ANTITHROMBOTIC TREATMENT AND RISK OF ISCHAEMIC STROKE RECURRENCE IN PATIENTS WITH NON-CARDIOEMBOLIC ISCHAEMIC STROKE IN ENGLAND: OBSERVATIONS FROM ASTRIS

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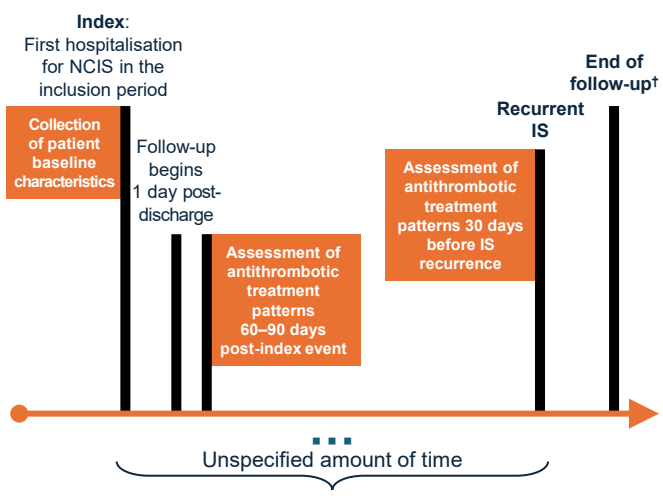
Introduction

- In England, ischaemic stroke (IS) represents 87% of first-ever strokes[1].
- Despite guideline-directed antithrombotic treatments, the risk of recurrent IS remains high[2–5].
- Risk of recurrent IS associated with real-world patterns of antithrombotic treatment use is not well characterised.
- The present study aims to evaluate antithrombotic use after a non-cardioembolic IS (NCIS) in England and examine the association with risk of IS recurrence.

Methods

- ASTRIS UK is a retrospective cohort study that used data from the Clinical Practice Research Datalink-Aurum database (CPRD-A) combined with hospital data from Hospital Episodes Statistics in England to follow patients after first hospitalisation due to NCIS, between 2012 and 2021 (**Figure 1**).
  - The index date was 1 day after discharge of the index NCIS.
- Patients ≥18 years, hospitalised due to an IS, registered with their general practice and who had at least one recorded prescription of any drug >1 year before the index date were included.
- Patients were excluded if they had:
  - A history of atrial fibrillation before index IS hospitalisation and ≤15 days post-discharge.
  - Oral anticoagulant therapy within 90 days before the index NCIS and no record of deep vein thrombosis or pulmonary embolism any time before the index IS hospitalisation.
- Patients were followed from the index date to the occurrence of first recurrent IS, death, last date of data collection from the general practice, or the end of the study period (31 March 2021).
- Use of antithrombotics and other medications was assessed using prospectively collected data on prescriptions from CPRD-A.

Figure 1. Study design



†Patients were followed until the earliest of study endpoint (first recurrence of IS), all-cause death, last date of data collection from the general practice, or the end of study period (31 March 2021).

IS, ischaemic stroke; NCIS, non-cardioembolic ischaemic stroke.

Statistical analysis

- Patients were considered exposed to an antithrombotic treatment up to 30 days after prescription supply ended.
- IS incidence rates were calculated as cases during follow-up divided by the total person-years, with 95% confidence intervals (CIs) assuming a Poisson distribution.
- Recurrent IS risk was analysed using two approaches:
  - On-treatment: based on the initial antithrombotic treatment received from 1 day post-IS with follow-up ending if that treatment was discontinued.
  - As-treated: tracked actual antithrombotic use throughout follow-up, updating exposure status as it changed.
- The risk of recurrent stroke was calculated for each group using Cox proportional hazard regressions adjusted for age, sex and comorbidities at baseline.

References

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Results

Patient characteristics

- At baseline, most patients were aged >75 years (n=21,879; 41.7%) and were male (n=27,873; 53.2%) (**Table 1**).
- The mean follow-up was 3.0 years.
- Common comorbidities included hypertension (n=32,119; 61.3%), hyperlipidaemia (n=17,058; 32.5%) and diabetes (n=12,952; 24.7%).

