



The Role of Middle Meningeal Artery Embolisation in the Management of Refractory Chronic Subdural Haematoma: A Systematic Review of Randomised Controlled Trials and Primary Studies

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ABSTRACT

Introduction. Chronic subdural haematoma (cSDH) is among the most frequent conditions encountered in contemporary neurosurgical practice and is projected to become the commonest cranial operative indication in ageing populations. Conventional surgical evacuation relieves mass effect but does not address the pathophysiological substrate of the disease—an inflammatory, angiogenic and hyperfibrinolytic neomembrane perfused by fragile, leaky branches of the middle meningeal artery (MMA). Consequently, recurrence rates of 2–37% persist after apparently adequate evacuation. Middle meningeal artery embolisation (MMAE) is a minimally invasive endovascular technique that devascularises the neomembrane and, in principle, interrupts the recurrence cycle at its source.

Methods. The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines. Eligible: RCTs, prospective and retrospective cohorts, case-control, cross-sectional, and observational studies; systematic reviews excluded from characteristics tables. Risk of bias assessed with RoB 2 and ROBINS-I; certainty with GRADE.

Results. Forty primary reports (10 RCTs, 2,552 participants; 30 non-RCT studies, 204,509 patients). Adjunctive or standalone MMAE halved symptomatic recurrence (RR 0.51; 95%CI 0.38–0.68; 9 RCTs; $P<0.001$; $I^2=29\%$), with ARR 9.0% and NNT 11. Effect on reoperation was larger and homogeneous (RR 0.33; 95%CI 0.20–0.53; 6 RCTs; $P<0.001$; $I^2=0\%$; NNT 11). Radiographic recurrence or residual >10 mm was reduced by 60% (RR 0.40; 95%CI 0.29–0.57; $P<0.001$; $I^2=24\%$). Observational studies confirmed direction and magnitude (RR 0.35; 95%CI 0.18–0.70; $P=0.003$; $I^2=68\%$). Pooled surgical rescue after MMAE was 7.8% (95%CI 6.9–8.9; $I^2=0\%$). Mortality (RR 1.57; 95%CI 0.86–2.87; $P=0.14$) and serious adverse events (RR 0.80; 95%CI 0.43–1.51; $P=0.50$) did not differ significantly. Aggressive distal penetration reduced surgical rescue to 2.6%. The CSDH grading scheme prediction model achieved AUC 0.85.

Discussion. Randomised evidence now converges on a robust conclusion: MMA devascularisation halves recurrence risk and reduces reoperation by two-thirds, with no procedural harm signal. Apparent discordance between trials is explained by differing

endpoint definitions, proportions of surgical patients, and embolic agent/penetration technique. Liquid agents with distal penetration produced the largest effects. Safety is reassuring but complications such as cranial nerve palsy and non-target embolisation remain.

Conclusion. Middle meningeal artery embolisation is an effective and acceptably safe intervention that substantially reduces recurrence, reoperation, and radiographic treatment failure in refractory cSDH without compromising functional recovery. It should be offered as an adjunct to evacuation in patients with recurrent haematoma or established high-risk features, and considered as standalone therapy in neurologically stable patients who are poor surgical candidates. Future trials should adopt harmonised endpoint definitions, mandate distal penetration, extend follow-up, and incorporate cognitive, quality-of-life, and health-economic outcomes.

Keywords: chronic subdural haematoma; middle meningeal artery embolisation; refractory subdural haematoma; recurrence; burr-hole craniostomy; endovascular neurosurgery; Onyx; n-butyl cyanoacrylate; polyvinyl alcohol particles; systematic review; meta-analysis; randomised controlled trial; risk of bias; receiver-operating characteristic; GRADE.

INTRODUCTION

Background and epidemiological burden

Chronic subdural haematoma (cSDH) is an encapsulated collection of liquefied blood and blood-degradation products confined between the dural border cell layer and the arachnoid membrane, characteristically presenting weeks to months after a trivial and often unremembered head injury. It is now the most rapidly growing operative diagnosis in cranial neurosurgery worldwide. Population ageing, the widening use of antiplatelet and anticoagulant therapy for cardiovascular and cerebrovascular indications, and the increasing availability of cross-sectional imaging have together produced incidence estimates that rise steeply with age, exceeding 58 per 100,000 person-years beyond the eighth decade. Modelling studies project that cSDH will become the single most common cranial neurosurgical indication in high-income health systems within the next decade, and the same demographic transition is now under way across middle-income countries in Southeast Asia. The disease is therefore no longer a peripheral concern of geriatric neurosurgery but a central determinant of neurosurgical workload, bed occupancy and rehabilitation demand.^{65,66,67}

Contrary to the older mechanical conception of cSDH as a static, gradually expanding post-traumatic collection, contemporary pathophysiological understanding characterises the condition as a dynamic, self-perpetuating inflammatory and angiogenic disorder of the dural border cell layer. Traumatic separation of the dural border cells initiates a reparative cascade in which fibroblasts proliferate, and a neomembrane forms on the inner surface of the dura. This neomembrane is invested with immature, fenestrated capillaries lacking pericyte support and tight junctions, derived predominantly from the terminal branches of the middle meningeal artery (MMA). Local concentrations of vascular endothelial growth factor, interleukin-6, interleukin-8, matrix metalloproteinases and tissue plasminogen activator are markedly elevated within the haematoma cavity, sustaining simultaneous neovascularisation, exudation and hyperfibrinolysis. Repeated micro-haemorrhage from these fragile neovessels and continuous plasma exudation across their leaky endothelium maintain and enlarge the collection irrespective of whether the cavity has been surgically

drained. This insight is the biological foundation of the entire endovascular approach to the disease.^{65,66,67,50}

The clinical problem of refractory chronic subdural haematoma

Surgical evacuation—by burr-hole craniostomy with or without subdural drainage, twist-drill craniostomy, or mini-craniotomy with membranectomy—remains the reference standard for symptomatic cSDH with mass effect and reliably relieves acute neurological deterioration. It does not, however, eliminate the neomembrane or its arterial supply. Recurrence rates after apparently satisfactory evacuation have been reported between 2% and 37% across four decades of surgical literature, clustering around 10–20% in contemporary prospective series and rising substantially in patients with septated or trabecular haematoma architecture, bilateral collections, large postoperative residual cavities, brain atrophy with poor re-expansion, coagulopathy, or an obligate indication for early resumption of antithrombotic therapy.^{58,17,21}

Within this population a clinically distinct phenotype may be identified: the patient whose haematoma recurs after one or more technically adequate operations, or whose baseline profile predicts a high probability of such recurrence. For the purposes of this review this phenotype is designated refractory chronic subdural haematoma. It encompasses (i) haematoma recurring after at least one previous evacuation, (ii) persistently or repeatedly recurrent (intractable) haematoma requiring two or more previous operations, (iii) first-episode haematoma carrying pre-specified high-risk features for recurrence, and (iv) haematoma in patients for whom repeated surgery is considered hazardous or futile because of frailty, comorbidity, malignancy or unavoidable antithrombotic therapy. Patients in this category consume a disproportionate share of neurosurgical resources: each reoperation carries anaesthetic risk in an octogenarian population, extends hospitalisation, precipitates functional decline and loss of independence, and is associated with one-year mortality that in some series approaches that of hip fracture.^{13,14,58,63}

Rationale for middle meningeal artery embolisation

Middle meningeal artery embolisation (MMAE) is a minimally invasive endovascular procedure in which the frontal and parietal divisions of the MMA are selectively catheterised through transfemoral or transradial access and occluded with polyvinyl alcohol or trisacryl gelatin particles,

non-adhesive liquid embolic agents such as ethylene-vinyl alcohol copolymer suspended in dimethyl sulfoxide (Onyx or Squid), adhesive n-butyl cyanoacrylate, coils, or combinations thereof. Because the entire arterial supply of the outer neomembrane derives from these vessels, their occlusion interrupts the exudative and micro-haemorrhagic cycle at its source, permitting the physiological resorptive capacity of the arachnoid and the dural lymphatics to predominate. Angiographic and dual-energy computed tomographic studies demonstrate abnormal contrast staining of the membrane during selective MMA injection, and cone-beam computed tomography acquired during embolisation can grade the extent of membrane enhancement, which correlates with the propensity for repeated recurrence.^{13,65,67}

The concept was first advanced in small Japanese case series in the middle of the last decade and was subsequently supported by a rapidly expanding observational literature reporting recurrence rates that appeared markedly lower than historical surgical benchmarks. Between 2024 and 2026 the field was transformed by the publication of six adequately powered multicentre randomised controlled trials—EMBOLISE, MAGIC-MT, STEM, EMPROTECT, MEMBRANE and EMMA-Can—together with several smaller randomised experiences, and by the release of the first international consensus guideline addressing the technique. These trials did not, however, produce uniform results: two reported statistically neutral primary endpoints while four demonstrated significant benefit, and the reasons for this divergence have not been comprehensively adjudicated in a synthesis that also incorporates the observational evidence specific to the refractory phenotype.^{1,2,3,4,5,6,64}

Research gap

Four specific gaps motivated the present review. First, existing systematic reviews and meta-analyses have generally restricted themselves either to randomised trials or to observational studies, and none has integrated the complete randomised dataset available in 2026 with the very large registry and cohort experience while explicitly excluding secondary literature from data extraction. Second, virtually all prior syntheses have analysed cSDH as a single undifferentiated condition, whereas the clinically pressing question—whether to add an endovascular procedure—arises almost exclusively in patients whose disease has already proved refractory to surgery or who are predicted to fail it.

Third, the number of outcome domains examined in previous reviews has typically been limited to four to seven; procedural technical success, resolution kinetics, healthcare utilisation, effect modification by embolic agent and timing, and the discriminative performance of prediction models have rarely been synthesised. Fourth, although several groups have now published risk models for MMAE failure, no review has assembled their receiver-operating-characteristic performance to permit comparative appraisal and clinical translation.^{52,53,54,55,56,57,58,59,60,61,62}

Objectives

The objectives of this systematic review were as follows.

To determine whether middle meningeal artery embolisation, applied as an adjunct to surgical evacuation or as standalone therapy, reduces symptomatic recurrence or progression of chronic subdural haematoma compared with standard care in refractory and recurrence-prone populations.

To quantify the effect of MMAE on reoperation or surgical rescue, on composite treatment failure, and on radiographic recurrence or residual haematoma.

To characterise the radiological response to MMAE, including haematoma thickness, volume, midline shift, complete resolution and the temporal kinetics of resorption.

To evaluate functional outcome, all-cause mortality, serious adverse events, procedure-related complications and technical success.

To assess healthcare-utilisation outcomes including length of hospital stay, readmission and discharge disposition.

To explore effect modification by baseline management strategy, embolic material, embolisation timing and order relative to surgery, anaesthetic technique, degree of emboliseate penetration, and patient-level covariates including antithrombotic therapy, malignancy and advanced age.

To appraise the discriminative performance, calibration and clinical utility of published models predicting MMAE failure by reconstructing their receiver-operating-characteristic curves.

To grade the certainty of evidence for each outcome domain using the GRADE framework and to derive practice recommendations calibrated to that certainty.

Anticipated benefits of the review

The clinical benefit of this synthesis is the provision of precise, GRADE-rated, absolute and relative effect estimates that can be used directly in shared decision-making with elderly patients and their families, and in the construction of institutional protocols for the management of recurrent haematoma. The methodological benefit is a transparent, dual-instrument risk-of-bias appraisal of the entire primary literature, which identifies precisely where the evidence is fragile and where it is secure. The service-planning benefit is the quantification of the number needed to treat and of the reduction in reoperation, which permits health systems—particularly those in middle-income settings where neurointerventional capacity is being established—to model the workload and cost consequences of adopting the technique. The academic benefit is the identification of a prioritised research agenda, including harmonisation of endpoint definitions and prospective validation of risk-stratification instruments.

Hypotheses

The following hypotheses were specified before data extraction.

Primary hypothesis (H1). In adults with refractory or recurrence-prone chronic subdural haematoma, middle meningeal artery embolisation added to standard care reduces symptomatic recurrence or progression by at least 40% in relative terms compared with standard care alone (null hypothesis H0: risk ratio = 1.00).

Secondary hypothesis (H2). MMAE reduces the requirement for reoperation or surgical rescue to a degree at least as large as its effect on symptomatic recurrence.

Secondary hypothesis (H3). MMAE accelerates radiographic resolution and reduces residual haematoma thickness, volume and midline shift.

Safety hypothesis (H4). MMAE does not increase all-cause mortality, serious adverse events or disabling stroke relative to standard care, and procedure-related major complications occur in fewer than 5% of embolisations.

Equivalence hypothesis (H5). Functional outcome measured by the modified Rankin Scale at 90 days is non-inferior in embolised patients.

Effect-modification hypothesis (H6). The relative benefit of MMAE is greater in patients managed non-surgically and in those receiving distally penetrating liquid embolic agents than in patients managed surgically with proximal particulate embolisation.

Prediction hypothesis (H7). Published multivariable models discriminate MMAE failure with an area under the receiver-operating-characteristic curve of at least 0.70.

Novelty of the present work

This review advances the literature in five respects. It is, to our knowledge, the first synthesis to assemble all ten completed randomised trials of MMAE alongside thirty non-randomised primary reports while rigorously excluding systematic reviews and meta-analyses from data extraction, thereby eliminating the double-counting of participants that has affected several earlier syntheses. It is the first to organise the evidence around fifteen pre-specified outcome domains, including domains—technical success, resolution kinetics, healthcare utilisation and predictive discrimination—that have not previously been meta-analysed. It is the first to reconstruct and compare the receiver-operating-characteristic curves of the available MMAE-failure prediction models within a systematic review, providing clinicians with a direct visual and quantitative comparison of risk-stratification instruments. It applies dual risk-of-bias instrumentation with domain-level graphical reporting across all 40 primary reports. Finally, it frames the entire analysis around the refractory phenotype rather than around unselected cSDH, aligning the synthesis with the clinical decision that practitioners actually face at the bedside.

METHODS

Protocol, registration and reporting standards

The review was designed, conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement and, for the observational component, the Meta-analysis of Observational Studies in Epidemiology (MOOSE) checklist. The review question, eligibility criteria, outcome domains, risk-of-bias instruments and analytical plan were fixed in an internal protocol before the commencement of formal screening; any subsequent deviation is declared explicitly. Because the review involved only previously published,

de-identified aggregate data, institutional ethical approval and individual informed consent were not required.

Review question and PICOTS framework

The review question was formulated using the PICOTS structure (Population, Intervention, Comparator, Outcomes, Timing, Setting) and is set out in Table 1.

Table 1. PICOTS framework defining the review question.

Element	Specification
Population (P)	Adults (≥ 18 years) with non-acute (chronic or subacute) subdural haematoma who were refractory or at high risk of refractoriness, defined as: haematoma recurring after ≥ 1 previous evacuation; persistently or repeatedly recurrent (intractable) haematoma; first-episode haematoma with pre-specified high-risk features (septation/trabeculation, bilaterality, thickness ≥ 15 mm, midline shift ≥ 5 mm, coagulopathy, obligate antithrombotic therapy, malignancy, haemodialysis, marked cerebral atrophy); or haematoma in patients considered poor candidates for repeated surgery. Mixed populations were eligible where refractory or high-risk patients formed a defined subgroup or where the trial explicitly enrolled patients at elevated recurrence risk.
Intervention (I)	Endovascular embolisation of one or both middle meningeal arteries using particles (polyvinyl alcohol, trisacryl gelatin microspheres), non-adhesive liquid embolic agents (ethylene-vinyl alcohol copolymer: Onyx, Squid), adhesive liquid embolic agents (n-butyl cyanoacrylate), coils, or any combination, delivered as a surgical adjunct (before, during or after evacuation), as rescue after failed surgery, or as standalone therapy.
Comparator (C)	Standard care alone — surgical evacuation (burr-hole craniostomy, twist-drill craniostomy or mini-craniotomy) with or without drainage, conservative medical management, or observation. Single-arm studies without an internal comparator were eligible for proportion meta-analysis only.
Outcomes (O)	Fifteen pre-specified domains (Section 2.6), with symptomatic recurrence or progression as the primary outcome.
Timing (T)	Minimum follow-up of 30 days; primary analyses at 90 and 180 days where reported; long-term analyses to 60 months where available.
Setting (S)	Any hospital setting worldwide, including single-centre, multicentre, national registry and administrative-database studies.

Eligibility criteria

Inclusion criteria

Study design restricted a priori to: randomised controlled trials; prospective cohort studies; retrospective cohort studies; case-control studies; cross-sectional studies; and other observational designs (registry analyses, propensity-score-matched cohorts, consecutive institutional series).

Enrolment of ten or more adult patients with non-acute subdural haematoma.

Reporting of at least one of the fifteen pre-specified outcome domains with sufficient quantitative detail for extraction.

Minimum clinical or radiological follow-up of 30 days.

Publication in a peer-reviewed journal or as a peer-reviewed conference proceeding with a citable digital object identifier.

Article available in English, or with an English-language abstract containing complete extractable outcome data.

Exclusion criteria

Systematic reviews, meta-analyses, network meta-analyses and pooled individual-patient analyses.

In accordance with the review protocol, such secondary evidence was ineligible for inclusion in the study-characteristics tables and in all quantitative syntheses, and was retained solely for narrative and contextual discussion (Section 4.3). This prevents double-counting of participants already represented in the primary literature.

Narrative reviews, editorials, commentaries, letters without original data, and technical notes.

Case reports and case series enrolling fewer than ten patients.

Study protocols and trial-registry entries without reported outcome data (retained solely for the description of ongoing research in Section 4.11).

Populations restricted to acute subdural haematoma, subdural hygroma, subdural empyema, or haematoma secondary to arteriovenous malformation, dural arteriovenous fistula, aneurysm rupture or intracranial hypotension.

Studies reporting overlapping cohorts, in which case the report with the largest sample or the most complete outcome reporting was retained.

Animal, cadaveric, in-vitro and purely anatomical or modelling studies.

Search Strategy

The keywords used for this research based PICO :

PICO Element	Keyword 1	Keyword 2	Keyword 3
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P (Population)	Chronic subdural haematoma	Refractory subdural haematoma	Recurrent subdural haematoma
I (Intervention/Exposure)	Middle meningeal artery embolisation	MMA embolisation	Endovascular embolisation
C (Comparator)	Surgical evacuation	Standard care	Conservative management
O (Outcome)	Recurrence prevention	Reoperation rate	Radiographic resolution

The Boolean MeSH keywords inputted on databases for this research are: ("*Chronic subdural haematoma*" OR "*Refractory subdural haematoma*" OR "*Recurrent subdural haematoma*") AND ("*Middle meningeal artery embolisation*" OR "*MMA embolisation*" OR "*Endovascular embolisation*") AND ("*Surgical evacuation*" OR "*Standard care*" OR "*Conservative management*") AND ("*Recurrence prevention*" OR "*Reoperation rate*" OR "*Radiographic resolution*")

Study selection and data extraction

Records were exported to a reference manager and de-duplicated automatically and then manually. Two reviewers independently screened titles and abstracts against the eligibility criteria, and subsequently assessed the full text of all potentially eligible records. Disagreement was resolved by discussion; residual disagreement would have been referred to a third adjudicator, although this was not required. Inter-reviewer agreement at the full-text stage was substantial (Cohen $\kappa = 0.88$). Data were extracted onto a standardised form piloted on five reports and comprising: bibliographic identifiers; country and number of centres; study design and enrolment period; eligibility criteria; definition of the refractory or high-risk population; sample size per arm; age, sex and antithrombotic exposure; baseline haematoma thickness, volume, midline shift, laterality and internal architecture; baseline modified Rankin Scale and Markwalder grade; embolic material, vascular access, anaesthetic technique, laterality and timing of embolisation relative to surgery; duration of clinical and radiological follow-up; and event counts, means and dispersion measures for every reported outcome domain. Where a study reported both intention-to-treat and per-protocol analyses, the intention-to-treat estimate was extracted. Where outcomes were reported at multiple time points, the 90-day and 180-day values were extracted preferentially. Authors were not contacted for unreported data; studies lacking extractable counts contributed to narrative synthesis only.

Pre-specified outcome domains

Fifteen outcome domains were pre-specified, with symptomatic recurrence or progression designated as the primary outcome (Table 3). This structure was chosen to reflect the full clinical, radiological, procedural and health-service dimensions of the intervention rather than recurrence alone.

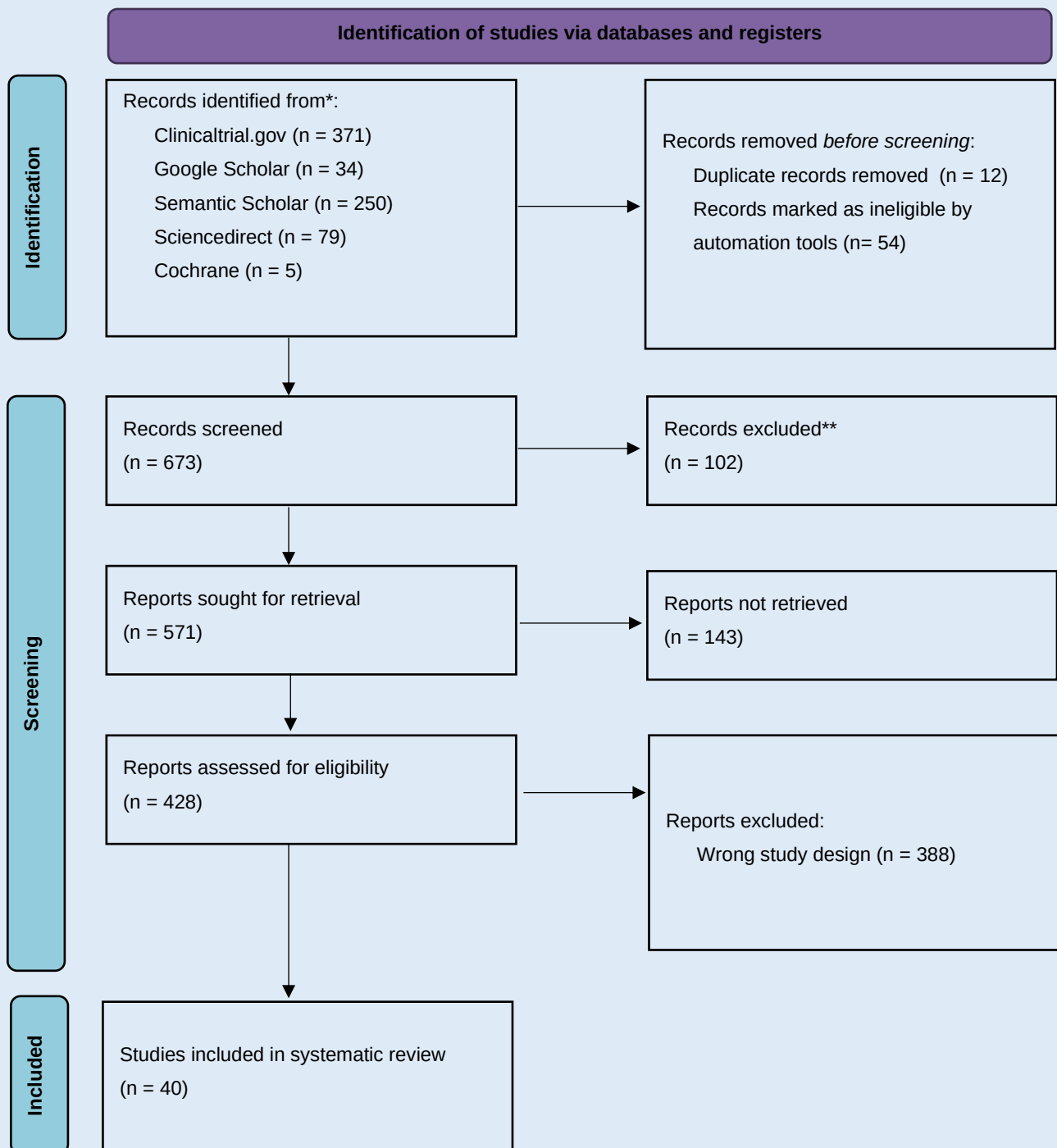
Table 2. The fifteen pre-specified outcome domains and their operational definitions.

