multivariable HR (95% CI)
Sex (ref: women)				
Men	0.812 (0.726–0.908)	0.880 (0.781–0.991)	0.963 (0.926–1.003)	1.090 (1.045–1.138)
Age, y (ref: 18–54)				
55–64	1.700 (1.268–2.279)	1.554 (1.152–2.097)	1.388 (1.238–1.557)	1.247 (1.110–1.402)
65–74	3.349 (2.583–4.343)	2.933 (2.241–3.838)	1.922 (1.735–2.130)	1.690 (1.522–1.877)
75–84	4.285 (3.314–5.541)	3.489 (2.656–4.584)	2.616 (2.366–2.892)	2.256 (2.032–2.506)
≥85	4.459 (3.384–5.875)	3.516 (2.608–4.741)	3.112 (2.805–3.453)	2.721 (2.435–3.042)
Year (ref: 2012)				
2013	0.985 (0.813–1.193)	0.969 (0.798–1.177)	0.948 (0.887–1.013)	0.939 (0.878–1.004)
2014	1.052 (0.865–1.278)	1.036 (0.850–1.262)	0.870 (0.811–0.933)	0.862 (0.804–0.925)
2015–2016	0.854 (0.711–1.026)	0.860 (0.714–1.035)	0.796 (0.747–0.848)	0.782 (0.733–0.833)
2017–2018	0.851 (0.699–1.036)	0.864 (0.708–1.055)	0.771 (0.719–0.826)	0.764 (0.713–0.820)
2019–2020	0.923 (0.720–1.183)	0.912 (0.708–1.175)	0.812 (0.745–0.886)	0.798 (0.730–0.871)
Consciousness at hospital admission (ref: alert)				
Unknown	1.031 (0.682–1.558)	1.220 (0.796–1.870)	0.880 (0.715–1.083)	0.894 (0.720–1.111)
Drowsy	0.824 (0.702–0.967)	0.904 (0.766–1.066)	0.960 (0.877–1.051)	0.908 (0.828–0.997)
Unconscious	0.604 (0.431–0.846)	0.890 (0.630–1.258)	0.629 (0.479–0.826)	0.689 (0.519–0.916)
Living alone before stroke (ref: no)				
Yes	1.218 (1.088–1.364)	1.023 (0.905–1.157)	1.224 (1.176–1.275)	1.078 (1.032–1.126)
Dependent in personal activities of daily living before stroke (ref: no)				
Yes	1.466 (1.145–1.877)	1.156 (0.896–1.493)	1.239 (1.132–1.355)	0.998 (0.910–1.094)
Atrial fibrillation (ref: no)				
Yes	1.901 (1.676–2.157)	1.452 (1.266–1.664)	1.328 (1.270–1.389)	1.116 (1.065–1.170)
Diabetes (ref: no)				
Yes	1.336 (1.156–1.545)	1.179 (1.011–1.375)	1.413 (1.350–1.480)	1.333 (1.271–1.398)
Hypertensive medication before stroke (ref: no)				
Yes	1.391 (1.242–1.558)	1.019 (0.901–1.153)	1.522 (1.459–1.588)	1.270 (1.214–1.329)
Smoker (ref: no)				
Unknown	0.811 (0.673–0.978)	0.839 (0.686–1.026)	0.997 (0.926–1.074)	0.982 (0.906–1.063)
Yes	0.847 (0.702–1.022)	1.166 (0.960–1.417)	0.875 (0.826–0.927)	1.130 (1.063–1.202)

Overall, the cumulative incidence of stroke recurrence was 3.7% (95% CI, 3.6%–3.8%) after 1 year, 7.0% (95% CI, 6.8%–7.1%) after 3 years, and 9.1% (95% CI, 8.9%–9.3%) after 5 years. In univariable analysis, factors that were associated with an increased risk of recurrence included female sex (P=0.004), higher age (P<0.001), hemorrhagic stroke (P<0.001), living alone (P<0.001), activities of daily living -dependency (P<0.001), atrial fibrillation (P<0.001), diabetes (P<0.001), and hypertensive medication before stroke (P<0.001). Patients who were unconscious at the time of hospital admission had a lower risk of stroke recurrence than patients who were alert or drowsy at hospital admission (P<0.001).The risk of recurrence decreased substantially during the study period (crude HR 2019–2020 versus 2012, 0.824 [95% CI, 0.759–0.894]; P<0.001; Figure 1), with no significant difference in time trend between men and women (P for sex-by-period interaction=0.384).

