

Appendix 1: Search strategy (MEDLINE via OVID)

1. exp brain ischemia/ or exp stroke/ or exp brain infarction/
2. exp "Intracranial Embolism and Thrombosis"/
3. (isch?emi\$ adj6 (stroke\$ or apoplexy\$ or cerebral vasc\$ or cerebrovasc\$ or cva)).ti,ab.
4. ((brain or cerebr\$ or cerebell\$ or vertebrobasil\$ or hemispher\$ or intracran\$ or intracerebral or infratentorial or supratentorial or middle cerebr\$ or mca\$ or anterior circulation) adj5 (isch?emi\$ or infarct\$ or thrombo\$ or emboli\$ or occlu\$ or hypoxi\$ or accident?)).ti,ab.
5. stroke.ti,ab.
6. or/1-5
7. infusions, intra-arterial/ or injections, intra-arterial/
8. (Intra?arterial or intra arterial).tw.
9. (thrombol* or embolus or thrombus or endovascular device or thromboaspiration or embolectom* or thrombectom* or recanali?ation).ti,ab.
10. ((clot or thrombus or thrombi or embol\$) adj5 (aspirat\$ or remov\$ or retriev\$ or fragmentation or retract\$ or extract\$ or obliterated\$ or dispers\$)).ti,ab.
11. Thrombolytic therapy/ or exp plasminogen activators/ or "Intracranial Embolism and Thrombosis"/dt or thrombosis/dt
12. (tPA or t-PA or rtPA or rt-PA or plasminogen or alteplase or urokinase or reteplase or tenecteplase or streptokinase).ti,ab.
13. ("standard treatment?" or balloon*).ti,ab.
14. ((retrieval or extraction) adj5 device\$).ti,ab.
15. endovascular procedures/ or radiography, interventional/ or radiology, interventional/ or stents/ or catheters, indwelling/ or thrombosis/su or "Intracranial Embolism and Thrombosis"/su
16. or/7-15
17. (mRS or rankin).tw.
18. (NIHSS or "National Institutes of Health Stroke Scale?" or "NIH Stroke Scale?" or "NIH Stroke Score?").tw.
19. "Functional Independen* Measure*".tw.
20. "Oxford Handicap Scale?".tw.
21. ("Barthel Index" or "Barthel score?").tw.
22. (EuroQoL* or EQ-5D or EQ5D).tw.
23. HRQoL.tw.
24. "quality of life".tw.
25. ss-qol*.tw.
26. "stroke impact scale?".tw.

27. "Stroke-specific Quality of Life".tw.
28. "glasgow outcome scale?".tw.
29. Treatment outcome/ or "quality of life"/
30. glasgow outcome scale/
31. ("clinical effectiveness" or safety).tw.
32. "Outcome Assessment (Health Care)"/
33. or/17-32
34. 6 and 16 and 33
35. ("clinical trial" or "clinical trial, phase i" or "clinical trial, phase ii" or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or "multicenter study" or "randomized controlled trial").pt. or double-blind method/ or clinical trials as topic/ or clinical trials, phase i as topic/ or clinical trials, phase ii as topic/ or clinical trials, phase iii as topic/ or clinical trials, phase iv as topic/ or controlled clinical trials as topic/ or randomized controlled trials as topic/ or early termination of clinical trials as topic/ or multicenter studies as topic/ or ((randomi?ed adj7 trial*) or (controlled adj3 trial*) or (clinical adj2 trial*) or ((single or doubl* or tripl* or treb*) and (blind* or mask*))).ti,ab.
36. cohort studies/ or longitudinal studies/ or follow-up studies/ or prospective studies/ or retrospective studies/ or cohort.ti,ab. or longitudinal.ti,ab. or prospective.ti,ab. or retrospective.ti,ab.
37. or/35-36
38. 34 and 37
39. (cardiac or coronary or myocardi* or aorta or aortic).ti,ab.
40. 38 not 39
41. limit 40 to humans

Appendix 2: Study selection form

Study ID:

1. STUDY DESIGN	Circle one response
RCT, non-randomised trial, controlled before-and-after study or cohort study (with prospective assessment) <ul style="list-style-type: none"> • Exclude if single center study, case control study, cross-sectional study or case series 	Yes / No / Unsure
2. PARTICIPANTS	
Adult patients (aged ≥ 18) presenting with acute ischaemic stroke	Yes / No / Unsure
3. INTERVENTION	
At least 10 patients received intra-arterial mechanical thrombectomy (MT) with or without adjuvant IV rt-PA or intra-arterial (IA) thrombolysis with rt-PA.	Yes / No / Unsure
4. OUTCOMES:	
Includes an assessment of change in one of the following outcomes at ≥ 90 days follow-up? <ul style="list-style-type: none"> • modified Rankin Scale (mRS) • Oxford Handicap Scale (OHS) • Barthel Index • National Institute of Health Stroke Scale (NIHSS) 	Yes / No / Unsure
Comments:	

