National Institute for Health and Care Excellence

Guideline version (Consultation)

Subarachnoid haemorrhage

[C] Evidence review for severity scoring systems

NICE guideline <number>

Evidence review underpinning

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Draft for Consultation

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ISBN
[add for final publication version only, delete this text for consultation version]

Contents

1 Severity scoring systems

Evidence review underpinning recommendations 1.1.13 and 1.2.7 and research recommendations in the NICE guideline.

1.1 Review question: What is the prognostic utility of severity scoring systems in adults with suspected or confirmed subarachnoid haemorrhage?

1.2 Introduction

SAH typically causes sudden severe headache rising to a peak within minutes, associated with vomiting and possibly altered level of consciousness. Over time, patients with subarachnoid haemorrhage may recover with little or no neurological consequence, may survive with significant disability, or may deteriorate and die.

SAH severity scoring systems have been developed in an attempt to codify the clinical findings that indicate the severity of a bleeding event. These have typically combined indicators of a patient's level of consciousness and neurological function. In current practice SAH severity scoring systems are used to guide decisions on patient care.

To be effective, a scoring system should contain simple, commonly understood criteria that facilitate rapid assessment of a patient's condition (should be easy to use). A system should have low intra- and inter-user variation in scores, and thresholds should have significant correlation with patient outcome.

This review was carried out to evaluate the prognostic accuracy of these severity scoring systems in people with SAH.

1.3 PICO table

For full details see the review protocol in Appendix A:.

Table 1: PICO characteristics of review question

Population	Adults (16 and older) with a suspected or confirmed subarachnoid haemorrhage caused by a suspected or confirmed ruptured aneurysm.

Prognostic variables under consideration	Severity scoring system such as:
	• World Federation of Neurosurgical Societies grading scale
	  ○ Grade1
	  ○ Grade 2
	  ○ Grade 3
	  ○ Grade 4
	  ○ Grade 5
	• Fisher scale
	  ○ Grade1
	  ○ Grade 2
	  ○ Grade 3
	  ○ Grade 4
	• Hunt and Hess Scale
	  ○ Grade1
	  ○ Grade 2
	  ○ Grade 3

	○ Grade 4 ○ Grade 5 • Glasgow Coma Scale ○ 3-15 • Prognosis on Admission of Aneurysmal Subarachnoid Haemorrhage (PAASH) scale ○ Grade1 ○ Grade 2 ○ Grade 3 ○ Grade 4 ○ Grade 5
Confounding factors	• Age
Outcome(s)	Markers of poor outcome: • Mortality • Functional status ○ Modified Rankin Scale (MRS) ○ Glasgow Outcome Score (GOS) ○ Oxford Handicap Score (OHS) • Rebleed subarachnoid haemorrhage Measured by: • Accuracy data ○ Sensitivity, specificity, positive predictive value, negative predictive value • Association data ○ Adjusted Risk Ratio or Odds Ratio Short term outcomes <30 days will be grouped. Outcomes will be reported monthly for the first year and grouped at yearly time-points thereafter.
Study design	• Cohort studies • Cross-sectional studies Studies will only be included if all the key confounders have been accounted for in a multivariate analysis. In the absence of multivariate analysis, studies that account for key confounders with univariate analysis or matched groups will be considered.

1 **Hunt & Hess scale (1968)**

Category	Criteria
Grade I	Asymptomatic, or minimal headache and slight nuchal rigidity.
Grade II	Moderate to severe headache, nuchal rigidity, no neurological deficit other than cranial nerve palsy.
Grade III	Drowsiness, confusion, or mild focal deficit.
Grade IV	Stupor, moderate to severe hemiparesis, possibly early decerebrate rigidity and vegetative disturbances.
Grade V	Deep coma, decerebrate rigidity, moribund appearance.

2

Fisher scale (1980)

Grade	Descriptions
Fisher I	No Blood detected
Fisher II	Diffuse deposition or thin layer with all vertical layers of blood (interhemispheric fissure, insular cistern, ambient cistern) <1 mm thick
Fisher III	Localized clots and/or vertical layers of blood >= 1mm in thickness
Fisher IV	Diffuse or no subarachnoid blood, but with intracerebral or intraventricular clots

Glasgow Coma Scale (1974)

	1	2	3	4	5
Eye (E)	Does not open eyes	Opens eyes in response to painful stimuli	Opens eyes in response to voice	Opens eyes spontaneously	N/A
Verbal (V)	Makes no sounds	Incomprehensible sounds	Utters inappropriate words	Confused/disoriented	Oriented, converses normally
Motor (M)	Makes no movements	Extension to painful stimuli (decerebrate response)	Abnormal flexion to painful stimuli (decorticate response)	Flexion/withdrawal to painful stimuli	Localizes painful stimuli

World Federation of Neurological Surgeons score (1988)

Grade	Original WFNS	Modified WFNS
I	GCS 15	GCS 15
II	GCS 13 – 14 with focal neurologic deficits	GCS14
III	GCS 13-14 without focal neurologic deficits	GCS 13
IV	GCS 7-12	GCS 7-12
V	GCS 3-6	GCS 3-6

Modified Rankin Scale (mRS) (1988)

0	No symptoms.
1	No significant disability. Able to carry out all usual activities, despite some symptoms.
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
3	Moderate disability. Requires some help, but able to walk unassisted.
4	Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
6	Dead.

Glasgow Outcome Scale (1975)

GOS Category	Proposed description of category
5 - Death	Ascribable to particular incident and due to original brain damage. Potentially subcategorize death according to whether occur before or after regaining consciousness to distinguish initial recovery from brain damage
4 - Persistent Vegetative State	Unresponsive and speechless for weeks or months after acute brain damage. Sleep wake cycles after 2-3 weeks
3 - Severe disability (conscious but disabled)	Dependent on daily support because of physical and/or mental causes
2 - Moderate disability (disabled but independent)	Independent in 'daily life' (for example, can use public transport and work in a sheltered environment). Able to maintain self-care and 'activities for daily living'. Considerable family disruption possible
1 - Good recovery	Resumption of normal life, although there may be minor neurological and psychological deficits. Return to work could lead to false impressions in either direction (for example, socioeconomic factors in work availability, attitude of past employers; included here are leisure interests and family relationships.

1.4 Clinical evidence

1.4.1 Included studies

Twenty-three observational studies were included in the review;[1, 31, 51, 57, 74, 78, 83, 106, 110, 117, 125, 126, 140, 163, 190, 196, 203, 240, 249, 250, 261, 266, 292] these are summarised in Table 2 below. Of the 23 studies included within the review, 16 studies were retrospective cohort studies and 7 were prospective cohort studies. Evidence from these studies is summarised in the clinical evidence summary below (Table 3).

See also the study selection flow chart in Appendix C:, study evidence tables in Appendix D:, forest plots in Appendix E: and GRADE tables in Appendix H:.

1.4.2 Excluded studies

See the excluded studies list in Appendix I:.

1.4.3 1 Summary of clinical studies included in the evidence review

2 **Table 2: Summary of studies included in the evidence review**

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments

Abulhasan 2018[1]	Single cohort study (n=434)
	all patients with spontaneous SAH admitted to the neurologic ICU (all patients admitted with nontraumatic SAH, proven by computed tomography (CT) scan or cerebrospinal fluid analysis)
		multivariate analysis	Hunt & Hess grades 4 & 5	• Age
				  ○ <60
				  ○ 60-79 years
				  ○ ≥80 years
				• Intracerebral haemorrhage
				• Intraventricular haemorrhage
				• Rebleeding within 24 hours
				• Maximum lumen size ≥7mm
					In hospital mortality	This study is an external validation study of the HAIR score.
						The study does not appropriately describe the follow up period for the outcomes.

Claasen 2004[31]	Prospective cohort study (n=467) Patients with SAH admitted to Neurological intensive care unit between July 1 1996 and June 1 2002, admitted within 3 days of onset (follow up: 3 months)	forward stepwise multiple logistic regression analysis	Hunt and Hess grade	• In hospital bleeding • Aneurysm size >10mm • Intraventricular haemorrhage • Loss of consciousness • Age (per decile)	Functional status: mRS 4-6	Outcome given as an odds ratio per grade increase (not individual grade odds ratios)
Dijkland 2016[51]	Retrospective cohort study (n=2,435) of two data sets.	multivariate logistic regression analysis	Fisher grade 1 – 4 WFNS 1 – 6	• Age	Mortality	Study uses the ISAT and Rotterdam cohort for external model validation

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
	Patients were 18 years or older, admitted to hospital less than or equal to 28 days after ictus, SAH proven by CT or CSF spectrophotometry and ruptured intracranial aneurysm as the presumed cause. (follow up: 60 days)			• Maximum lumen size aneurysm (mm)		
Duan 2016[57]	Prospective cohort study (n=520) Patients were age ≥ 60 years; and with aSAH treated endovascularly (follow up: 1 year)	multivariate logistic regression analysis	Hunt & Hess score 4 – 5 Fisher score 3 – 4	• Age ≥ 75 • Hypertension • Located on and distal the circle of Willis • Periprocedural complications	Functional status: mRS ≥ 3	
Galea 2017[74]	Prospective cohort study (n=3341) Patients with an aSAH were included and data were collected from 14 centres in the United Kingdom (follow up: at discharge)	multivariate analysis	WFNS grade (per grade increase)	• Age • Pre-op bleed • DCI • Hypertension • IHD • Treatment • CSF diversion • CSF infection Age • Pre-op bleed • DCI	GOS 1 - 3	GOS was dichotomized into favourable outcome (GOS score 4 and 5) and unfavourable outcome (GOS score 1–3).

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
				• Hypertension • IHD • Treatment • CSF diversion • CSF infection		
Germanson 1998[78]	Cohort study (n=751) Patients were selected according to the NICSAH I study (unclear of inclusion criteria) (follow up: 3 months)	logistic regression	GCS	• Age • Sex • Location of aneurysm • Level of consciousness	Functional status: GOS 1 – 3	Not all prognostic information given and unclear regarding which predictors are used within the regression model. Unable to meta-analyse outcome.

Goldberg 2018[83]	Retrospective cohort study (n=146)
	Bernese SAH database for poor grade patients (WFNS grade IV – V), elderly patients (age ≥ 60 years) suffering from aSAH admitted between 2005 to 2017
	(follow up: 23.5 months)
		multivariate cox regression analysis	WFNS grade V compared to WFNS grade IV	• Age:
				  ○ 60-69
				  ○ 70-79
				  ○ 80-90
				• ICH
					Survival Analyses	

Inamasu 2016[106]	Single centre retrospective cohort study with	multivariable analysis	GCS score 3 – 4	• Age • Female sex • GCS score 3 – 4	In hospital mortality	The study does not appropriately describe the follow

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
	multivariate analysis (n=115) Patients with WFNS grade V SAH who were considered suitable candidates for endovascular treatment, who were taken to the angiographic suite within 24 hours of symptom onset. The coil selection was at the discretion of the attending EVT specialist			• Intraoperative / postoperative rebleeding • Delayed cerebral ischaemia • Years of experience of EVT specialist		up period for the outcomes.
Jabbarli 2015[110]	Retrospective cohort study (n=157) Patients with non-traumatic non aneurysmal subarachnoid haemorrhage admitted between January 2005 to December 2012 (follow up: 6 months)	multivariate analysis	Hunt & Hess grade	• Age > 65 • Diffuse basal bleeding pattern • Acute hydrocephalus • Leucocytosis at mission • Rebleeding • Vasospasm on TCS • Cerebral infarction • Meningitis • Severe anaemia	Functional status: mRS 3-6	

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
Karamanakos 2012[117]	Retrospective cohort study (n=1657) Admission alive to the hospital within 24 hours from the start of the acute aneurysmal SAH verified by CT, spinal tap or autopsy (follow up: 1 – 3 days; 4 – 30 days; 1 – 12 months)	multivariate analysis	Hunt and Hess grade I - V	• Age • Gender • Time period of SAH • ICT • IVH • SDH • Hydrocephalus • Site of aneurysm • Size of aneurysm • Number of saccular aneurysms	Mortality	Not clearly specified which confounders were used in multivariate analysis, only reports only those that were statistically significant
Konzalla 2016[125] / Konzalla 2018[126]	Retrospective cohort study (n=193) Patients with aneurysms of carotid bifurcation and posterior communicating artery between 1999 and 2013 (follow up: 6 months)	multivariate analysis	WFNS grade I – III Fisher grade 3	• Age • Admission status • Aneurysms of carotid bifurcation artery • Absence of mild or severe cerebrovascular spasm	Functional status: mRS >2	
Lee 2014[140]	Retrospective cohort study (n=400) Patients were identified from the GET with the guidelines stroke database (patients	multivariate analysis	Hunt & Hess grades	• Age • IVH • Rebleed within 24hours	In hospital mortality	Validation of the HAIR score for SAH. The study does not appropriately describe the follow up period for the outcomes.

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
	were excluded if CT negative SAH and traumatic SAH) (follow up:)					
Mocco 2006[163]	Retrospective cohort study (n=98) Patients with aneurysmal SAH admitted to Columbia University Medical Center and enrolled in our Subarachnoid Hemorrhage Outcomes Project. Of these, 148 patients were of poor clinical grade, defined as Hunt and Hess Grades IV and V. SAH was confirmed in all patients by head computed tomographic scans and was rated according to the Fisher scale. (follow up: 12 months)	multivariable analysis	Admission Hunt & Hess IV – V Worst Hunt & Hess of V Fisher grade 3 – 4	• Aged ≥ 64 years of age • Hyperglycaemia • Worst Hunt and Hess grade V • Aneurysm size 13mm or greater	Functional status: mRS 4 – 6	

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
Orakdogen 2016[190]	Retrospective cohort study (n=104) Evidence of SAH from a computerized tomography (CT) scan and the presence of an angiographically-confirmed saccular aneurysm as the cause of the haemorrhage	logistic regression analysis	WFNS (IV – V)	• Age > 55 • Size of aneurysm >7mm • Clinical vasospasm	Mortality	The study does not appropriately describe the follow up period for the outcomes.
Ozono 2020[196]	Retrospective cohort study (n=1123) All patients with aSAH who were age 20 years or older and the interval between symptom onset and admission was ≤72 hours. (follow up: 3 months)	multivariate logistic regression analysis	Age Modified WFNS (I – V)	• Endovascular Coiling • Mean age • Sex • Location of aneurysm • Vasospasm • Duration from onset to treatment	Mortality mRS ≥3	Results for elderly and non-elderly were combined for analysis.
Rabinstein 2004[203]	Retrospective cohort study (n=81) consecutive patients with symptomatic cerebral	multivariate analysis	Poor grade WFNS	• Age • Coiling	Functional status: mRS >2	

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
	vasospasm from aneurysmal SAH treated with percutaneous balloon angioplasty or selective intra-arterial papaverine infusion between 1990 and 2000 (follow up: 3 months)					
Starke 2009[240]	Retrospective cohort study (n=160) Poor grade aSAH patients (follow up: 1 year)	multivariate analysis	GCS	• Gender • Age > 70	Functional status: mRS 4 - 6	Authors have grouped outcomes from admission GCS and refer to outcomes as mRS 0-3 (favourable outcome) and mRS 4-6 (unfavourable outcome)
Taki 2011[249]	Retrospective cohort study (n=614) Patients with SAH who were ≥20 years old at onset; SAH on CT scans or lumbar puncture; saccular aneurysm as the cause of the SAH confirmed on three dimensional CTA, MRA or DSA and aneurysmal	multivariate logistic regression analysis	Admission WFNS grade IV – V	• Age • Admission WFNS • Preadmission aneurysm rupture • Vasospasm induced cerebral infarct • Infection • Shunt dependent hydrocephalus • Seizure	Functional status: mRS Mortality	

