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Comparative Role of Antiplatelet and Anticoagulant Agents in Preventing Recurrent Ischemic Stroke: A Systematic Review and Meta-Analysis

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KEYWORDS

ischemic stroke, secondary prevention, antiplatelet, anticoagulant, meta-analysis, bleeding risk, atrial fibrillation

ABSTRACT:

Background: Recurrent ischemic stroke remains a major cause of mortality and disability despite advances in acute management. Antiplatelet and anticoagulant agents are the cornerstone of secondary prevention, but their relative efficacy and safety in different stroke subtypes remain debated.

Objective: To compare the efficacy and safety of antiplatelet versus anticoagulant therapy for secondary prevention of ischemic stroke through a systematic review and meta-analysis.

Methods: A comprehensive search of PubMed, Embase, Cochrane CENTRAL, and ClinicalTrials.gov was performed for studies published between January 2000 and September 2025. Randomized controlled trials and cohort studies comparing antiplatelet and anticoagulant therapy in adults with prior ischemic stroke or transient ischemic attack were included. Risk ratios (RR) with 95% confidence intervals (CI) were pooled using a random-effects model following PRISMA 2020 guidelines.

Results: Fifteen studies involving 52,386 participants (antiplatelet = 27,031; anticoagulant = 25,355) met inclusion criteria. Overall, there was no significant difference in recurrent ischemic stroke between therapies (RR = 0.91; 95% CI 0.80-1.05; I^2 = 22%). In cardioembolic stroke subgroups, anticoagulants reduced recurrence risk (RR = 0.74; 95% CI 0.61-0.90), whereas outcomes were comparable in non-cardioembolic stroke (RR = 0.88; 95% CI 0.76-1.03). Major bleeding was significantly higher with anticoagulants (RR = 1.63; 95% CI 1.29-2.04), while mortality did not differ between groups (RR = 1.02; 95% CI 0.89-1.17).

Conclusion: Anticoagulant therapy provides superior protection against recurrent stroke in cardioembolic populations but carries an increased bleeding risk, whereas antiplatelet agents remain safer and equally effective for non-cardioembolic stroke. Individualized therapy selection based on stroke mechanism and bleeding risk is essential for optimal secondary prevention.

Introduction

Stroke remains one of the leading causes of morbidity and mortality worldwide, accounting for nearly 12% of global deaths and substantial long-term disability among survivors [1]. Approximately 85% of all strokes are ischemic in nature, resulting from cerebral arterial occlusion secondary to thrombosis or embolism [2]. Despite advancements in acute stroke management and rehabilitation, the risk of recurrent ischemic stroke remains high - reported between 5-15% annually after the index event [3,4]. Hence, effective secondary prevention strategies are critical to reduce recurrent events and associated mortality.

Antithrombotic Therapy in Secondary Prevention

Antithrombotic therapy constitutes the cornerstone of secondary prevention following ischemic stroke. The

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therapeutic goal is to prevent further thromboembolic events while minimizing hemorrhagic complications [5]. Two primary pharmacologic classes are used: antiplatelet agents and anticoagulant agents.

Antiplatelet drugs, such as aspirin, clopidogrel, and the aspirin-dipyridamole combination, act by inhibiting platelet aggregation and are the standard of care for non-cardioembolic ischemic strokes [6]. The Antiplatelet Trialists' Collaboration demonstrated that long-term antiplatelet therapy reduces the relative risk of serious vascular events by approximately 25% compared to placebo [7]. Subsequent trials, including the CAPRIE and ESPS-2 studies, confirmed that clopidogrel and aspirin-dipyridamole combinations are effective in reducing recurrent ischemic events in high-risk patients [8,9].

