eTables:

eTable 1. Table of excluded studies with reasons for exclusion.

eTable 2. Pooled rates with corresponding 95%CI (confidence intervals) of safety and efficacy outcomes among acute ischemic stroke patients treated with endovascular therapy (EVT) and best medical treatment (BMT) compared to BMT alone.

eReferences used in the Supplement.

eFigures:

eFigures 1-23

Palaiodimou L, *et al. J Neurol Neurosurg Psychiatry* 2023; 94:781–785. doi: 10.1136/jnnp-2023-331513

eTable 1. Table of excluded studies with reasons for exclusion.

Study Name	**Reason(s) for Exclusion**
Roman et al.[1]	Individual patient data meta-analysis
Hill et al.[2]	Subgroup analysis of Interventional Management of Stroke (IMS)-III Trial, with ASPECTS-range of 0-4

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eTable 2. Pooled rates, risk differences with corresponding 95%CI (confidence intervals), and numbers needed to treat (or harm) of safety and efficacy outcomes among acute ischemic stroke patients treated with endovascular therapy (EVT) and best medical treatment (BMT) compared to BMT alone.

The corresponding pooled proportions with 95% confidence intervals (95%CI) were calculated after the implementation of the variance-stabilizing double arcsine transformation, as previously described.[3]

Outcomes	**mRS 0-3***	**mRS 0-2***	**mRS 0-1***	**sICH**	**Any ICH**	**Mortality***
EVT+ BMT (95%CI)	37 (29-45)	20 (13-28)	8 (5-12)	4 (1-9)	42 (11-78)	28 (19-38)
BMT (95%CI)	21 (13-30)	9 (7-11)	5 (1-10)	2 (1-4)	19 (5-40)	29 (20-40)
RD%(95%CI)	15 (10-20)	11 (5-17)	3 (1-6)	2 (-1 – 4)	23 (3 – 44)	-1 (-5– 4)
NNT	7	9	33	50 (NNH)	4 (NNH)	100

*At three months; mRS: modified Rankin Scale; sICH: symptomatic intracranial hemorrhage; ICH: intracranial hemorrhage; RD: risk difference; NNT: number needed to treat; NNH: number needed to harm.

Palaiodimou L, *et al. J Neurol Neurosurg Psychiatry* 2023; 94:781–785. doi: 10.1136/jnnp-2023-331513

eReferences used in the Supplement.

1. Román LS, Menon BK, Blasco J, et al. Imaging features and safety and efficacy of endovascular stroke treatment: a meta-analysis of individual patient-level data. *Lancet Neurol.* 2018;17(10):895-904.
2. Hill MD, Demchuk AM, Goyal M, et al. Alberta Stroke Program early computed tomography score to select patients for endovascular treatment: Interventional Management of Stroke (IMS)-III Trial. *Stroke.* 2014;45(2):444-449.
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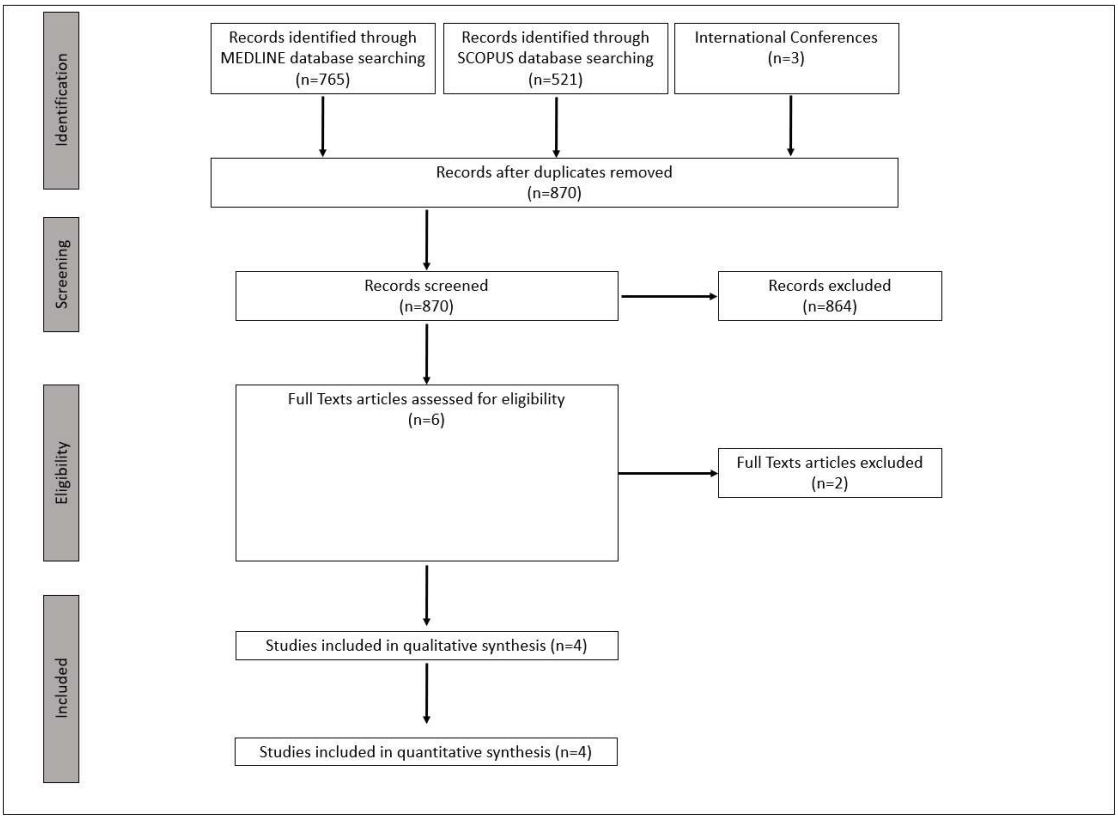
8. Huo X, Ma G, Tong X, et al. Trial of Endovascular Therapy for Acute Ischemic Stroke with Large Infarct. *N Engl J Med.* 2023;388(14):1272-1283.
9. Sarraj A, Hassan AE, Abraham MG, et al. Trial of Endovascular Thrombectomy for Large Ischemic Strokes. *N Engl J Med.* 2023;388(14):1259-1271.
10. Yoshimura S, Sakai N, Yamagami H, et al. Endovascular Therapy for Acute Stroke with a Large Ischemic Region. *N Engl J Med.* 2022;386(14):1303-1313.
11. von Kummer R, Broderick JP, Campbell BC, et al. *The Heidelberg Bleeding Classification: Classification of Bleeding Events After Ischemic Stroke and Reperfusion Therapy.* Stroke. 2015 Oct;46(10):2981-6. doi: 10.1161/STROKEAHA.115.010049. Epub 2015 Sep 1.
12. Wahlgren N, Ahmed N, Dávalos A, et al. Thrombolysis with alteplase for acute ischaemic stroke in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST): an observational study. *Lancet.* 2007;369(9558):275-282.

eFigure 1. PRISMA flowchart presenting the selection of eligible studies.



