Antiplatelet regimens after ischemic stroke or transient ischemic attack: a systematic review and updated network meta-analysis

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Background: It is still uncertain which antiplatelet regimen had the greatest net clinical benefit in patients who have suffered a transient ischemic attack or non-cardioembolic ischemic stroke, and it is necessary to choose the optimal regimen according to the clinical situation.

Methods: We utilized 3 databases of Medline, Embase, and the Cochrane Central Register of Controlled Trials to find randomized controlled trials that met our criteria, and performed network meta-analyses in recurrent stroke, composite outcomes, major bleeding events, recurrent ischemic stroke, and all bleeding events. Three-dimensional clustered rank plots were used to obtain the net clinical benefit. Subgroup analyses were performed according to the symptom-onset-to-treatment time (<72 and >72 h), stroke subtypes (large artery atherosclerosis and small vessel occlusion), and dual antiplatelet agent treatment duration.

Results: A total of 69 trials were enrolled. Cilostazol was associated with a lower risk of recurrent stroke, major bleeding events, composite outcomes, recurrent ischemic stroke, and all bleeding events compared to low to medium dose aspirin. The three-dimensional rank plot showed that cilostazol had the highest net clinical benefit. The combination of aspirin plus clopidogrel had greater efficacy in the <72 h after stroke onset and large artery atherosclerosis subgroups, and when it was restricted to1 month of use major bleeding risk was not higher than aspirin. The combination of aspirin plus dipyridamole had greater efficacy and safety comparable to aspirin in terms of small vessel occlusion.

Conclusions: The efficacy and safety profiles among antiplatelet regimens may differ according to clinical situation, although cilostazol, aspirin plus clopidogrel, and aspirin plus dipyridamole may be considered as preferable options.

Keywords: Antiplatelet; network meta-analysis; ischemic stroke; transient ischemic attack

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Introduction

Non-cardioembolic ischemic stroke is an episode of neurologic dysfunction due to the permanent cerebral, retinal, or spinal infarction, caused by other than cardioembolism (1). Approximately 75% of ischemic stroke (IS) was attributed to the non-cardioembolism (2). Unlike IS, transient ischemic attack (TIA) is a brief and non-lasting focal neurological dysfunction, not result in the permanent infarction (3). Global prevalence of IS was 77.2 million people in 2019 (4), and the overall prevalence of TIA was about 2% (4,5). Patients with IS or TIA have a higher risk of recurrent stroke, with about 10–20% having a recurrent stroke within 3 months, most of which occur during the first few days (6-9).

The cornerstone for secondary non-cardioembolic ischemic stroke prevention is antiplatelet therapy, which includes aspirin (10-12). Although antiplatelet therapy reduces the incidence of atherosclerotic cardiovascular disease (10,13), it also increases the risk of major bleeding such as intracranial hemorrhage and gastrointestinal bleeding requiring blood transfusions (13). Therefore, various antiplatelet agents and combinations of agents have been investigated to find regimens that demonstrate the best net clinical benefit regarding both potency and risk. However, as the number of available antiplatelet agents increase, it is becoming difficult to assess the effectiveness and safety of various treatment regimens directly. In the absence of direct comparisons, a network meta-analysis (NMA) can be a useful alternative to compare various antiplatelet treatment regimens (14-18). However, NMAs have historically had low clinical application for real-world clinicians since they have not considered several complicated conditions that patients may face.

The risk of stroke recurrence is fairly high during the first few days after an initial stroke or TIA (6,9). Several trials (19-22) have suggested that intensive antiplatelet therapy should be administered as early as possible to reduce the high recurrence rate of acute stroke in that critical period. However, long-term intensive antiplatelet therapy failed to show benefit regarding the increased risk of bleeding. Therefore, the most appropriate antiplatelet regimen may differ depending on the time interval between symptom onset and treatment initiation. Moreover, since there are several studies (21,23) that have demonstrated that limiting the duration of dual antiplatelet therapy (DAPT) is necessary to reduce the risk of major bleeding, DAPT treatment duration is an important safety consideration. In addition, the most appropriate antiplatelet therapy may depend on the subtype of ischemic stroke (2). Lastly, the degree of thrombotic and bleeding tendency differs according to race and should also be considered (24,25).

In this study, we performed an updated NMA, which included recently published randomized controlled trials (RCTs), to determine which antiplatelet regimen had the greatest net clinical benefit in terms of both efficacy and safety. This was determined through diverse subgroup analyses, which included the duration of DAPT treatment, the time interval between symptom onset and treatment initiation, and stroke subtypes [large artery atherosclerosis (LAA) and small vessel occlusion (SVO)].

We present the following article in accordance with the PRISMA NMA reporting checklist (26) (available at https://atm.amegroups.com/article/view/10.21037/atm-21-3748/rc).

Methods

We registered this NMA to the International Prospective Register of Systematic Reviews (PROSPERO) in July 2020 (CRD42020186926).

Search strategy

We searched multiple comprehensive databases (Medline, Embase, and the Cochrane Central Register of Controlled Trials) for relevant studies from inception until November 9, 2020. The search terms were “ischemic stroke”, “TIA”, and “antiplatelet agents”. Neither language nor the year of publication were restricted. A detailed search strategy, which was identical to that from a study of NMA (25), was presented in Table S1. The systematic search was performed by an independent collaborator (EJK). An additional manual search was conducted by two independent reviewers (SJJ and JMJ) to prevent the omission of any relevant study. When necessary, the authors were contacted to obtain more data.

Study selection

We included all eligible studies that were randomized controlled trials that assessed the effectiveness or safety of antiplatelet regimens in TIA or non-cardioembolic ischemic stroke patients for the secondary prevention. Studies that involved cardiovascular or peripheral arterial diseases other than IS or TIA were excluded. However, for the CAPRIE (27) and CHARISMA (28) trials, we were

able to extract the relevant outcomes from the IS or TIA patients through the subgroup analyses. While several trials had extended follow-up periods, only the results from the follow-up period included in the original study were analyzed. All disagreements concerning inclusion and exclusion were discussed until a consensus was reached.

Data extraction and processing

Data was extracted from the selected studies by two reviewers independently. A predefined data extraction template was used for the data extraction, and the following data were retrieved: baseline characteristics [age, sex, race, stroke subtypes, percentage of prior TIA, initial modified Rankin Scale (mRS) or National Institutes of Health Stroke Scale (NIHSS) score, and comorbidities including hypertension, diabetes, peripheral arterial disease, and myocardial infarction], study design (interventions, medication dosage, sample size, time interval between onset of symptoms and treatment initiation, treatment duration, and period of follow-up), and treatment outcome indicators, including the number of recurrent IS, recurrent stroke (ischemic + hemorrhagic stroke), recurrent TIA, recurrent myocardial infarction, vascular death, all-cause death, composite outcome (stroke, myocardial infarction, and vascular death), major bleeding event, and all bleeding events.

Primary efficacy and safety outcomes were recurrent stroke and major bleeding event respectively, and secondary outcomes were recurrent IS, composite outcomes, and all bleeding events. Major bleeding was defined as intracranial hemorrhage and extracranial bleeding requiring blood transfusions, which corresponds severe (life threatening) or moderate bleeding criteria in GUSTO classification (29). For trials that did not report outcomes, but whose outcomes could be obtained manually by adding or subtracting others, the value obtained manually was used as the number of outcomes. When we performed subgroup analyses using trials that did not include the relevant information, we obtained outcome data from the original study, from other sub-analyses (30-32) or from meta-analyses (33,34). In case of multi-arm trials, we took out only comparison arms that met inclusion criteria. The primary principle used to group antiplatelet regimens was the active ingredient of a specific drug. Different doses of the same active ingredient were grouped as the same antiplatelet regimen. However, since the purpose of a NMA was to assess the effectiveness and safety of the current standard antiplatelet therapy (low to medium dose aspirin) with other antiplatelet regimens, aspirin was grouped into three categories according to dosage [very low (<50 mg), low to medium (50–330 mg), and high dose (>330 mg)]. Low to medium dose aspirin was used as the common comparator.

Quality assessment

We assessed risks of bias of enrolled studies and the entire NMA using the Cochrane risk of bias assessment tool (35). Two reviewers evaluated seven domains of the risk of bias independently, and each domain was expressed as low risk, unclear risk, or high risk. Disagreement was resolved through discussion or adjudicated by a third reviewer when necessary.

Statistical analysis

We performed the NMA through the Bayesian method, using the R software "gemtc" package (36), and the relative risk ratio and 95% credible interval (CrI) were estimated. The counted number of patients in each study was subtracted based on the intention-to-treat population. Based on the outcomes mentioned previously, the efficacy and safety of different antiplatelet therapies were estimated. After a network setup, we performed Markov chain Monte Carlo simulation under the random effects model and performed a convergence diagnosis to choose the optimized network model (37). For the consistency test (37), we performed node-splitting methods to confirm that there is no statistical difference between direct and indirect evidence for a certain comparison. We also measured I^2 values to consider the degree of inconsistency in the network as a whole (38). Publication bias was examined using funnel plots (39). We obtained the forest plot, league table, and the surface under the cumulative ranking curve (SUCRA) (40). The ranking of antiplatelet therapy regimens was presented using ranking probabilities. For assessing the efficacy and safety simultaneously, we made a three-dimensional clustered rank plot, which was obtained using SUCRA ranking probabilities in recurrent stroke, composite outcome, and major bleeding events.

We performed subgroup analyses for the time interval between onset of symptoms and treatment initiation (<72 and >72 h), the duration of DAPT treatment, and stroke subtypes (LAA and SVO).

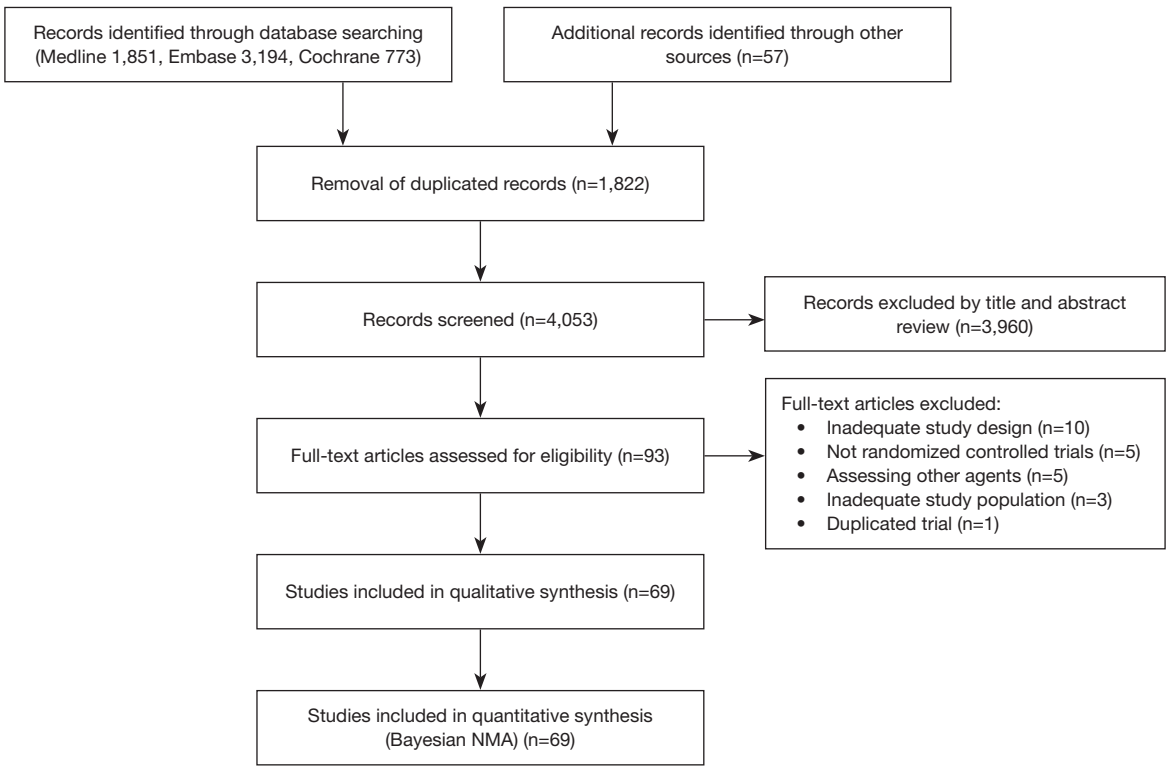

Figure 1 PRISMA flow chart.

Results

Literature search

Total 5,818 relevant studies (1,851 from Medline, 3,194 from Embase, and 773 from Cochrane Central Register of Controlled Trials) were initially detected. According to our inclusion and exclusion criteria, total 69 eligible articles published between March 1969 and November 2020 were incorporated into the NMA (*Figure 1*).

Characteristics of the included studies

The 69 included trials assessed 16 antiplatelet regimens including very low dose of aspirin (41), low to medium dose of aspirin [low dose (19-21,28,42-60); medium dose (27,41,61-72); low to medium dose (22,73-75)], high dose of aspirin (61,76-86), cilostazol (48,50,52,59,68,87), clopidogrel (63,88-93), dipyridamole (94), prasugrel (93), sarpogrelate (49), ticagrelor (57), ticlopidine (81,84,86,91,95-98), triflusal (62,65,66,92), aspirin plus cilostazol (47,54,55,69,75,99), aspirin plus clopidogrel (19,21,22,28,45,46,51,56,58,70-72,74,90,99-101), aspirin plus dipyridamole (20,43,53,67,73,79,82,85,89,90,102,103), aspirin plus ticagrelor (60,101), and aspirin plus ticlopidine (98). Detailed characteristics of these 69 studies are exhibited in Table S2. Sixty-five trials were two-arm studies, and three trials (58,79,90) had three intervention arms. One three-arm trial (58) compared two dosages of clopidogrel (50 *vs.* 75 mg) in aspirin plus clopidogrel combination, and we merged the two intervention arms into an aspirin plus clopidogrel regimen and analyzed. Additionally, one trial (43) had four intervention arms.

At baseline, the patients were 65 years old on average. The mean prevalence of diabetes, hyperlipidemia, hypertension, and smoking was 28%, 40%, 64%, and 38% respectively. The average period of follow-up was 15 months, while 14 trials had a duration of follow-up of one month (44,46,56,60,71,90) or less (27,45,51,64,72,85,95,102).

Risk of bias

The assessments of biases for all enrolled studies and the entire NMA were performed using the Cochrane Collaboration tool and we showed them in Figures S1,S2.

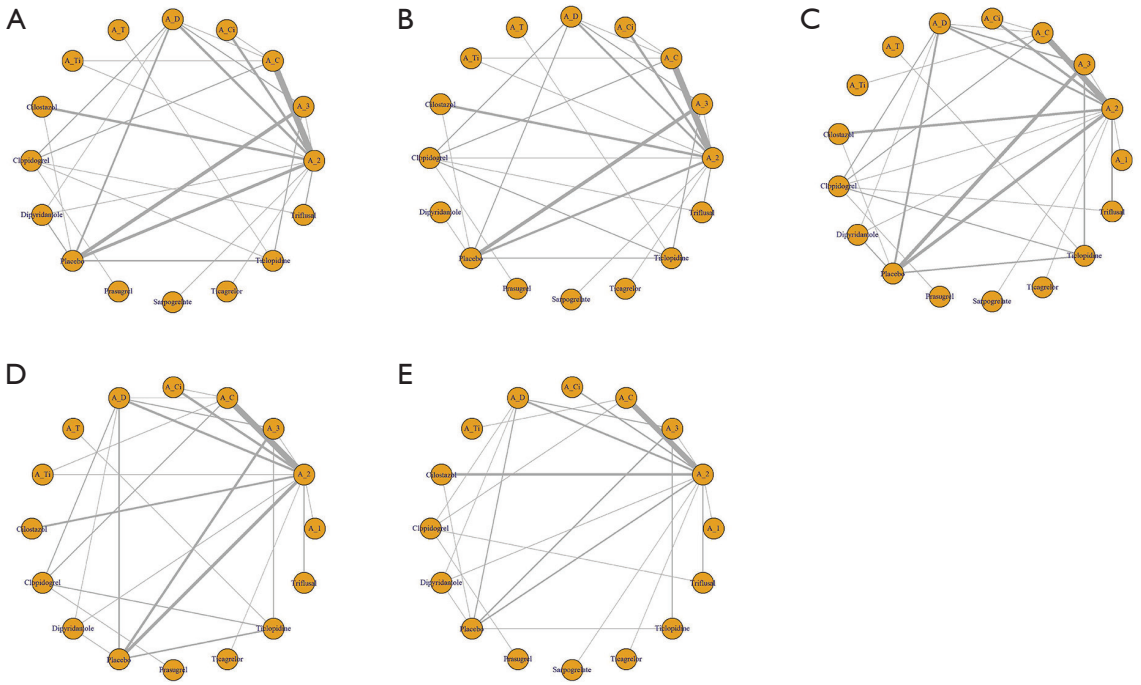

Figure 2 Network plots of the antiplatelet regimens. Antiplatelet treatment regimens are represented by nodes, and direct comparison trials between treatment regimens are linked with a line. The width of the line corresponds the sample size for each treatment regimen. (A) Recurrent stroke; (B) recurrent ischemic stroke; (C) composite outcomes; (D) major bleeding event; (E) all bleeding events. A_1, aspirin very low dose; A_2, aspirin low to medium dose; A_3, aspirin high dose; A_C, combination of aspirin plus clopidogrel; A_Ci, combination of aspirin plus cilostazol; A_D, combination of aspirin plus dipyridamole; A_T, combination of aspirin plus ticlopidine; A_Ti, combination of aspirin plus ticagrelor.

