

Supplemental Material

Cilostazol for secondary prevention of stroke and cognitive decline: Systematic review and meta-analysis

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Search Strategy

- 1) brain ischemia/ or brain infarction/ or cerebral infarction/ or hypoxia-ischemia, brain/ or stroke.tw.
- 2) cerebral vascular attack/ or cerebrovascular attack/ or cerebral vascular accident/ or cerebrovascular accident/ or CVA.tw.
- 3) (lacuna\$ or small vessel\$ or small infarct\$ or microinfarct\$ or subcortical lesion\$ or subcortical infarct\$).tw.
- 4) leukoencephalopathy/ or Binswanger's disease.tw.
- 5) (white matter hyperintensity\$ or WMH).tw.
- 6) (small vessel disease or SVD).tw.
- 7) (white matter lesion\$ or WML).tw.
- 8) vascular dementia.tw
- 9) dementia.tw
- 10) Alzheimer's disease/ Alzheimer\$.tw
- 11) mild cognitive impairment / or MCI/ or cognitive impairment.tw
- 12) 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
- 13) cilostazol.tw.
- 14) pletal.tw.
- 15) 13 or 14
- 16) 12 AND 15
- 17) limit 16 to humans
- 18) remove duplicates from 17

Supplement Table I: Outcomes reported by each study

Study	Outcome								
	Stroke reoccurrence			MACE	Adverse symptoms ^{\$}	Functional outcome (mRS)	Death*	Cognition	Radiological findings
	All stroke	Ischaemic stroke	Haemorrhagic stroke						
ARCC ¹					✓				
CAIST ²	✓	✓		✓	✓	✓	✓		
CASID ³					✓			✓	
CASISP ⁴	✓	✓	✓		✓	✓#	✓		✓
CATHARSIS ⁵	✓	✓	✓	✓	✓	✓	✓		✓
CSPS ⁶⁻⁸	✓	✓	✓	✓	✓		✓		
CSPS2 ⁹⁻¹¹	✓	✓	✓	✓	✓		✓		
CSPS.com ^{12, 13}	✓	✓	✓	✓	✓	✓#	✓		
ECLIPse ^{14, 15}	✓	✓	✓		✓		✓		
Guo ¹⁶	✓	✓	✓		✓	✓#	✓		
Johkura ¹⁷	✓	✓	✓		✓		✓		
LACI-1 ¹⁸⁻²⁰	✓	✓	✓		✓		✓	✓	✓
Lee ²¹	✓	✓	✓		✓		✓		
Nakamura ²²	✓	✓	✓	✓	✓	✓	✓		
Ohnuki ²³	✓	✓	✓		✓		✓		
PICASSO ²⁴⁻²⁶	✓	✓	✓	✓	✓		✓		
Sakurai ²⁷	✓	✓					✓	✓	
Shimizu ²⁸	✓	✓	✓	✓	✓	✓	✓		
TOSS ²⁹	✓	✓	✓	✓			✓		
TOSS-2 ³⁰	✓	✓	✓	✓	✓		✓		✓
TOTAL	18	18	16	10			18	3	4

= not reported; \$ = see Supplementary Table 2 for details of adverse symptoms; mRS = modified Rankin Scale

