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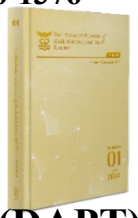

Effectiveness of Dual Antiplatelet Therapy (DAPT) to Reduce Stroke Recurrence in Patients with Minor Stroke or High Risk Transient Ischemic Attach (TIA): A Comprehensive Systematic Review

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ABSTRACT

Background Patients who experience a minor stroke or a high-risk transient ischemic attack (TIA) are at an increased risk of stroke recurrence. Effective secondary prevention strategies are critical to reducing the burden of stroke-related morbidity and mortality. This systematic review aims to evaluate the effectiveness of DAPT in reducing stroke recurrence in patients with minor stroke or high-risk TIA. **Methods:** The study followed PRISMA 2020 guidelines, reviewing English-language publications from 2015 to 2025. Editorials, duplicate reviews from the same journal, and papers lacking a DOI were excluded. The literature search was conducted using PubMed, SagePub, SpringerLink, and Google Scholar. **Result:** A total of 1.800 articles were initially identified through online databases (PubMed, SagePub, SpringerLink, and Google Scholar). After three rounds of screening, eight relevant studies were selected for full-text analysis. **Conclusion:** DAPT is a superior strategy compared to SAPT in reducing stroke recurrence in patients with minor stroke or high-risk TIA. However, its safety concerns, particularly regarding major bleeding, necessitate careful patient selection and treatment duration optimization. Current data suggest that a 21-day DAPT regimen followed by SAPT offers the best balance of efficacy and safety, particularly in patients with atherosclerotic stroke. Future studies should continue refining treatment approaches to maximize the benefits of DAPT while minimizing risks.

Keywords: dual antiplatelet therapy, transient ischemic attack, ischemic stroke

INTRODUCTION

Stroke remains a leading cause of mortality and long-term disability worldwide, with a significant proportion of cases attributed to recurrent ischemic events. Patients who experience a minor stroke or a high-risk transient ischemic attack (TIA) are at an increased risk of stroke recurrence, especially within the first few weeks following the initial event. Effective secondary prevention strategies are critical to reducing the burden of stroke-related morbidity and mortality. Dual antiplatelet therapy (DAPT), which typically combines aspirin and a P2Y12 inhibitor such as clopidogrel or ticagrelor, has been proposed as a more effective treatment strategy compared to single antiplatelet therapy in reducing the risk of recurrent stroke in this vulnerable population.[1,2]

The rationale for DAPT in secondary stroke prevention is based on its potential to provide enhanced platelet inhibition, thereby mitigating the risk of thrombus formation in patients with underlying cerebrovascular disease. Unlike single antiplatelet therapy, which primarily targets a single pathway in platelet aggregation, DAPT exerts a synergistic effect by blocking multiple pathways involved in platelet activation. This dual mechanism of action is hypothesized to offer superior protection against recurrent stroke, particularly in patients with underlying atherosclerotic disease or other high-risk features.[3,4]

Several landmark clinical trials, including the CHANCE (Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events) and POINT (Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke) trials, have provided evidence supporting the short-term benefits of DAPT in reducing the risk of stroke recurrence. These studies demonstrated that a short-term course of DAPT, initiated soon after a minor stroke or high-risk TIA, significantly reduces the risk of recurrent stroke compared to aspirin alone. However, the duration of therapy remains a topic of ongoing debate, as prolonged use of DAPT has been associated with an increased risk of bleeding complications.[5,6]

Despite the promising findings from clinical trials, the real-world effectiveness and safety of DAPT for stroke prevention remain areas of active

investigation. Variability in patient characteristics, stroke etiology, and adherence to treatment guidelines may influence the overall outcomes of DAPT in diverse clinical settings. Furthermore, the balance between efficacy and bleeding risk must be carefully evaluated, particularly in populations with a high propensity for hemorrhagic complications. Recent studies have provided substantial evidence supporting the use of DAPT in reducing the risk of recurrent stroke, particularly within the first 90 days following a minor stroke or high-risk TIA.[7] This systematic review aims to evaluate the effectiveness of DAPT in reducing stroke recurrence in patients with minor stroke or high-risk TIA by synthesizing evidence from clinical trials and observational studies.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate the effectiveness of DAPT in reducing stroke recurrence in patients with minor stroke or high-risk TIA based on literatures of the last decade. The review aimed to provide insights to improve patient treatment strategies, with an emphasis on the significance of key findings in the reviewed studies. Inclusion criteria for the study included: 1) Papers published in English, and 2) Papers published between 2015 and 2025. Exclusion criteria were: 1) Editorials, 2) Papers without a DOI, 3) Previously published review articles, and 4) Duplicate entries in journals.