Most of the 69 studies were found to have a low risk of bias in the six domains. However, seven studies (58,67,69,81,85,90,98) did not describe the randomization methods in detail. The CAPRIE (27) and the CHARISMA studies (28) were subgroup analyses. The procedures, utilized to blind the participants and staffs or the outcome assessments, were not described in ten studies (46,50,55,58, 69,71,74,85,90,98). Five studies (20,72,73,75,92) were open-label trials. And five studies (27,51,64,67,101) were assessor-masked open-label trials.

Outcomes of interest

Figure 2 depicts the network plots for each outcome. We displayed the main results of the NMA in *Figure 3*, Tables S3-S8, and Figure S3.

Recurrent stroke

Sixty-three trials reported recurrent stroke events with a total sample size of 159,461. Cilostazol, aspirin plus clopidogrel, aspirin plus ticagrelor, clopidogrel, and aspirin plus dipyridamole had a decreased risk of recurrent stroke to aspirin alone. Cilostazol has the highest SUCRA value, the combination of aspirin plus clopidogrel had the second highest, and the combination of aspirin plus ticagrelor had the third highest value.

Recurrent IS

Sixty-two trials with a sample size of 160,772 reported recurrent IS. Aspirin plus clopidogrel, cilostazol, aspirin plus ticagrelor, aspirin plus dipyridamole, and clopidogrel alone had a decreased risk of recurrent IS to aspirin alone. The combination of aspirin plus clopidogrel had the highest SUCRA value, cilostazol had the second highest, and the combination of aspirin plus ticagrelor had the third highest value.

Composite outcomes

Sixty-six trials reported composite outcomes with a sample size of 160,344. Aspirin plus ticagrelor, cilostazol, aspirin

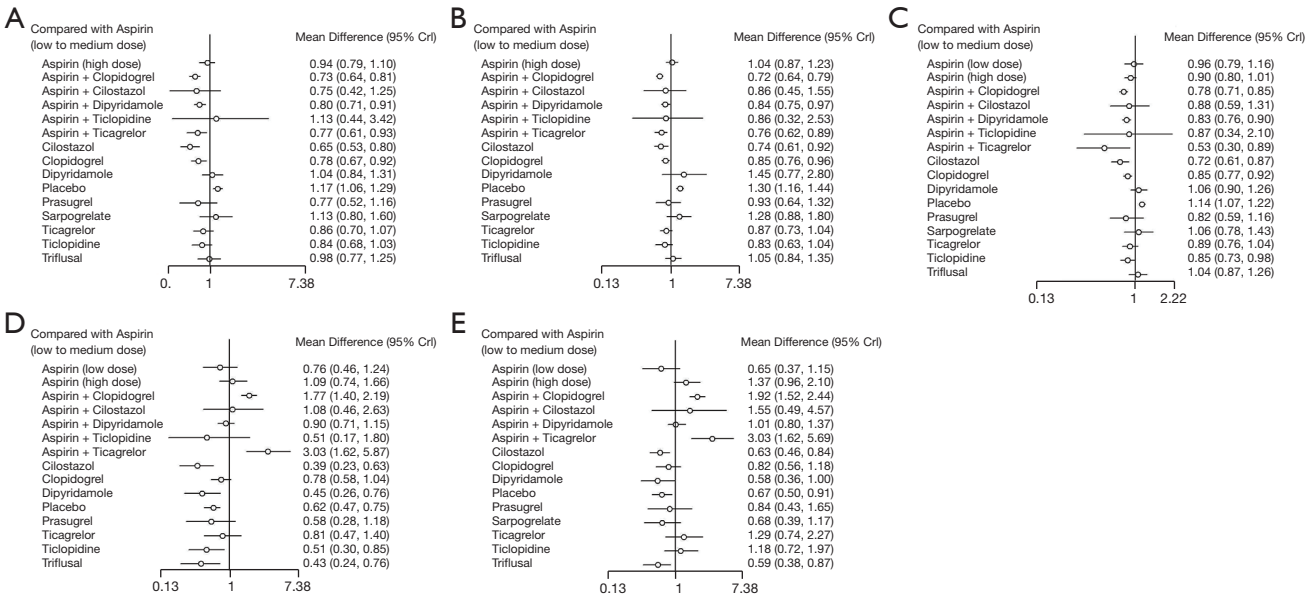

Figure 3 Forrest plots of the antiplatelet regimens compared to aspirin (low to medium dose). (A) Recurrent stroke; (B) recurrent ischemic stroke; (C) composite outcomes; (D) major bleeding event; (E) all bleeding events.

plus clopidogrel, aspirin plus dipyridamole, and clopidogrel had a decreased risk of composite outcomes to aspirin alone. The combination of aspirin plus ticagrelor had the highest SUCRA value, cilostazol had the second highest, and the combination of aspirin plus clopidogrel had the third highest value.

Major bleeding event

Fifty-seven trials reported major bleeding with a sample size of 156,436. Compared to aspirin, cilostazol, triflusal, dipyridamole, and ticlopidine were associated with a lower risk of major bleeding. However, aspirin plus ticagrelor and aspirin plus clopidogrel had an increased risk of major bleeding events to aspirin alone. Cilostazol had the highest SUCRA value and aspirin plus ticagrelor had the lowest value.

All bleeding events

Forty-three trials reported bleeding with a sample size of 102,102. Triflusal and cilostazol had a decreased risk of all bleeding events to aspirin alone. However, aspirin plus ticagrelor and aspirin plus clopidogrel had an increased risk of all bleeding events to aspirin. Triflusal had the highest SUCRA value, cilostazol had the third highest, and aspirin plus ticagrelor had the lowest value.

Net clinical benefit

We supposed that the antiplatelet regimen, which had the high probabilities of first ranking in efficacy (recurrent stroke and composite outcomes) and safety (major bleeding events) simultaneously, had the greatest net clinical benefit. As shown at *Figure 4*, cilostazol had the greatest net clinical benefit.

Consistency assessment and publication bias

Figure S4 shows the results of node-splitting assessments. There were no loop inconsistencies when comparing effect estimates for all outcomes measured based on direct *vs.* indirect evidence (all P>0.05). In addition, very low heterogeneity was noticed when assessing inconsistency across trials (all I^2<5%). The symmetry of the comparison-adjusted funnel plots indicated that there was no evidence of publication bias (Figure S5).

Subgroup analyses

Time interval from stroke onset to treatment initiation <72 hours

Twenty-six studies (19-22,27,31,33,44,51,56,57,60,64,67-69,71,72,74,75,85,101) were included in this subgroup

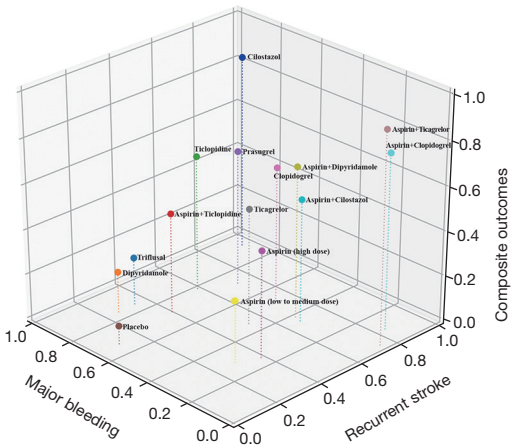

Figure 4 Three-dimensional clustered rank plot. Values of each axis are the probabilities which antiplatelet regimens had the first ranking for recurrent stroke, composite outcomes, and major bleeding event using values of surface under the cumulative ranking curve. The point (1, 1, 1) is the hypothetical point with 100% probability of first ranking for all interesting events. Since cilostazol is the closest antiplatelet therapy regimen to the point (1, 1, 1), it was considered to have the greatest net clinical benefit.

analysis. The total sample size was 83,306 and the mean follow-up period was 2.3 months. Among included studies, outcome data from one subgroup or post hoc analysis (31) and one meta-analysis (33) were used. The overall heterogeneity was low (all I^2<5%), and no inconsistency was noticed except at composite outcomes. The node-splitting assessment was not evaluated in the analysis of composite outcomes because of a lack of outcome data. Four DAPT treatments (aspirin plus clopidogrel, aspirin plus ticagrelor, aspirin plus cilostazol, and aspirin plus dipyridamole) and four monotherapies (low to medium dose aspirin, high dose aspirin, cilostazol, and ticagrelor) were compared (Figure S6). The combination of aspirin plus clopidogrel had decreased risks of recurrent stroke, recurrent IS, and composite outcomes to aspirin alone. The combination of aspirin plus ticagrelor had decreased risks of recurrent IS and composite outcomes to aspirin alone. Although cilostazol ranked high, it was not associated with better efficacy than aspirin. Safety in terms of all bleeding events was not obtained due to a lack of outcome data. Two DAPT combinations (aspirin plus ticagrelor and aspirin plus clopidogrel) had an increased risk of major bleeding events to aspirin alone. Other regimens did not have a higher risk of major bleeding than aspirin.

Time interval from stroke onset to treatment initiation >72 hours

Forty-nine studies were included with a sample size of 90,665 (Table S2). None of the included studies limited or included only patients who received treatment after 72 h of symptom onset. However, majority of index events for enrollment occurred 72 h following the beginning of symptoms, and most trials included a three-month or longer follow-up period, which could reflect the chronic and stable stage after the index event. No inconsistency was observed in node-splitting assessments (all P>0.05), and an overall heterogeneity in the network was low (all I^2<8%).

Cilostazol, aspirin plus clopidogrel, clopidogrel, and aspirin plus dipyridamole had decreased risks of recurrent stroke, recurrent IS, and composite outcomes to aspirin alone (Figure S7). Cilostazol had the highest SUCRA values for recurrent stroke and composite outcomes. Cilostazol had also decreased risks of major bleeding event and all bleeding events compared to aspirin alone, and it had the second highest SUCRA value for major and all bleeding events. Although aspirin plus clopidogrel had the highest SUCRA value for recurrent IS, it was the only regimen that had a higher risk of major and all bleeding events than aspirin, and its SUCRA ranks were the lowest.

Stroke subtype—LAA

Ten studies (30,32,45,47,51,55,56,58,71,99) were included with a sample size of 3,092. The outcome data from two sub-analyses (30,32), which had analyzed only patients with LAA in the original trials, were used. There was no inconsistency in node-splitting assessments (all P>0.05), and no heterogeneity in the network (all I^2=0%). The antiplatelet regimens included two DAPTs (aspirin plus clopidogrel and aspirin plus cilostazol), low to medium dose aspirin, and cilostazol (Figure S8). The combination of aspirin plus clopidogrel had decreased risks of recurrent stroke, recurrent IS, and composite outcomes to aspirin alone. In terms of safety, the combination of aspirin plus clopidogrel had increased risks of major bleeding event and all bleeding events compared to aspirin alone. Cilostazol was analyzed only in terms of recurrent stroke and ischemic stroke due to a lack of other outcome data.

Stroke subtype—SVO

Five studies (30,32,34,54,70) with the total sample size of 32,690 were used as outcome extraction sources of 13 included trials (43,44,52,54,70,73,79,86,87,89,91,97,100). Two trials investigated the comparative effects of antiplatelet

regimens in only patients with SVO (54,70). Outcome data of 2 trials from subgroup or post hoc analyses (30,32) and 9 trials from one meta-analysis (34) which had been extracted and pooled in only patients with SVO of the original trial population, were included. The overall heterogeneity was low (all I^2<8%), and no inconsistency was observed in the analyses of IS and composite outcomes (all P>0.05). The node-splitting assessment was not performed in the analysis of recurrent stroke because of a lack of outcome data. Three DAPTs (aspirin plus cilostazol, aspirin plus clopidogrel, and aspirin plus dipyridamole) as well as ticlopidine, clopidogrel, cilostazol, low to medium dose aspirin, and dipyridamole were included (Figure S9). Bleeding outcomes were not analyzed due to the absence of data. All included antiplatelet regimens were comparable to aspirin in terms of recurrent stroke, recurrent IS, and composite outcomes. However, the combination of aspirin plus dipyridamole was associated with the highest SUCRA value for recurrent IS and composite outcomes, and the second highest for recurrent stroke.

Treatment duration of DAPT

All 69 trials were included with the total sample size of 171,595. The overall heterogeneity was low (all I^2<5%), and there was no inconsistency in node-splitting assessments except at aspirin *vs.* aspirin plus clopidogrel (P=0.02) and aspirin plus clopidogrel *vs.* aspirin plus ticagrelor (P=0.02). Combination regimens including aspirin plus cilostazol, aspirin plus clopidogrel, and aspirin plus dipyridamole were divided according to DAPT treatment duration (< or >1 month). As shown in Figure S10, aspirin plus clopidogrel (<1 month) had greater efficacy with preserved safety compared to both aspirin plus clopidogrel (>1 month) and aspirin alone. However, the major bleeding risk associated with aspirin plus clopidogrel (>1 month) was higher than that with aspirin. The combination of aspirin plus cilostazol had comparable efficacy and safety to aspirin regardless of the duration of therapy. For the combination of aspirin plus dipyridamole, however, only a duration >1 month had greater efficacy for recurrent stroke, recurrent IS, and composite outcomes, and safety similar to aspirin.

Discussion

Our Bayesian NMA showed that cilostazol had the highest net clinical benefit and decreased risks of recurrent stroke, recurrent IS, composite outcomes, major bleeding event, and all bleeding events to aspirin alone. This finding was similar with conclusions of previous NMAs, but we revealed additionally that several regimens have different efficacy and safety profiles according to the treatment initiation, stroke subtype, and DAPT treatment duration. Most of all, cilostazol was found to have the highest net clinical benefit especially in the >72 hours from stroke onset subgroup analysis. And the combination of aspirin plus clopidogrel had a higher efficacy than aspirin and a high SUCRA value in the <72 hours from stroke onset subgroup analysis, and in the DAPT duration subgroup analysis, the major bleeding risk of the <1 month group was not higher than that of aspirin. Also, it had higher efficacy without increasing major bleeding risk compared to aspirin in the LAA subgroup analysis. In the case of SVO, there was no antiplatelet regimen with higher efficacy than aspirin, but in the SUCRA ranking, the combination of aspirin plus dipyridamole had the highest value. Therefore, efficacy and safety profiles among antiplatelet regimens may differ according to the clinical situation, stroke subtypes, and treatment duration of dual antiplatelet agents.