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
	obliteration by clipping or coiling within 14 days of onset (follow up: 12 months)			• Post clipping haemorrhagic complication • Post coiling ischemic complication		
Taweesomboonyat 2019 [250]	Retrospective observational cohort study (n=189) Patients who underwent neurosurgical clipping or endovascular coiling for SAH (follow up: 6 months)	multivariate logistic regression analyses	Hunt & Hess grade	• Age • Seizure • Deterioration before intervention • Side of aneurysm • Aneurysm horizontal orientation • Intervention	mRS 3 - 6	Poor outcomes defined as mRS 3 – 6
Van Donkelaar 2017[261]	Prospective observational cohort study (n=1620) patients with a nontraumatic SAH (follow up: 2 months)	multivariate logistic regression analyses	rWFNS	• Age • Gender • History • Initial WFNS • Type of SAH • Aneurysm location • Aneurysm size • mFisher grade • Intracerebral hematoma • Subdural hematoma • Hydrocephalus • Type of treatment	Functional status: mRS 4 - 6	rWFNS equates to WFNS score post resuscitation. Poor outcome (modified Rankin Scale Score 4–6)

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Comments
Wang 2019[266]	Prospective cohort study with multivariate analysis n = 104 All these patients underwent early microsurgical clipping or endovascular coiling within three days after SAH (follow up: 6 – 36 months)	Multivariate analysis	Fisher grade I – II WFNS grade IV	• Low density area on CT • Hydrocephalus • Endovascular coiling • External ventricular drainage • Intraventricular drainage • Decompressive craniectomy • Intracranial hematoma • Cerebral Hernia	mRS 0 - 2	Favourable outcome was defined as mRS ≤2
Zhao 2017[292]	Prospective and observational cohort study n = 136 Patients who presented with poor-grade aSAH at the time of treatment (Poor-grade aSAH was defined as a WFNS grade of IV or V) (follow up: 12 months)	multivariate analysis	WFNS grade V modified Fisher grade	• Age • Aneurysm neck size • Postop pneumonia	Functional status: mRS 4 - 6	Poor-grade aSAH was defined as a mRS 4 - 6

1 See Appendix D:for full evidence tables.

2

1.4.4 Quality assessment of clinical studies included in the evidence review

Table 3: Clinical evidence summary: Hunt and Hess grade (per grade increase)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
mRS 4 - 6 scale 0-6; high score represents poorer outcome	467 (1 study) 3 months	⨁⨁⨁⊖ MODERATE1 due to indirectness	OR 1.8 (1.3 to 2.49) per clinical grade increase
mRS 3 - 6 scale 0-6; high score represents poorer outcome	157 (1 study) 6 months	⨁⨁⨁⊖ MODERATE1 due to indirectness	OR 2.03 (1.13 to 3.65) per clinical grade increase
1 The majority of the evidence had indirect outcomes (outcome per grade increase) and population (non aneurysmal SAH)			

Table 4: Clinical evidence summary: Hunt and Hess grade two

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Hunt and Hess grade 1 as reference			
Mortality	1657 (1 study) 1 - 3 days	⨁⨁⊖⊖ LOW1,2 due to risk of bias, imprecision	OR 0.6 (0.1 to 3.6)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Mortality	1657 (1 study) 4 - 30 days	⨁⨁⨀⨀ LOW1,2 due to risk of bias, imprecision	OR 1.4 (0.4 to 4.9)
Mortality	1657 (1 study) 1 - 12 months	⨁⨁⨀⨀ LOW1,2 due to risk of bias, imprecision	OR 0.6 (0.2 to 1.8)
mRS 3 – 6 scale 0-6; high score represents poorer outcome	185 (1 study) 6 months	⨁⨁⨀⨀ LOW1,2 due to risk of bias, imprecision	OR 1.19 (0.13 to 10.89)
1 Downgraded by 1 increment if the confidence interval crossed the null line 2 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias			

1

1 **Table 5: Clinical evidence summary: Hunt and Hess grade three**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Hunt and Hess grade 1 as reference			
Mortality	1657 (1 study) 1 - 3 days	⨁⨁⊖⊖ LOW1,2 due to risk of bias, imprecision	OR 1.1 (0.2 to 6.05)
Mortality	1657 (1 study) 4 - 30 days	⨁⨁⨁⊖ MODERATE2 due to risk of bias	OR 3.3 (1 to 10.89)
Mortality	1657 (1 study) 1 - 12 months	⨁⨁⊖⊖ LOW1,2 due to risk of bias, imprecision	OR 2.8 (0.8 to 9.8)
mRS 3 – 6 scale 0-6; high score represents poorer outcome	185 (1 study) 6 months	⨁⨁⊖⊖ LOW1,2 due to risk of bias, imprecision	OR 1.43 (0.13 to 15.73)

1 Downgraded by 1 increment if the confidence interval crossed the null line

2 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

1 **Table 6: Clinical evidence summary: Hunt and Hess grade four**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Hunt and Hess grades 1-3 as reference			
In-hospital mortality	848 (2 studies)	⊕⊕⊕⊖ MODERATE2 due to risk of bias	OR 5.11 (2.67 to 9.77)
Hunt and Hess grade 1 as reference			
Mortality	1657 (1 study) 1 - 3 days	⊕⊕⊕⊖ MODERATE2 due to risk of bias	OR 6 (1.3 to 27.69)
Mortality	1657 (1 study) 4-30 days	⊕⊕⊕⊖ MODERATE2 due to risk of bias	OR 10 (3 to 33.33)
Mortality	1657 (1 study) 1-12 months	⊕⊕⊕⊖ MODERATE2 due to risk of bias	OR 3.4 (1 to 11.56)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
mRS 3 – 6 scale 0-6; high score represents poorer outcome	185 (1 study) 6 months	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision	OR 6.07 (0.6 to 61.12)
mRS 4 - 6 scale 0-6; high score represents poorer outcome	98 (1 study) 12 months	⊕⊕⊕⊖ MODERATE1 due to imprecision	HR 1.1 (0.21 to 5.87)
1 Downgraded by 1 increment if the confidence interval crossed the null line 2 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias			

1

2

3 **Table 7: Clinical evidence summary: Hunt and Hess grade five**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Hunt and Hess grade 1-3 as reference			
In-hospital mortality	848 (2 studies)	⊕⊕⊕⊖ MODERATE2 due to risk of bias	OR 42.02 (22.01 to 80.24)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Hunt and Hess grade 1 as reference			
Mortality	1657 (1 study) 1-3 days	⨁⨁⨁⨀ MODERATE2 due to risk of bias	OR 92 (21 to 403.04)
Mortality	1657 (1 study) 4-30 days	⨁⨁⨁⨀ MODERATE2 due to risk of bias	OR 43 (11 to 168.1)
Mortality	1657 (1 study) 1-12 months	⨁⨁⨁⨀ MODERATE2 due to risk of bias	OR 12 (1.8 to 79.99)
mRS 4 - 6 scale 0-6; high score represents poorer outcome	98 (1 study) 12 months	⨁⨁⨁⨀ MODERATE1 due to imprecision	HR 3.83 (0.61 to 24.01)
1 Downgraded by 1 increment if the confidence interval crossed the null line			

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
2 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias			

1

2 **Table 8: Clinical evidence summary: Hunt and Hess grade 4 – 5**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Hunt and Hess grade 1-3 as reference			
mRS >3 scale 0-6; high score represents poorer outcome	520 (1 study) 12 months	⨁⨁⨁⊖ MODERATE1 due to indirectness	OR 1.76 (1.13 to 2.73)
1 The majority of the evidence had indirect outcomes (outcome included multiple scores – grade 4 and 5)			

3

1 **Table 9: Clinical evidence summary: Fisher grade (per grade increase)**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
mRS 4 - 6 scale 0-6; high score represents poorer outcome	136 (1 study) 12 months	⨁⨁⨁⨀ MODERATE1 due to indirectness	OR 2.3 (1.5 to 3.53)
1 The majority of the evidence had indirect outcomes (outcome per grade increase)			

2

3

4 **Table 10: Clinical evidence summary: Fisher grade 1**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Fisher grade 4 as reference			
Mortality	2435 (1 study) 60 days	⨁⨁⨀⨀ LOW1,2 due to risk of bias and imprecision	OR 0.36 (0.09 to 1.44)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Fisher grade 0 as reference			
mRS 4 - 6 scale 0-6; high score represents poorer outcome	1620 (1 study) 2 months	⨁⨁⨁⊖ MODERATE1 due to imprecision	OR 0.8 (0.3 to 2.13)
1 Downgraded by 1 increment if the confidence interval crossed the null line 2 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias			

1

2 **Table 11: Clinical evidence summary: Fisher grade 1 - 2**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Fisher grade 3-4 as reference			
mRS 0 – 2 scale 0-6; high score represents poorer outcome	104 (1 study) 6 months	⨁⨁⊖⊖ LOW1,2 due to risk of bias and indirectness	OR 12.10 (2.10 to 69.72)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 The majority of the evidence had indirect outcomes (outcome included multiple scores – grade 1 and 2)			

1

2 **Table 12: Clinical evidence summary: Fisher grade 2**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Fisher grade 4 as reference			
Mortality	2435 (1 study) 60 days	⨁⨁⨁⊖ MODERATE2 due to risk of bias	OR 0.52 (0.27 to 1)
Fisher grade 0 as reference			
mRS 4 - 6 scale 0-6; high score represents poorer outcome	1620 (1 study) 2 months	⨁⨁⨁⊖ MODERATE1 due to imprecision	OR 1.1 (0.4 to 3.02)
1Downgraded by 1 increment if the confidence interval crossed the null line			

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
2 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias			

1

2 **Table 13: Clinical evidence summary: Fisher grade 3**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Fisher grade 4 as reference			
Mortality	2335 (1 study) 60 days	⨁⨁⊖⊖ LOW1,2 due to risk of bias and imprecision	OR 0.97 (0.7 to 1.34) Pooled
Fisher grade 1 as reference			
mRS >2 scale 0-6; high score represents poorer outcome	193 (1 study) 6 months	⨁⨁⊖⊖ LOW2,3 due to risk of bias, indirectness	OR 0.49 (0.25 to 0.96)
mRS 4 - 6			

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
scale 0-6; high score represents poorer outcome	98 (1 study) 12 months	⊕⊕⊕⊖ MODERATE1 due to imprecision	OR 1.41 (0.44 to 4.51)
Fisher grade 0 as reference			
mRS 4 - 6 scale 0-6; high score represents poorer outcome	1620 (1 study) 2 months	⊕⊕⊕⊖ MODERATE1 due to imprecision	OR 1.6 (0.4 to 6.4)

1 Downgraded by 1 increment if the confidence interval crossed the null line
2 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
3 The majority of the evidence had an indirect population (Patients with aneurysms of carotid bifurcation and posterior communicating artery)

1

1 **Table 14: Clinical evidence summary: Fisher grade 3 – 4**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Fisher grade 1-2 as reference			
mRS >3 scale 0-6; high score represents poorer outcome	520 (1 study) 12 months	⨁⨁⨁⊖ MODERATE1 due to indirectness	OR 3.23 (2.43 to 4.3)
1 The majority of the evidence had indirect outcomes (outcome included multiple scores – grade 3 and 4)			

2

3 **Table 15: Clinical evidence summary: Fisher grade 4**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Fisher grade 0 as reference			
mRS 4 - 6 scale 0-6; high score represents poorer outcome	1620 (1 study) 2 months	⨁⨁⨁⨁ HIGH	OR 4.1 (1.7 to 9.89)
Fisher grade 1 as reference			
mRS 4 - 6			

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
scale 0-6; high score represents poorer outcome	98 (1 study) 12 months	⊕⊕⊕⊖ MODERATE1 due to imprecision	OR 1.09 (0.33 to 3.58)
1 Downgraded by 1 increment if the confidence interval crossed the null line			

1

2 **Table 16: Clinical evidence summary: WFNS (per grade increase)**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
GOS 1 – 3 scale 1-5; high score represents positive outcome.	3341 (1 study) At discharge	⊕⊕⊖⊖ LOW1,2 due to risk of bias, indirectness	OR 2.06 (1.91 to 2.22)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 The majority of the evidence had indirect outcomes (outcome per grade increase)			

3

4

1 **Table 17: Clinical evidence summary: WFNS 1-3**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
WFNS grade 4-5 as reference			
mRS >2 scale 0-6; high score represents poorer outcome	193 (1 study) 6 months	⨁⨁⨀⨀ LOW1,2 due to risk of bias, indirectness	OR 9.6 (4.9 to 18.81)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 The majority of the evidence had indirect outcomes (outcome included multiple scores – grade 1 to 3)			

2

3 **Table 18: Clinical evidence summary: WFNS 2**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
WFNS grade 1 as reference			
Mortality	2335 (1 study; 2 cohorts) 60 days	⨁⨁⨁⨁ MODERATE2 due to risk of bias	OR 1.94 (1.3 to 2.87) Pooled
Mortality	1123 (1 study; 2 cohorts) 90 days	⨁⨁⨀⨀ MODERATE1 due to imprecision	OR 2.07 (0.87 to 4.9)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
mRS ≥3 scale 0-6; high score represents poorer outcome	1123 (1 study; 2 cohorts) 90 days	⊕⊕⊖⊖ MODERATE1 due to imprecision	OR 1.64 (0.93 to 2.92)
mRS 4 - 6 scale 0-6; high score represents poorer outcome	1620 (1 study) 2 months	⊕⊕⊕⊕ HIGH	OR 1.6 (1.1 to 2.33)

1 Downgraded by 1 increment if the confidence interval crossed the null line

2 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

1

2 **Table 19: Clinical evidence summary: WFNS 3**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
WFNS grade 1 as reference			
Mortality	2335 (1 study; 2 cohorts) 60 days	⊕⊕⊖⊖ LOW1,2 due to risk of bias and imprecision	OR 1.82 (0.95 to 3.47)
Mortality	1123 (1 study; 2 cohorts) 90 days	⊕⊕⊕⊖ MODERATE1 due imprecision	OR 2.26 (0.8 to 6.34)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
mRS ≥3 scale 0-6; high score represents poorer outcome	1123 (1 study; 2 cohorts) 90 days	⨁⨁⨁⨁ HIGH	OR 4.35 (2.29 to 8.27)
mRS 4 - 6 scale 0-6; high score represents poorer outcome	1620 (1 study) 2 months	⨁⨁⨁⨁ HIGH	OR 3.2 (1.4 to 7.31)
1 Downgraded by 1 increment if the confidence interval crossed the null line 2 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias			

1

2 **Table 20: Clinical evidence summary: WFNS 4**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
WFNS grade 1 as reference			
Mortality	2335 (1 study; 2 cohorts) 60 days	⨁⨁⨁⊖ MODERATE1 due to risk of bias	OR 5.05 (2.91 to 8.77)
Mortality	1123 (1 study; 2 cohorts) 90 days	⨁⨁⨁⨁ HIGH	OR 2.54 (1.11 to 5.81)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Mortality	614 (1 study) 12 months	⨁⨁⨁⨀ MODERATE1 due to risk of bias	OR 3.71 (1.03 to 13.36)
mRS 3-6 scale 0-6; high score represents poorer outcome	614 (1 study) 12 months	⨁⨁⨁⨀ MODERATE1 due to risk of bias	OR 3.46 (1.49 to 8.04)
mRS ≥3 scale 0-6; high score represents poorer outcome	1123 (1 study; 2 cohorts) 90 days	⨁⨁⨁⨁ HIGH	OR 10.50 (6.35 to17.38)
mRS 4 - 6 scale 0-6; high score represents poorer outcome	1620 (1 study) 2 months	⨁⨁⨁⨁ HIGH	OR 5.7 (3.7 to 8.78)
WFNS grade 5 as reference			
mRS 0 – 2 scale 0-6; high score represents poorer outcome	104 (1 study) 6 months	⨁⨁⨁⨀ MODERATE1 due to risk of bias	OR 10.82 (3.73 to 31.37)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias			