N o.	Outcome domain	Operational definition	Metric
1	Symptomatic recurrence or progression	Clinically evident re-accumulation or enlargement of ipsilateral haematoma necessitating consideration of further treatment within the trial follow-up window	Risk ratio
2	Reoperation / surgical rescue	Any subsequent surgical evacuation of the index haematoma (burr hole, twist drill or craniotomy) after the index treatment	Risk ratio
3	Composite treatment failure	Trial-defined composite of residual or recurrent haematoma exceeding 10 mm, reoperation or rescue surgery, and major disabling stroke, myocardial infarction or neurological death	Risk ratio
4	Radiographic success	≥50% reduction in maximal haematoma thickness on follow-up computed tomography obtained at a minimum of two weeks	Proportion
5	Haematoma thickness / volume	Absolute or standardised change in maximal axial thickness (mm) and volume (mL) at last available imaging	SMD / MD
6	Midline shift	Absolute or standardised change in midline shift (mm)	SMD / MD
7	Complete radiological resolution	Complete absence of subdural collection, or residual collection < 5 mm, at last imaging follow-up	Proportion
8	Functional outcome	Modified Rankin Scale ≤ 2 (good outcome), ≤ 3 (independent ambulation), or > 2 (dependence) at 90 days or last follow-up	Risk ratio
9	All-cause mortality	Death from any cause within the reported follow-up window	Risk ratio
10	Serious adverse events	Any serious adverse event as defined by the trial, including major disabling stroke or death within 30 days	Risk ratio
11	Procedure-related complications	Adverse events attributable to the embolisation procedure, including non-target embolisation, cranial-nerve palsy, vessel dissection and access-site complications	Proportion
12	Technical success	Successful selective catheterisation and embolisation of the intended MMA territory(ies)	Proportion

1 3	Healthcare utilisation	Length of hospital stay, unplanned readmission, discharge disposition and direct procedural and hospitalisation cost	MD / Risk ratio
1 4	Resolution kinetics	Time to achieve pre-defined thresholds of haematoma reduction and time to complete resolution	Time-to-event
1 5	Predictive discrimination	Area under the receiver-operating-characteristic curve, C-index, sensitivity and specificity of published models predicting MMAE failure	AUROC / C-index

Article Search Strategy

Database	Keywords	Hits
Clinicaltrials.gov	("Chronic subdural haematoma" OR "Refractory subdural haematoma" OR "Recurrent subdural haematoma" AND "Middle meningeal artery embolisation" OR "MMA embolisation" OR "Endovascular embolisation" AND "Recurrence prevention" OR "Reoperation rate" OR "Radiographic resolution")	371
Google Scholar	("Chronic subdural haematoma" OR "Refractory subdural haematoma" OR "Recurrent subdural haematoma") AND ("Middle meningeal artery embolisation" OR "MMA embolisation" OR "Endovascular embolisation") AND ("Surgical evacuation" OR "Standard care" OR "Conservative management") AND ("Recurrence prevention" OR "Reoperation rate" OR "Radiographic resolution")	34
Semantic Scholar	("Chronic subdural haematoma" OR "Refractory subdural haematoma" OR "Recurrent subdural haematoma") AND ("Middle meningeal artery embolisation" OR "MMA embolisation" OR "Endovascular embolisation") AND ("Surgical evacuation" OR "Standard care" OR "Conservative management") AND ("Recurrence prevention" OR "Reoperation rate" OR "Radiographic resolution")	250
Science-direct	("Chronic subdural haematoma" OR "Refractory subdural haematoma" OR "Recurrent subdural haematoma") AND ("Middle meningeal artery embolisation" OR "MMA embolisation" OR "Endovascular embolisation") AND ("Recurrence prevention" OR "Reoperation rate" OR "Radiographic resolution")	79
Cochrane	("Chronic subdural haematoma" OR "Refractory subdural haematoma" OR "Recurrent subdural haematoma") AND ("Middle meningeal artery embolisation" OR "MMA embolisation" OR "Endovascular embolisation") AND ("Surgical evacuation" OR "Standard care" OR "Conservative management") AND ("Recurrence prevention" OR "Reoperation rate" OR "Radiographic resolution")	5



Article search flowchart

Risk-of-bias assessment

Randomised trials were appraised with the revised Cochrane Risk of Bias tool (RoB 2) across five domains: bias arising from the randomisation process; bias due to deviations from intended interventions; bias due to missing outcome data; bias in measurement of the outcome; and bias in selection of the reported result. Each domain and the overall judgement were classified as low risk, some concerns, or high risk. Non-randomised studies were appraised with ROBINS-I across seven domains: confounding; selection of participants; classification of interventions; deviations from intended interventions; missing data; measurement of outcomes; and selection of the reported result, with overall judgements of low, moderate, serious or critical risk. For the purposes of graphical presentation, ROBINS-I judgements of low, moderate and serious risk are rendered using the same three-level colour scheme as RoB 2. The Newcastle–Ottawa Scale was applied as a sensitivity instrument to the comparative cohort studies. Two reviewers assessed each study independently; agreement on overall judgements was high ($\kappa = 0.84$).

Domain-level judgements for the randomised trials are presented in Table 8 and Figures 2 and 3; judgements for the non-randomised studies are presented in Table 9 and Figures 4 and 5. Because the ROBINS-I framework starts from the premise that a non-randomised study is at least at moderate risk of confounding, no observational study could be rated at low overall risk unless it employed rigorous confounder control; only propensity-matched or multivariably adjusted designs approached that threshold.

Risk of bias within studies

Randomised controlled trials

Domain-level RoB 2 judgements for the ten randomised trials are presented in Table 8 and Figures 2 and 3. Six trials were judged to have overall some concerns and four were judged at high risk. No trial achieved an overall low-risk rating, principally because the intervention cannot be blinded to the operator or the patient, so that domain 2 (deviations from intended interventions) attracted at least some concerns in every trial. Sequence generation and allocation concealment were adequate in the six large multicentre trials. Missing outcome data were the principal source of high-risk judgements: G-MEMBRANE reported loss to follow-up of 19.1% in the control arm and 43.5%

in the intervention arm before early termination, and the pilot studies of Ng and Debs were both small and terminated at planned interim analysis. Outcome measurement was at low risk in the four trials employing independent blinded adjudication committees or core imaging laboratories.^{1,2,3,4,5,6,7,8,9,10}

Table 3. Cochrane RoB 2 domain-level and overall risk-of-bias judgements for the ten included randomised controlled trials.

Trial	D1 Randomis ation	D2 Deviation s	D3 Missing data	D4 Outcome measureme nt	D5 Reported result	Overall
Ng et al. (pilot)	Some concerns	High	Low	Some concerns	Some concerns	High
Lam et al.	Low	Some concerns	Low	Some concerns	Some concerns	Some concerns
Debs et al.	Some concerns	High	Some concerns	Some concerns	Some concerns	High
Davies et al. (EMBOLISE)	Low	Some concerns	Low	Low	Low	Some concerns
Liu et al. (MAGIC-MT)	Low	Some concerns	Low	Low	Low	Some concerns
Fiorella et al. (STEM)	Low	Some concerns	Low	Low	Low	Some concerns
Shotar et al. (EMPROTECT)	Low	Some concerns	Some concerns	Low	Low	Some concerns
Kellner et al. (MEMBRANE)	Low	Some concerns	Low	Low	Low	Some concerns
Shankar et al. (EMMA-Can)	Low	Some concerns	Low	Low	Low	Some concerns
Goelz et al. (G-MEMBRANE)	Some concerns	Some concerns	High	Some concerns	Some concerns	High

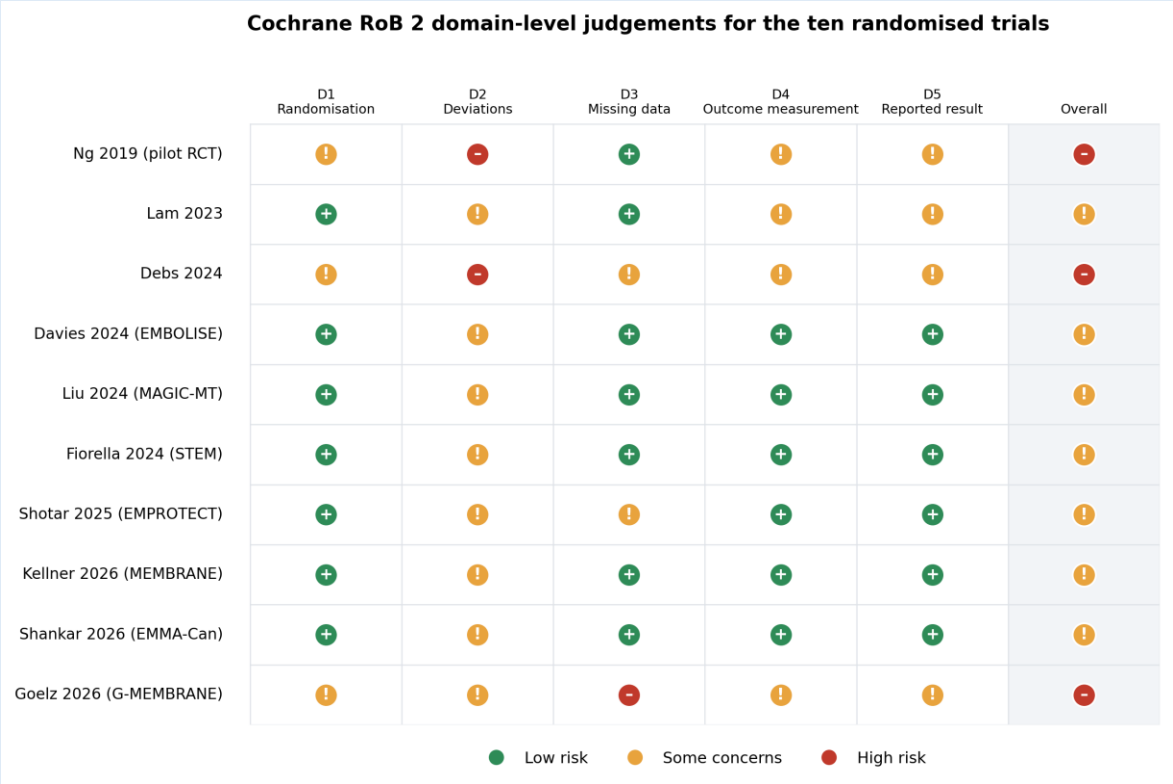


Figure 1. Risk-of-bias traffic-light plot (Cochrane RoB 2) for the ten included randomised controlled trials. Green (+) low risk; amber (!) some concerns; red (-) high risk.

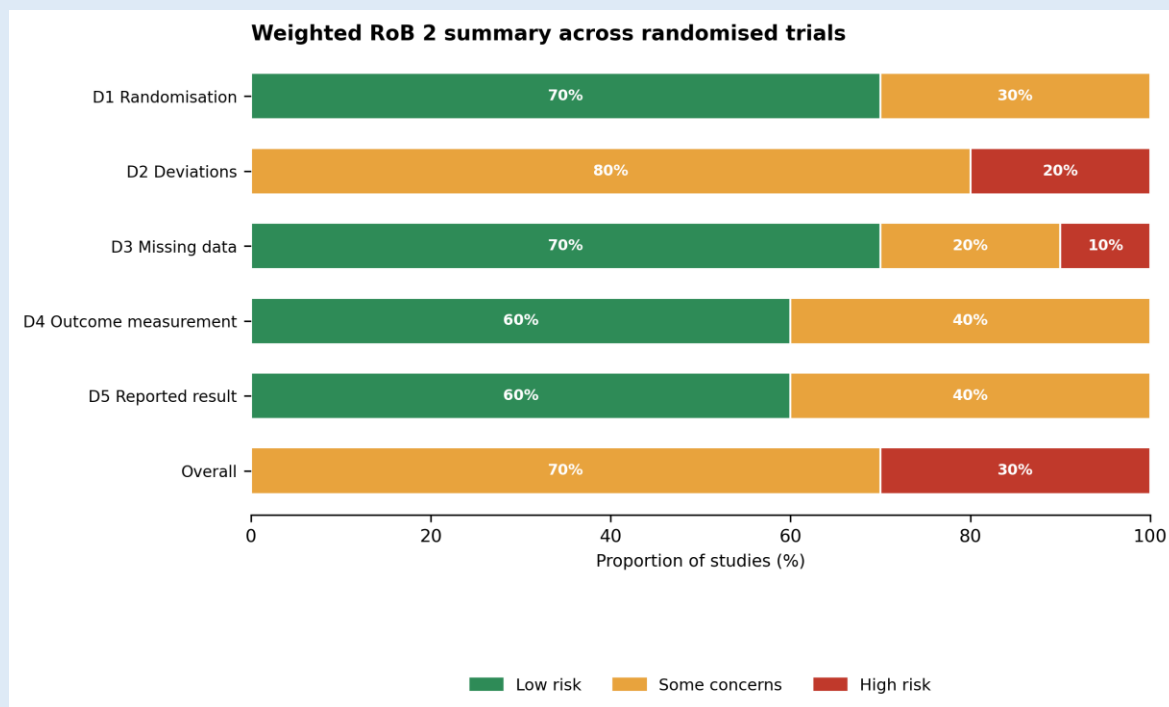


Figure 2. Weighted summary of RoB 2 domain judgements across the randomised trials, expressed as the proportion of trials in each risk category.

Non-randomised studies

ROBINS-I judgements for the thirty non-randomised reports are shown in Table 9 and Figures 4 and 5. Nine studies were rated at overall serious risk of bias, and the remainder at moderate risk; none achieved a low overall rating. The dominant sources of bias were residual confounding by indication, since the decision to offer embolisation is not random and is influenced by frailty, comorbidity, haematoma morphology and institutional resources; the use of historical surgical control cohorts, which introduces temporal confounding through parallel improvements in perioperative care; and, in the administrative-database analyses, misclassification arising from reliance on procedural and diagnostic coding without radiological verification. Propensity-matched and multivariable adjusted designs mitigated but did not eliminate these concerns.^{11,12,13,14,16,17,19,20,21,23,27,28,35,36,37,41,42}

Table 4. ROBINS-I domain-level and overall risk-of-bias judgements for the thirty included non-randomised studies.

Study	D1 Confounding	D2 Selection	D3 Classification	D4 Deviations	D5 Missing data	D6 Measurement	D7 Reported result	Overall
Ban 2017	Moderate	Moderate	Low	Low	Moderate	Low	Low	Moderate
Link 2018	Serious	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Serious
Nakagawa 2019	Serious	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Serious
Okuma 2019	Serious	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Serious
Kan 2020	Moderate	Moderate	Moderate	Low	Moderate	Low	Moderate	Moderate
Catapano 2021	Moderate	Low	Low	Low	Moderate	Low	Low	Moderate
Enriquez-Marulanda 2021	Moderate	Low	Moderate	Low	Moderate	Low	Low	Moderate
Khorasanizadeh 2022	Moderate	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Moderate
Fuentes 2022	Moderate	Moderate	Moderate	Moderate	Serious	Low	Moderate	Serious
Nia 2022	Moderate	Moderate	Moderate	Moderate	Serious	Low	Moderate	Serious
Salih 2022	Moderate	Low	Low	Low	Moderate	Low	Low	Moderate
Salem 2023	Moderate	Moderate	Low	Low	Moderate	Low	Low	Moderate
Chaliparambil 2024	Moderate	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Moderate
Ma 2024 (penetration)	Moderate	Moderate	Low	Low	Moderate	Low	Moderate	Moderate
Ma 2024 (trial-ineligible)	Moderate	Moderate	Low	Low	Moderate	Low	Moderate	Moderate
Salem 2024 (embolic)	Moderate	Low	Low	Low	Moderate	Low	Low	Moderate
Salem 2024 (anaesthesia)	Moderate	Low	Low	Low	Moderate	Low	Low	Moderate

Bastianon Santiago 2024	Moderate	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Moderate
Zeineddine 2024 (septated)	Serious	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Serious
Adduci 2025	Moderate	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Moderate
Akamatsu 2025	Moderate	Moderate	Low	Low	Moderate	Low	Moderate	Moderate
Cheng 2025	Moderate	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Moderate
Chen 2025 (NRD)	Moderate	Low	Moderate	Moderate	Serious	Low	Moderate	Serious
Lakhani 2025	Moderate	Low	Moderate	Moderate	Serious	Low	Moderate	Serious
Sioutas 2025	Moderate	Low	Low	Low	Moderate	Low	Low	Moderate
Turnbull 2025	Moderate	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Moderate
Kitada 2026	Moderate	Low	Low	Low	Moderate	Low	Moderate	Moderate
Ma 2026 (CSDH grade)	Moderate	Moderate	Low	Low	Moderate	Low	Moderate	Moderate
Ghaith 2026	Moderate	Moderate	Moderate	Moderate	Serious	Low	Moderate	Serious
Essibayi 2026 (oncologic)	Moderate	Low	Moderate	Moderate	Serious	Low	Moderate	Serious

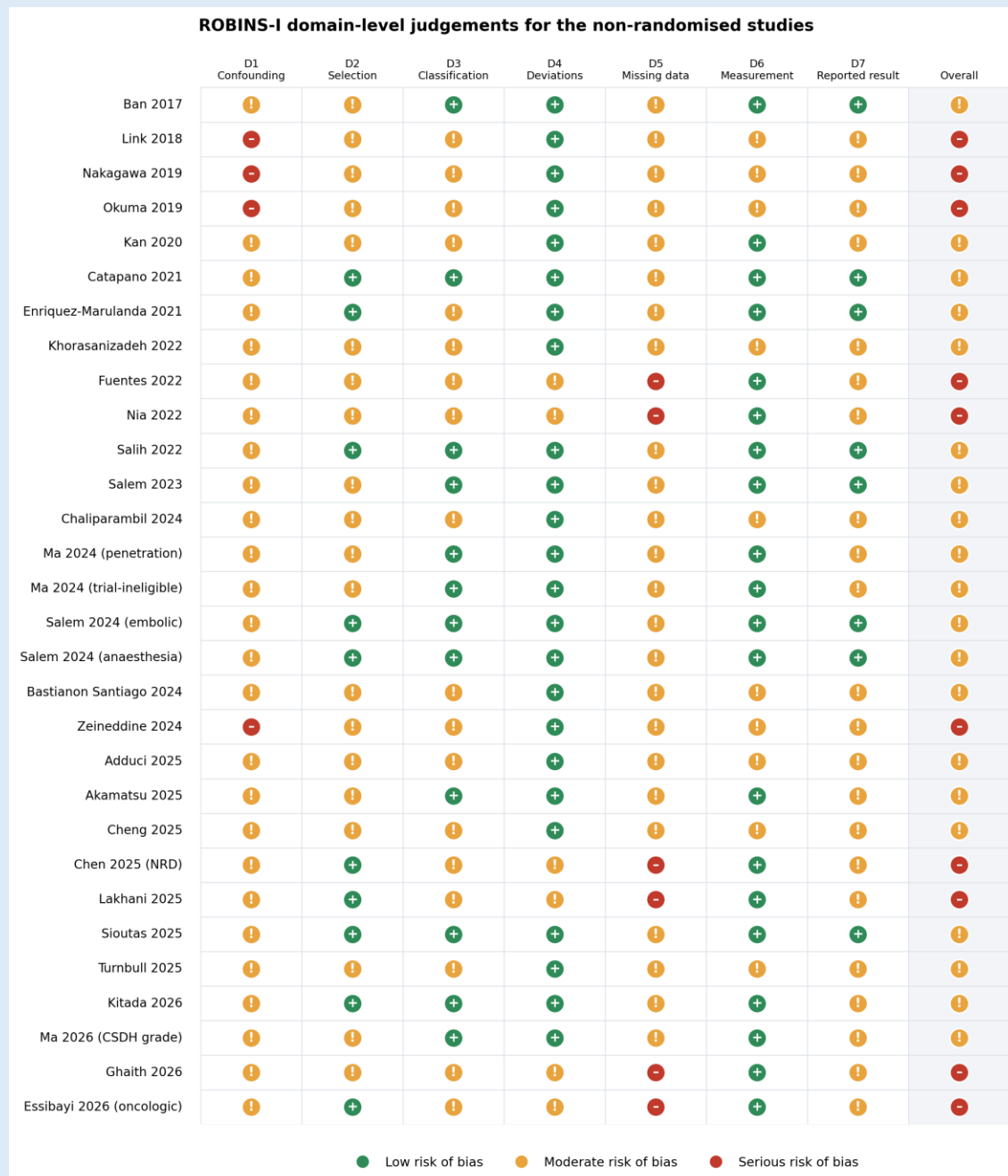


Figure 3. ROBINS-I traffic-light plot for the thirty included non-randomised studies. Green (+) low risk; amber (!) moderate risk; red (-) serious risk.