Cilostazol was found to have the potential to be a first option for the secondary prevention of subacute and chronic stroke. The high efficacy and safety of cilostazol were due to the lower risk of bleeding and pleiotropic mechanisms in the vascular endothelium associated with phosphodiesterase type-3 (PDE3) inhibitors (104). However, cilostazol has been studied mainly in Asian populations, and evidence has shown a higher bleeding tendency (105) and a difference in the mechanism of stroke (106) in Asians compared to non-Asians. Therefore, the high net clinical benefit may be more prominent in Asians (25), and it is necessary to evaluate the efficacy and safety of cilostazol in non-Asian populations. In other hands, although cilostazol did not have a higher efficacy than aspirin in the subgroup analysis of stroke onset to treatment initiation time interval <72 h, there is a need for further evaluation of the role of cilostazol in the acute phase of stroke since its SUCRA value was ranked highly. In addition, more clinical evidence concerning the combination of aspirin and cilostazol is needed because a recent study (107), which reported that cilostazol-based DAPT was beneficial and safe, was excluded from this NMA for its unique study design which cannot be analyzed in this NMA. There is some evidence for the clinical applicability of aspirin plus cilostazol since superior efficacy and safety was seen with aspirin plus dipyridamole, which has a similar mechanism of action to that of cilostazol after longer treatment compared to aspirin alone.

The combination of aspirin plus clopidogrel was found

to be the optimal antiplatelet regimen in patients within the acute period of stroke because it had a higher efficacy than aspirin and a high SUCRA value in the <72 hours from stroke onset subgroup analysis. Although aspirin plus clopidogrel had a higher bleeding risk, if the increased bleeding risk was not higher than the high recurrence rate in the acute period of stroke, it may have a positive net benefit. In addition, in the DAPT duration subgroup analysis, the major bleeding risk of the <1 month group was not higher than that of aspirin; therefore, the use of aspirin plus clopidogrel for <1 month is thought to have a clear positive net clinical benefit. However, since patients with a minor stroke or TIA were mainly included in the RCTs using DAPT during the acute phase, the low risk for intracerebral hemorrhage should be carefully interpreted.

The combination of aspirin plus ticagrelor showed almost similar efficacy and safety profiles to the combination of aspirin plus clopidogrel, but unlike aspirin plus clopidogrel, the risk of major bleeding with aspirin plus ticagrelor was higher than that with aspirin, even though it was administered for <1 month. However, it is worth noting that aspirin plus ticagrelor had the highest SUCRA value in composite outcomes, although it ranked third in recurrent stroke. This finding suggests that the prevention of cardiovascular events with the combination of aspirin plus ticagrelor is considerably greater in patients with IS. Therefore, we recommend the combination of aspirin plus ticagrelor in patients with a high risk of cardiovascular events after IS.

In case of SVO, the combination of aspirin plus dipyridamole had the highest SUCRA value. It is thought that dipyridamole played a role in SVO prevention as a vasodilator. It is important to note that cilostazol, which had high SUCRA values throughout this NMA, did not rank high in the SVO subgroup analysis. However, of the RCTs included, only a few were conducted on SVO. Therefore, in this subgroup analysis, a lot of data were from sub-analyses and meta-analyses, which may have increased the likelihood of a bias. More clinical trials regarding SVO are needed for a definite conclusion.

This study has several limitations. Although there was no evidence of inconsistency in the entire NMA, some node-splitting assessments were not evaluated in the subgroup analyses because of a lack of outcome data. And there was an inconsistency in two loops (aspirin *vs.* aspirin plus clopidogrel, and aspirin plus clopidogrel *vs.* aspirin plus ticagrelor) in recurrent IS of the DAPT duration subgroup analysis. However, it is possible that one or a few may show inconsistency by chance when multiple loops are tested for inconsistency (26), and since this is not related to differences according to the DAPT duration, we determined it would not affect the overall conclusion. Likewise, though inconsistency tests were not conducted in some subgroup analyses, these were largely irrelevant to our main conclusions. Second, in subgroup analyses, some among outcome data were extracted from post hoc analyses or meta-analyses due to the difficulty of data assess. Thus, there is a possibility of randomization error and bias in selective reporting. Third, there is a possibility of design inconsistency. We included 69 trials and the total 171,595 patients. Although the overall heterogeneity in the whole network was very low, the conclusions of each subgroup analysis were somewhat different from that of the entire NMA. So, there may be another unexpected variable that could affect the NMA conclusions. For example, some studies focused patients with minor stroke or high-risk TIA.

In conclusion, efficacy and safety profiles among antiplatelet regimens may differ according to the clinical situation, stroke subtypes, and treatment duration of dual antiplatelet agents although cilostazol, aspirin plus clopidogrel, and aspirin plus dipyridamole were considered as preferable options in patients with non-cardioembolic stroke or TIA. More randomized investigations are therefore needed to identify the most suitable antiplatelet therapy regimens for different clinical conditions and stroke subtypes, particularly SVO.

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Footnote

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Supplementary

Table S1 Search strategy

Search No.	PubMed	Results	Embase	Results	Cochrane Trials	Results
#1	Stroke, Lacunar[mh] OR lacunar stroke*[tw] OR lacunar infarct*[tw] OR lacunar syndrome*[tw] OR ischemic stroke*[tw] OR ischaemic stroke*[tw] OR ischemic brain stroke*[tw] OR ischaemic brain stroke*[tw] OR brain ischemia*[tw] OR brain ischaemia*[tw] OR cerebral ischemia*[tw] OR cerebral ischaemia*[tw] OR cerebrovascular ischemia*[tw] OR cerebrovascular ischaemia*[tw] OR ischemic brain[tw] OR ischaemic brain[tw] OR ischemic encephalopath*[tw] OR ischaemic encephalopath*[tw]	111,773	('lacunar stroke'/de OR (lacunar NEAR/3 (stroke* OR infarct* OR syndrome*)):ti,ab OR (isch*mic NEAR/5 stroke*):ti,ab OR (brain NEAR/5 isch*mi*):ti,ab OR (cerebral NEAR/5 isch*mia*):ti,ab OR (cerebrovascular NEAR/5 isch*mia*):ti,ab OR (isch*mic NEAR/5 encephalopath*):ti,ab)	171,132	[mh "Stroke, Lacunar"] OR (lacunar NEAR/3 (stroke* OR infarct* OR syndrome*)):ti,ab OR (isch*mic NEAR/5 stroke*):ti,ab OR (brain NEAR/5 isch*mi*):ti,ab OR (cerebral NEAR/5 isch*mia*):ti,ab OR (cerebrovascular NEAR/3 isch*mia*):ti,ab OR (isch*mic NEAR/5 encephalopath*):ti,ab	14,082
#2	Brain Infarction[mh] OR brain infarct*[tw] OR brain stem infarct*[tw] OR brain venous infarct*[tw] OR cerebral infarct*[tw] OR cerebral artery infarct*[tw] OR cerebrovascular infarct*[tw] OR cortical infarct*[tw] OR subcortical infarct*[tw] OR hemisphere infarct*[tw] OR hemispheric infarct*[tw]	52,031	('brain infarction'/exp OR ((brain OR cerebral OR cerebrovascular OR cortical OR hemispher*) NEAR/5 infarct*):ti,ab)	93,661	[mh "Cerebral Infarction"] OR ((brain OR cerebral OR cerebrovascular OR cortical OR hemispher*) NEAR/5 infarct*):ti,ab	4,878
#3	Ischemic Attack, Transient[mh] OR transient ischemic attack*[tw] OR transient ischaemic attack*[tw] OR transient brain ischemia*[tw] OR transient brain ischaemia*[tw] OR transient cerebral ischemia*[tw] OR transient cerebral ischaemia*[tw] OR (brain[tw] AND (TIA[tw] OR TIAs[tw]))	30,088	('transient ischemic attack'/exp OR (transient NEAR/5 isch*mic NEAR/5 attack*):ti,ab OR (transient NEAR/5 (brain OR cerebral) NEAR/5 isch*mia*):ti,ab OR (brain NEAR/5 (TIA OR TIAs)):ti,ab)	47,458	[mh "Ischemic Attack, Transient"] OR (transient NEAR/5 isch*mic NEAR/5 attack*):ti,ab OR (transient NEAR/5 (brain OR cerebral) NEAR/5 isch*mia*):ti,ab OR (brain NEAR/5 (TIA OR TIAs)):ti,ab	2,660
#4	#1 OR #2 OR #3	160,882	#1 OR #2 OR #3	259,013	#1 OR #2 OR #3	18,119
#5	Platelet Aggregation Inhibitors[mh] OR platelet aggregation inhibitor*[tw] OR platelet antiaggregant*[tw] OR platelet anti-aggregant*[tw] OR platelet inhibitor*[tw] OR antiplatelet agent*[tw] OR antiplatelet drug*[tw] OR anti-platelet agent*[tw] OR anti-platelet drug*[tw] OR platelet antagonist*[tw] OR antithrombocytic agent*[tw] OR anti-thrombocytic agent*[tw] OR thrombocyte aggregation inhibitor*[tw]	43,502	('antithrombocytic agent'/de OR ((platelet OR thrombocyte) NEAR/3 (inhibitor* OR antiaggregant* OR anti-aggregant* OR antagonist*)):ti,ab OR ((antiplatelet OR anti-platelet OR antithrombocytic OR anti-thrombocytic) NEAR/3 (drug* OR agent*)):ti,ab)	58,684	[mh "Platelet Aggregation Inhibitors"] OR ((platelet OR thrombocyte) NEAR/3 (inhibitor* OR antiaggregant* OR anti-aggregant* OR antagonist*)):ti,ab OR ((antiplatelet OR anti-platelet OR antithrombocytic OR anti-thrombocytic) NEAR/3 (drug* OR agent*)):ti,ab	5,954
#6	Aspirin[mh] OR aspirin[tw] OR acetylsalicylic acid[tw] OR acetyl salicylic acid[tw] OR acetosalicylic acid[tw] OR Acylpyrin[tw] OR Colfarit[tw] OR Ecotrin[tw] OR Endosprin[tw] OR Magnecyl[tw] OR Micristin[tw] OR Polopirin[tw] OR Polopiryna[tw] OR Solupsan[tw] OR Zorprin[tw] OR Acetysal[tw] OR Aloxiprimum[tw] OR Dispril[tw] OR Easprin[tw] OR Solprin[tw]	71,184	('acetylsalicylic acid'/de OR (aspirin OR 'acetylsalicylic acid' OR 'acetyl salicylic acid' OR 'acetosalicylic acid' OR Acylpyrin OR Colfarit OR Ecotrin OR Endosprin OR Magnecyl OR Micristin OR Polopirin OR Polopiryna OR Solupsan OR Zorprin OR Acetysal OR Aloxiprimum OR Dispril OR Easprin OR Solprin):ti,ab)	226,793	[mh Aspirin] OR (aspirin OR "acetylsalicylic acid" OR "acetyl salicylic acid" OR "acetosalicylic acid" OR Acylpyrin OR Colfarit OR Ecotrin OR Endosprin OR Magnecyl OR Micristin OR Polopirin OR Polopiryna OR Solupsan OR Zorprin OR Acetysal OR Aloxiprimum OR Dispril OR Easprin OR Solprin):ti,ab	14,748

Table S1 *(continued)*

https://dx.doi.org/10.21037/atm-21-3748

Table S1 *(continued)*

Search No.	PubMed	Results	Embase	Results	Cochrane Trials	Results
#7	Ticlopidine[mh] OR ticlopidine[tw] OR ticlodix[tw] OR ticlodone[tw] OR 53-32C[tw] OR 5332C[tw] OR ticlid[tw]	11,945	ticlopidine/de OR (ticlopidine OR ticlodix OR ticlodone OR 53-32C OR 5332C OR ticlid):ti,ab	14,688	[mh Ticlopidine] OR (ticlopidine OR ticlodix OR ticlodone OR "53-32C" OR 5332C OR ticlid):ti,ab	2,635
#8	Clopidogrel[tw] OR SC 25989C[tw] OR SC 25990C[tw] OR SR 25989[tw] OR Iscover[tw] OR PCR-4099[tw] OR Plavix[tw]	14,755	clopidogrel/de OR (Clopidogrel OR SC-25989C OR SC-25990C OR SR-25989 OR Iscover OR PCR-4099 OR Plavix):ti,ab	62,606	[mh Clopidogrel] OR (Clopidogrel OR SC-25989C OR SC-25990C OR SR-25989 OR Iscover OR PCR-4099 OR Plavix):ti,ab	4,919
#9	Cilostazol[mh] OR Cilostazol[tw] OR OPC-13013[tw] OR Pletal[tw] OR pletaal[tw]	1,911	cilostazol/de OR (Cilostazol OR OPC-13013 OR Pletal OR pletaal):ti,ab	5,975	[mh Cilostazol] OR (Cilostazol OR OPC-13013 OR Pletal OR pletaal):ti,ab	802
#10	Ticagrelor[mh] OR Ticagrelor[tw] OR Brilique[tw] OR AZD 6140[tw] OR Brilinta[tw]	2,989	ticagrelor/de OR (Ticagrelor OR Brilique OR AZD-6140 OR Brilinta):ti,ab	9,772	[mh Ticagrelor] OR (Ticagrelor OR Brilique OR AZD-6140 OR Brilinta):ti,ab	1,706
#11	Prasugrel Hydrochloride[mh] OR Prasugrel[tw] OR CS 747[tw] OR Efient[tw] OR Effient[tw] OR LY 640315[tw]	2,532	prasugrel/de OR (Prasugrel OR CS-747 OR Efient OR Effient OR LY-640315):ti,ab	8,976	[mh "Prasugrel Hydrochloride"] OR (Prasugrel OR CS-747 OR Efient OR Effient OR LY-640315):ti,ab	1,057
#12	triflusal[tw] OR 2-acetoxy-4-trifluoromethylbenzoic acid[tw] OR Disgren[tw] OR tecnosal[tw] OR triflux[tw] OR aflen[tw]	192	triflusal/de OR (triflusal OR '2-acetoxy-4-trifluoromethylbenzoic acid' OR Disgren OR tecnosal OR triflux OR aflen):ti,ab	621	(triflusal OR "2-acetoxy-4-trifluoromethylbenzoic acid" OR Disgren OR tecnosal OR triflux OR aflen):ti,ab	113
#13	Dipyridamole[mh] OR Dipyridamole[tw] OR Dipyramidole[tw] OR Cerebrovase[tw] OR Persantine[tw] OR Persantin[tw] OR Curantil[tw] OR Curantyl[tw] OR Kurantil[tw] OR Miosen[tw] OR Novo-Dipiradol[tw] OR Antistenocardin[tw] OR Cléridium[tw] OR Cleridium[tw]	10,561	dipyridamole/de OR (Dipyridamole OR Dipyramidole OR Cerebrovase OR Persantine OR Persantin OR Curantil OR Curantyl OR Kurantil OR Miosen OR Novo-Dipiradol OR Antistenocardin OR Cléridium OR Cleridium):ti,ab	25,496	[mh Dipyridamole] OR (Dipyridamole OR Dipyramidole OR Cerebrovase OR Persantine OR Persantin OR Curantil OR Curantyl OR Kurantil OR Miosen OR Novo-Dipiradol OR Antistenocardin OR Cléridium OR Cleridium):ti,ab	1,299
#14	sarpogrelate[tw] OR MCI-9042[tw] MCI9042[tw] OR anplag[tw]	29	sarpogrelate/de OR (sarpogrelate OR MCI-9042 MCI9042 OR anplag):ti,ab	652	(sarpogrelate OR MCI-9042 MCI9042 OR anplag):ti,ab	95
#15	Placebos[mh] OR Control Groups[mh] OR placebo[tw] OR placebos[tw] OR control group*[tw]	689,855	placebo/de OR 'control group'/de OR (placebo* OR 'control group*'):ti,ab	1,126,149	[mh Placebos] OR [mh "Control Groups"] OR (placebo* OR "control group*"):ti,ab	471,321
#16	OR #5 to #15	793,523	OR #5 to #15	1,396,246	OR #5 to #15	485,357
#17	Secondary Prevention[mh] OR ((secondary[tw] OR relapse[tw] OR recurren*[tw]) AND preventi*[tw]) OR early therap*[tw]	169,633	('secondary prevention'/de OR ((secondary OR relapse OR recurren*) AND prevention*):ti,ab OR 'early therap*':ti,ab)	109,216	[mh "Secondary Prevention"] OR ((secondary OR relapse OR recurrence) AND prevention*):ti,ab OR "early therap*":ti,ab	24,628
#18	#4 AND #16 AND #17	2,322	#4 AND #16 AND #17	3,840	#4 AND #16 AND #17	791