Table 21: Clinical evidence summary: WFNS 4 - 5

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
WFNS grade 1-3 as reference			
Mortality	104 (1 study)	⨁⨁⊖⊖ LOW1,2 due to risk of bias, indirectness	OR 88.81 (8.61 to 916.19)
mRS >2 scale 0-6; high score represents poorer outcome	81 (1 study) 3 months	⨁⨁⊖⊖ LOW1,2 due to risk of bias, indirectness	OR 3.58 (1.28 to 10.01)
1 The majority of the evidence had indirect outcomes (outcome included multiple scores – grade 4 and 5) 2 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias			

1 **Table 22: Clinical evidence summary: WFNS 5**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
WFNS grade 1 as reference			
Mortality (Pooled)	2335 (1 study, 2 cohorts) 60 days	⨁⨁⨀⨀ LOW1,2 due to risk of bias, inconsistency	OR 42.38 (1.17 to 1534.17)
Mortality	1123 (1 study, 2 cohorts) 90 days	⨁⨁⨁⨁ HIGH	OR 9.22 (4.35 to 19.52)
Mortality	614 (1 study) 12 months	⨁⨁⨁⨀ MODERATE1 due to risk of bias	OR 9.43 (2.5 to 35.57)
mRS ≥3 scale 0-6; high score represents poorer outcome	1123 (1 study, 2 cohorts) 90 days	⨁⨁⨁⨀ MODERATE2 due to inconsistency	OR 31.80 (13.75 to 73.53)
mRS 4 - 6 scale 0-6; high score represents poorer outcome	1620 (1 study) 2 months	⨁⨁⨁⨁ HIGH	OR 12.1 (7.3 to 20.06)
mRS 3-6 scale 0-6; high score represents poorer outcome	614 (1 study) 12 months	⨁⨁⨁⨀ MODERATE1 due to risk of bias	OR 13.48 (5.09 to 35.7)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
mRS 4 - 6 scale 0-6; high score represents poorer outcome	136 (1 study) 12 months	⨁⨁⨁⨁ HIGH	OR 8.6 (3.1 to 23.86)
WFNS grade 4 as reference			
Survival Analyses	146 (1 study) 23.5 months	⨁⨁⨁⊖ MODERATE1 due to risk of bias	HR 2.78 (1.69 to 4.57)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 Downgraded by 1 or 2 increments because of heterogeneity, I2>50%, p>0.04, subgroup analysis not possible; <2 studies per subgroup.			

1

1 **Table 23: Clinical evidence summary: WFNS 6**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
WFNS grade 1 as reference			
Mortality	2435 (1 study) 60 days	⨁⨁⨁⊖ MODERATE1 due to risk of bias	OR 5.75 (2.41 to 13.72)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias			

2

3 **Table 24: Clinical evidence summary: Glasgow Coma Scale 3 - 4**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
GCS grades 5-6 as reference			
In-hospital mortality	115 (1 study)	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision, indirectness	OR 2.27 (0.91 to 5.68)
1 Downgraded by 1 increment if the confidence interval crossed the null line			

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
2 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 3 The majority of the evidence had indirect outcomes (outcome included multiple scores – GCS 3 – 4)			

1

2 **Table 25: Clinical evidence summary: Glasgow Coma Scale 8 - 9**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
GCS grades 10-12 as reference			
mRS 4 – 6 scale 0-6; high score represents poorer outcome	160 (1 study) 1 year	⨁⨁⊖⊖ LOW1,2 due to risk of bias, indirectness	OR 14.2 (1.5 to 134.41)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 The majority of the evidence had indirect outcomes (outcome included multiple scores – GCS 8 – 9)			

3

4 **Table 26: Clinical evidence summary: Glasgow Coma Scale 5 - 7**

5

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
GCS grades 10-12 as reference			
mRS 4 – 6 scale 0-6; high score represents poorer outcome	160 (1 study) 1 year	⨁⨁⊖⊖ LOW1,2 due to risk of bias, indirectness	OR 38.5 (4.2 to 352.92)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 The majority of the evidence had indirect outcomes (outcome included multiple scores – GCS 5 – 7)			

1

2 **Table 27: Clinical evidence summary: Glasgow Coma Scale 3 - 4**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
GCS grades 10-12 as reference			
mRS 4 – 6 scale 0-6; high score represents poorer outcome	160 (1 study) 1 year	⨁⨁⊖⊖ LOW1,2 due to risk of bias, indirectness	OR 63.4 (5.6 to 717.76)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias			

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
2 The majority of the evidence had indirect outcomes (outcome included multiple scores – GCS 3 – 4)			

1

2 **Table 28: Clinical evidence summary for evidence not suitable for GRADE – GCS per grade**

Outcomes	No of Participants (studies) Follow up	Risk of bias	Relative effect
GOS 1 – 3 scale 1-5; high score represents positive outcome.	751 Germanson 1998 [78] 3 months	High risk of bias	OR 1.5 for a three-point difference between two GCS scores 1

3 1 The study provides no information on statistical variance, therefore the committee were unable to ascertain the statistical significance of this outcome

4 See Appendix F: for full GRADE tables.

1.5 Economic evidence

1.5.1 Included studies

No health economic studies were included.

1.5.2 Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix G:.

1.6 Evidence statements

1.6.1 Clinical evidence statements

One outcome measure for quality of life from 1 study was not suitable for inclusion in the GRADE summary tables.

The study found a trend towards mortality or severe impairment (GOS 1 - 3) in quality of life if there was a three-point difference in Glasgow Coma Scale. (n=751, low risk of bias).

1.6.2 Health economic evidence statements

No relevant economic evaluations were identified.

1.7 The committee's discussion of the evidence

1.7.1 Interpreting the evidence

1.7.1.1 The outcomes that matter most

The critical outcomes in this review were mortality, functional status and rate of recurrent subarachnoid haemorrhage. The committee considered these critical outcomes would, if predicted accurately, guide discussion around treatment decisions. The committee agreed that accurately predicting risk of morbidity and mortality would help clinicians to identify people with SAH who would likely benefit from intervention and those in whom outcomes are so poor that intervention would be unlikely to be clinically justified. Functional status was to be measured by validated grading systems such as the Modified Rankin Scale, Glasgow Outcome Score or Oxford Handicap Score.

The evidence review intended to assess the prognostic accuracy of validated severity scoring systems in predicting these outcomes. The committee did not define any thresholds for risk scores providing a significant prognostic value. Therefore, the committee assessed the magnitude of effect.

No evidence was found for the statistical significance for prognostic accuracy of severity scoring systems.

1.7.1.2 The quality of the evidence

The evidence ranged from high to very low quality, however the majority of the evidence was of low quality, using small datasets with retrospective validation. The committee had

particular concerns over the accuracy of the outcome data, agreeing that the accuracy of the data presented was unclear. The committee also noted some inconsistency in the magnitude of the risk association between different scoring tools and the specified outcomes. The committee agreed that some outcomes were indirect due to the inclusion of an indirect population (non-aneurysmal SAH and aneurysm of the carotid bifurcation); pooling of outcome data across multiple risk score thresholds also added uncertainty to the prognostic accuracy of some scores.

Due to the uncertainty in the clinical evidence, the committee did not consider it possible to recommend the use of a single severity scoring tool as a prognostic indicator. The committee also considered this uncertainty as the basis for a recommendation not to use a subarachnoid haemorrhage severity score in isolation to determine the need for, or timing of, transfer of care to a specialist neurosurgical centre.

The committee agreed that it would be useful to have a universal severity scoring system as a clinical descriptor that also reliably and accurately predicts outcome following SAH as this would assist clinical decision making and utilisation of resources. The committee made a high priority research recommendation to determine which factors best predict mortality or disability for people with aneurysmal subarachnoid haemorrhage (see Appendix J:).

1.7.1.3 Benefits and harms

The benefits of a well validated severity score include a global assessment of a patient's clinical condition in an easily understood format, which can help communication, and inform further interventions and care, and prognosis. The harms from a poorly validated score can include a bias against active treatment of patients with a poor predicted outcome.

The committee experience is that a proportion of patients that are initially in 'poor grade' categories (typically characterised by the aneurysmal subarachnoid haemorrhage resulting in altered consciousness and/or a need for ventilation for more than 48 hours) will achieve a meaningful or independent recovery with rapid resuscitation, critical care and neurosurgical or neurointerventional management. The committee agreed that the risk of this harm was such that they could only recommend a severity score on the basis of robust good quality evidence.

The available evidence examined association between clinical outcomes and severity scoring systems including Hunt & Hess (grade I-V), Fisher grade (I-IV), WFNS (1-5) and Glasgow Coma Score (3-15). All of these systems showed associations between worse scores and poorer clinical outcomes but the committee noted that the scores were assessed in small datasets and used different predictor variables in their multivariate analysis and outcomes, so comparisons across scores and studies are of limited value. Individual severity scoring systems showed association for some outcomes and not others at different cut offs or time points. However, none of the systems were consistent for all outcomes and cut offs or time points, which meant that the committee were unable to pick one scoring system over another.

There was a trend of an increased risk of morbidity and mortality with a higher Hunt & Hess score. Two studies showed an incremental increase in risk of poor functional status (as indicated by a high mRS) with each Hunt & Hess grade increase, with an odds ratio for poor functional status of 1.8 and 2.03 per Hunt and Hess grade increase, respectively, in each study. Several studies also showed an increase in risk of mortality up to a year after ictus with higher Hunt and Hess scores.

Three studies reported an increase in mortality with each increase in Fisher grade, with 1 large study showing a low risk of mortality at the lowest Fisher grade (OR 0.36) when compared to those with the highest grading (grade 4). A higher Fisher grade was also associated with a higher mRS score, indicating a greater risk of poor functional status.

The evidence showed that a higher WFNS score was associated with a higher risk of morbidity and mortality, with a significantly increased risk of mortality at the highest grading of WFNS. There was also a trend for every WFNS score increase to be associated with a higher risk of morbidity (indicated by a high mRS).

The evidence on Glasgow Coma Score showed that between 2 groups with lower levels of consciousness (multivariate analysis of patients with GCS 3-6; GCS 5 – 6 versus GCS 3 – 4), there was an increased risk of in-hospital mortality with a lower GCS score. One study also indicated that every decrease in GCS score was associated with a higher risk of increased morbidity indicated by a high mRS score (4 – 6).

The committee acknowledged that the evidence was generally of low quality but showed associations between the individual severity scores and poor outcomes. The committee noted that the severity scoring systems had not been prospectively validated in appropriately powered datasets from large cohorts of people with SAH and information about discrimination and calibration of the individual scoring systems is lacking. The committee was concerned that the potential harm from use of the scoring systems to support decision making in clinical practice may outweigh any benefit.

The committee agreed that the scoring systems in this review may be useful as clinical descriptors, but from their experience were aware that severity score can vary over time, especially soon after symptom onset. The committee were also aware that severity scoring systems are used in current clinical practice to influence decisions about transfer of care to a specialist neurosurgical centre. Thus, transfer into a specialist centre may be delayed or denied to people with SAH and a score indicating a poor prognosis (often referred to as ‘poor grade’). Due to the uncertainty in the evidence and their experience the committee agreed that this practice should not be supported, but decisions about transfer to a neurosurgical centre should be based on a broader assessment of the person’s clinical condition, the radiological findings, and comorbidities.

The committee were aware that scoring systems are also used to support treatment decisions for people with a confirmed diagnosis of aneurysmal SAH. The committee agreed that the evidence on severity scoring systems does not support this practice and that treatment decisions should be based on a holistic patient assessment rather than solely on a severity score. On the basis of the evidence and their experience the committee recommended that SAH severity scores should not be used in isolation to determine the suitability of any management option.

1.7.2 Cost effectiveness and resource use

No published economic evaluations were identified for inclusion in this review. The committee noted that use of severity scoring systems does not directly incur additional costs as the scores are primarily based on clinical observation and assessment. The Fisher score is based on CT scan findings, but this will have been carried out for all patients with an aneurysmal subarachnoid haemorrhage as part of diagnosis and also does not incur an additional cost.

The committee commented that in some cases severity scoring systems are being used as the sole indicator to determine whether a person with a confirmed subarachnoid haemorrhage is transferred to a neurosurgical centre for specialist assessment and care. They expressed concern that this often means that ‘poor grade’ patients are not transferred unless their condition improves. Consequently, these people may not receive timely specialist care, which may lead to poorer outcomes.

The committee acknowledged that there is little evidence available to compare the effects of neurosurgery or neurointervention in a specialist centre with conservative management in a general district hospital in people with ‘poor grade’ subarachnoid haemorrhage. However, the

committee considered that based on the specific expertise available and evidence in other clinical areas, better outcomes would be expected in a specialist centre.

The committee considered that the recommendation not to use severity scoring systems in isolation to determine suitability of interventions may lead to additional transfers to neurosurgical centres. However, overall this was not considered likely to result in a substantial resource impact due to the small number of additional transfers as a result of the recommendation.

1.7.3 Other factors the committee took into account

The committee noted that although there are numerous severity scoring systems, with the majority being based on or adapted from the GCS, there is no single severity scoring system that is used universally to predict morbidity and mortality in people with aSAH. The committee were concerned that scores are used inappropriately whereby people are denied assessment at neurosurgical centres and this informed their recommendation.

The committee added that severity scoring systems are used by healthcare professionals to assess a patient's clinical state at a single timepoint, but clinical state and severity score may vary over time, especially soon after symptom onset. The committee acknowledged that in practice severity scoring systems can be a useful clinical descriptor to provide the person with aSAH and their family or carers information about their current condition. However, severity scoring systems need to be used together with radiological findings, medical history and comorbidities. The committee considered that this reinforces the need to base clinical management decisions on a holistic patient assessment rather than solely on a severity scoring system. Therefore, the committee made the recommendation to not use a severity scoring system in isolation.