Yes for 1, 2, 3 AND 4 → INCLUDE

No for 1, 2, 3 OR 4 → EXCLUDE (note reason[s] in comments box)

Appendix 3: Data extraction form

BASIC INFORMATION

Study id: enter text.
Name (1st reviewer): enter text.
Name (checker): enter text.
Author details: enter text.
Title: enter text.
Type of publication: enter text.

STUDY CHARACTERISTICS

Study design enter text.
Inclusion and exclusion criteria enter text.
Recruitment procedures enter text.
Number of Centres enter text.

Interventions

Outline details of control enter text.
Outline details of intervention Select enter text.

CONTROL GROUP (BASELINE) (BASELINE)

Age: Choose an item.
n (CI or IQ range) enter text.
Gender: Choose an item.
n (%) enter text.

INTERVENTION GROUP

Age: Choose an item.
n (CI or IQ range) enter text.
Gender: Choose an item.
n (%) enter text.

CONTROL GROUP CLINICAL CHARACTERISTICS

Previous stroke n (%) Click here to enter text.
Previous TIA n (%) Click here to enter text.
Previous ICH n (%) Click here to enter text.
Hypertension n (%) Click here to enter text.
Diabetes n (%) Click here to enter text.
Atrial fibrillation n (%) Click here to enter text.
NIHSS score select n (SD, CI or IQ range) Click here
Systolic blood pressure select n (SD, CI or IQ range) Click here
Glucose level on arrival (mmol) select n (SD, CI or IQ range) Click here
ASPECTS on CT select n (SD, CI or IQ range) Click here
Baseline functioning select no./total no (%) Click here
Internal carotid artery no. (%) Click here to enter text.
M1 middle cerebral artery no. (%) Click here to enter text.
M2 middle cerebral artery no. (%) Click here to enter text.

For multi-arm trials select intervention being reported in this form here: Select

INTERVENTION GROUP CLINICAL CHARACTERISTICS

Previous stroke n (%) Click here to enter text.
Previous TIA n (%) Click here to enter text.
Previous ICH n (%) Click here to enter text.
Hypertension n (%) Click here to enter text.
Diabetes n (%) Click here to enter text.
Atrial fibrillation n (%) Click here to enter text.
NIHSS score select n (SD, CI or IQ range) Click here

Systolic blood pressure	select	n (SD, CI or IQ range)	Click here
Glucose level on arrival (mmol)	select	n (SD, CI or IQ range)	Click here
ASPECTS on CT	select	n (SD, CI or IQ range)	Click here
Baseline functioning	select	no./total no (%)	Click here
Internal carotid artery no. (%)	Click here		
M1 middle cerebral artery no. (%)	Click here		
M2 middle cerebral artery no. (%)	Click here		

CONTROL GROUP (process times)

Stroke onset to randomisation	select	minutes (SD or CI or IQ range)	Click here
Stroke onset to CT	select	minutes (SD or CI or IQ range)	Click here
Stroke onset to stroke onset to start of intravenous thrombolysis (alteplase)	select	minutes (SD or CI or IQ range)	Click here
Stroke onset to randomisation	select	minutes (SD or CI or IQ range)	Click here

INTERVENTION GROUP (process times)

Stroke onset to randomisation	select	minutes (SD or CI or IQ range)	Click here
Stroke onset to CT	select	minutes (SD or CI or IQ range)	Click here
Stroke onset to start of intravenous thrombolysis (alteplase)	select	minutes (SD or CI or IQ range)	Click here
CT to groin puncture	select	minutes (SD or CI or IQ range)	Click here
CT to first reperfusion	select	minutes (SD or CI or IQ range)	Click here
Stroke onset to first reperfusion	select	minutes (SD or CI or IQ range)	Click here
Time to best recanalization achieved	select	minutes (SD or CI or IQ range)	Click here
Stroke onset to first reperfusion	select	minutes (SD or CI or IQ range)	Click here
Treatment with IV thrombolysis no. (%)	Click here.		