Table S1 *(continued)*

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Table S1 *(continued)*

Search No.	PubMed	Results	Embase	Results	Cochrane Trials	Results
#19	(Animals[mh] NOT Humans[mh]) OR Models, Animal[mh:noexp] OR Disease Models, Animal[mh] OR Animal Experimentation[mh]	4,935,274	(animal/exp NOT human/exp) OR 'animal model'/exp OR 'animal experiment'/exp OR 'animal cell'/de OR 'animal tissue'/de OR 'in vitro study'/de OR 'nonhuman'/de	9,510,924	Cochrane Reviews 18 Trials 773	
#20	#18 NOT #19	2,277	#18 NOT #19	3,640		
#21	Clinical Trial[pt] OR Clinical Trials as Topic[mh] OR Random Allocation[mh] OR Double-Blind Method[mh] OR Single-Blind Method[mh] OR Multicenter Study[pt] OR Multicenter Studies as Topic[mh] OR randomiz*[tw] OR randomis*[tw] OR randomly[tw] OR trial[tw] OR trials[tw] OR groups[tw] OR placebo[tw] OR placebos[tw] OR ((single*[tw] OR double*[tw] OR treb*[tw] OR tripl*[tw]) AND (blind*[tw] OR mask*[tw])) OR (random*[tw] AND (allocat*[tw] OR assign*[tw])) OR drug therapy[sh]	5,567,516	('clinical trial'/exp OR 'clinical trial (topic)'/exp OR randomization/exp OR 'double blind procedure'/de OR 'single blind procedure'/de OR (randomiz* OR randomis* OR randomly OR trial OR trials OR groups OR placebo OR placebos):ti,ab OR ((single* OR double* OR treb* OR tripl*) AND (blind* OR mask*)):ti,ab OR (random* AND (allocat* OR assign*)):ti,ab OR 'drug therapy':lnk)	8,220,832		
#22	#20 AND #21	1,851	#20 AND #21	3,194	Trials	773

Table S2 Characteristics of the enrolled trials

Trial	Antiplatelet therapy regimens	F/U	Tx.	Patients	N	T	C	Male	Age	HTN	DM
1969 Acheson (94)	Dipyridamole *vs* Placebo	25M		Stroke/TIA	169	85	84	70%	58	59%	NC
1977 AITIA, Fields (76)	Aspirin (high) *vs* Placebo	6M		TIA	178	88	90	62%	60	47%	14%
1978 Canadian Coop (77)	Aspirin (high) *vs* Placebo	26M		TIA	283	144	139	67%	NC	NC	NC
1980 Reuther (78)	Aspirin (high) *vs* Placebo	24M		TIA	60	30	30	65%	58	50%	17%
1981 Pince J (102)	Aspirin+Dipyridamole *vs* Placebo	10D		IS	80	40	40	62%	66	NC	NC
1983 AICLA, Bousser (79)	Aspirin (high) *vs* Aspirin+Dipyridamole *vs* Placebo	36M		IS/TIA	604	198/202	204	70%	63	63%	22%
1983 Danish Coop (80)	Aspirin (high) *vs* Placebo	25M		TIA	203	101	102	73%	59	27%	NC
1983 Turpie (95)	Ticlopidine *vs* Placebo	16D		IS	53	27	26	40%	NC	NC	NC
1984 Tohgi (81)	Aspirin (high) *vs* Ticlopidine	12M		TIA	340	170	170	NC	NC	NC	NC
1985 ACCSG (82)	Aspirin+Dipyridamole *vs* Aspirin (high)	61M		TIA	890	448	442	67%	64	48%	15%
1985 Ross Russel (96)	Ticlopidine *vs* Placebo	3M		TIA	22	11	11	NC	NC	NC	NC
1987 Swedish Coop (83)	Aspirin (high) *vs* Placebo	24M		IS	505	253	252	62%	68	46%	17%
1989 CATS, Gent (97)	Ticlopidine *vs* Placebo	24M		IS	1,053	525	528	62%	65	68%	32%
1989 TASS, Hass (84)	Aspirin (high) *vs* Ticlopidine	40M		IS/TIA	3,069	1,529	1,540	65%	63	39%	20%
1990 ESPS (103)	Aspirin+Dipyridamole *vs* Placebo	24M		IS/TIA	2,500	1,250	1,250	58%	63	37%	NC
1990 Kaye (85)	Aspirin+Dipyridamole *vs* Aspirin (high)	2W	<72h	IS	183	88	95	38%	NC	NC	NC

Table S2 *(continued)*

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Table S2 *(continued)*

Trial	Antiplatelet therapy regimens	F/U	Tx.	Patients	N	T	C	Male	Age	HTN	DM
1991 DUTCH TIA (41)	Aspirin (very low) *vs* Aspirin (low to medium)	31M		IS/TIA	3,131	1,555	1,576	65%	NC	42%	8%
1991 SALT (42)	Aspirin (low to medium) *vs* Placebo	29M		IS/TIA	1,360	676	684	66%	67	48%	13%
1991 UK-TIA, Farrell (61)	Aspirin (low to medium) *vs* Aspirin (high) *vs* Placebo	50M		IS/TIA	2,435	806/815	814	73%	60	40%	5%
1995 MAST-I (27)	Aspirin (low to medium) *vs* Placebo	10D	<6h	IS	309	153	156	53%	NC	NC	NC
1995 Smirne (62)	Triflusal *vs* Aspirin (low to medium)	6M		TIA	183	90	93	58%	66	51%	10%
1996 CAPRIE (63)	Aspirin (low to medium) *vs* Clopidogrel	14M		IS	6,428	3,233	3198	64%	65	65%	25%
1996 ESPS2, Diener (43)	Aspirin+Dipyridamole *vs* Aspirin (low to medium) *vs* Dipyridamole *vs* Placebo	24M		IS/TIA	6,602	1,650/1,649/1,654	1,649	58%	66	61%	16%
1997 CAST, Chen (44)	Aspirin (low to medium) *vs* Placebo	1M	<48h	IS	20,655	10,335	10,320	64%	63	25%	NC
1997 IST (64)	Aspirin (low to medium) *vs* Placebo	2W	<48h	IS	19,435	9,720	9,715	54%	70	82%	NC
2000 CSPS, Gotoh (87)	Cilostazol *vs* Placebo	22M		IS	1,067	533	534	66%	65	61%	25%
2003 AAASPS, Gorelick (86)	Ticlopidine *vs* Aspirin (high)	24M		IS	1,809	902	907	47%	61	86%	41%
2003 TACIP, Matias-Guiu (65)	Triflusal *vs* Aspirin (low to medium)	30M		IS/TIA	2,107	1,055	1,052	66%	64	62%	25%
2003 TOPALS, Ito (98)	Aspirin+Ticlopidine *vs* Ticlopidine	19M		IS/TIA	270	132	138	65%	67	47%	23%
2004 MATCH, Diener (100)	Aspirin+Clopidogrel *vs* Clopidogrel	18M		IS/TIA	7,599	3,797	3,802	63%	66	78%	68%
2004 TAPIRSS, Culebras (66)	Triflusal *vs* Aspirin (low to medium)	19M		IS/TIA	429	213	216	69%	65	71%	19%
2005 CARESS, Markus (45)	Aspirin+Clopidogrel *vs* Aspirin (low to medium)	1W		IS/TIA	107	51	56	70%	66	65%	32%
2005 Chairangsarit (67)	Aspirin+Dipyridamole *vs* Aspirin (low to medium)	6M	<48h	IS	38	20	18	53%	64	50%	32%
2005 PLUTO-Stroke, Serebruany (46)	Aspirin+Clopidogrel *vs* Aspirin (low to medium)	1M		IS	70	35	35	50%	68	50%	39%
2005 TOSS, Kwon (47)	Aspirin+Cilostazol *vs* Aspirin (low to medium)	6M		IS	135	67	68	61%	62	58%	40%
2006 ESPRIT, Halkes (73)	Aspirin+Dipyridamole *vs* Aspirin (low to medium)	42M		IS/TIA	2,739	1,363	1,376	66%	63	60%	19%
2006 FASTER, Kennedy (19)	Aspirin+Clopidogrel *vs* Aspirin (low to medium)	3M	<24h	IS/TIA	392	198	194	53%	68	51%	11%
2008 CASISP, Huang (48)	Cilostazol *vs* Aspirin (low to medium)	15M		IS	719	360	359	69%	60	79%	18%
2008 Fukuuchi (88)	Clopidogrel *vs* Ticlopidine	12M		IS	1,151	573	578	73%	65	68%	19%
2008 PRoFESS, Sacco (89)	Aspirin+Dipyridamole *vs* Clopidogrel	30M		IS	20,332	10,181	10,151	64%	66	74%	29%
2008 S-ACCESS, Shinohara (49)	Sarpogrelate *vs* Aspirin (low to medium)	19M		IS	1,510	752	758	72%	65	70%	28%
2008 Serebruany (90)	Aspirin+Dipyridamole *vs* Asipirin+Clopidogrel *vs* Clopidogrel	1M		TIA	60	20/20	20	64%	61	70%	100%
2009 Guo (50)	Cilostazol *vs* Aspirin (low to medium)	12M		IS	68	34	34	35%	60	NC	NC
2009 Uchiyama (91)	Clopidogrel *vs* Ticlopidine	12M		IS	1,869	941	928	72%	64	70%	22%
2010 CLAIR, Wong (51)	Aspirin+Clopidogrel *vs* Aspirin (low to medium)	1W	<72h	IS/TIA	98	46	52	78%	59	64%	38%
2010 CSPS2, Shinohara (52)	Cilostazol *vs* Aspirin (low to medium)	29M		IS	2,757	1,379	1,378	72%	63	74%	29%

Table S2 *(continued)*

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Table S2 *(continued)*

Trial	Antiplatelet therapy regimens	F/U	Tx.	Patients	N	T	C	Male	Age	HTN	DM
2010 EARLY, Dengler (20)	Aspirin+Dipyridamole *vs* Aspirin (low to medium)	1W	<24h	IS TIA	543	283	260	63%	69	74%	24%
2011 CAIST, Lee (68)	Cilostazol *vs* Aspirin (low to medium)	3M	<48h	IS	458	231	227	62%	63	65%	35%
2011 CHARISMA, Hankey (28)	Aspirin+Clopidogrel *vs* Aspirin (low to medium)	25M		IS/TIA	4,320	2,157	2,163	63%	65	76%	29%
2011 JASAP, Uchiyama (53)	Aspirin+Dipyridamole *vs* Aspirin (low to medium)	15M		IS	1,291	652	639	72%	66	89%	41%
2011 TOSS2, Kwon (99)	Aspirin+Cilostazol *vs* Aspirin+Clopidogrel	7M		IS	457	232	225	52%	65	72%	43%
2012 Nakamura (69)	Aspirin+Cilostazol *vs* Aspirin (low to medium)	6M	<48h	IS	76	38	38	74%	66	82%	35%
2012 SPS3, Benavente (70)	Aspirin+Clopidogrel *vs* Aspirin (low to medium)	40M		IS	3,020	1,517	1,503	63%	63	75%	37%
2013 CHANCE, Wang (21)	Aspirin+Clopidogrel *vs* Aspirin (low to medium)	3M	<24h	IS/TIA	5,170	2,584	2586	67%	63	66%	22%
2013 ECLIPse, Han (54)	Aspirin+Cilostazol *vs* Aspirin (low to medium)	3M		IS	203	100	103	75%	65	57%	29%
2014 Yi (71)	Aspirin+Clopidogrel *vs* Aspirin (low to medium)	1M	<48h	IS	574	286	288	55%	69	73%	38%
2015 CATHARSIS, Uchiyama (55)	Aspirin+Cilostazol *vs* Aspirin (low to medium)	24M		IS	163	83	80	66%	68	77%	37%
2015 He (72)	Aspirin+Clopidogrel *vs* Aspirin (low to medium)	2W	<72h	IS/TIA	690	343	347	57%	62	68%	42%
2015 Yi (74)	Aspirin+Clopidogrel *vs* Aspirin (low to medium)	6M	<48h	IS	979	490	489	56%	69	71%	34%
2016 COMPRESS, Hong (56)	Aspirin+Clopidogrel *vs* Aspirin (low to medium)	1M	<48h	IS	358	178	180	64%	67	67%	33%
2016 SOCRATES, Johnston (57)	Ticagrelor *vs* Aspirin (low to medium)	3M	<24h	IS/TIA	13,199	6,589	6,610	59%	65	74%	25%
2017 MAESTRO, Han (92)	Triflusal *vs* Clopidogrel	32M		IS	784	391	393	68%	61	61%	29%
2017 Zuo (58)	Aspirin+Clopidogrel *vs* Aspirin (low to medium)	3M		IS/TIA	200	66/66	68	61%	61	65%	32%
2018 PICASSO, Kim (59)	Cilostazol *vs* Aspirin (low to medium)	23M		IS/TIA	1,534	766	768	62%	65	89%	33%
2018 POINT, Johnston (22)	Aspirin+Clopidogrel *vs* Aspirin (low to medium)	3M	<12h	IS/TIA	4,881	2,432	2,449	56%	65	70%	28%
2019 ADS, Aoki (75)	Aspirin+Cilostazol *vs* Aspirin (low to medium)	3M	<48h	IS	1201	600	601	66%	69	76%	32%
2019 PRASTRO-I, Ogawa (93)	Prasugrel *vs* Clopidogrel	25M		IS	3,747	1,885	1,862	79%	62	80%	33%
2019 PRINCE, Wang (101)	Aspirin+Ticagrelor *vs* Aspirin+Clopidogrel	3M	<24h	IS/TIA	675	336	339	74%	60	61%	25%
2020 THALES, Johnston (60)	Aspirin+Ticagrelor *vs* Aspirin (low to medium)	1M	<24h	IS/TIA	11,016	5,523	5,493	62%	65	78%	29%

F/U, follow-up period; Tx., time interval from symptom onset to treatment initiation; N, number of total participants; T, number of treatment groups; C, number of comparator groups; IS, ischemic stroke; TIA, transient ischemic stroke; M, month; D, day; W, week

https://dx.doi.org/10.21037/atm-21-3748

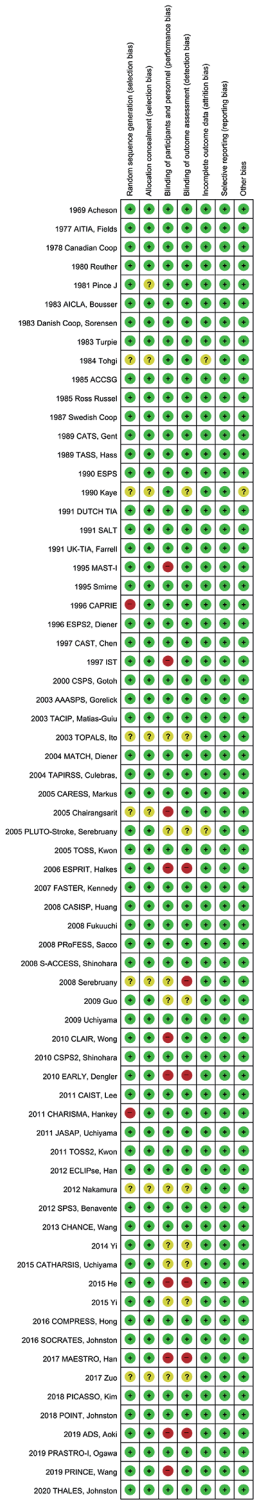

Figure S1 Risk of bias summaries depicted using colors (red: high risk; green: low risk; yellow: unclear).