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1 Appendices

2 Appendix A: Review protocols

3 **Table 29: Review protocol: Severity scoring systems in subarachnoid haemorrhage**

ID	Field	Content
0.	PROSPERO registration number	CRD42019132514
1.	Review title	What is the prognostic utility of severity scoring systems in adults with suspected or confirmed subarachnoid haemorrhage?
2.	Review question	What is the prognostic utility of severity scoring systems in adults with suspected or confirmed subarachnoid haemorrhage?
3.	Objective	To determine the prognostic utility of different scoring systems in adults with a suspected or confirmed subarachnoid haemorrhage.
4.	Searches	The following databases will be searched: • Embase • MEDLINE Searches will be restricted by: • English language only The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review.
5.	Condition or domain being studied	Aneurysmal subarachnoid haemorrhage
6.	Population	Inclusion: Adults (16 and older) with a suspected or confirmed subarachnoid haemorrhage caused by a suspected or confirmed ruptured aneurysm. Exclusion: • Adults with subarachnoid haemorrhage caused by head injury, ischaemic stroke or an arteriovenous malformation. • Children and young people aged 15 years and younger.
7.	Intervention/Exposure/Test	Prognostic factors: Severity scoring system such as: • World Federation of Neurosurgical Societies grading scale: ○ Grade1 ○ Grade 2 ○ Grade 3 ○ Grade 4 ○ Grade 5

		• Fisher scale:
		  ○ Grade1
		  ○ Grade 2
		  ○ Grade 3
		  ○ Grade 4
		• Hunt and Hess Scale:
		  ○ Grade1
		  ○ Grade 2
		  ○ Grade 3
		  ○ Grade 4
		  ○ Grade 5
		• Glasgow Coma Scale:
		  ○ 3-15
		• PAASH:
		  ○ Grade1
		  ○ Grade 2
		  ○ Grade 3
		  ○ Grade 4
		  ○ Grade 5

8.	Comparator/Reference standard/Confounding factors	Confounding factors: • Age
9.	Types of study to be included	• Cohort studies • Cross-sectional studies Studies will only be included if all the key confounders have been accounted for in a multivariate analysis. In the absence of multivariate analysis, studies that account for key confounders with univariate analysis or matched groups will be considered.
10.	Other exclusion criteria	Exclusions: • Studies that do not account for key confounders. • Adults with subarachnoid haemorrhage caused by head injury, ischaemic stroke or an arteriovenous malformation. • Children and young people aged 15 years and younger.
11.	Context	

12.	Primary outcomes (critical outcomes)	Markers of poor outcome:
		• Mortality
		• Functional status
		  ○ Modified Rankin Scale (MRS)
		  ○ Glasgow Outcome Score (GOS)
		  ○ Oxford Handicap Score (OHS)
		• Rebleed subarachnoid haemorrhage
		
		Measured by:
		• Accuracy data
		  ○ SN, SP, PPV, NPV

		• Association data ○ Adjusted RR or OR Short term outcomes <30 days will be grouped. Outcomes will be reported monthly for the first year and grouped at yearly time-points thereafter.	
13.	Secondary outcomes (important outcomes)	n/a	
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. If not an intervention review, add: A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4).	
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. QUIPS will be used to critically appraise risk prediction studies. Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.	
16.	Strategy for data synthesis	Aggregate data on prognostic accuracy and prognostic association of severity scoring systems will be collected and synthesized in a quantitative data analysis. Endnote will be used for bibliography, citations, sifting and reference management. If more than one study covered the same combination of population, risk factor and outcome then meta-analysis will be used to pool results. Meta-analysis will be carried out using the generic inverse variance function on Review Manager using fixed effect model. Data synthesis will be completed by two reviewers, with any disagreements resolved by discussion, or if necessary a third independent reviewer.	
17.	Analysis of sub-groups	Subgroups (if heterogeneity): • Timing of scoring from ictus ○ <7 days ○ 7-14 days ○ >14-28 days ○ >28 days	
18.	Type and method of review	☐	Intervention
		☐	Diagnostic

		☒	Prognostic
		☐	Qualitative
		☐	Epidemiologic
		☐	Service Delivery
		☐	Other (please specify)
19.	Language	English	
20.	Country	England	
21.	Anticipated or actual start date		
22.	Anticipated completion date	3 February 2021	
23.	Stage of review at time of this submission	Review stage	Started / Completed
		Preliminary searches	☑ / ☑
		Piloting of the study selection process	☑ / ☑
		Formal screening of search results against eligibility criteria	☑ / ☑
		Data extraction	☑ / ☑
		Risk of bias (quality) assessment	☑ / ☑
		Data analysis	☑ / ☑
24.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail SAH@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre	
25.	Review team members	From the National Guideline Centre: • Ms Gill Ritchie • Mr Ben Mayer • Mr Audrius Stonkus • Mr Vimal Bedia • Ms Emma Cowles • Ms Jill Cobb • Ms Amelia Unsworth	

26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.	
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.	
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website.	
29.	Other registration details		
30.	Reference/URL for published protocol		
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
32.	Keywords	Subarachnoid haemorrhage, scoring system	
33.	Details of existing review of same topic by same authors	None	
34.	Current review status	☐	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated

		☐	Discontinued
35..	Additional information		
36.	Details of final publication	www.nice.org.uk	

1

2 **Table 30: Health economic review protocol**

Review question	All questions where health economic evidence applicable
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2003, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual.[174] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will decide based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded based on applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below.

	The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2003 or later but that depend on unit costs and resource data entirely or predominantly from before 2003 will be rated as 'Not applicable'. • Studies published before 2003 will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

This literature search strategy was used for the following review;

- What is the prognostic utility of severity scoring systems in adults with suspected or confirmed subarachnoid haemorrhage?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[174]

For more information, please see the Methods Report published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

Searches were constructed using the following approach:

- Population AND Prognostic/risk factor terms AND Study filters

Table 31: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 24 June 2020	Exclusions Observational studies Prognostic studies

Database	Dates searched	Search filter used
Embase (OVID)	1974 – 24 June 2020	Exclusions Observational studies Prognostic studies

1 **Medline (Ovid) search terms**

1.	exp Subarachnoid Hemorrhage/
2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)).ti,ab.
3.	(SAH or aSAH).ti,ab.
4.	exp Intracranial Aneurysm/
5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain) adj3 (aneurysm* or aneurism* or hematoma* or haematoma*)).ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23
25.	6 not 24
26.	limit 25 to English language
27.	World Federation of Neurosurgical Societ*.ti,ab.
28.	(WFNS or m-WFNS or mWFNS or h-WFNS or hWFNS).ti,ab.
29.	(Glasgow adj coma).ti,ab.
30.	GCS.ti,ab.
31.	Glasgow Coma Scale/
32.	(Fisher* adj (grade* or scale* or score*)).ti,ab.
33.	mFS.ti,ab.
34.	(Hunt adj2 Hess).ti,ab.
35.	(PAASH or Prognosis on Admission of Aneurysmal Subarachnoid Hemorrhage).ti,ab.
36.	or/27-35
37.	((risk* or predict* or prognos* or severity or grading or diagnos*) adj4 (tool* or rule* or index* or indices or score* or scoring or scale* or model* or system* or algorithm* or stratif* or criteria or calculat* or classification* or grade*)).ti,ab.

38.	((score* or scoring or stratif*) adj3 (system* or schem* or scale*)).ti,ab.
39.	Severity of Illness Index/
40.	or/37-39
41.	26 and (36 or 40)
42.	predict.ti.
43.	(validat* or rule*).ti,ab.
44.	(predict* and (outcome* or risk* or model*)).ti,ab.
45.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
46.	decision*.ti,ab. and Logistic models/
47.	(decision* and (model* or clinical*)).ti,ab.
48.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
49.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.
50.	ROC curve/
51.	or/42-50
52.	prognosis/
53.	(predict* or prognos*).ti,ab.
54.	Logistic models/
55.	Disease progression/
56.	or/52-55
57.	Epidemiologic studies/
58.	Observational study/
59.	exp Cohort studies/
60.	(cohort adj (study or studies or analys* or data)).ti,ab.
61.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
62.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
63.	Controlled Before-After Studies/
64.	Historically Controlled Study/
65.	Interrupted Time Series Analysis/
66.	(before adj2 after adj2 (study or studies or data)).ti,ab.
67.	exp case control study/
68.	case control*.ti,ab.
69.	Cross-sectional studies/
70.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
71.	or/57-70
72.	41 and (51 or 56 or 71)

1 **Embase (Ovid) search terms**

1.	*subarachnoid hemorrhage/
2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)).ti,ab.
3.	(SAH or aSAH).ti,ab.
4.	exp intracranial aneurysm/

5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain or saccular or berry or wide-neck*) adj3 (aneurysm* or aneurism* or hematoma* or haematoma*)).ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	Case report/ or Case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	Nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental animal/
19.	Animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice).ti.
22.	or/14-21
23.	6 not 22
24.	limit 23 to English language
25.	World Federation of Neurosurgical Societ*.ti,ab.
26.	(WFNS or m-WFNS or mWFNS or h-WFNS or hWFNS).ti,ab.
27.	(Glasgow adj coma).ti,ab.
28.	GCS.ti,ab.
29.	Glasgow coma scale/
30.	(Fisher* adj (grade* or scale* or score*)).ti,ab.
31.	mFS.ti,ab.
32.	(Hunt adj2 Hess).ti,ab.
33.	(PAASH or Prognosis on Admission of Aneurysmal Subarachnoid Hemorrhage).ti,ab.
34.	or/25-33
35.	((risk* or predict* or prognos* or severity or grading or diagnos*) adj4 (tool* or rule* or index* or indices or score* or scoring or scale* or model* or system* or algorithm* or stratif* or criteria or calculat* or classification* or grade*)).ti,ab.
36.	((score* or scoring or stratif*) adj3 (system* or schem* or scale*)).ti,ab.
37.	"severity of illness index"/
38.	or/35-37
39.	24 and (34 or 38)
40.	predict.ti.
41.	(validat* or rule*).ti,ab.
42.	(predict* and (outcome* or risk* or model*)).ti,ab.
43.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
44.	decision*.ti,ab. and Statistical model/
45.	(decision* and (model* or clinical*)).ti,ab.

46.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
47.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.
48.	Receiver operating characteristic/
49.	or/40-48
50.	prognosis/
51.	(predict* or prognos*).ti,ab.
52.	Logistic models/
53.	Disease progression/
54.	or/50-53
55.	Clinical study/
56.	Observational study/
57.	family study/
58.	longitudinal study/
59.	retrospective study/
60.	prospective study/
61.	cohort analysis/
62.	follow-up/
63.	cohort*.ti,ab.
64.	62 and 63
65.	(cohort adj (study or studies or analys* or data)).ti,ab.
66.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
67.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
68.	(before adj2 after adj2 (study or studies or data)).ti,ab.
69.	exp case control study/
70.	case control*.ti,ab.
71.	cross-sectional study/
72.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
73.	or/55-61,64-72
74.	39 and (49 or 54 or 73)

B.21 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to subarachnoid haemorrhage population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase.

Table 32: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2003 – 23 June 2020	Exclusions Health economics studies
Embase	2003 – 23 June 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 23 June 2020 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

1.	exp Subarachnoid Hemorrhage/
2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)).ti,ab.
3.	(SAH or aSAH).ti,ab.
4.	exp Intracranial Aneurysm/
5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain or saccular or berry or wide-neck*) adj3 (aneurysm* or aneurism* or hematoma* or haematoma*)).ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23

25.	6 not 24
26.	limit 25 to English language
27.	Economics/
28.	Value of life/
29.	exp "Costs and Cost Analysis"/
30.	exp Economics, Hospital/
31.	exp Economics, Medical/
32.	Economics, Nursing/
33.	Economics, Pharmaceutical/
34.	exp "Fees and Charges"/
35.	exp Budgets/
36.	budget*.ti,ab.
37.	cost*.ti.
38.	(economic* or pharmaco?economic*).ti.
39.	(price* or pricing*).ti,ab.
40.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
41.	(financ* or fee or fees).ti,ab.
42.	(value adj2 (money or monetary)).ti,ab.
43.	or/27-42
44.	26 and 43

1 **Embase (Ovid) search terms**

1.	subarachnoid hemorrhage/
2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)).ti,ab.
3.	(SAH or aSAH).ti,ab.
4.	exp intracranial aneurysm/
5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain or saccular or berry or wide-neck*) adj3 (aneurysm* or aneurism* or hematoma* or haematoma*)).ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/

21.	(rat or rats or mouse or mice).ti.
22.	or/14-21
23.	6 not 22
24.	limit 23 to English language
25.	health economics/
26.	exp economic evaluation/
27.	exp health care cost/
28.	exp fee/
29.	budget/
30.	funding/
31.	budget*.ti,ab.
32.	cost*.ti.
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
38.	or/25-37
39.	24 and 38

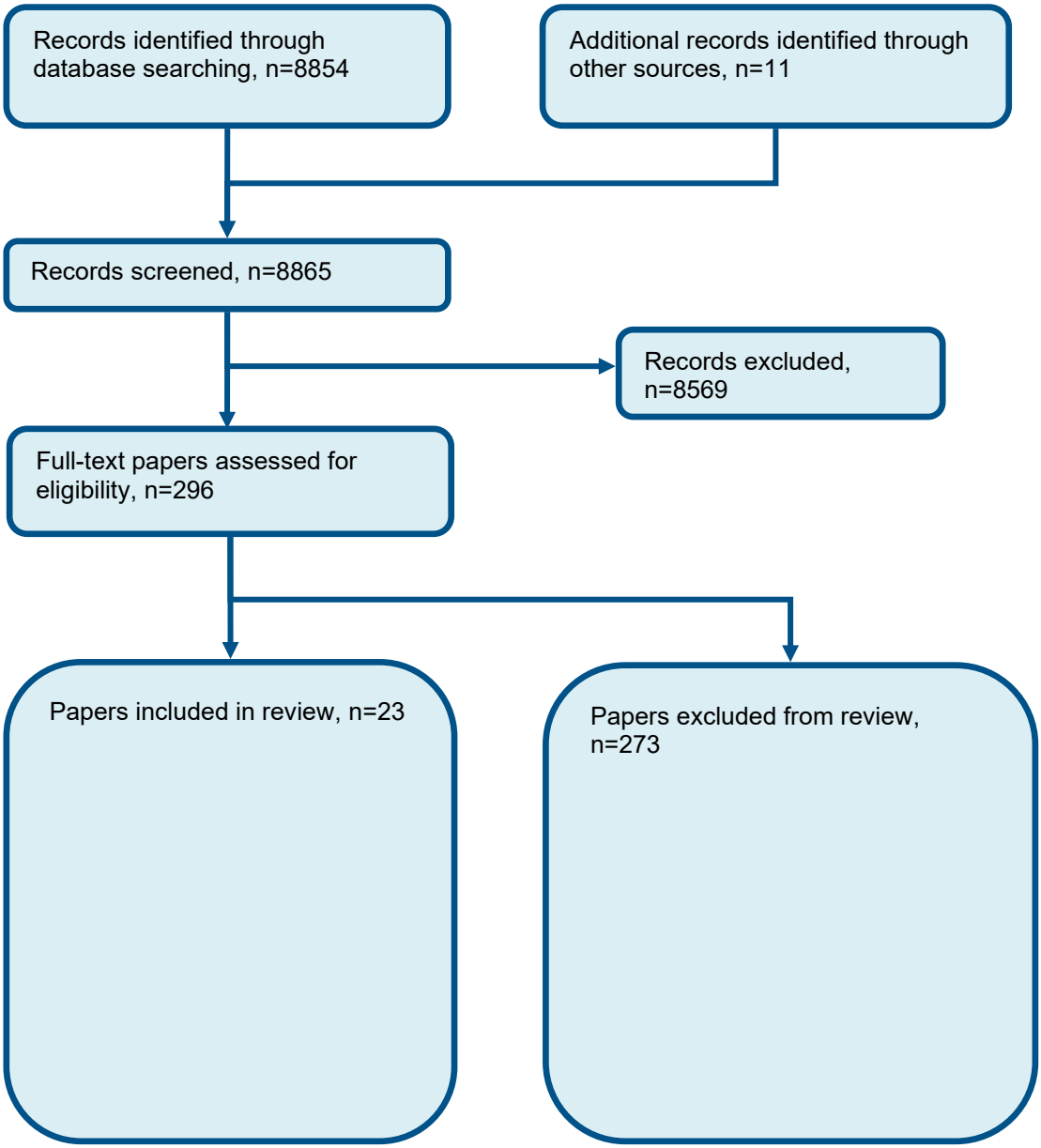
1 **NHS EED and HTA (CRD) search terms**

#1.	MeSH DESCRIPTOR Subarachnoid Hemorrhage EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Intracranial Hemorrhages EXPLODE ALL TREES
#3.	(((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)))
#4.	((SAH or aSAH))
#5.	#1 OR #2 OR #3 OR #4
#6.	MeSH DESCRIPTOR Aneurysm EXPLODE ALL TREES
#7.	((aneurysm* or hematoma* or haematoma*))
#8.	#6 OR #7
#9.	MeSH DESCRIPTOR Intracranial Aneurysm EXPLODE ALL TREES
#10.	(((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (aneurysm* or hematoma* or haematoma*)))
#11.	#9 OR #10
#12.	MeSH DESCRIPTOR Aneurysm, ruptured
#13.	(((ruptur* or weak* or brain or trauma*) adj3 (aneurysm* or hematoma* or haematoma*)))
#14.	#12 OR #13
#15.	(#5 or #8 or #11 or #14)

