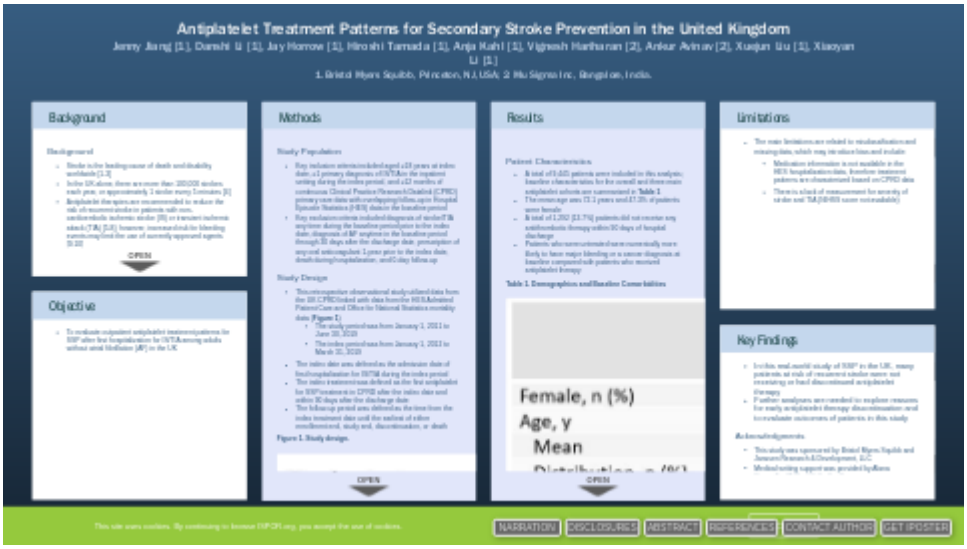
Antiplatelet Treatment Patterns for Secondary Stroke Prevention in the United Kingdom



Jenny Jiang [1], Danshi Li [1], Jay Horrow [1], Hiroshi Tamada [1], Anja Kahl [1], Vignesh Hariharan [2], Ankur Avinav [2], Xuejun Liu [1], Xiaoyan Li [1]

1. Bristol Myers Squibb, Princeton, NJ, USA; 2. Mu Sigma Inc, Bangalore, India.

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BACKGROUND

Background

- Stroke is the leading cause of death and disability worldwide [1-3]
- In the UK alone, there are more than 100,000 strokes each year, or approximately 1 stroke every 5 minutes [4]
- Antiplatelet therapies are recommended to reduce the risk of recurrent stroke in patients with non-cardioembolic ischemic stroke (IS) or transient ischemic attack (TIA) [5-8]; however, increased risk for bleeding events may limit the use of currently approved agents [9,10]
- Real-world data on the effectiveness and safety of antiplatelet regimens are lacking
- It is important to understand treatment patterns for secondary stroke prevention (SSP) after IS/TIA in a real-world setting

OBJECTIVE

- To evaluate outpatient antiplatelet treatment patterns for SSP after first hospitalization for IS/TIA among adults without atrial fibrillation (AF) in the UK

METHODS

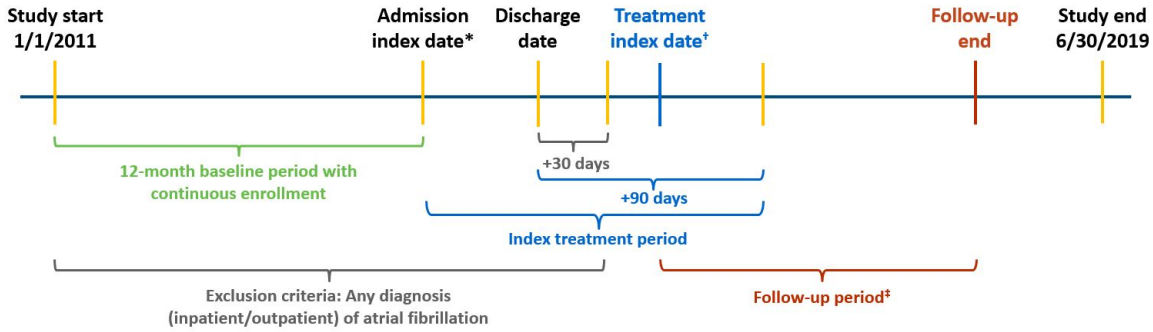
Study Population

- Key inclusion criteria included aged ≥18 years at index date, ≥1 primary diagnosis of IS/TIA in the inpatient setting during the index period, and ≥12 months of continuous Clinical Practice Research Datalink (CPRD) primary care data with overlapping follow-up in Hospital Episode Statistics (HES) data in the baseline period
- Key exclusion criteria included diagnosis of stroke/TIA any time during the baseline period prior to the index date, diagnosis of AF anytime in the baseline period through 30 days after the discharge date, prescription of any oral anticoagulant 1-year prior to the index date, death during hospitalization, and 0-day follow-up