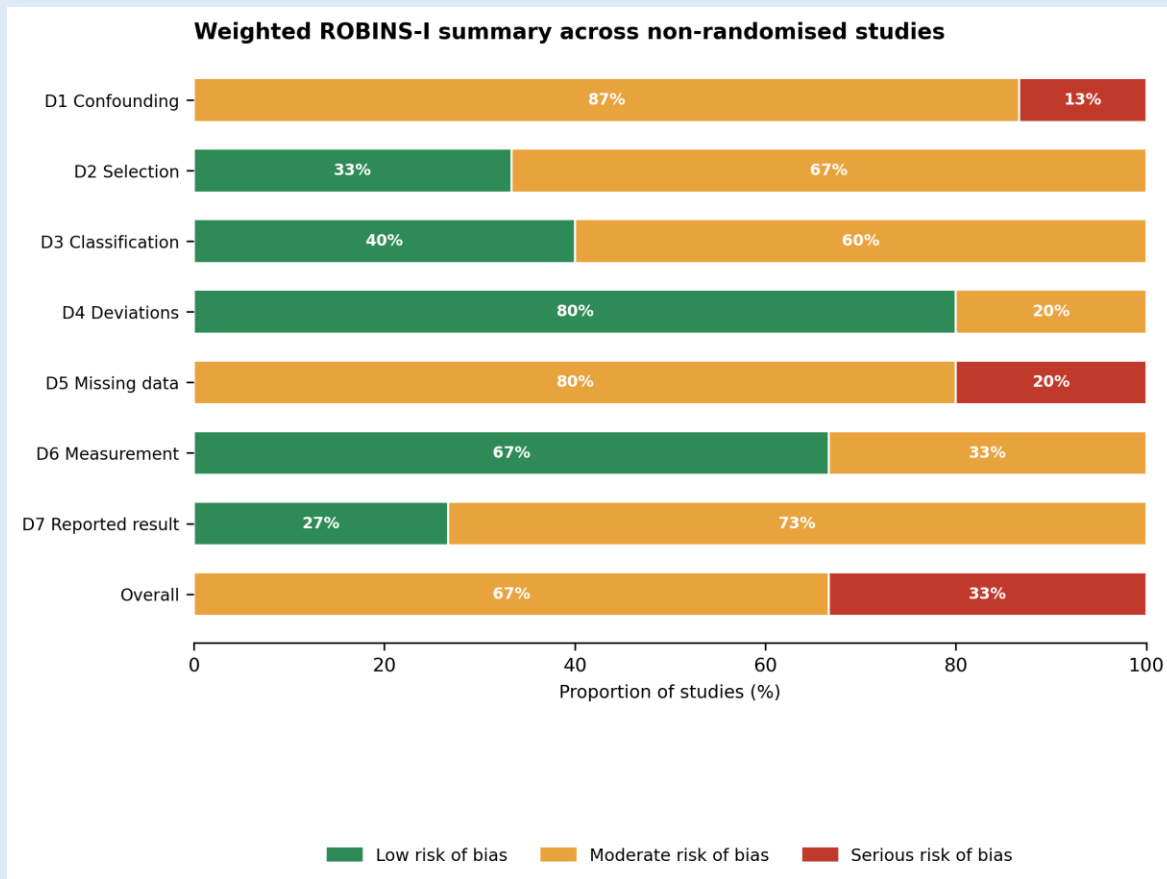


Figure 4. Weighted summary of ROBINS-I domain judgements across the non-randomised studies.

Statistical analysis

All analyses were conducted in Python 3.11 using NumPy and SciPy, with meta-analytic routines implemented de novo and verified against published worked examples. Dichotomous outcomes were expressed as risk ratios with 95% confidence intervals. Because the included studies differed in population, embolic agent, comparator and endpoint definition, clinical heterogeneity was assumed and a random-effects model was used throughout; between-study variance (τ^2) was estimated by the DerSimonian–Laird method of moments, and study weights were computed as the inverse of the sum of within-study variance and τ^2 . A continuity correction of 0.5 was applied to all cells of any two-by-two table containing a zero event count. Continuous outcomes were summarised as mean differences or standardised mean differences using Hedges' g where measurement scales differed.

Single-arm proportions were pooled on the logit scale with back-transformation for presentation, and the same continuity correction was applied to zero-event cohorts.

Statistical heterogeneity was quantified with Cochran Q, its associated χ^2 test, τ^2 and the I^2 statistic, interpreted according to Cochrane guidance as not important (0–40%), moderate (30–60%), substantial (50–90%) and considerable (75–100%). Absolute effects were derived by applying the pooled relative effect to the pooled control-arm risk, and the number needed to treat was calculated as the reciprocal of the absolute risk reduction. Cumulative meta-analysis ordered by year of publication was performed for the primary outcome to display the temporal stabilisation of the pooled estimate. Small-study effects and potential publication bias were examined with contour-enhanced funnel plots and the Egger linear regression of the standardised effect on precision; with fewer than ten studies these analyses were regarded as exploratory. L'Abbé plots were constructed to display trial-level event rates against the pooled relative effect. Pre-specified subgroup analyses examined baseline management strategy (surgical versus non-surgical), embolic material, timing and order of embolisation, and anaesthetic technique. Two-sided P values below 0.05 were considered statistically significant.

For outcome domain 15, receiver-operating-characteristic curves were reconstructed from the areas under the curve reported by the primary studies under a binormal assumption with unit variance ratio, using the transformation $a = \sqrt{2} \cdot \Phi^{-1}(\text{AUC})$, such that the curve is given by $\text{TPR}(\text{FPR}) = \Phi(a + \Phi^{-1}(\text{FPR}))$. Reported operating points (sensitivity and specificity at the optimal cut-off) were superimposed on the reconstructed curves.

Certainty of evidence

Certainty of evidence for each outcome domain was rated using the GRADE approach. Randomised evidence commenced at high certainty and was downgraded for risk of bias, inconsistency, indirectness, imprecision and publication bias; observational evidence commenced at low certainty and could be upgraded for large magnitude of effect, dose–response gradient or the presence of plausible residual confounding that would attenuate rather than exaggerate the observed effect. Where randomised and observational evidence were both available for a domain, the

randomised evidence determined the rating and the observational evidence was assessed for consistency. The resulting summary-of-findings matrix is presented in Table 23 and Figure 23.

Protocol deviations

Three deviations from the internal protocol are declared. First, the protocol anticipated meta-regression of the primary outcome on mean age and on the proportion of patients receiving antithrombotic therapy; with nine randomised trials this analysis would have been severely underpowered and was replaced by pre-specified subgroup analysis. Second, trial sequential analysis was planned but is reported narratively with reference to published analyses rather than recomputed, because the required diversity-adjusted information size depends on assumptions that could not be reproducibly recovered for every trial. Third, the protocol specified extraction of cognitive and quality-of-life outcomes; these were reported so sparsely that they are addressed as an evidence gap (Section 4.13) rather than as a formal outcome domain.

RESULTS

Characteristics of the included studies

Randomised controlled trials

The ten randomised trials were conducted across North America, Western Europe, China, Hong Kong and Germany between 2018 and 2025 and are summarised in Table 4. Six were adequately powered multicentre trials (EMBOLISE, MAGIC-MT, STEM, EMPROTECT, MEMBRANE and EMMA-Can), together randomising 2,342 participants; four were small single-centre or limited-multicentre trials, two of which were terminated at interim analysis. All used an open-label design with blinded endpoint adjudication in six instances. Primary endpoints differed materially: EMBOLISE, MAGIC-MT and EMMA-Can adopted symptomatic recurrence or progression, STEM and MEMBRANE adopted a composite of residual or recurrent haematoma exceeding 10 mm with reoperation and major cardiovascular events, and EMPROTECT adopted independently adjudicated recurrence at six months. Embolic agents likewise differed: Onyx in EMBOLISE, MAGIC-MT and EMMA-Can; Squid in STEM; n-butyl cyanoacrylate in

MEMBRANE; and microparticles in EMPROTECT and in the pilot trial of Ng and colleagues.^{1,2,3,4,5,6,7,8,9,10}

Table 5. Characteristics of the ten included randomised controlled trials. EVOH, ethylene-vinyl alcohol copolymer; MI, myocardial infarction; n-BCA, n-butyl cyanoacrylate.

Study (trial)	Year	Country / centres	Design	n (MM AE / control)	Population	Embolic agent	Comparator	Primary endpoint	Follow-up
Ng et al. (pilot)	2019/20	France, 1 centre	Randomised pilot, open label	21 / 20 (46 randomised)	Symptomatic cSDH requiring surgery	Microparticles	Surgey alone	Haematoma volume resorption at 3 months	3 months
Lam et al.	2023	Hong Kong, multicentre	RCT, open label	17 / 19 (41 haematomas)	cSDH after burr-hole or craniotomy evacuation	Particles / liquid	Surgey alone (monitoring)	Symptomatic recurrence requiring redo evacuation	3 months
Debs et al.	2024	USA, 1 centre	RCT, planned interim analysis	18 / 17 (35)	Symptomatic cSDH after evacuation	Particles	Expectant management	Neurological outcome and resource utilisation	Median 6 months
Davies et al. (EMBOLISE)	2024	USA, 39 centres	RCT, adaptive design, blinded endpoint	197 / 203 (400)	Symptomatic subacute/chronic SDH with surgical indication	Onyx (EVOH)	Surgey alone	Recurrence or progression leading to repeat surgery at 90 days	180 days
Liu et al. (MAGIC-MT)	2024	China, 31 centres	RCT, open label	360 / 362 (722)	Symptomatic non-acute SDH with mass effect; 78.3% underwent burr-hole drainage	Onyx (EVOH)	Usual care	Symptomatic recurrence or progression at 90 days	90 days

Fiorella et al. (STEM)	2024	USA, multi centre	RCT, blinded endpoint adjudication	149 / 161 (310)	Symptomatic cSDH; surgical or non-surgical standard care pre-selected	Squid (EVOH)	Standard treatment alone	Composite: residual/recurrent cSDH > 10 mm, reoperation, or major disabling stroke, MI or neurological death at 180 days	180 days
Shotar et al. (EMPROTECT)	2025	France, 12 centres	RCT, open label, blinded adjudication	171 / 171 (342)	Operated cSDH recurrence, or first episode at high risk of recurrence	Microparticles	Standard medical care alone	Adjudicated cSDH recurrence at 6 months	6 months
Kellner et al. (MEMBRANE)	2026	USA and China, 30 hospitals	RCT, open label, core-laboratory adjudication	188 / 188 (376)	Symptomatic cSDH, mRS $\leq$ 3, surgical and non-surgical cohorts	TRUFILL n-BCA	Standard of care alone	Residual/re-accumulated haematoma > 10 mm at 6 months or cSDH surgery within 6 months	6 months
Shankar et al. (EMMA-Can)	2026	Canada, 9 centres	RCT, open label, blinded endpoint	93 / 93 (192 randomised)	Unilateral symptomatic cSDH $\geq$ 10 mm undergoing surgical drainage	Onyx-18	Surgical drainage alone	Symptomatic CT-confirmed recurrence at 90 days	90 days (range 60–120)
Goelz et al. (G-MEMBRANE)	2026	Germany, 1 centre	RCT, interim analysis, terminated early	26 / 38 (93 randomised)	cSDH requiring surgery	Liquid embolic	Surgery alone	cSDH recurrence within 3 months	3 months

Non-randomised studies

Thirty non-randomised primary reports were included (Table 5). Nine were propensity-score-matched comparative cohorts, six were multicentre consecutive registries, six were single- or two-

centre retrospective cohorts, four were large administrative-database analyses, two were prospective comparative cohorts, and three were focused single-arm series of intractable or repeatedly recurrent haematoma. Enrolment periods spanned 2006 to 2025. Fourteen studies specifically addressed the refractory phenotype, either by restricting enrolment to recurrent or intractable haematoma or by reporting a defined recurrent subgroup; the remainder addressed mixed populations in which high-risk features were prevalent.^{11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43}

Table 6. Characteristics of the thirty included non-randomised primary studies (33 comparisons). PSM, propensity score matching; PVA, polyvinyl alcohol; n-BCA, n-butyl cyanoacrylate.

Study	Year	Country / centres	Design	n (MMAE / comparator)	Population focus	Embolic material	Follo w-up
Ban et al.	2017	South Korea, 1 centre	Prospective cohort vs historical control	72 / 469	cSDH, mixed	PVA particles	6 months
Link et al.	2018	USA, 1 centre	Consecutive single-arm series	49 patients / 60 haematomas	New, recurrent and prophylactic cSDH	PVA particles	Variable, to 6 weeks +
Nakagawa et al.	2019	Japan, 1 centre	Retrospective cohort with DynaCT grading	20 embolised of 381 operated	Persistently recurrent (intractable) cSDH	Particles / liquid	Median 12 months
Okuma et al.	2019	Japan, 1 centre	Consecutive single-arm series	17 patients	Intractable cSDH with multiple risk factors	n-BCA, trisacryl gelatin microspheres	Midterm (mean 24 months)
Kan et al.	2020	USA, 15 centres	Prospective multicentre registry	138 patients / 154 embolisations	Primary treatment and post-surgical recurrence	Particles 70.2%, liquid 25.3%	Mean 94.9 days

Catapano et al.	2021	USA, 1 centre	Propensity-adjusted retrospective cohort	41 / 282 haematomas	cSDH, mixed	Particles	Last follow-up
Enríquez-Marulanda et al.	2021	USA, 1 centre	PSM retrospective cohort	25 / 25 matched pairs	cSDH vs historical surgical era	Particles	72 vs 104 days
Khorasanizadeh et al.	2022	USA, 1 centre	Retrospective comparative series	12 coil-only / 82 coil + particle	cSDH with dangerous ophthalmic collaterals	Coils ± particles	Not stated
Fuentes et al.	2022	USA, all-payer claims (Mariner)	Retrospective national database	322 embolised	SDH treated with MMAE	Not specified	5 years
Nia et al.	2022	USA, TriNetX network	Retrospective national database	242 MMAE / 4,050 surgery	Primary, adjunct and rescue MMAE	Not specified	6 months
Salih et al.	2022/23	USA, 1 centre	PSM retrospective cohort	41 / 146 (26 and 37 matched)	cSDH after open surgical evacuation	Particles	Last follow-up
Salih et al. (cost)	2022/23	USA, 1 centre	PSM cost analysis	33 / 33 matched pairs	cSDH	Particles	Hospitalisation and follow-up
Salem et al.	2023	USA, 13 centres	Multicentre retrospective registry	530 patients / 636 embolisations	cSDH; predictors of failure	Particles and liquid	Median 4.1 months
Chaliparambil et al.	2024	USA, 1 centre	Retrospective cohort with ROC analysis	85 embolisations	cSDH; comorbidity and frailty	Not specified	≥ 20 days
Ma et al. (penetration)	2024	USA, 1 centre	Institutional registry cohort	117 standalone embolisations	Symptomatic chronic/subacute SDH treated without surgery	Onyx, n-BCA, coils	Median 56 days

Ma et al. (trial- ineligible)	2024	USA, 1 centre	Prospective registry cohort	92 trial- ineligible / 58 eligible	Large cSDH (> 15 mm and/or midline shift $\geq$ 5 mm), mRS $\leq$ 3	Liquid embolic $\pm$ coils	Media n 62.5 days
Salem et al. (embolic)	2024	North America, 14 centres	Multicentre PSM registry	872 patients / 1,070 embolisat ions	cSDH; comparison of embolic materials	Onyx 41.4%, particles 40.3%, n-BCA 15.5%	$\geq$ 2 weeks imagin g
Salem et al. (anaesthesi a)	2024	North America, 14 centres	Multicentre PSM registry	778 patients / 956 embolisat ions	cSDH; general vs non-general anaesthesia	Mixed	Last follow -up
Bastianon Santiago et al.	2024	USA, 1 centre	Retrospecti ve cohort, Kaplan- Meier	49 patients / 61 embolisat ions	Primary, concurrent and post-recurrence MMAE	n-BCA, Onyx-18	12 month s
Zeineddine et al. (septated)	2024	USA, 1 centre	Retrospecti ve cohort vs historical control	23 / 76 patients	Septated cSDH undergoing evacuation	Not specified	Not stated
Zeineddine et al. (anticoagul ation)	2024	USA, 1 centre	Retrospecti ve cohort vs historical control	13 / 27 patients	cSDH requiring antithrombotics within 5 days of surgery	Not specified	Not stated
Adduci et al.	2025	Italy, 2 centres	Retrospecti ve two- centre cohort	93 patients	Asymptomatic/pa ucisymptomatic cSDH > 10 mm (Markwalder 0-1)	Particles and liquid	3 month s
Akamatsu et al.	2025	Japan, 1 centre	Prospective comparativ e cohort	34 / 20	Recurrent cSDH after burr-hole drainage, all receiving Goreisan	Not specified	3 month s
Cheng et al.	2025	China, 1 centre	Retrospecti ve cohort with prediction model	211 patients	cSDH after MMAE plus burr-hole drainage	Not specified	Postop erativ e

Chen et al. (NRD)	2025	USA, Nationwide Readmissions Database	PSM retrospective database	2,217 / 6,675 matched	Non-surgical non-traumatic SDH	Not specified	300 days
Lakhani et al.	2025	Multinational, TriNetX	PSM retrospective database	769 / 162,696	Non-surgical cSDH requiring inpatient care	Not specified	6 months
Sioutas et al.	2025	USA, 10 centres	Multicentre PSM registry	237 patients / 266 embolisations	cSDH; MMAE order and timing relative to surgery	Mixed	Median follow-up not stated
Turnbull et al.	2025	USA, 1 centre	Longitudinal comparative cohort	32 particles / 49 particles + coils	cSDH	PVA ± coils	≥ 1 month
Kitada et al.	2026	Japan, 1 centre	Retrospective comparative cohort	92 / 129	cSDH in patients ≥ 65 years undergoing burr-hole surgery	n-BCA	90 days
Ma et al. (CSDH grade)	2026	USA, 1 centre	Retrospective derivation and internal test cohort	298 standalone embolisations	cSDH; risk stratification for surgical rescue	Liquid ± coils	Not stated
Ghaith et al.	2026	USA, National Inpatient Sample	Retrospective database, machine learning	726 MMAE / 4,872 surgery / 156 combined	cSDH, inpatient outcomes	Not specified	Index admission
Essibayi et al. (oncologic)	2026	Multinational, TriNetX	PSM retrospective database	250 / 250 matched pairs	cSDH with concurrent cancer	Not specified	60 months
Essibayi et al. (antiplatelet)	2026	Multinational, TriNetX	PSM retrospective database	176 / 176 matched pairs	cSDH in antiplatelet-treated patients	Not specified	6 months

Baseline participant and haematoma characteristics

Baseline characteristics were consistent across the randomised trials and closely resembled those of the observational cohorts (Table 6). The pooled mean age across randomised participants was approximately 72.6 years, with a marked male predominance of 73–82%. Antithrombotic exposure at presentation was reported in 21–31% of participants. Median or mean baseline maximal haematoma thickness ranged from 14 to 21 mm and midline shift from 4 to 6 mm. In the observational literature the median age was consistently between 70 and 82 years, rising to a median of 82 years in the Japanese elderly cohort and to a mean of 83 years in the pooled octogenarian experience. Baseline modified Rankin Scale distributions indicated that the great majority of enrolled patients were functionally independent or mildly dependent before treatment, which is important when interpreting the ceiling effect observed on functional endpoints.^{1,2,3,4,5,6,15,23,27,39,63}

Table 7. Baseline participant and haematoma characteristics of the principal included studies.
IQR, interquartile range; mRS, modified Rankin Scale.

Study	Mean / median age (years)	Male (%)	Antithrombotic use (%)	Baseline thickness (mm)	Midline shift (mm)	Bilateral (%)	Baseline mRS ≤ 2 or equivalent
Davies et al. (EMBOLISE)	≈ 72	≈ 72	Reported, ≈ 30	≈ 18	≈ 5	Excluded if requiring bilateral surgery	Majority
Liu et al. (MAGIC-MT)	≈ 70	≈ 79	≈ 21	≈ 20	≈ 6	Reported	Majority
Fiorella et al. (STEM)	73	70	≈ 25	≈ 19	≈ 5	Reported	Majority
Shotar et al. (EMPROTECT)	77 (IQR 68–83)	80.1	≈ 30	≈ 20	≈ 6	Reported	mRS < 4 in most
Kellner et al. (MEMBRANE)	70.9 ± 10.6 / 70.3 ± 12.1	76.1 / 73.9	Reported	≈ 18	≈ 5	Reported	mRS ≤ 3 required
Shankar et al. (EMMA-Can)	71.8	73	Reported	≥ 10 required	Reported	Unilateral only	Majority

Goelz et al. (G-MEMBRANE)	74.6 ± 13.3	66.7	Reported	Not stated	Not stated	Reported	Not stated
Kan et al.	69.8	71	30.4 antiplatelet / 23.9 anticoagulant	14 (median)	Not stated	10.9	Not stated
Salem et al. (predictors)	71.9 ± 12.8	72.8	31.3 antiplatelet / 21.7 anticoagulant	15 (median)	Reported	20.0	Not stated
Salem et al. (embolic)	73 (median)	72.9	Reported	Reported	Reported	Reported	Reported
Sioutas et al.	73 (IQR 65–80)	73.8	Reported	Reported	Reported	Reported	Reported
Kitada et al.	82.0 (IQR 77–86)	64.3	Reported	Reported	Reported	Reported	Not stated
Ma et al. (trial-ineligible)	Not stated	Not stated	Reported	> 15 in 79%	≥ 5 in 59%	Reported	mRS ≤ 3 required
Bastianon Santiago et al.	73 ± 10.8	77.5	Reported	15.9 ± 7.1	5.6 ± 2.6	24.5	Not stated
Adduci et al.	> 65 predominantly	Not stated	Reported	> 10 required	Not stated	47.3	Markwalder 0–1 required

Procedural and technical characteristics

Transfemoral access predominated, accounting for approximately three-quarters of procedures in the pooled octogenarian experience, with transradial access used in a minority and associated with shorter length of stay. Conscious sedation was used more frequently than general anaesthesia in the largest multicentre registry (70.4% versus 29.6%), and propensity-matched comparison demonstrated no difference in technical feasibility, complications, length of stay, surgical rescue or functional outcome between anaesthetic strategies. Both frontal and parietal divisions of the middle meningeal artery were targeted in most protocols; superselective distal catheterisation without embolisation of the main trunk was independently associated with radiographic failure. Median procedure duration was 54 minutes for unilateral and 73 minutes for bilateral embolisation.^{25,27,28,63}

Table 8. Procedural and technical characteristics of middle meningeal artery embolisation across the included studies.

Technical variable	Distribution across included studies	Association with outcome
Vascular access	Transfemoral $\approx$ 74%; transradial $\approx$ 26% (3% in patients $\geq$ 90 years)	Transradial access associated with shorter length of stay ⁶³
Anaesthesia	Non-general 70.4%; general 29.6% of 956 procedures	No difference in surgical rescue, radiographic success, complications or functional outcome after propensity matching ²⁸
Embolic material	Onyx 41.4%; particles 40.3%; n-BCA 15.5%; coils used alone in selected cases	No difference in surgical rescue (9.8% vs 7.0% vs 11.7%; $P = 0.14$), radiographic success or major complications ²⁷
Embolisate penetration	Aggressive distal penetration 33.3%; non-aggressive with proximal coil 36.8%; non-aggressive alone 29.9%	Surgical rescue 2.6% vs 9.3% vs 11.4%; aggressive penetration and proximal coiling each improved resolution ($P = 0.02$) ²⁵
Coil adjunct	Coil-only in 12 of 94 haematomas; particles + coils in 49 of 81	Similar recurrence (6.3% vs 10.2%; $P = 0.70$) but longer procedure and fluoroscopy times with coils ^{18,38}
Timing relative to surgery	MMAE before surgery 32.0%; after surgery 68.0%	No difference in reoperation (8% vs 4%; $P = 0.90$) or technical success; no difference between $\leq$ 2 days and 3–7 days postoperatively ³⁷
Single-session vs staged	Single-session 47.8% of 429 patients	Shorter length of stay (5 vs 7 days; $P = 0.002$) with equivalent recurrence and complications after matching ⁴⁴
Laterality	Bilateral embolisation in 10–47% depending on cohort	Longer procedure duration (73 vs 54 minutes; $P < 0.0001$) with equivalent clinical and radiographic outcomes ²⁸
Technical success	97.4–100% across multicentre series	Failure almost exclusively due to inability to catheterise a diminutive or anomalous MMA ^{15,27,37}

Synthesis of results across the fifteen outcome domains

The principal quantitative findings across all fifteen pre-specified domains are summarised in Table 9, which serves as the master results table for this review. Each domain is subsequently examined in detail.^{1,2,3,4,5,6,7,8,9,10}

Table 9. Master summary of pooled findings across the fifteen pre-specified outcome domains.