2

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of severity scoring systems for subarachnoid haemorrhage



Appendix D: Clinical evidence tables

Reference	Abulhasan 2018[1]	
Study type and analysis	Retrospective cohort study with multivariate analysis	
Number of participants and characteristics	All patients with spontaneous SAH admitted to the neurologic ICU (included all patients admitted with non-traumatic SAH, proven by computed tomography (CT) scan or cerebrospinal fluid analysis, regardless of the documented source of bleed.) (n=434) Age (Median, IQR): 56 (48-65) Male: 158 Female: 276	
	Fisher grade 1: 22	Hunt & Hess 1: 141
	Fisher grade 2: 30	Hunt & Hess 2: 83
	Fisher grade 3: 56	Hunt & Hess 3: 75
	Fisher grade 4: 322	Hunt & Hess 4: 82
		Hunt & Hess 5: 53
Prognostic variable(s)	Hunt & Hess grade 4 Hunt & Hess grade 5	
Confounders OR Stratification strategy	Age • <60 • 60-79 years • ≥80 years Intracerebral haemorrhage Intraventricular haemorrhage Rebleeding within 24 hours Maximum lumen size ≥7mm	
Outcomes and effect sizes	In-Hospital Mortality: Area under curve: 0.89	

Reference	Abulhasan 2018[1]		
	Hunt & Hess Grade	SAH	aSAH
	1 – 3 (reference)	1	1
	4	6.48 (2.56 – 16.4) OR (95% CI) p value <0.001	4.66 (1.76 – 12.3) OR (95% CI) p value 0.002
	5	43 (16 – 116) OR (95% CI) p value <0.001	19 (6.70 – 53.8) OR (95% CI) p value <0.001
Comments	Study is an external validation study of the HAIR score. The study does not appropriately describe the follow up period for the outcomes		
Risk of Bias	Low risk (assessed with QUIPS checklist)		

1

Reference	Claasen 2004[31]
Study type and analysis	Prospective cohort study with forward stepwise multiple logistic regression analysis
Number of participants and characteristics	Patients with SAH admitted to Neurological intensive care unit between July 1 1996 and June 1 2002, admitted within 3 days of onset (n=467) Mean age (SD): 54 (14) Female: 291
Prognostic variable(s)	Hunt and Hess grade
Confounders OR Stratification strategy	In hospital bleeding Aneurysm size >10mm Intraventricular haemorrhage Loss of consciousness Age (per decile)
Outcomes and effect sizes	Severe disability or mortality at 3 months (mRS 4 – 6)
	Hunt & Hess grade (OR 95% CI): 1.8 (1.3-2.3) per Hunt and Hess grade p value <0.001
Comments	The outcome was indirect as it gave an OR per grade increase rather than individual grade increases.
Risk of Bias	Low risk (assessed with QUIPS checklist)

2

Reference	Dijkland 2016[51]		
Study type and analysis	Retrospective cohort study with multivariate logistic regression analysis		
Number of participants and characteristics	Patients were 18 years or older, admitted to hospital less than or equal to 28 days after ictus, SAH proven by CT or CSF spectrophotometry and ruptured intracranial aneurysm as the presumed cause. (Prediction model (n=2,128) = ISAT cohort, Validation Cohort (n=307) = Rotterdam University medical centre) Age: ISAT cohort – 52 (44-60) Rotterdam cohort – 56 (47-66) Male: 896 Female: 1539		
Prognostic variable(s)	Fisher Grade 1 – 4 WFNS 1 - 6		
Confounders OR Stratification strategy	Age Maximum lumen size aneurysm (mm)		
Outcomes and effect sizes	• Mortality (60 days)		
		ISAT cohort OR (95% CI)	Rotterdam Cohort OR (95% CI)
	Fisher grade 1	0.36 (0.09-1.49)	-
	Fisher grade 2	0.52 (0.27-1.02)	-
	Fisher grade 3	0.97 (0.69-1.37)	0.93 (0.31-2.81)
	Fisher grade 4	Reference	Reference
	WFNS 1	Reference	Reference
	WFNS 2	1.87 (1.23-2.83)	2.56 (0.78-8.42)
	WFNS 3	1.70 (0.87-3.32)	4.45 (0.39-50.61)
	WFNS 4	4.87 (2.60-9.14)	5.71 (1.79-18.24)
	WFNS 5	7.0 (2.54-19.28)	272.82 (68.97-1079.24)
	WFNS 6	5.75 (2.41-13.73)	NA
Comments			
Risk of Bias	Moderate risk due to differences between the two data sets and incomplete outcome comparisons (assessed with QUIPS checklist)		

1

Reference	**Duan 2016[57]**		
Study type and analysis	Prospective cohort study with multivariate logistic regression analysis		
Number of participants and characteristics	Patients were age ≥ 60 years; and with aSAH treated endovascularly. (n=520) Mean age (SD): 67.88 (6.44) Male: 128 Female: 288		
	Fisher scale 1 – 2: 297	Hunt & Hess scale 1 - 3 : 374	
	Fisher scale 3 – 4: 119	Hunt & Hess scale 4 - 5 : 42	
Prognostic variable(s)	Hunt & Hess score 4 – 5 Fisher score 3 – 4		
Confounders OR Stratification strategy	Age ≥ 75 Hypertension Located on and distal the circle of Willis Periprocedural complications		
Outcomes and effect sizes	(mRS ≥ 3) 1-year after coiling		
	Covariate	Odds ratio	95% CI, p value
	Hunt & Hess score 4 – 5	1.758	1.133 – 2.729, p value 0.012
	Fisher score 3 – 4	3.229	2.427 – 4.295, p value 0.000
Comments	Reference assumed as Hunt & Hess 1 – 2 and Fisher score 1 – 2 for analysis		
Risk of Bias	Low risk (assessed with QUIPS checklist)		

2

3

Reference	**Galea 2017[74]**
Study type and analysis	Prospective cohort study with multivariate analysis

Reference	Galea 2017[74]			
Number of participants and characteristics	Patients (n=3341) with an aSAH were included and data were collected from 14 centers in the United Kingdom over a period of 4 years (September 2011–2015).			
	Median age (IQR)		55 (18)	
	M / F		1052 / 2289	
	WFNS	Grade 1	1715	
		Grade 2	682	
		Grade 3	202	
		Grade 4	412	
		Grade 5	442	
Prognostic variable(s)	WFNS			
Confounders OR Stratification strategy	Age Pre-op bleed DCI Hypertension IHD Treatment CSF diversion CSF infection			
Outcomes and effect sizes	OR of unfavourable outcome			
	WNFS grade	Odds Ratio	95% CI	P value
		1.04	1.03 – 1.05	< 0.001
Comments	GOS was dichotomized into favourable outcome (GOS score 4 and 5) and unfavourable outcome (GOS score 1–3). Outcomes were measured at discharge.			
Risk of Bias	Moderate risk due to study attrition (assessed with QUIPS checklist)			

1

2

Reference	Germanson 1998[78]
Study type and analysis	Cohort study with logistic regression
Number of participants and characteristics	Patients were selected according to the NICSAH I study (unclear of inclusion criteria) from September 1989 to January 1991 (n=751) Patient demographic data not given
Prognostic variable(s)	GCS
Confounders OR Stratification strategy	Age Sex Location of aneurysm Level of consciousness
Outcomes and effect sizes	unfavourable outcome (GOS 1 – 3)
	GOS 1.5 (for a three-point difference between two GCS scores)
Comments	Not all prognostic information given and unclear regarding which predictors are used within the regression model.
Risk of Bias	High risk due to missing patient information and unclear outcome definition (assessed with QUIPS checklist)

1

Reference	Goldberg 2018[83]
Study type and analysis	Retrospective cohort study with multivariate cox regression analysis
Number of participants and characteristics	Bernese SAH database for poor grade patients (WFNS grade IV – V), elderly patients (age ≥ 60 years) suffering from aSAH admitted between 2005 to 2017 (n=146) Mean age (SD): 71.1 (7.7) years Male:38 Female: 108 WFNS grade IV: 39 WFNS grade V: 107
Prognostic variable(s)	WFNS grade V compared to WFNS grade IV

Reference	Goldberg 2018[83]		
Confounders OR Stratification strategy	Age: 60-69; 70-79; 80-90 ICH		
Outcomes and effect sizes	survival analyses (HR 98% CI):		
	WFNS grade V compared to WFNS grade IV	2.78 (1.69 – 4.57)	P value<0.001
Comments	145 of 146 patients were included in the survival analyses, amounting to 282 follow up years with a mean follow up of 23.51±38.14 months		
Risk of Bias	Moderate risk due to no information on missing patients (assessed with QUIPS checklist)		

1

Reference	Inamasu 2016[106]
Study type and analysis	Single centre retrospective cohort study with multivariate analysis
Number of participants and characteristics	Patients with WFNS grade V SAH who were considered suitable candidates for endovascular treatment, who were taken to the angiographic suite within 24 hours of symptom onset. The coil selection was at the discretion of the attending EVT specialist N=115 Mean age (SD): 62.46 (12.68 Male: 43 Female: 73
Prognostic variable(s)	GCS score 3 – 4
Confounders OR Stratification strategy	Age Female sex Intraoperative / postoperative re-bleeding Delayed cerebral ischaemia Years of experience of EVT specialist
Outcomes and effect sizes	GOS 1 – in hospital mortality OR (95% CI): GCS 3 – 4: 2.274 (0.911-5.673) p value 0.078

Reference	Inamasu 2016[106]		
Comments	GCS 3 – 4 compared to 5 – 6 for multivariate analysis. The study does not appropriately describe the follow up period for the outcomes.		
Risk of Bias	Moderate risk due to unclear outcome definition and no information on patients lost to follow up (assessed with QUIPS checklist)		

1

Reference	Jabbarli 2015[110]		
Study type and analysis	Retrospective cohort study with multivariate analysis		
Number of participants and characteristics	Patients with non-traumatic non aneurysmal subarachnoid haemorrhage admitted between January 2005 to December 2012 (n=157) Age (mean SD): 59.37 (12.92) Female: 73 Male: 84 Poor Hunt and Hess grade (>3): 8		
Prognostic variable(s)	Hunt and Hess grade		
Confounders OR Stratification strategy	Age ≥ 65 Diffuse basal bleeding pattern Acute hydrocephalus Leucocytosis at mission Rebleeding Vasospasm on TCS Cerebral infarction Meningitis Severe anaemia		
Outcomes and effect sizes	Multivariate analysis of outcome predictors (poor grade mRS 3 – 6) at 6 months after NASAH (OR 95% CI)		
	Hunt & Hess grade	2.03 (1.13-3.63)	P value 0.013
Comments	Hunt & Hess OR increase per clinical grade increase		
Risk of Bias	Low risk (assessed with QUIPS checklist)		

Reference	Karamanakos 2012[117]			
Study type and analysis	Retrospective cohort study with multivariate analysis			
Number of participants and characteristics	Admission alive to the hospital within 24 hours from the start of the acute aneurysmal SAH verified by CT, spinal tap or autopsy (n=1657) Age: ≤39: 865 40 – 64: 2785 ≥65: 773			
Prognostic variable(s)	Hunt and Hess grades I – V			
Confounders OR Stratification strategy	Age Gender Time period of SAH ICT IVH SDH Hydrocephalus Site of aneurysm Size of aneurysm Number of saccular aneurysms			
Outcomes and effect sizes	Mortality			
	Hunt and Hess grade	1-3 days (OR 95% CI)	4 – 30 days (OR 95% CI)	1 – 12 months (OR 95% CI)
	I	1	1	1
	II	0.6 (0.1-2.8)	1.4 (0.4-5.0)	0.6 (0.2-2.0)
	III	1.1 (0.2-5.1)	3.3 (1.0-11)	2.5 (0.8-7.7)
	IV	6.0 (1.3-27) p value 0.019	10 (3.0-36) p value 0.0	3.4 (1.0-11) p value 0.042
	V	92 (21-418) p value 0.0	43 (11-180) p value 0.0	12 (1.8-74) p value 0.009
Comments	Not clearly specified which confounders were used in multivariate analysis, only reports only those that were statistically significant			

Reference	Karamanakos 2012[117]	
Risk of Bias	Moderate risk due to unclear confounders for multivariate analysis (assessed with QUIPS checklist)	

1

Reference	Konzalla 2016[125] merged with Konzalla 2018[126]	
Study type and analysis	Retrospective cohort study with multivariate analysis	
Number of participants and characteristics	Patients with aneurysms of carotid bifurcation and posterior communicating artery between 1999 and 2013 (n=193) Mean age: 55.2 Female: 156 Male: 37 WFNS I – III: 114 Fisher grade 3: 141	
Prognostic variable(s)	WFNS grade I – III Fisher grade 3	
Confounders OR Stratification strategy	Age Admission status Aneurysms of carotid bifurcation artery Absence of mild or severe cerebrovascular spasm	
Outcomes and effect sizes	Unfavourable outcome (mRS >2) OR (95% CI)	
	WFNS I – III	9.6 (4.9 – 18.8) p value <0.001
	Fisher grade 3	0.49 (0.25 – 0.97) p value 0.04
Comments	Outcome was assessed by Modified Rankin score 6 months after aneurysmal SAH Reference assumed as WFNS IV – V and Fisher grade 1 for analysis.	
Risk of Bias	Moderate risk due to no information on patients lost to follow up (assessed with QUIPS checklist)	

2

Reference	Lee 2014[140]
Study type and analysis	Retrospective cohort study with multivariate analysis

Reference	Lee 2014[140]		
Number of participants and characteristics	Patients were identified from the GET with the guidelines stroke database (patients were excluded if CT negative SAH and traumatic SAH) (n=400) Mean age: 56.9 Female:261		
Prognostic variable(s)	Hunt & Hess grades		
Confounders OR Stratification strategy	Age IVH Rebleed within 24hours		
Outcomes and effect sizes	in-hospital mortality		
	Hunt & Hess	OR (95% CI)	
	1 – 3 (reference)	1	P value < 0.0001
	4	4.08 (1.65 – 10.09)	
	5	41.3 (17.56 – 97.11)	
Comments	Validation of the HAIR score for SAH. The study does not appropriately describe the follow up period for the outcomes.		
Risk of Bias	Moderate risk due to no information on patients lost to follow up (assessed with QUIPS checklist)		

1

Reference	Mocco 2006[163]
Study type and analysis	Retrospective cohort study with multivariable analysis
Number of participants and characteristics	Patients with aneurysmal SAH admitted to Columbia University Medical Center and enrolled in our Subarachnoid Hemorrhage Outcomes Project. Of these, 148 patients were of poor clinical grade, defined as Hunt and Hess Grades IV and V. SAH was confirmed in all patients by head computed tomographic scans and was rated according to the Fisher scale. The presence and location of an intracranial aneurysm was confirmed with four-vessel cerebral angiography in a majority of patients, including all patients who underwent aneurysm securing intervention.