The sex-related difference in stroke recurrence showed different patterns after an ischemic and after a hemorrhagic stroke (P for sex-by-stroke type interaction=0.019). Cumulative incidence function plots did not reveal any serious deviations from the proportional hazard assumption. After adjustments for women's higher age and differences in other patient characteristics, men had a lower risk of recurrence than women after a hemorrhagic stroke (adjusted HR, 0.880 [95% CI, 0.781–0.991]; Table 2). Following ischemic stroke, men had a slightly higher risk of stroke recurrence (ischemic, hemorrhagic, or unspecified stroke) than women (adjusted HR, 1.090 [95% CI, 1.045–1.138]; Figure 2). The observed differences after a hemorrhagic or an ischemic

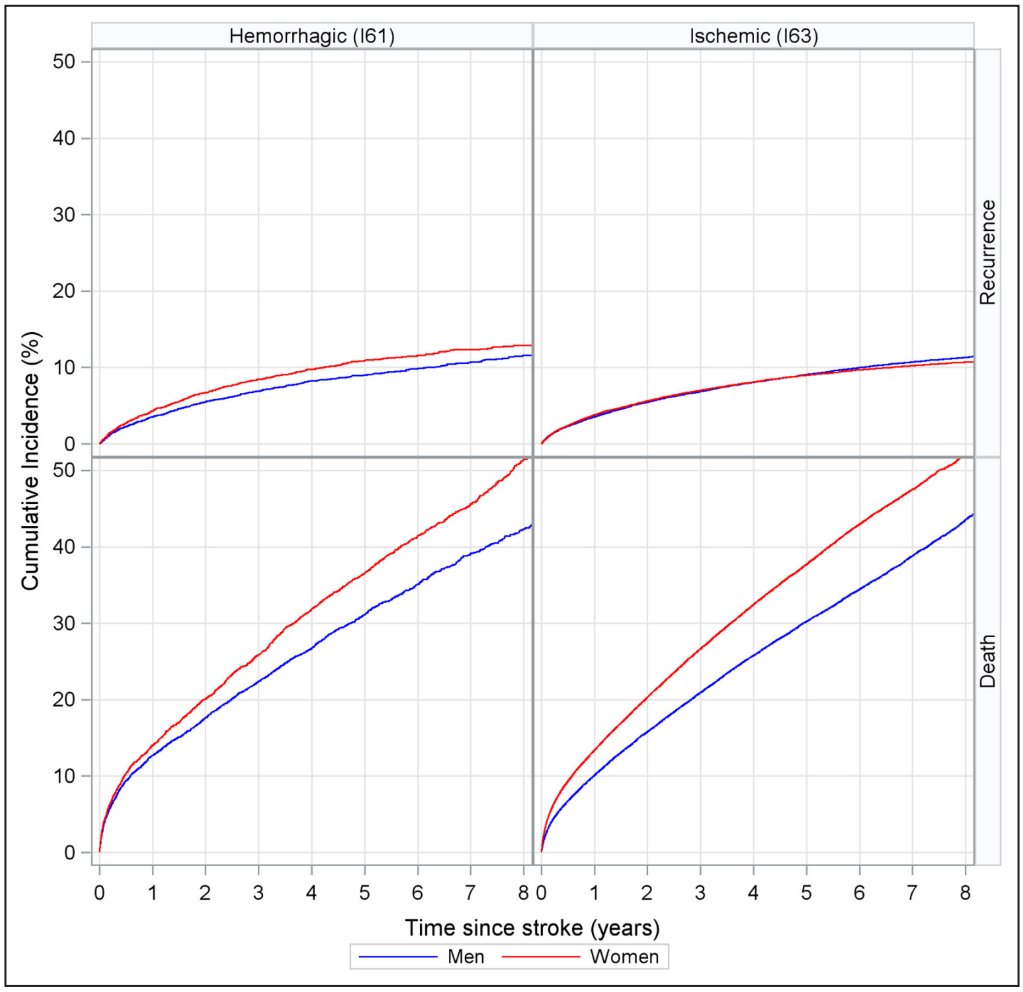

Figure 2. Estimated crude (unadjusted) cumulative incidence of stroke recurrence (of any type) or death following 28 days after stroke, in men and women after intracerebral hemorrhage (I61) or after ischemic stroke (I63).

Adjusted cause-specific hazard ratio (HR) of stroke recurrence in men compared with women: 0.880 (95% CI, 0.781–0.991) after I61, and 1.090 (1.045–1.138) after I63. Numbers at risk 28 days after stroke: 7829 men (I61), 6210 women (I61), 63 706 men (I63), 55 907 women (I63). Number of recurrent strokes (any type) during follow-up: 635 men (I61), 598 women (I61), 5139 men (I63), 4471 women (I63). Number of deaths during follow-up: 2246 men (I61), 2138 women (I61), 17 750 men (I63), 19 564 women (I63).

stroke remained at a similar level throughout the study period (*P* for sex-by-year interaction=0.453 and 0.539, respectively).