INTERVENTION PROCEDURAL INFORMATION

Targeted occluded vessel(s)	Click here to enter text.		
Tandem extracranial vessel occlusion	Click here to enter text.		
Classification of thrombectomy (if possible)	<input type="checkbox"/>	Image guided	
	<input type="checkbox"/>	Adjunctive	
	<input type="checkbox"/>	Failed IVT	
	<input type="checkbox"/>	Primary	
Thrombectomy technology used	<input type="checkbox"/>	First Generation	
	<input type="checkbox"/>	Second Generation Retrieval	
	<input type="checkbox"/>	Second Generation Aspiration	
Adjunctive IA lytic	Select		
Were operators experienced neurointerventionists?	Select		
Procedures performed in centres in specialist neuroangiographic facilities?	Select		
Rate of non-intervention in intervention allocated arm	enter text.		
Crossover rates allocated to control received IAT	enter text.		
Crossover rates allocated to IAT, but not received	enter text.		

Appendix 4. Discrepancies in primary study data between the current and previous meta-analyses

The HERMES collaboration meta-analysis of five trials published in 2015, MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, and EXTEND-IA reported for reduced disability an adjusted OR = 2.49 [1.76 to 3.53]. This was based on data from 1,287 patients (634 thrombectomy and 653 standard care), across the 5 trials. Comparative summed data in our meta-analysis were 1,278 patients (633 thrombectomy and 645 standard care; a difference of -1 and +8 totals respectively).

Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, Dávalos A, Majoie CB, van der Lugt A, de Miquel MA, Donnan GA, Roos YB, Bonafe A, Jahan R, Diener HC, van den Berg LA, Levy EI, Berkhemer OA, Pereira VM, Rempel J, Millán M, Davis SM, Roy D, Thornton J, Román LS, Ribó M, Beumer D, Stouch B, Brown S, Campbell BC, van Oostenbrugge RJ, Saver JL, Hill MD, Jovin TG; HERMES collaborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet* 2016;387(10029):1723-31.

Differences in primary study data between our meta-analysis and those from two others are highlighted in the tables below:

Hussain et al 2016	Thrombectomy		Difference in data	Standard Care		Difference in data
	Events	Total		Events	Total	
MR CLEAN	77	233	+1 event	51	267	=
ESCAPE	89	164	+2 events	43	147	=
EXTEND-IA	25	35	=	14	35	=
SWIFT PRIME	59	98	=	33	93	=
REVASCAT	44	103	-1 event	29	103	=
THERAPY	21	55	-2 events +5 total	16	53	+2 events +7 total

Hussain M, Moussavi M, Korya D, Mehta S, Brar J, Chahal H, Qureshi I, Mehta T, Ahmad J, Zaidat OO, Kirmani JF. Systematic Review and Pooled Analyses of Recent Neurointerventional Randomized Controlled Trials: Setting a New Standard of Care for Acute Ischemic Stroke Treatment after 20 Years. *Intervent Neurol* 2016;5:39-50.

Phan et al 2016	Thrombectomy		Difference in data	Standard Care		Difference in data
	Events	Total		Events	Total	
MR CLEAN	76	233		51	267	
ESCAPE	87	165	+1 total	43	150	+3 total
EXTEND-IA	25	35		14	35	
SWIFT PRIME	59	98		33	98	+5 total
REVASCAT	45	103		29	103	

Phan K, Zhao DF, Phan S, Huo YR, Mobbs RJ, Rao PJ, Mortimer AM. Endovascular therapy including thrombectomy for acute ischemic stroke: A systematic review and meta-analysis with trial sequential analysis. *J Clin Neurosci* 2016; 29:38-45.

