Supplementary Material

Antiplatelet Therapy after Aneurysmal Subarachnoid Hemorrhage: A Meta-Analysis

Supplemental Methodology

Literature Search Details

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) Inception to Present - Search ran 04/15/2021

1. subarachnoid hemorrhage/
2. intracranial hemorrhage/ or cerebral hemorrhage/
3. Aneurysm, intracranial/
4. Rupture, spontaneous/
5. 3 and 4
6. Aneurysm, rupture/
7. exp brain/ or exp meninges/
8. 6 and 7
9. ((subarachnoid hemorrhage) adj6 (hemorrhage$ or bleed$).tw
10. Vasospasm, intracranial/ or ischemia, cerebral/
11. ((cerebral or intracranial) adj6 (vasospasm or spasm)).tw.
12. sah.tw.
13. 1 or 2 or 5 or 8 or 9 or 9 or 10 or 11 or 12
14. exp antiplatelet therapy/
15. (platelet aggregation inhibitors or anti-platelet).tw.
16. (aspirin$ or acetyl salicylic acid$ or salicylate$ or clopidogrel$ or ticlopidine$ or dipyridamole$ or Persantin$).tw.
17. ((glycoprotein iib$ or gp iib$ or glycoprotein iiia$ or gp iiia$)).tw.
18. (abciximab$ or tirofiban$ or eptifibatide$ or ReoPro$ or prasugrel$ or ticagrelor$).tw.
19. or/ 14-18
20. 13 and 19
21. limit 20 to human

The first search was conducted in Ovid MEDLINE. Subject headings and key words were adapted for the other databases.

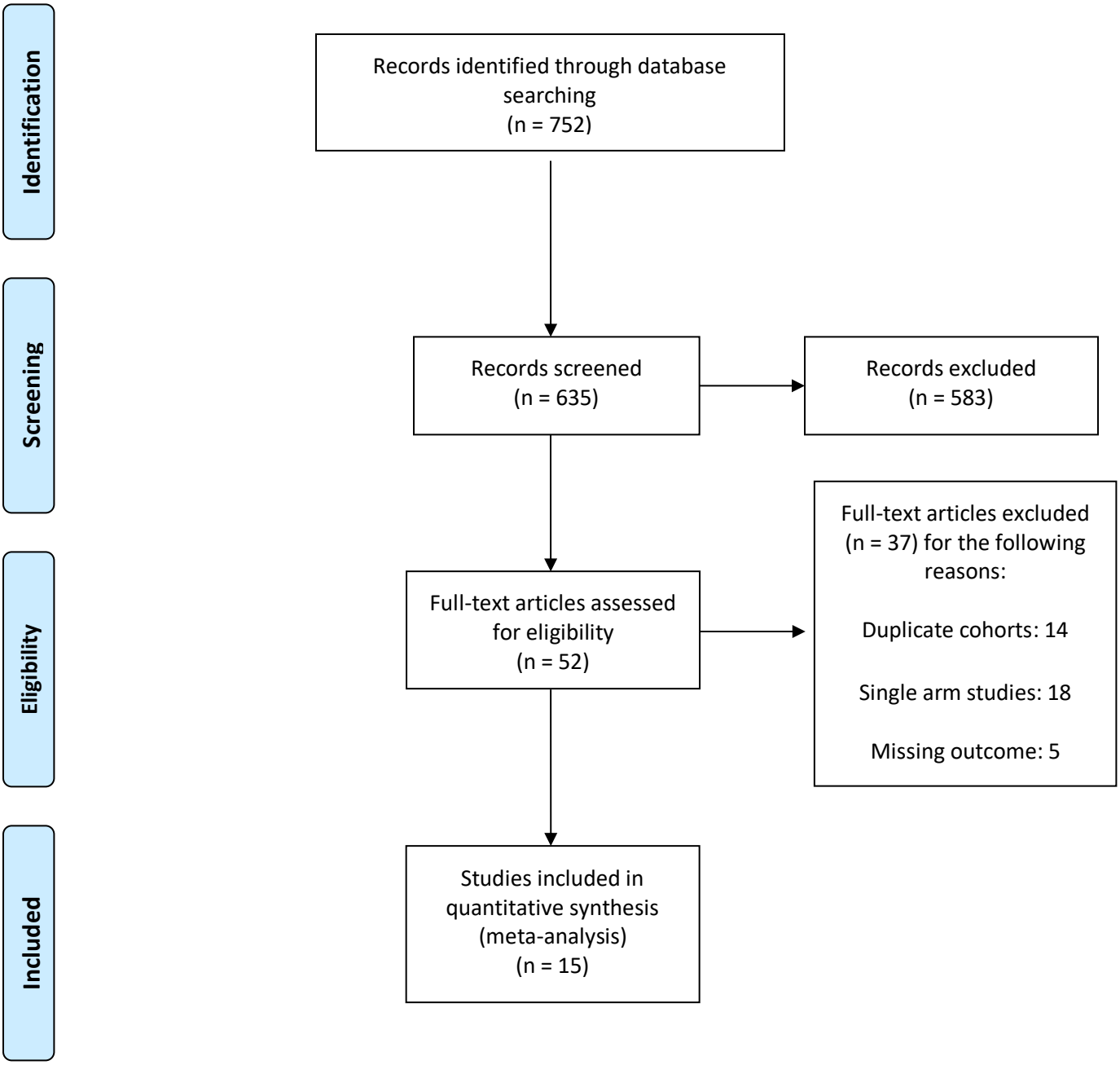
Supplemental Table I. Rates of Intracranial Hemorrhage in the Included Studies

