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Research article

Antiplatelet treatment patterns and outcomes of secondary stroke prevention in the United States

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ABSTRACT

Objective: Patients who have an ischemic stroke (IS) or transient ischemic attack (TIA) are at risk of having a secondary stroke. Single antiplatelet therapy (SAPT) or dual antiplatelet therapy (DAPT) may be recommended for secondary stroke prevention (SSP), depending on severity and etiology. This study evaluated outpatient antiplatelet treatment patterns for SSP and outcomes after first hospitalization for IS/TIA among adults without atrial fibrillation in the United States.
Materials and methods: This retrospective observational study utilized data from an adjudicated administrative health claims database. Eligible patients had an imputed National Institutes of Health Stroke Scale index event score ≤7. Over-the-counter medication use (eg, aspirin) was not captured.
Results: Of 154,273 patients, 41,622 (27%) were prescribed antiplatelet therapy within 90 days of the event; 93.8% received SAPT, 6.1% received DAPT. The first line of antiplatelet therapy after discharge was started a mean of 17.0 days after the event; mean treatment duration was 61.9 days. The incidence rate for secondary IS was 5.53, 2.03, and 1.17 per person-year 90-days, 1-year, and 3-years following treatment initiation, respectively. Among patients matched for demographic and clinical characteristics, the risk of secondary IS was increased with DAPT versus SAPT (hazard ratio [95% CI]: 1.27 [1.20–1.34]; $p < 0.0001$).
Conclusions: Many patients were not prescribed or discontinued antiplatelet therapy within 90 days of hospitalization for IS/TIA and, in most cases, prescriptions were not compliant with SSP consensus guidelines. Patients remained at risk for IS, which was highest within 90 days. More effective strategies for SSP are needed to improve outcomes in this patient population.

1. Introduction

Stroke is the second leading cause of death worldwide and was responsible for 143 million disability-adjusted life-years and 6.55 million deaths in 2019 [1]. In the United States, the prevalence of stroke among adults was 3.0% in 2017 and is expected to reach 3.9% by 2030 due to the aging population and accumulation of risk factors [2]. Currently, approximately 795,000 people in the United

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States experience a stroke each year [2]. The direct medical cost for stroke in the United States was $36.7 billion in 2015 and is projected to more than double to $94.3 billion by 2035 [2].

Patients who have a minor ischemic stroke (IS) or transient ischemic attack (TIA) have an estimated 3%–4% risk of secondary stroke within 90 days of the initial event [3–5]. Longer term, the risk of secondary stroke persists between 5.1% at year 1 and 9.5% at year 5 [6].

Use of antiplatelet therapy is widely recommended for secondary stroke prevention (SSP) in patients with IS or TIA [7–9]. In those with minor IS [National Institutes of Health Stroke Scale (NIHSS) score ≤3 [7,8]] or high-risk TIA [ABDC^2 score ≥3 [10]], dual antiplatelet therapy (DAPT) with clopidogrel and aspirin started within 12–24 h of symptom onset and continued for 21–90 days, followed by single antiplatelet therapy (SAPT), is now recommended in several consensus guidelines to maximize benefit [7–9]. Long-term use of DAPT, or the use of multiple antiplatelet therapy (MAPT) for any length of time, should be avoided due to an increased risk of bleeding [8].

Currently, real-world US data on antiplatelet treatment patterns and outcomes after the first IS/TIA are limited [11,12]. Given the recent updates to consensus guidelines, there is a need for up-to-date real-world information. This study used a US health claims database to evaluate treatment patterns and outcomes in patients without atrial fibrillation (AF) who were prescribed antiplatelet therapy for SSP following hospitalization for the initial IS or TIA and who had an NIHSS score ≤7.