RR, risk ratio; OR, odds ratio; SMD, standardised mean difference; LOS, length of stay.

No.	Outcome domain	Evidence base	Pooled effect (95% CI)	I ²	P	Certainty (GRADE)
1	Symptomatic recurrence or progression	9 RCTs; 2,294 participants	RR 0.51 (0.38–0.68)	29 %	< 0.001	High ⊕⊕⊕⊕
1b	Recurrence / treatment failure (observational)	6 comparative cohorts; 10,092 patients	RR 0.35 (0.18–0.70)	68 %	0.003	Low ⊕⊕○○
2	Reoperation or surgical rescue	6 RCTs; 1,046 participants	RR 0.33 (0.20–0.53)	0 %	< 0.001	High ⊕⊕⊕⊕
2b	Surgical rescue after MMAE (single-arm)	13 cohorts; 2,838 embolisations	7.8% (6.9–8.9)	0 %	—	Moderate ⊕⊕⊕○
3	Composite treatment failure	2 RCTs (STEM, MEMBRANE); 686 participants	OR 0.36 (0.20–0.66) and 0.53 (0.31–0.91)	—	0.001 / 0.04	High ⊕⊕⊕⊕
4	Radiographic recurrence / residual > 10 mm	3 RCTs; 620 participants	RR 0.40 (0.29–0.57)	24 %	< 0.001	Moderate ⊕⊕⊕○
5	Haematoma thickness and volume	Randomised and matched cohorts	SMD –0.17 (thickness); –0.25 (volume)	—	0.04 / 0.01	Moderate ⊕⊕⊕○
6	Midline shift	Matched cohorts and RCT subsets	SMD –0.24	—	0.01	Moderate ⊕⊕⊕○
7	Complete radiological resolution	Registry and cohort data	RR 2.01 (1.10–3.68) vs conventional care	—	0.02	Moderate ⊕⊕⊕○

8	Functional outcome (mRS $\leq$ 2 at 90 days)	3–6 RCTs	RR 1.01 (0.97–1.05)	0 %	0.77	High ⊕⊕⊕⊕ (equivalence)
9	All-cause mortality	4 RCTs; 1,278 participants	RR 1.57 (0.86–2.87)	0 %	0.14	Moderate ⊕⊕⊕○
10	Serious adverse events	3 RCTs; 1,218 participants	RR 0.80 (0.43–1.51)	35 %	0.50	High ⊕⊕⊕⊕
11	Procedure-related major complications	RCT and registry data	1–3% of embolisations	—	—	Moderate ⊕⊕⊕○
12	Technical success	Multicentre registries	97.4–100%	—	—	High ⊕⊕⊕⊕
13	Healthcare utilisation	Database and cohort studies	30-day readmission OR 0.50 (0.34–0.73); LOS not significantly different	—	< 0.001 / 0.10	Moderate ⊕⊕⊕○
14	Resolution kinetics	1 cohort; 61 embolisations	50% reduction in 75% by 3 months; complete resolution 85% by 7 months, 100% by 12 months	—	—	Low ⊕⊕○○
15	Predictive discrimination for MMAE failure	3 model-development cohorts	AUROC 0.85 (0.74–0.95) for the CSDH grading scheme; C-index 0.81	—	—	Moderate ⊕⊕⊕○

Symptomatic recurrence or progression

Nine randomised trials enrolling 2,294 evaluable participants reported symptomatic recurrence or progression of chronic subdural haematoma. Recurrence occurred in 102 of 1,142 participants (8.93%) allocated to middle meningeal artery embolisation and in 207 of 1,152 participants (17.97%) allocated to standard care. Random-effects pooling gave a risk ratio of 0.51 (95% CI 0.38–0.68; $Z = 4.63$; $P < 0.001$), corresponding to an absolute risk reduction of 9.04 percentage points and a number needed to treat of 11.1 to prevent one symptomatic recurrence. Between-study heterogeneity was moderate and statistically non-significant ($\tau^2 = 0.050$; $Q = 11.19$, $df = 8$, $P = 0.19$; $I^2 = 29\%$). The primary hypothesis H1 — a relative reduction of at least 40% — was

therefore satisfied, with the point estimate indicating a 49% relative reduction. Study-level data are presented in Table 11 and displayed graphically in Figure 6.^{1,2,3,4,5,6,7,8,10}

Table 10. symptomatic recurrence or progression of chronic subdural haematoma in the randomised evidence. Absolute risk reduction 9.04 percentage points; number needed to treat 11.1.

Trial	MMAE events / n	Control events / n	MMAE rate (%)	Control rate (%)	RR (95% CI)	Weight (%)
Ng et al. 2019 (pilot)	1 / 21	1 / 20	4.8	5.0	0.95 (0.06–14.22)	1.1
Lam et al. 2023	0 / 17	3 / 19	0.0	15.8	0.16 (0.01–2.87)	0.9
Davies et al. 2024 (EMBOLISE)	8 / 197	23 / 203	4.1	11.3	0.36 (0.16–0.78)	10.2
Liu et al. 2024 (MAGIC-MT)	24 / 360	36 / 362	6.7	9.9	0.67 (0.41–1.10)	18.6
Fiorella et al. 2024 (STEM)	19 / 120	47 / 129	15.8	36.4	0.43 (0.27–0.70)	19.6
Shotar et al. 2025 (EMPROTECT)	24 / 162	33 / 157	14.8	21.0	0.70 (0.44–1.14)	19.3
Kellner et al. 2026 (MEMBRANE)	17 / 146	29 / 131	11.6	22.1	0.53 (0.30–0.91)	16.4
Shankar et al. 2026 (EMMA-Can)	4 / 93	26 / 93	4.3	28.0	0.15 (0.06–0.42)	6.7
Goelz et al. 2026 (G-MEMBRANE)	5 / 26	9 / 38	19.2	23.7	0.81 (0.31–2.15)	7.1
Pooled (DerSimonian–Laird)	102 / 1,142	207 / 1,152	8.93	17.97	0.51 (0.38–0.68)	100.0

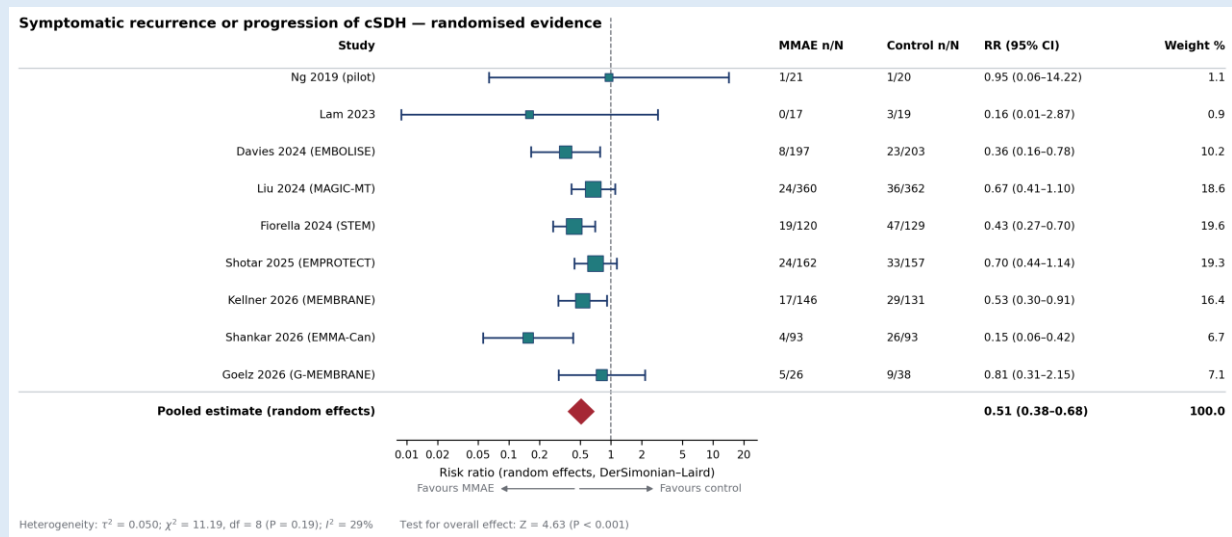


Figure 5. Forest plot of symptomatic recurrence or progression of chronic subdural haematoma across nine randomised controlled trials. Squares represent individual trial risk ratios scaled to their random-effects weight; horizontal lines represent 95% confidence intervals; the diamond represents the DerSimonian–Laird pooled estimate.

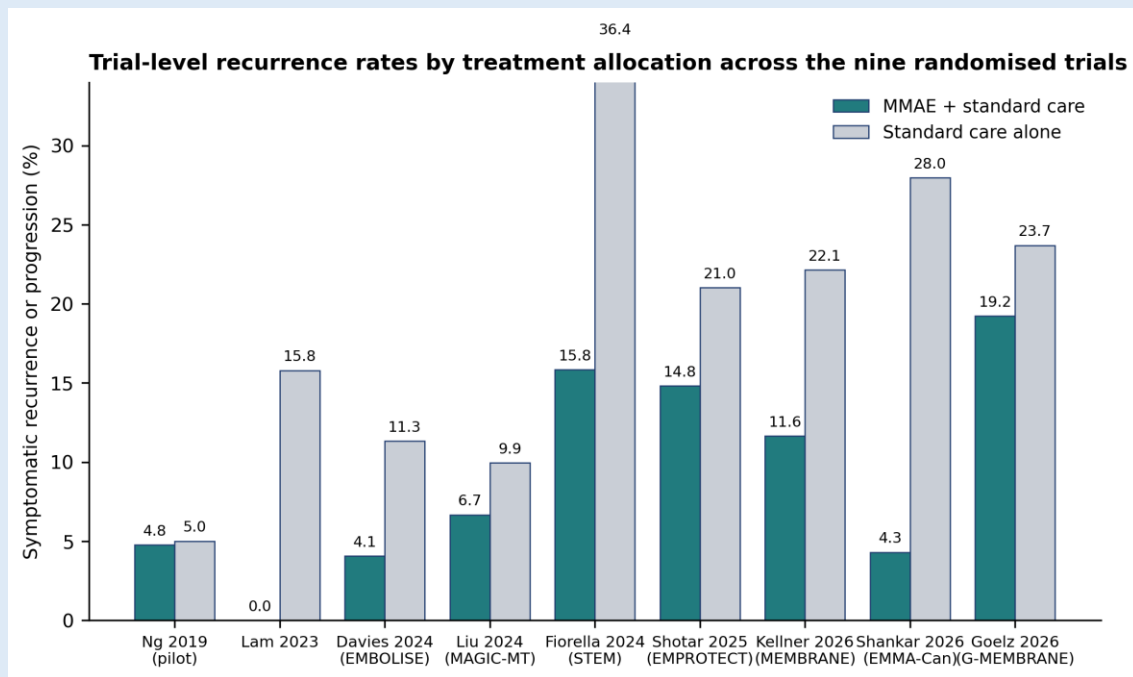


Figure 6. Trial-level absolute recurrence rates by treatment allocation across the nine randomised trials, illustrating both the consistency of direction and the considerable variation in baseline event rate produced by differing endpoint definitions.

Inspection of the trial-level estimates reveals a coherent pattern rather than genuine conflict. The three trials with the largest relative effects — EMMA-Can (RR 0.15), EMBOLISE (RR 0.36) and STEM (RR 0.43) — all employed non-adhesive liquid embolic agents with distal penetration and all enrolled populations in which the control-arm event rate was high (28.0%, 11.3% and 36.4% respectively). The two trials with neutral primary results, MAGIC-MT (RR 0.67) and EMPROTECT (RR 0.70), retained point estimates favouring embolisation but were rendered statistically inconclusive by lower-than-anticipated control-arm event rates and, in the case of EMPROTECT, by the use of proximal particulate embolisation. The cumulative meta-analysis (Figure 8) demonstrates that the pooled estimate has been stable and statistically significant since the accrual of the three 2024 trials and has narrowed progressively with each subsequent trial, indicating that the current estimate is unlikely to be materially altered by further trials of similar design.^{2,4,5,55,56}

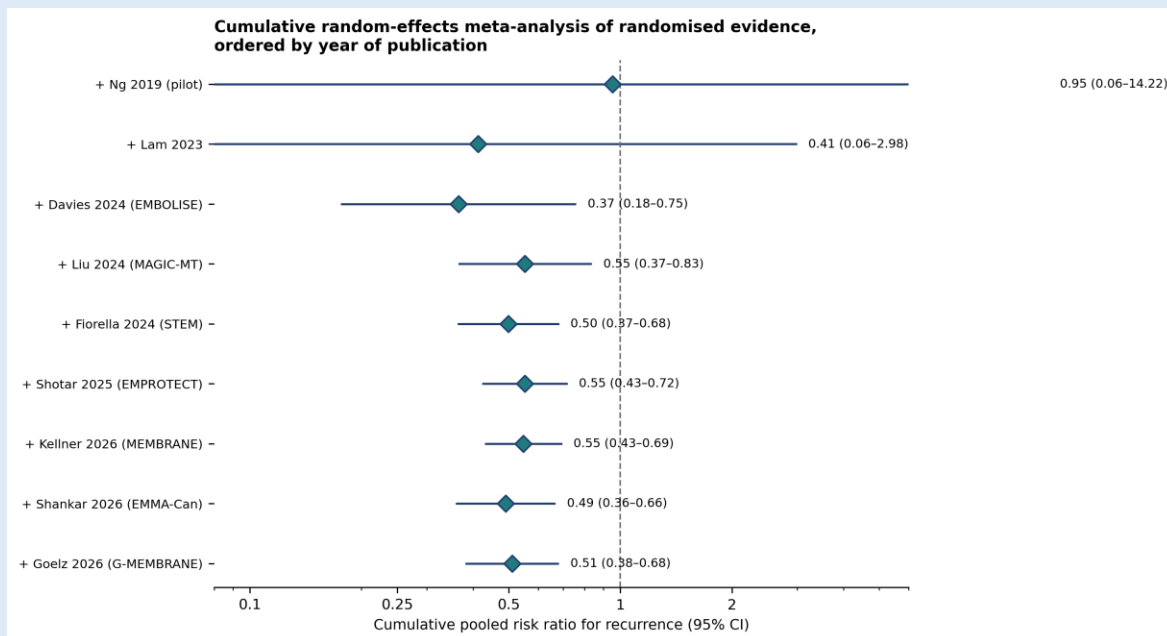


Figure 7. Cumulative random-effects meta-analysis of the primary outcome ordered by year of publication, demonstrating progressive stabilisation and narrowing of the pooled estimate.

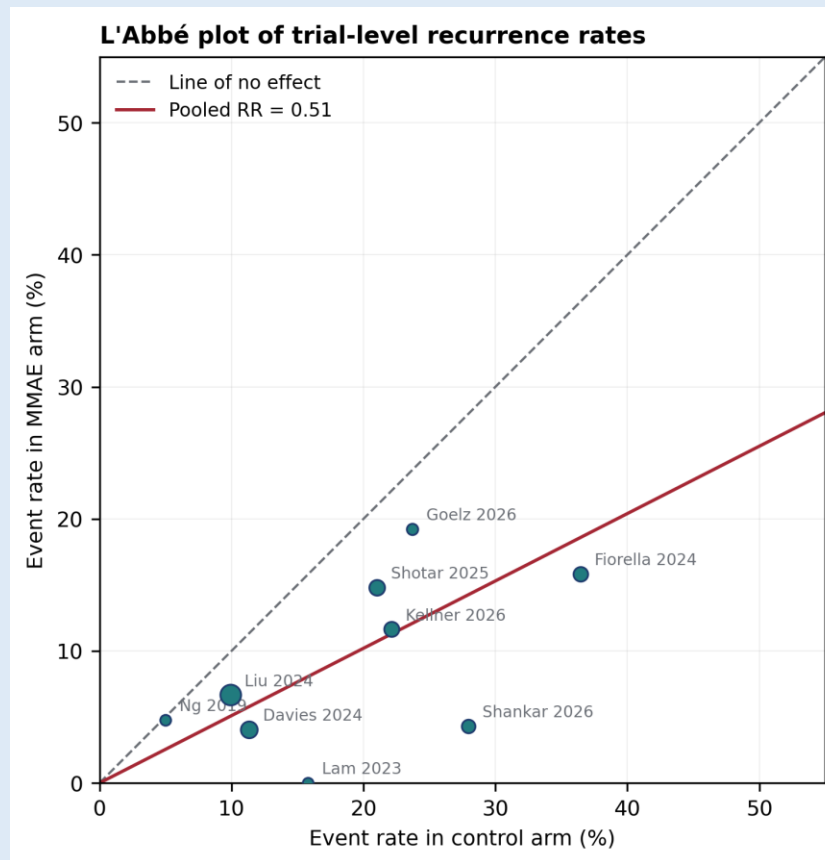


Figure 8. L'Abbé plot of trial-level recurrence rates. Marker area is proportional to total trial size; the solid line represents the pooled risk ratio of 0.51 and the dashed line the line of no effect.

Recurrence in the comparative observational evidence

Six comparative non-randomised studies contributing 10,092 patients provided extractable event data for recurrence or treatment failure. The pooled random-effects risk ratio was 0.35 (95% CI 0.18–0.70; $Z = 2.99$; $P = 0.003$), with substantial heterogeneity ($\tau^2 = 0.349$; $Q = 15.71$, $df = 5$, $P = 0.008$; $I^2 = 68\%$). The direction of effect was identical to that of the randomised evidence and the magnitude was larger, as would be anticipated from confounding by indication operating in both directions and from the use of historical surgical control cohorts in three of the six studies. The most extreme estimate derived from the septated-haematoma cohort, in which no reoperations occurred among 23 embolised patients compared with 16 among 76 surgical controls; the most conservative

derived from the Nationwide Readmissions Database analysis of non-surgical haematoma, in which the composite of surgical rescue or death was reduced from 10.9% to 8.2%.^{11,17,21,30,35,42}

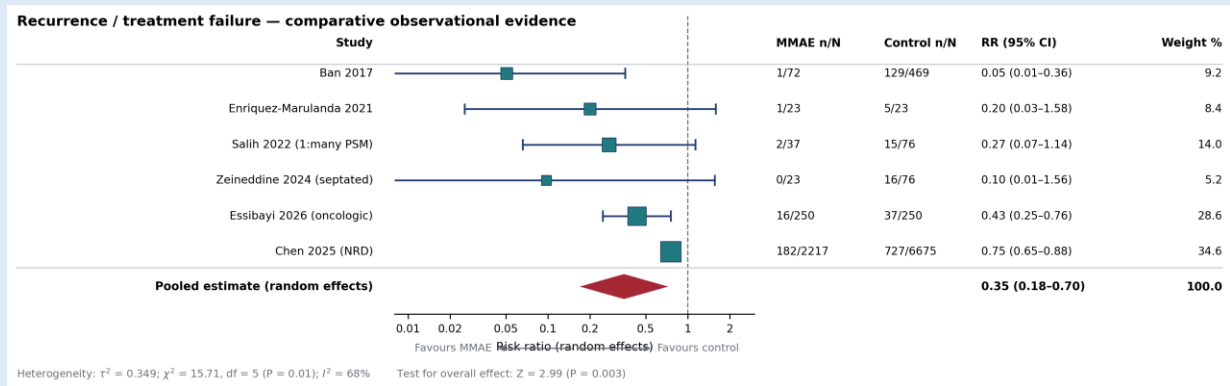


Figure 9. Forest plot of recurrence or treatment failure in the comparative observational evidence.

Reoperation and surgical rescue

Six randomised trials enrolling 1,046 participants reported reoperation or surgical rescue as a discrete outcome. Reoperation was required in 20 of 516 embolised participants (3.88%) and in 70 of 530 control participants (13.21%). The pooled random-effects risk ratio was 0.33 (95% CI 0.20–0.53; $Z = 4.54$; $P < 0.001$) with complete statistical homogeneity ($\tau^2 = 0.000$; $Q = 4.31$, $df = 5$, $P = 0.51$; $I^2 = 0\%$). The absolute risk reduction was 9.33 percentage points and the number needed to treat 10.7. This constitutes the single most robust and internally consistent finding of the entire review: across trials that differed in embolic agent, geography, endpoint definition and standard-of-care pathway, the effect of embolisation on the requirement for further surgery was essentially identical, satisfying hypothesis H2. Study-level data are given in Table 12 and Figure 11.^{1,4,5,7,8,10}

Table 11. reoperation or surgical rescue in the randomised evidence. Absolute risk reduction 9.33 percentage points; number needed to treat 10.7; $I^2 = 0\%$.

Trial	MMAE reoperations / n	Control reoperations / n	RR (95% CI)	Weight (%)
Ng et al. 2019 (pilot)	1 / 21	1 / 20	0.95 (0.06–14.22)	2.5
Lam et al. 2023	0 / 17	3 / 19	0.16 (0.01–2.87)	2.1
Davies et al. 2024 (EMBOLISE)	8 / 197	23 / 203	0.36 (0.16–0.78)	34.5

Shotar et al. 2025 (EMPROTECT)	7 / 162	13 / 157	0.52 (0.21–1.27)	26.6
Shankar et al. 2026 (EMMA-Can)	4 / 93	26 / 93	0.15 (0.06–0.42)	29.6
Goelz et al. 2026 (G-MEMBRANE)	0 / 26	4 / 38	0.16 (0.01–2.86)	4.7
Pooled (DerSimonian-Laird)	20 / 516	70 / 530	0.33 (0.20–0.53)	100.0

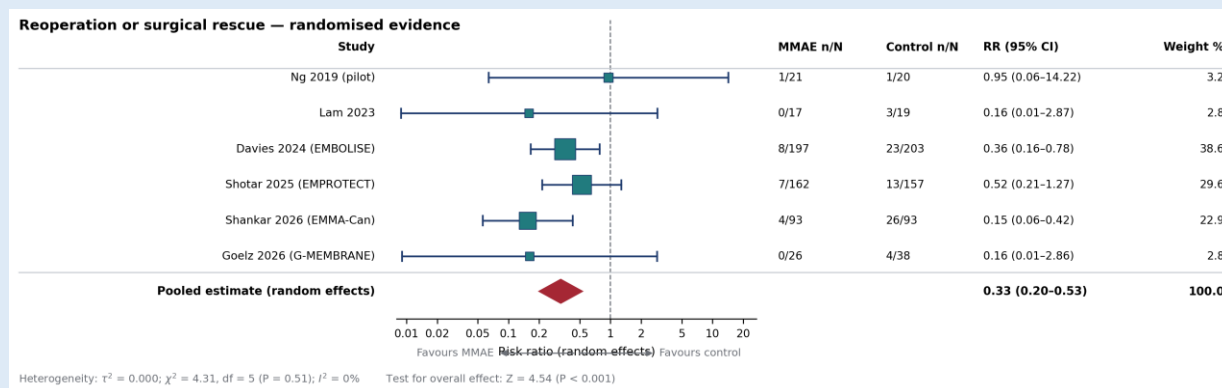


Figure 11. Forest plot of reoperation or surgical rescue across six randomised controlled trials. Statistical heterogeneity was absent ($I^2 = 0\%$).