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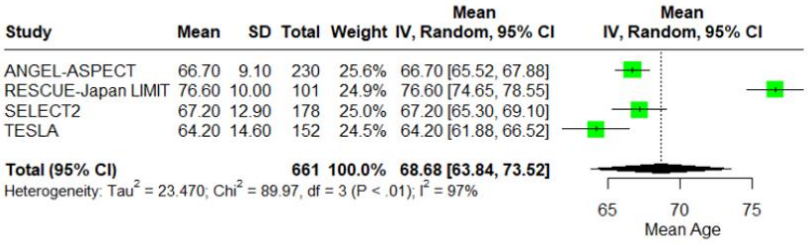
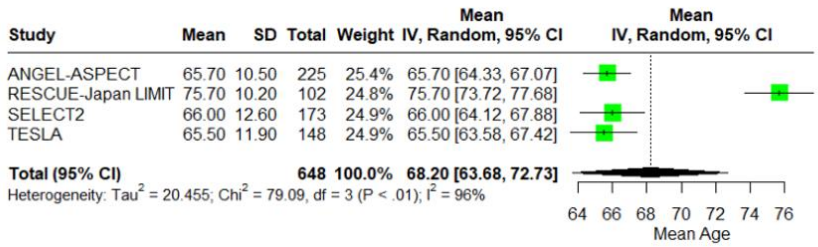
eFigure 2. Forest plots presenting the pooled mean of age (in years) of the patients enrolled in the EVT arm (panel A), the pooled mean of age (in years) of the patients enrolled in the BMT arm (panel B), and the mean difference of age (in years) among the patients in the EVT versus the BMT arm (panel C).

SD: standard deviation; CI: confidence interval; IV: inverse variance; EVT: endovascular treatment; BMT: best medical treatment.

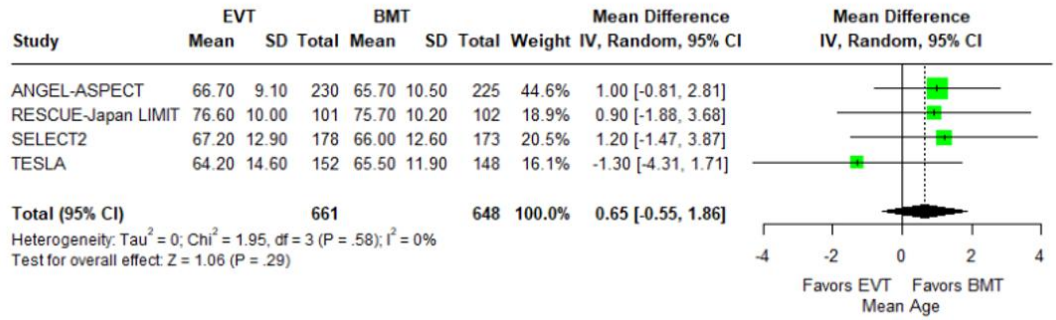
A.



B.

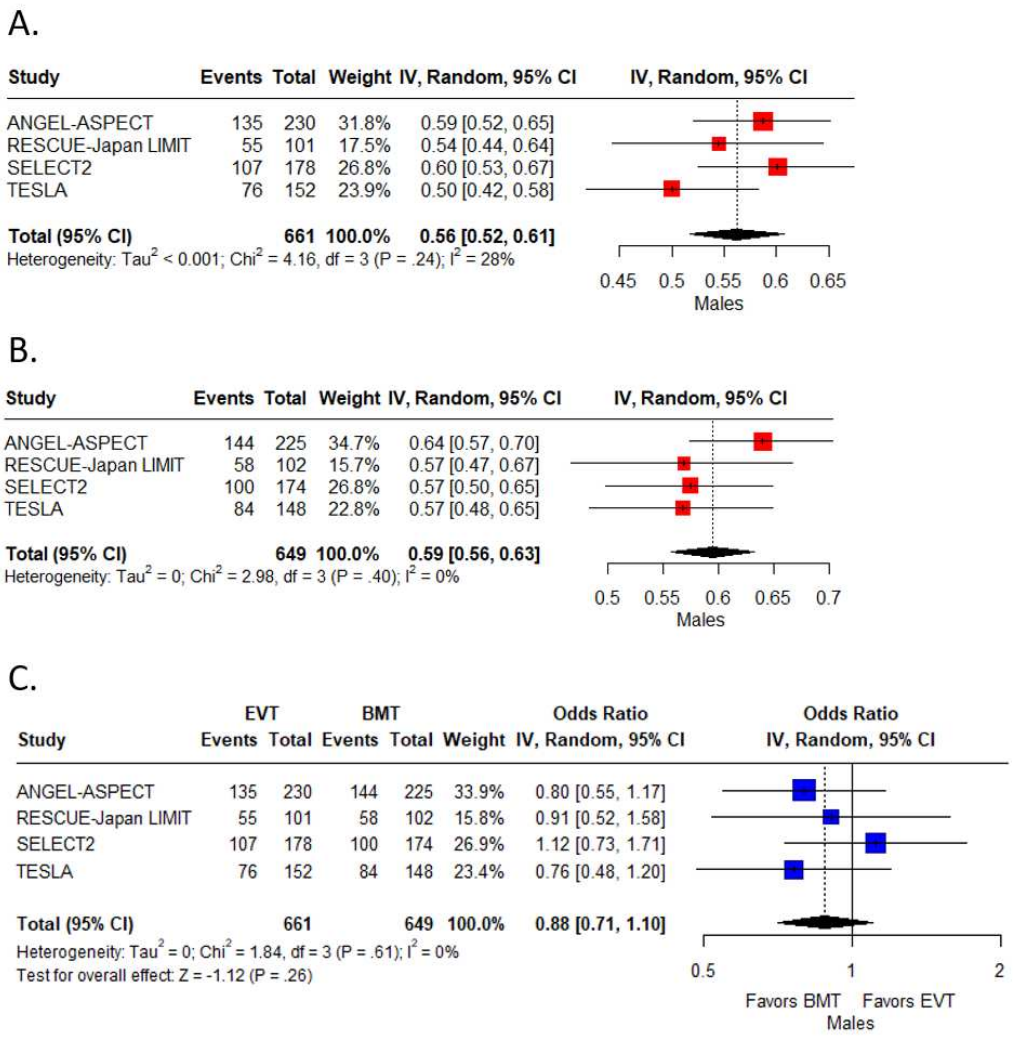


C.