This study contributes valuable knowledge in the IS/TIA disease space:

- Provides up-to-date, real-world data on treatment patterns for SSP after mild to moderate IS/TIA
- Is the first of its kind to use a validated machine learning algorithm to assess stroke severity

2. Methods

2.1. Study design

This was a retrospective, observational study of treatment patterns and outcomes in hospitalized patients diagnosed with primary IS or TIA without AF. Data were obtained from the Optum® Clinformatics® Data Mart Date of Death database (Optum DOD). Optum DOD is an adjudicated US administrative health claims database for members of private health insurance. It includes data on inpatient and outpatient medical services, prescriptions as dispensed, outpatient lab tests processed by some vendors, and date of death. It does not cover the use of over-the-counter medications such as aspirin.

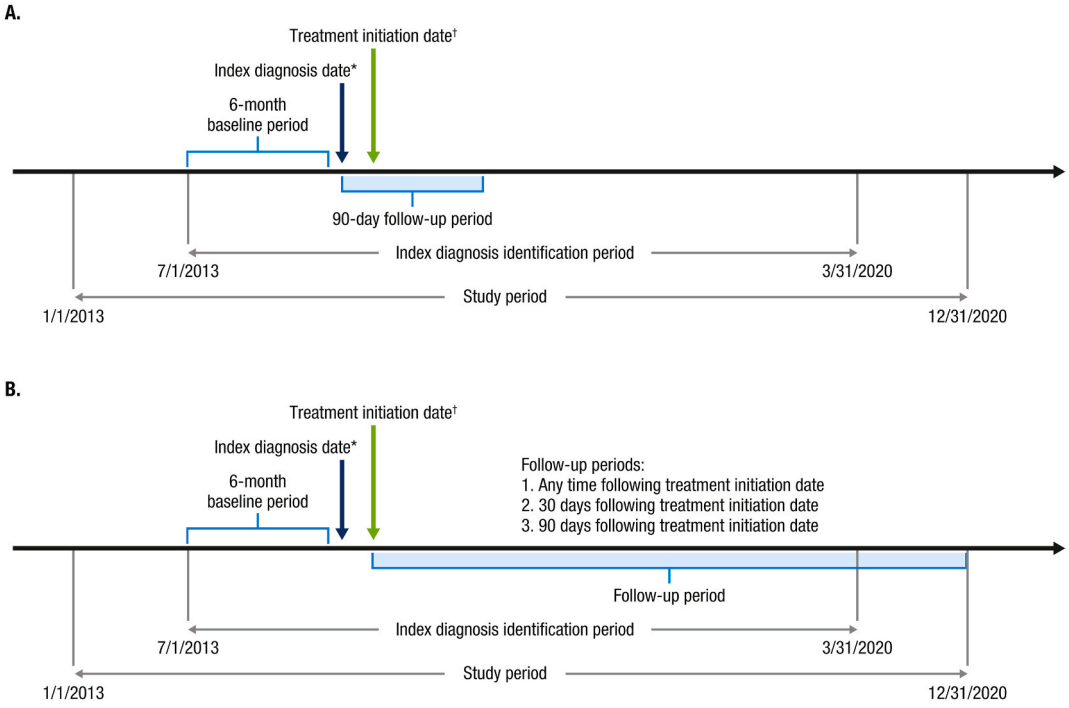

Fig. 1. Study timeframes for (A) analysis of treatment patterns and (B) analysis of clinical outcomes. IS, ischemic stroke; TIA, transient ischemic attack. *First hospitalized IS/TIA event. †First antiplatelet therapy for secondary IS/TIA prevention.

2.2. Participants

Adults ≥18 years of age with ≥1 inpatient hospitalization with a primary diagnosis of IS or TIA (index event), continuous health insurance eligibility for ≥6 months prior to and ≥90 days after the index event, and an imputed NIHSS score for the index event ≤7 were included in the analyses. The index date was defined as the date of admission to the hospital for the index event. Patients were excluded if they had a diagnosis of AF at any time prior to the index event to 30 days after the index event; a diagnosis of IS, TIA, or hemorrhagic stroke at any time prior to the index event; and/or ≥1 pharmacy claim for anticoagulants from 6 months prior to the index event to 90 days following the index event.