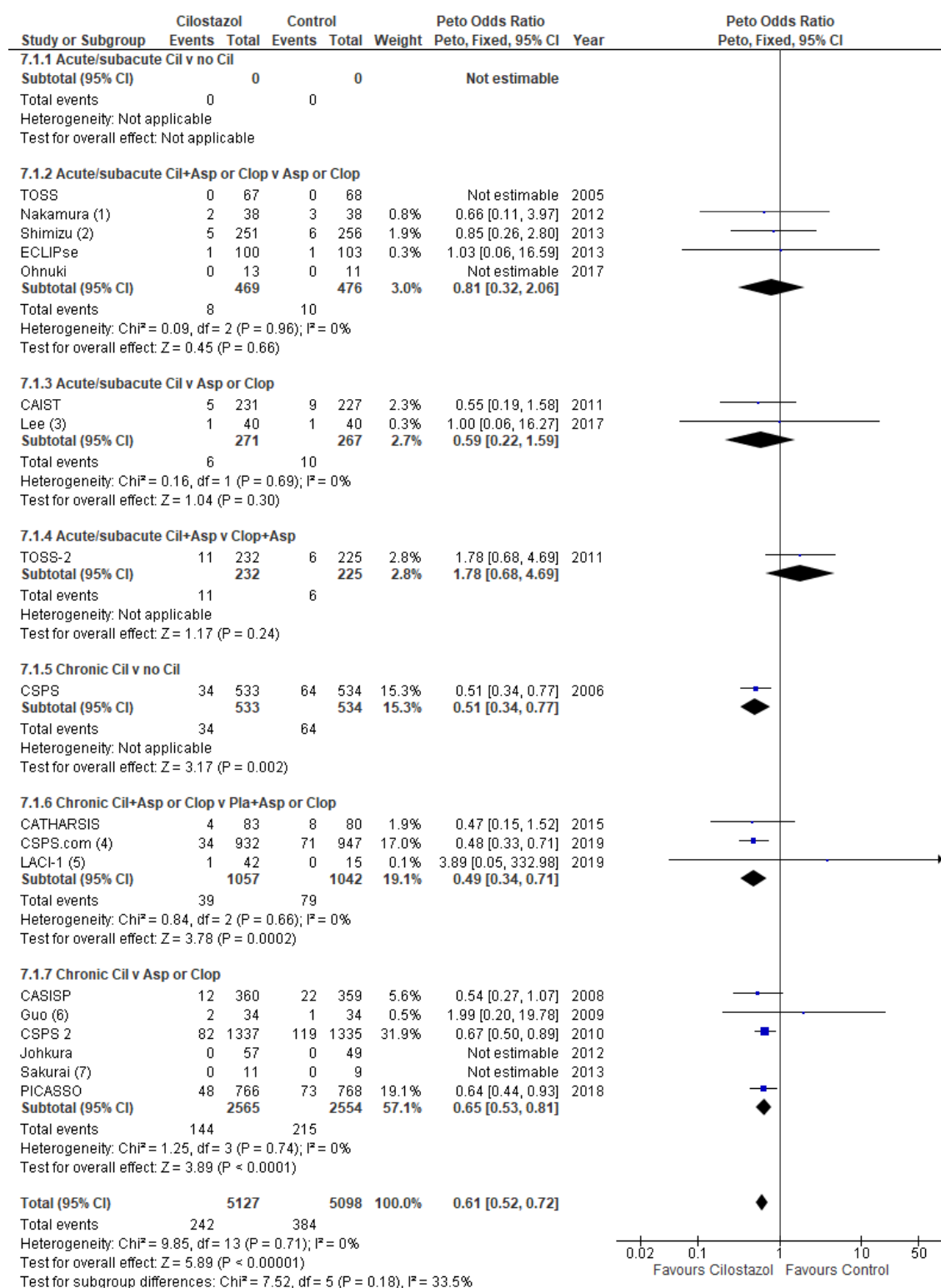
Supplement Table II: Adverse symptoms reported by each study (references are given in Supplement Table 1)

Study	Outcome							
	Adverse events							
	Headaches	Palpitations	Dizziness	Nausea	Constipation	Diarrhoea	Tachycardia	Bleeding
ARCC	✓							✓
CAIST	✓	✓	✓	✓	✓	✓		
CASID	✓		✓	✓		✓		
CASISP	✓	✓	✓				✓	✓
CATHARSIS								
CSPS	✓	✓	✓	✓				
CSPS2	✓	✓	✓		✓	✓	✓	✓
CSPS.com	✓	✓					✓	✓
ECLIPse	✓	✓	✓					
Guo	✓		✓				✓	✓
Johkura	✓						✓	✓
LACI-1	✓							✓
Lee	✓	✓	✓			✓		
Nakamura		✓						✓
Ohnuki								✓
PICASSO	✓	✓	✓	✓	✓	✓		✓
Sakurai								
Shimizu	✓	✓						✓
TOSS								
TOSS-2								✓
TOTAL	14	10	9	4	3	5	5	12

Supplement Table III. Study Quality by CONSORT criteria section. CONSORT consists of 37 items rating the presence (yes/no) of information included in each study. Where criterion is met, a score of one for the item was given (possible scores ranged from 0 to 37). Overall study quality ranged from 14-35 (mean=24, SD=5.88).

