INCIDENCE OF ISCHAEMIC STROKE RECURRENCE IN PATIENTS AFTER NON-CARDIOEMBOLIC ISCHAEMIC STROKE IN DENMARK:

OBSERVATIONS FROM ASTRIS

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Recurrent IS poses a significant challenge to patients, healthcare systems, and public health

- Stroke is the second leading cause of death and a significant contributor to disability[1]
- Despite advances in acute stroke management, the risk of recurrent IS has remained unchanged in the past 20 years[2]
- Understanding the incidence of IS recurrence is important for shaping SSP strategies and improving patient outcomes

The ASTRIS-Denmark real-world study aims to describe the incidence of IS recurrence in survivors of NCIS in Denmark

1. Feigin VL, et al. *Lancet Neurol.* 2023;22(12):1160–1206; 2. Kolmos M, et al. *J Stroke Cerebrovasc Dis.* 2021;30(8):105935.
IS, ischaemic stroke; NCIS, non-cardioembolic ischaemic stroke; SSP, secondary stroke prevention.

ASTRIS-Denmark study design

Retrospective cohort study based on **five** nationwide Danish registries†

Inclusion criteria

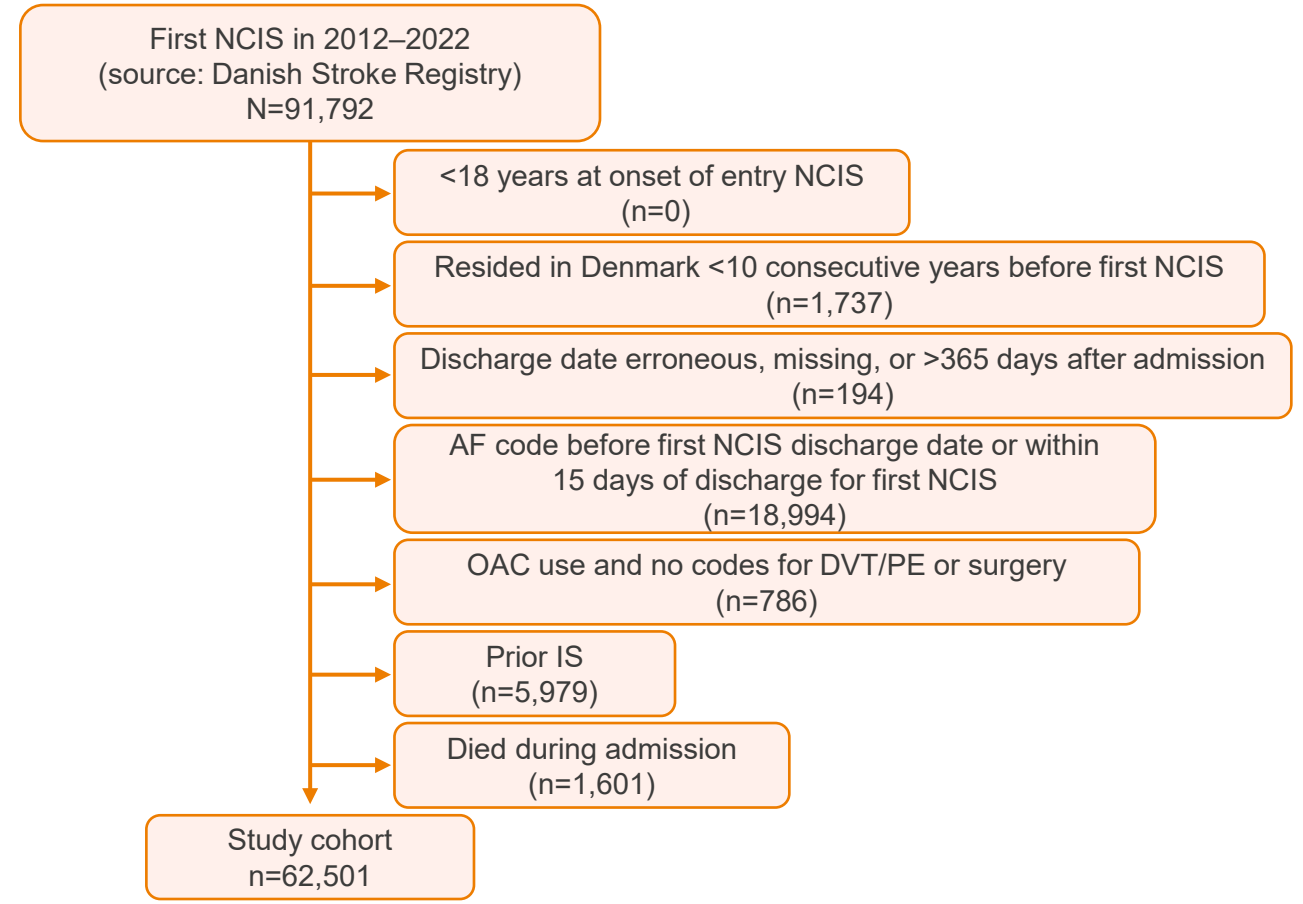
- At least 18 years of age
- First (index) NCIS between 2012 and 2022‡
- Resided in Denmark ≥10 consecutive years before first NCIS§