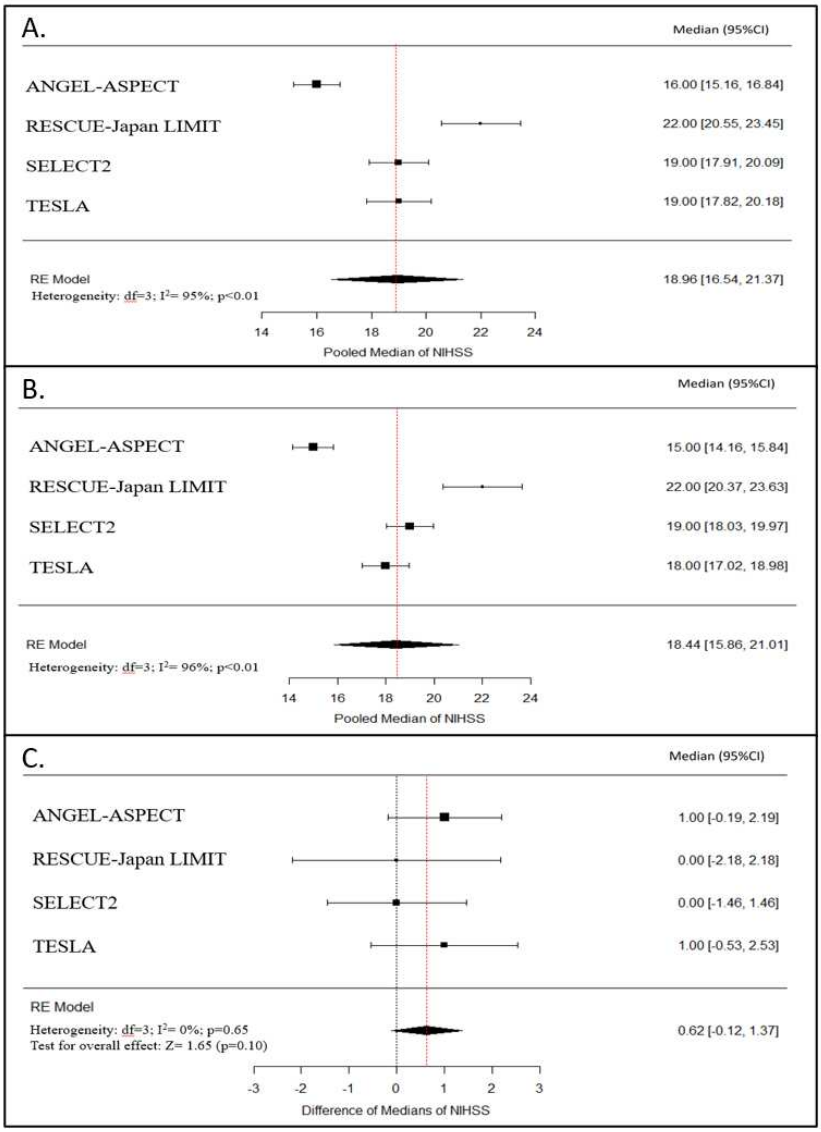
eFigure 3. Forest plots presenting the pooled proportion of men among the patients enrolled in the EVT arm (panel A), the pooled proportion of men among the patients enrolled in the BMT arm (panel B), and the odds ratio of men in the EVT versus the BMT arm (panel C).

CI: confidence interval; IV: inverse variance; EVT: endovascular treatment; BMT: best medical treatment.



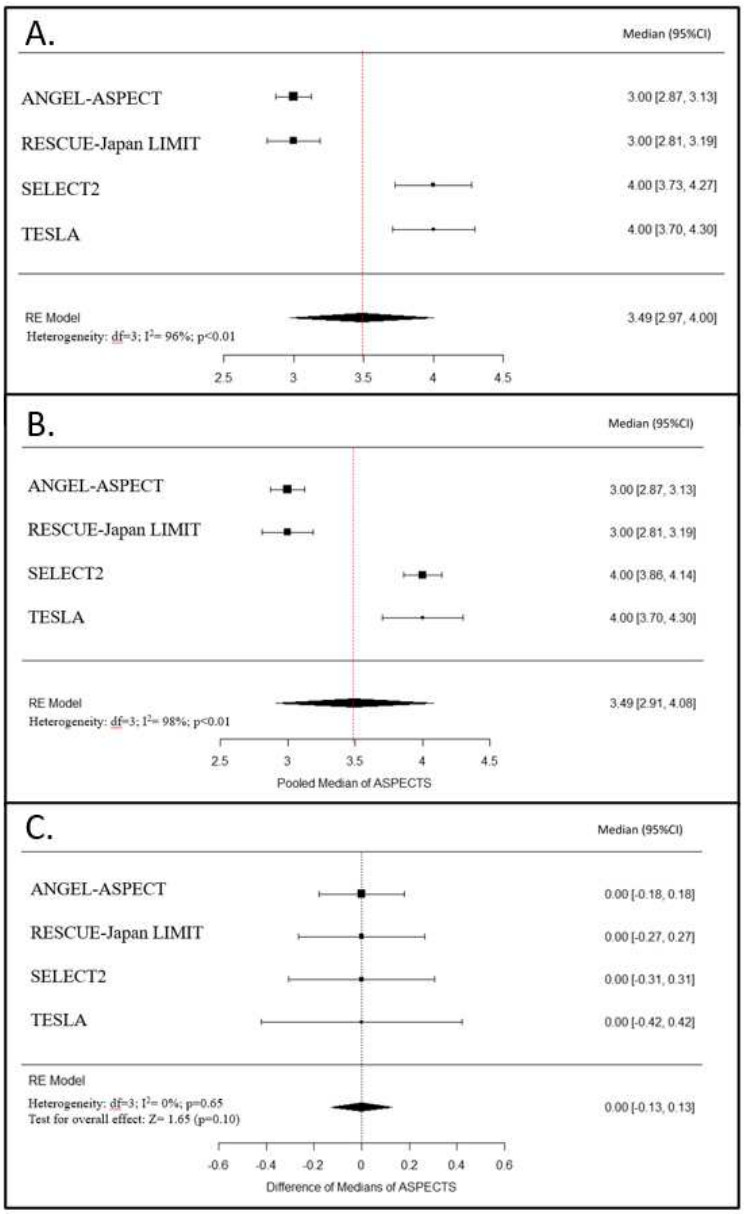
eFigure 4. Forest plots presenting the pooled median of NIHSS of the patients enrolled in the EVT arm (panel A), the pooled median of NIHSS of the patients enrolled in the BMT arm (panel B), and the difference of medians of NIHSS among the patients in the EVT versus the BMT arm (panel C), as calculated by the quantile estimation (QE) method.[4]

CI: confidence interval; RE: random effect; NIHSS: National Institutes of Health Stroke Scale.



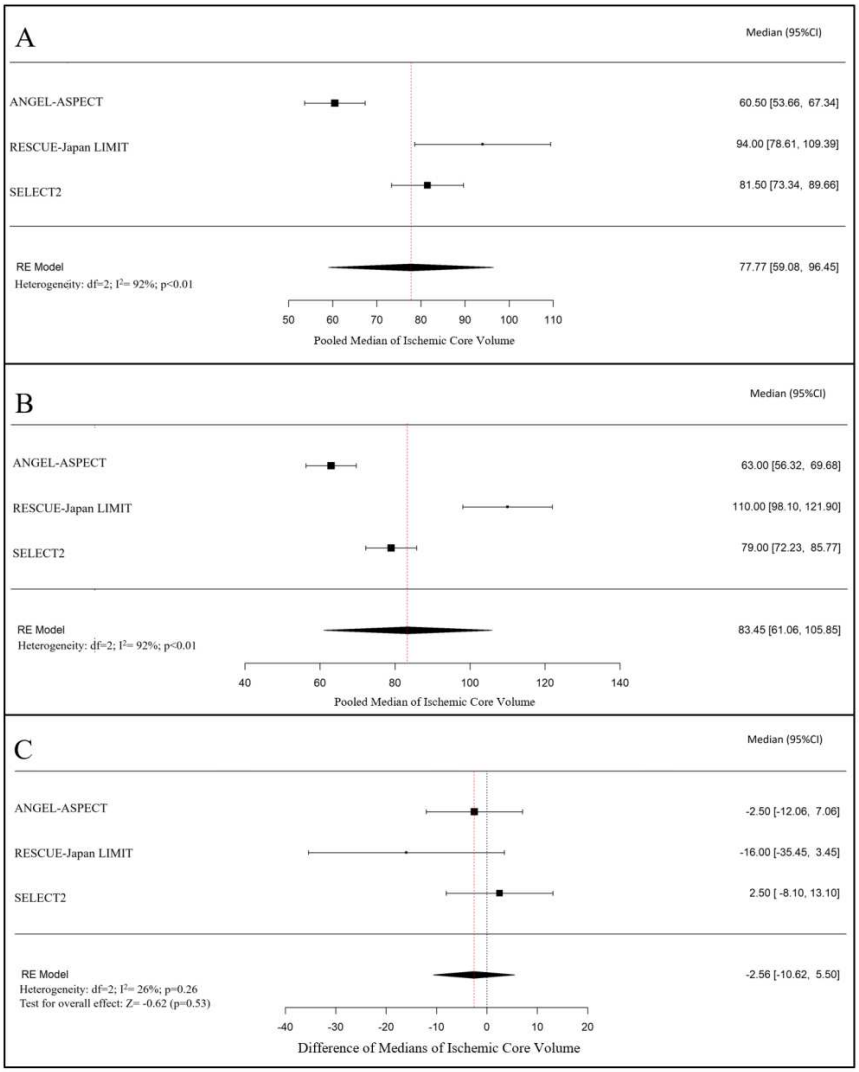
eFigure 5. Forest plots presenting the pooled median of ASPECTS of the patients enrolled in the EVT arm (panel A), the pooled median of ASPECTS of the patients enrolled in the BMT arm (panel B), and the difference of medians of ASPECTS among the patients in the EVT versus the BMT arm (panel C), as calculated by the quantile estimation (QE) method.[4]