DISCUSSION

Between 2012 and 2020, we observed a decreasing incidence of stroke recurrence following the first 28 days after the initial stroke. One year after stroke, the incidence was reduced by nearly 20%. Overall, men had a slightly lower incidence of stroke recurrence than women. After adjustments for women's higher age and other differences in patient characteristics, men had a lower risk of recurrence (of any type) after a hemorrhagic stroke but a slightly higher risk after ischemic stroke compared with women.

The estimated incidence of stroke recurrence is consistent with what has been reported previously from populations-based register studies in Denmark,[6] south London,[8] and from a rural population in central Pennsylvania, United States.[9] While no evident sex differences were seen in the studies from the United Kingdom or the United States, the Danish study, similar to our findings, reported a higher risk of stroke recurrence in men compared with women after ischemic stroke and, in contrast to our findings, a similar risk in men and women after intracerebral hemorrhage. One cause of the differences in the Danish and the Swedish study could be that the Danish study had a definition

of 21 days in contrast with ours of 28 days after stroke onset. Although Sweden and Denmark are close, basic patient characteristics differ, particularly regarding smoking in men, which is more common in Denmark.[14]

Our study focused on patient and stroke characteristics recorded during the acute phase. We did not include time-varying covariates related to, for example, treatment. Previously observed differences in treatment and persistent use of secondary preventive drugs between men and women,[3,15] may contribute to differences in stroke recurrence. A major part of the observed decrease in stroke recurrence after ischemic stroke took place up until 2016, whereafter the incidence stabilized. This coincides with a previously observed increase in the use of statins and that of anticoagulants in patients with atrial fibrillation after stroke during that time. The latter increase was particularly marked in women.[3] A Swedish study estimated improved anticoagulant treatment of atrial fibrillation to explain an absolute reduction of 10% in the decreasing incidence of stroke seen during the period 2012 to 2017.[16] The remaining absolute 27% decrease was hypothesized to be attributable to an overall healthier population with healthier lifestyles, better blood pressure control, and better-managed preventive drug treatment in general in the elderly.[16,17] In congruence with this, a meta-analysis of 17 statin trials found statin treatment to reduce the risk of all-cause mortality and recurrent stroke.[18]

A major strength of this nationwide study is the high coverage, estimated to include >90% of all patients with stroke treated in hospitals in Sweden.[19] A systematic review of *ICD* coding for acute stroke reported a positive predictive value of 89% for intracerebral hemorrhage and 82% for ischemic stroke.[20] With the reporting to Riksstroke and the subsequent follow-up with a questionnaire, the diagnosis of stroke is double- or triple-checked, improving diagnostic accuracy. Hence, the bias attributable to misdiagnosis is likely to be small. Our study excluded recurrent strokes during the first 28 days after the first stroke. A previous review estimated that the cumulative incidence of stroke at 30 days was 3.1%.[4] Hence, the total risk of recurrence is higher than the incidence reported here, following the first 28 days. A previous study based on data from Riksstroke showed that the sex-related difference in 28-day case fatality was small after adjustment for differences in age and other risk factors.[3] The current study included potential confounding factors (such as age and cardiovascular risk factors). However, unmeasured confounding attributable to social status, for example, and selection of patients surviving 28 days may still have biased the estimated incidences.