Reference	Mocco 2006[163]	
	(n=98) Mean age (range): 55 (19-89) Male: 29 Female: 69 Hunt & Hess grade V at admission: 29 Fisher grade 1 – 2: 17 Fisher grade 3: 45 Fisher grade 4: 36	
Prognostic variable(s)	Admission Hunt & Hess IV – V Worst Hunt & Hess of V Fisher grade 3 – 4	
Confounders OR Stratification strategy	Aged ≥ 64 years of age Hyperglycaemia Worst Hunt and Hess grade V Aneurysm size 13mm or greater	
Outcomes and effect sizes	Poor outcome (mRS 4 – 6) at 12 months (Hazard ratio; 95% CI)	
	Admission Hunt & Hess grade IV	1.100 (0.206-5.872)
	Admission Hunt & Hess grade V	3.833 (0.612-24.023)
	Fisher grade 3	1.410 (0.441-4.502)
	Fisher grade 4	1.089 (0.331-3.577)
Comments	Reference assumed as Hunt & Hess I and Fisher grade 1 for analysis	
Risk of Bias	Low risk (assessed with QUIPS checklist)	

1

Reference	Orakdogen 2016[190]
Study type and analysis	Retrospective cohort study with logistic regression analysis
Number of participants	Evidence of SAH from a computerized tomography (CT) scan and the presence of an angiographically-confirmed saccular aneurysm as the cause of the haemorrhage (n=104)

Reference	Orakdogen 2016[190]		
and characteristics	Age: <55 – 62; ≥55 – 42 Male: 53 Female: 51 WFNS I – III: 86 WFNS IV – V: 18		
Prognostic variable(s)	WFNS (high)		
Confounders OR Stratification strategy	Age ≥ 55 Size of aneurysm (>7.0mm) Clinical vasospasm (positive)		
Outcomes and effect sizes	Mortality (OR 95% CI)		
	WFNS (IV - V)	88.809 (8.609 – 916.152)	P value 0.001
Comments	Reference assumed as WFNS I – III for analysis. The study does not appropriately describe the follow up period for the outcomes.		
Risk of Bias	Moderate risk as unclear which other confounders were used within MVA (assessed with QUIPS checklist)		

1

Reference	Ozono 2020[196]		
Study type and analysis	Retrospective cohort study with multivariate analysis		
Number of participants and characteristics	Data for the present study were obtained from the 1863 participants enrolled in the mWFNS Scale study. This was a multicentre prospective observational study, which included a total of 38 neurosurgical institutions across Japan. Patients were enrolled from October 2010 to March 2013. All patients were age 20 years or older and the interval between symptom onset and admission was ≤72 hours. The 1124 patients were divided into 2 groups: those who were non-elderly, age <65 years (n = 613), and those who were elderly, age ≥65 years (n = 511).		
	Variable	Non elderly (n=613)	Elderly (n=511)
	Age, years, mean (SD)	52.5 (9.1)	74.3 (6.6)
	Male / Female	255 / 358	97 / 414

Reference	Ozono 2020[196]				
	Surgical clipping	438		337	
	mWFNS grade	I	272	157	
		II	111	94	
		III	49	46	
		IV	97	112	
		V	84	102	
	Fisher grade	1	30	29	
		2	85	63	
		3	492	414	
		4	2	2	
Prognostic variable(s)	Age mWFNS				
Confounders OR Stratification strategy	Endovascular Coiling Mean age Sex Location of aneurysm Vasospasm Duration from onset to treatment				
Outcomes and effect sizes	**Mortality (mRS 6) at 3 months after onset of SAH**				
	mWFNS	Non elderly		Elderly	
		Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
	I	Reference		Reference	
	II	2.76 (0.69 - 11.00)	0.151	1.72 (0.57 - 5.19)	0.339
	III	3.36 (0.68 - 16.61)	0.138	1.70 (0.44 - 6.50)	0.44
	IV	4.22 (1.10 - 16.18)	0.035	1.86 (0.65 - 5.35)	0.248
	V	16.70 (5.03 - 55.46)	<0.001	6.30 (2.41 - 16.45)	<0.001
	Poor Outcome of mRS Score ≥3 at 3 Months After Onset of SAH				
	mWFNS	Non elderly		Elderly	

Reference	Ozono 2020[196]				
		Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
	I	Reference		Reference	
	II	1.29 (0.50 - 3.34)	0.601	1.89 (0.92 - 3.90)	0.084
	III	3.54 (1.30 - 9.64)	0.013	5.02 (2.17 - 11.59)	<0.001
	IV	11.60 (5.50 - 24.46)	<0.001	9.67 (4.89 - 19.12)	<0.001
	V	49.59 (22.17 - 110.91)	<0.001	21.07 (10.10 - 43.94)	<0.001
Comments	Results for elderly and non-elderly were combined for analysis.				
Risk of Bias	Moderate risk due to analysis without calibration (assessed with QUIPS checklist)				

1

2

Reference	Rabinstein 2004[203]
Study type and analysis	Retrospective cohort study with multivariate analysis
Number of participants and characteristics	consecutive patients with symptomatic cerebral vasospasm from aneurysmal SAH treated with percutaneous balloon angioplasty or selective intra-arterial Papaverine infusion between 1990 and 2000 (n=81) Mean age (range): 54 years (29 – 88) WFNS I : 29 WFNS II : 16 WFNS III : 7 WFNS IV : 25 WFNS V : 4
Prognostic variable(s)	WFNS
Confounders OR Stratification strategy	Age Coiling
Outcomes and effect sizes	Poor outcome (mRS >2) 3 months (median follow up period)
	Poor WFNS grade IV – V (OR 95% CI): 3.58 (1.28-11) p value 0.02

Reference	Rabinstein 2004[203]		
Comments	Reference assumed as WFNS I – III for analysis		
Risk of Bias	Moderate risk due to no information on patients lost to follow up (assessed with QUIPS checklist)		

1

Reference	Starke 2009[240]		
Study type and analysis	Retrospective cohort study with multivariate analysis		
Number of participants and characteristics	Poor grade aSAH patients (n=160) Mean age (SD): 59.1 (15) Male: 45 Female: 115		
Prognostic variable(s)	GCS		
Confounders OR Stratification strategy	Female gender Age >70		
Outcomes and effect sizes	unfavourable outcome (mRS 4 – 6) (OR 95% CI)		
	A (GCS 10-12)	1.0	
	B (GCS 8-9)	14.2 (1.5-140.5)	P value 0.022
	C (GCS 5-7)	38.5 (4.2-340)	P value 0.001
	D (GCS 3-4)	63.4 (5.6-707.1)	P value 0.001
Comments	Authors have grouped outcomes from admission GCS and refer to outcomes as mRS 0-3 (favourable outcome) and mRS 4-6 (unfavourable outcome) and the follow up period assumed to be one year as stated by authors		
Risk of Bias	Moderate risk due to confounder used in MVA and no information on patients lost to follow up (assessed with QUIPS checklist)		

2

Reference	Taki 2011[249]
Study type and analysis	Retrospective cohort study with multivariate logistic regression analysis

Reference	Taki 2011[249]	
Number of participants and characteristics	Patients with SAH who were ≥20 years old at onset; SAH on CT scans or lumbar puncture; saccular aneurysm as the cause of the SAH confirmed on three dimensional CTA, MRA or DSA and aneurysmal obliteration by clipping or coiling within 14 days of onset (n=614) Mean age (SD): 61.01 (12.5) Female: 361 Male: 163	
	WFNS I: 167	Fisher grade 1: 7
	WFNS II: 140	Fisher grade 2: 113
	WFNS III: 55	Fisher grade 3: 341
	WFNS IV: 108	Fisher grade 4: 73
	WFNS V: 65	
Prognostic variable(s)	Admission WFNS grade IV – V	
Confounders OR Stratification strategy	Age Sex WFNS grade Fisher grade Re-rupture Date of obliteration Interval from admission to obliteration Symptomatic vasospasm Vasospasm cerebral infarct Cardiopulmonary dysfunction Infection Hydrocephalus Seizure Ileus Femur fracture Acute renal failure Size of aneurysm	

Reference	Taki 2011[249]	
	Location of aneurysm	
Outcomes and effect sizes	Multivariate logistic regression with Modified Rankin scale as a binary outcome (mRS 0-2 = good; mRS 3-6 = poor) at 12 months after SAH	
	Admission WFNS grade	Odds Ratio (95% CI) P value
	IV	3.46 (1.49 – 8.04) p value <0.005
	V	13.48 (5.09-35.71) p value < 0.001
	Multivariate logistic regression with Survival or death as a binary outcome	
	Admission WFNS grade	Odds Ratio (95% CI) P value
	IV	3.71 (1.03-13.39) p value <0.05
	V	9.43 (2.50-35.55) p value <0.005
Comments	Reference assumed as WFNS grade I for analysis	
Risk of Bias	Moderate risk due to outcome assessed as binary outcomes (assessed with QUIPS checklist)	

1

Reference	Taweesomboonyat 2019[250]	
Study type and analysis	Retrospective cohort study with multivariate analysis	
Number of participants and characteristics	Patients who underwent neurosurgical clipping or endovascular coiling between November 2002 to March 2018 (n=189) Age (mean SD): Clipping: 56.5 (11.4); Coiling: 64.3 (13.9) Female: 146 Male: 43	
	Hunt & Hess grade 1 - 7	WFNS grade 1 – 127
	Hunt & Hess grade 2 - 122	WFNS grade 2 – 14
	Hunt & Hess grade 3 - 27	WFNS grade 3 – 3
	Hunt & Hess grade 4 - 33	WFNS grade 4 – 38
		WFNS grade 5 – 7
Prognostic variable(s)	Hunt & Hess grade (reference = grade 1)	

Reference	Taweesomboonyat 2019[250]	
Confounders OR Stratification strategy	Age Seizure Deterioration before intervention Side of aneurysm Aneurysm horizontal orientation Intervention	
Outcomes and effect sizes	Multivariate analysis of factors associated with poor outcomes (OR 95% CI) 6 months	
	HH grade 2	1.19 (0.13 – 11.39)
	HH grade 3	1.43 (0.13 – 15.68)
	HH grade 4	6.07 (0.6 – 61.12)
Comments	Poor outcomes defined as mRS 3 – 6	
Risk of Bias	Moderate risk of bias due no information on patients lost to follow up (assessed with QUIPS checklist)	

1

2

Reference	Van Donkelaar 2017[261]
Study type and analysis	Prospective observational cohort study multivariate logistic regression analyses
Number of participants and characteristics	patients with a nontraumatic SAH (n=1620) Median age (IQR): 55 (46-65) Female: 1001 WFNS I: 848 WFNS II: 313 WFNS III: 34 WFNS IV: 230 WFNS V: 195
Prognostic variable(s)	rWFNS (WFNS score post resuscitation)

Reference	Van Donkelaar 2017[261]		
Confounders OR Stratification strategy	Age Gender History Initial WFNS Type of SAH Aneurysm location Aneurysm size mFisher grade Intracerebral hematoma Subdural hematoma Hydrocephalus Type of treatment		
Outcomes and effect sizes	poor outcome (mRS 4 – 6) 2 months after SAH		
	Covariate	Adjusted Odds Ratio (95% CI)	P value
	rWFNS I	1.0	
	rWFNS II	1.6 (1.1-2.5)	0.02
	rWFNS III	3.2 (1.4-7.4)	0.005
	rWFNS IV	5.7 (3.7-8.8)	<0.001
	rWFNS V	12.1 (7.3-19.9)	<0.001
	mFisher grade 0	1.0	
	mFisher grade 1	0.8 (0.3-1.9)	0.55
	mFisher grade 2	1.1 (0.4-2.7)	0.85
	mFisher grade 3	1.6 (0.6-4.3)	0.30
	mFisher grade 4	4.1 (1.7-9.8)	0.002
Comments	Poor outcome (modified Rankin Scale Score 4–6)		
Risk of Bias	Low risk (assessed with QUIPS checklist)		

1

Reference	Wang 2019[266]			
Study type and analysis	Prospective cohort study with multivariate analysis			
Number of participants and characteristics	n = 104 All these patients underwent early microsurgical clipping or endovascular coiling within three days after SAH Male – 39 / Female – 65 Age: < 60 – 63; ≥60 – 41			
	Fisher Grade		WFNS grade	
	I - II	21	IV	58
	III – IV	83	V	46
Prognostic variable(s)	CT fisher grade I – II WFNS grade IV			
Confounders OR Stratification strategy	Low density area on CT Hydrocephalus Endovascular coiling External ventricular drainage Intraventricular drainage Decompressive craniectomy Intracranial hematoma Cerebral Hernia			
Outcomes and effect sizes	Multivariate analysis of favourable outcome (OR 95% CI) 6 – 36 months post onset			
	Fisher Grade I – II (compared to grade III – IV)	12.102 (2.101-69.712)	P value 0.005	
	WFNS grade IV (compared to grade V)	3.852 (1.094-13.562)	P value 0.036	
Comments	Favourable outcome was defined as mRS ≤2			
Risk of Bias	Moderate risk of bias as unclear which of the cofounders were used within MVA (assessed with QUIPS checklist)			

1

2

Reference	**Zhao 2017[292]**				
Study type and analysis	prospective and observational cohort study (from registries) with multivariate analysis				
Number of participants and characteristics	Patients who presented with poor-grade aSAH at the time of treatment (Poor-grade aSAH was defined as a World Federation of Neurosurgical Societies (WFNS) grade of IV or V) (n=136) Mean age (SD): 54.6 (11.8) Female: 64 Male: 72 Fisher grade I – II: 33 Fisher grade III – IV: 103				
Prognostic variable(s)	WFNS grade V mFisher grade				
Confounders OR Stratification strategy	Age Aneurysm neck size Postop pneumonia				
Outcomes and effect sizes	poor outcome mRS 4- 6 at 12 months				
		Pre-op model		Post-op model	
	Predictors	OR (95% CI)	P value	OR (95% CI)	P value
	WFNS grade V	8.6 (3.1-23.8)	<0.001	7.6 (2.7-21.8)	<0.001
	Modified fisher grade	2.3 (1.5-3.7)	<0.001	2.3 (1.5-3.7)	<0.001
Comments	(Poor-grade aSAH was defined as a mRS 4 - 6) Reference assumed as WFNS 1 for analysis				
Risk of Bias	Moderate risk of bias as no information on patients lost to follow up (assessed with QUIPS checklist)				

Appendix E: Forest plots

E.1 Hunt & Hess grade (per grade increase)

Figure 2: mRS 4 – 6 (3 months). Scale 0-6; high score represents poorer outcome.

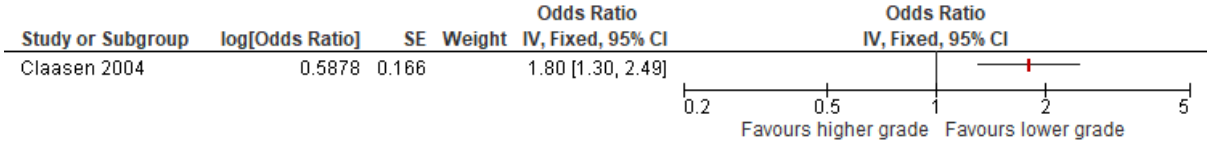
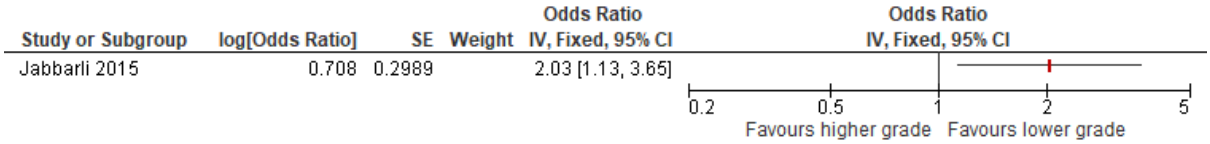


Figure 3: mRS 3 – 6 (6 months). Scale 0-6; high score represents poorer outcome.