Study Design

- This retrospective observational study utilized data from the UK CPRD linked with data from the HES Admitted Patient Care and Office for National Statistics mortality data (**Figure 1**)
  - The study period was from January 1, 2011 to June 30, 2019
  - The index period was from January 1, 2012 to March 31, 2019
- The index date was defined as the admission date of first hospitalization for IS/TIA during the index period
- The index treatment was defined as the first antiplatelet for SSP treatment in CPRD after the index date and within 90 days after the discharge date
- The follow-up period was defined as the time from the index treatment date until the earliest of either enrollment end, study end, discontinuation, or death

Figure 1. Study design.



IS, ischemic stroke; TIA, transient ischemic attack
*First hospitalization with principal diagnosis of IS/TIA between 1/1/2012 to 3/31/2019.
†First antiplatelet treatment.
‡Any time from treatment index date until minimum of enrollment end, study end, discontinuation or death.

Study Assessments

- Antiplatelet treatment patterns for SSP among patients without AF who experienced their first hospitalized IS/TIA event were evaluated, including:
  - Type of treatment (ie, single antiplatelet therapy [SAPT], dual antiplatelet therapy [DAPT], no antithrombotic therapy)
  - Duration of treatment
  - Treatment patterns (ie, discontinuation, switch, non-treatment)
- Antiplatelet therapies were identified in CPRD by the relevant codes for aspirin, clopidogrel, dipyridamole, prasugrel, ticagrelor, aspirin + dipyridamole (Aggrenox)
- No treatment was defined as no antithrombotic prescription observed in CPRD from the index date to 90 days after the discharge date

Statistical Analyses

- Baseline patient characteristics were summarized using frequencies and percentages for categorical values and descriptive statistics for continuous variables
- Descriptive statistics were used to report treatment patterns

RESULTS

Patient Characteristics

- A total of 9,445 patients were included in this analysis; baseline characteristics for the overall and three main antiplatelet cohorts are summarized in **Table 1**
- The mean age was 72.1 years and 47.3% of patients were female
- A total of 1,292 (13.7%) patients did not receive any antithrombotic therapy within 90 days of hospital discharge
- Patients who were untreated were numerically more likely to have major bleeding or a cancer diagnosis at baseline compared with patients who received antiplatelet therapy

Table 1. Demographics and Baseline Comorbidities

	Overall (N = 9,445)	Untreated (n = 1,292)	Clopidogrel SAPT (n = 5,971)	Aspirin SAPT (n = 1,332)	Clopidogrel + aspirin DAPT (n = 470)
Female, n (%)	4,465 (47.3)	666 (51.5)	2,789 (46.7)	668 (50.2)	179 (38.1)
Age, y					
Mean	72.1	71.8	71.8	74.3	70.2
Distribution, n (%)					
18-54 y	1,143 (12.1)	226 (17.5)	685 (11.5)	114 (8.6)	68 (14.5)
55-64 y	1,462 (15.5)	172 (13.3)	986 (16.5)	174 (13.1)	79 (16.8)
65-74 y	2,228 (23.6)	232 (18.0)	1,494 (25.0)	296 (22.2)	120 (25.5)
75-79 y	1,376 (14.6)	171 (13.2)	847 (14.2)	211 (15.8)	73 (15.5)
≥80 y	3,236 (34.3)	491 (38.0)	1,959 (32.8)	537 (40.3)	130 (27.7)
Comorbidities, n (%)					
Hypertension	4,503 (47.7)	555 (43.0)	2,817 (47.2)	683 (51.3)	262 (55.7)
Diabetes	1,593 (16.9)	169 (13.1)	985 (16.5)	259 (19.4)	120 (25.5)
Renal disease	1,556 (16.5)	211 (16.3)	919 (15.4)	269 (20.2)	86 (18.3)
Chronic obstructive pulmonary disease	1,396 (14.8)	207 (16.0)	829 (13.9)	215 (16.1)	88 (18.7)
Cancer	828 (8.8)	154 (11.9)	500 (8.4)	105 (7.9)	35 (7.4)
Myocardial infarction	730 (7.7)	76 (5.9)	360 (6.0)	138 (10.4)	102 (21.7)
Peripheral vascular disease	560 (5.9)	83 (6.4)	325 (5.4)	84 (6.3)	44 (9.4)
Major bleeding	490 (5.2)	84 (6.5)	287 (4.8)	74 (5.6)	23 (4.9)
Heart failure	397 (4.2)	49 (3.8)	226 (3.8)	63 (4.7)	26 (5.5)