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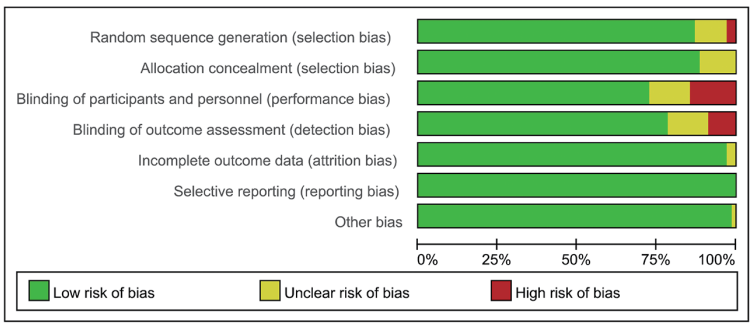

Figure S2 Graph of the total risk of bias of the entire network meta-analysis

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Table S3 League table of antiplatelet regimens with the relative risks and 95% credible intervals for recurrent stroke

Antiplatelet Regimens	A_2	A_3	A_C	A_Ci	A_D	A_T	A_Ti	Cilostazol	Clopidogrel	Dipyridamole	Placebo	Prasugrel	Sarpogrelate	Ticagrelor	Ticlopidine	Triflusal
A_2		1.05(0.90,1.26)	1.36(1.22,1.54)	1.32(0.79,2.34)	1.24(1.09,1.39)	0.87(0.29,2.22)	1.29(1.06,1.63)	1.52(1.24,1.85)	1.27(1.08,1.48)	0.95(0.76,1.18)	0.85(0.76,0.93)	1.28(0.86,1.9)	0.88(0.62,1.24)	1.15(0.92,1.42)	1.18(0.96,1.46)	1.01(0.79,1.29)
A_3	0.94(0.79,1.1)		1.29(1.05,1.58)	1.26(0.71,2.29)	1.17(0.97,1.40)	0.83(0.29,2.08)	1.22(0.95,1.63)	1.43(1.10,1.87)	1.20(0.96,1.49)	0.90(0.68,1.15)	0.80(0.67,0.92)	1.21(0.79,1.84)	0.83(0.57,1.22)	1.08(0.82,1.42)	1.12(0.94,1.32)	0.96(0.70,1.27)
A_C	0.73(0.64,0.81)	0.77(0.63,0.94)		0.96(0.57,1.70)	0.91(0.77,1.04)	0.63(0.22,1.62)	0.94(0.76,1.20)	1.11(0.88,1.38)	0.93(0.78,1.08)	0.69(0.53,0.88)	0.62(0.53,0.71)	0.93(0.62,1.39)	0.64(0.44,0.91)	0.84(0.65,1.06)	0.86(0.68,1.09)	0.74(0.56,0.95)
A_Ci	0.75(0.42,1.25)	0.79(0.43,1.39)	1.03(0.58,1.72)		0.93(0.52,1.59)	0.64(0.19,1.86)	0.97(0.54,1.73)	1.14(0.63,1.98)	0.95(0.53,1.62)	0.71(0.39,1.25)	0.64(0.36,1.07)	0.96(0.49,1.84)	0.66(0.34,1.21)	0.87(0.47,1.51)	0.88(0.48,1.58)	0.75(0.41,1.34)
A_D	0.80(0.71,0.91)	0.85(0.71,1.02)	1.09(0.95,1.29)	1.06(0.62,1.88)		0.70(0.23,1.79)	1.04(0.83,1.36)	1.22(0.97,1.53)	1.02(0.88,1.19)	0.76(0.60,0.97)	0.68(0.59,0.78)	1.03(0.69,1.52)	0.70(0.49,1.02)	0.92(0.72,1.18)	0.95(0.76,1.20)	0.81(0.62,1.07)
A_T	1.13(0.44,3.42)	1.20(0.47,3.42)	1.56(0.61,4.48)	1.54(0.53,5.05)	1.41(0.55,4.22)		1.49(0.58,4.26)	1.73(0.67,5.47)	1.45(0.56,4.34)	1.08(0.42,3.22)	0.96(0.38,2.88)	1.46(0.54,4.71)	1.00(0.38,2.97)	1.30(0.50,4.01)	1.34(0.55,4.01)	1.15(0.44,3.63)
A_Ti	0.77(0.61,0.93)	0.81(0.61,1.04)	1.05(0.82,1.30)	1.02(0.57,1.84)	0.96(0.73,1.19)	0.67(0.23,1.72)		1.16(0.86,1.56)	0.98(0.73,1.25)	0.73(0.52,0.97)	0.65(0.50,0.81)	0.98(0.62,1.52)	0.67(0.44,1.00)	0.88(0.64,1.17)	0.91(0.66,1.20)	0.78(0.55,1.06)
Cilostazol	0.65(0.53,0.80)	0.69(0.53,0.90)	0.89(0.72,1.12)	0.87(0.50,1.57)	0.81(0.64,1.02)	0.57(0.18,1.47)	0.85(0.64,1.15)		0.83(0.64,1.07)	0.62(0.46,0.84)	0.55(0.45,0.69)	0.84(0.54,1.31)	0.58(0.38,0.85)	0.75(0.56,1.00)	0.77(0.58,1.04)	0.66(0.48,0.91)
Clopidogrel	0.78(0.67,0.92)	0.83(0.67,1.03)	1.07(0.91,1.28)	1.04(0.61,1.85)	0.97(0.83,1.13)	0.68(0.22,1.77)	1.01(0.79,1.35)	1.19(0.92,1.54)		0.74(0.57,0.97)	0.66(0.56,0.79)	1.00(0.69,1.44)	0.69(0.47,1.01)	0.90(0.69,1.17)	0.93(0.73,1.19)	0.79(0.60,1.05)
Dipyridamole	1.04(0.84,1.31)	1.10(0.86,1.45)	1.43(1.12,1.86)	1.39(0.79,2.53)	1.30(1.02,1.65)	0.92(0.31,2.37)	1.36(1.02,1.89)	1.59(1.18,2.16)	1.33(1.02,1.74)		0.89(0.71,1.12)	1.34(0.85,2.12)	0.92(0.62,1.39)	1.20(0.89,1.64)	1.24(0.93,1.68)	1.06(0.77,1.48)
Placebo	1.17(1.06,1.29)	1.23(1.07,1.47)	1.60(1.40,1.87)	1.56(0.92,2.77)	1.46(1.27,1.66)	1.03(0.34,2.60)	1.52(1.22,1.96)	1.78(1.44,2.21)	1.49(1.25,1.78)	1.12(0.88,1.39)		1.50(1.00,2.25)	1.03(0.72,1.48)	1.35(1.07,1.70)	1.39(1.14,1.71)	1.19(0.92,1.55)
Prasugrel	0.77(0.52,1.16)	0.82(0.54,1.25)	1.06(0.71,1.60)	1.03(0.54,2.00)	0.96(0.65,1.43)	0.68(0.21,1.83)	1.01(0.65,1.60)	1.19(0.76,1.85)	0.99(0.69,1.43)	0.74(0.47,1.16)	0.66(0.44,0.99)		0.68(0.40,1.17)	0.89(0.57,1.40)	0.92(0.59,1.41)	0.78(0.50,1.24)
Sarpogrelate	1.13(0.80,1.60)	1.19(0.81,1.75)	1.54(1.08,2.24)	1.50(0.82,2.88)	1.41(0.97,2.01)	0.99(0.33,2.63)	1.47(0.99,2.23)	1.71(1.16,2.57)	1.44(0.98,2.10)	1.08(0.71,1.61)	0.96(0.67,1.38)	1.45(0.85,2.46)		1.30(0.86,1.95)	1.34(0.89,1.99)	1.14(0.76,1.74)
Ticagrelor	0.86(0.70,1.07)	0.91(0.70,1.20)	1.18(0.94,1.53)	1.14(0.65,2.11)	1.07(0.84,1.37)	0.76(0.24,1.97)	1.12(0.84,1.56)	1.31(0.99,1.77)	1.10(0.84,1.44)	0.82(0.60,1.12)	0.73(0.58,0.93)	1.11(0.70,1.74)	0.76(0.51,1.15)		1.02(0.77,1.38)	0.87(0.64,1.21)
Ticlopidine	0.84(0.68,1.03)	0.88(0.75,1.05)	1.15(0.91,1.46)	1.12(0.63,2.05)	1.04(0.83,1.30)	0.74(0.24,1.80)	1.09(0.82,1.50)	1.28(0.96,1.71)	1.07(0.83,1.36)	0.80(0.59,1.07)	0.71(0.58,0.87)	1.08(0.70,1.67)	0.74(0.50,1.11)	0.97(0.72,1.29)		0.85(0.61,1.16)
Triflusal	0.98(0.77,1.25)	1.03(0.78,1.41)	1.34(1.04,1.76)	1.32(0.74,2.41)	1.22(0.93,1.59)	0.86(0.27,2.22)	1.27(0.94,1.79)	1.50(1.09,2.04)	1.25(0.95,1.65)	0.93(0.67,1.29)	0.83(0.64,1.08)	1.26(0.80,1.98)	0.87(0.57,1.30)	1.13(0.82,1.55)	1.17(0.85,1.62)	

A_2, low to medium dose aspirin; A_3, high dose aspirin; A_C, aspirin plus clopidogrel; A_Ci, aspirin plus cilostazol; A_D, aspirin plus dipyridamole; A_T, aspirin plus ticlopidine; A_Ti, aspirin plus ticagrelor

Table S4 League table of antiplatelet regimens with the relative risks and 95% credible intervals for recurrent ischemic stroke

Antiplatelet Regimens	A_2	A_3	A_C	A_Ci	A_D	A_T	A_Ti	Cilostazol	Clopidogrel	Dipyridamole	Placebo	Prasugrel	Sarpogrelate	Ticagrelor	Ticlopidine	Triflusal
A_2		0.96(0.81,1.14)	1.37(1.25,1.53)	1.15(0.64,2.19)	1.17(1.02,1.32)	1.15(0.39,3.06)	1.31(1.11,1.60)	1.34(1.08,1.62)	4.57(1.04,1.31)	0.68(0.35,1.29)	0.76(0.69,0.85)	1.06(0.75,1.54)	0.78(0.55,1.12)	1.14(0.95,1.36)	1.19(0.95,1.56)	0.94(0.73,1.18)
A_3	1.04(0.87,1.23)		1.43(1.18,1.74)	1.22(0.67,2.33)	1.21(1.00,1.47)	1.18(0.41,3.12)	1.37(1.06,1.77)	1.37(1.06,1.82)	1.21(1.00,1.47)	0.70(0.35,1.36)	0.80(0.65,0.95)	1.11(0.76,1.67)	0.81(0.55,1.21)	1.19(0.92,1.52)	1.24(1.02,1.52)	0.97(0.72,1.30)
A_C	0.72(0.64,0.79)	0.69(0.57,0.84)		0.84(0.47,1.59)	0.85(0.72,0.98)	0.83(0.28,2.23)	0.95(0.79,1.17)	0.97(0.76,1.21)	0.84(0.73,0.95)	0.49(0.25,0.93)	0.55(0.47,0.64)	0.77(0.54,1.11)	0.56(0.39,0.82)	0.83(0.66,1.00)	0.86(0.67,1.14)	0.68(0.52,0.87)
A_Ci	0.86(0.45,1.55)	0.81(0.42,1.49)	1.18(0.62,2.10)		1.01(0.53,1.76)	1.01(0.25,2.94)	1.13(0.58,2.05)	1.15(0.59,2.03)	1.00(0.52,1.78)	0.59(0.22,1.28)	0.65(0.34,1.16)	0.92(0.45,1.74)	0.67(0.32,1.32)	0.98(0.50,1.79)	1.01(0.51,1.83)	0.81(0.40,1.45)
A_D	0.84(0.75,0.97)	0.82(0.67,0.99)	1.17(1.01,1.38)	0.98(0.56,1.87)		0.97(0.32,2.59)	1.12(0.91,1.43)	1.13(0.89,1.44)	0.98(0.89,1.13)	0.58(0.30,1.10)	0.65(0.56,0.77)	0.91(0.63,1.32)	0.66(0.46,0.98)	0.97(0.78,1.21)	1.02(0.80,1.34)	0.79(0.61,1.04)
A_T	0.86(0.32,2.53)	0.84(0.31,2.43)	1.19(0.44,3.49)	0.98(0.33,3.97)	1.02(0.38,3.03)		1.11(0.42,3.45)	1.15(0.42,3.49)	1.01(0.38,2.97)	0.59(0.18,2.07)	0.65(0.25,1.96)	0.90(0.32,2.94)	0.66(0.23,2.08)	0.99(0.37,2.94)	1.03(0.41,3.03)	0.80(0.29,2.41)
A_Ti	0.76(0.62,0.89)	0.72(0.56,0.93)	1.04(0.85,1.26)	0.87(0.48,1.71)	0.89(0.69,1.09)	0.89(0.28,2.34)		1.01(0.76,1.31)	0.88(0.70,1.07)	0.51(0.26,1.00)	0.58(0.46,0.70)	0.81(0.55,1.21)	0.59(0.39,0.88)	0.86(0.65,1.10)	0.90(0.66,1.24)	0.71(0.51,0.94)
Cilostazol	0.74(0.61,0.92)	0.72(0.54,0.94)	1.02(0.82,1.30)	0.86(0.49,1.69)	0.87(0.69,1.11)	0.86(0.28,2.32)	0.98(0.76,1.31)		0.86(0.69,1.10)	0.51(0.26,1.00)	0.57(0.45,0.72)	0.79(0.54,1.21)	0.58(0.39,0.89)	0.85(0.65,1.12)	0.90(0.65,1.24)	0.69(0.51,0.96)
Clopidogrel	0.85(0.76,0.96)	0.82(0.67,0.99)	1.17(1.04,1.35)	0.99(0.55,1.89)	1.01(0.87,1.12)	0.98(0.33,2.61)	1.13(0.92,1.41)	1.15(0.90,1.44)		0.59(0.30,1.10)	0.65(0.56,0.76)	0.91(0.65,1.29)	0.67(0.45,0.98)	0.98(0.79,1.20)	1.02(0.81,1.33)	0.80(0.61,1.03)
Dipyridamole	1.45(0.77,2.80)	1.41(0.73,2.80)	2.00(1.06,3.93)	1.68(0.77,4.39)	1.71(0.90,3.32)	1.69(0.48,5.41)	1.92(0.99,3.81)	1.94(0.99,3.81)	1.69(0.90,3.28)		1.11(0.60,2.16)	1.54(0.76,3.35)	1.12(0.57,2.51)	1.66(0.85,3.28)	1.73(0.87,3.59)	1.34(0.70,2.77)
Placebo	1.30(1.16,1.44)	1.24(1.04,1.52)	1.79(1.56,2.08)	1.51(0.85,2.85)	1.53(1.28,1.76)	1.51(0.50,3.93)	1.71(1.41,2.13)	1.74(1.43,2.17)	1.52(1.30,1.75)	0.89(0.46,1.65)		1.39(0.97,2.04)	1.02(0.71,1.48)	1.49(1.20,1.81)	1.56(1.23,2.02)	1.23(0.93,1.57)
Prasugrel	0.93(0.64,1.32)	0.89(0.59,1.30)	1.29(0.90,1.82)	1.08(0.57,2.19)	1.09(0.75,1.58)	1.10(0.33,3.03)	1.22(0.82,1.81)	1.25(0.82,1.83)	1.08(0.77,1.51)	0.64(0.29,1.31)	0.71(0.48,1.02)		0.74(0.43,1.17)	1.07(0.70,1.57)	1.12(0.72,1.68)	0.88(0.57,1.28)
Sarpogrelate	1.28(0.88,1.80)	1.22(0.82,1.81)	1.75(1.21,2.51)	1.47(0.75,3.06)	1.50(1.01,2.16)	1.49(0.47,4.17)	1.67(1.12,2.53)	1.71(1.11,2.50)	1.48(1.01,2.17)	0.88(0.39,1.72)	0.97(0.67,1.40)	1.34(0.84,2.28)		1.46(0.96,2.13)	1.52(0.99,2.34)	1.19(0.78,1.79)
Ticagrelor	0.87(0.73,1.04)	0.84(0.65,1.07)	1.19(0.99,1.49)	1.01(0.55,1.99)	1.02(0.82,1.26)	1.00(0.33,2.66)	1.15(0.90,1.51)	1.16(0.88,1.52)	1.01(0.82,1.26)	0.60(0.30,1.17)	0.66(0.54,0.82)	0.93(0.63,1.40)	0.68(0.46,1.03)		1.03(0.78,1.44)	0.82(0.60,1.09)
Ticlopidine	0.83(0.63,1.04)	0.80(0.65,0.97)	1.15(0.87,1.47)	0.98(0.54,1.84)	0.97(0.74,1.23)	0.96(0.32,2.38)	1.10(0.80,1.49)	1.10(0.80,1.52)	0.97(0.75,1.22)	0.57(0.27,1.13)	0.64(0.49,0.81)	0.89(0.59,1.37)	0.65(0.42,1.00)	0.96(0.69,1.28)		0.78(0.54,1.10)
Triflusal	1.05(0.84,1.35)	1.02(0.76,1.37)	1.45(1.14,1.90)	1.22(0.68,2.46)	1.25(0.95,1.62)	1.23(0.41,3.38)	1.39(1.06,1.92)	1.42(1.03,1.94)	1.23(0.96,1.61)	0.74(0.36,1.42)	0.81(0.63,1.07)	1.12(0.77,1.74)	0.83(0.55,1.27)	1.21(0.91,1.64)	1.27(0.90,1.82)	