	Number of items	Min	Max	Median	IQR
Title & abstract	2	0	2	2	1-2
Introduction	2	2	2	2	2-2
Methods	17	4	16	9.5	5-11.25
Results	10	3	10	8	6.75-9
Discussion	3	1	3	3	2-3
Other information	3	0	3	1.5	0-2
TOTAL	37	14	35	23.5	20-27.5

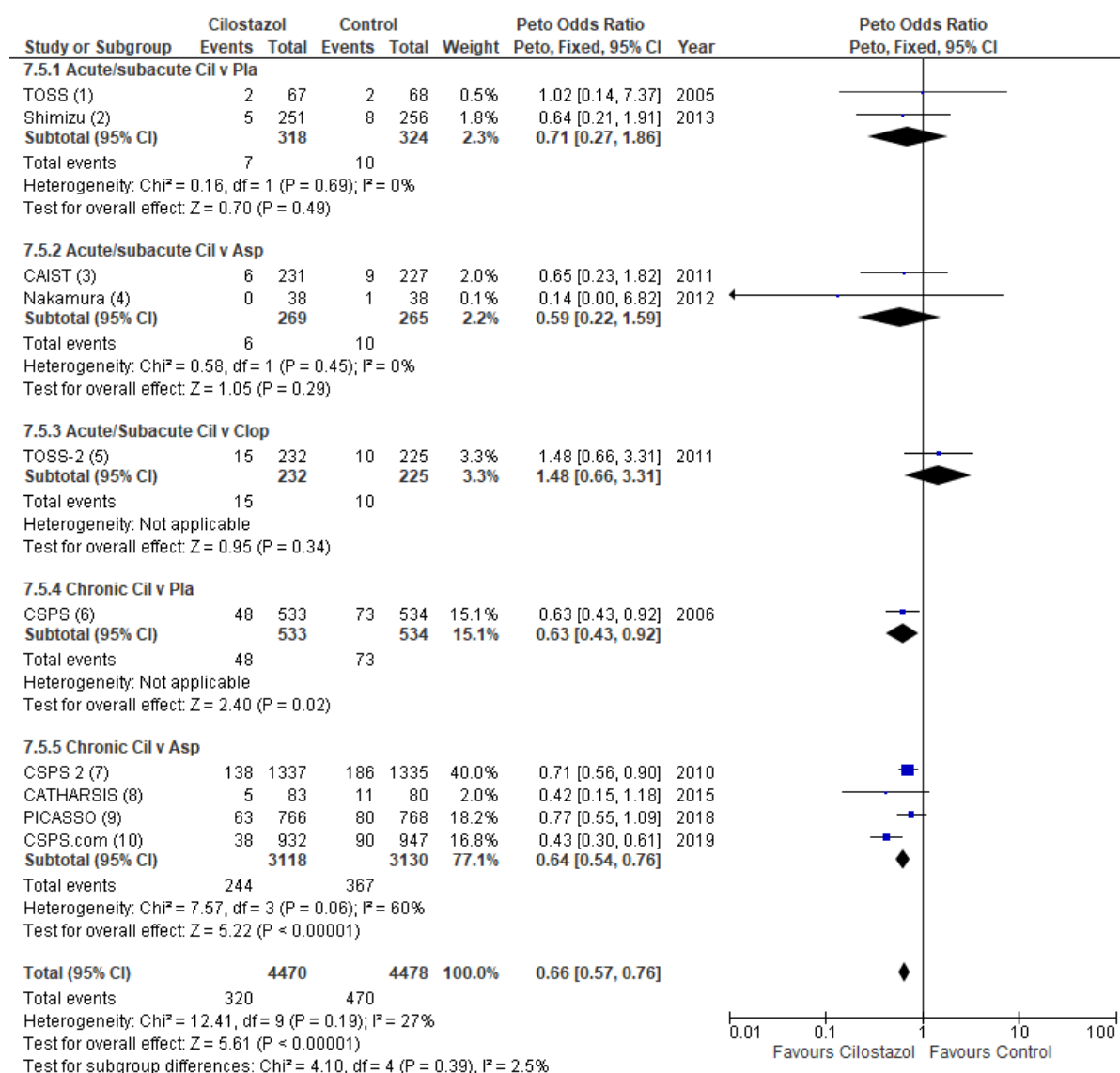
Supplement Figure I. Effect of cilostazol on recurrent stroke, all types.