Table 1. Patient characteristics at index NCIS and incidence of recurrent IS since index NCIS

	Index IS, n (%)†	Recurrent IS, n (%)	IR per 100 P-Ys
Sex			
Male	27,873 (53.2)	3019 (51.5)	3.5
Female	24,546 (46.8)	2838 (48.5)	4.0
Age at index NCIS, years			
<65	16,082 (30.7)	1401 (23.9)	2.5
65–75	14,458 (27.6)	1577 (26.9)	3.3
>75	21,879 (41.7)	2879 (49.2)	5.5
Smoker status			
Never smoker	17,219 (32.8)	1924 (32.8)	3.8
Current	10,586 (20.2)	1087 (18.6)	3.3
Past smoker	20,692 (39.5)	2388 (40.8)	4.0
Missing smoker status	3922 (7.5)	458 (7.8)	3.7
No. of primary care visits in previous year, any diagnosis			
0–4	8596 (16.4)	690 (11.8)	2.4
5–9	8975 (17.1)	835 (14.3)	2.9
10–19	15,671 (29.9)	1800 (30.7)	3.8
>20	19,177 (36.6)	2532 (43.2)	4.9
Baseline eGFR, ml/min/1.73 m^2			
≥90	4311 (8.2)	423 (7.2)	3.0
60–89	12,926 (24.7)	1453 (24.8)	3.8
45–59	4924 (9.4)	632 (10.8)	4.8
30–44	2669 (5.1)	409 (7.0)	6.9
15–29	854 (1.6)	140 (2.4)	9.3
<15	234 (0.4)	46 (0.8)	12.1
Unknown	26,501 (50.6)	2754 (47.0)	3.3
Comorbidity prior to index NCIS			
Hypertension	32,119 (61.3)	4072 (69.5)	4.6
Diabetes	12,952 (24.7)	1865 (31.8)	5.4
Hyperlipidaemia	17,058 (32.5)	2192 (37.4)	4.6
Peripheral artery disease	3147 (6.0)	480 (8.2)	6.2
Ischaemic heart disease	11,926 (22.8)	1769 (30.2)	5.5
Congestive heart failure	2614 (5.0)	360 (6.1)	6.2
Prior transient ischaemic attack	4848 (9.2)	758 (12.9)	5.8
Prior intracranial haemorrhage	1120 (2.1)	137 (2.3)	4.9
Major bleeding event	15,314 (29.2)	1811 (30.9)	4.2
Deep vein thrombosis	3542 (6.8)	461 (7.9)	5.0
Dementia	2879 (5.5)	337 (5.8)	8.5
Cancer	8942 (17.1)	1043 (17.8)	4.8
COPD	6429 (12.3)	800 (13.7)	4.8
Alcohol misuse	4590 (8.8)	505 (8.6)	3.9
Antiplatelet use prior to index NCIS	15,129 (28.9)	2296 (39.2)	5.5

†An index stroke event was defined as NCIS if the patient had no history of AF prior to, or AF ≤15 days from, hospitalisation for IS and had not received oral anticoagulant therapy within 90 days before hospitalisation for IS unless they had a record of either DVT/PE or hip/knee surgery.

AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease; DVT, deep vein thrombosis; eGFR, estimated glomerular filtration rate; IR, incidence rate; IS, ischaemic stroke; NCIS, non-cardioembolic ischaemic stroke; P-Y, patient-years; PE, pulmonary embolism.

Antithrombotic treatment patterns after NCIS and before recurrence

- The antithrombotic treatment patterns of 46,548 patients were assessed 60–90 days after first NCIS.
- Among patients with a NCIS, 42,257 patients (90.8%) received antithrombotic treatment 60–90 days after their first NCIS, with the vast majority being single antiplatelet therapy. Antithrombotic treatment use was comparable between age groups (**Table 2**).
- In patients with a recurrent IS (n=5857), 1570 (26.8%) did not receive antithrombotic treatment 30 days before stroke recurrence.