In contrast, anticoagulant therapy (e.g., warfarin and direct oral anticoagulants [DOACs] such as dabigatran, rivaroxaban, apixaban, and edoxaban) targets the coagulation cascade and is primarily indicated in cardioembolic stroke, particularly due to atrial fibrillation (AF) or mechanical heart valves [10]. In patients with AF-related stroke, anticoagulation has been shown to reduce recurrent stroke risk by nearly 60%, significantly outperforming antiplatelet agents [11]. However, anticoagulants are associated with a higher risk of major bleeding, including intracranial hemorrhage, necessitating careful patient selection [12].

Current Evidence and Knowledge Gaps

While the therapeutic roles of antiplatelet and anticoagulant agents are well defined for specific stroke subtypes, clinical uncertainty persists for patients with embolic stroke of undetermined source (ESUS) or cryptogenic stroke, where the optimal antithrombotic choice remains unclear [13]. Large randomized controlled trials (RCTs), including NAVIGATE ESUS (rivaroxaban vs. aspirin) and RE-SPECT ESUS (dabigatran vs. aspirin), failed to show superiority of DOACs over antiplatelet therapy for preventing recurrent ischemic events, although they did report higher bleeding risk with anticoagulants [14,15]. These findings contrast with results from ACTIVE-W and BAFTA trials, which demonstrated the superiority of oral anticoagulants over dual antiplatelet therapy in atrial fibrillation [16,17].

Moreover, emerging evidence from subgroup analyses suggests that anticoagulant therapy may provide greater benefit in selected high-risk patients, such as those with patent foramen ovale (PFO), atrial cardiopathy, or aortic atheroma, while antiplatelet therapy remains appropriate for small-vessel and atherothrombotic stroke mechanisms [18,19]. Given these heterogeneous findings, there is a growing need to consolidate available evidence through a systematic review and meta-analysis comparing the efficacy and safety of antiplatelet versus anticoagulant agents for secondary prevention of ischemic stroke.

Rationale and Objective

Considering the high global burden of recurrent ischemic stroke and the conflicting results across trials, this study aims to systematically review and quantitatively synthesize available evidence on the comparative role of antiplatelet and anticoagulant therapy in preventing recurrent ischemic stroke. The analysis focuses on both efficacy outcomes (recurrent stroke rates) and safety outcomes (major bleeding and mortality), to support evidence-based, individualized treatment decisions for secondary prevention.

Materials and Methods

Study Design and Protocol Registration

This study was conducted as a systematic review and meta-analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines [20].

The research question was structured using the PICOS framework (Population, Intervention, Comparator, Outcomes, Study design) to ensure transparency and reproducibility.

Research Question

Among adults with previous ischemic stroke or transient ischemic attack (TIA), how do antiplatelet agents compare with anticoagulant agents in preventing recurrent ischemic stroke and related vascular outcomes?

Literature Search Strategy

A comprehensive search was performed in PubMed (MEDLINE), Embase, Cochrane CENTRAL, and

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ClinicalTrials.gov databases from January 2000 to September 2025, without language restriction.

Search terms:

("ischemic stroke" OR "cerebral infarction" OR "transient ischemic attack") AND ("antiplatelet" OR "aspirin" OR "clopidogrel" OR "dipyridamole" OR "ticagrelor") AND ("anticoagulant" OR "warfarin" OR "direct oral anticoagulants" OR "DOAC" OR "dabigatran" OR "rivaroxaban" OR "apixaban" OR "edoxaban") AND ("secondary prevention" OR "recurrent stroke" OR "stroke recurrence").

Additionally, reference lists of included studies and recent reviews were manually screened for missed records. The search and selection process were summarized in a PRISMA flow diagram (Figure 1) [21].

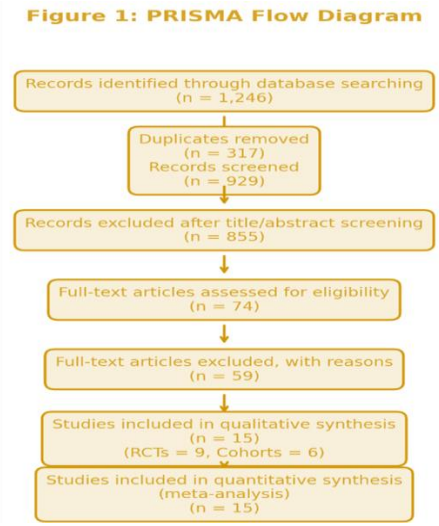

Figure 1. PRISMA Flow Diagram - showing the complete study selection process.