E.2 Hunt & Hess grade 2

Figure 4: Mortality (1 – 3 days)

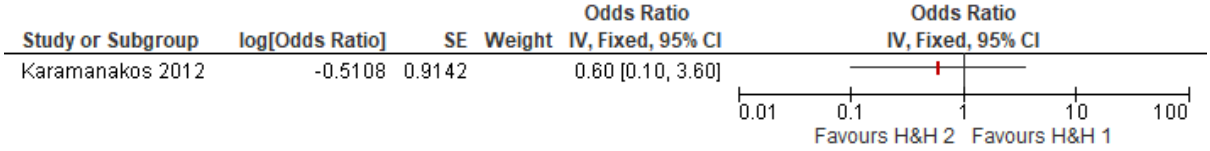


Figure 5: Mortality (4 – 30 days)

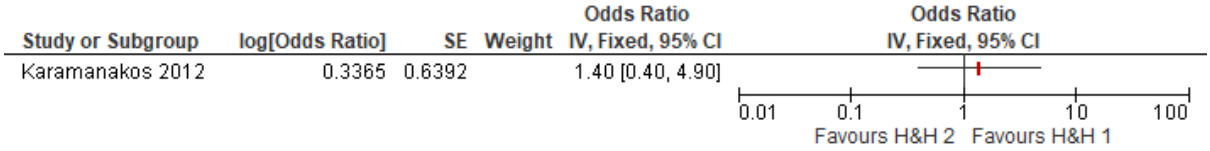


Figure 6: Mortality (1 – 12 months)

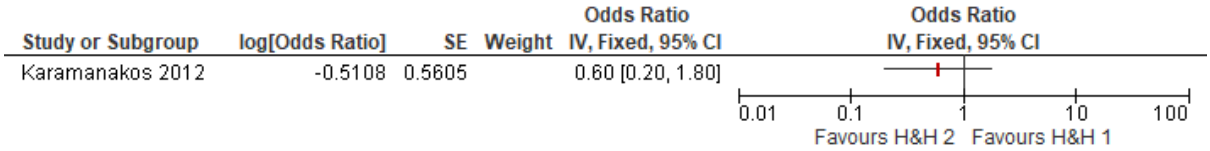


Figure 7: mRS 3 – 6 (6 months). Scale 0-6; high score represents poorer outcome.

E.31 Hunt & Hess grade 3

Figure 8: Mortality (1 – 3 days)

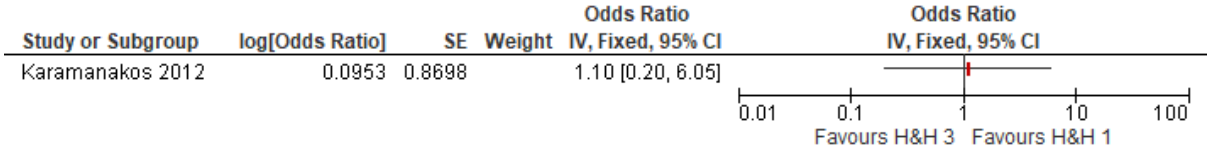


Figure 9: Mortality (4 – 30 days)

Figure 10: Mortality (1 – 12 months)

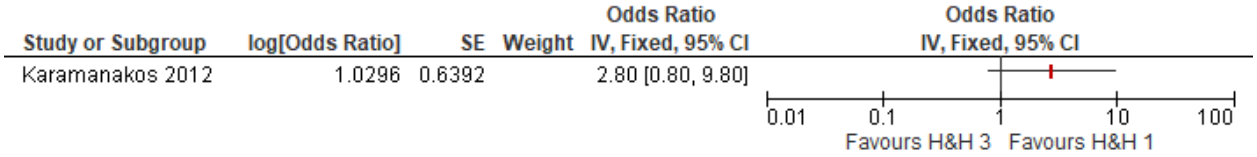
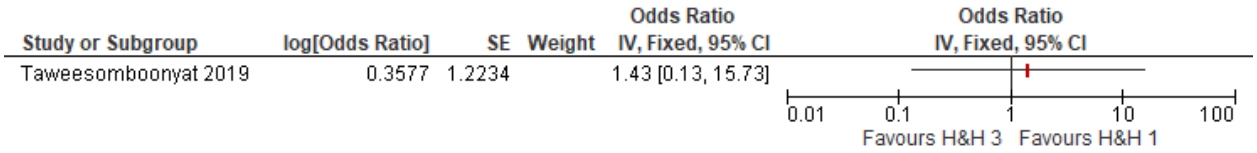
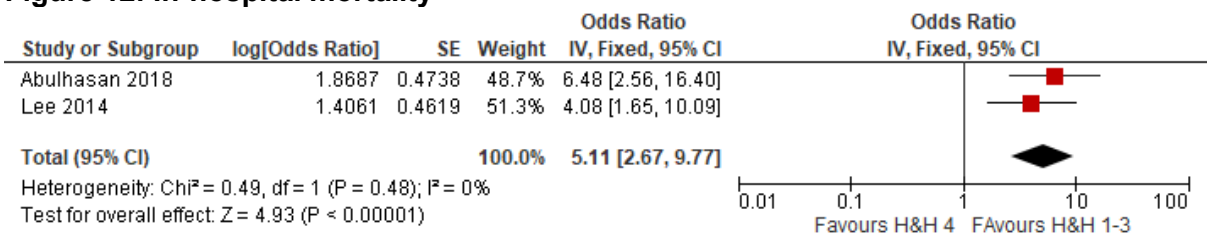


Figure 11: mRS 3 – 6 (6 Months). Scale 0-6; high score represents poorer outcome.



E.42 Hunt & Hess grade 4

Figure 12: In-hospital mortality



Confounder for meta-analysis: age

Figure 13: Mortality (1 – 3 days)

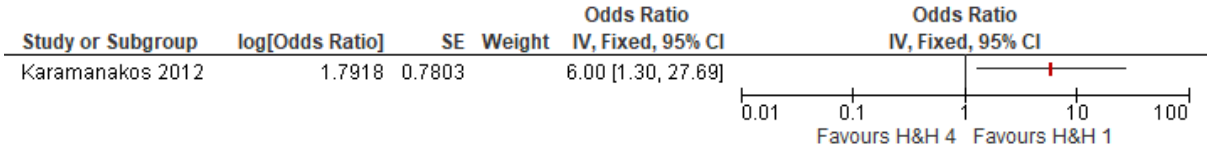


Figure 14: Mortality (4 – 30 days)

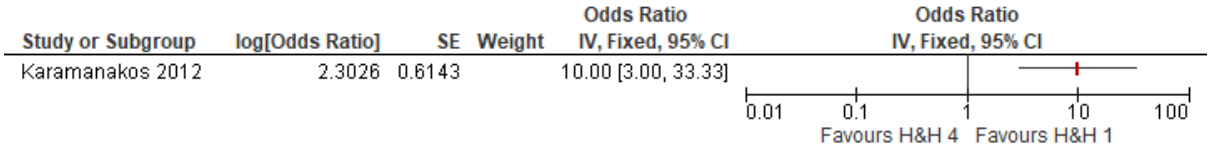


Figure 15: Mortality (1 – 12 months)

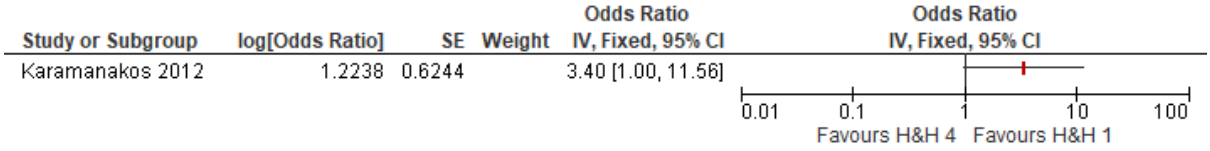
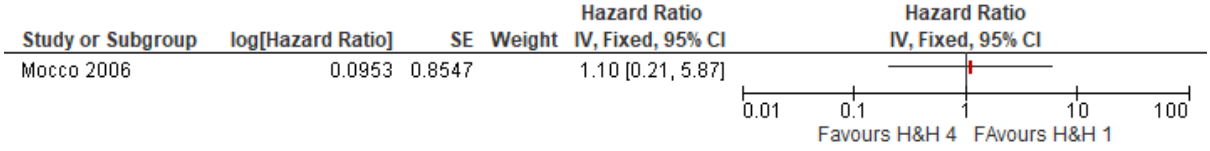


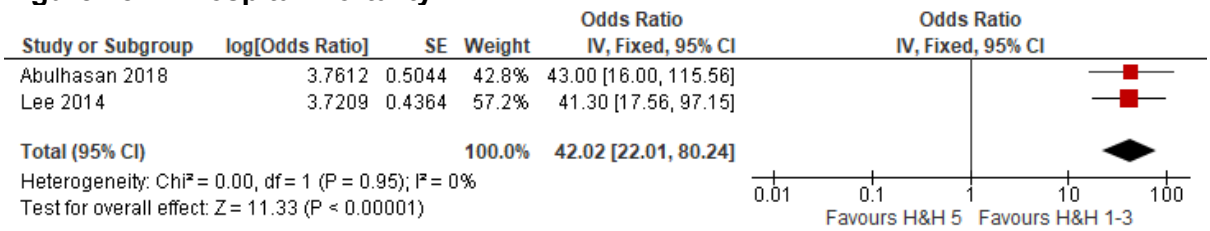
Figure 16: mRS 3 – 6 (6 Months). Scale 0-6; high score represents poorer outcome.

Figure 17: mRS 4 – 6 (12 months). Scale 0-6; high score represents poorer outcome.



E.54 Hunt & Hess grade 5

Figure 18: In-hospital mortality



Confounder for meta-analysis: age

Figure 19: Mortality (1 – 3 days)

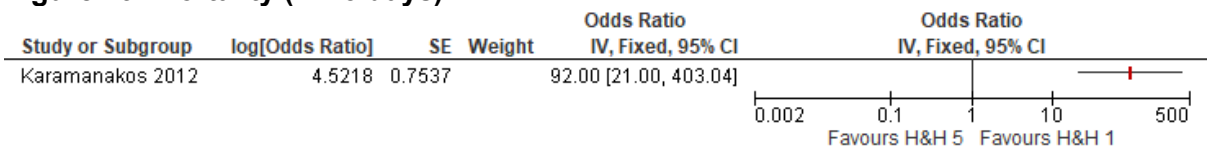
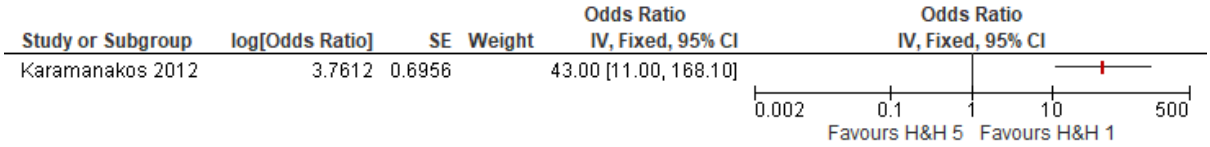
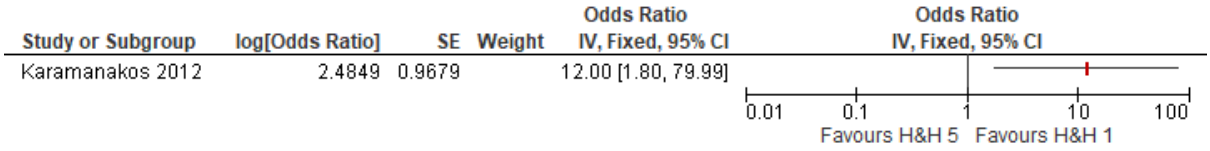


Figure 20: Mortality (4 – 30 days)



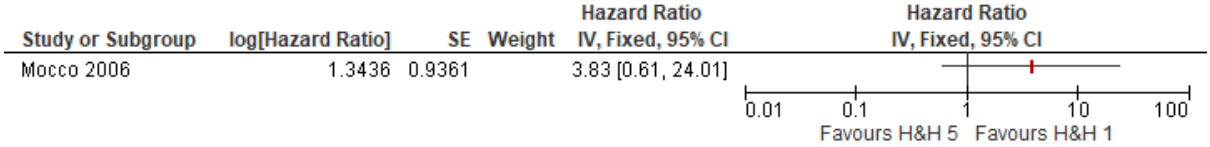
1

Figure 21: Mortality (1 – 12 months)



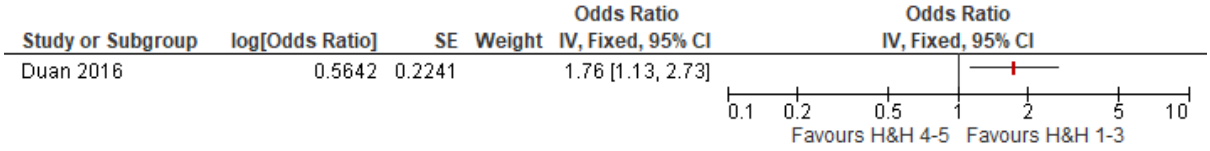
2

Figure 22: mRS 4 – 6 (12 months). Scale 0-6; high score represents poorer outcome.



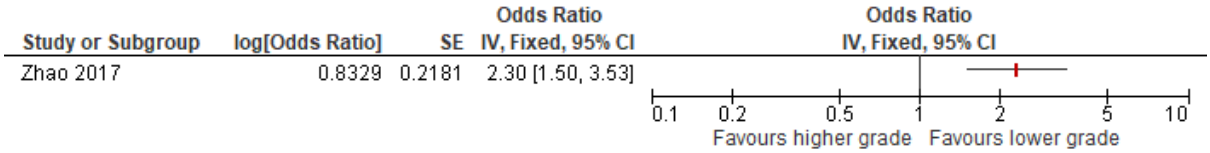
E.63 Hunt & Hess grade 4 – 5

Figure 23: mRS >3 (12 months). Scale 0-6; high score represents poorer outcome.



E.74 Fisher grade (per grade increase)

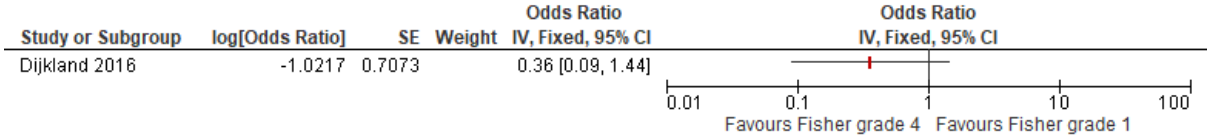
Figure 24: mRS 4 – 6 (12 months). Scale 0-6; high score represents poorer outcome.



5

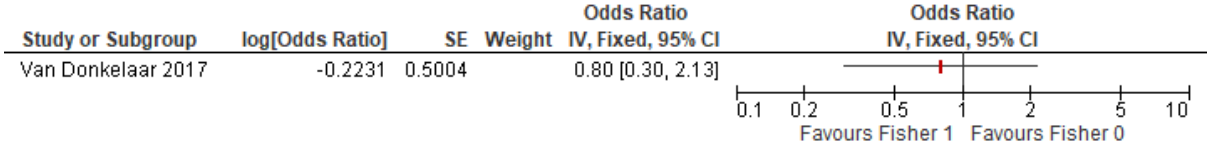
E.81 Fisher grade 1

Figure 25: Mortality (60 days)



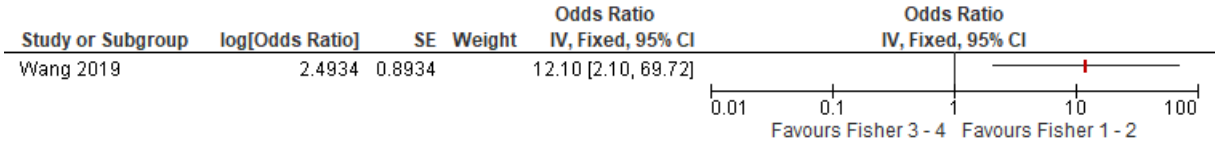
2

Figure 26: mRS 4 – 6 (2 months). Scale 0-6; high score represents poorer outcome.