Footnotes

- (1) Cilostazol group received aspirin AND Cilostazol.
- (2) Comparison group received placebo OR no treatment.
- (3) Comparison group received aspirin OR placebo.
- (4) Comparison group treated with aspirin OR Clopidogrel.
- (5) Comparison group received aspirin OR Clopidogrel.
- (6) Includes TIA.
- (7) Comparison group received aspirin AND Clopidogrel.

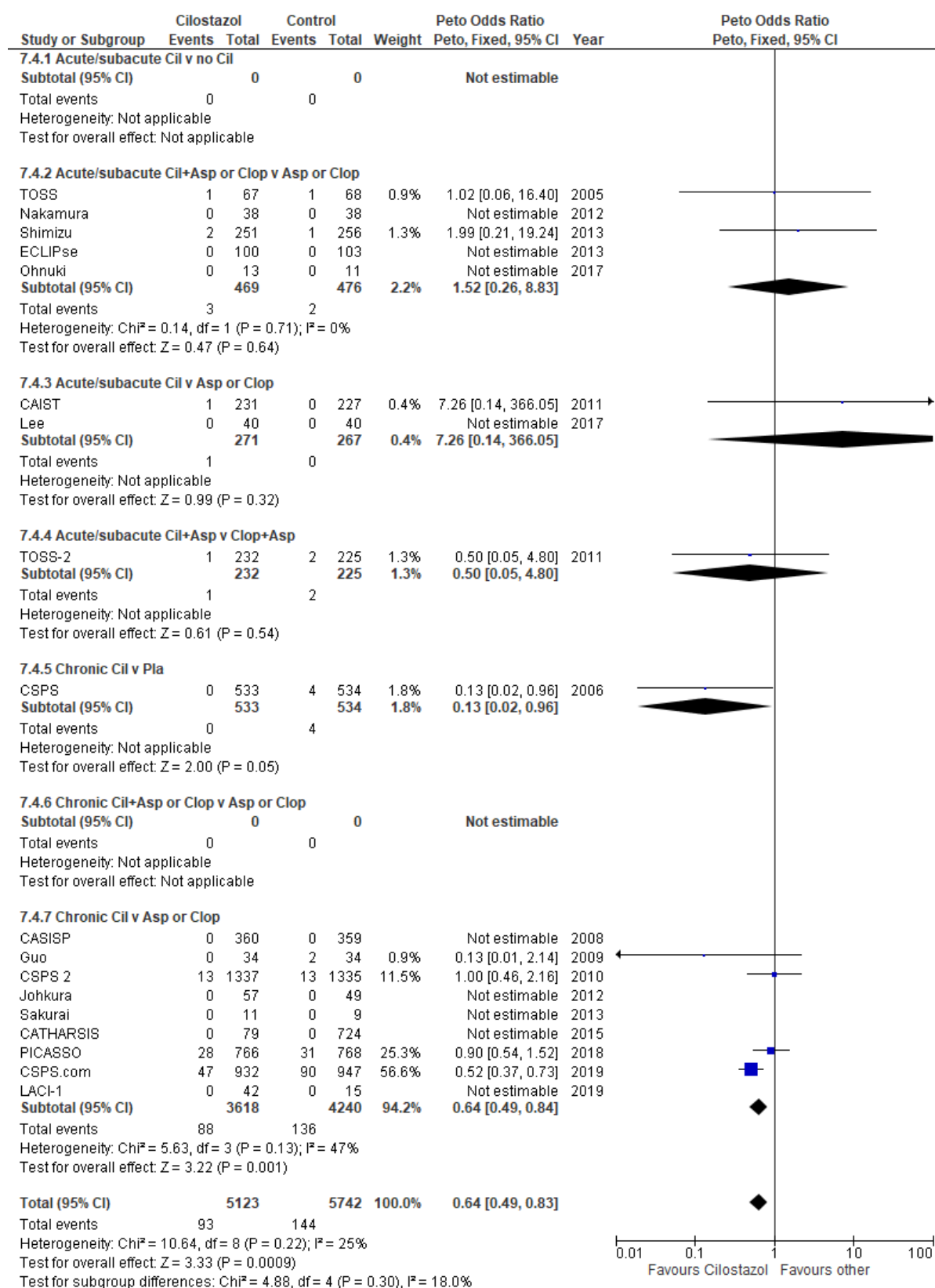
Supplement Figure II Effect of cilostazol on Major Adverse Cardiovascular Events (MACE)