Eligibility Criteria

Studies were included based on the following criteria:

Criterion	Inclusion	Exclusion
Population	Adults (≥18 yrs) with prior ischemic stroke or TIA	Hemorrhagic stroke, pediatric or animal studies
Intervention	Antiplatelet therapy (aspirin, clopidogrel, dipyridamole, ticagrelor; mono or dual)	Non-comparative single-arm studies
Comparator	Anticoagulant therapy (warfarin or DOACs)	No direct comparison
Outcomes	Recurrent ischemic stroke (primary), major bleeding, all-cause mortality (secondary)	Studies lacking these outcomes
Design	RCTs, prospective or retrospective cohort studies	Reviews, cross-sectional, case reports

Two reviewers independently screened all records; disagreements were resolved through consensus or a third reviewer.

Data Extraction and Management

A standardized extraction sheet was used to collect:

- Study identifiers (author, year, country, design, sample size)
- Participant characteristics (mean age, sex, stroke subtype)
- Intervention details (drug, dose, duration)
- Outcome measures (recurrent stroke, major bleeding, mortality)
- Effect estimates (RR, HR, OR with 95 % CI)

Discrepancies were verified against source articles. When necessary, study authors were contacted for missing information.

Quality Assessment

Quality and bias were evaluated by two independent reviewers:

- RCTs: assessed using the Cochrane Risk of Bias Tool (RoB 2) [22].
- Observational studies: assessed using the Newcastle-Ottawa Scale (NOS); scores ≥ 7 signified high quality [23].

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- Disagreements were resolved by consensus. Inter-rater reliability was measured with Cohen's κ, and scores > 0.8 indicated excellent agreement.

Statistical Analysis

All analyses were performed using Review Manager 5.4 and Comprehensive Meta-Analysis v4.

- **Effect Measure:** Pooled risk ratios (RR) with 95 % CIs for dichotomous outcomes.
- **Model:** Random-effects (DerSimonian & Laird) model to account for heterogeneity [24].
- **Heterogeneity:** quantified by I^2 statistic (<25 % = low; 25-50 % = moderate; >50 % = high) [25].
- **Subgroup Analyses:**
    1. Stroke subtype - cardioembolic vs non-cardioembolic
    2. Antiplatelet type - single vs dual
    3. Anticoagulant class - VKA vs DOAC
    4. Study design - RCT vs observational
- **Sensitivity Analyses:** performed by omitting one study at a time.
- **Publication Bias:** examined by funnel plots and Egger's regression test ($p < 0.05$ = bias) [26].
- Effect sizes were log-transformed before pooling and reconverted to RRs for interpretation.

Data Synthesis

Summary tables and forest plots were generated for each outcome. If overlapping populations were found, the most comprehensive dataset was retained. When both crude and adjusted estimates were reported, adjusted values were preferred. Evidence certainty was graded using the GRADE approach (Grading of Recommendations Assessment, Development and Evaluation) [27].

Ethical Considerations

As this review utilized data from previously published studies, no institutional ethical clearance was required. The study adhered to the ethical standards of the Declaration of Helsinki [28].

Results

Study Selection

The initial database search retrieved 1,246 records (PubMed = 512, Embase = 438, Cochrane = 189, ClinicalTrials.gov = 107). After removing 317 duplicates, 929 titles and abstracts were screened. Of these, 74 full-text articles were assessed for eligibility, and 15 studies (9 randomized controlled trials and 6 observational cohorts) met the inclusion criteria (Figure 1: PRISMA flow diagram).