Study (Year)	Antiplatelet Therapy		No Antiplatelet Therapy	
	ICH (%)	Total Population	ICH (%)	Total Population
Bruder (2018)[1]	6	129	1	129
Ditz (2021)[2]	5	85	5	75
Hop (2000)[3]	1	24	2	26
MASH (Combined 2009)[4]	2	87	1	74
Nagahama (2018)[5]	2	85	3	76
Oppong (2019)[6]	29	329	10	251
Shaw (1985)[7]	3	173	2	175
Sun (2020)[8]	5	65	7	101
Suzuki (1989)[9]	7	172	3	86
Tokiyoshi (1991)[10]	2	13	0	11
Total Events	**62**	**1162**	**34**	**1004**

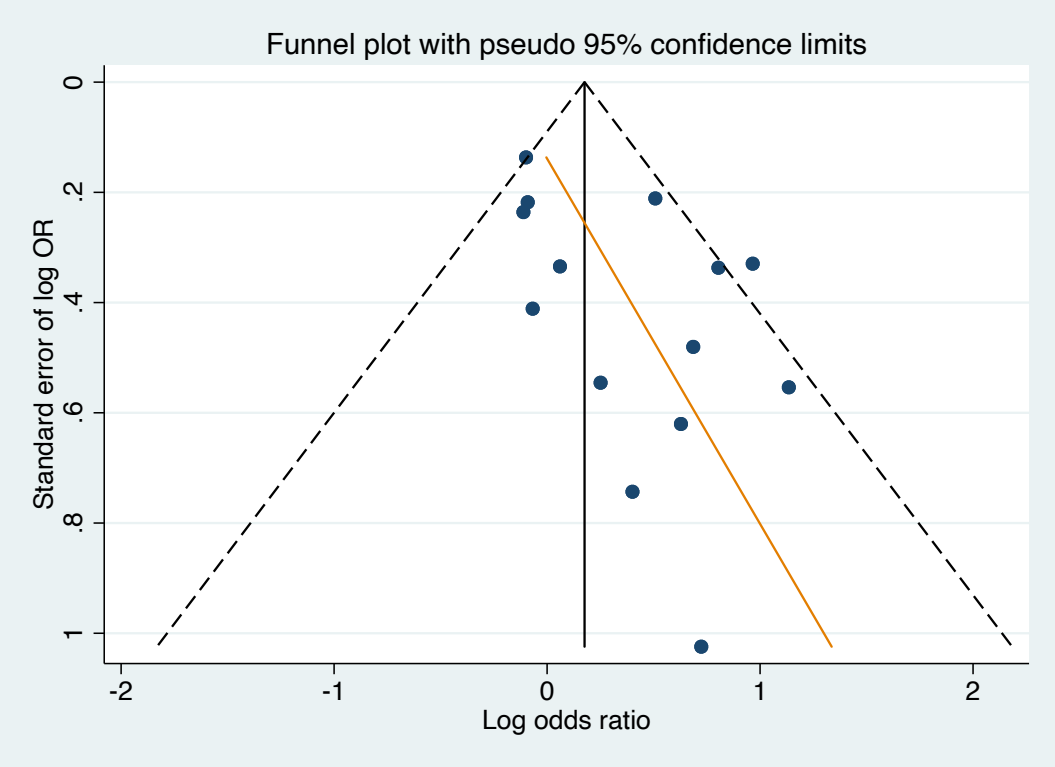
Abbreviations: ICH, intracranial hemorrhage.