Exclusion criteria

- AF diagnosis anytime before and up to 15 days after discharge for first NCIS‖
- OAC use within 90 days before IS hospitalisation with no record for DVT/PE any time up to 1 day before first NCIS, and no record for hip/knee surgery from 180 days up to 1 day before first NCIS

Follow-up

- From discharge after first NCIS and until the earliest of the following events:
  - Recurrent IS¶
  - Emigration
  - All-cause death
  - End of study period (August 2022)



†Danish Stroke Registry, Danish National Patient Registry, Danish Death Registry, Danish National Prescription Registry, and Civil Registration System. ‡First stroke severity was assessed by the Scandinavian Stroke Scale. §To ensure coverage of comorbidity and medication use by the Danish registries. ‖The cohort was not censored for AF during follow-up. ¶Day 1–14 post-discharge (Stroke Registry) or day 15 (Danish Stroke, Danish National Patient, or Danish Death Registry).
AF, atrial fibrillation; DVT, deep vein thrombosis; IS, ischaemic stroke; NCIS, non-cardioembolic ischaemic stroke; OAC, oral anticoagulant; PE, pulmonary embolism.

Patient demographic and disease characteristics

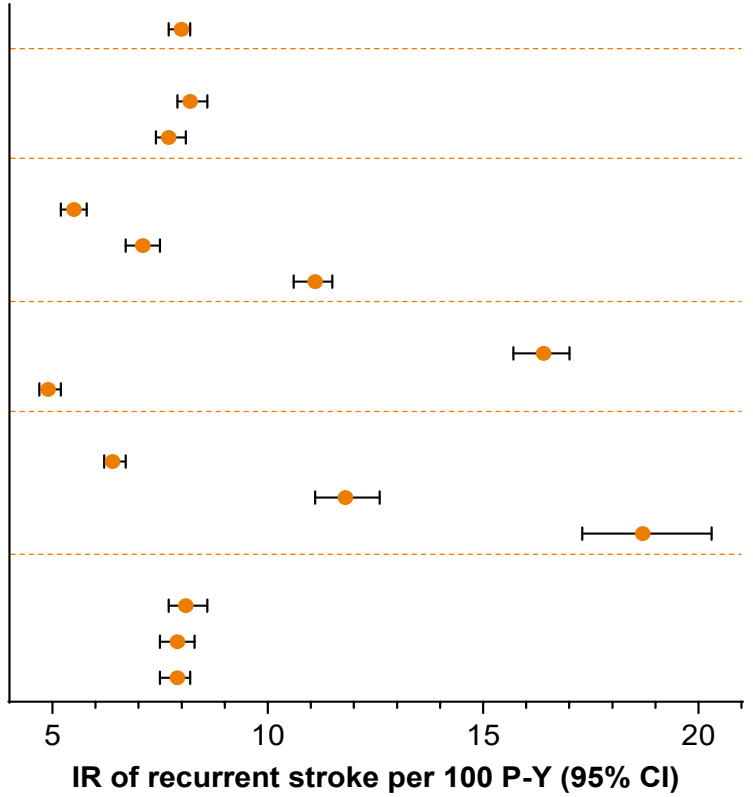
Cohort characteristics (n=62,501)	Patients, n (%)
Demographics and risk factors	
Men	34,952 (55.9)
Age, years, mean (SD)	70.0 (13.2)
Current smoker	18,675 (29.9)
High alcohol use†	6,342 (10.1)
Comorbidities	
Hypertension	41,670 (66.7)
Diabetes	10,208 (16.3)
Hyperlipidaemia	17,377 (27.8)
Peripheral artery disease	3,530 (5.6)
Ischaemic heart disease	9,819 (15.7)
Medical history	
Transient ischaemic attack	5,027 (8.0)
Medication use at time of first NCIS	
Antiplatelets	15,691 (25.1)
OACs	593 (0.9)
Statins	15,930 (25.5)

†Disorders indicative of high alcohol use.
NCIS, non-cardioembolic ischaemic stroke; OAC, oral anticoagulant; SD, standard deviation.