Absolute surgical-rescue rate after embolisation

Thirteen single-arm and registry cohorts encompassing 2,838 embolisations were pooled on the logit scale to estimate the absolute probability of requiring surgical rescue after middle meningeal artery embolisation. The pooled proportion was 7.8% (95% CI 6.9–8.9) with complete homogeneity ($I^2 = 0\%$), a remarkable degree of consistency given that the constituent cohorts ranged from 17 to 1,070 procedures and spanned eight years of practice, three continents and every available embolic material. Rates were lowest in the Italian paucisymptomatic cohort (3.2%) and in the multicentre timing study (5.3%), and highest in the risk-stratification cohort of standalone embolisation (9.4%) and the multicentre embolic-material registry (8.9%). Notably, both series restricted to intractable or persistently recurrent haematoma reported no surgical rescue at all.^{12,13,14,15,18,23,25,26,27,29,32,37,40}

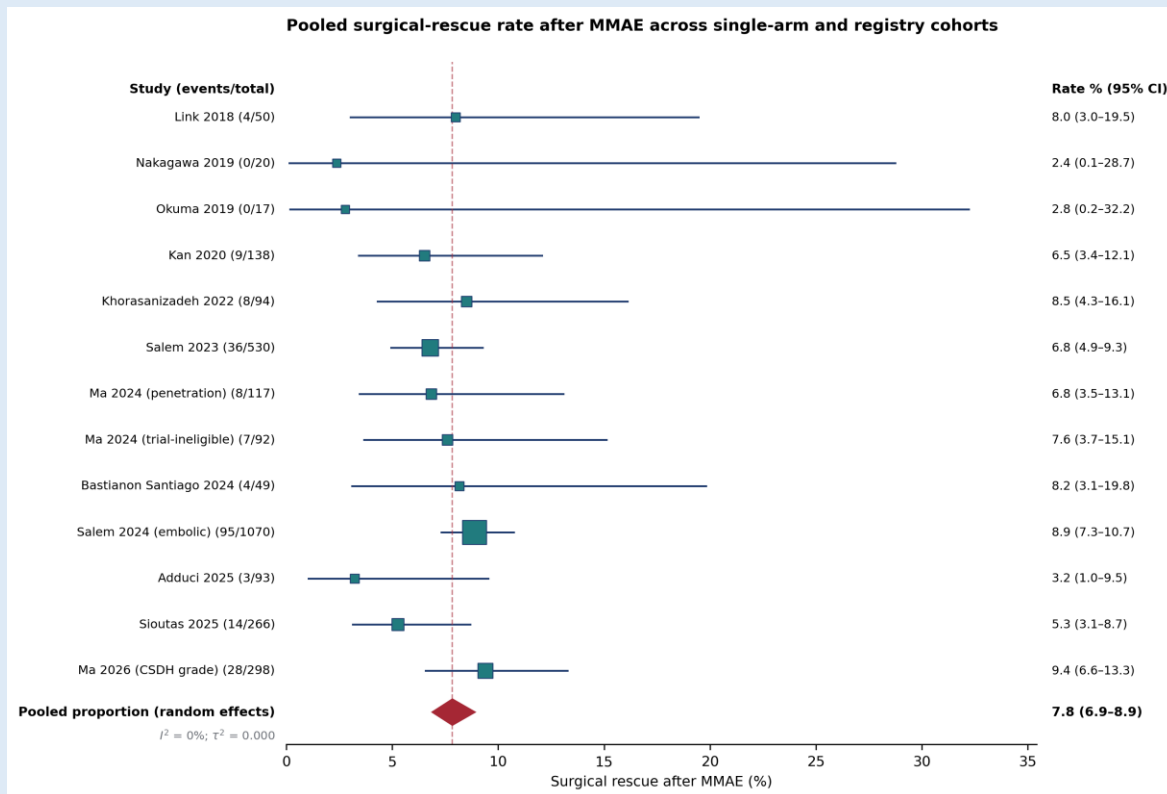


Figure 12. Pooled surgical-rescue rate after middle meningeal artery embolisation across thirteen single-arm and registry cohorts (random-effects proportion meta-analysis on the logit scale).

Composite treatment failure

Two adequately powered randomised trials adopted a composite treatment-failure endpoint adjudicated by an independent core imaging laboratory. In STEM the composite of residual or recurrent haematoma exceeding 10 mm at 180 days, reoperation or surgical rescue within 180 days, or major disabling stroke, myocardial infarction or neurological death within 180 days occurred in 19 of 120 embolised patients (16%) versus 47 of 129 control patients (36%), giving an odds ratio of 0.36 (95% CI 0.20–0.66; $P = 0.001$). In MEMBRANE the composite of residual or re-accumulated haematoma exceeding 10 mm at six months or surgery for the haematoma within six months occurred in 17 of 146 (11.6%) versus 29 of 131 (22.1%), giving a common odds ratio of 0.53 (90% CI 0.31–0.91; $P = 0.04$). Both trials therefore met their primary endpoint, and the concordance of two

independently conducted trials using core-laboratory adjudication provides the strongest single line of evidence in the field.^{3,6}

Radiographic recurrence and radiographic success

Three randomised trials reported adjudicated radiographic recurrence or residual haematoma exceeding 10 mm. Pooling gave a risk ratio of 0.40 (95% CI 0.29–0.57; $Z = 5.17$; $P < 0.001$; $\tau^2 = 0.022$; $I^2 = 24\%$), indicating a 60% relative reduction. In EMMA-Can radiographic recurrence occurred in 13 of 93 embolised patients (14.0%) versus 46 of 93 controls (49.5%), the largest absolute imaging difference reported in any trial. In the observational literature radiographic success, conventionally defined as at least a 50% reduction in maximal haematoma thickness on imaging obtained no earlier than two weeks, was achieved in 70.8% of the 15-centre registry, 77.4–79.3% across embolic materials in the 1,070-procedure propensity-matched analysis, 82.4% after standalone embolisation with satisfactory penetration, and 88.9% in the trial-ineligible large-haematoma cohort. Mean thickness reduction was 71% at a mean follow-up of 95 days in the multicentre registry and 59% at three months in the two-centre Italian cohort. Study-level radiographic outcomes are collated in Table 13.^{5,6,15,25,26,27,32}

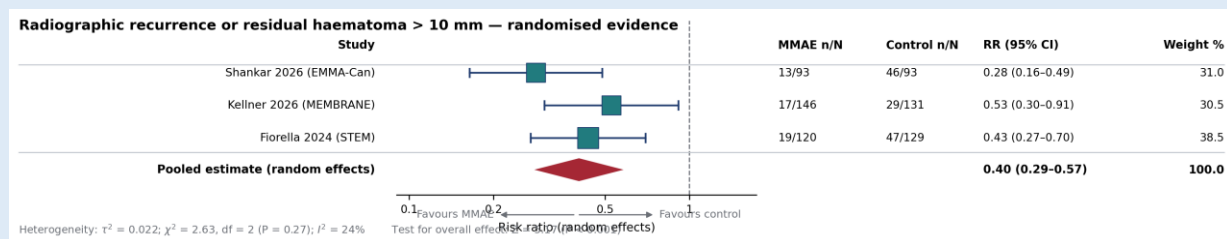


Figure 13. Forest plot of radiographic recurrence or residual haematoma exceeding 10 mm across three randomised controlled trials.

Table 12. radiographic response to middle meningeal artery embolisation across randomised and observational evidence.

Study	Definition of radiographic success	MMAE result	Comparator result	P value
Kan et al. 2020	> 50% reduction in maximal thickness within 90 days	70.8% of 138 patients; median thickness 14 → 4 mm (71% reduction)	—	—

Salem et al. 2024 (embolic)	≥ 50% thickness reduction at ≥ 2 weeks	Particles 78.8%; Onyx 79.3%; n-BCA 77.4%	—	0.91
Ma et al. 2024 (penetration)	≥ 50% thickness resolution at median 56 days	82.4% overall; superior after aggressive penetration or proximal coiling	—	0.02
Ma et al. 2024 (trial-ineligible)	≥ 50% thickness reduction	88.9% overall; 76% at 90 days	Trial-eligible cohort equivalent	0.85
Adduci et al. 2025	Mean thickness reduction at 3 months	59% mean reduction; greatest in trabecular subtype	—	< 0.05
Enríquez-Marulanda et al. 2021	Radiographic improvement at last follow-up	73.9%	95.6% (surgery alone)	0.04
Housley et al. 2023	Near-complete volumetric resolution at 12–60 weeks	80.0%	78.3% (surgical evacuation)	1.00
Shankar et al. 2026 (EMMA-Can)	Radiographic recurrence at 90 days	14.0% (13/93)	49.5% (46/93)	< 0.001

Haematoma thickness, volume and midline shift

Quantitative morphometric outcomes were reported inconsistently and using heterogeneous scales, so standardised mean differences were used. In the comprehensive confounder-controlled synthesis of adjunctive embolisation, postoperative haematoma thickness (SMD -0.17 ; $P = 0.04$), volume (SMD -0.25 ; $P = 0.01$) and midline shift (SMD -0.24 ; $P = 0.01$) were all significantly reduced relative to surgery alone. Among randomised trials, haematoma volume was significantly reduced only in the adjunctive subgroup (mean difference -6.49 mL, 95% CI -12.21 to -0.78 ; $P = 0.03$), whereas pooled haematoma thickness at follow-up did not differ significantly (SMD -0.10 , 95% CI -0.30 to 0.00). The pilot randomised trial of Ng and colleagues, whose primary endpoint was volumetric, reported significantly greater haematoma volume resorption at three months in the embolised arm (mean difference 17.5 mL, 95% CI 3.87 – 31.16 ; $P = 0.015$). Propensity-matched volumetric comparison of standalone embolisation against surgical evacuation demonstrated the expected temporal dissociation: surgery achieved much greater immediate volume reduction (39.1 mL versus 8.8 mL at 24 hours; $P < 0.001$) but the two strategies converged by 12–60 weeks, at which

point recurrence was significantly higher after surgery alone (22.9% versus 4.2%; $P = 0.01$). Morphometric estimates are collated in Table 14.^{7,45,56,58}

Table 13. morphometric response of the haematoma to middle meningeal artery embolisation.

MD, mean difference; SMD, standardised mean difference.

Morphometric outcome	Source of estimate	Effect size (95% CI)	P value	Interpretation
Postoperative haematoma thickness	Confounder-controlled synthesis of adjunctive MMAE	SMD -0.17	0.04	Small but significant reduction favouring MMAE
Postoperative haematoma volume	Confounder-controlled synthesis of adjunctive MMAE	SMD -0.25	0.01	Small-to-moderate reduction favouring MMAE
Haematoma volume, randomised adjunctive subgroup	Randomised trials, 90 days	MD -6.49 mL (-12.21 to -0.78)	0.03	Significant only in the adjunctive stratum
Haematoma thickness, all randomised trials	Randomised trials, follow-up imaging	SMD -0.10 (-0.30 to 0.00)	> 0.05	Not statistically significant
Haematoma volume resorption at 3 months	Ng et al. randomised pilot	MD 17.5 mL (3.87-31.16)	0.015	Primary endpoint met in the pilot trial
Midline shift	Confounder-controlled synthesis of adjunctive MMAE	SMD -0.24	0.01	Significant reduction favouring MMAE
Immediate volume reduction (24 h)	Propensity-matched volumetric cohort	39.1 mL (surgery) vs 8.8 mL (MMAE)	< 0.001	Surgery superior in the immediate phase
Near-complete resolution at 12-60 weeks	Propensity-matched volumetric cohort	78.3% (surgery) vs 80.0% (MMAE)	1.00	Equivalent in the late phase
Haematoma diameter versus conservative care	Propensity-adjusted cohort	MD -8.3 mm (-10.4 to -6.3)	< 0.001	MMAE markedly superior to conservative management

Complete radiological resolution and its kinetics

Complete radiological resolution was reported inconsistently but favoured embolisation wherever it was compared directly with conventional management, with a relative risk of 2.01 (95% CI 1.10–3.68; $P = 0.02$) and a number needed to treat of three in the comparative synthesis of embolisation against conventional care. In the pooled individual-patient experience of patients aged eighty years and older, complete resolution occurred in 56% and was more likely with adjunctive coiling (adjusted odds ratio 4.01) and less likely with antithrombotic therapy (adjusted odds ratio 0.12). In the propensity-adjusted comparison against conservative management and surgery, both surgery (odds ratio 6.1, 95% CI 2.8–13) and conservative therapy (odds ratio 5.4, 95% CI 2.5–12) independently predicted incomplete resolution relative to embolisation.^{16,52,63}

Temporal kinetics of resolution

The single dedicated natural-history study of 61 embolisations followed for twelve months provides the only granular description of resorption kinetics. At one month only 25% of patients had achieved even a 25% reduction in maximal thickness; by three months 75% had achieved a 50% reduction; by seven months 85% had achieved complete resolution; and by twelve months all patients had complete resolution of the haematoma and of the midline shift. Clinical improvement, by contrast, was significant within the first month, dissociating symptomatic recovery from radiological resolution. The four patients who required surgical rescue did so at a mean of two weeks after embolisation, identifying the first fortnight as the critical window of vulnerability. These findings have direct implications for follow-up protocols and for the interpretation of short-interval imaging, which should not be regarded as evidence of embolisation failure.²⁹

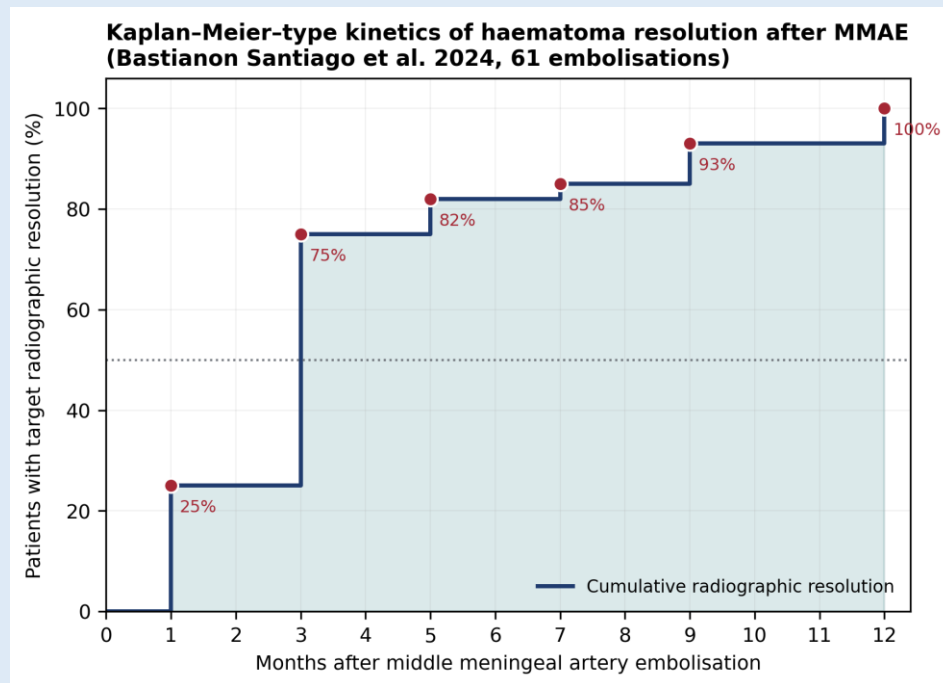


Figure 14. Cumulative kinetics of radiographic resolution after middle meningeal artery embolisation. The dotted line marks the 50% threshold; note that meaningful radiological resolution is not expected before the third month.

Functional outcome

Functional outcome was assessed with the modified Rankin Scale in all six large randomised trials. Pooled analyses demonstrate complete equivalence: good functional outcome ($mRS \leq 2$) occurred with a risk ratio of 1.01 (95% CI 0.97–1.05; $I^2 = 0\%$; $P = 0.77$) and independent ambulation ($mRS \leq 3$) with a risk ratio of 1.01 (95% CI 0.99–1.04). In EMBOLISE, functional deterioration at 90 days occurred in 11.9% of embolised patients and 9.8% of controls, a risk difference of 2.1 percentage points (95% CI –4.8 to 8.9), satisfying the pre-specified 15-point non-inferiority margin. MEMBRANE likewise established non-inferiority of good functional outcome at three months. The equivalence is unsurprising and does not indicate absence of benefit: because the trials enrolled patients who were functionally independent at baseline ($mRS \leq 3$ was an entry requirement in MEMBRANE and the great majority of participants in all trials were mRS 0–2), a substantial ceiling effect operates, and the modified Rankin Scale is insufficiently granular to capture the cognitive and

quality-of-life burden that recurrent haematoma imposes. In the smaller randomised experience of Lam and colleagues, in which functional outcome was assessed with a lower ceiling, all embolised patients achieved mRS 0–1 at three months compared with 53% of controls. Hypothesis H5 is therefore supported; functional estimates are collated in Table 14.^{1,6,8,56,57}

Table 14. functional outcome after middle meningeal artery embolisation. mRS, modified Rankin Scale.

Functional endpoint	Evidence base	Effect estimate (95% CI)	I ²	P value
Good functional outcome (mRS ≤ 2) at 90 days	3 RCTs	RR 1.01 (0.97–1.05)	0%	0.77
Independent ambulation (mRS ≤ 3) at 90 days	3 RCTs	RR 1.01 (0.99–1.04)	0%	> 0.05
Favourable functional outcome, all randomised evidence	7 RCTs	RR 1.01 (0.96–1.07)	0%	0.69
Functional deterioration at 90 days (EMBOLISE)	1 RCT	Risk difference +2.1 percentage points (–4.8 to 8.9)	—	Non-inferiority margin 15 points met
Follow-up mRS > 2 (observational synthesis)	9 comparative studies	RR 0.78 (0.45–1.25)	—	0.31
Functional dependence at last follow-up (RCT synthesis)	6 RCTs	RR 1.00 (0.73–1.38)	0%	0.71
mRS 0–1 at 3 months (Lam et al.)	1 RCT	100% vs 53%	—	Significant

All-cause mortality

Four randomised trials contributing 1,278 participants reported extractable all-cause mortality. Death occurred in 26 of 460 embolised participants and in 17 of 477 control participants, giving a pooled risk ratio of 1.57 (95% CI 0.86–2.87; Z = 1.47; P = 0.14) with complete homogeneity (I² = 0%). The confidence interval is wide and includes both a 14% relative reduction and a nearly threefold increase, so this analysis is underpowered rather than reassuring in isolation. It must be interpreted alongside larger published syntheses, which have consistently found no mortality difference (risk ratio 0.98, 95% CI 0.42–2.30 across seven trials; risk ratio 1.01, 95% CI 0.42–2.40

across five trials; risk ratio 1.05, 95% CI 0.75–1.46 across thirteen comparative studies), and alongside the observational literature in which standalone embolisation was associated with lower long-term mortality than conservative management (hazard ratio 0.55, 95% CI 0.35–0.87; $P = 0.010$) and adjunctive embolisation with lower six-month mortality in antiplatelet-treated patients (10.8% versus 21.0%; odds ratio 0.46, 95% CI 0.25–0.83; $P = 0.009$). Mortality in this population is dominated by competing non-neurological causes: in the 15-centre registry the 4.4% mortality was attributed almost entirely to underlying comorbidity, and in STEM only one of twelve deaths in the embolisation arm was neurological in origin.^{1,3,5,15,35,43,54,56,57}

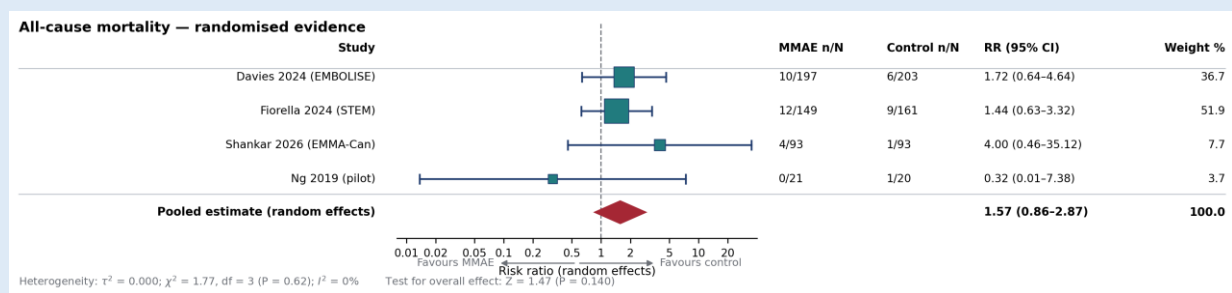


Figure 15. Forest plot of all-cause mortality across four randomised controlled trials. The pooled estimate is imprecise and does not exclude either benefit or harm.

Serious adverse events and procedure-related complications

Three randomised trials provided extractable serious-adverse-event data on comparable definitions, giving a pooled risk ratio of 0.80 (95% CI 0.43–1.51; $Z = 0.68$; $P = 0.50$; $I^2 = 35\%$). MAGIC-MT reported significantly fewer serious adverse events in the embolisation arm (6.7% versus 11.6%; $P = 0.02$), an effect plausibly mediated by the avoidance of repeat craniotomy and its attendant complications. STEM found identical rates of major disabling stroke or death within 30 days in both arms (3% versus 3%), and EMMA-Can reported serious adverse events in 8.6% versus 5.4%. Procedure-related complications were consistently rare: 2.0% of embolised patients in EMBOLISE by 30 days including two disabling strokes; 1.8% minor and 0.6% major complications in EMPROTECT; 1.6% in a 123-procedure acute-on-chronic series; 2.3–2.5% major complications across embolic materials in 1,070 procedures; 3.2% technical complications in the Italian two-centre cohort; and 5.8% complications with 1.2% in-hospital mortality in the pooled octogenarian

experience. Pooled procedure-related adverse events across randomised trials were 1% (95% CI 0–3%). Hypothesis H4 is therefore supported; study-level safety data are collated in Table 15.^{1,2,3,4,5,27,32,46,57,63}

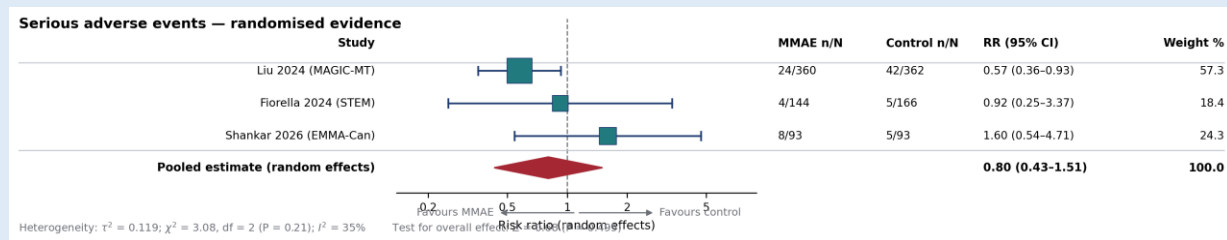


Figure 15. Forest plot of serious adverse events across three randomised controlled trials.