2.3. Assessments

Primary study objectives were to evaluate treatment patterns of prescribed outpatient antiplatelet therapies after the first hospitalization for IS or TIA, to evaluate clinical outcomes of interest after antiplatelet therapy initiation, and to investigate the risk of clinical outcomes in patients prescribed SAPT versus DAPT (defined as 2 antiplatelet agents initiated on the same day, including aspirin/dipyridamole) within 90 days of the index event.

Analysis of treatment patterns included type of treatment, treatment sequence, and duration of each line of treatment. Patient demographics and comorbidities were stratified according to treatment with SAPT, DAPT, or MAPT (3 antiplatelet agents on the same day, including aspirin/dipyridamole), or no treatment based on the index prescription. Study antiplatelet agents included aspirin, aspirin/dipyridamole, cilostazol, clopidogrel, dipyridamole, prasugrel, ticagrelor, and ticlopidine.

Clinical outcomes of interest were secondary IS/TIA, myocardial infarction (MI), major bleeding, and death. The probability of having a claim with a primary diagnosis of IS, TIA, or MI during the follow-up period was analyzed.

2.4. Data collection

The study was conducted between January 1, 2013 and December 31, 2020 (Fig. 1). For the analysis of treatment patterns, patients were followed for a period of 90 days after the index event. For the analysis of clinical outcomes, patients were followed from the treatment initiation date to the earliest of first outcome of interest, death, end of health insurance eligibility, or end of study. The treatment initiation date was defined as the first outpatient prescription for antiplatelet therapy for secondary IS/TIA prevention within 90 days of the index event.

A validated prediction model based on Optum integrated databases of electronic health records and claims data was used to impute NIHSS scores for all IS/TIA patients. This machine learning algorithm analyzed 127 clinically relevant predictors from patients who had an inpatient stroke diagnosis and a NIHSS score recorded on claims data [13,14].

To calculate CHA_2DS_2-VASc score using claims data, the original scoring algorithm was slightly modified to consider a prescription fill for antidiabetic medication as equivalent to a diagnosis of diabetes mellitus [15]. The HAS-BLED scoring algorithm was slightly

Table 1
Patient demographics and comorbidities according to first prescription of antiplatelet therapy.

	Overall (N = 154,273)	First prescription of antiplatelet therapy (n = 41,622)			No prescription antiplatelet therapy (n = 112,651)
		SAPT (n = 39,062)	DAPT (n = 2,537)	MAPT (n = 23)	
Female, n (%)	85,862 (55.7)	19,257 (49.3)	1,148 (45.3)	9 (39.1)	65,448 (58.1)
Age, years, mean (SD)	69.6 (12.9)	69.5 (11.6)	65.6 (12.3)	73.4 (8.0)	69.8 (13.4)
QCI, mean (SD)	1.2 (1.7)	1.1 (1.6)	0.8 (1.4)	1.1 (1.6)	1.2 (1.7)
Modified CHA_2DS_2-VASc score, mean (SD)	2.7 (1.7)	2.9 (1.8)	2.3 (1.8)	2.9 (2.1)	2.7 (1.7)
Modified HAS-BLED score, mean (SD)	2.1 (1.4)	2.2 (1.5)	1.8 (1.5)	2.2 (1.8)	2.0 (1.4)
Comorbidities, n (%)					
Hypertension	98,582 (63.9)	26,402 (67.6)	1,460 (57.5)	13 (56.5)	70,707 (62.8)
Hyperlipidemia	77,346 (50.1)	21,485 (55.0)	1,206 (47.5)	10 (43.5)	54,645 (48.5)
Diabetes	51,342 (33.3)	15,358 (39.3)	907 (35.8)	10 (43.5)	35,067 (31.1)
CAD	27,000 (17.5)	10,163 (26.0)	413 (16.3)	5 (21.7)	16,419 (14.6)
Anemia	24,242 (15.7)	5,365 (13.7)	267 (10.5)	4 (17.4)	18,606 (16.5)
PVD	20,816 (13.5)	6,313 (16.2)	297 (11.7)	3 (13.0)	14,203 (12.6)
CHF	11,419 (7.4)	3,384 (8.7)	150 (5.9)	3 (13.0)	7,882 (7.0)
CKD	10,174 (6.6)	2,679 (6.9)	118 (4.7)	1 (4.3)	7,376 (6.5)
Old MI[a]	5,227 (3.4)	2,174 (5.6)	61 (2.4)	2 (8.7)	2,990 (2.7)
Acute MI	2,957 (1.9)	1,295 (3.3)	43 (1.7)	–	1,619 (1.4)
VTE	2,215 (1.4)	389 (1.0)	14 (0.6)	–	1,812 (1.6)

CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; DAPT, dual antiplatelet therapy; MAPT, multiple antiplatelet therapy; MI, myocardial infarction; PVD, peripheral vascular disease; QCI, Quan-Charlson comorbidity index; SAPT, single antiplatelet therapy; SD, standard deviation; VTE, venous thromboembolism.

[a] Includes healed MI or past MI diagnosed by electrocardiogram or other investigation, but currently presenting no symptoms.

modified to consider treatment with an antihypertensive as equivalent to a diagnosis of hypertension, remove the labile international normalized ratio condition, and consider treatment with nonsteroidal anti-inflammatory drugs or antiplatelets as concomitant drug use [16].

2.5. Statistical analyses

Descriptive statistics were used to summarize baseline patient characteristics and outcomes. Frequencies and percentages were used to describe categorical variables; means and standard deviations were used for continuous variables. Clinical outcomes were investigated with time-to-event analyses using standard Kaplan-Meier methods. Cox proportional hazard regression, with adjustment for baseline confounders, was used to assess the association between type of antiplatelet therapy (SAPT vs DAPT) and risk of clinical outcomes with hazard ratios (HRs) and 95% confidence intervals (CIs).

The propensity of receiving SAPT was predicted using a logistic regression model with potential confounders of age, sex, index year, baseline comorbidities, and comorbidity risk scores (ie, Quan-Charlson comorbidity index [QCI], CHA_2DS_2-VASc, and HAS-BLED), and baseline medication use. Patients receiving SAPT were matched 1:1 with patients receiving DAPT based on demographic and baseline clinical characteristics without replacement on the logit of the propensity score using calipers of width equal to 20% of the standard deviation of the logit of the propensity score. Descriptive statistics were used to summarize demographic and baseline characteristics for each treatment cohort. Standardized differences in baseline characteristics of $<10\%$ were considered a negligible imbalance.

3. Results

3.1. Patient characteristics

A total of 154,273 patients with IS or TIA during the index period were included, of whom 41,622 (27%) received a prescription for antiplatelet therapy and 112,651 (73%) did not receive any prescribed antiplatelet therapy within 90 days of the index event (Table 1). In the overall population, mean patient age was 69.6 years and 55.7% of patients were female. Mean QCI was 1.2, mean modified CHA_2DS_2-VASc score was 2.7, and mean modified HAS-BLED score was 2.1. Cardiovascular-related comorbidities in the overall study population included hypertension (63.9%), hyperlipidemia (50.1%), diabetes (33.3%), coronary artery disease (17.5%), anemia (15.7%), and peripheral vascular disease (13.5%). Baseline characteristics were generally similar in patients who received antiplatelet therapy and the untreated population.

3.2. Treatment patterns

Of the 41,622 patients who were prescribed antiplatelet therapy within 90 days of hospitalization for IS/TIA, 93.8% received SAPT, 6.1% received DAPT, and 0.1% received MAPT as their first line of antiplatelet therapy (Table 2). The most commonly used prescription antiplatelet therapies were clopidogrel (79.5%), aspirin (11.4%), and aspirin/dipyridamole (3.4%; Table 3).

The mean duration for the first line of prescribed antiplatelet therapy was 61.9 days. 28.6% of patients had a treatment change within 90 days following the index event, and most patients continued the first line of therapy beyond 90 days. Of patients who had a change in first line of therapy within 90 days, the most common reason was discontinuation of prescribed antiplatelet therapy (57.7%).

Table 2
Treatment sequence and line of antiplatelet therapy duration.