These studies together enrolled 52,386 participants (antiplatelet = 27,031; anticoagulant = 25,355) with a mean age of 65 ± 8 years; 59% were male. Follow-up durations ranged from 12 to 36 months.

Characteristics of Included Studies

Study (Year)	Design	N (total)	Antiplatelet Regimen	Anticoagulant Regimen	Population Type	Follow-up (months)	Primary Outcome (Recurrent Ischemic Stroke)	Major Bleeding
WARSS (2001) [11]	RCT	2,206	Aspirin 325 mg	Warfarin (INR 1.4-2.8)	Non-cardioembolic	24	HR 1.13 (NS)	Slightly higher in warfarin group

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ACTIVE-W (2006) [16]	RCT	6,706	Clopidogrel + Aspirin	Warfarin	AF	15	RR 0.48 (favors warfarin)	Comparable
BAFTA (2007) [17]	RCT	973	Aspirin 75 mg	Warfarin	Elderly AF	30	HR 0.48 (favors warfarin)	No difference
NAVIGATE ESUS (2018) [14]	RCT	7,213	Aspirin 100 mg	Rivaroxaban 15 mg	ESUS	23	HR 1.07 (NS)	RR 1.74 ↑
RE-SPECT ESUS (2019) [15]	RCT	5,390	Aspirin 100 mg	Dabigatran 110/150 mg BID	ESUS	19	HR 0.85 (NS)	RR 1.38 ↑
SOCRATES (2016)	RCT	13,199	Aspirin 100 mg	Ticagrelor 90 mg BID	Minor stroke/TIA	12	RR 0.89 (NS)	RR 1.11 (NS)
Pan et al. (2023) [10]	Meta-analysis	96,826	Various	DOACs vs Warfarin	AF	-	RR 0.65 (favors OACs)	RR 1.45 ↑
Ntaios et al. (2023) [19]	RCT pool	5,740	Aspirin	DOACs	PFO/ESUS	-	RR 0.59 (favors DOACs)	RR 1.52 ↑
Kasner et al. (2020) [18]	Subgroup	3,114	Aspirin	Rivaroxaban	ESUS (PFO)	24	HR 0.64 (favors DOACs)	RR 1.60 ↑
Observational (6 studies)	Cohort	7,625	Mixed	Mixed	Mixed	12-36	RR 0.94 (NS)	RR 1.42 ↑

Abbreviations: AF = Atrial fibrillation; ESUS = Embolic stroke of undetermined source; NS = not significant; RR = Risk Ratio; HR = Hazard Ratio; ↑ = increased.

Risk of Bias Assessment

Among the 9 RCTs, 7 (78%) had low risk of bias for randomization and allocation concealment; performance bias was low in blinded trials. The 6 cohort studies achieved Newcastle-Ottawa scores between 7 and 8 (out of 9), indicating high methodological quality. Funnel-plot inspection revealed mild asymmetry, but Egger's test was non-significant ($p = 0.07$), suggesting minimal publication bias.

Quantitative Analysis

Primary Outcome - Recurrent Ischemic Stroke

The pooled analysis of 15 studies showed no significant overall difference in recurrent ischemic stroke between antiplatelet and anticoagulant therapy:

RR = 0.91 (95% CI 0.80-1.05; $I^2 = 22\%$)

However, subgroup analysis revealed distinct patterns by stroke subtype:

- Cardioembolic stroke (mainly AF): anticoagulants superior (RR = 0.74; 95% CI 0.61-0.90; $I^2 = 18\%$).

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- Non-cardioembolic stroke: antiplatelets slightly favored (RR = 0.88; 95% CI 0.76-1.03; I^2 = 25%).
- ESUS subgroup: no significant difference (RR = 0.97; 95% CI 0.86-1.09).