Supplementary Table I: Results of Risk of Bias Questions to Assess the Quality of Included Studies								
Type of Bias	**Selection**				**Detection**		**Attrition**	**Confounding**
Question:	Was the study sample randomly selected?	Were the inclusion and exclusion criteria adequately described?	Was the primary objective to assess functional outcome?	Was the primary objective to assess DCI?	Was the study prospective in nature?	Were the investigators blinded to the APT status?	Were losses to follow up systematically reported?	Were the data adjusted for covariate risk?
Bruder (2018)[1]	-	+	+	+	+	-	-	+
Ditz (2021)[2]	-	+	+	+	-	-	-	+
Hop (2000)[3]	+	+	+	+	+	+	+	+
ISAT (2009)[11]	-	+	+	-	-	-	-	+
Juvela (1995)[12]	-	+	+	+	+	-	-	+
MASH Clipping (2009)[4]	+	+	+	+	+	+	+	+
MASH Coiling (2009))[4]	+	+	+	+	+	+	+	+
Nagahama (2018)[5]	-	+	+	+	-	-	-	+
Ono (1984)[13]	+	+	+	+	+	+	+	+
Oppong (2019)[6]	-	+	+	+	-	-	-	+
Shaw (1985)[7]	+	+	+	+	+	-	+	+
Sun (2020)[8]	-	+	+	+	-	-	-	-
Suzuki (1989)[9]	+	+	+	+	+	+	+	+
Tokiyoshi (1991)[10]	+	+	+	+	+	+	+	+
Toussaint (2004)[14]	-	+	+	+	-	-	-	+
Abbreviations: ICH, intracranial hemorrhage								

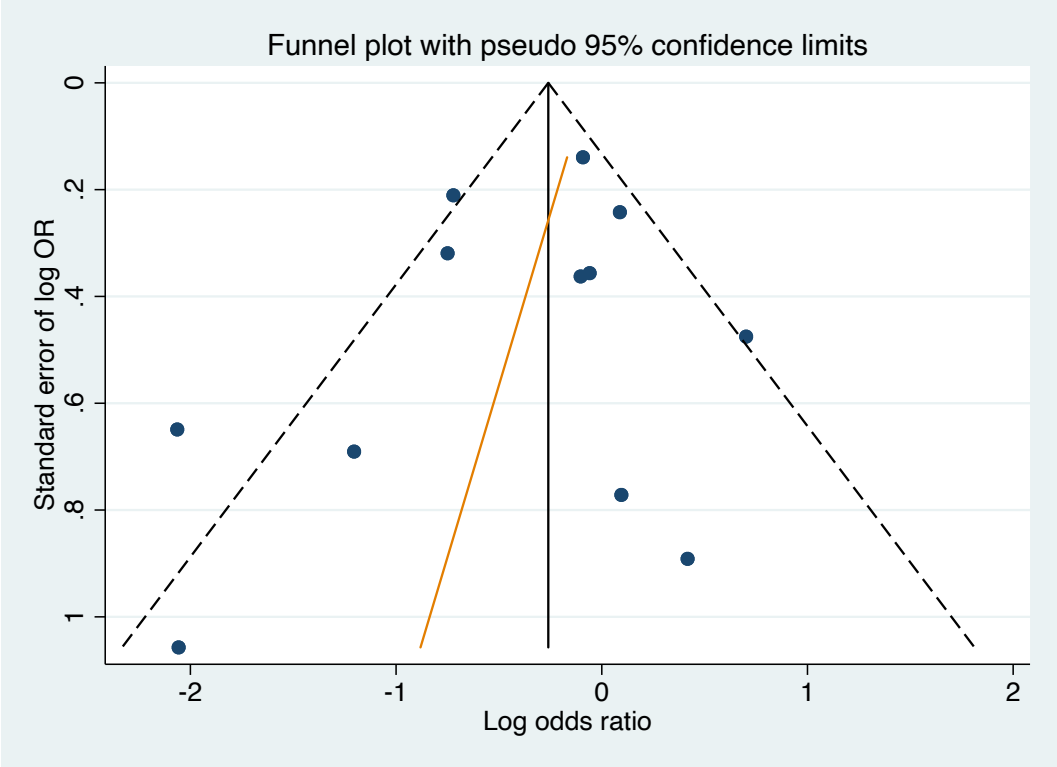
Supplemental Figure I: Study selection flow diagram