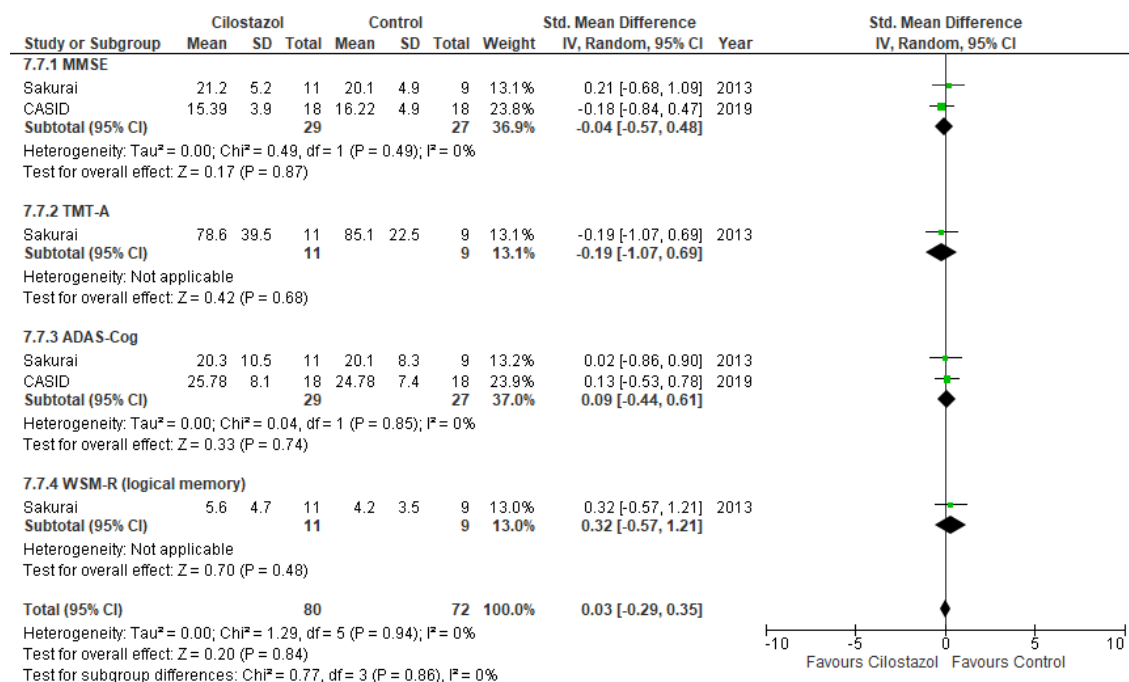
Footnotes

- (1) Includes acute coronary events.
- (2) Includes cerebral infarction, intracranial haemorrhage and congestive heart failure. Comparison group received placebo OR no treatment.
- (3) Includes non-fatal stroke, non-fatal MI, vascular death or other cardiovascular events requiring hospitalisation.
- (4) Cilostazol group received aspirin AND Cilostazol.
- (5) Includes non-fatal stroke, non-fatal MI and vascular death.
- (6) Includes cerebral infarction, TIA, MI, intracranial hemorrhage and other vascular events.
- (7) Includes cerebral infarction, ischaemic cerebrovascular disease and death from any cause.
- (8) Includes ischaemic stroke, cerebral hemorrhage and other vascular events.
- (9) Includes stroke, MI and vascular death.
- (10) Includes stroke, MI and vascular death. Comparison group treated with aspirin OR Clopidogrel.