	First line of antiplatelet therapy (n = 41,622)	Second line of antiplatelet therapy (n = 2,519)
Type of treatment, n (%)		
SAPT	39,062 (93.8)	1,296 (51.4)
DAPT	2,537 (6.1)	907 (36.0)
MAPT	23 (0.1)	316 (12.5)
Duration of treatment, days, mean (SD)	61.9 (27.1)	31.5 (21.4)
Time to start of treatment, days, mean (SD)[a]	17.0 (21.3)	11.7 (16.9)
Change in treatment within 90 days of first IS/TIA hospitalization, n (%)	11,886 (28.6)	901 (35.8)
Add-on	1,183 (10.0)	51 (5.7)
Switching	560 (4.7)	24 (2.7)
De-escalation	618 (5.2)	667 (74.0)
Restart[b]	2,670 (22.5)	40 (4.4)
Discontinue[c]	6,855 (57.7)	119 (13.2)

DAPT, dual antiplatelet therapy; IS, ischemic stroke; MAPT, multiple antiplatelet therapy; SAPT, single antiplatelet therapy; SD, standard deviation; TIA, transient ischemic attack.

[a] First line of antiplatelet therapy: time from first IS/TIA hospitalization admission to start of first line of therapy; second line of antiplatelet therapy: time from end of first line of therapy to start of second line of therapy.

[b] Restart of the same antiplatelet therapy.

[c] Discontinuation of the current antiplatelet therapy with no further therapy identified.

Table 3
Initial prescription for antiplatelet therapy within 90 Days of ischemic stroke or transient ischemic event.

Antiplatelet agent prescribed for first line of antiplatelet therapy, n (%)	Patients (n = 41,622)
Clopidogrel	33,074 (79.5)
Aspirin	4,764 (11.4)
Aspirin/dipyridamole	1,397 (3.4)
Aspirin + clopidogrel	1,054 (2.5)
Ticagrelor	628 (1.5)
Other[a]	705 (1.7)

[a] Includes cilostazol, prasugrel, cilostazol + clopidogrel, dipyridamole, aspirin + ticagrelor, aspirin/dipyridamole + clopidogrel, aspirin/dipyridamole + aspirin, cilostazol + ticagrelor, clopidogrel + prasugrel, clopidogrel + ticagrelor, aspirin/dipyridamole + cilostazol, aspirin + prasugrel, and ticlopidine.

Among the 2,519 patients who received a second line of prescribed antiplatelet therapy within 90 days of the index date, the mean treatment duration was 31.5 days; SAPT was prescribed for 51.4% of these patients, DAPT for 36.0%, and MAPT for 12.5%. Of patients who had a change in second line of therapy within 90 days, the most common reason was de-escalation of prescribed antiplatelet therapy (74.0%).

4. Outcomes

The incidence of clinical outcomes was assessed in 46,148 patients who initiated prescribed antiplatelet therapy for secondary

Table 4
Incidence of clinical outcomes of interest following initiation of antiplatelet therapy.

	Patients prescribed antiplatelet therapy (n = 46,148)	
	Cases (n)	Incidence rate (per PY)
IS		
30 days	25,305	12.62
90 days	27,383	5.53
1 year	29,326	2.03
2 years	30,174	1.38
3 years	30,555	1.17
Overall	30,850	1.01
TIA		
30 days	12,223	4.11
90 days	13,725	1.73
1 year	15,546	0.63
2 years	16,403	0.43
3 years	16,784	0.36
Overall	17,106	0.32
MI		
30 days	2,497	0.68
90 days	3,633	0.36
1 year	5,922	0.18
2 years	7,177	0.14
3 years	7,714	0.12
Overall	8,213	0.11
Major bleeding[a]		
30 days	126	0.03
90 days	320	0.03
1 year	736	0.02
2 years	1,032	0.02
3 years	1,200	0.02
Overall	1,368	0.02
Death[b]		
30 days	147	0.04
90 days	642	0.06
1 year	2,062	0.06
2 years	3,220	0.06
3 years	3,962	0.06
Overall	4,941	0.06

HIPAA, Health Insurance Portability and Accountability Act; IS, ischemic stroke; MI, myocardial infarction; PY, person-year; TIA, transient ischemic attack.