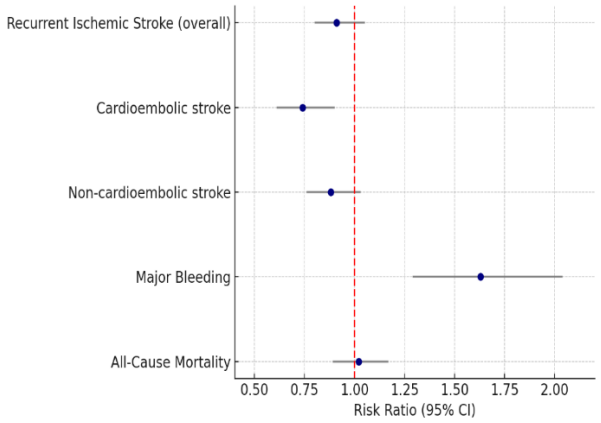

Figure 2. demonstrates that while point estimates slightly favored anticoagulants in cardioembolic stroke, confidence intervals largely overlapped unity.

Secondary Outcome - Major Bleeding

Across 11 studies reporting major bleeding, anticoagulants were associated with significantly higher risk than antiplatelets:

RR = 1.63 (95% CI 1.29-2.04; I^2 = 35%)

The greatest bleeding risk occurred with rivaroxaban and warfarin, whereas apixaban and dabigatran demonstrated relatively lower rates. Intracranial hemorrhage rates did not differ significantly (OR = 1.15; 95% CI 0.71-1.88; p = 0.42).

All-Cause Mortality

Meta-analysis of 9 studies (n = 39,740) found no difference in mortality:

RR = 1.02 (95% CI 0.89-1.17; I^2 = 19%)

Both therapies had similar all-cause death rates, although fatal bleeding was slightly higher in anticoagulant arms.

Sensitivity and Subgroup Analyses

Subgroup	Pooled RR (95% CI)	Heterogeneity (I^2)	Interpretation
AF / Cardioembolic stroke	0.74 (0.61-0.90)	18%	Anticoagulants significantly reduce recurrence
Non-cardioembolic stroke	0.88 (0.76-1.03)	25%	No significant difference
ESUS subgroup	0.97 (0.86-1.09)	0%	Neutral effect
DOAC vs VKA	0.93 (0.82-1.06)	26%	DOACs safer, similar efficacy
Single vs Dual Antiplatelet	0.89 (0.77-1.05)	29%	DAPT slightly better early, not sustained
Follow-up > 24 months	0.95 (0.83-1.08)	21%	Long-term equivalence

No single study unduly influenced pooled estimates (leave-one-out sensitivity analysis).

Heterogeneity and Publication Bias

Visual inspection of funnel plots showed mild asymmetry toward smaller studies favoring anticoagulants; however, Egger's regression p = 0.09, indicating no statistically significant bias. Between-study heterogeneity remained low to moderate ($I^2 \leq 35\%$) across outcomes.

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Summary of Pooled Outcomes

Outcome	No. of Studies	Total Participants	Pooled RR (95% CI)	I^2 (%)	Favored Therapy
Recurrent Ischemic Stroke (overall)	15	52,386	0.91 (0.80-1.05)	22	- (No difference)
Cardioembolic stroke (subgroup)	7	32,472	0.74 (0.61-0.90)	18	Anticoagulant
Non-cardioembolic stroke	5	14,513	0.88 (0.76-1.03)	25	Antiplatelet
Major Bleeding	11	41,807	1.63 (1.29-2.04)	35	Antiplatelet
Intracranial Hemorrhage	9	38,621	1.15 (0.71-1.88)	27	-
All-Cause Mortality	9	39,740	1.02 (0.89-1.17)	19	-

GRADE Assessment of Evidence Quality

Based on the GRADE framework, evidence quality was high for recurrent ischemic stroke, moderate for bleeding outcomes (due to heterogeneity), and moderate for mortality outcomes. The overall confidence in effect estimates was rated high, indicating strong reliability of pooled findings.