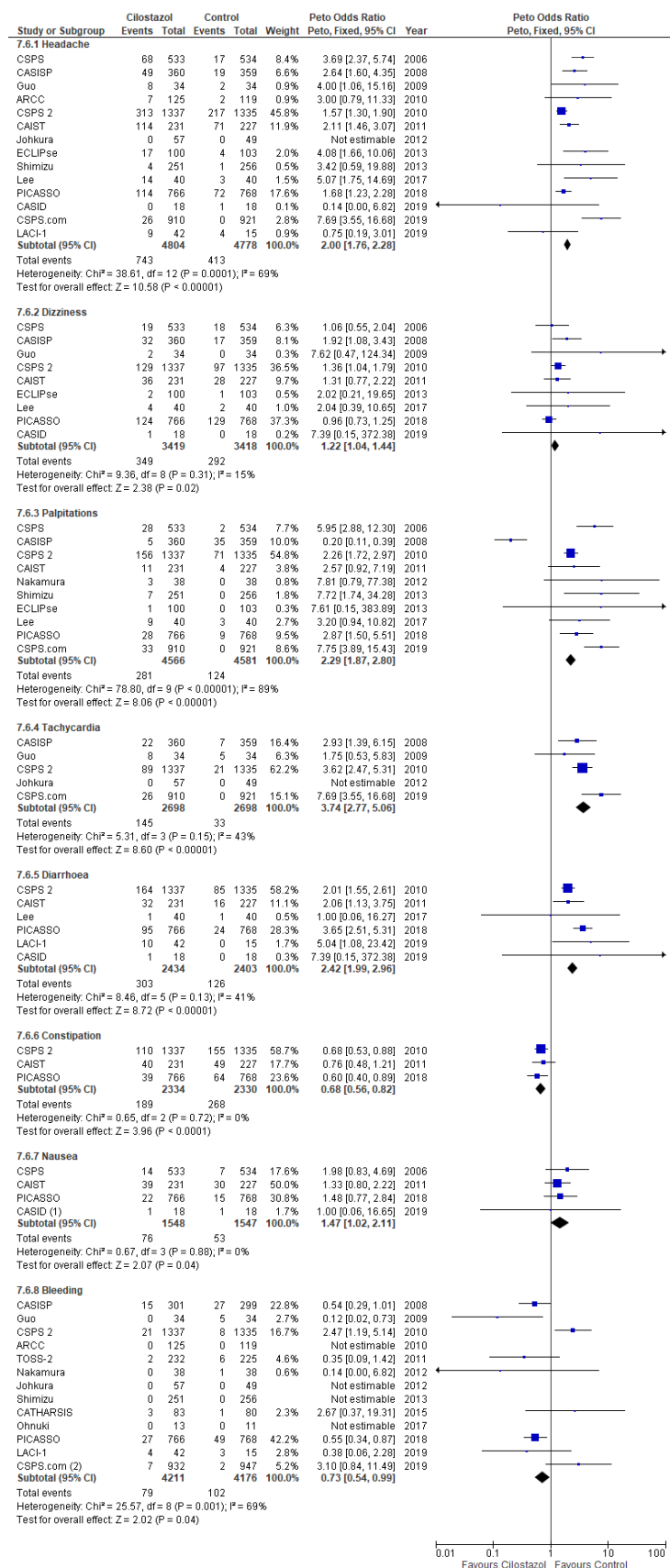
Supplement Figure III Effect of cilostazol on death from all causes by the end of follow-up