CI: confidence interval; RE: random effect; ASPECTS: Alberta Stroke Program Early CT Score.



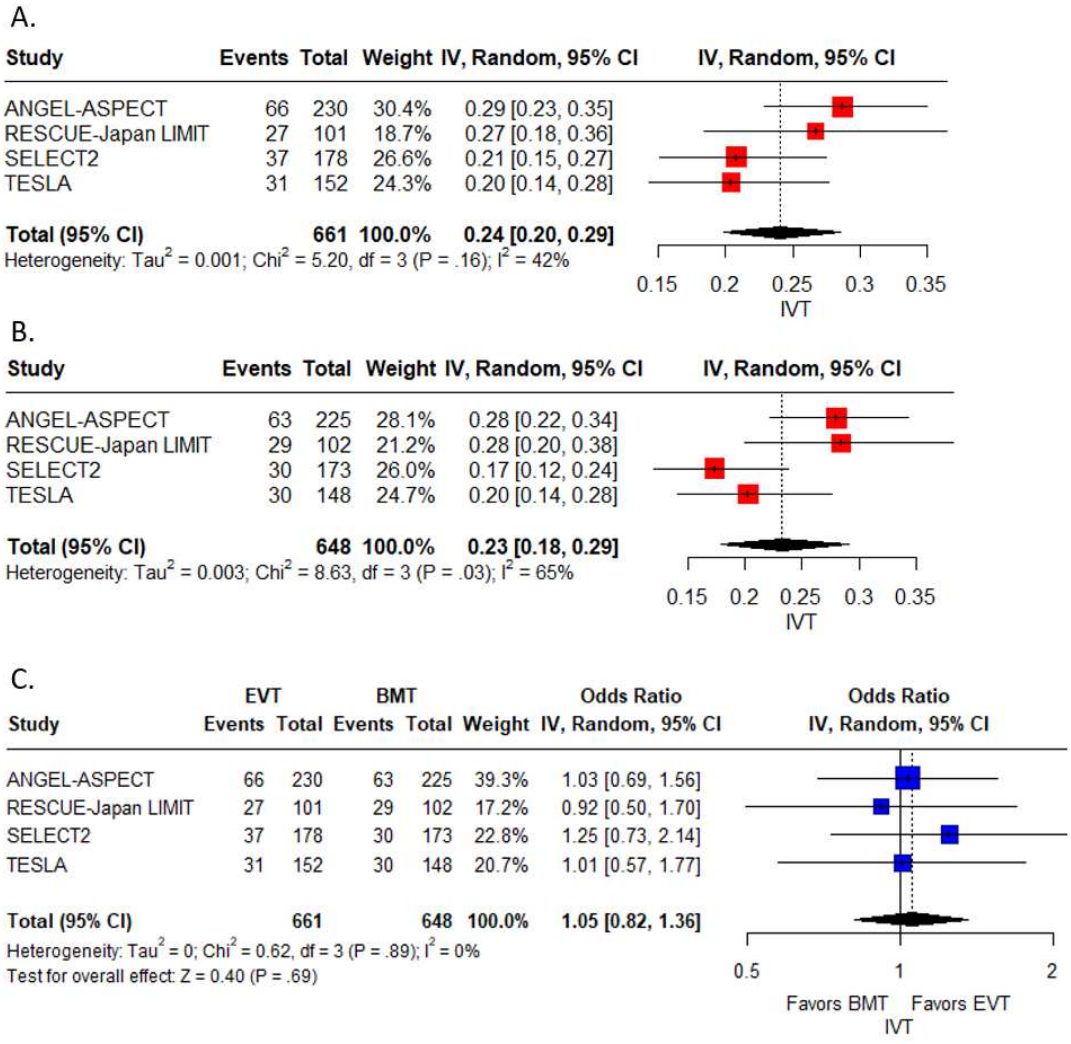
eFigure 6. Forest plots presenting the pooled median of ischemic-core volume (in ml) of the patients enrolled in the EVT arm (panel A), the pooled median of ischemic-core volume (in ml) of the patients enrolled in the BMT arm (panel B), and the difference of medians of ischemic-core volume (in ml) among the patients in the EVT versus the BMT arm (panel C), as calculated by the quantile estimation (QE) method.[4]

CI: confidence interval; RE: random effect.



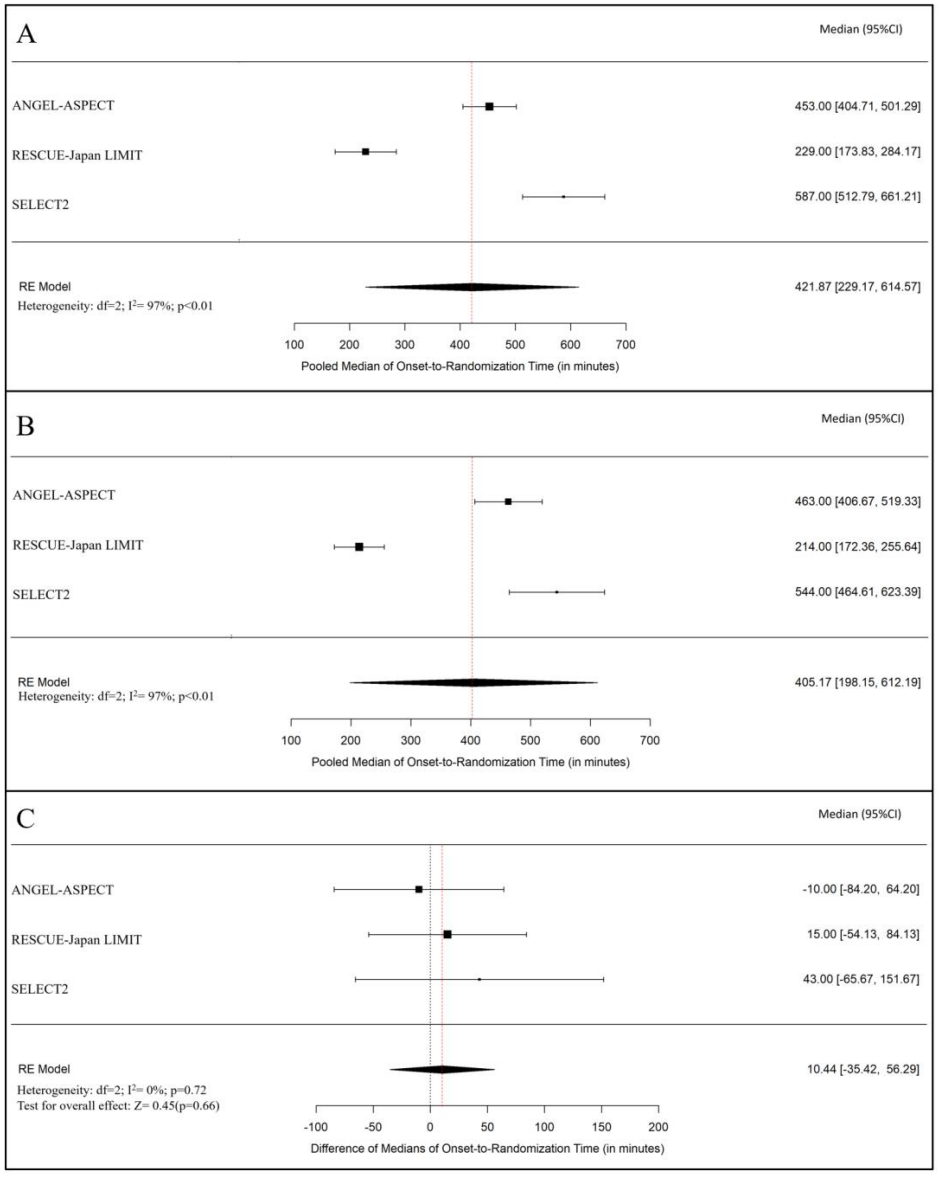
eFigure 7. Forest plots presenting the pooled proportion of IVT pretreatment among the patients enrolled in the EVT arm (panel A), the pooled proportion of IVT pretreatment among the patients enrolled in the BMT arm (panel B), and the odds ratio of IVT pretreatment in the EVT versus the BMT arm (panel C).