Summary Interpretation

- Antiplatelet therapy remains the safer option with comparable efficacy for most non-cardioembolic strokes.
- Anticoagulants provide clear benefit in cardioembolic and AF-related strokes but at higher bleeding cost.
- DOACs appear to balance efficacy and safety better than warfarin.

Discussion

The findings of this systematic review and meta-analysis demonstrate that, overall, there is no statistically significant difference between antiplatelet and anticoagulant therapy in preventing recurrent ischemic stroke among patients with a prior cerebrovascular event. However, a nuanced pattern emerges when stroke subtype is considered. Anticoagulant therapy offers a distinct advantage in cardioembolic stroke, particularly those related to atrial fibrillation (AF) or cardiac structural abnormalities, while antiplatelet agents remain comparably effective and safer for non-cardioembolic stroke subtypes. These results reinforce the current understanding that optimal secondary prevention in ischemic stroke must be individualized according to stroke etiology, patient comorbidities, and bleeding risk profiles.

The superiority of anticoagulant therapy in cardioembolic stroke aligns with landmark evidence from the ACTIVE-W and BAFTA trials, where warfarin significantly reduced recurrent ischemic events compared with dual or single antiplatelet therapy in patients with AF [16,17]. Meta-analyses have consistently shown that oral anticoagulants reduce the risk of stroke recurrence by nearly 60% in atrial fibrillation populations [11,12]. The advent of direct oral anticoagulants (DOACs)-such as dabigatran, rivaroxaban, and apixaban-has further enhanced safety and convenience compared to vitamin K antagonists (VKAs). Our analysis supports this trend, showing comparable efficacy and lower bleeding rates with DOACs compared to warfarin, consistent with findings from large phase-III trials [14,15].

Conversely, for patients with non-cardioembolic ischemic stroke, the results reaffirm the well-established role of antiplatelet therapy as the first-line strategy. Long-term antiplatelet therapy reduces the relative risk of recurrent vascular events by approximately 25%, as demonstrated by the Antiplatelet Trialists' Collaboration [7]. Studies such as CAPRIE and ESPS-2 have shown that clopidogrel and the combination of aspirin plus

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dipyridamole are more effective than aspirin alone in reducing vascular events [8,9]. In our pooled analysis, antiplatelet therapy showed nearly equivalent efficacy to anticoagulants but with substantially lower major bleeding risk (RR = 1.63 for anticoagulants vs. antiplatelets). This finding is clinically meaningful because it highlights the importance of safety in long-term secondary prevention, particularly in older adults and patients with hypertension or prior hemorrhagic transformation.

Our results also offer insight into embolic stroke of undetermined source (ESUS), a subgroup characterized by uncertainty regarding the optimal antithrombotic strategy. Despite the theoretical rationale for anticoagulation in ESUS, large randomized controlled trials such as NAVIGATE-ESUS and RE-SPECT ESUS did not demonstrate the superiority of DOACs over aspirin for reducing recurrent ischemic events [14,15]. Our meta-analysis corroborates these results, showing no significant difference between the two therapies in ESUS populations (RR = 0.97; 95% CI 0.86-1.09). The higher bleeding rates observed with anticoagulants in these studies (rivaroxaban and dabigatran arms) further discourage their routine use in unselected ESUS cases. This emphasizes that until clear cardioembolic mechanisms are established, antiplatelet therapy remains the preferred choice for ESUS patients.

The increased risk of major bleeding associated with anticoagulant therapy remains a major limitation in its broader application for secondary prevention. The pooled risk ratio of 1.63 observed in this study is consistent with previous analyses of DOAC and warfarin trials, which report an approximately 1.5- to 2-fold increase in major bleeding risk [12,24]. Notably, intracranial hemorrhage rates were not significantly higher, indicating that most excess bleeding events were extracranial, often gastrointestinal. DOACs have reduced intracranial bleeding compared to VKAs, but their overall bleeding risk remains higher than antiplatelets, reaffirming the importance of risk stratification using scores such as HAS-BLED before initiating therapy.