Supplement Figure IV Effect of cilostazol on cognition by the end of follow-up

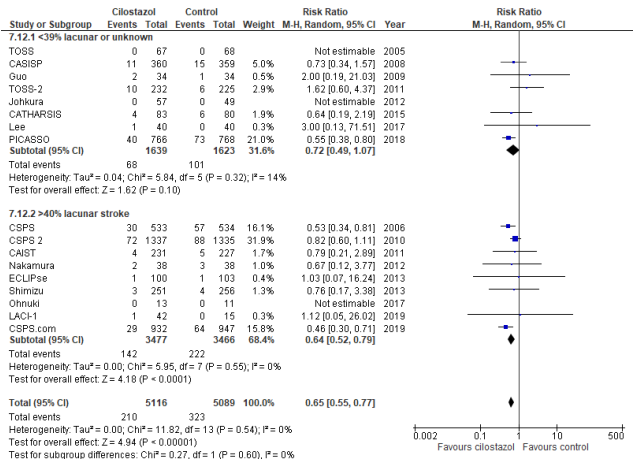


Supplement Figure V. Adverse symptoms including systemic bleeding

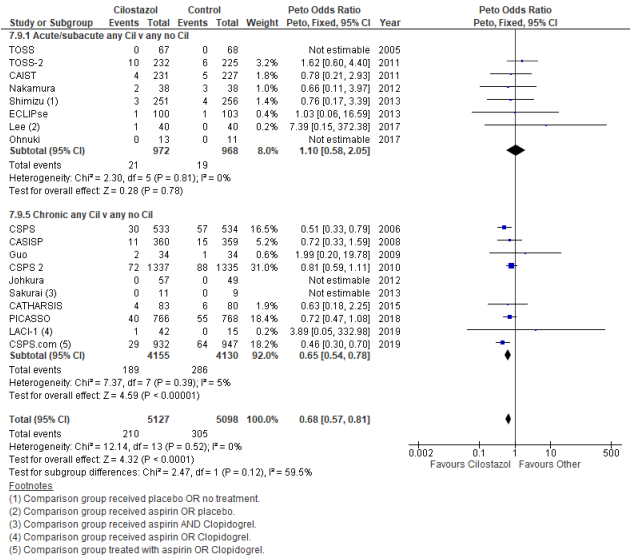


Supplement Figure VI. Sensitivity analyses

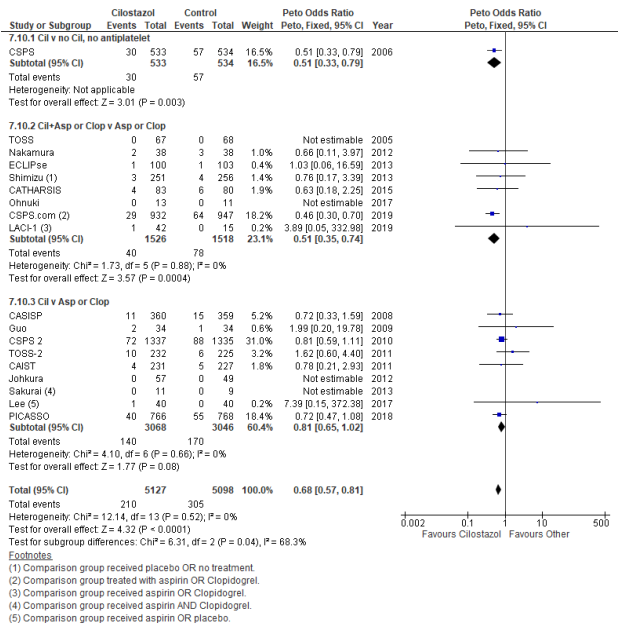
A. Proportion with lacunar stroke