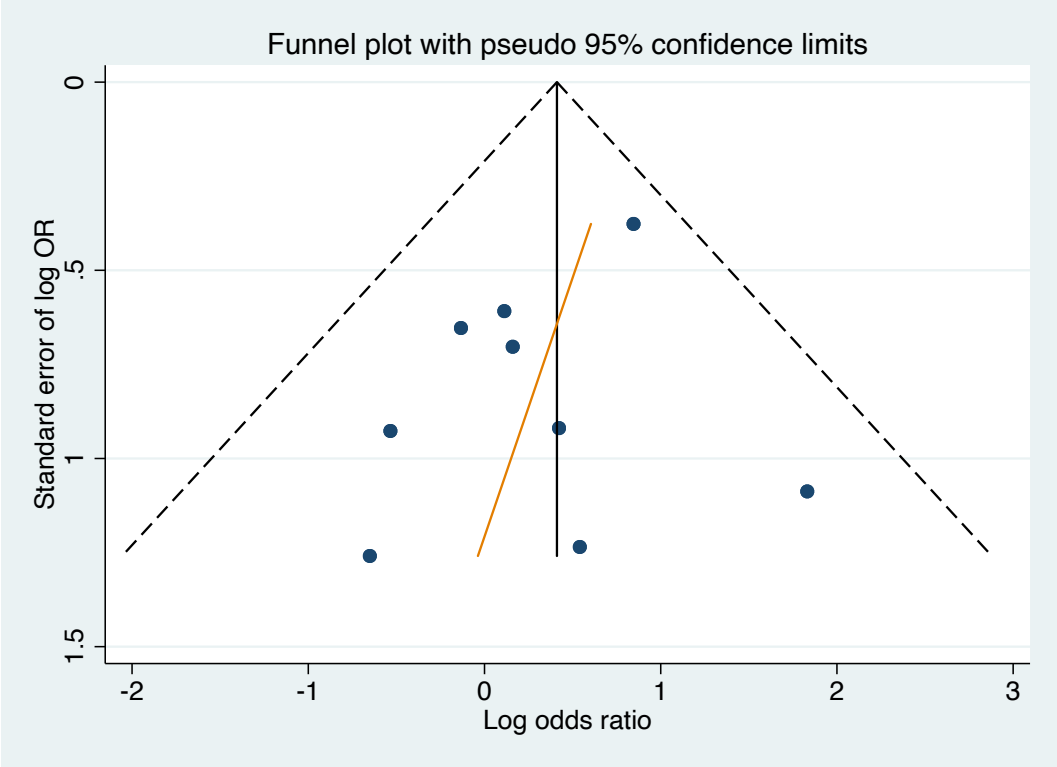
Supplemental Figure II: Funnel Plot to Evaluate Publication Bias of Functional Outcome after Subarachnoid Hemorrhage.