A_2, low to medium dose aspirin; A_3, high dose aspirin; A_C, aspirin plus clopidogrel; A_Ci, aspirin plus cilostazol; A_D, aspirin plus dipyridamole; A_T, aspirin plus ticlopidine; A_Ti, aspirin plus ticagrelor

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Table S5 League table of antiplatelet regimens with the relative risks and 95% credible intervals for composite outcomes

Antiplatelet Regimens	A_1	A_2	A_3	A_C	A_Ci	A_D	A_T	A_Ti	Cilostazol	Clopidogrel	Dipyridamole	Placebo	Prasugrel	Sarpogrelate	Ticagrelor	Ticlopidine	Triflusal
A_1		0.96(0.79,1.16)	1.07(0.85,1.35)	1.23(0.99,1.51)	1.09(0.69,1.67)	1.16(0.94,1.43)	1.10(0.43,2.80)	1.81(1.03,3.28)	1.32(1.03,1.72)	1.13(0.91,1.40)	0.90(0.69,1.16)	0.84(0.68,1.03)	1.16(0.79,1.72)	0.90(0.63,1.29)	1.08(0.84,1.38)	1.13(0.88,1.45)	0.92(0.70,1.20)
A_2	1.03(0.85,1.25)		1.10(0.98,1.24)	1.27(1.16,1.39)	1.13(0.76,1.67)	1.20(1.10,1.30)	1.14(0.47,2.85)	1.88(1.12,3.32)	1.37(1.14,1.63)	1.17(1.07,1.28)	0.93(0.78,1.10)	0.87(0.81,0.93)	1.21(0.85,1.68)	0.93(0.69,1.26)	1.12(0.95,1.30)	1.17(1.01,1.35)	0.95(0.78,1.14)
A_3	0.93(0.73,1.17)	0.90(0.80,1.01)		1.14(0.99,1.32)	1.01(0.66,1.54)	1.08(0.95,1.22)	1.03(0.43,2.58)	1.70(0.98,3.00)	1.23(0.98,1.54)	1.05(0.93,1.21)	0.84(0.68,1.03)	0.78(0.70,0.88)	1.08(0.76,1.54)	0.84(0.60,1.17)	1.01(0.83,1.23)	1.05(0.93,1.18)	0.85(0.68,1.06)
A_C	0.81(0.65,1.00)	0.78(0.71,0.85)	0.87(0.75,1.00)		0.89(0.59,1.31)	0.94(0.83,1.05)	0.89(0.36,2.28)	1.47(0.88,2.55)	1.07(0.89,1.30)	0.92(0.82,1.02)	0.73(0.60,0.88)	0.68(0.61,0.76)	0.95(0.66,1.33)	0.73(0.53,1.01)	0.88(0.73,1.04)	0.91(0.77,1.09)	0.74(0.60,0.91)
A_Ci	0.91(0.59,1.44)	0.88(0.59,1.31)	0.98(0.64,1.49)	1.12(0.76,1.68)		1.06(0.71,1.60)	1.01(0.37,2.80)	1.69(0.86,3.12)	1.21(0.78,1.90)	1.04(0.69,1.56)	0.82(0.53,1.27)	0.77(0.52,1.15)	1.07(0.62,1.83)	0.83(0.51,1.40)	0.98(0.65,1.52)	1.04(0.67,1.58)	0.84(0.55,1.34)
A_D	0.86(0.69,1.05)	0.83(0.76,0.90)	0.92(0.81,1.04)	1.05(0.94,1.19)	0.93(0.62,1.40)		0.94(0.39,2.39)	1.56(0.92,2.77)	1.14(0.93,1.38)	0.97(0.89,1.07)	0.78(0.64,0.93)	0.72(0.66,0.79)	1.00(0.71,1.40)	0.77(0.57,1.06)	0.93(0.77,1.11)	0.97(0.83,1.13)	0.79(0.64,0.96)
A_T	0.90(0.35,2.30)	0.87(0.34,2.10)	0.96(0.38,2.30)	1.11(0.43,2.70)	0.98(0.35,2.65)	1.05(0.41,2.51)		1.61(0.57,4.71)	1.19(0.48,3.00)	1.02(0.41,2.45)	0.81(0.31,2.07)	0.76(0.30,1.82)	1.05(0.38,2.66)	0.81(0.31,2.10)	0.98(0.38,2.42)	1.02(0.41,2.39)	0.83(0.32,2.08)
A_Ti	0.55(0.30,0.96)	0.53(0.30,0.89)	0.58(0.33,1.01)	0.67(0.39,1.12)	0.59(0.31,1.15)	0.64(0.36,1.08)	0.62(0.21,1.72)		0.73(0.41,1.23)	0.62(0.35,1.05)	0.49(0.27,0.84)	0.46(0.26,0.78)	0.64(0.33,1.16)	0.49(0.26,0.93)	0.59(0.32,1.02)	0.62(0.34,1.07)	0.51(0.28,0.87)
Cilostazol	0.75(0.58,0.97)	0.72(0.61,0.87)	0.80(0.64,1.01)	0.92(0.76,1.11)	0.82(0.52,1.26)	0.87(0.72,1.06)	0.83(0.33,2.07)	1.36(0.80,2.41)		0.85(0.70,1.05)	0.68(0.53,0.87)	0.63(0.53,0.77)	0.88(0.59,1.27)	0.67(0.48,0.96)	0.81(0.64,1.02)	0.85(0.67,1.09)	0.69(0.53,0.89)
Clopidogrel	0.88(0.70,1.08)	0.85(0.77,0.92)	0.94(0.82,1.07)	1.08(0.97,1.20)	0.96(0.63,1.43)	1.02(0.93,1.12)	0.97(0.40,2.43)	1.60(0.94,2.82)	1.16(0.94,1.42)		0.79(0.65,0.95)	0.74(0.66,0.82)	1.02(0.73,1.41)	0.79(0.58,1.09)	0.95(0.79,1.13)	0.99(0.85,1.16)	0.81(0.65,0.99)
Dipyridamole	1.10(0.85,1.43)	1.06(0.90,1.26)	1.18(0.96,1.45)	1.35(1.13,1.65)	1.20(0.78,1.85)	1.28(1.07,1.54)	1.22(0.48,3.12)	2.00(1.18,3.59)	1.46(1.14,1.87)	1.25(1.04,1.52)		0.93(0.78,1.11)	1.28(0.88,1.87)	1.00(0.70,1.41)	1.19(0.95,1.51)	1.25(1.01,1.56)	1.02(0.78,1.30)
Placebo	1.18(0.96,1.45)	1.14(1.07,1.22)	1.26(1.13,1.41)	1.45(1.31,1.62)	1.29(0.86,1.91)	1.37(1.25,1.51)	1.30(0.54,3.28)	2.14(1.27,3.78)	1.56(1.29,1.88)	1.33(1.21,1.49)	1.06(0.89,1.26)		1.38(0.97,1.94)	1.06(0.78,1.45)	1.28(1.07,1.52)	1.34(1.15,1.54)	1.08(0.89,1.32)
Prasugrel	0.85(0.57,1.26)	0.82(0.59,1.16)	0.92(0.64,1.31)	1.05(0.74,1.50)	0.93(0.54,1.59)	0.99(0.71,1.40)	0.94(0.37,2.56)	1.54(0.85,2.97)	1.13(0.78,1.67)	0.97(0.70,1.35)	0.77(0.53,1.13)	0.72(0.51,1.02)		0.77(0.48,1.23)	0.92(0.64,1.35)	0.97(0.68,1.39)	0.78(0.53,1.16)
Sarpogrelate	1.11(0.77,1.57)	1.06(0.78,1.43)	1.19(0.85,1.65)	1.36(0.98,1.86)	1.19(0.71,1.92)	1.28(0.93,1.74)	1.22(0.47,3.22)	2.02(1.07,3.78)	1.47(1.03,2.06)	1.25(0.91,1.71)	0.99(0.70,1.42)	0.93(0.68,1.26)	1.29(0.81,2.07)		1.19(0.85,1.67)	1.25(0.88,1.77)	1.01(0.70,1.49)
Ticagrelor	0.92(0.72,1.18)	0.89(0.76,1.04)	0.98(0.81,1.20)	1.13(0.95,1.36)	1.01(0.65,1.53)	1.07(0.90,1.28)	1.01(0.41,2.63)	1.67(0.97,3.03)	1.22(0.97,1.54)	1.04(0.87,1.25)	0.83(0.65,1.04)	0.78(0.65,0.92)	1.08(0.73,1.55)	0.83(0.59,1.17)		1.04(0.84,1.29)	0.85(0.66,1.09)
Ticlopidine	0.88(0.68,1.12)	0.85(0.73,0.98)	0.94(0.84,1.06)	1.08(0.91,1.28)	0.95(0.63,1.47)	1.02(0.87,1.19)	0.97(0.41,2.41)	1.60(0.92,2.85)	1.17(0.91,1.47)	1.00(0.85,1.17)	0.79(0.63,0.98)	0.74(0.64,0.86)	1.02(0.71,1.46)	0.79(0.56,1.12)	0.95(0.77,1.18)		0.81(0.63,1.03)
Triflusal	1.08(0.82,1.42)	1.04(0.87,1.26)	1.16(0.93,1.45)	1.33(1.09,1.65)	1.18(0.74,1.81)	1.25(1.03,1.55)	1.19(0.47,3.09)	1.95(1.13,3.56)	1.43(1.11,1.87)	1.22(1.00,1.51)	0.97(0.76,1.26)	0.91(0.75,1.12)	1.26(0.86,1.87)	0.98(0.67,1.41)	1.17(0.91,1.50)	1.22(0.96,1.57)	

A_1, very low dose aspirin; A_2, low to medium dose aspirin; A_3, high dose aspirin; A_C, aspirin plus clopidogrel; A_Ci, aspirin plus cilostazol; A_D, aspirin plus dipyridamole; A_T, aspirin plus ticlopidine; A_Ti, aspirin plus ticagrelor

Table S6 League table of antiplatelet regimens with the relative risks and 95% credible intervals for major bleeding events

Antiplatelet Regimens	A_1	A_2	A_3	A_C	A_Ci	A_D	A_T	A_Ti	Cilostazol	Clopidogrel	Dipyridamole	Placebo	Prasugrel	Ticagrelor	Ticlopidine	Triflusal
A_1		0.76(0.46,1.24)	0.69(0.36,1.34)	0.43(0.25,0.73)	0.70(0.25,1.84)	0.83(0.48,1.88)	1.46(0.38,4.95)	0.25(0.11,0.55)	1.95(0.96,4.05)	0.97(0.55,1.71)	1.66(0.80,3.38)	1.21(0.72,2.17)	1.29(0.56,3.03)	0.92(0.45,1.92)	1.49(0.72,3.03)	1.75(0.82,3.74)
A_2	1.31(0.80,2.16)		0.91(0.59,1.34)	0.56(0.45,0.71)	0.91(0.37,2.15)	1.10(0.86,1.39)	1.92(0.55,5.87)	0.32(0.17,0.61)	2.54(1.58,4.26)	1.27(0.95,1.71)	2.20(1.29,3.70)	1.58(1.32,2.10)	1.70(0.84,3.52)	1.22(0.71,2.09)	1.95(1.16,3.28)	2.29(1.31,4.09)
A_3	1.44(0.74,2.74)	1.09(0.74,1.66)		0.62(0.40,1.00)	0.99(0.38,2.67)	1.22(0.80,1.84)	2.08(0.61,6.42)	0.36(0.17,0.74)	2.77(1.57,5.47)	1.41(0.90,2.18)	2.39(1.27,4.66)	1.75(1.17,2.80)	1.86(0.88,4.09)	1.34(0.70,2.61)	2.15(1.24,3.63)	2.53(1.30,5.20)
A_C	2.32(1.36,3.93)	1.77(1.40,2.19)	1.60(0.99,2.46)		1.66(0.65,3.70)	1.95(1.42,2.59)	3.42(0.96,10.3)	0.58(0.29,1.11)	4.48(2.67,8.16)	2.25(1.67,3.00)	3.89(2.19,6.75)	2.82(2.09,4.01)	3.00(1.48,6.23)	2.18(1.19,3.89)	3.45(1.99,5.92)	4.05(2.22,7.53)
A_Ci	1.41(0.54,3.89)	1.08(0.46,2.63)	1.00(0.37,2.61)	0.59(0.26,1.52)		1.20(0.51,3.06)	2.02(0.47,8.84)	0.36(0.12,0.95)	2.74(1.06,7.53)	1.36(0.57,3.59)	2.36(0.86,7.02)	1.74(0.72,4.43)	1.82(0.62,6.23)	1.33(0.48,3.63)	2.02(0.79,6.11)	2.44(0.90,7.38)
A_D	1.19(0.69,2.06)	0.90(0.71,1.15)	0.81(0.54,1.23)	0.51(0.38,0.69)	0.83(0.32,1.95)		1.74(0.49,5.31)	0.30(0.14,0.57)	2.31(1.36,4.13)	1.15(0.89,1.51)	1.97(1.14,3.52)	1.43(1.07,2.08)	1.53(0.78,3.12)	1.10(0.62,2.02)	1.76(1.04,3.06)	2.06(1.15,3.97)
A_T	0.68(0.20,2.59)	0.51(0.17,1.80)	0.47(0.15,1.62)	0.29(0.09,1.03)	0.49(0.11,2.08)	0.57(0.18,2.00)		0.17(0.04,0.68)	1.33(0.38,5.20)	0.65(0.22,2.31)	1.14(0.32,4.30)	0.88(0.27,3.00)	0.88(0.25,3.63)	0.63(0.18,2.61)	1.02(0.37,3.12)	1.17(0.33,4.61)
A_Ti	3.93(1.80,8.75)	3.03(1.62,5.87)	2.71(1.35,5.69)	1.72(0.89,3.42)	2.77(1.04,7.84)	3.32(1.73,6.68)	5.64(1.46,21.1)		7.76(3.49,17.4)	3.85(1.96,7.92)	6.55(2.97,15.3)	4.80(2.52,9.97)	5.10(2.07,13.8)	3.70(1.61,8.67)	5.87(2.57,13.7)	6.88(2.91,16.9)
Cilostazol	0.51(0.24,1.03)	0.39(0.23,0.63)	0.36(0.18,0.63)	0.22(0.12,0.37)	0.36(0.13,0.94)	0.43(0.24,0.73)	0.74(0.19,2.61)	0.12(0.05,0.28)		0.50(0.27,0.87)	0.86(0.41,1.70)	0.62(0.37,1.06)	0.67(0.28,1.59)	0.47(0.22,0.97)	0.75(0.36,1.56)	0.88(0.43,1.88)
Clopidogrel	1.03(0.58,1.80)	0.78(0.58,1.04)	0.70(0.45,1.10)	0.44(0.33,0.59)	0.73(0.27,1.72)	0.86(0.65,1.11)	1.51(0.43,4.52)	0.25(0.12,0.50)	1.98(1.14,3.66)		1.71(0.95,3.09)	1.24(0.90,1.88)	1.33(0.70,2.55)	0.96(0.51,1.79)	1.52(0.91,2.58)	1.78(0.96,3.45)
Dipyridamole	0.60(0.29,1.23)	0.45(0.26,0.76)	0.41(0.21,0.78)	0.25(0.14,0.45)	0.42(0.14,1.15)	0.50(0.28,0.87)	0.87(0.23,3.06)	0.15(0.06,0.33)	1.15(0.58,2.43)	0.58(0.32,1.04)		0.72(0.42,1.30)	0.77(0.33,1.93)	0.55(0.26,1.19)	0.88(0.42,1.87)	1.04(0.47,2.32)
Placebo	0.82(0.45,1.38)	0.62(0.47,0.75)	0.57(0.35,0.85)	0.35(0.24,0.47)	0.57(0.22,1.38)	0.69(0.47,0.92)	1.19(0.33,3.63)	0.20(0.10,0.39)	1.60(0.93,2.69)	0.80(0.53,1.10)	1.37(0.76,2.34)		1.06(0.50,2.23)	0.76(0.41,1.34)	1.21(0.68,2.05)	1.43(0.77,2.61)
Prasugrel	0.76(0.32,1.76)	0.58(0.28,1.18)	0.53(0.24,1.12)	0.33(0.16,0.67)	0.54(0.16,1.59)	0.65(0.31,1.27)	1.12(0.27,3.93)	0.19(0.07,0.48)	1.47(0.62,3.56)	0.74(0.39,1.41)	1.28(0.51,3.00)	0.94(0.44,1.99)		0.72(0.28,1.70)	1.12(0.50,2.56)	1.32(0.54,3.38)
Ticagrelor	1.08(0.51,2.20)	0.81(0.47,1.40)	0.74(0.38,1.42)	0.45(0.25,0.83)	0.74(0.27,2.07)	0.90(0.49,1.61)	1.58(0.38,5.41)	0.26(0.11,0.61)	2.09(1.02,4.39)	1.03(0.55,1.92)	1.80(0.83,3.81)	1.30(0.74,2.42)	1.38(0.58,3.49)		1.58(0.73,3.38)	1.87(0.87,4.17)
Ticlopidine	0.66(0.32,1.37)	0.51(0.30,0.85)	0.46(0.27,0.80)	0.28(0.16,0.50)	0.49(0.16,1.25)	0.56(0.32,0.95)	0.97(0.31,2.67)	0.17(0.07,0.38)	1.32(0.63,2.71)	0.65(0.38,1.09)	1.13(0.53,2.32)	0.82(0.48,1.45)	0.89(0.38,1.98)	0.63(0.29,1.35)		1.18(0.53,2.51)
Triflusal	0.56(0.26,1.21)	0.43(0.24,0.76)	0.39(0.19,0.76)	0.24(0.13,0.44)	0.40(0.13,1.09)	0.48(0.25,0.86)	0.84(0.21,2.94)	0.14(0.05,0.34)	1.12(0.53,2.31)	0.56(0.28,1.03)	0.95(0.42,2.08)	0.69(0.38,1.28)	0.75(0.29,1.84)	0.53(0.23,1.14)	0.84(0.39,1.87)	