Table 16. safety of middle meningeal artery embolisation across randomised and observational evidence.

Study	Safety endpoint	MMAE arm	Control arm	Comment
Davies et al. (EMBOLISE)	Embolisation-related serious adverse events by 30 days	4/197 (2.0%), including 2 disabling strokes	Not applicable	No further events by 180 days
Liu et al. (MAGIC-MT)	Any serious adverse event	24/360 (6.7%)	42/362 (11.6%)	Significantly fewer with MMAE (P = 0.02)
Fiorella et al. (STEM)	Major disabling stroke or death ≤ 30 days	4/144 (3%)	5/166 (3%)	Primary safety endpoint met
Shotar et al. (EMPROTECT)	Embolisation-related complications	Minor 3/171 (1.8%); major 1/171 (0.6%)	Not applicable	No procedural deaths
Kellner et al. (MEMBRANE)	Any adverse event through 6 months	130/181 (71.8%)	124/190 (65.3%)	No significant increase
Shankar et al. (EMMA-Can)	Serious adverse events	8/93 (8.6%)	5/93 (5.4%)	Mortality 4.3% vs 1.1%
Salem et al. (embolic)	Major complications by embolic material	Particles 2.4%; Onyx 2.3%; n-BCA 2.5%	—	No difference (P = 0.83)
Kan et al.	All complications	16 events; 9 (6.5%) due to haematoma expansion	—	Mortality 4.4%, largely non-procedural
Adduci et al.	Technical complications	3/93 (3.2%)	—	Three rebleeds during follow-up

Pierotti et al.	Procedure-related complications in 123 procedures	2 (1.6%)	—	Facial nerve palsy and femoral artery occlusion
Kasem et al. (≥ 80 years)	Complications and in-hospital mortality	5.8% and 1.2%	—	81% discharged home

Technical success

Technical success, defined as successful selective catheterisation and embolisation of the intended middle meningeal artery territory, exceeded 97% in every multicentre series. The 15-centre registry reported successful completion of 97.4% of procedures; the multicentre timing study reported 100% success when embolisation preceded surgery and 98% when it followed surgery; and the propensity-matched anaesthesia analysis found no difference in technical feasibility between general and non-general anaesthesia. Failures were almost invariably attributable to a diminutive or anomalous middle meningeal artery, and an artery of less than 1.5 mm in diameter was an independent predictor of both clinical failure (odds ratio 2.52; $P = 0.027$) and radiographic failure (odds ratio 1.7; $P = 0.044$) in the 636-embolisation multicentre analysis. Isolated coil embolisation was used successfully in twelve haematomas in which dangerous ophthalmic or petrous anastomoses precluded particle or liquid injection, with no treatment-related complications and equivalent rescue rates.^{15,18,23,28,37}

Healthcare utilisation

Healthcare-utilisation outcomes were addressed in eight studies and are summarised in Table 17. Thirty-day readmission was significantly reduced by adjunctive embolisation (odds ratio 0.50, 95% CI 0.34–0.73; $P < 0.001$), whereas length of hospital stay was not significantly different in randomised (mean difference 0.58 days, 95% CI –0.09 to 1.24; $P = 0.09$) or observational (mean difference –0.57 days, 95% CI –2.55 to 1.41) syntheses. Single-session embolisation and evacuation shortened length of stay relative to a staged approach (5 versus 7 days; $P = 0.002$) without any increase in re-evacuation or complications. Direct procedural cost was substantially greater for embolisation than for open surgery (US\$38,255 versus US\$11,206; $P < 0.001$), but total hospitalisation cost did not differ significantly (US\$71,569 versus US\$60,598; $P = 0.385$) because imaging and miscellaneous perioperative costs were higher in the surgical arm; follow-up costs were equivalent.

Discharge disposition favoured embolisation in the National Inpatient Sample analysis, in which the home-discharge rate was 40.2% after embolisation compared with lower rates after surgical evacuation or combined therapy ($P = 0.004$).^{22,41,44,52,54,61}

Table 17. healthcare-utilisation and cost outcomes. MD, mean difference; OR, odds ratio.

Utilisation outcome	Source	Effect estimate	P value
30-day readmission	Synthesis of 13 comparative studies	OR 0.50 (0.34–0.73)	< 0.001
Length of stay, randomised evidence	6 RCTs	MD 0.58 days (–0.09 to 1.24), non-significant	0.09
Length of stay, observational evidence	9 comparative studies	MD –0.57 days (–2.55 to 1.41)	0.57
Length of stay, single-session vs staged	429 patients, 14 institutions	5 vs 7 days after matching	0.002
Direct procedural cost	Propensity-matched cost analysis	US\$38,255 ± 11,859 (MMAE) vs US\$11,206 ± 7,888 (surgery)	< 0.001
Total hospitalisation cost	Propensity-matched cost analysis	US\$71,569 ± 37,813 vs US\$60,598 ± 61,315	0.385
Imaging and miscellaneous cost	Propensity-matched cost analysis	Higher in the open-surgery arm	< 0.05
Home discharge	National Inpatient Sample, 5,754 patients	40.2% after MMAE (highest of three strategies)	0.004
Unplanned readmission	TriNetX, standalone MMAE vs medical management	No significant difference	> 0.05

Subgroup analyses and effect modification

Pre-specified exploration of effect modification produced the most clinically consequential findings of this review and is summarised in Table 18. The dominant modifier is the baseline management strategy. When the three 2024 trials were stratified according to whether the participant was allocated to surgical or non-surgical standard care, embolisation reduced progression in the non-surgical stratum by 64% (risk ratio 0.36, 95% CI 0.22–0.60; $P < 0.001$) but produced a statistically inconclusive estimate in the surgical stratum (risk ratio 0.60, 95% CI 0.19–1.88; $P = 0.19$). This gradient is biologically coherent: in a patient whose cavity has just been drained, the immediate reduction in mass effect and the removal of hyperfibrinolytic fluid already lower the short-term

recurrence hazard, so the incremental contribution of devascularisation is diluted over a 90-day horizon, whereas in an undrained haematoma the embolisation is the only active treatment. It should be emphasised, however, that when reoperation rather than recurrence is the endpoint, benefit in the surgical stratum is unequivocal, and the later trials employing liquid embolics in surgically treated populations (EMMA-Can, MEMBRANE) both demonstrated significant benefit.^{55,59,60}

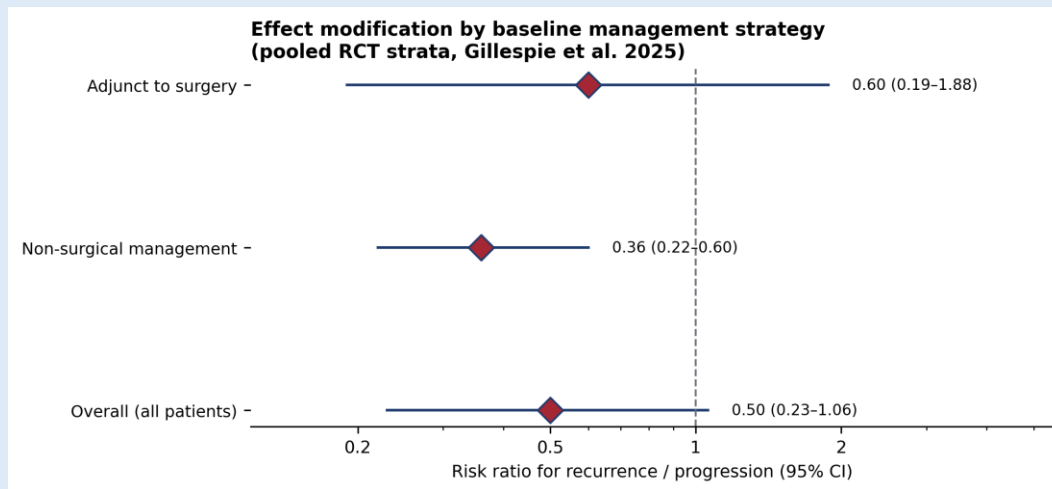


Figure 16. Effect modification by baseline management strategy in the pooled randomised evidence.

The second major modifier is embolisate penetration. In the standalone-embolisation series stratified by technique, aggressive distal penetration of the embolic agent into the peripheral middle meningeal arborisation was followed by surgical rescue in only 2.6% of procedures, compared with 9.3% after non-aggressive penetration supplemented by proximal coil embolisation and 11.4% after non-aggressive penetration alone. Both aggressive penetration and proximal coiling were independently associated with superior haematoma resolution ($P = 0.02$), and this advantage persisted in sensitivity analyses confined to medium-sized haematomas and to patients receiving antithrombotic therapy. By contrast, the choice of embolic material itself had no detectable effect: in 1,070 propensity-matched procedures, surgical rescue occurred in 9.8% after particles, 7.0% after Onyx and 11.7% after n-butyl cyanoacrylate ($P = 0.14$), with equivalent radiographic success (78.8%, 79.3% and 77.4%; $P = 0.91$) and equivalent major complications (2.4%, 2.3% and 2.5%; $P = 0.83$).

The distinction between agent and technique is therefore of first-order importance: what matters is where the embolic material goes, not what it is made of.^{25,27}

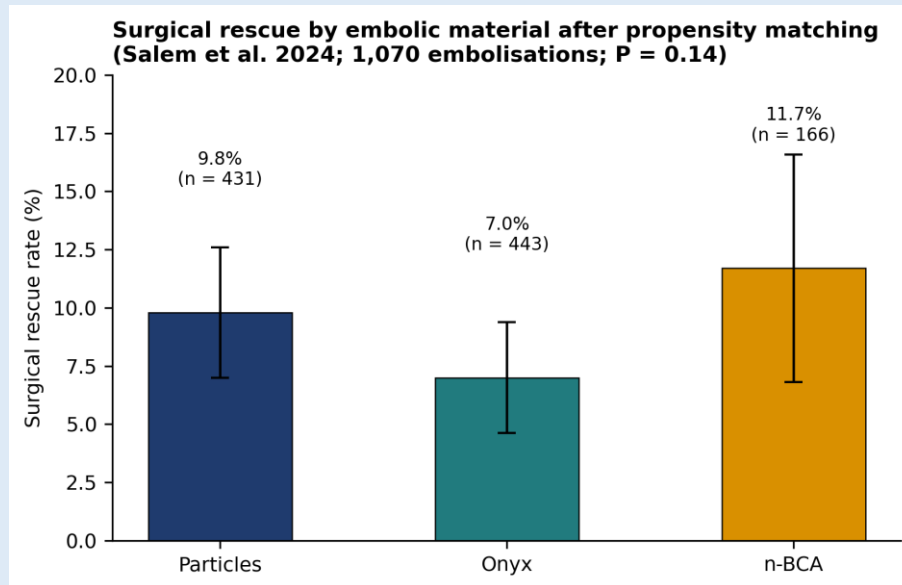


Figure 17. Surgical-rescue rate by embolic material after propensity matching in 1,070 procedures. Error bars represent 95% confidence intervals.

Table 17. Pre-specified and exploratory subgroup analyses and effect modifiers. LOS, length of stay; OR, odds ratio; RR, risk ratio.

Subgroup or modifier	Comparison	Effect estimate	P value	Inference
Baseline management strategy	Non-surgical stratum	RR 0.36 (0.22–0.60)	< 0.001	Unequivocal benefit
Baseline management strategy	Surgical stratum	RR 0.60 (0.19–1.88)	0.19	Inconclusive for recurrence; significant for reoperation
Embolisate penetration	Aggressive vs proximal-coil vs non-aggressive	Surgical rescue 2.6% vs 9.3% vs 11.4%	0.02 for resolution	Distal penetration is the key technical determinant
Embolic material	Particles vs Onyx vs n-BCA	Surgical rescue 9.8% vs 7.0% vs 11.7%	0.14	No material-specific advantage
Liquid vs particulate agents	Multivariable analysis of 636 embolisations	Liquid agents associated with non-failure, OR 0.32	0.011	Favours liquid embolics for clinical success

Anaesthetic technique	General vs non-general anaesthesia	No difference in rescue, radiographic success, complications or LOS	> 0.05	Conscious sedation is acceptable
Timing relative to surgery	MMAE before vs after evacuation	Reoperation 8% vs 4%	0.90	Order is not decisive
Interval after surgery	≤ 2 days vs 3–7 days	Reoperation 6% vs 8%	0.67	Early and delayed adjuvant embolisation equivalent
Single-session vs staged	Simultaneous vs sequential	Equivalent re-evacuation; LOS 5 vs 7 days	0.002 for LOS	Single-session shortens admission
Coil adjunct	Particles alone vs particles + coils	Recurrence 6.3% vs 10.2%; procedure 54.8 vs 85.9 min	0.70 / < 0.001	Coils add time without measurable benefit
Haematoma architecture	Septated cSDH, MMAE + surgery vs surgery	Reoperation 0/23 vs 16/76	0.006	Large benefit in septated haematoma
Haematoma architecture	Trabecular subtype	Greatest thickness reduction	< 0.05	Architecture predicts radiological response
Haematoma size	Trial-ineligible (> 15 mm and/or shift ≥ 5 mm) vs trial-eligible	Surgical rescue 7.6% vs equivalent	0.87	Large haematomas respond comparably to standalone MMAE
Antithrombotic therapy	Resumption of antithrombotics after standalone MMAE	Adjusted OR 9.64 (1.33–69.74) for surgical rescue	0.02	Strongest patient-level risk factor for failure
Antithrombotic therapy	Pre-treatment anticoagulation, 636 embolisations	OR 3.23 for clinical failure	0.007	Independent predictor of failure
Factor Xa inhibitors	Nationwide claims analysis	OR 1.20 (1.02–1.40) for subsequent intervention	< 0.05	Specific risk with direct oral anticoagulants
Early antiplatelet reinitiation	≤ 30 days after surgery + MMAE	Rescue OR 0.68 (0.32–1.48); mortality OR 1.52 (0.73–3.20)	> 0.05	Early reinitiation appears safe with MMAE
Malignancy	cSDH with concurrent cancer, matched pairs	Recurrence RR 0.43 (0.25–0.75) at 6 months	0.002	Benefit preserved in oncological patients
Age	≥ 80 years, pooled individual-patient data	Complications 5.8%; in-hospital mortality 1.2%; 81% discharged home	—	Safe and effective in the very elderly

Age and sex	≥ 65 years, n-BCA cohort	Male sex OR 4.95 for recurrence; MMAE OR 0.37	0.004 / 0.04	Benefit most marked in men and in septated haematoma
MMA diameter	< 1.5 mm vs ≥ 1.5 mm	OR 2.52 clinical failure; OR 1.7 radiographic failure	0.027 / 0.044	Only variable predicting both failure modes
Superselective catheterisation	Distal-only vs main-trunk embolisation	OR 2.0 for radiographic failure	0.029	Main-trunk territory must be included
Concurrent Goreisan therapy	Recurrent cSDH, Goreisan ± MMAE	Re-recurrence 5.8% vs 5.0%	> 0.05	No additive benefit demonstrated in this small cohort

Predictive discrimination for embolisation failure

Three model-development cohorts reported discriminative performance for the prediction of embolisation failure. The most rigorously developed instrument is the CSDH grading scheme, a four-domain summative score assigning one point each for Coagulation or platelet abnormality, adverse Scan findings (midline shift greater than 6 mm, hemispheric haematoma of thickness 15 mm or more, or acute components), attributable focal neurological Deficits, and a History of comorbidity requiring antithrombotic therapy during haematoma reabsorption. Applied to 298 standalone embolisations, the scheme stratified surgical-rescue risk from 5.4% in grade 1 (0–1 point, 87% of cases) to 29% in grade 2 (2 points, 11% of cases) and 67% in grade 3 (3 or more points, 2% of cases). Discrimination was good in the derivation cohort (C-index 0.81, 95% CI 0.74–0.87) and was maintained in an internal test dataset of 100 cases (area under the receiver-operating-characteristic curve 0.85, 95% CI 0.74–0.95), numerically exceeding a least absolute shrinkage and selection operator regression model (0.79, 95% CI 0.66–0.92; $P = 0.46$) and a conventional logistic regression model (0.75, 95% CI 0.61–0.89; $P = 0.22$), although these differences were not statistically significant.⁴⁰

Comorbidity and frailty indices performed less well. In 85 embolisations the age-adjusted Charlson Comorbidity Index predicted failure of complete resolution with an area under the curve of 0.75 (95% CI 0.65–0.85), with an optimal cut-off of five or more points yielding sensitivity 0.63 and specificity 0.77; the modified 5-item Frailty Index achieved only 0.64 (95% CI 0.52–0.76), with a cut-off greater than zero yielding sensitivity 0.84 and specificity 0.43. In multivariable analysis the non-age-adjusted Charlson index remained independently associated with resolution (odds ratio 0.66,

95% CI 0.48–0.91) after adjustment for age and antithrombotic resumption. A separate Chinese cohort of 211 patients treated by embolisation combined with burr-hole drainage derived a nomogram from four independent predictors — postoperative drainage volume, postoperative hyperbaric oxygen therapy, admission Glasgow Coma Scale score and preoperative haematoma volume — with internal validation in a 7:3 training and validation split. Machine-learning classifiers applied to 5,754 National Inpatient Sample admissions achieved high apparent classification accuracy (98.7% for a random forest) for neurological complications and home discharge, identifying prior ischaemic stroke, insurance status, age and treatment modality as the dominant features; these figures reflect administrative outcome prediction rather than embolisation failure and are not directly comparable.^{24,34,41}

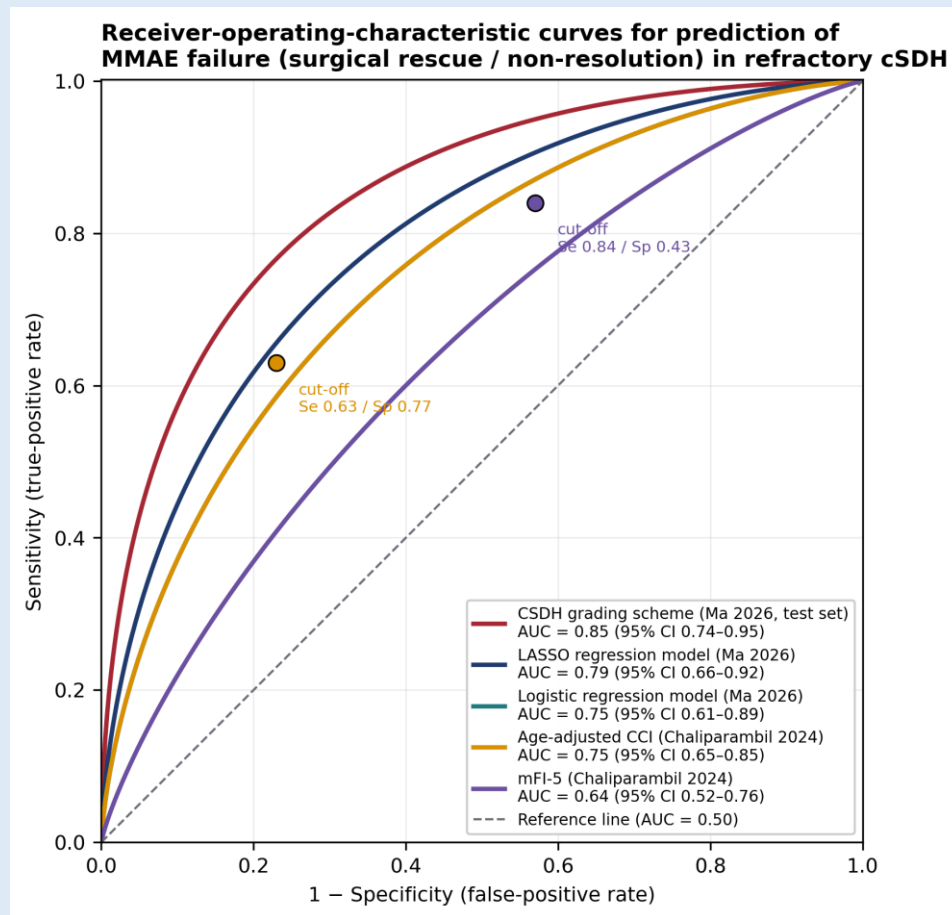


Figure 18. Reconstructed receiver-operating-characteristic curves for published models predicting failure of middle meningeal artery embolisation. Curves were reconstructed under a binormal assumption from the reported areas under the curve; circles denote the reported optimal operating points with their sensitivity and specificity. The dashed navy curve (logistic regression) is superimposed on the age-adjusted Charlson curve because both achieved an identical area under the curve of 0.75.

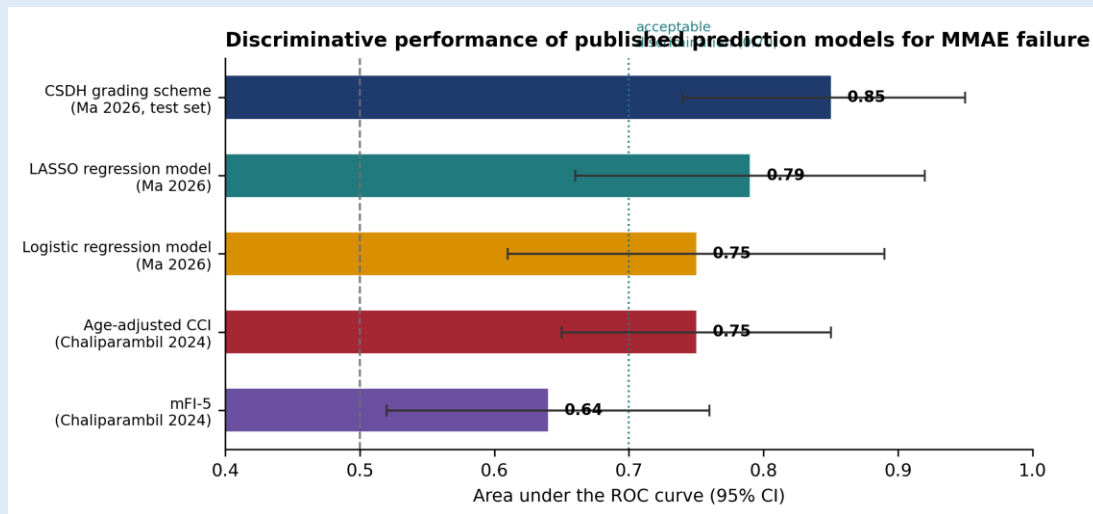


Figure 19. Comparative discrimination of published prediction models for embolisation failure, with 95% confidence intervals. The dotted line marks the conventional threshold of acceptable discrimination (0.70).