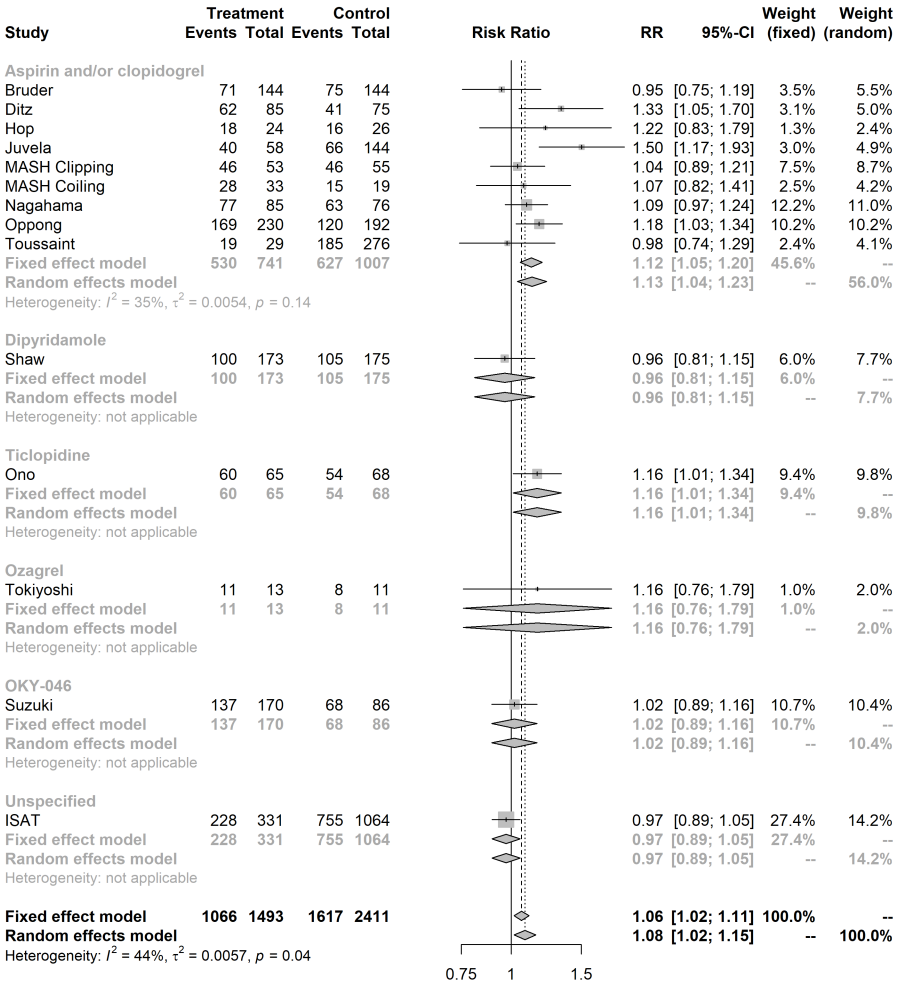
Supplemental Figure III: Funnel Plot to Evaluate Publication Bias of Delayed Cerebral Ischemia after Subarachnoid Hemorrhage.



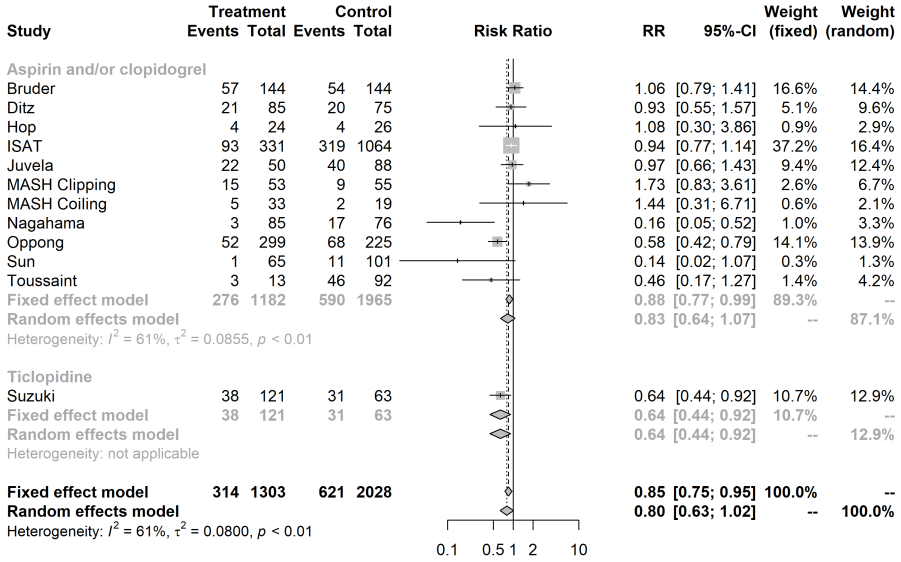
Supplemental Figure IV: Funnel Plot to Evaluate Publication Bias of Intracranial Hemorrhage after Subarachnoid Hemorrhage.