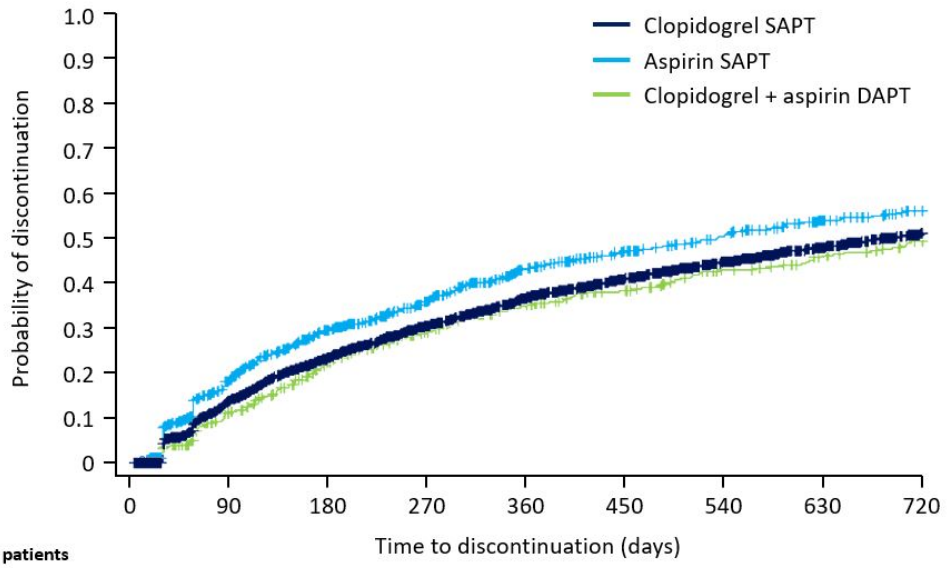
Treatment Patterns

- Altogether, 7,978 patients received antiplatelet treatment within 90 days of hospital discharge
  - Among those patients, the most common treatments were clopidogrel SAPT (n = 5,971; 74.8%), aspirin SAPT (n = 1,332; 16.7%), and clopidogrel + aspirin DAPT (n = 470; 5.9%)
- Among patients treated with any antiplatelet therapy in the index or follow-up periods, the median (range) duration of therapy was 294 (1 to 2,715), 232 (1 to 2,645), and 300 (1 to 2,463) days for patients who initiated clopidogrel SAPT, aspirin SAPT, and clopidogrel + aspirin DAPT, respectively
- Of the 470 patients initiating clopidogrel + aspirin DAPT, 293 (62.3%) switched to SAPT with a median time to switch of 56 days; among those who switched to SAPT, 242 (82.6%) switched to clopidogrel and 51 (17.4%) switched to aspirin
- Two years after initial hospitalization for IS/TIA, 2,386 (40.0%), 588 (44.1%), and 182 (38.7%) patients were observed without antiplatelet treatment among those who previously received clopidogrel SAPT, aspirin SAPT, and clopidogrel + aspirin DAPT, respectively (**Table 2**)
- Two years after initial hospitalization for IS/TIA, the probabilities of discontinuation among patients treated with clopidogrel SAPT, aspirin SAPT, and clopidogrel + aspirin DAPT were 51.2%, 56.3%, and 49.4% respectively (**Figure 2**)
- The median (range) length of stay for the initial hospitalization for IS/TIA was 4 (1 to 232), 4 (1 to 152), and 4 (1 to 83) days for patients who initiated clopidogrel SAPT, aspirin SAPT, and clopidogrel + aspirin DAPT, respectively, and 8 (1 to 388) days for those who were untreated