Search Strategy

The keywords used for this research are dual antiplatelet therapy, transient ischemic attack, ischemic stroke. The Boolean MeSH keywords inputted on databases for this research are: *"dual"[All Fields] AND ("antiplatelet"[All Fields]*

OR "antiplatelets"[All Fields]) AND ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "therapies"[All Fields] OR "therapy"[MeSH Subheading] OR "therapy"[All Fields] OR "therapy s"[All Fields] OR "therapys"[All Fields]) AND ("transient ischaemic attack"[All Fields] OR "ischemic attack, transient"[MeSH Terms] OR ("ischemic"[All Fields] AND "attack"[All Fields] AND "transient"[All Fields]) OR "transient ischemic attack"[All Fields] OR ("transient"[All Fields] AND "ischemic"[All Fields] AND "attack"[All Fields])) AND ("ischemic stroke"[MeSH Terms] OR ("ischemic"[All Fields] AND "stroke"[All Fields]) OR "ischemic stroke"[All Fields]).

Data retrieval

Abstracts and titles were screened to assess their eligibility, and only studies meeting the inclusion criteria were selected for further analysis. Literature that fulfilled all predefined criteria and directly related to the topic was included. Studies that did not meet these criteria were excluded. Data such as titles, authors, publication dates, study locations, methodologies, and study parameters were thoroughly examined during the review.

Quality Assessment and Data Synthesis

Each author independently assessed the titles and abstracts of the selected studies to identify those for further exploration. Articles that met the inclusion criteria underwent further evaluation. Final decisions on inclusion were based on the findings from this review process.

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	"dual"[All Fields] AND ("antiplatelet"[All Fields] OR "antiplatelets"[All Fields]) AND ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "therapies"[All Fields] OR "therapy"[MeSH Subheading] OR "therapy"[All Fields] OR "therapys"[All Fields] OR "therapys"[All Fields]) AND ("transient ischaemic attack"[All Fields] OR "ischemic attack, transient"[MeSH Terms] OR ("ischemic"[All Fields] AND "attack"[All Fields] AND "transient"[All Fields]) OR "transient ischemic attack"[All Fields] OR ("transient"[All Fields] AND "ischemic"[All Fields] AND "attack"[All Fields])) AND ("ischemic stroke"[MeSH Terms] OR ("ischemic"[All Fields] AND "stroke"[All Fields]) OR "ischemic stroke"[All Fields])	550
Springer Link	((dual antiplatelet therapy) AND (transient ischemic attack)) AND (ischemic stroke)	640
Sagepub	((dual antiplatelet therapy) AND (transient ischemic attack)) AND (ischemic stroke)	200
Google Scholar	((dual antiplatelet therapy) AND (transient ischemic attack)) AND (ischemic stroke)	410

Table 2. JBI *Critical appraisal of Study*

Parameters	Pan (2017)	Wang (2025)	Trifan (2021)	Li (2016)	Johnston (2019)	Bhatia (2019)	Suryawanshi (2025)
1. Bias related to temporal precedence							
Is it clear in the study what is the "cause" and what is the "effect" (ie, there is no confusion about which variable comes first)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Bias related to selection and allocation							
Was there a control group?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Bias related to confounding factors							
Were participants included in any comparisons similar?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Bias related to administration of intervention/exposure							
Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	No.	No.	No.	No.	No.	No.	No.
5. Bias related to assessment, detection, and measurement of the outcome							
Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the outcomes of participants included in any comparisons measured in the same way?	No.	No.	No.	No.	No.	No.	No.
Were outcomes measured in a reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Bias related to participant retention							
Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Statistical conclusion validity							
Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes

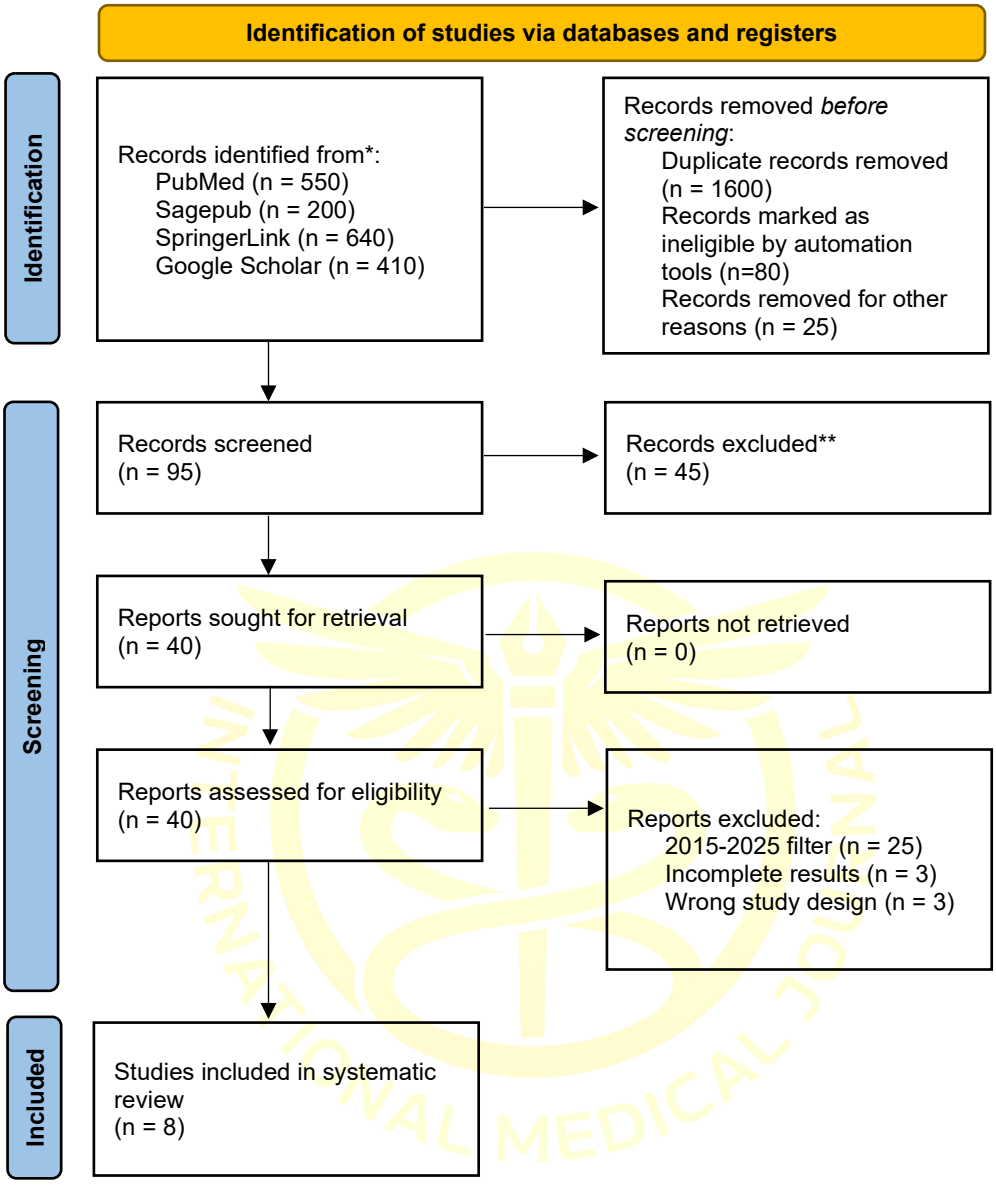

Figure 1. Article search flowchart

RESULT

The initial number of articles retrieved from online databases (PubMed, SagePub, SpringerLink, and Google Scholar) is 1,800 articles. After conducting three levels of screening, eight articles that directly relate to the current systematic review have been chosen for further assessment through full-text reading and analysis. Table 3 presents the selected literature included in this analysis.

Table 3. The literature included in this study

No.	Authors (Year)	Country	Study Design	Sample Size	Results
1	Pan et al. (2017)	China	Randomized Controlled Trial (CHANCE)	5,170	DAPT (clopidogrel + aspirin) reduced the 90-day stroke recurrence rate to 8.2% vs. 11.7% in the aspirin-only group (HR: 0.68, 95% CI: 0.57–0.81, P < 0.001). However, the major bleeding rate was 0.3% vs. 0.1% (P = 0.09).
2	Wang et al. (2015)	China	Randomized Controlled Trial (CHANCE)	5,170	Clopidogrel + aspirin reduced the risk of recurrent stroke at 90 days to 8.2% vs. 11.7% in aspirin-alone (HR: 0.68, 95% CI: 0.57–0.81, P < 0.001). Major bleeding was similar between groups (0.3% vs. 0.1%, P = 0.09).
3	Trifan et al. (2021)	Multiple	Systematic Review & Meta-Analysis	Varies	DAPT was associated with a 24% relative risk reduction (RRR) for recurrent stroke