A_1, very low dose aspirin; A_2, low to medium dose aspirin; A_3, high dose aspirin; A_C, aspirin plus clopidogrel; A_Ci, aspirin plus cilostazol; A_D, aspirin plus dipyridamole; A_T, aspirin plus ticlopidine; A_Ti, aspirin plus ticagrelor

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Table S7 League table of antiplatelet regimens with the relative risks and 95% credible intervals for all bleeding events

Antiplatelet Regimens	A_1	A_2	A_3	A_C	A_Ci	A_D	A_Ti	Cilostazol	Clopidogrel	Dipyridamole	Placebo	Prasugrel	Sarpogrelate	Ticagrelor	Ticlopidine	Triflusal
A_1		0.65(0.37,1.15)	0.47(0.22,0.90)	0.33(0.18,0.62)	0.42(0.12,1.50)	0.64(0.33,1.15)	0.21(0.09,0.50)	1.02(0.55,1.97)	0.79(0.41,1.58)	1.11(0.51,2.31)	0.97(0.51,1.82)	0.77(0.32,1.83)	0.96(0.44,2.09)	0.50(0.23,1.10)	0.55(0.25,1.16)	1.09(0.57,2.26)
A_2	1.52(0.86,2.65)		0.72(0.47,1.04)	0.51(0.40,0.65)	0.64(0.21,2.02)	0.98(0.72,1.23)	0.32(0.17,0.61)	1.56(1.17,2.12)	1.21(0.84,1.77)	1.69(0.99,2.77)	1.48(1.09,1.99)	1.17(0.60,2.28)	1.46(0.84,2.52)	0.77(0.43,1.34)	0.84(0.50,1.38)	1.67(1.14,2.59)
A_3	2.09(1.10,4.34)	1.37(0.96,2.10)		0.71(0.46,1.15)	0.89(0.28,2.97)	1.34(0.90,2.02)	0.45(0.22,0.97)	2.16(1.39,3.63)	1.67(1.03,2.91)	2.34(1.29,4.34)	2.05(1.40,3.09)	1.61(0.79,3.56)	2.01(1.06,4.09)	1.06(0.55,2.18)	1.16(0.79,1.78)	2.31(1.39,4.30)
A_C	2.94(1.60,5.41)	1.92(1.52,2.44)	1.39(0.86,2.14)		1.24(0.41,4.01)	1.89(1.31,2.56)	0.63(0.35,1.13)	3.03(2.10,4.43)	2.33(1.61,3.45)	3.25(1.84,5.64)	2.85(1.95,4.17)	2.27(1.17,4.43)	2.82(1.55,5.10)	1.48(0.81,2.71)	1.63(0.92,2.80)	3.22(2.12,5.25)
A_Ci	2.34(0.66,8.00)	1.55(0.49,4.57)	1.11(0.33,3.52)	0.80(0.24,2.43)		1.50(0.46,4.57)	0.51(0.13,1.77)	2.43(0.76,7.53)	1.88(0.56,5.98)	2.61(0.75,8.75)	2.29(0.70,7.17)	1.81(0.49,6.55)	2.27(0.63,7.61)	1.19(0.33,4.05)	1.30(0.38,4.34)	2.62(0.77,8.33)
A_D	1.54(0.86,2.97)	1.01(0.80,1.37)	0.74(0.49,1.10)	0.52(0.38,0.75)	0.66(0.21,2.13)		0.33(0.17,0.67)	1.59(1.12,2.45)	1.23(0.87,1.87)	1.72(1.02,2.94)	1.51(1.08,2.20)	1.19(0.63,2.41)	1.49(0.83,2.82)	0.78(0.43,1.49)	0.86(0.51,1.47)	1.70(1.12,2.88)
A_Ti	4.61(1.99,10.5)	3.03(1.62,5.69)	2.20(1.02,4.48)	1.57(0.87,2.82)	1.96(0.56,7.17)	2.97(1.47,5.64)		4.75(2.40,9.58)	3.70(1.86,7.53)	5.15(2.25,11.3)	4.52(2.24,8.93)	3.56(1.47,8.75)	4.48(1.94,10.3)	2.33(1.01,5.52)	2.56(1.13,5.69)	5.10(2.5,11.02)
Cilostazol	0.97(0.50,1.80)	0.63(0.46,0.84)	0.46(0.27,0.71)	0.32(0.22,0.47)	0.41(0.13,1.31)	0.62(0.40,0.89)	0.21(0.10,0.41)		0.77(0.48,1.23)	1.07(0.58,1.88)	0.94(0.63,1.38)	0.74(0.36,1.53)	0.93(0.49,1.72)	0.49(0.25,0.91)	0.53(0.29,0.92)	1.06(0.65,1.78)
Clopidogrel	1.25(0.63,2.43)	0.82(0.56,1.18)	0.59(0.34,0.96)	0.42(0.28,0.62)	0.53(0.16,1.76)	0.81(0.53,1.13)	0.26(0.13,0.53)	1.29(0.81,2.06)		1.39(0.74,2.51)	1.22(0.75,1.90)	0.96(0.56,1.67)	1.20(0.61,2.32)	0.63(0.32,1.24)	0.69(0.37,1.24)	1.38(0.88,2.25)
Dipyridamole	0.89(0.43,1.93)	0.58(0.36,1.00)	0.42(0.22,0.77)	0.30(0.17,0.54)	0.38(0.11,1.33)	0.57(0.33,0.97)	0.19(0.08,0.44)	0.92(0.52,1.70)	0.71(0.39,1.35)		0.87(0.51,1.51)	0.69(0.30,1.60)	0.86(0.41,1.88)	0.45(0.21,0.98)	0.49(0.25,0.97)	0.98(0.53,1.97)
Placebo	1.02(0.54,1.94)	0.67(0.50,0.91)	0.48(0.32,0.71)	0.34(0.23,0.51)	0.43(0.13,1.41)	0.65(0.45,0.92)	0.22(0.11,0.44)	1.05(0.72,1.58)	0.81(0.52,1.31)	1.13(0.65,1.94)		0.78(0.39,1.63)	0.98(0.52,1.85)	0.51(0.27,0.98)	0.56(0.34,0.91)	1.12(0.70,1.93)
Prasugrel	1.29(0.54,3.03)	0.84(0.43,1.65)	0.61(0.28,1.25)	0.44(0.22,0.85)	0.54(0.15,2.02)	0.83(0.41,1.57)	0.28(0.11,0.67)	1.33(0.65,2.74)	1.03(0.59,1.77)	1.44(0.62,3.25)	1.26(0.61,2.56)		1.24(0.52,2.94)	0.65(0.27,1.56)	0.72(0.31,1.60)	1.42(0.71,3.00)
Sarpogrelate	1.03(0.47,2.26)	0.68(0.39,1.17)	0.49(0.24,0.93)	0.35(0.19,0.64)	0.43(0.13,1.57)	0.66(0.35,1.19)	0.22(0.09,0.51)	1.07(0.58,2.01)	0.82(0.43,1.62)	1.15(0.53,2.41)	1.01(0.53,1.89)	0.80(0.33,1.91)		0.52(0.23,1.14)	0.57(0.26,1.19)	1.14(0.59,2.32)
Ticagrelor	1.96(0.90,4.30)	1.29(0.74,2.27)	0.94(0.45,1.79)	0.67(0.36,1.22)	0.83(0.24,2.94)	1.27(0.66,2.30)	0.42(0.18,0.98)	2.02(1.09,3.89)	1.57(0.80,3.09)	2.20(1.01,4.61)	1.92(1.01,3.59)	1.52(0.64,3.66)	1.89(0.87,4.17)		1.09(0.51,2.29)	2.17(1.12,4.48)
Ticlopidine	1.79(0.85,3.85)	1.18(0.72,1.97)	0.85(0.56,1.25)	0.61(0.35,1.07)	0.76(0.22,2.62)	1.15(0.67,1.93)	0.39(0.17,0.87)	1.85(1.07,3.35)	1.43(0.80,2.68)	2.00(1.02,3.93)	1.75(1.09,2.85)	1.38(0.62,3.22)	1.73(0.83,3.70)	0.91(0.43,1.96)		1.98(1.08,3.89)
Triflusal	0.90(0.44,1.75)	0.59(0.38,0.87)	0.43(0.23,0.71)	0.31(0.19,0.47)	0.38(0.12,1.28)	0.58(0.34,0.88)	0.19(0.09,0.39)	0.93(0.55,1.51)	0.72(0.44,1.13)	1.01(0.50,1.85)	0.88(0.51,1.42)	0.70(0.33,1.39)	0.87(0.42,1.67)	0.45(0.22,0.89)	0.50(0.25,0.92)	

A_1, very low dose aspirin; A_2, low to medium dose aspirin; A_3, high dose aspirin; A_C, aspirin plus clopidogrel; A_Ci, aspirin plus cilostazol; A_D, aspirin plus dipyridamole; A_Ti, aspirin plus ticagrelor.

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Table S8 Surface under the cumulative ranking curve (SUCRA) values and ranks

Antiplatelet Regimens	Recurrent stroke		Recurrent ischemic stroke		Composite vascular events		Major bleeding		All bleeding events	
	SUCRA	Rank	SUCRA	Rank	SUCRA	Rank	SUCRA	Rank	SUCRA	Rank
Aspirin (very low dose)	-	-	-	-	0.3613	12	0.4971	8	0.7662	4
Aspirin (low to medium dose)	0.2742	13	0.3496	11	0.2799	13	0.2748	13	0.4321	9
Aspirin (high dose)	0.3649	10	0.3098	12	0.4786	11	0.2319	14	0.2220	14
Cilostazol	0.9199	1	0.8292	2	0.8587	2	0.8954	1	0.8075	3
Clopidogrel	0.6928	5	0.6121	6	0.6095	7	0.4792	9	0.5981	7
Dipyridamole	0.2228	14	0.1217	15	0.1833	16	0.8207	3	0.8433	2
Prasugrel	0.6740	6	0.4871	10	0.6319	5	0.6740	6	0.5692	8
Sarpogrelate	0.1694	15	0.1458	14	0.2242	14	-	-	0.7384	6
Ticagrelor	0.5114	9	0.5861	8	0.5125	10	0.4457	10	0.2815	12
Ticlopidine	0.5686	8	0.6635	4	0.6151	6	0.7604	4	0.3325	11
Triflusal	0.3148	11	0.2910	13	0.2198	15	0.8413	2	0.8532	1
Aspirin + Cilostazol	0.6998	4	0.5931	7	0.5131	9	0.2994	12	0.2637	13
Aspirin + Clopidogrel	0.8249	2	0.8933	1	0.7918	3	0.0736	15	0.1003	15
Aspirin + Dipyridamole	0.6479	7	0.6324	5	0.6735	4	0.3577	11	0.4119	10
Aspirin + Ticagrelor	0.7238	3	0.8166	3	0.9515	1	0.0067	16	0.0181	16
Aspirin + Ticlopidine	0.3084	12	0.5734	9	0.5142	8	0.6905	5	-	-

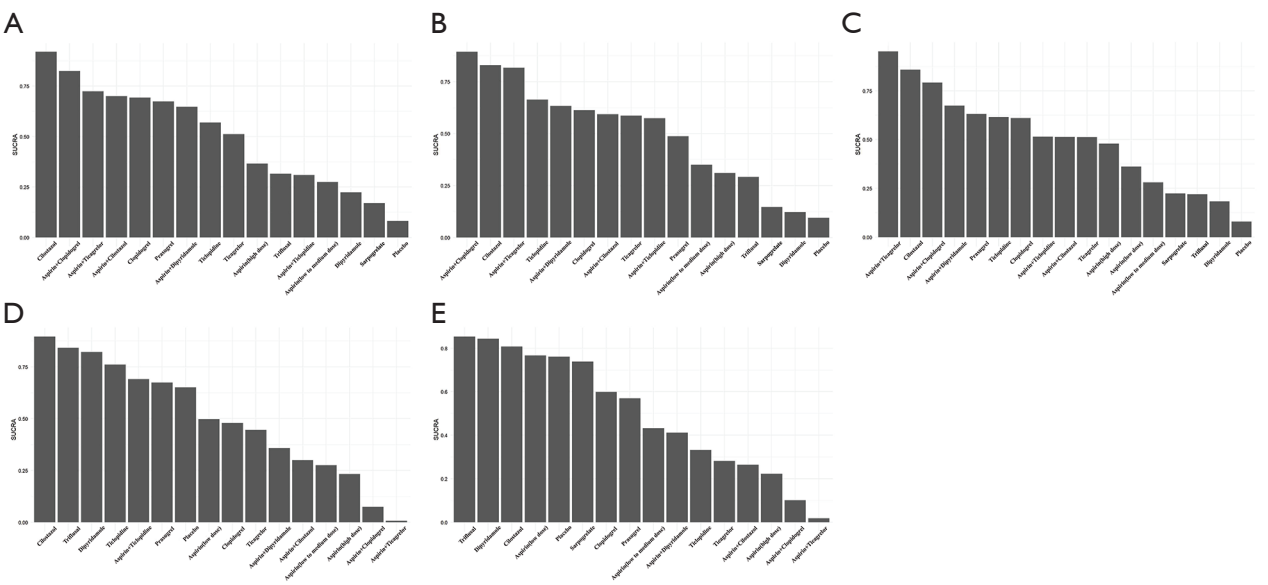

Figure S3 Surface under the cumulative ranking curve (SUCRA) rankograms for the antiplatelet regimens for (A) recurrent stroke, (B) recurrent ischemic stroke, (C) composite outcomes, (D) major bleeding events, and (E) all bleeding events.