[a] As defined using the Cunningham algorithm.

[b] To be compliant with HIPAA regulations, date of death was recorded as the last day of the month in which the death occurred.

prevention of IS/TIA within 90 days of the index event and had available data.

The rates of IS, TIA, MI, major bleeding, and death up to 3 years following prescribed antiplatelet therapy initiation are shown in Table 4. At 90 days following treatment initiation, the incidence rate for secondary IS per person-year was 5.53, dropping to 2.03 at 1 year and 1.17 at 3 years. The incidence rate for major bleeding per person-year was low across time at 0.03 at 90 days following treatment initiation and 0.02 at 3 years.

Patients who received DAPT (n = 2,537) were matched to those who received SAPT (n = 39,062) based on demographic and baseline clinical characteristics, including age, sex, index year of treatment, QCI, CHA_2DS_2-VASc score, HAS-BLED score, and comorbidities (Supplementary Table 1). In the matched sample, risk of secondary IS was increased in patients who received DAPT versus SAPT (HR [95% CI]: 1.27 [1.20–1.34]; $p < 0.0001$; Fig. 2). There were no significant differences in the risk of other outcomes, including TIA, MI, major bleeding, or death.

Patients who received DAPT were more likely to have a claim with a primary diagnosis of IS during the follow-up period compared with those who received SAPT (HR [95% CI]: 1.15 [1.00–1.32]; $p < 0.04$). There were no differences between the SAPT and DAPT groups in the probability of having a claim with a primary diagnosis of TIA or MI during follow-up.

5. Discussion

Data from the present study provide insight into the prescription treatment patterns and outcomes associated with secondary stroke prevention in the United States. The majority of patients from the Optum DOD database included in this analysis (73%) did not receive a prescription for antiplatelet therapy within 90 days of hospitalization for their first IS/TIA. It is important to note, however, that the Optum DOD database does not cover the use of over-the-counter medications such as aspirin, which likely resulted in the misclassification of treatment for some patients in this study. Of the 27% of patients who were prescribed antiplatelet therapy within 90 days of hospitalization, 93.8% received SAPT, 6.1% received DAPT, and 0.1% received MAPT as their first line of treatment. This treatment line was started an average of 17 days after the index event and was continued for a mean of 62 days. A total of 6% of patients received a second line of antiplatelet therapy within 90 days of the index event, and this was continued for an average of 32 days.

These results suggest some differences may exist between clinical guidelines and real-world practice. Current recommendations advise the early initiation of antiplatelet therapy after an IS/TIA, including short-term use of DAPT in those with minor IS or high-risk TIA [7–9]. However, the majority of patients in this study received no prescription for antiplatelet therapy, and of those who did receive a prescription, almost all received SAPT rather than DAPT. Although these findings suggest that there may be important differences between clinical recommendations and current practice, the present study did not capture in-patient antiplatelet therapy, which represents the true starting point of first-line therapy, nor did it capture the use of the over-the-counter aspirin. Failure to account for over-the-counter aspirin use may have resulted in some patients on DAPT being wrongly classified as receiving SAPT and some patients receiving over-the-counter aspirin classified as untreated.

These results are consistent with a study presented at the 2020 Congress of the International Society on Thrombosis and Haemostasis, which showed that the majority of US patients diagnosed with IS between 2008 and 2018 did not receive antiplatelet therapy for secondary prevention in the 30 days after hospitalization [12]. This study also did not capture data on over-the-counter aspirin use [12]. In contrast, a study using data from the US Get With The Guidelines®– Stroke Registry and Medicare claims found that almost all patients hospitalized with minor stroke or high-risk TIA between 2011 and 2014 were prescribed antiplatelet therapy upon discharge, with the majority of patients receiving SAPT [11].