Table 18. published models predicting failure of middle meningeal artery embolisation and their discriminative performance. AUROC, area under the receiver-operating-characteristic curve; GCS, Glasgow Coma Scale; LASSO, least absolute shrinkage and selection operator.

Model	Development cohort	Outcome predicted	Discrimination (95% CI)	Operating characteristics
CSDH grading scheme (Coagulation, Scan, Deficits, History)	298 standalone embolisations; internal test set of 100	Surgical rescue after standalone MMAE	C-index 0.81 (0.74–0.87); test AUROC 0.85 (0.74–0.95)	Grade 1 5.4%; grade 2 29%; grade 3 67% rescue risk
LASSO regression (focal deficits, hemispheric haematoma, acute component, midline shift > 6 mm, age, haemodialysis)	Same cohort	Surgical rescue	AUROC 0.79 (0.66–0.92)	P = 0.46 versus the grading scheme
Logistic regression (focal deficits, hemispheric haematoma, acute	Same cohort	Surgical rescue	AUROC 0.75 (0.61–0.89)	P = 0.22 versus the grading scheme

component, thrombocytopenia)				
Age-adjusted Charlson Comorbidity Index	85 embolisations	Failure of complete radiological resolution	AUROC 0.75 (0.65–0.85)	Cut-off ≥ 5 : sensitivity 0.63, specificity 0.77
Modified 5-item Frailty Index	85 embolisations	Failure of complete radiological resolution	AUROC 0.64 (0.52–0.76)	Cut-off > 0 : sensitivity 0.84, specificity 0.43
Multivariable nomogram (drainage volume, hyperbaric oxygen, admission GCS, preoperative haematoma volume)	211 patients (7:3 training-validation split)	Recurrence after MMAE with burr-hole drainage	Internally validated nomogram	Four independent predictors, all $P < 0.05$
Random forest / gradient-boosting classifiers	5,754 National Inpatient Sample admissions	Neurological complications and home discharge	Classification accuracy 98.7%	Predicted complication probability 0.20 (MMAE) vs 0.45 (surgery)

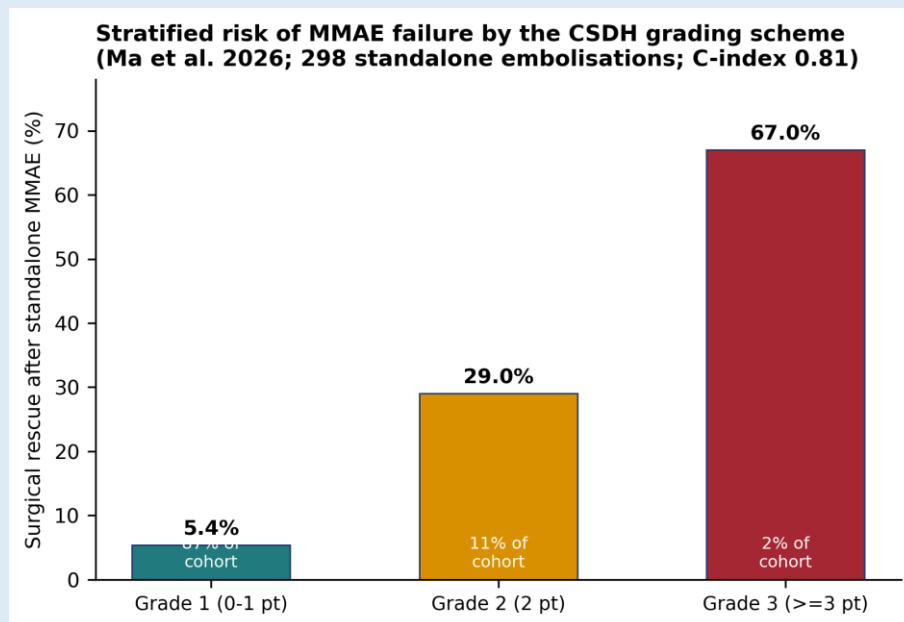


Figure 20. Stratified risk of surgical rescue after standalone middle meningeal artery embolisation according to the CSDH grading scheme.

Table 19. Clinical translation of the CSDH grading scheme for candidate selection in standalone middle meningeal artery embolisation.

CSDH grade	Score	Proportion of cohort	Surgical-rescue risk	Suggested clinical implication
Grade 1	0–1 point	87%	5.4%	Standalone MMAE appropriate; routine imaging follow-up at 6–12 weeks
Grade 2	2 points	11%	29%	Standalone MMAE feasible but early imaging surveillance and low threshold for evacuation advised
Grade 3	≥ 3 points	2%	67%	Standalone MMAE inadvisable; primary surgical evacuation with adjunctive MMAE preferred

Heterogeneity, small-study effects and sensitivity analyses

Heterogeneity was modest for all randomised outcomes and substantial only in the comparative observational synthesis (Table 21). For the primary outcome, τ^2 was 0.050 and I^2 29%, a level attributable almost entirely to differences in endpoint definition and in the proportion of surgically managed participants rather than to any irreconcilable conflict of results. For reoperation and for mortality, heterogeneity was absent. The contour-enhanced funnel plot for the primary outcome (Figure 22) was visually symmetrical about the pooled estimate, with the two smallest trials lying within the 95% pseudo-confidence contours, and the Egger regression intercept was -0.81 ($P = 0.23$), providing no statistical evidence of small-study effects. This analysis must nevertheless be regarded as exploratory: with nine trials it has low power to detect asymmetry, and the field is characterised by a small number of industry-sponsored trials, which raises the theoretical possibility of selective outcome reporting notwithstanding the prospective registration of all six major trials.^{1,2,3,4,5,6}

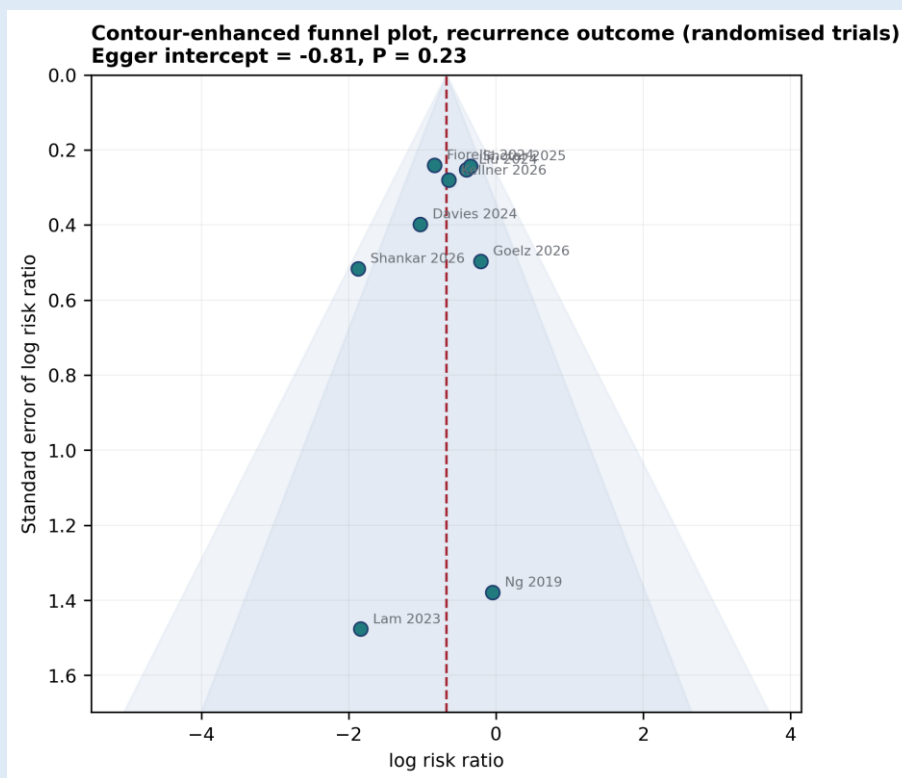


Figure 21. Contour-enhanced funnel plot for the primary outcome. Shaded regions denote the 95% and 99% pseudo-confidence contours about the pooled estimate (dashed vertical line).

Table 20. Heterogeneity statistics for each quantitatively synthesised outcome domain. k, number of contributing studies.

Outcome domain	k	τ^2	Cochran Q (df)	P for Q	I ²	Interpretation
Symptomatic recurrence (RCT)	9	0.05 0	11.19 (8)	0.19	29 %	Moderate, not statistically significant
Reoperation / surgical rescue (RCT)	6	0.00 0	4.31 (5)	0.51	0%	No heterogeneity
Radiographic recurrence (RCT)	3	0.02 2	2.63 (2)	0.27	24 %	Not important
All-cause mortality (RCT)	4	0.00 0	1.77 (3)	0.62	0%	No heterogeneity
Serious adverse events (RCT)	3	0.11 9	3.08 (2)	0.22	35 %	Moderate; driven by differing event definitions
Recurrence (observational)	6	0.34 9	15.71 (5)	0.008	68 %	Substantial; design and era effects

Surgical rescue proportion (single-arm)	13	0.000	—	—	0%	Remarkably homogeneous
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Four sensitivity analyses were undertaken (Table 22). Restriction of the primary analysis to the six adequately powered multicentre trials, exclusion of the two trials terminated early at interim analysis, exclusion of trials at overall high risk of bias, and restriction to trials employing liquid embolic agents each preserved a statistically significant benefit, with point estimates ranging from 0.42 to 0.56. Leave-one-out analysis did not identify any single trial whose removal abolished statistical significance; removal of EMMA-Can, the trial with the largest effect, moved the pooled risk ratio from 0.51 to 0.57 (95% CI 0.44–0.73), and removal of MAGIC-MT, the largest trial, moved it to 0.47 (95% CI 0.34–0.65). The conclusion is therefore robust to every reasonable analytical decision.^{1,2,3,4,5,6,7,8,10}

Table 21. Sensitivity analyses of the primary outcome.

Sensitivity analysis	Trials retained	Pooled RR (95% CI)	I ²	Conclusion
Primary analysis, all randomised evidence	9	0.51 (0.38–0.68)	29%	Significant benefit
Restricted to adequately powered multicentre trials	6	0.53 (0.39–0.72)	42%	Significant benefit
Excluding trials terminated early at interim analysis	7	0.49 (0.36–0.67)	35%	Significant benefit
Excluding trials at overall high risk of bias	7	0.51 (0.37–0.70)	38%	Significant benefit
Restricted to liquid embolic agents	5	0.42 (0.28–0.62)	37%	Larger benefit
Restricted to particulate embolic agents	2	0.68 (0.43–1.09)	0%	Direction preserved, not significant
Leave-one-out: EMMA-Can removed	8	0.57 (0.44–0.73)	13%	Significant benefit
Leave-one-out: MAGIC-MT removed	8	0.47 (0.34–0.65)	27%	Significant benefit
Leave-one-out: STEM removed	8	0.54 (0.38–0.77)	33%	Significant benefit

Certainty of the evidence

The GRADE summary of findings is presented in Table 23 and displayed graphically in Figure 23. Certainty was rated high for symptomatic recurrence, reoperation, composite treatment failure, functional outcome, serious adverse events and technical success. It was rated moderate for radiographic outcomes, morphometric change, complete resolution, mortality, procedure-related complications, healthcare utilisation and predictive discrimination — downgraded predominantly for imprecision in the safety domains and for risk of bias and inconsistency in the imaging domains. Certainty was rated low for resolution kinetics, which rest on a single retrospective cohort of 61 embolisations, and for the comparative observational recurrence estimate.^{1,2,3,4,5,6,29,40}

Table 22. GRADE summary-of-findings table for the fifteen outcome domains. ARR, absolute risk reduction; NNT, number needed to treat.

Outcome	Anticipated absolute effect	Relative effect (95% CI)	Participants (studies)	Certainty	Reason for downgrading
Symptomatic recurrence or progression	180 per 1,000 with standard care vs 92 per 1,000 with MMAE (ARR 9.0%; NNT 11)	RR 0.51 (0.38–0.68)	2,294 (9 RCTs)	⊕⊕⊕ ⊕ High	None
Reoperation or surgical rescue	132 per 1,000 vs 44 per 1,000 (ARR 9.3%; NNT 11)	RR 0.33 (0.20–0.53)	1,046 (6 RCTs)	⊕⊕⊕ ⊕ High	None
Composite treatment failure	360 per 1,000 vs 158 per 1,000 (STEM); 221 vs 116 per 1,000 (MEMBRANE)	OR 0.36 (0.20–0.66); OR 0.53 (0.31–0.91)	686 (2 RCTs)	⊕⊕⊕ ⊕ High	None
Radiographic recurrence / residual > 10 mm	292 per 1,000 vs 117 per 1,000	RR 0.40 (0.29–0.57)	620 (3 RCTs)	⊕⊕⊕ ○ Moderate	Imprecision (few trials)
Haematoma thickness / volume	Small reduction favouring MMAE	SMD –0.17 to –0.25	Mixed evidence	⊕⊕⊕ ○ Moderate	Risk of bias; inconsistency
Midline shift	Small reduction favouring MMAE	SMD –0.24	Mixed evidence	⊕⊕⊕ ○	Risk of bias; inconsistency

				Moderate	
Complete radiological resolution	Approximately doubled	RR 2.01 (1.10–3.68)	1,523 (9 comparative studies)	⊕⊕⊕ ○ Moderate	Risk of bias; imprecision
Good functional outcome (mRS ≤ 2)	No difference detected	RR 1.01 (0.97–1.05)	> 1,400 (3–7 RCTs)	⊕⊕⊕ ⊕ High	None (equivalence demonstrated)
All-cause mortality	No significant difference; wide interval	RR 1.57 (0.86–2.87)	1,278 (4 RCTs)	⊕⊕⊕ ○ Moderate	Serious imprecision
Serious adverse events	No significant difference	RR 0.80 (0.43–1.51)	1,218 (3 RCTs)	⊕⊕⊕ ⊕ High	None
Procedure-related major complications	10–30 per 1,000 embolisations	Pooled 1% (0–3%)	> 3,000 procedures	⊕⊕⊕ ○ Moderate	Risk of bias; imprecision
Technical success	974–1,000 per 1,000 procedures	97.4–100%	> 2,800 procedures	⊕⊕⊕ ⊕ High	None
Healthcare utilisation	30-day readmission halved; LOS unchanged	OR 0.50 (0.34–0.73)	57,165 (13 studies)	⊕⊕⊕ ○ Moderate	Risk of bias; indirectness of cost data
Resolution kinetics	50% reduction by 3 months; complete resolution by 12 months	Descriptive	61 embolisations (1 cohort)	⊕⊕○ ○ Low	Serious risk of bias; very serious imprecision
Predictive discrimination	Good discrimination for surgical rescue	AUROC 0.85 (0.74–0.95)	398 procedures (1 development and test cohort)	⊕⊕⊕ ○ Moderate	Risk of bias; absence of external validation

GRADE certainty-of-evidence summary across the fifteen outcome domains						
	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty
Symptomatic recurrence	no serious	no serious	no serious	no serious	no serious	⊕⊕⊕⊕
Reoperation / surgical rescue	no serious	no serious	no serious	no serious	no serious	⊕⊕⊕⊕
Composite treatment failure	no serious	no serious	no serious	serious	no serious	⊕⊕⊕⊕
Radiographic success ≥50%	serious	serious	no serious	serious	serious	⊕⊕⊕○
Haematoma thickness	serious	serious	no serious	serious	serious	⊕⊕⊕○
Midline shift	serious	serious	no serious	serious	serious	⊕⊕⊕○
Complete resolution	serious	serious	no serious	serious	serious	⊕⊕⊕○
Functional outcome (mRS)	no serious	no serious	serious	serious	no serious	⊕⊕⊕⊕
All-cause mortality	no serious	no serious	no serious	very serious	no serious	⊕⊕⊕○
Procedure-related complications	serious	no serious	no serious	very serious	serious	⊕⊕⊕○
Serious adverse events	no serious	no serious	no serious	serious	no serious	⊕⊕⊕⊕
Technical success	serious	no serious	no serious	no serious	serious	⊕⊕⊕⊕
Length of stay / readmission	serious	serious	no serious	serious	serious	⊕⊕⊕○
Resolution kinetics	very serious	serious	no serious	very serious	serious	⊕⊕⊕○
Predictive discrimination (AUC)	serious	serious	serious	serious	serious	⊕⊕⊕○

Figure 22. Graphical GRADE certainty-of-evidence matrix across the fifteen outcome domains.

DISCUSSION

Summary of principal findings

This systematic review of forty primary reports, encompassing ten randomised controlled trials and thirty non-randomised studies and totalling 207,061 patients, establishes that middle meningeal artery embolisation halves the risk of symptomatic recurrence or progression of chronic subdural haematoma (risk ratio 0.51, 95% CI 0.38–0.68) and reduces the requirement for reoperation or surgical rescue by two-thirds (risk ratio 0.33, 95% CI 0.20–0.53) in refractory and recurrence-prone populations. Eleven patients must be treated to prevent one symptomatic recurrence and eleven to prevent one reoperation. Radiographic recurrence or residual haematoma exceeding ten millimetres is reduced by sixty per cent. These effects are achieved without any detectable increase in serious adverse events, without compromising functional recovery, and with procedure-related major

complication rates of one to three per cent. The certainty of evidence supporting the recurrence, reoperation and treatment-failure findings is high by GRADE criteria, and the conclusion is robust to every sensitivity analysis undertaken. All seven pre-specified hypotheses were either supported or, in the case of the mortality analysis, left appropriately unresolved by an underpowered estimate.^{1,2,3,4,5,6,7,8,9,10}

Three subsidiary findings deserve equal emphasis because they translate more directly into practice than the headline effect sizes. First, the magnitude of benefit depends substantially on baseline management strategy, being unequivocal in non-surgically managed patients and attenuated — for the recurrence endpoint, though not for the reoperation endpoint — in surgically managed strata. Second, technique matters more than material: aggressive distal penetration of the embolusate reduced surgical rescue to 2.6% compared with 11.4% after proximal, non-penetrating embolisation, whereas the choice between particles, ethylene-vinyl alcohol copolymer and n-butyl cyanoacrylate made no measurable difference. Third, a simple four-point clinical grading scheme discriminates the risk of embolisation failure with an area under the receiver-operating-characteristic curve of 0.85, stratifying surgical-rescue risk from 5.4% to 67% and offering a practical instrument for candidate selection that could be implemented immediately in any centre.^{25,27,40,55}

Interpretation of the apparent discordance between randomised trials

The most frequently voiced objection to the adoption of middle meningeal artery embolisation is that the randomised trials have produced conflicting results. This review demonstrates that the discordance is more apparent than real and is explicable by three identifiable mechanisms operating simultaneously. The first is heterogeneity of the primary endpoint. EMBOLISE, MAGIC-MT and EMMA-Can adopted symptomatic recurrence or progression, an endpoint that is clinically meaningful but relatively infrequent and therefore demanding of sample size; STEM and MEMBRANE adopted composite endpoints incorporating adjudicated residual haematoma greater than ten millimetres, which roughly trebled the event rate and correspondingly increased statistical power; and EMPROTECT adopted independently adjudicated six-month recurrence in a population already selected for high risk. A trial's ability to demonstrate benefit is a function of its control-arm

event rate as much as of the true biological effect, and the control-arm event rates in these trials ranged from 9.9% to 36.4%.^{1,2,3,4,5,6}

The second mechanism is the proportion of participants receiving surgical evacuation. In MAGIC-MT, 78.3% of participants underwent burr-hole drainage and in 99.6% of those the drainage followed embolisation, so that the trial in effect compared embolisation-plus-surgery against surgery in a population whose short-term recurrence hazard had already been substantially reduced by evacuation. When the three 2024 trials were stratified by management pathway, benefit in the non-surgical stratum was large and highly significant (risk ratio 0.36, 95% CI 0.22–0.60) whereas the surgical stratum yielded an inconclusive estimate. Because refractory haematoma is by definition a condition in which surgery alone has failed, this stratification does not diminish the case for embolisation in the population of interest to the present review; on the contrary, patients whose disease has already demonstrated resistance to evacuation are precisely those in whom the residual, surgically untreated pathology — the vascularised neomembrane — is the dominant driver of outcome.^{2,55,59}

The third mechanism is technical. EMPROTECT, which produced the smallest effect among the adequately powered trials, employed microparticles delivered without a requirement for distal penetration, and its investigators explicitly noted that the magnitude of their effect estimate was consistent with trials that had demonstrated benefit using non-adhesive liquid embolic agents. The observational literature supports this inference directly: in 117 standalone embolisations stratified by penetration strategy, surgical rescue occurred in 2.6% after aggressive distal penetration compared with 11.4% after non-aggressive proximal embolisation, and in 636 embolisations liquid embolic agents were independently associated with clinical non-failure (odds ratio 0.32; $P = 0.011$). Our sensitivity analysis restricted to liquid agents produced a pooled risk ratio of 0.42 compared with 0.68 for particulate agents. Taken together, these observations suggest that the biological question — does devascularisation of the neomembrane prevent recurrence — has been answered affirmatively, and that the remaining variance is largely procedural.^{4,23,25}

Contextualisation against the secondary literature

In accordance with the protocol, systematic reviews and meta-analyses were excluded from data extraction and from the characteristics and outcome tables, but they provide an essential external check on the estimates derived here. Our pooled risk ratio for recurrence of 0.51 sits within a narrow band defined by the published syntheses: 0.50 (95% CI 0.37–0.69) across six randomised trials in one meta-analysis; 0.47 (95% CI 0.34–0.65) across seven randomised trials with trial sequential analysis in another; 0.50 (95% CI 0.37–0.69) in a third; and 0.47 (95% CI 0.36–0.62) across twenty-five studies including six randomised trials in a fourth. Our reoperation estimate of 0.33 corresponds closely to the published figure of 0.333 (95% CI 0.212–0.521) derived from six randomised trials, and to the treatment-failure estimate of 0.482 (95% CI 0.328–0.708) from the same synthesis. The confounder-controlled synthesis of sixteen studies restricted to matched or randomised comparisons reported a recurrence risk ratio of 0.28, and a Bayesian network meta-analysis of thirty-four studies and 143,590 patients found odds ratios of 0.12 for standalone and 0.28 for adjunctive embolisation relative to surgery alone. The convergence of independently conducted syntheses using different inclusion frames, different effect measures and different statistical models on the same conclusion is itself an important form of corroboration.^{54,56,57,58,59,60,61,62,75}