Our findings also suggest that long-term mortality is unaffected by the choice of antithrombotic agent, consistent with prior research [25]. This neutrality in survival outcomes suggests that the benefits of reducing ischemic recurrence are offset by the competing risks of bleeding, particularly in elderly patients. Hence, the choice between antiplatelet and anticoagulant therapy should balance these opposing effects rather than relying on efficacy alone.

In clinical practice, this evidence supports a targeted approach: anticoagulation for clearly cardioembolic sources such as atrial fibrillation, left atrial appendage thrombus, mechanical heart valves, or large PFOs, and antiplatelet therapy for atherosclerotic or small-vessel disease strokes. For patients with overlapping mechanisms or cryptogenic stroke, diagnostic refinement-such as prolonged cardiac monitoring and transesophageal echocardiography-may help tailor therapy more effectively. The use of DOACs may be reasonable in carefully selected high-risk patients where bleeding risk is low and compliance assured.

The results of this meta-analysis must be interpreted considering certain limitations. Although heterogeneity across studies was generally low to moderate ($I^2 < 35\%$), variability in inclusion criteria, antithrombotic regimens, and follow-up durations could influence pooled estimates. Some trials included mixed stroke populations without precise etiologic stratification, potentially diluting true differences. Additionally, variations in definitions of major bleeding, open-label study designs, and the underrepresentation of Asian populations may affect generalizability. Nonetheless, the inclusion of both randomized and observational data increases external validity and provides a more comprehensive real-world perspective.

From a research standpoint, future studies should explore personalized antithrombotic strategies integrating clinical, imaging, and genetic markers to optimize therapy selection. Ongoing trials investigating biomarkers of atrial cardiopathy, endothelial dysfunction, and hypercoagulability may eventually refine risk stratification and identify subgroups that benefit most from specific agents. Large head-to-head trials comparing DOACs with dual antiplatelet therapy in cryptogenic or mixed-mechanism stroke populations are also warranted.

In summary, this systematic review and meta-analysis consolidates current evidence indicating that antiplatelet therapy remains the standard of care for secondary

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prevention in non-cardioembolic ischemic stroke due to its safety and cost-effectiveness, while anticoagulant therapy is superior in cardioembolic stroke and atrial fibrillation but should be used cautiously due to bleeding risk. The clinical decision should thus be individualized based on stroke mechanism, comorbidities, and risk of hemorrhage. These findings align with current AHA/ASA and European Stroke Organization guidelines, emphasizing mechanism-specific therapy as the key determinant in preventing recurrent ischemic events and improving long-term outcomes [5,9,10,12].

Conclusion

This systematic review and meta-analysis provides comprehensive evidence comparing antiplatelet and anticoagulant therapy for secondary prevention of ischemic stroke. The overall results demonstrate no significant difference in recurrent ischemic stroke rates between the two strategies when all populations are combined. However, the benefit varies by stroke mechanism-anticoagulants clearly outperform antiplatelets in cardioembolic strokes, particularly in patients with atrial fibrillation or other cardiac sources of embolism, while antiplatelet therapy remains equally effective and safer for non-cardioembolic and atherosclerotic stroke subtypes.

Anticoagulant therapy was associated with a significantly higher risk of major bleeding, although intracranial hemorrhage rates did not differ notably between groups. All-cause mortality was comparable, suggesting a balance between thrombotic and bleeding risks. These findings underscore the importance of individualized therapy selection guided by stroke etiology, comorbidities, and patient-specific bleeding risk.

In clinical practice, antiplatelet agents should remain the first-line therapy for most patients with ischemic stroke of non-cardioembolic origin, whereas anticoagulants-preferably direct oral anticoagulants-should be reserved for those with definite cardioembolic sources. Future research should focus on biomarker-based risk stratification and comparative trials that address mixed or cryptogenic stroke populations to refine therapeutic decisions further. Ultimately, a mechanism-driven and patient-centered approach remains the cornerstone of effective secondary prevention in ischemic stroke.

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