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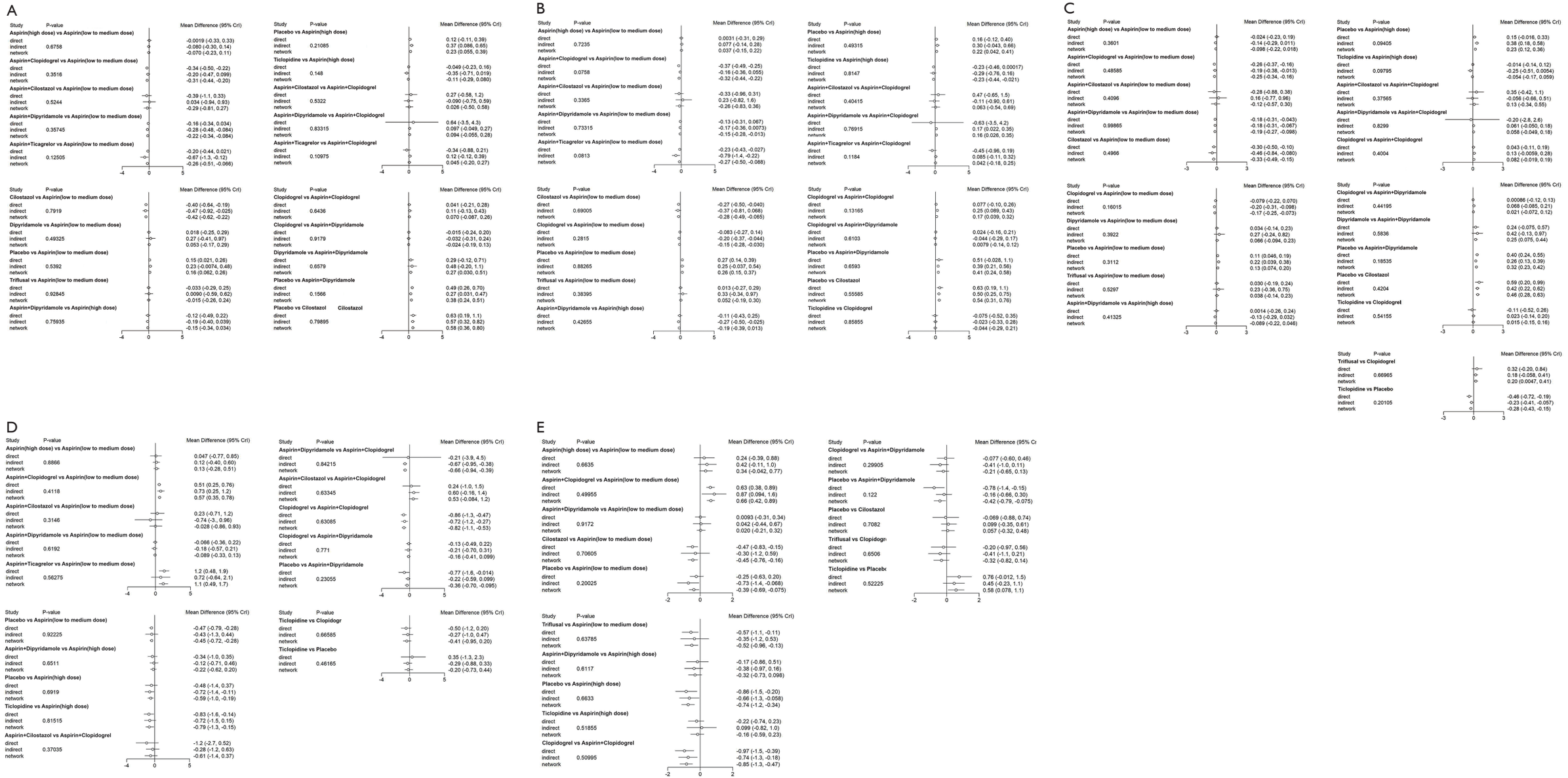

Figure S4 Inconsistency assessments using the node-splitting method for (A) recurrent stroke, (B) recurrent ischemic stroke, (C) composite outcomes, (D) major bleeding events, and (E) all bleeding events. Abbreviations: A_2, aspirin (low to medium dose); A_3, aspirin (high dose); A_C, aspirin plus clopidogrel; A_Ci, aspirin plus cilostazol; A_D, aspirin plus dipyridamole; A_T, aspirin plus ticlopidine; A_Ti, aspirin plus ticagrelor.

https://dx.doi.org/10.21037/atm-21-3748

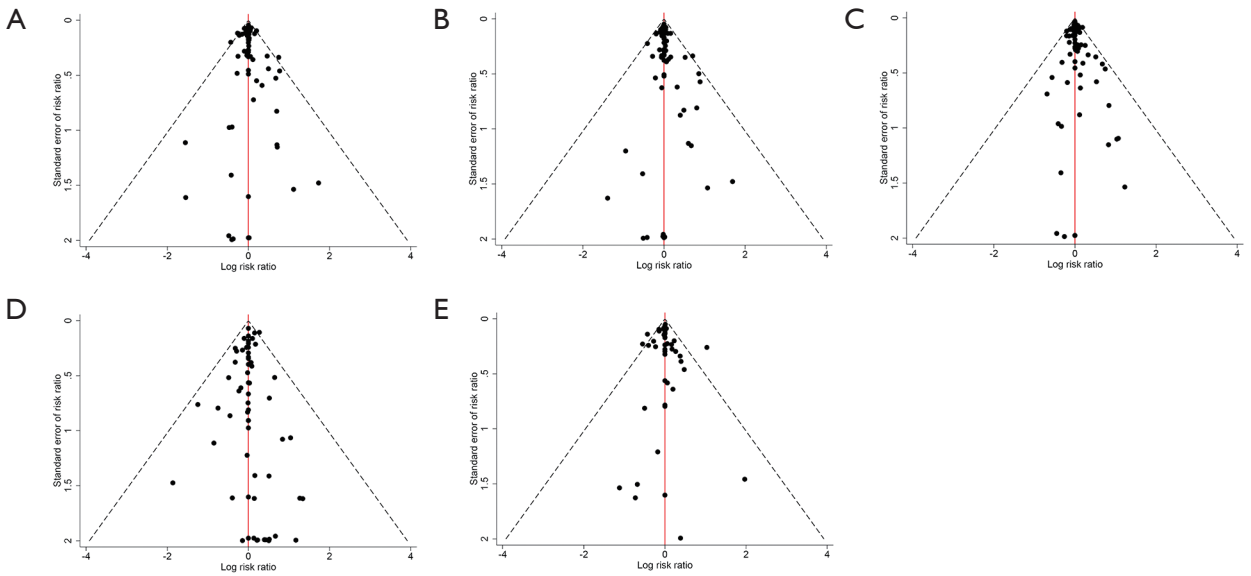

Figure S5 Funnel plots of the antiplatelet regimens of the enrolled trials. The symmetrical shape of the funnel plots demonstrates that there is no evidence of publication bias in this network meta-analysis for (A) recurrent stroke, (B) recurrent ischemic stroke, (C) composite outcomes, (D) major bleeding events, and (E) all bleeding events.

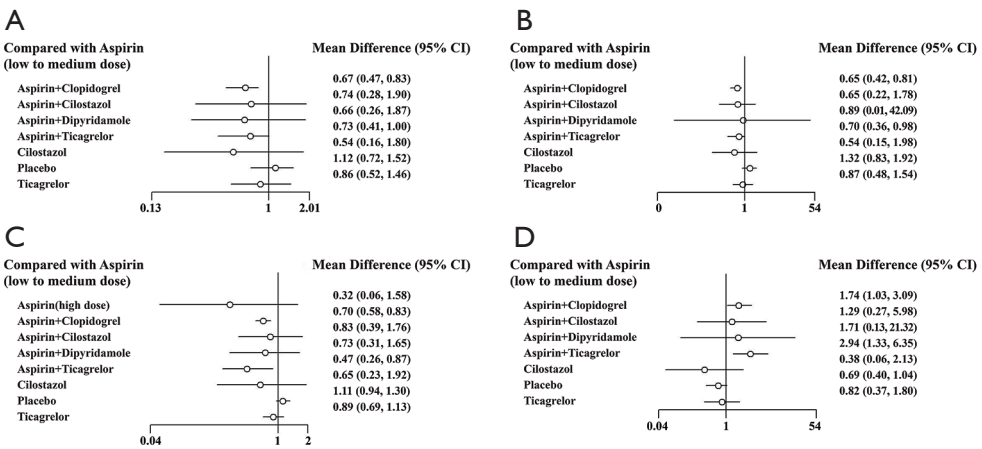

Figure S6 Forrest plots of the antiplatelet regimens compared with aspirin in the subgroup analysis (< 72 hours) for (A) recurrent stroke, (B) recurrent ischemic stroke, (C) composite outcomes, and (D) major bleeding events.

https://dx.doi.org/10.21037/atm-21-3748

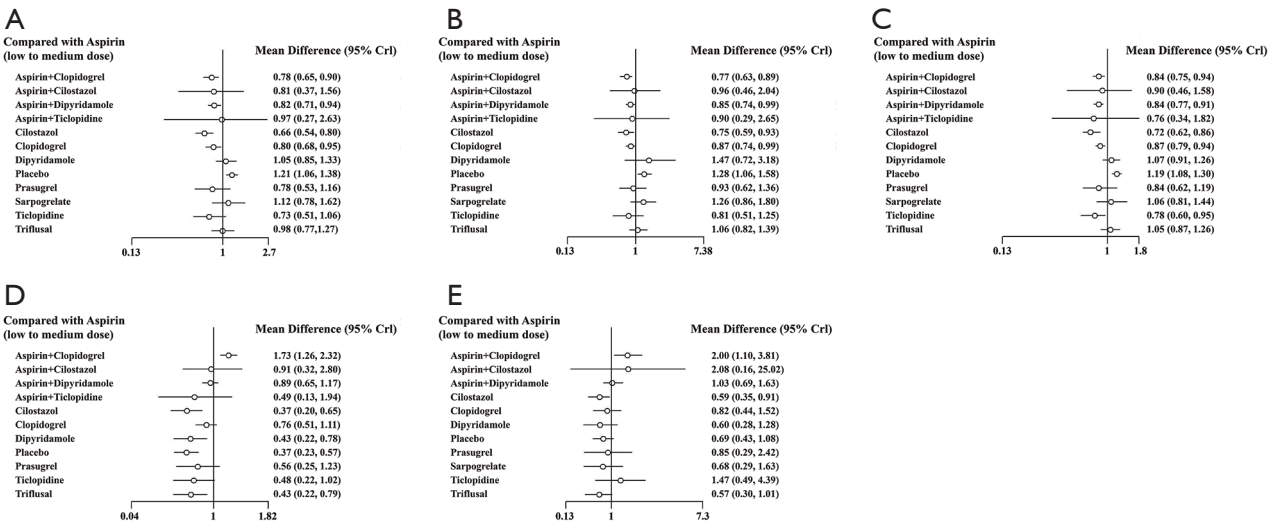

Figure S7 Forrest plots of the antiplatelet regimens compared with aspirin in the subgroup analysis (> 72 hours) for (A) recurrent stroke, (B) recurrent ischemic stroke, (C) composite outcomes, (D) major bleeding events, and (E) all bleeding events.

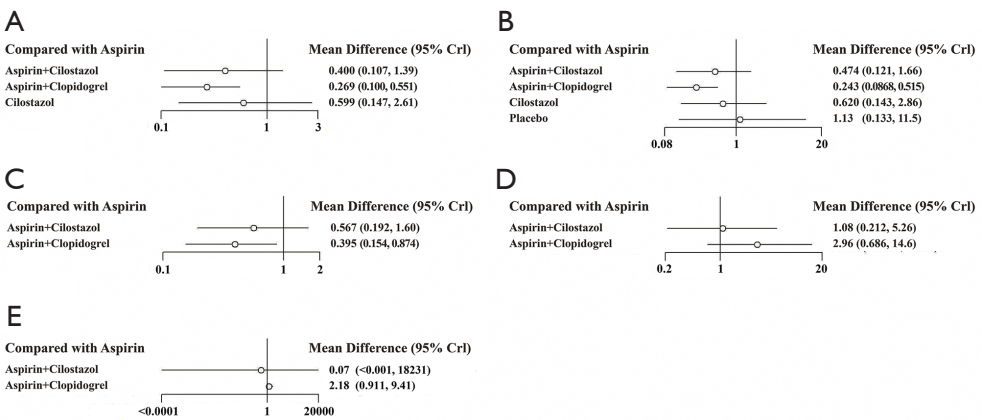

Figure S8 Forrest plots of the antiplatelet regimens compared with aspirin in the subgroup analysis for large artery atherosclerosis for (A) recurrent stroke, (B) recurrent ischemic stroke, (C) composite outcomes, (D) major bleeding events, and (E) all bleeding events.

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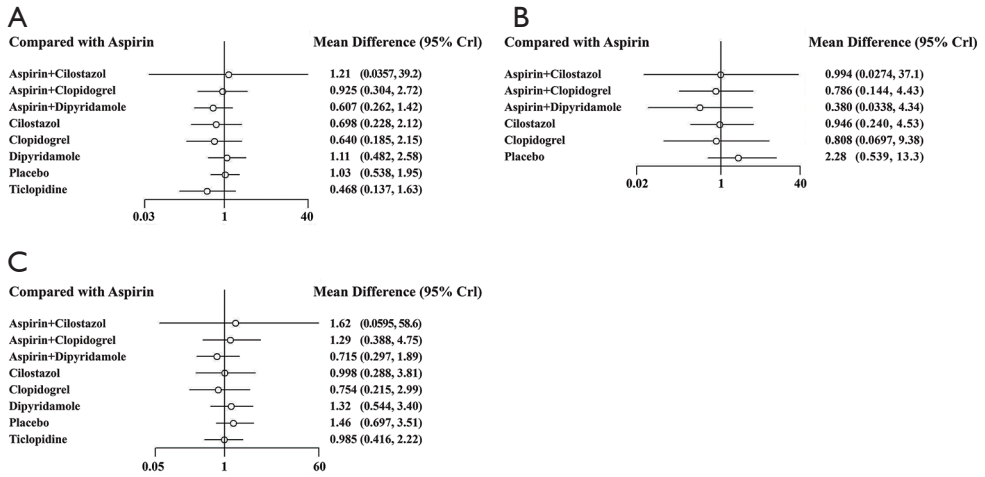

Figure S9 Forrest plots of the antiplatelet regimens compared with aspirin in the subgroup analysis for small vessel occlusion for (A) recurrent stroke, (B) recurrent ischemic stroke, and (C) composite outcomes.

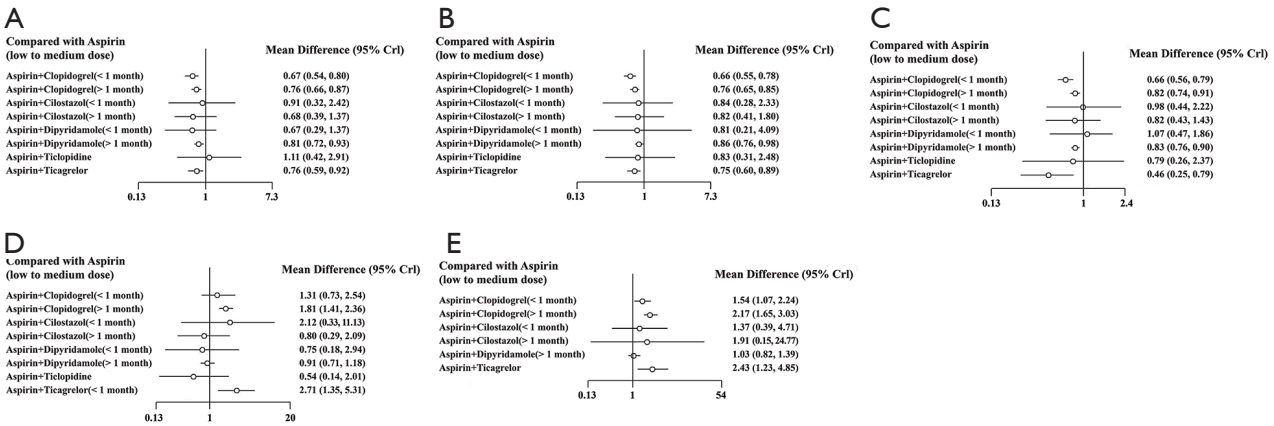

Figure S10 Forrest plots of the antiplatelet regimens compared with aspirin in the subgroup analysis for dual anti-platelet therapy, for (A) recurrent stroke, (B) recurrent ischemic stroke, (C) composite outcomes, (D) major bleeding events, and (E) all bleeding events.

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