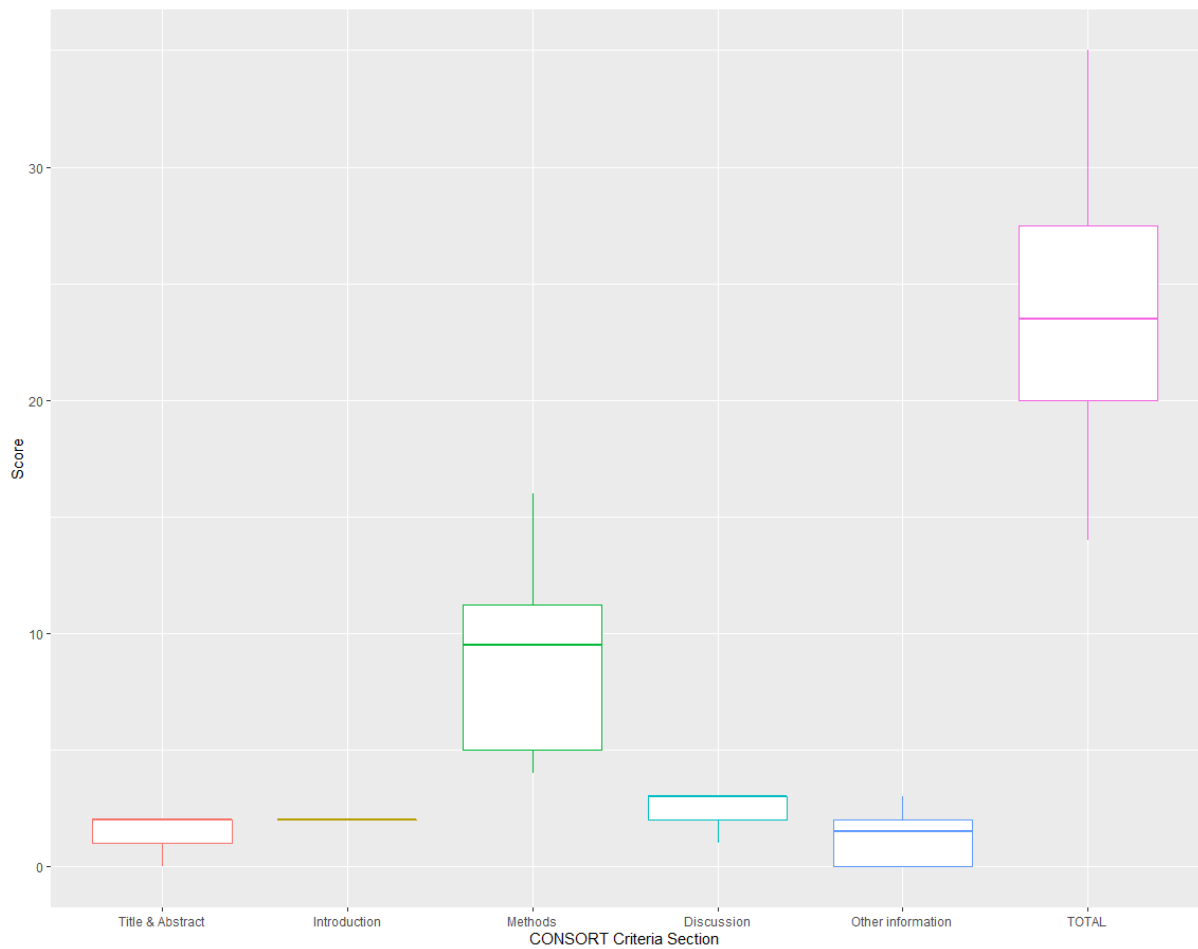
B Ischaemic stroke by time to treatment



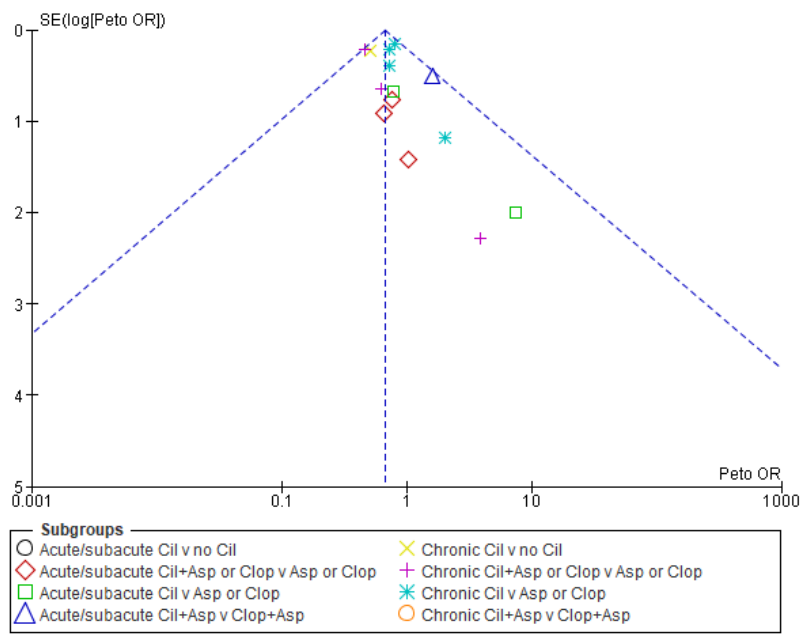
C Ischaemic stroke by additional antiplatelets



Supplement Figure VII. Chart of proportions of papers meeting CONSORT quality criteria



Supplement Figure VIII. Funnel plots



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