CI: confidence interval; IV: inverse variance; EVT: endovascular treatment; BMT: best medical treatment; IVT: intravenous thrombolysis.

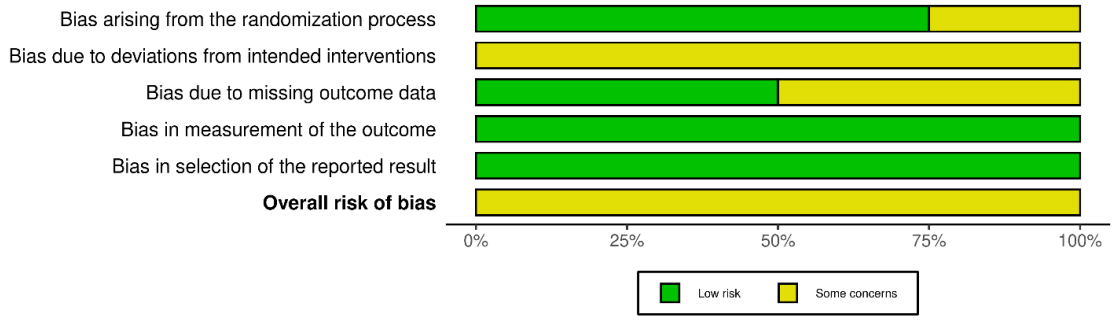


eFigure 8. Forest plots presenting the pooled median time onset-to-randomization (in minutes) of the patients enrolled in the EVT arm (panel A), the pooled median time onset-to-randomization (in minutes) of the patients enrolled in the BMT arm (panel B), and the difference of medians of time onset-to-randomization (in minutes) among the patients in the EVT versus the BMT arm (panel C), as calculated by the quantile estimation (QE) method.[4]

CI: confidence interval; RE: random effect.

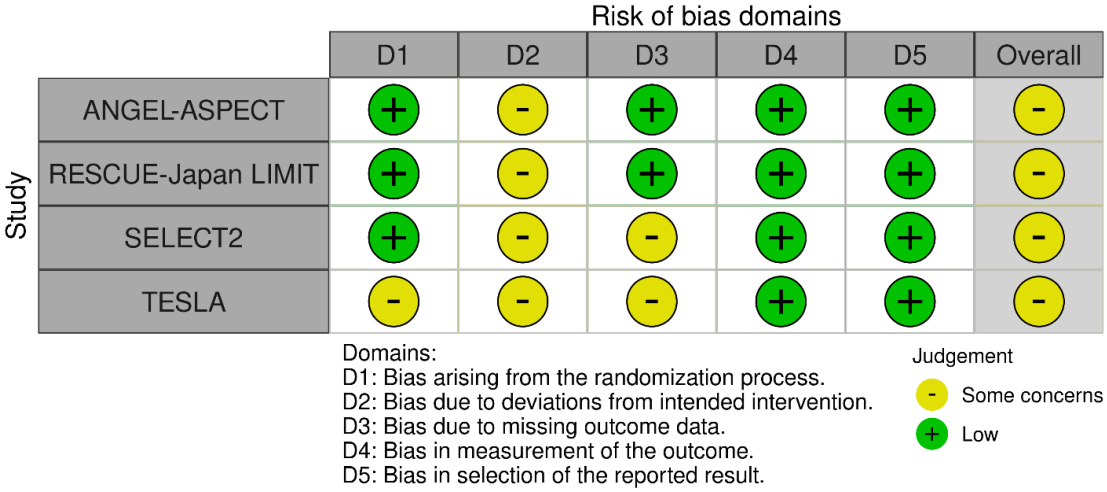


eFigure 9. Summary plot presenting the quality assessment of included randomized controlled clinical trials using the Cochrane Collaboration tool (RoB 2).[5]



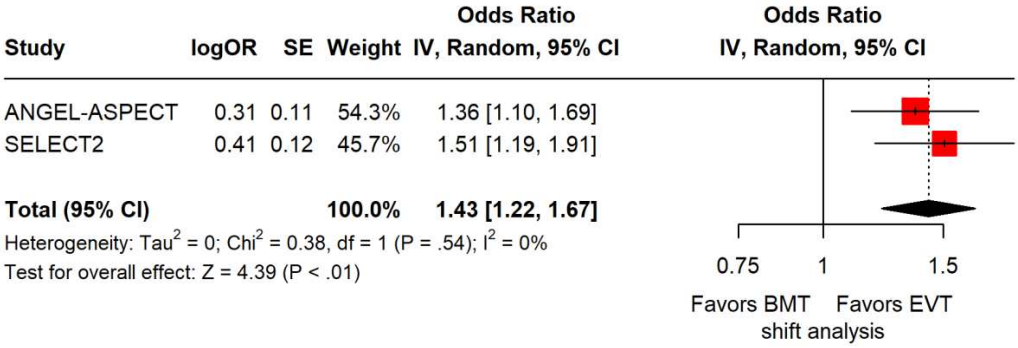
All of the studies were free of risk of bias in two domains: the measurement of outcomes (since all adjudicators were blinded to the patients' allocation) and the results' reporting. The TESLA[6,7] trial presented minor concerns in the randomization process due to the inclusion of more patients with diabetes mellitus in the interventional arm compared to control. Furthermore, due to the nature of the intervention, blinding of participants and investigators was not possible in any of the included trials. Additionally, in ANGEL-ASPECT,[8] SELECT2,[9] and TESLA[6,7] trials, minor deviations from intended interventions were noted; such a bias was not detected in RESCUE-Japan LIMIT[10] trial. Finally, in SELECT2[9] and TESLA[6,7] trials, there were minor concerns due to missing data regarding outcomes (due to lost to follow up patients).