Appendix 5: Trial Sequential Analysis Graphs

Figure S1. Functional independence at 90 days

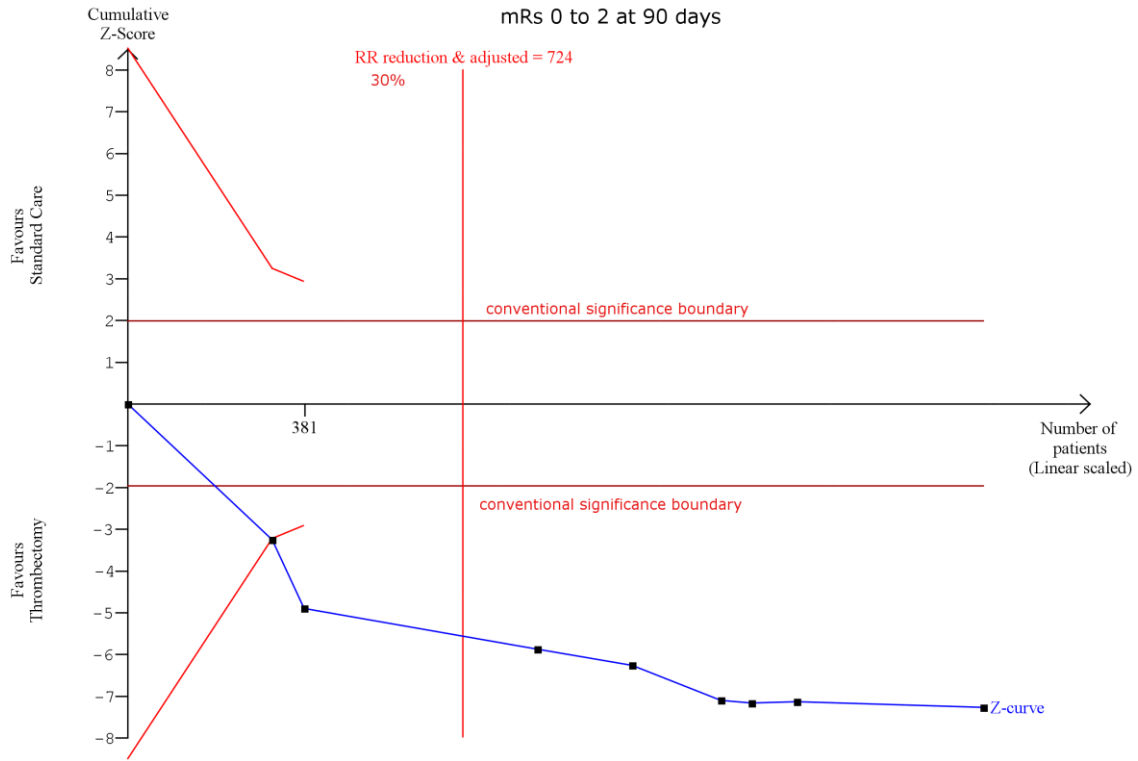


Figure S2. Mortality at 90 days

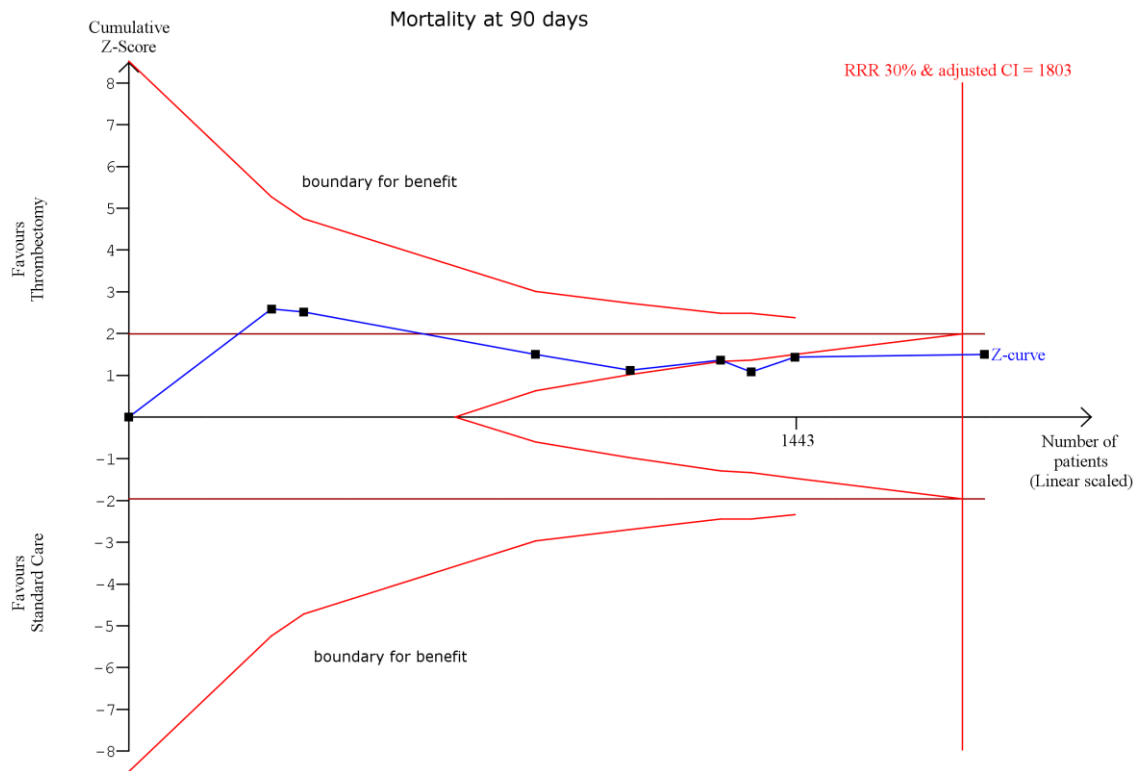


Figure S3. SICH with 7 days