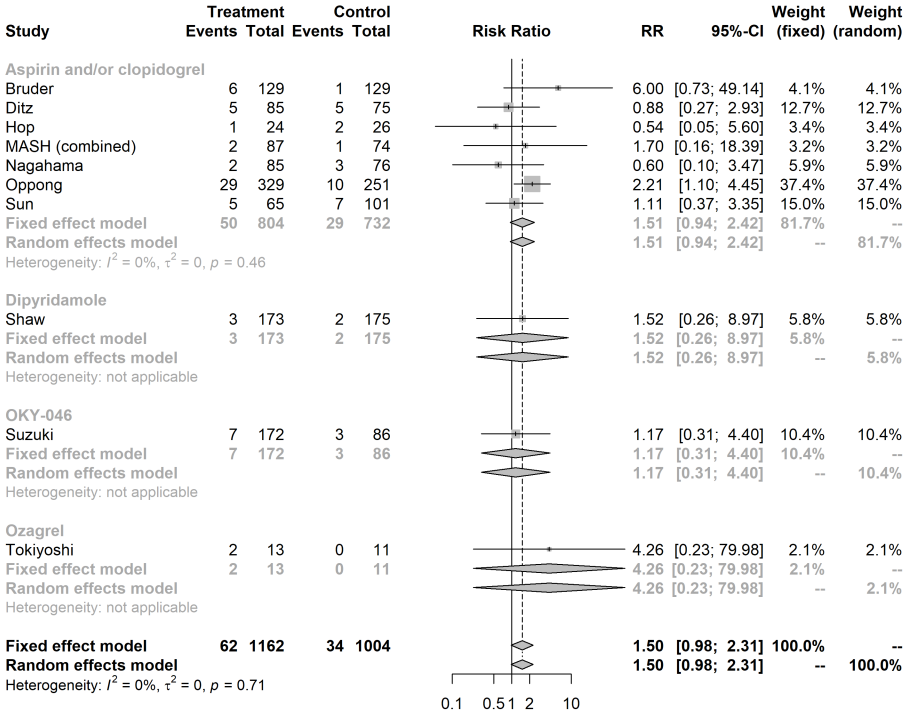
Supplemental Figure V. Forest plot of the association between antiplatelet therapy and good functional outcome after aneurysmal subarachnoid hemorrhage, stratified by type of antiplatelet medication.



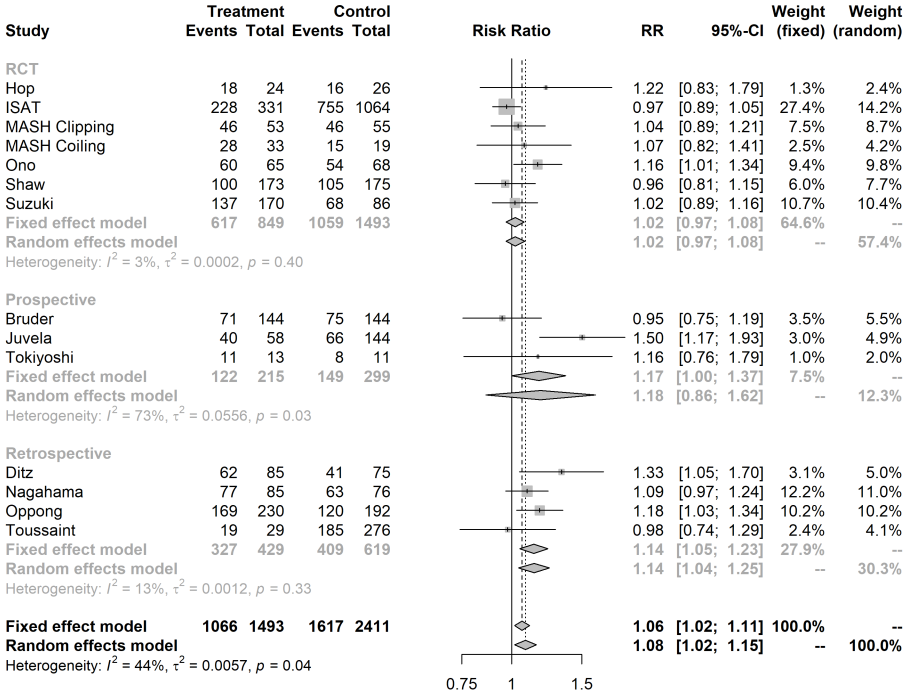
Supplemental Figure VI. Forest plot of the association between antiplatelet therapy and delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage, stratified by type of antiplatelet medication.