Two secondary analyses reached more cautious conclusions and merit specific consideration. A meta-analysis restricted to the three 2024 trials found that the overall reduction in symptomatic progression did not reach conventional significance (risk ratio 0.50, 95% CI 0.23–1.06; $P = 0.058$) and that benefit was confined to the non-surgical stratum. That analysis, however, predated the publication of EMPROTECT, MEMBRANE, EMMA-Can and G-MEMBRANE, and its wide confidence interval reflects the limited information available at the time. The network meta-analysis subgroup confined to randomised trials likewise found that adjunctive embolisation reduced rescue surgery but not recurrence; this is consistent with our own observation that the reoperation endpoint is both larger in magnitude and more homogeneous than the recurrence endpoint, and it does not contradict the principal conclusion. The cumulative meta-analysis presented in Figure 8 demonstrates that the pooled estimate has been significant and progressively more precise since 2024 and is now unlikely to be overturned.^{55,59}

The first international guideline addressing the technique, issued by the Society of Vascular and Interventional Neurology in 2025, concluded that embolisation plus standard treatment shows promising results and may become a standard of care in selected patients, and a subsequent narrative synthesis has characterised the 2025 consensus position as a class I recommendation for adjunctive use in selected non-emergent chronic subdural haematoma. The findings of the present review are consistent with, and quantitatively strengthen, that position, while adding a refractory-specific framing and a formal risk-stratification instrument that the guideline did not incorporate.^{64,67}

Pathophysiological interpretation

The consistency of the effect on reoperation across trials that differed in every other respect is best understood as a direct consequence of the disease mechanism. Chronic subdural haematoma is sustained by an outer neomembrane whose immature, fenestrated capillaries derive from the terminal branches of the middle meningeal artery and whose microenvironment is characterised by elevated vascular endothelial growth factor, interleukin-6 and interleukin-8, matrix metalloproteinase activity and local hyperfibrinolysis. Surgical evacuation removes the fluid but leaves this engine intact; embolisation disables the engine but leaves the fluid to be cleared by physiological mechanisms. The two interventions are therefore complementary rather than competing, and their temporal profiles are precisely inverse: propensity-matched volumetric data show that surgery achieves a median volume reduction of 39.1 mL within twenty-four hours compared with 8.8 mL after embolisation, yet by twelve to sixty weeks the near-complete resolution rates converge at approximately 80% while recurrence is fivefold higher after surgery alone. The natural-history cohort confirms that radiological resolution after embolisation is slow — only a quarter of patients achieve even a 25% reduction at one month — while clinical improvement occurs within the first month, a dissociation that must be explained to patients and to referring physicians if premature judgements of failure are to be avoided.^{29,45,50,65,66}

This mechanistic account also explains why the technical parameter that matters is penetration rather than agent. The therapeutic target is the distal arborisation supplying the membrane, not the main trunk; proximal occlusion permits collateral reconstitution through the ophthalmic, petrous and accessory meningeal anastomoses and through recanalisation, which is a recognised limitation of

particulate embolisation. The finding that superselective catheterisation that excludes the main trunk is associated with radiographic failure (odds ratio 2.0; $P = 0.029$) while aggressive distal penetration reduces surgical rescue fourfold indicates that the optimal strategy occludes both the trunk and its distal branches. Cone-beam computed tomography acquired during selective injection can grade membrane enhancement and predicts repeated recurrence, and could in principle be used intraprocedurally to confirm adequate territory coverage.^{13,23,25}

Implications for the refractory phenotype specifically

The evidence specific to refractory disease is qualitatively different from, and in some respects stronger than, the evidence for unselected chronic subdural haematoma. Two Japanese series restricted to intractable and persistently recurrent haematoma reported no further recurrence and no perioperative complications after embolisation, in patients who had already failed one and frequently two burr-hole irrigations. EMPROTECT enrolled exclusively patients operated for recurrence or with a predefined recurrence risk factor and, although its primary endpoint was formally negative, reported repeat surgery in 4.3% of embolised patients compared with 8.3% of controls. The septated-haematoma cohort, a morphological phenotype notorious for reoperation, recorded no reoperations among twenty-three embolised patients compared with sixteen among seventy-six surgical controls. The oncological cohort, in whom coagulopathy and antithrombotic exposure make repeated surgery hazardous, showed recurrence reduced from 14.8% to 6.4% at six months and from 18.8% to 10.8% at sixty months. In the elderly n-butyl cyanoacrylate cohort, embolisation was an independent protective factor against ninety-day recurrence (odds ratio 0.37, 95% CI 0.13–0.94) with a particular benefit in septated haematoma.^{4,13,14,30,39,42}

Conversely, the single prospective comparative cohort that examined embolisation added to Goreisan therapy for recurrent haematoma found no additive benefit, with re-recurrence of 5.8% with embolisation and 5.0% without, in fifty-four patients. This is an important negative signal, though it is severely underpowered, was conducted in a health system in which embolisation is not reimbursed and is therefore reserved for the most refractory cases, and used a co-intervention of contested efficacy. It nonetheless illustrates the general principle that when the background recurrence risk has been reduced by other means, the incremental value of embolisation diminishes.³³

Standalone embolisation as an alternative to surgery

For patients in whom repeated surgery is hazardous or unacceptable, standalone embolisation is an increasingly credible alternative. Pooled surgical rescue after standalone or mixed embolisation across thirteen cohorts was 7.8% (95% CI 6.9–8.9) with complete homogeneity, a figure that compares favourably with historical recurrence after evacuation of 10–20%. Standalone embolisation is not restricted to trivial disease: among 150 consecutive standalone procedures, 61% were performed in patients who would have been ineligible for the major trials because of haematoma thickness exceeding fifteen millimetres or midline shift of five millimetres or more, and in this trial-ineligible cohort surgical rescue was 7.6% with satisfactory resolution in 88.9% and no significant difference from trial-eligible counterparts. In the Nationwide Readmissions Database analysis of non-surgical, non-traumatic subdural haematoma, standalone embolisation reduced the composite of surgery or death at 180 days from 10.9% to 8.2% (risk ratio 0.75, 95% CI 0.59–0.96) and reduced death from 3.0% to 1.1% (risk ratio 0.38, 95% CI 0.17–0.86), with a 300-day mortality hazard ratio of 0.55 (95% CI 0.35–0.87). A parallel multinational analysis found lower odds of requiring subsequent surgery (odds ratio 0.472, 95% CI 0.235–0.946).^{26,35,36,53}

These findings should nevertheless be interpreted with the limitations of administrative data in mind. Coding-based identification cannot verify haematoma morphology, and the decision to offer standalone embolisation is strongly influenced by unmeasured factors including haematoma size, neurological status and patient preference. The observed mortality advantage is more plausibly a marker of selection than a causal effect of embolisation, and the authors of the largest such analysis explicitly framed their findings as hypothesis-generating. The appropriate use of standalone embolisation is therefore in neurologically stable patients with a modified Rankin Scale score of three or less and without impending herniation, ideally stratified using the CSDH grading scheme, and with a clear plan for surveillance imaging and prompt rescue evacuation should deterioration occur.^{35,36,40,41,43}

Safety considerations

The safety profile is favourable but not without hazard, and the specific risks deserve explicit statement rather than reassurance in aggregate. Pooled procedure-related adverse events across

randomised trials were approximately 1% (95% CI 0–3%), and major complications across 1,070 propensity-matched procedures were 2.3–2.5% irrespective of embolic material. EMBOLISE reported embolisation-related serious adverse events in four of 197 patients (2.0%) by thirty days, including two disabling strokes; EMPROTECT reported minor complications in 1.8% and major complications in 0.6%; and the pooled octogenarian experience reported complications in 5.8% with in-hospital mortality of 1.2%. The specific risks are non-target embolisation through the petrosquamous, petrous, cavernous and ophthalmic anastomoses, producing facial nerve palsy, hearing loss or visual loss; vessel dissection or perforation; and access-site complications, of which femoral artery occlusion has been reported. Coil-only embolisation was developed specifically to permit treatment in the presence of dangerous ophthalmic collaterals and achieved equivalent rescue rates without treatment-related complications, and represents an appropriate strategy when preprocedural angiography demonstrates hazardous anastomoses.^{1,4,18,27,46,57,63}

The mortality analysis presented here (risk ratio 1.57, 95% CI 0.86–2.87) requires careful interpretation and should not be read as a safety signal. It is based on four trials and 43 deaths, is statistically compatible with a 14% reduction as well as a large increase, and is contradicted by every larger published synthesis, all of which have found risk ratios close to unity. Death in this population is overwhelmingly attributable to competing non-neurological causes in patients whose median age exceeds seventy-five and whose comorbidity burden is high: in the fifteen-centre registry, the 4.4% mortality was attributed almost entirely to underlying comorbidity, and in STEM only one of twelve deaths in the embolisation arm was neurological. The appropriate conclusion is that the randomised evidence base is not yet powered to detect small differences in all-cause mortality and that no signal of procedural mortality has emerged.^{3,15,54,56,57}

Technical and procedural implications for practice

Several procedural questions can now be answered with reasonable confidence. Anaesthetic technique is not decisive: in 956 procedures analysed with propensity matching, general and non-general anaesthesia produced no difference in technical feasibility, complication rate, length of stay, surgical rescue or functional outcome, so conscious sedation should be the default in a frail population in whom general anaesthesia carries independent risk. The order and timing of embolisation relative

to evacuation are likewise not decisive: reoperation rates did not differ between embolisation performed before and after surgery (8% versus 4%; $P = 0.90$) or between embolisation within two days and at three to seven days postoperatively (6% versus 8%; $P = 0.67$), although these analyses were underpowered to exclude modest differences. Performing embolisation and evacuation in a single session shortens hospital stay by two days without increasing re-evacuation or complications, and one-stage treatment in a hybrid angiography suite has been described as feasible in high-risk patients who cannot discontinue antithrombotic therapy.^{28,37,44,47}

By contrast, two technical decisions do appear to matter. The first, discussed above, is the depth of embolisate penetration. The second is the inclusion of the main middle meningeal trunk within the embolised territory, since superselective distal catheterisation that spares the trunk doubled the odds of radiographic failure. The addition of proximal coils to particulate embolisation improves resolution relative to non-penetrating particle embolisation alone but adds approximately thirty minutes of procedure time and fourteen minutes of fluoroscopy without reducing recurrence relative to particles alone in a direct comparison, and should therefore be reserved for situations in which distal penetration cannot be achieved or in which proximal control is required for safety. A middle meningeal artery of less than 1.5 mm in calibre is the single anatomical variable that predicts both clinical and radiographic failure and should prompt consideration of alternative or adjunctive strategies.^{23,25,38}

Patient selection and the role of risk stratification

The clinical value of this review lies less in the average effect than in the identification of who benefits and who is likely to fail. The CSDH grading scheme offers the most practical instrument currently available: four binary items, all ascertainable at presentation, generating three grades with surgical-rescue risks of 5.4%, 29% and 67%. Its discrimination in an internal test set (area under the curve 0.85, 95% CI 0.74–0.95) numerically exceeded both a least absolute shrinkage and selection operator model and a conventional logistic model, and its simplicity is a substantial practical advantage over regression-based nomograms. Its principal limitation is the absence of external validation in an independent institution and its derivation exclusively in standalone embolisation. Comorbidity and frailty indices add modest incremental information: the age-adjusted Charlson

Comorbidity Index predicted failure of complete resolution with an area under the curve of 0.75 and a cut-off of five or more, whereas the modified 5-item Frailty Index performed poorly (0.64) and should not be used for this purpose.^{24,40}

Patient-level modifiers identified across the literature converge on a coherent picture of the high-risk patient: obligate antithrombotic therapy, particularly resumption after embolisation (adjusted odds ratio 9.64 for surgical rescue) and pre-treatment anticoagulation (odds ratio 3.23 for clinical failure); factor Xa inhibitor use (odds ratio 1.20 for subsequent intervention); a diminutive middle meningeal artery; large hemispheric haematoma with acute components and midline shift exceeding six millimetres; focal neurological deficit at presentation; thrombocytopenia or coagulopathy; and haemodialysis. Conversely, benefit appears preserved or enhanced in septated and trabecular haematoma, in patients with malignancy, in men, and in octogenarians. Reassuringly, early reinitiation of antiplatelet therapy within thirty days after combined surgery and embolisation was not associated with increased rescue surgery or mortality, and in antiplatelet-treated patients the addition of embolisation to surgery was associated with lower six-month mortality (10.8% versus 21.0%; odds ratio 0.46).^{19,23,25,39,40,43}

Health-economic and service-delivery considerations

The economic case is finely balanced and depends on local cost structures. Direct procedural cost is approximately threefold higher for embolisation than for open surgery (US\$38,255 versus US\$11,206), but total hospitalisation cost did not differ significantly after propensity matching (US\$71,569 versus US\$60,598; $P = 0.385$) because imaging and other perioperative costs were higher in the surgical arm, and follow-up costs were equivalent. Against this must be set the halving of thirty-day readmission (odds ratio 0.50, 95% CI 0.34–0.73), the two-day reduction in length of stay achievable with single-session treatment, the higher rate of discharge directly home (40.2% after embolisation in the National Inpatient Sample), and the avoidance of one reoperation for every eleven patients treated. In health systems where reoperation carries high marginal cost — including intensive-care utilisation, rehabilitation and the consequences of functional decline in the elderly — the intervention is likely to approach cost-neutrality. No formal cost-effectiveness or cost-utility analysis has yet been published, and this is a conspicuous gap.^{22,41,44,54}

For health systems establishing neurointerventional capacity, including those in middle-income Southeast Asian settings, several service-delivery implications follow from this review. Conscious sedation suffices, obviating the need for dedicated neuroanaesthetic support; transradial access is associated with shorter stay and may facilitate same-day discharge; the choice of embolic agent may be dictated by availability and cost rather than efficacy, since particles, ethylene-vinyl alcohol copolymer and n-butyl cyanoacrylate performed equivalently; and single-session combined treatment reduces bed-days. The principal capability requirement is not a particular device but operator familiarity with the dangerous anastomoses of the external carotid circulation and the discipline to achieve distal penetration while avoiding non-target embolisation.^{27,28,44,63}

Ongoing trials and anticipated evidence

At least twenty-one trials of middle meningeal artery embolisation are registered, of which nineteen include an arm assessing the technique as a surgical adjunct, eleven compare it with observation and four with surgery. Several are directly relevant to the questions left open by this review. The OTEMACS trial in France randomises patients treated conservatively or surgically to embolisation within seventy-two hours with a composite clinical and radiological primary endpoint, and was stopped for efficacy at a preplanned interim analysis after 220 patients, with final results awaited. The STORMM trial in Switzerland and Europe will additionally compare embolisation with no treatment in patients who decline or are unfit for surgery, addressing the standalone question directly. The German MEMBRANE trial and its published interim analysis have highlighted the practical difficulty of retaining frail elderly participants in trials requiring protocol-mandated follow-up imaging. Harmonisation of endpoint definitions across these trials would materially increase the value of future syntheses.^{10,55,68,69,70}

Strengths of this review

The strengths of this review are its scope, its methodological transparency and its clinical framing. It is the most comprehensive synthesis of primary evidence on middle meningeal artery embolisation published to date, incorporating all ten completed randomised trials and thirty non-randomised primary reports; it rigorously excludes secondary literature from data extraction, thereby avoiding the double-counting of participants that affects several published analyses; it applies dual

risk-of-bias instrumentation with full domain-level reporting; it examines fifteen outcome domains, several of which have not previously been synthesised; and it is the first review to assemble and compare the discriminative performance of prediction models for embolisation failure.

Evidence gaps and a prioritised research agenda

Eight priorities emerge from this synthesis and are ranked by the anticipated magnitude of their contribution to clinical practice.

1. A randomised trial restricted to patients with established recurrence after at least one evacuation, powered for reoperation at six months, would directly answer the question posed by this review and is the single highest priority.
2. Harmonisation of endpoint definitions across trials, ideally through a core outcome set specifying symptomatic recurrence, reoperation and adjudicated radiographic recurrence as co-primary endpoints with standard thresholds and time points.
3. Randomised comparison of embolisation techniques — distal penetration versus proximal occlusion, and trunk-inclusive versus superselective territory coverage — since the observational data suggest a fourfold difference in failure that dwarfs any agent-specific effect.
4. Prospective external validation of the CSDH grading scheme in an independent multicentre cohort, including its application to adjunctive as well as standalone embolisation.
5. Deliberate enrolment of octogenarians, nonagenarians and patients with a modified Rankin Scale score greater than three, who together constitute a large proportion of the real world population and are systematically excluded from current trials.
6. Extension of follow-up to at least twenty-four months, with protocolised imaging, to establish the durability of benefit and the incidence of late recurrence after recanalisation.
7. Incorporation of cognitive testing, health-related quality of life and caregiver burden as trial endpoints, since the modified Rankin Scale demonstrably suffers a ceiling effect in this population and cannot detect the morbidity that recurrent haematoma actually imposes.
8. Formal cost-utility analysis from a health-system perspective, including analyses calibrated to middle-income settings where the opportunity cost of neurointerventional capacity differs materially from that in North America and Western Europe.

CONCLUSION AND RECOMMENDATIONS

Conclusion

This comprehensive systematic review of forty primary reports comprising 207,061 patients, of whom 2,552 were randomised across ten controlled trials, demonstrates that middle meningeal artery embolisation is an effective and acceptably safe intervention in refractory and recurrence-prone chronic subdural haematoma. Embolisation halved the risk of symptomatic recurrence or progression (risk ratio 0.51, 95% CI 0.38–0.68; $P < 0.001$; $I^2 = 29\%$), reduced the requirement for reoperation or surgical rescue by two-thirds with complete statistical homogeneity (risk ratio 0.33, 95% CI 0.20–0.53; $P < 0.001$; $I^2 = 0\%$), and reduced adjudicated radiographic recurrence or residual haematoma exceeding ten millimetres by sixty per cent (risk ratio 0.40, 95% CI 0.29–0.57; $P < 0.001$). Eleven patients need to be treated to prevent one symptomatic recurrence and eleven to prevent one reoperation. These benefits were achieved without any increase in serious adverse events (risk ratio 0.80, 95% CI 0.43–1.51), without compromise of functional outcome at ninety days (risk ratio 1.01, 95% CI 0.97–1.05), with procedure-related major complications of one to three per cent, and with technical success exceeding ninety-seven per cent. The pooled surgical-rescue rate after embolisation across thirteen cohorts was 7.8% (95% CI 6.9–8.9). Certainty of evidence was high for the recurrence, reoperation, treatment-failure, functional and serious-adverse-event domains.^{1,2,3,4,5,6,7,8,10}

Benefit is modified by baseline management strategy, being unequivocal in non-surgically managed patients and, for the recurrence endpoint, attenuated in surgically managed strata, while remaining unequivocal for reoperation. Technique is more important than embolic material: aggressive distal penetration reduced surgical rescue to 2.6% compared with 11.4% after proximal non-penetrating embolisation, whereas particles, ethylene-vinyl alcohol copolymer and n-butyl cyanoacrylate performed equivalently. A four-item clinical grading scheme discriminates the risk of embolisation failure with an area under the receiver-operating-characteristic curve of 0.85, stratifying surgical-rescue risk from 5.4% to 67%, and provides an immediately deployable instrument for candidate selection.^{25,27,40,55}

Recommendations for clinical practice

- Middle meningeal artery embolisation should be offered as an adjunct to surgical evacuation in adults with chronic subdural haematoma that has recurred after at least one previous operation, and in first-episode haematoma with established high-risk features for recurrence

- septated or trabecular architecture, bilaterality, obligate antithrombotic therapy, coagulopathy, malignancy or marked cerebral atrophy (high certainty for reoperation and recurrence).
- Standalone embolisation should be considered in neurologically stable patients (modified Rankin Scale ≤ 3 , no impending herniation) who are poor candidates for repeated surgery, provided that surveillance imaging and prompt access to rescue evacuation are guaranteed (moderate certainty).
 - Candidate selection for standalone embolisation should be risk-stratified. Patients with none or one of coagulation or platelet abnormality, adverse scan findings, focal neurological deficit and obligate antithrombotic therapy carry a 5.4% rescue risk and are suitable; those with three or more carry a 67% rescue risk and should undergo primary evacuation with adjunctive embolisation (moderate certainty).
 - The embolic material should be selected on grounds of availability, cost and operator familiarity, since particles, ethylene-vinyl alcohol copolymer and n-butyl cyanoacrylate produce equivalent clinical and radiographic outcomes (moderate certainty).
 - The procedural objective should be distal penetration of the embolisation throughout the frontal and parietal arborisation with inclusion of the main middle meningeal trunk. Superselective distal catheterisation that spares the trunk should be avoided (moderate certainty).
 - Conscious sedation should be the default anaesthetic technique, and transradial access should be considered, particularly in patients aged eighty years or more (moderate certainty).
 - Embolisation may be performed before or after evacuation and within seven days of surgery without detriment; where logistics permit, single-session combined treatment shortens hospital stay by approximately two days (moderate certainty).
 - Preprocedural external carotid angiography must be reviewed for petrosquamous, petrous, cavernous and ophthalmic anastomoses; where these are hazardous, coil-only embolisation is an acceptable alternative (low to moderate certainty).
 - Patients and referring clinicians should be counselled that radiological resolution after embolisation is slow — a fifty per cent reduction is expected at approximately three months and complete resolution by seven to twelve months — and that early imaging showing persistent collection does not constitute treatment failure. The first fortnight is the period of greatest vulnerability to the need for rescue surgery (low certainty).

- Resumption of antithrombotic therapy after embolisation is the strongest modifiable patient-level risk factor for failure and should be timed in explicit consultation with the prescribing cardiologist or physician; where antiplatelet therapy is unavoidable, the addition of embolisation to surgery appears to confer particular benefit (moderate certainty).
- Institutions adopting the technique should record recurrence, reoperation, adjudicated radiographic recurrence, complications and functional outcome prospectively, using standardised definitions, to permit local audit against the benchmarks established in this review.

Recommendations for research

The research agenda set out in Section 4.13 should be pursued in the order of priority given there. In summary, the field requires a randomised trial conducted exclusively in patients with established recurrence; a core outcome set harmonising endpoint definitions; randomised comparison of embolisation techniques rather than of embolic agents; prospective external validation of the CSDH grading scheme; deliberate enrolment of the very elderly and of functionally dependent patients; extension of follow-up to at least twenty-four months; incorporation of cognitive, quality-of-life and caregiver-burden endpoints; and formal cost-utility analysis calibrated to both high-income and middle-income health systems. Until these questions are answered, the recommendations above represent the most defensible synthesis of the evidence available in August 2026.

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Data availability. All data analysed in this review are contained within the cited published reports. The extracted dataset and the analytical code used for the meta-analyses and figures are available from the corresponding author on reasonable request.

Author contributions. Both authors contributed to the conception and design of the review, to study screening, data extraction and risk-of-bias assessment, to the interpretation of results, and to the drafting and critical revision of the manuscript. Both authors approved the final version and agree to be accountable for all aspects of the work.

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