Among patients who received a prescription for antiplatelet therapy at any time point during the follow-up period, the incidence rate for secondary IS remained high at 90 days following treatment initiation but decreased at 3 years. The 90-day incidence rate for

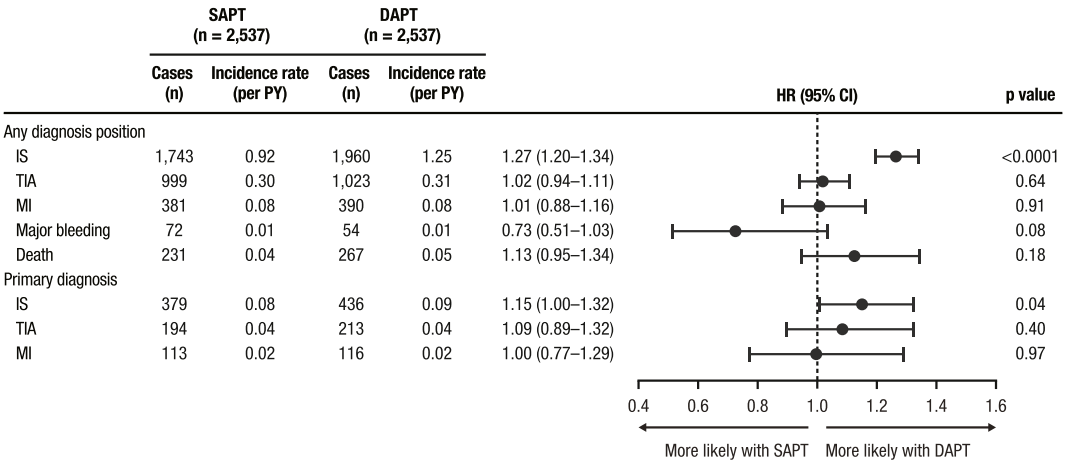

Fig. 2. Risk of clinical outcomes of interest in patients prescribed SAPT versus DAPT. CI, confidence interval; DAPT, dual antiplatelet therapy; HR, hazard ratio; IS, ischemic stroke; MI, myocardial infarction; PY, person-year; SAPT, single antiplatelet therapy; TIA, transient ischemic attack.

secondary IS in our study was consistent with previously published reports [3–5]. The incidence rate for major bleeding remained relatively constant over time. These findings highlight the residual risk of secondary IS in patients receiving antiplatelet therapy, suggesting a need for new treatment strategies that are safe and effective for long-term SSP.

These results showed an increased risk of secondary IS in patients who received DAPT versus SAPT and a tendency toward a lower risk of major bleeding. These results were unexpected and are likely to be at least somewhat confounded by the relatively limited sample size of the matched SAPT versus DAPT populations and a failure to capture over-the-counter aspirin use. Of note, these data contrast with the findings of randomized controlled trials that have informed consensus guidelines [17–21]. The Clopidogrel in High-Risk Patients with Acute Non-disabling Cerebrovascular Events (CHANCE) and Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) trials both showed clear reductions in the risk of recurrent IS with clopidogrel + aspirin versus aspirin alone when treatment was initiated within 1 day of the event [17,18]. The POINT trial also showed an increased risk of major bleeding in patients who received DAPT, but a secondary analysis found this was only evident in patients who continued DAPT for longer than 21 days [18,19]. The Acute Stroke or Transient Ischaemic Attack Treated with Ticagrelor and Aspirin for Prevention of Stroke and Death (THALES) trial showed a reduced risk of recurrent IS with a 30-day regimen of ticagrelor + aspirin versus aspirin alone, albeit at the cost an increased risk of severe bleeding [20]. Unlike in clinical trials, the current study may have been impacted by use of over-the-counter aspirin, as patients assigned to the SAPT group could have been treated with DAPT, consisting of a prescription antiplatelet and over-the-counter aspirin. Additionally, it is possible that a higher proportion of patients who were prescribed DAPT discontinued treatment compared to those who were prescribed SAPT. These results should be interpreted with caution due to the potential for confounding bias that cannot be fully addressed by matching and misclassification bias.