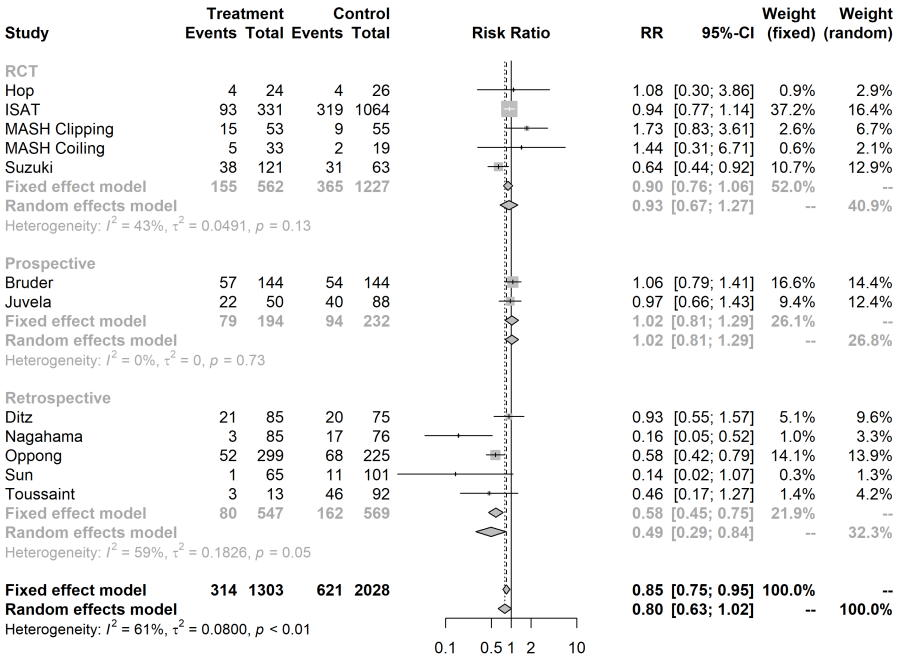
Supplemental Figure VII. Forest plot of the association between antiplatelet therapy and intracranial hemorrhage after aneurysmal subarachnoid hemorrhage, stratified by type of antiplatelet medication.



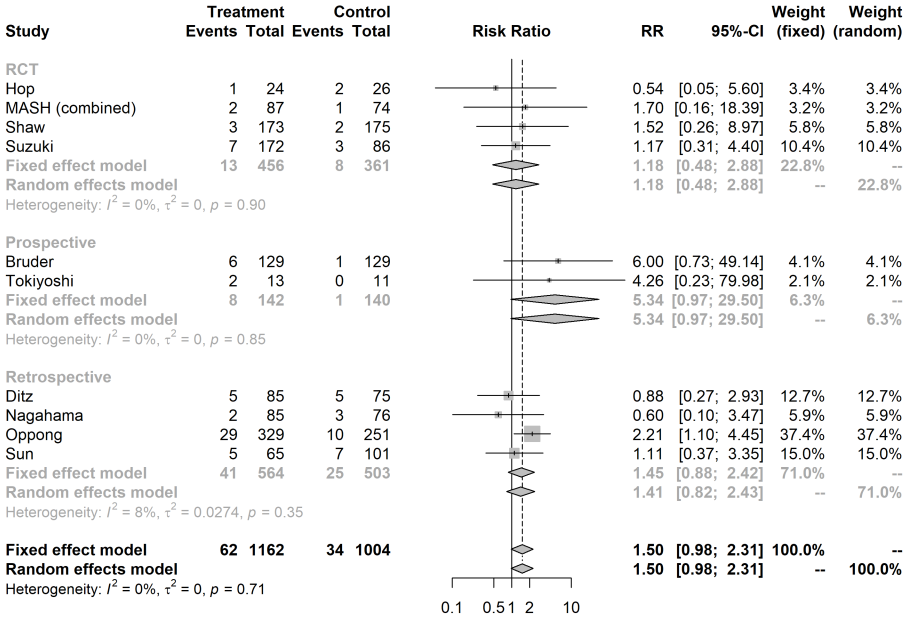
Supplemental Figure VIII. Forest plot of the association between antiplatelet therapy and functional outcome after aneurysmal subarachnoid hemorrhage, stratified by study type.