Table 2. Antiplatelet Therapy Duration by Time Intervals

Discontinued therapy, n (%)	Clopidogrel SAPT (n = 5,971)	Aspirin SAPT (n = 1,332)	Clopidogrel + aspirin DAPT (n = 470)
<90 days from index treatment	796 (13.3)	235 (17.6)	50 (10.6)
<180 days from index treatment	1,292 (21.6)	360 (27.0)	96 (20.4)
<270 days from index treatment	1,629 (27.3)	425 (31.9)	122 (26.0)
<360 days from index treatment	1,894 (31.7)	492 (36.9)	141 (30.0)
<450 days from index treatment	2,062 (34.5)	524 (39.3)	153 (32.6)
<540 days from index treatment	2,191 (36.7)	551 (41.4)	166 (35.3)
<630 days from index treatment	2,298 (38.5)	574 (43.1)	174 (37.0)
<720 days from index treatment	2,386 (40.0)	588 (44.1)	182 (38.7)

Figure 2. Probability of discontinuation of antiplatelet therapies.



Number of patients									
Clopidogrel SAPT	5,971	4,684	3,756	3,121	2,583	2,196	1,872	1,577	1,325
Aspirin SAPT	1,332	968	756	614	492	417	363	305	262
Clopidogrel + aspirin DAPT	470	379	306	253	214	186	155	138	121

Probability of discontinuation									
Clopidogrel SAPT	0	0.141	0.237	0.307	0.369	0.412	0.448	0.481	0.512
Aspirin SAPT	0	0.186	0.296	0.362	0.434	0.473	0.511	0.540	0.563
Clopidogrel + aspirin DAPT	0	0.114	0.224	0.293	0.351	0.386	0.431	0.462	0.494

LIMITATIONS

- The main limitations are related to misclassification and missing data, which may introduce bias and include:
    - Medication information is not available in the HES hospitalization data, therefore treatment patterns are characterized based on CPRD data
    - There is a lack of measurement for severity of stroke and TIA (NIHSS score not available)

KEY FINDINGS

- In this real-world study of SSP in the UK, many patients at risk of recurrent stroke were not receiving or had discontinued antiplatelet therapy
- Further analyses are needed to explore reasons for early antiplatelet therapy discontinuation and to evaluate outcomes of patients in this study

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DISCLOSURES

J. Jiang, D. Li, J. Horrow, H. Tamada, A. Kahl, X. Liu, and X. Li are employees of Bristol Myers Squibb. V. Hariharan and A. Avinav are employees of Mu Sigma Inc.

ABSTRACT

OBJECTIVES: Antiplatelet therapies are recommended to reduce the risk of recurrent stroke in patients with non-cardioembolic ischemic stroke (IS) or transient ischemic attack (TIA); however, increased risk for bleeding may limit the use of currently approved agents. Real-world data on effectiveness and safety of antiplatelet regimens are lacking. This study evaluated outpatient antiplatelet treatment patterns for secondary stroke prevention (SSP) after first hospitalization for IS/TIA among UK adults without atrial fibrillation (AF).

METHODS: This retrospective observational study utilized data from the UK Clinical Practice Research Datalink linked with Hospital Episode Statistics data from 1/1/2011–6/30/2019. Patients with AF diagnosis or oral anticoagulant use before index hospitalization were excluded. Outcomes included type and duration of treatments received for SSP and treatment patterns, including use of single antiplatelet therapy (SAPT) and dual antiplatelet therapy (DAPT).

RESULTS: Of the 9,568 patients in this analysis, mean age was 72.1 years and 47.4% were female; 85.3% were treated with antiplatelet or anticoagulant therapy and 14.7% were untreated within 90 days of hospital discharge. Among 8,162 treated patients, 97.9% received antiplatelets, 2.0% received anticoagulants, and 0.1% received both; the most commonly used antiplatelet therapies were clopidogrel (5,975) or aspirin (1,336) SAPT and clopidogrel+aspirin DAPT (470). The median duration of any antiplatelet therapy was 293, 232, and 300 days for patients who initiated clopidogrel, aspirin, and DAPT, respectively. Of patients initiating DAPT, 62.3% switched to SAPT (83% clopidogrel, 17% aspirin; median time to switch=56 days). Two years after initial hospitalization for IS/TIA, 39.9%, 44.1%, and 38.7% of patients no longer took antiplatelet treatment among those previously receiving clopidogrel, aspirin, and DAPT, respectively.

CONCLUSION: Many patients at risk of secondary stroke were not receiving or had discontinued antiplatelet therapy. Further analyses are needed to explore reasons for early antiplatelet discontinuation and evaluate outcomes of patients in this study.

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