ARTICLE INFORMATION

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Disclosures

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REFERENCES

1. Feigin VL, Vos T, Nichols E, Owolabi MO, Carroll WM, Dichgans M, Deuschl G, Parmar P, Brainin M, Murray C. The global burden of neurological disorders: translating evidence into policy. *Lancet Neurol.* 2020;19:255–265. doi: 10.1016/S1474-4422(19)30411-9
2. Arnao V, Acciarresi M, Cittadini E, Caso V. Stroke incidence, prevalence and mortality in women worldwide. *Int J Stroke.* 2016;11:287–301. doi: 10.1177/1747493016632245
3. Eriksson M, Asberg S, Sunnerhagen KS, von Euler M. Sex differences in stroke care and outcome 2005-2018: observations from the Swedish stroke register. *Stroke.* 2021;52:3233–3242. doi: 10.1161/STROKEAHA.120.033893
4. Mohan KM, Wolfe CD, Rudd AG, Heuschmann PU, Kolominsky-Rabas PL, Grieve AP. Risk and cumulative risk of stroke recurrence: a systematic review and meta-analysis. *Stroke.* 2011;42:1489–1494. doi: 10.1161/STROKEAHA.110.602615
5. Amarenco P, Lavallee PC, Monteiro Tavares L, Labreuche J, Albers GW, Abboud H, Anticoli S, Audebert H, Bornstein NM, Caplan LR, et al. Five-year risk of stroke after TIA or minor ischemic stroke. *N Engl J Med.* 2018;378:2182–2190. doi: 10.1056/NEJMoa1802712
6. Skajaa N, Adelborg K, Horvath-Puho E, Rothman KJ, Henderson VW, Thygesen LC, Sorensen HT. Risks of stroke recurrence and mortality after first and recurrent strokes in Denmark: a nationwide registry study. *Neurology.* 2022;98:e329–e342. doi: 10.1212/WNL.0000000000013118
7. Basu E, Salehi Omran S, Kamel H, Parikh NS. Sex differences in the risk of recurrent ischemic stroke after ischemic stroke and transient ischemic attack. *Eur Stroke J.* 2021;6:367–373. doi: 10.1177/23969873211058568
8. Xu M, Amarilla Vallejo A, Cantalapiedra Calvete C, Rudd A, Wolfe C, O'Connell MDL, Douiri A. Stroke outcomes in women: a population-based cohort study. *Stroke.* 2022;53:3072–3081.
9. Lambert C, Chaudhary D, Olulana O, Shahjouei S, Avula V, Li J, Abedi V, Zand R. Sex disparity in long-term stroke recurrence and mortality in a rural population in the United States. *Ther Adv Neurol Disord.* 2020;13:1756286420971895. doi: 10.1177/1756286420971895
10. Asplund K, Hulter Asberg K, Appelros P, Bjarne D, Eriksson M, Johansson A, Jonsson F, Norrving B, Stegmayr B, Terent A, et al. The Riks-Stroke story: building a sustainable national register for quality assessment of stroke care. *Int J Stroke.* 2011;6:99–108. doi: 10.1111/j.1747-4949.2010.00557.x
11. Soderholm A, Stegmayr B, Glader EL, Asplund K, Riksstroke C. Validation of hospital performance measures of acute stroke care quality. Riksstroke, the Swedish stroke register. *Neuroepidemiology.* 2016;46:229–234. doi: 10.1159/000444679
12. Austin PC, Lee DS, Fine JP. Introduction to the analysis of survival data in the presence of competing risks. *Circulation.* 2016;133:601–609. doi: 10.1161/CIRCULATIONAHA.115.017719
13. Stensrud MJ, Hernan MA. Why test for proportional hazards? *JAMA.* 2020;323:1401–1402. doi: 10.1001/jama.2020.1267
14. Sundhedsstyrelsen. Danskernes Rygevaner 2020. https://www.sst.dk/-/media/Udgivelser/2021/Tobak/Danskernes-Rygevaner-2020_delrapport-1_04_03_2021.ashx?la=da&hash=8077A894BA39F6DC18B6A4CCFFFC4120768D1BD0. Accessed November 24, 2022.

15. Glader EL, Sjölander M, Eriksson M, Lundberg M. Persistent use of secondary preventive drugs declines rapidly during the first 2 years after stroke. *Stroke.* 2010;41:397–401. doi: 10.1161/STROKEAHA.109.566950
16. Forslund T, Komen JJ, Andersen M, Wettermark B, von Euler M, Mantel-Teeuwisse AK, Braunschweig F, Hjemdahl P. Improved stroke prevention in atrial fibrillation after the introduction of non-vitamin K antagonist oral anticoagulants. *Stroke.* 2018;49:2122–2128. doi: 10.1161/STROKEAHA.118.021990
17. Krishnamurthi RV, Feigin VL, Forouzanfar MH, Mensah GA, Connor M, Bennett DA, Moran AE, Sacco RL, Anderson LM, Truelsen T, et al. Global and regional burden of first-ever ischaemic and haemorrhagic stroke during 1990-2010: findings from the global burden of disease study 2010. *Lancet Glob Health.* 2013;1:e259–e281. doi: 10.1016/S2214-109X(13)70089-5
18. Zhai C, Hou K, Li R, Hu Y, Zhang J, Zhang Y, Wang L, Zhang R, Cong H. Efficacy of statin treatment based on cardiovascular outcomes in elderly patients: a standard meta-analysis and Bayesian network analysis. *J Int Med Res.* 2020;48:300060520926349. DOI: 10.1177/0300060520926349
19. Koster M, Asplund K, Johansson A, Stegmayr B. Refinement of Swedish administrative registers to monitor stroke events on the national level. *Neuroepidemiology.* 2013;40:240–246. doi: 10.1159/000345953
20. McCormick N, Bhole V, Lacaille D, Avina-Zubieta JA. Validity of diagnostic codes for acute stroke in administrative databases: a systematic review. *PLoS One.* 2015;10:e0135834. doi: 10.1371/journal.pone.0135834