Supplemental Figure IX. Forest plot of the association between antiplatelet therapy and delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage, stratified by study type.



Supplemental Figure X. Forest plot of the association between antiplatelet therapy and intracranial hemorrhage after aneurysmal subarachnoid hemorrhage, stratified by study type.



References (Also included in the main manuscript)

1. Bruder M, Won SY, Wagner M, Brawanski N, Dinc N, Kashefiolasl S, et al. Continuous acetylsalicylic acid treatment does not influence bleeding pattern or outcome of aneurysmal subarachnoid hemorrhage: A matched-pair analysis. *World Neurosurg*. 2018;113:e122-e128
2. Ditz C, Machner B, Schacht H, Neumann A, Schramm P, Tronnier VM, et al. Effects of post-interventional antiplatelet therapy on angiographic vasospasm, delayed cerebral ischemia, and clinical outcome after aneurysmal subarachnoid hemorrhage: A single-center experience. *Neurosurg Rev*. 2021
3. Hop JW, Rinkel GJ, Algra A, Berkelbach van der Sprenkel JW, van Gijn J. Randomized pilot trial of postoperative aspirin in subarachnoid hemorrhage. *Neurology*. 2000;54:872-878
4. van den Bergh WM, Algra A, Rinkel GJ, Group MS. Magnesium and aspirin treatment in patients with subarachnoid haemorrhage. Comparison of effects after endovascular and neurosurgical aneurysm occlusion. *J Neurol*. 2009;256:213-216
5. Nagahama Y, Allan L, Nakagawa D, Zanaty M, Starke RM, Chalouhi N, et al. Dual antiplatelet therapy in aneurysmal subarachnoid hemorrhage: Association with reduced risk of clinical vasospasm and delayed cerebral ischemia. *J Neurosurg*. 2018;129:702-710
6. Darkwah Oppong M, Gembruch O, Pierscianek D, Kohrmann M, Kleinschnitz C, Deuschl C, et al. Post-treatment antiplatelet therapy reduces risk for delayed cerebral ischemia due to aneurysmal subarachnoid hemorrhage. *Neurosurgery*. 2019;85:827-833
7. Shaw MD, Foy PM, Conway M, Pickard JD, Maloney P, Spillane JA, et al. Dipyridamole and postoperative ischemic deficits in aneurysmal subarachnoid hemorrhage. *J Neurosurg*. 1985;63:699-703
8. Sun GU, Park E, Kim DW, Kang SD. Dual antiplatelet treatment associated with reduced risk of symptomatic vasospasm and delayed cerebral ischemia in aneurysmal subarachnoid hemorrhage. *J Cerebrovasc Endovasc Neurosurg*. 2020;22:134-140
9. Suzuki S, Iwabuchi T, Tanaka T, Kanayama S, Ottomo M, Hatanaka M, et al. Prevention of cerebral vasospasm with oky-046 an imidazole derivative and a thromboxane synthetase inhibitor. A preliminary co-operative clinical study. *Acta Neurochir (Wien)*. 1985;77:133-141
10. Tokiyoshi K, Ohnishi T, Nii Y. Efficacy and toxicity of thromboxane synthetase inhibitor for cerebral vasospasm after subarachnoid hemorrhage. *Surg Neurol*. 1991;36:112-118
11. van den Bergh WM, Kerr RS, Algra A, Rinkel GJ, Molyneux AJ, International Subarachnoid Aneurysm Trial Collaborative G. Effect of antiplatelet therapy for endovascular coiling in aneurysmal subarachnoid hemorrhage. *Stroke*. 2009;40:1969-1972
12. Juvela S. Aspirin and delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage. *J Neurosurg*. 1995;82:945-952
13. Dorhout Mees SM, van den Bergh WM, Algra A, Rinkel GJ. Antiplatelet therapy for aneurysmal subarachnoid haemorrhage. *Cochrane Database Syst Rev*. 2007:CD006184

14. Toussaint LG, 3rd, Friedman JA, Wijdicks EF, Piepgras DG, Pichelmann MA, McIver JI, et al. Influence of aspirin on outcome following aneurysmal subarachnoid hemorrhage. *J Neurosurg*. 2004;101:921-925