					compared to monotherapy (RR: 0.76, 95% CI: 0.67–0.86). However, the risk of major bleeding was significantly higher (RR: 1.84, 95% CI: 1.30–2.60).
4	Li et al. (2016)	China	Prospective Cohort Study	1,168	DAPT within 12 hours of minor stroke/TIA reduced stroke recurrence at 90 days (5.2% vs. 12.1%, HR: 0.41, 95% CI: 0.25–0.68, P < 0.01). No significant increase in major bleeding events (0.4% vs. 0.3%, P = 0.67).
5	Johnston et al. (2019)	USA	Randomized Controlled Trial (POINT)	4,881	DAPT reduced major stroke at 90 days (5.0% vs. 6.5%, HR: 0.75, 95% CI: 0.59–0.95, P = 0.02), but increased major bleeding (0.9% vs. 0.4%, HR: 2.32, 95% CI: 1.10–4.87, P = 0.02).
6	Bhatia et al. (2019)	Multiple	Randomized Controlled Trial (TARDIS)	3,096	Intensive DAPT did not significantly reduce recurrent stroke risk (7.8% vs. 7.6%, P = 0.84), but increased bleeding risk (4.7% vs. 1.5%, OR: 3.16, 95% CI: 2.19–4.56, P < 0.001).

7	Suryawanshi et al. (2025)	India	Prospective Observational Cohort Study	160	DAPT (1–21 days) followed by SAPT reduced early neurological deterioration (2.4% vs. 7.7%, HR: 0.66, 95% CI: 0.42–0.91, P = 0.08) and new stroke/TIA (4.8% vs. 11.5%, HR: 0.75, 95% CI: 0.61–0.93, P = 0.06). Bleeding events were 4.7% higher in DAPT group.
8	He et al. (2015)	China	Randomized Controlled Trial	690	DAPT within 72 hours of non-cardioembolic ischemic stroke reduced early neurological deterioration (2.8% vs. 5.8%, P = 0.03) and stroke recurrence (3.1% vs. 6.8%, P = 0.01) with no significant difference in major bleeding (0.6% vs. 0.5%, P = 0.87).

DISCUSSION

The effectiveness of dual antiplatelet therapy (DAPT) in reducing stroke recurrence among patients with minor stroke or high-risk transient ischemic attack (TIA) has been well-documented across multiple clinical trials and observational studies. The CHANCE trial (Wang et al., 2015) demonstrated a significant reduction in the 90-day risk of recurrent stroke in patients treated with a combination of clopidogrel and aspirin (8.2%) compared to those receiving aspirin monotherapy (11.7%).[8] Similarly, the POINT trial (Johnston et al., 2019) showed a 90-day stroke recurrence rate of 5.0% in the DAPT group versus 6.5% in the aspirin-alone group. Additionally, Li et al. (2016) reported that DAPT initiated within 12 hours of symptom onset significantly reduced stroke recurrence at 90 days (5.2% vs. 12.1%, HR: 0.41, $P < 0.01$). These findings consistently highlight the superiority of DAPT over single antiplatelet therapy (SAPT) in reducing the risk of recurrent ischemic events.[9]

Beyond primary stroke recurrence prevention, DAPT has demonstrated benefits in preventing early neurological deterioration (END) and improving functional outcomes. The Suryawanshi et al. (2025) study reported that END occurred in only 2.4% of patients receiving 21-day DAPT followed by SAPT, compared to 7.7% in those receiving SAPT alone (HR: 0.66; $P = 0.08$). Moreover, a new stroke or TIA occurred in 4.8% of the DAPT group compared to 11.5% in the SAPT group (HR: 0.75; $P = 0.06$). Functional outcomes assessed using the modified Rankin Scale (mRS) showed a greater likelihood of achieving a favorable outcome in the DAPT group (OR: 3.12; $P = 0.001$). These data reinforce that DAPT not only reduces recurrent stroke but also contributes to improved recovery and functional independence in patients with minor stroke or high-risk TIA.[10]

While DAPT is effective, its safety profile remains a critical concern, particularly the risk of major bleeding. The POINT trial (Johnston et al., 2019) found that major bleeding occurred in 0.9% of patients receiving DAPT compared to 0.4% in those receiving SAPT (HR: 2.32; $P = 0.02$).[9] Similarly, the TARDIS trial

(Bhatia et al., 2019) reported a significantly higher risk of bleeding with intensive DAPT, with rates of 4.7% in the DAPT group compared to 1.5% in the SAPT group ($P < 0.001$).[11] The Suryawanshi et al. (2025) study also noted a slight increase in bleeding events and muscle-toxic effects in the DAPT group, with a 4.7% higher bleeding rate than SAPT. These findings underscore the need to balance the benefits of stroke prevention with the potential risks of hemorrhagic complications when prescribing DAPT.[10]