eFigure 10. Traffic Light Plot presenting the quality assessment of included randomized controlled clinical trials using the Cochrane Collaboration tool (RoB 2).[5]



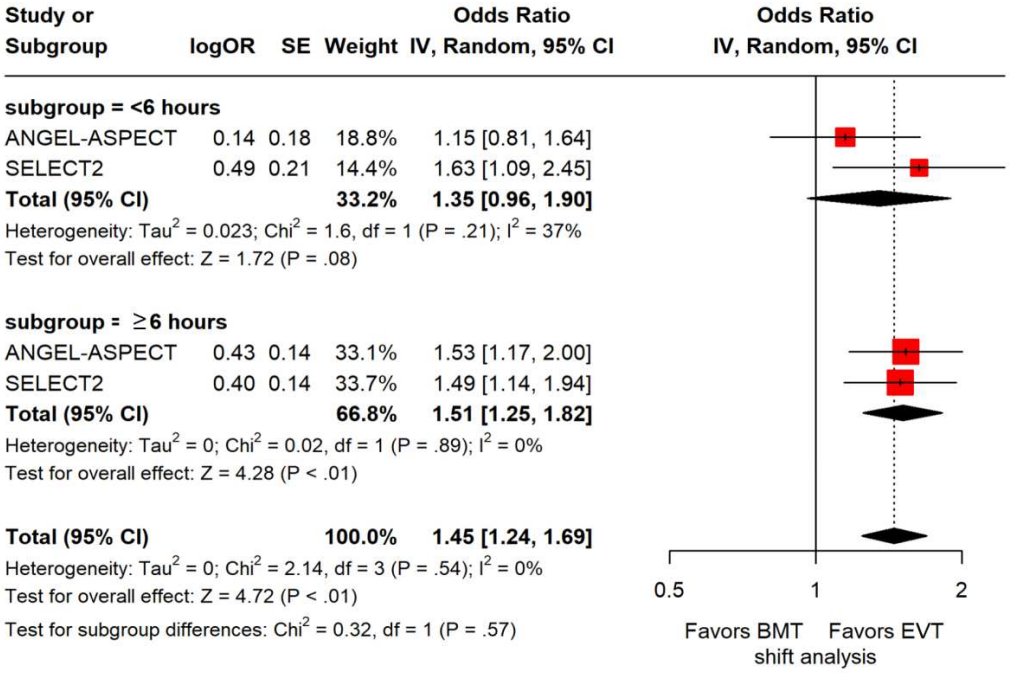
eFigure 11: Sensitivity analysis regarding the association of EVT compared to BMT with reduced disability at 3 months, using the generalized OR as reported by 2 studies.[8,9]

SE: standard error; CI: confidence interval; IV: inverse variance; EVT: endovascular treatment; BMT: best medical treatment.



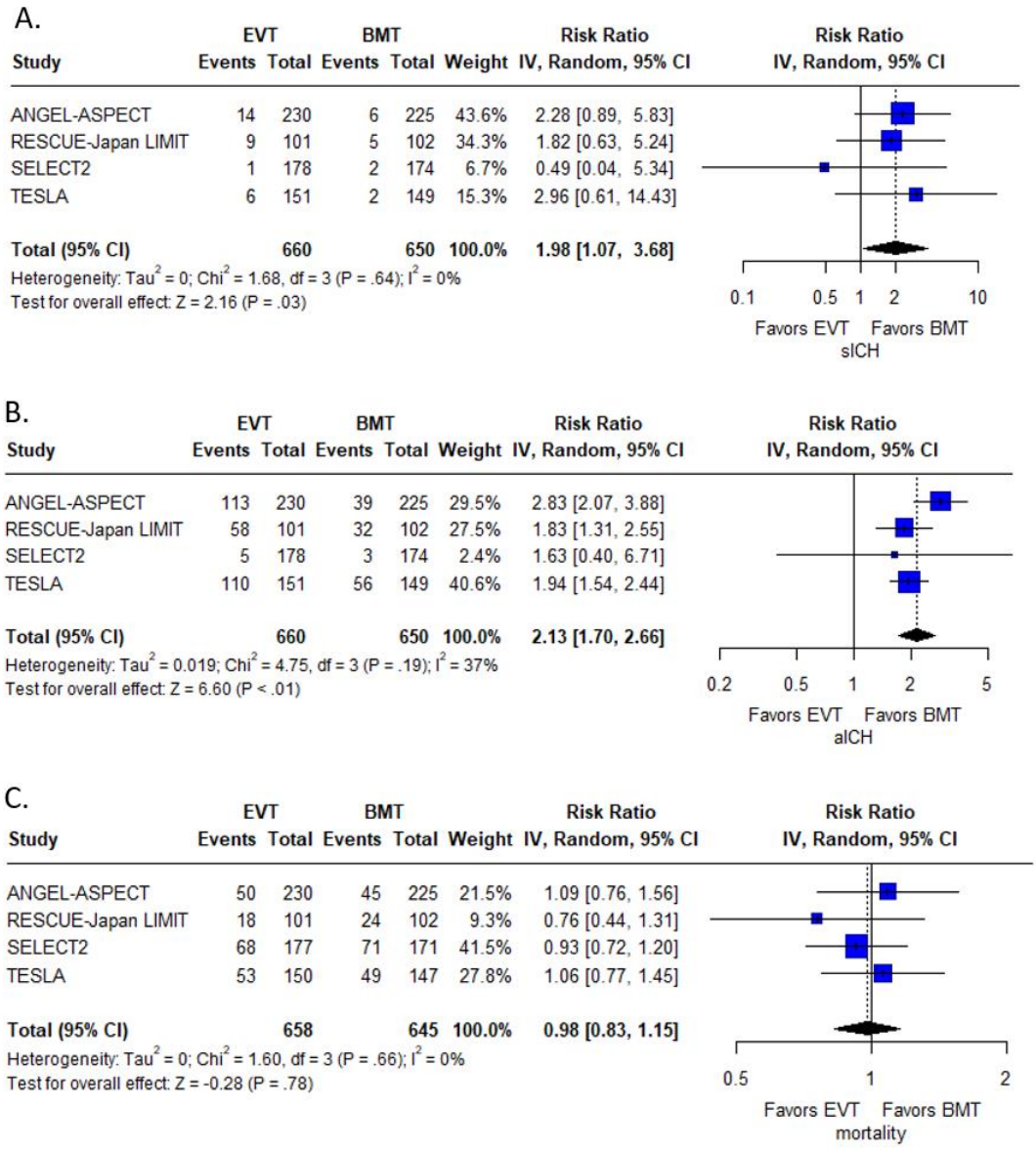
eFigure 12: Forest plot presenting the association of EVT compared to BMT with reduced disability at 3 months (using the generalized OR), stratified by onset-to randomization time (<6 hours vs. ≥ 6 hours).

SE: standard error; CI: confidence interval; IV: inverse variance; EVT: endovascular treatment; BMT: best medical treatment.