IS recurrence rates overall and by subgroup

Incidence of recurrent IS within 12 months since first NCIS

	Patients, n (%)	Events†, n	IR per 100 P-Y (95% CI)
All patients	62,501 (100.0)	4,462	**8.0 (7.7–8.2)**
Sex			
Female	27,549 (44.1)	2,012	**8.2 (7.9–8.6)**
Male	34,952 (55.9)	2,450	**7.7 (7.4–8.1)**
Age at index stroke, years			
<65	20,495 (32.8)	1,059	**5.5 (5.2–5.8)**
65–75	18,220 (29.2)	1,176	**7.1 (6.7–7.5)**
>75	23,786 (38.1)	2,227	**11.1 (10.6–11.5)**
Time since index NCIS			
<3 months	–	2,424	**16.4 (15.7–17.0)**
3–12 months	–	2,038	**4.9 (4.7–5.2)**
Index stroke severity‡			
Mild	47,182 (75.5)	2,825	**6.4 (6.2–6.7)**
Moderate	9,538 (15.3)	941	**11.8 (11.1–12.6)**
Severe	4,333 (6.9)	573	**18.7 (17.3–20.3)**
Calendar years			
2012–2014	17,123 (27.4)	1,254	**8.1 (7.7–8.6)**
2015–2017	18,467 (29.5)	1,321	**7.9 (7.5–8.3)**
2018–2021	26,911 (43.1)	1,887	**7.9 (7.5–8.2)**



Recurrence rates did not improve between 2012 and 2022 in Denmark

†An index stroke event was defined as NCIS if the patient had no history of AF prior to, or within 30 days after, hospitalisation for IS and had not received OAC therapy within 90 days before hospitalisation for IS unless they had a record of either DVT/PE or hip/knee surgery. ‡SSS scores: mild, 43–58; moderate, 26–42; severe, 0–25; 1448 (2.3%) patients had missing index stroke severity data.

AF, atrial fibrillation; CI, confidence interval; DVT, deep vein thrombosis; IR, incidence rate; IS, ischaemic stroke; NCIS, non-cardioembolic ischaemic stroke; OAC, oral anticoagulant; PE, pulmonary embolism; P-Y, person-years; SSS, Scandinavian Stroke Scale.

Risk of recurrent IS by year

Recurrent IS per year of follow-up after first NCIS

Follow-up	Patients, n	P-Y of follow-up	Events, n	IR per 100 P-Y (95% CI)	Cumulative risk† (95% CI)
Year 1	62,501	56,137	4,462	8.0 (7.7–8.2)	7.7 (7.5–8.0)
Year 2	51,578	46,655	1,591	3.4 (3.2–3.6)	11.1 (10.9–11.4)
Year 3	41,964	37,708	1,070	2.8 (2.7–3.0)	14.0 (13.6–14.3)
Year 4	33,728	30,294	787	2.6 (2.4–2.8)	16.6 (16.2–17.0)
Year 5	26,987	23,942	551	2.3 (2.1–2.5)	18.9 (18.5–19.3)

The cumulative risk of IS recurrence after 5 years was substantial despite the incidence peaking in the first year after a NCIS

†Nelson–Aalen cumulative hazard estimate by the end of each period.
CI, confidence interval; IR, incidence rate; IS, ischaemic stroke; NCIS, non-cardioembolic ischaemic stroke; P-Y, person-years.

ASTRIS-Denmark strengths and limitations

Strengths

- Nationwide data, limited exclusion criteria
- Use of high-quality registries with prospectively collected data
- Virtually no loss to follow-up
- Availability of stroke severity data

Limitations

- Registries as data source; no influence on which data were collected or how they were collected
- Danish Stroke Registry may be less complete in recent years
- Some degree of misclassification of stroke diagnoses particularly for recurrent IS during follow-up solely identified through the Danish National Patient Registry or Danish Death Registry

Conclusions

- Despite advances in SSP, IS recurrence rates after NCIS did not improve in 2012–2022 in Denmark
- The 5-year risk of IS recurrence was 18.9%; younger age and less severe first strokes were associated with lower IS recurrence rates
- However, these results demonstrate an unmet need in all patient subgroups; all presented subgroups had a 12-month IS recurrence rate of greater than 5 per 100 person-years
- Improved secondary prevention strategies are needed for NCIS survivors

IS, ischaemic stroke; NCIS, non-cardioembolic ischaemic stroke; SSP, secondary stroke prevention.