Conflicts of interest / Disclosures

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Table 2. Antithrombotic treatment patterns after NCIS and before IS recurrence

Antithrombotic treatment, n (%)	60–90 days after first NCIS	30 days before IS recurrence
All patients	N=46,548	N=5857
No antithrombotic treatment	4291 (9.2)	1570 (26.8)
Any antithrombotic treatment	42,257 (90.8)	4287 (73.2)
SAPT	36,806 (79.1)	3675 (62.7)
DAPT	3580 (7.7)	327 (5.6)
Patients <65 years old	N=15,008	N=1401
No antithrombotic treatment	1668 (11.1)	462 (33.0)
Any antithrombotic treatment	13,340 (88.9)	939 (67.0)
SAPT	11,473 (76.4)	801 (57.2)
DAPT	1161 (7.7)	89 (6.4)
Patients 65–75 years old	N=13,322	N=1577
No antithrombotic treatment	1039 (7.8)	403 (25.6)
Any antithrombotic treatment	12,283 (92.2)	1174 (74.4)
SAPT	10,690 (80.2)	977 (62.0)
DAPT	1093 (8.2)	99 (6.3)
Patients >75 years old	N=18,218	N=2879
No antithrombotic treatment	1584 (8.7)	705 (24.5)
Any antithrombotic treatment	16,634 (91.3)	2174 (75.5)
SAPT	14,643 (80.4)	1897 (65.9)
DAPT	1326 (7.3)	139 (4.8)

DAPT, dual antiplatelet therapy; IS, ischaemic stroke; NCIS, non-cardioembolic ischaemic stroke; SAPT, single antiplatelet therapy.

Risk of IS recurrence associated with antithrombotic treatment

- A higher risk of IS recurrence in patients not receiving antithrombotic treatment at the start of follow-up was observed when compared with patients receiving aspirin only (**Table 3**).
  - On-treatment analysis for no antithrombotics: adjusted hazard ratio (aHR [95% CI]), 1.6 (1.2–2.0).
  - As-treated analysis for no antithrombotics: aHR (95% CI), 1.6 (1.4–1.8).
- Similar risks of IS recurrence were observed in patients receiving aspirin, P2Y12 inhibitors and DAPT.

Table 3. Risk of recurrent IS and antithrombotic treatment

	Events, n	P-Y	Recurrent IS	IR per 100 P-Y	aHR† (95% CI)
On-treatment analysis‡					
No antithrombotics	9928	6081	313	5.2	1.6 (1.2–2.0)
ASA only	2230	2171	90	4.2	1 (ref)
P2Y12i only	29,960	56,890	1843	3.2	1.1 (0.9–1.3)
DAPT	3981	1906	131	6.9	1.2 (0.9–1.6)
As-treated analysis‡					
No antithrombotics	26,839	17,900	775	4.3	1.6 (1.4–1.8)
ASA only	5576	8497	279	3.3	1 (ref)
P2Y12i only	39,839	104,947	3107	3.0	1.0 (0.9–1.1)
DAPT	8567	5844	287	4.9	1.1 (0.9–1.3)

For this analysis, follow-up started on Day 30 of follow-up.

†Estimates adjusted for age, sex, Townsend index, BMI, smoking, health services utilisation in the year before index NCIS, comorbidity, renal function (eGFR) and drug use at admission for the index NCIS using a Cox proportional hazard regression model.

‡An adjusted 'on-treatment' approach censored follow-up when initial antithrombotic treatment (treatment received from 1 day post-IS) was discontinued, while the 'as-treated' approach continuously updated antithrombotic exposure status throughout follow-up regardless of initial treatment following an index NCIS.

aHR, adjusted hazard ratio; ASA, acetylsalicylic acid (aspirin); BMI, body mass index; CI, confidence interval; DAPT, dual antiplatelet therapy; eGFR, estimated glomerular filtration rate; IR, incidence rate; IS, ischaemic stroke; NCIS, non-cardioembolic ischaemic stroke; P-Y, person-years; P2Y12i, P2Y12 inhibitor; ref, reference treatment.

Conclusions

- ASTRIS UK shows patients in England had excellent adherence (over 90%) to antithrombotic treatment in the 60–90 days following an index NCIS.
- Patients untreated with antithrombotics had an elevated risk of IS recurrence, highlighting the importance of adhering to guideline-recommended therapy following a NCIS.
- Approximately three out of four patients who suffered a recurrent IS were receiving antithrombotic treatment in the 30 days before the event, underlining the need for improved secondary stroke prevention strategies.
- ASTRIS Denmark, a similarly designed study, is being presented at WSC 2025 as an e-poster highlight (22 October 2025 at 11:45).

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