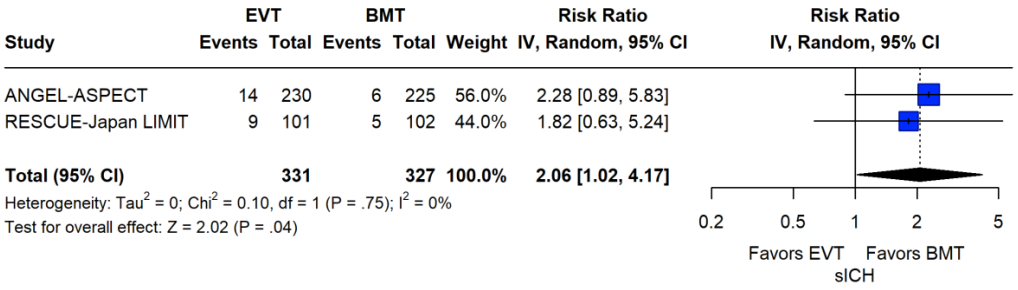
eFigure 13: Analysis of Safety Outcomes. Forest plot presenting the association of EVT compared to BMT with sICH (panel A), any-ICH (panel B) and 3-month mortality (panel C).

CI: confidence interval; IV: inverse variance; EVT: endovascular treatment; BMT: best medical treatment; sICH: symptomatic intracranial hemorrhage; aICH: any intracranial hemorrhage.



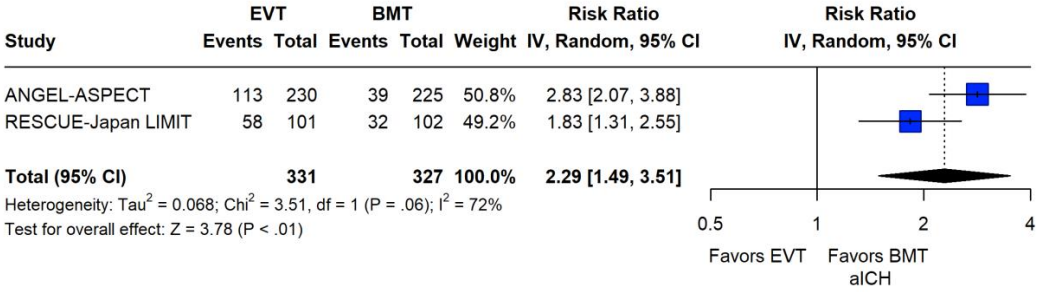
eFigure 14: Sensitivity analysis regarding the association of EVT compared to BMT with sICH, including the studies that reported this outcome up to 48 hours post intervention.[8,10]

CI: confidence interval; IV: inverse variance; EVT: endovascular treatment; BMT: best medical treatment; sICH: symptomatic intracranial hemorrhage.



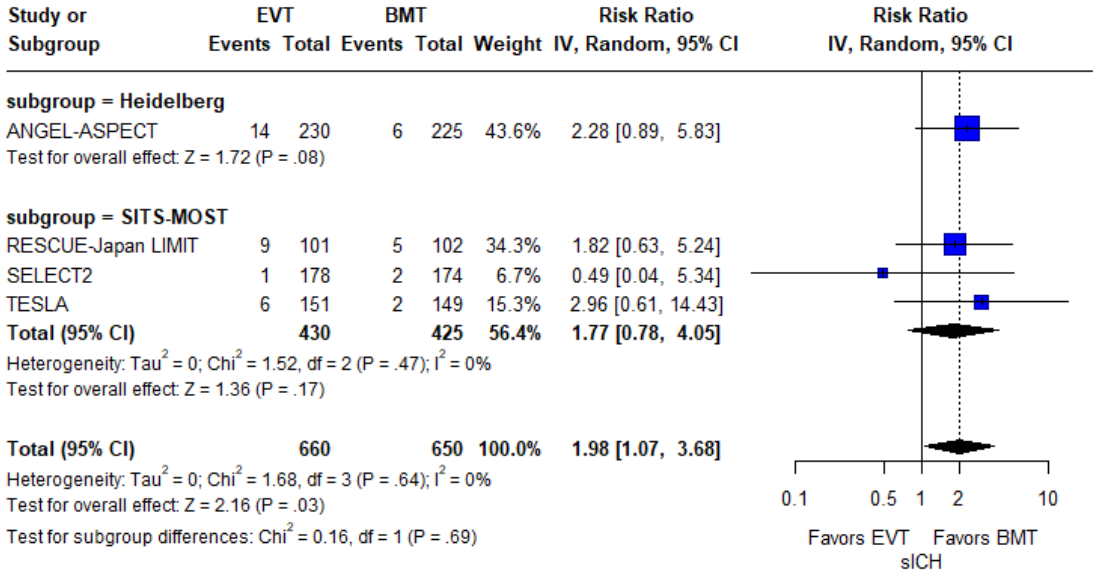
eFigure 15: Sensitivity analysis regarding the association of EVT compared to BMT with any ICH, including the studies that reported this outcome up to 48 hours post intervention.[8,10]

CI: confidence interval; IV: inverse variance; EVT: endovascular treatment; BMT: best medical treatment; aICH: any intracranial hemorrhage.



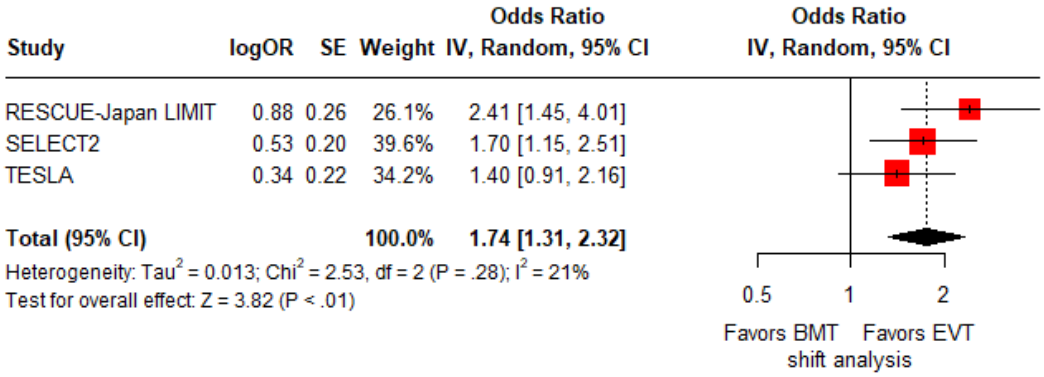
eFigure 16: Forest plot presenting the association of EVT compared to BMT with sICH, stratified by the different definitions used by each study. The ANGEL-ASPECT trial[8] used the Heidelberg bleeding classification (NIHSS-score increase of ≥4 points or an increase in the score for an NIHSS subcategory of ≥2 points with any intracranial hemorrhage on imaging),[11] while the SELECT2,[9] RESCUE-Japan LIMIT,[10] and TESLA[6,7] trials used the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) definition (parenchymal hematoma type 2 and NIHSS-score increase by at least 4 points).[12]

CI: confidence interval; IV: inverse variance; EVT: endovascular treatment; BMT: best medical treatment; sICH: symptomatic intracranial hemorrhage; SITS-MOST: Safe Implementation of Thrombolysis in Stroke-Monitoring Study.