To date, few studies have examined antiplatelet treatment patterns and clinical outcomes for secondary stroke prevention in patients without atrial fibrillation. One multicenter retrospective cohort study conducted in the United States used data from hospitals participating in the Get With The Guidelines-Stroke program, an ongoing voluntary national stroke registry, evaluated DAPT prescription upon hospital discharge after minor versus nonminor acute ischemic stroke [22]. Despite updated American Heart Association/American Stroke Association guidelines, >50% of patients with minor acute ischemic stroke did not receive DAPT, and >40% of patients with nonminor stroke received DAPT at discharge [22]. Other studies include a multicenter analysis of patients with stroke in Korea which showed that a high percentage of patients received antithrombotics after the initial stroke event, and outcomes were most favorable in those patients receiving aspirin monotherapy [23]. A database study from Taiwan showed that the recurrence of stroke was similar between patients treated with aspirin and clopidogrel [24]. Moreover, a retrospective study from China assessed the long-term efficacy and safety of clopidogrel versus aspirin after the initial stroke event [25]. The current study is unique in its use of a US health claims database and its evaluation of treatment patterns focused on the use of SAPT versus DAPT.

Strengths of the current study include the large sample size with longitudinal follow-up data, offering an up-to-date, real-world view of treatment patterns for SSP after mild to moderate IS/TIA. The CHA_2DS_2-VASc score was utilized in the present study despite it originally being developed for use in patients with AF. Recent evidence has shown that this scale predicts IS/TIA events with similar accuracy in AF and non-AF patients, and may therefore permit the earlier initiation of treatment in patients without AF [26,27]. This study was also the first of its kind to assess stroke severity (NIHSS score) using a machine learning algorithm. In addition, to our knowledge, the study is the first to examine patients from the United States using claims data focusing on the use of SAPT versus DAPT. The main limitation of this study is the fact that claims data do not include over-the-counter medications, in particular aspirin or those provided as samples by a physician, potentially leading to underestimation of treatment use. Efforts are underway to develop and validate methods for using electronic medical record data to determine over-the-counter aspirin use [28,29]. Future observational studies of US patients that account for over-the-counter aspirin use may be able to provide more meaningful insights. Other study limitations include the fact that data in the Optum DOD database are limited to the commercially insured population and cannot be generalized to the US population. Although a large population was initially included, matched analyses of patients who received SAPT versus DAPT had a substantially reduced the sample size (n = 2,537). There is also potential for misclassification bias from inability to identify any stroke occurring before the timeframe examined. Finally, this analysis also failed to capture the nature or duration of in-patient treatment and hospitalization, and whether patients were discharged to a rehabilitation facility, which may have influenced future outpatient treatment decisions.

In conclusion, this analysis of a large real-world database shows that the majority of patients at risk of secondary stroke in the United States are not prescribed antiplatelet therapy within 90 days of hospitalization for IS/TIA; however, this does not account for over-the-counter aspirin use. In addition, almost all patients received SAPT as their first prescription and, on average, treatment was not started until more than 2 weeks after the index event. Patients who received prescription antiplatelet therapy had a residual risk of recurrent IS, which was highest immediately following the first IS/TIA event, highlighting the need for more effective SSP strategies to improve outcomes in this patient population.

Disclosures

Ellen O'Brien is an employee of Janssen Global Services, LLC. Dejan Milentijevic and Cindy Y. Chen are employees of Janssen Scientific Affairs, LLC. Rajarshi Roychowdhury and Smita Mitra are employees of Janssen Business Technology Commercial Data Services. Medical writing support was provided by Dana Tabor, PhD, of Lumanity Communications, Inc., and was funded by Bristol Myers Squibb and Janssen Global Services, LLC.

Author contributions

Ellen O'Brien and Dejan Milentijevic conceived and designed the experiments, analyzed and interpreted the data, and wrote the paper.

Rajarshi Roychowdhury and Smita Mitra performed the experiments and wrote the paper.

Cindy Y. Chen conceived and designed the experiments, performed the experiments, analyzed and interpreted the data, and wrote the paper.

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Appendix A. Supplementary data

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