The optimal duration of DAPT is another crucial factor in determining its safety and effectiveness. Most studies support a short-term DAPT strategy, typically lasting between 21 and 90 days. The CHANCE trial utilized DAPT for 21 days, after which patients transitioned to SAPT, leading to a significant reduction in stroke recurrence while maintaining an acceptable bleeding risk. The POINT trial extended DAPT use to 90 days but observed a notable increase in major bleeding events, suggesting that prolonged therapy may not offer additional benefits. The Suryawanshi et al. (2025) study further supported this approach, with DAPT for 21 days followed by SAPT demonstrating superior outcomes compared to continuous SAPT. These results indicate that a short-duration DAPT regimen, particularly within the first three weeks post-stroke, may offer the best balance between efficacy and safety.[10]

The choice of antiplatelet agents in DAPT is also a key consideration. Most studies, including CHANCE, POINT, and Li et al. (2016), utilized clopidogrel (300 mg loading dose followed by 75 mg daily) in combination with aspirin (initial 300 mg followed by 100 mg daily). He et al. (2015) examined a similar regimen and found that stroke deterioration occurred in nine patients in the DAPT group compared to 19 in the SAPT group, further supporting the efficacy of clopidogrel-aspirin therapy.[12,13] However, newer P2Y12 inhibitors such as ticagrelor have been explored in recent studies. The THALES trial (Johnston et al., 2020) found that ticagrelor (180 mg loading dose, 90 mg twice daily) combined with aspirin reduced stroke recurrence compared to aspirin alone but was associated with a higher

bleeding risk. These findings suggest that while ticagrelor may be an alternative to clopidogrel, careful patient selection is required to minimize adverse effects.[9]

DAPT is consistently found to be superior to monotherapy in preventing recurrent strokes in high-risk patients. The meta-analysis by Trifan et al. (2021) confirmed that DAPT reduces stroke recurrence by 24% compared to SAPT (RR: 0.76, 95% CI: 0.67–0.86).[14] He et al. (2015) also found that stroke recurrence after TIA occurred in only one patient in the DAPT group compared to three in the SAPT group.[12] Furthermore, Li et al. (2016) demonstrated that DAPT significantly lowered the hazard ratio for stroke recurrence (HR: 0.41, $P < 0.01$) compared to SAPT. These results strongly support the use of DAPT as the preferred strategy in patients with minor stroke or high-risk TIA, particularly in the acute phase following an ischemic event.[13]

Despite these advantages, patient selection remains critical to optimize DAPT use. The CHANCE and POINT trials specifically targeted patients with minor stroke (NIHSS ≤ 3) or high-risk TIA (ABCD2 score ≥ 4), and both showed significant benefits in these populations. However, the TARDIS trial, which included patients with a broader range of stroke severities, did not find a significant reduction in stroke recurrence but observed a substantial increase in bleeding complications. The Suryawanshi et al. (2025) study, which focused on atherosclerotic-origin strokes, further emphasized that DAPT is particularly effective in this subgroup, suggesting that DAPT should be primarily reserved for patients with large artery atherosclerosis rather than all stroke patients.[10]

Another critical consideration is real-world application. While clinical trials provide strong evidence, observational studies such as those by He et al. (2015) and Suryawanshi et al. (2025) offer insights into how DAPT performs outside controlled settings. These studies highlight that while DAPT remains effective in preventing stroke recurrence, real-world bleeding risks may be slightly higher than in clinical trials due to variations in adherence and patient comorbidities. This underscores the need for individualized risk assessment when prescribing DAPT in routine practice.[10,12]

Future research should focus on refining DAPT protocols to further improve its risk-benefit ratio. Genetic testing for clopidogrel metabolism may help identify patients who would benefit more from alternative P2Y12 inhibitors such as ticagrelor. Additionally, studies investigating risk stratification models to predict bleeding risks could help guide DAPT duration in different patient populations. Further research is also needed to determine whether alternative DAPT regimens, such as cilostazol-based combinations, may offer comparable efficacy with lower bleeding risks.[15]

CONCLUSION

DAPT is a superior strategy compared to SAPT in reducing stroke recurrence in patients with minor stroke or high-risk TIA. However, its safety concerns, particularly regarding major bleeding, necessitate careful patient selection and treatment duration optimization. Current data suggest that a 21-day DAPT regimen followed by SAPT offers the best balance of efficacy and safety, particularly in patients with atherosclerotic stroke. Future studies should continue refining treatment approaches to maximize the benefits of DAPT while minimizing risks.

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