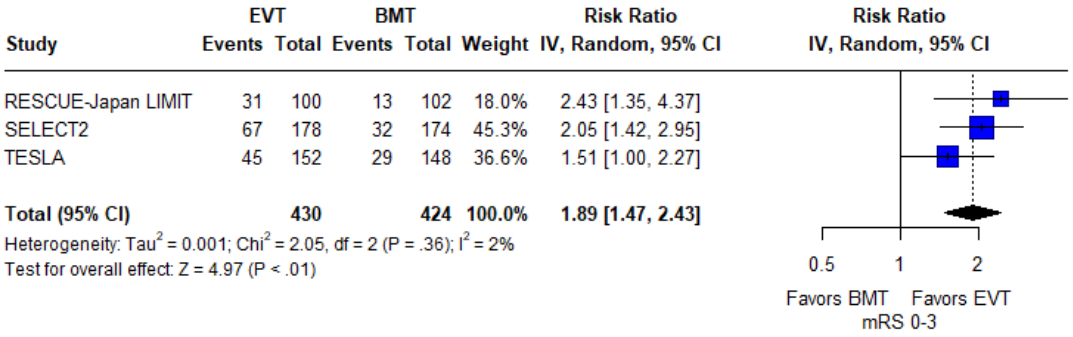
eFigure 17: Sensitivity analysis regarding the association of EVT compared to BMT with reduced disability at 3 months, after excluding the ANGEL-ASPECT trial.[8]

SE: standard error; CI: confidence interval; IV: inverse variance; EVT: endovascular treatment; BMT: best medical treatment.



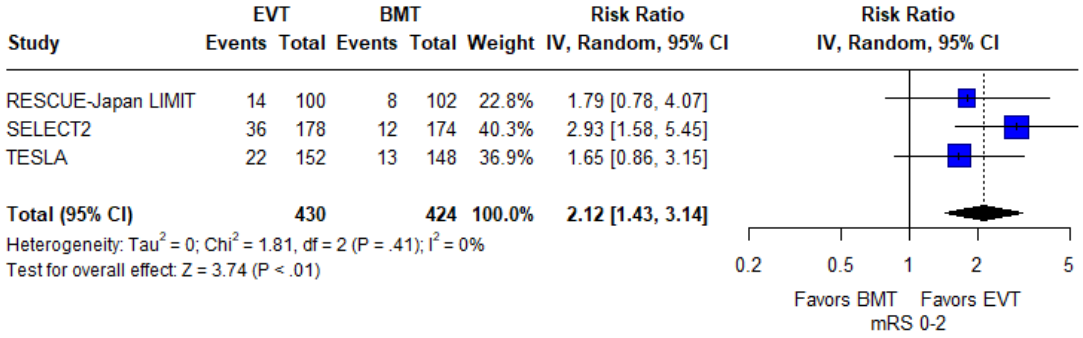
eFigure 18: Sensitivity analysis regarding the association of EVT compared to BMT with independent ambulation at 3 months, after excluding the ANGEL-ASPECT trial.[8]

CI: confidence interval; IV: inverse variance; EVT: endovascular treatment; BMT: best medical treatment; mRS: modified Rankin Scale.



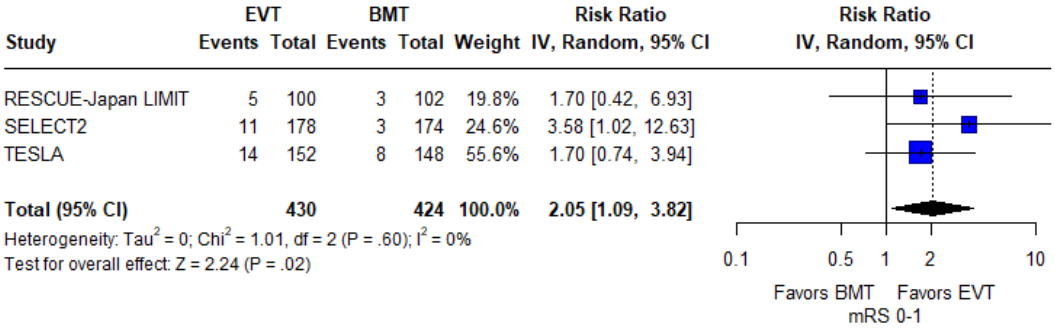
eFigure 19: Sensitivity analysis regarding the association of EVT compared to BMT with good functional outcome at 3 months, after excluding the ANGEL-ASPECT trial.[8]

CI: confidence interval; IV: inverse variance; EVT: endovascular treatment; BMT: best medical treatment; mRS: modified Rankin Scale.



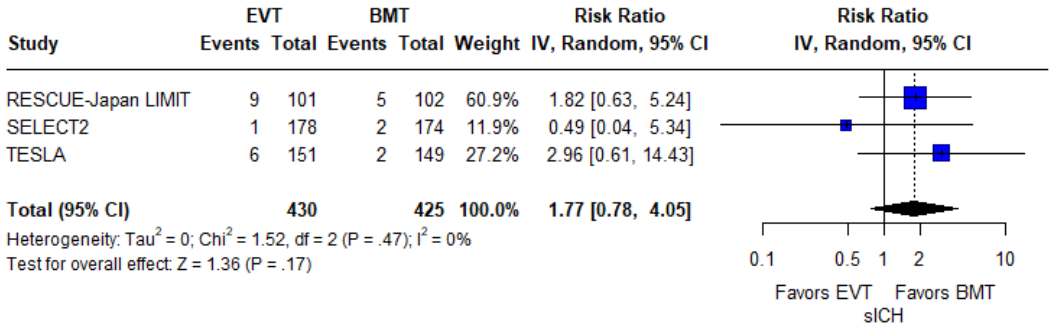
eFigure 20: Sensitivity analysis regarding the association of EVT compared to BMT with excellent functional outcome at 3 months, after excluding the ANGEL-ASPECT trial.[8]

CI: confidence interval; IV: inverse variance; EVT: endovascular treatment; BMT: best medical treatment; mRS: modified Rankin Scale.



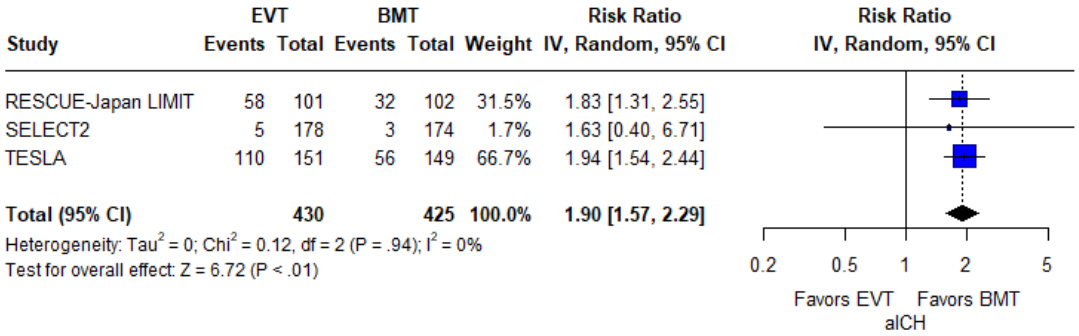
eFigure 21: Sensitivity analysis regarding the association of EVT compared to BMT with sICH, after excluding the ANGEL-ASPECT trial.[8]

CI: confidence interval; IV: inverse variance; EVT: endovascular treatment; BMT: best medical treatment; sICH: symptomatic intracranial hemorrhage.



eFigure 22: Sensitivity analysis regarding the association of EVT compared to BMT with any ICH, after excluding the ANGEL-ASPECT trial.[8]

CI: confidence interval; IV: inverse variance; EVT: endovascular treatment; BMT: best medical treatment; aICH: any intracranial hemorrhage.



eFigure 23: Sensitivity analysis regarding the association of EVT compared to BMT with mortality at 3 months, after excluding the ANGEL-ASPECT trial.[8]

CI: confidence interval; IV: inverse variance; EVT: endovascular treatment; BMT: best medical treatment.