E.93 Fisher grade 1 – 2

4 **Figure 27: mRS 0 – 2 (6 months). Scale 0-6; high score represents poorer outcome.**



5

E.106 Fisher grade 2

Figure 28: Mortality (60 days)

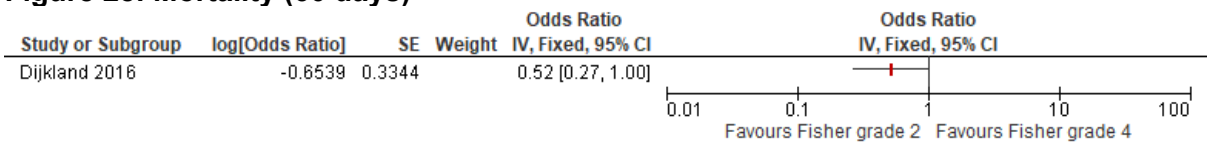
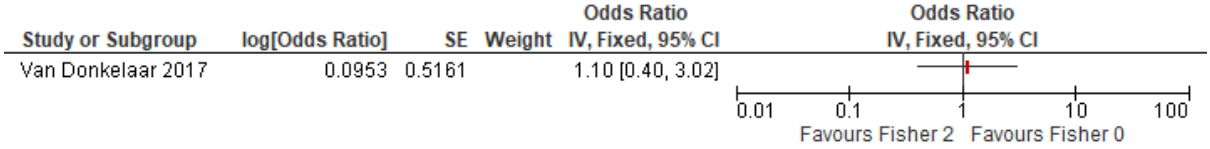


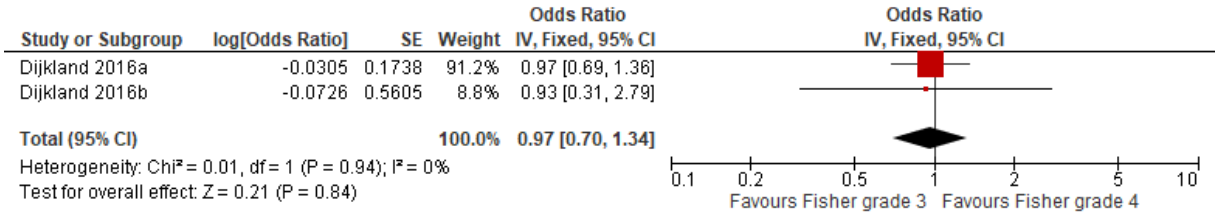
Figure 29: mRS 4 – 6 (2 months). Scale 0-6; high score represents poorer outcome.



7

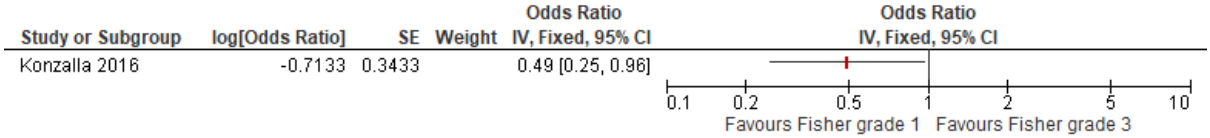
E.118 Fisher grade 3

Figure 30: Mortality (60 days)



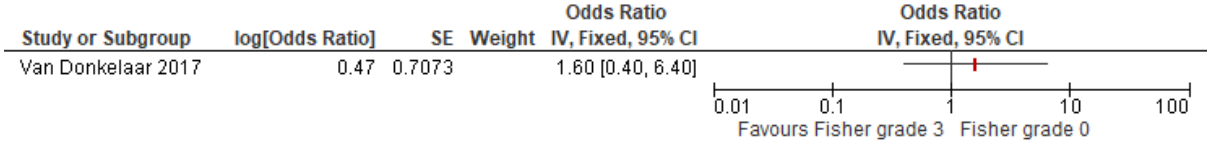
1

Figure 31: mRS >2 (6 months). Scale 0-6; high score represents poorer outcome.



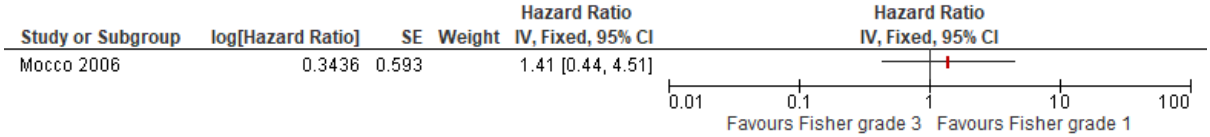
2

Figure 32: mRS 4 – 6 (2 months). Scale 0-6; high score represents poorer outcome.



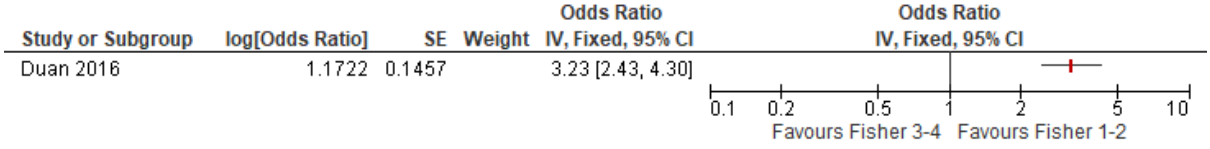
3

Figure 33: mRS 4 – 6 (12 months). Scale 0-6; high score represents poorer outcome.



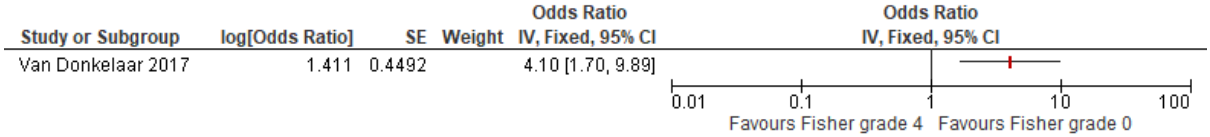
E.12 4 Fisher grade 3 – 4

Figure 34: mRS >3 (12 months). Scale 0-6; high score represents poorer outcome.



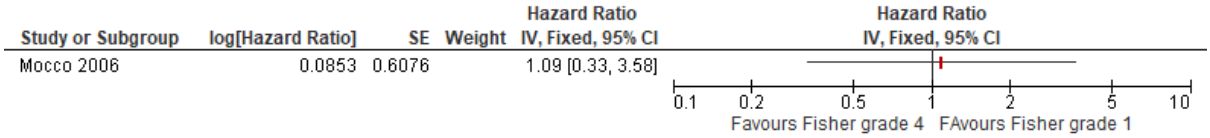
E.13 5 Fisher grade 4

Figure 35: mRS 4 – 6 (2 months). Scale 0-6; high score represents poorer outcome.



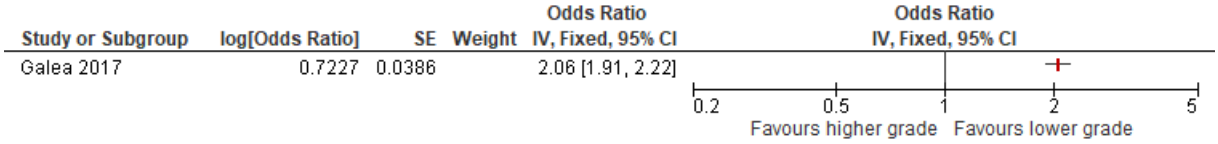
6

Figure 36: mRS 4 – 6 (12 months). Scale 0-6; high score represents poorer outcome.



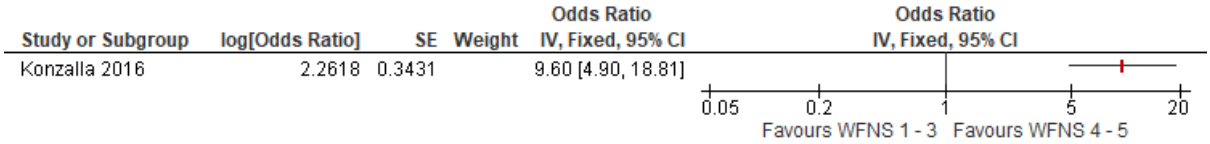
E.14 WFNS (per grade increase)

Figure 37: GOS 1 – 3 (at discharge). Scale 1-5; high score represents positive outcome.



E.15 WFNS 1 – 3

Figure 38: mRS >2 (6 months). Scale 0-6; high score represents poorer outcome.



E.16 WFNS 2

Figure 39: Mortality (60 days)

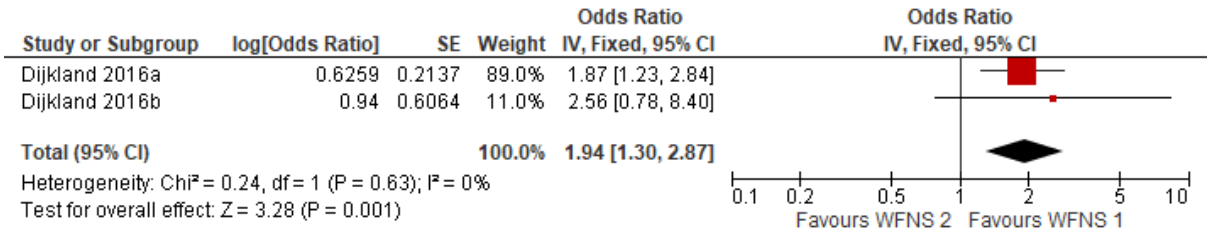


Figure 40: Mortality (90 days)

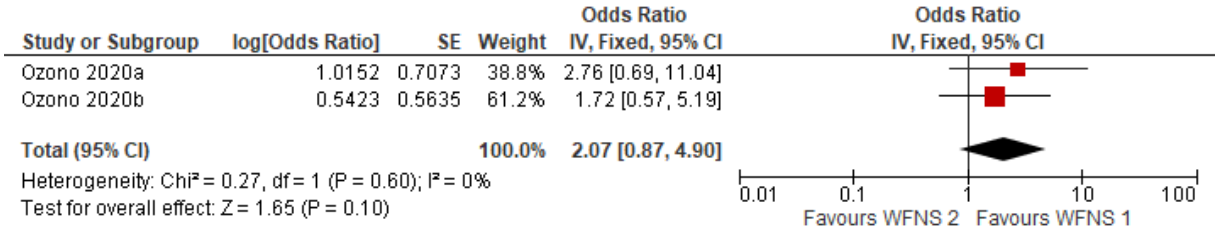


Figure 41: mRS ≥3 (3 months). Scale 0-6; high score represents poorer outcome.

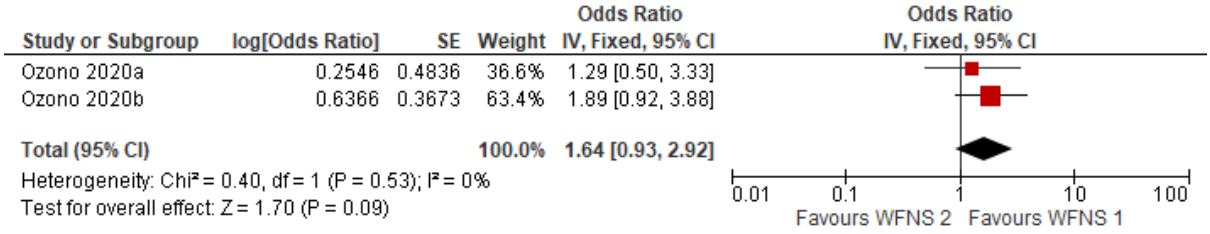
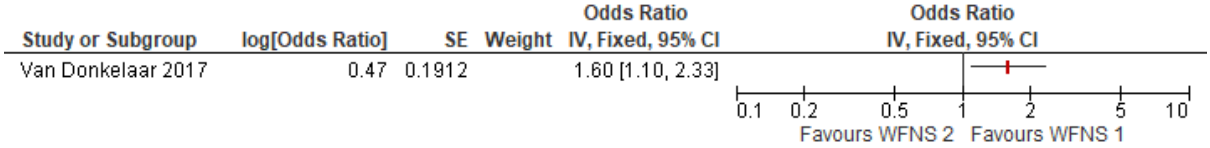


Figure 42: mRS 4 – 6 (2 months). Scale 0-6; high score represents poorer outcome.



E.17 1 WFNS 3

Figure 43: Mortality (60 days)

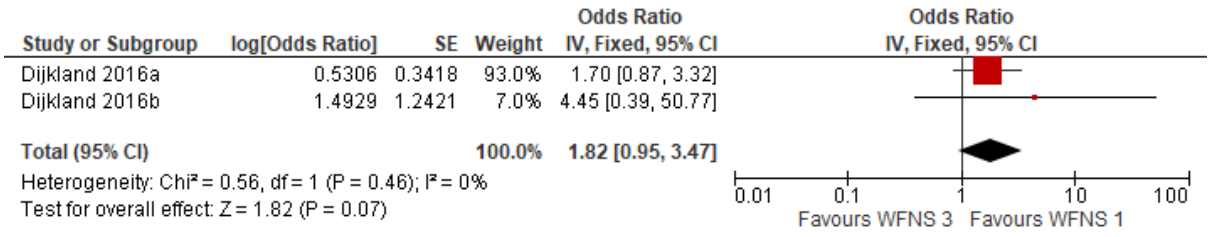


Figure 44: Mortality (90 days)

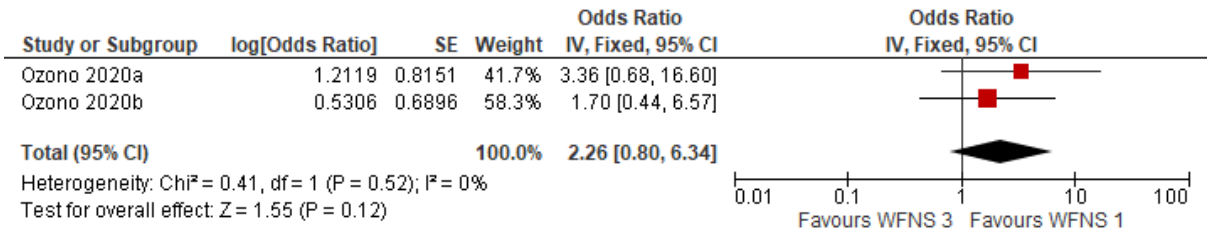


Figure 45: mRS ≥3 (3 months). Scale 0-6; high score represents poorer outcome.

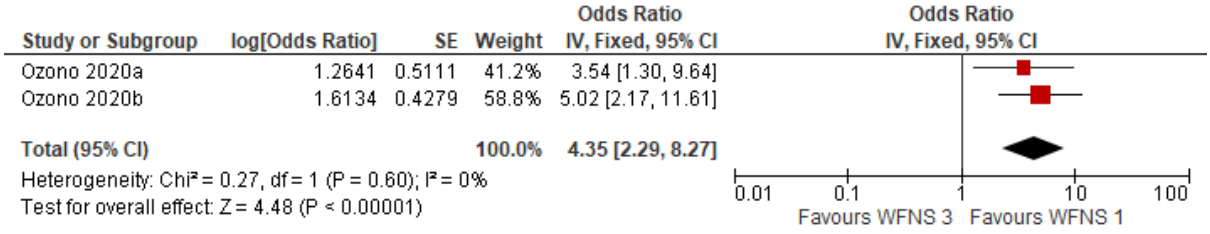


Figure 46: mRS 4 – 6 (2 months). Scale 0-6; high score represents poorer outcome.

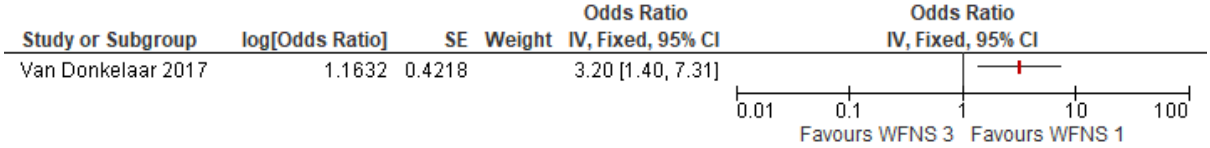


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Figure 47: Mortality (60 days)

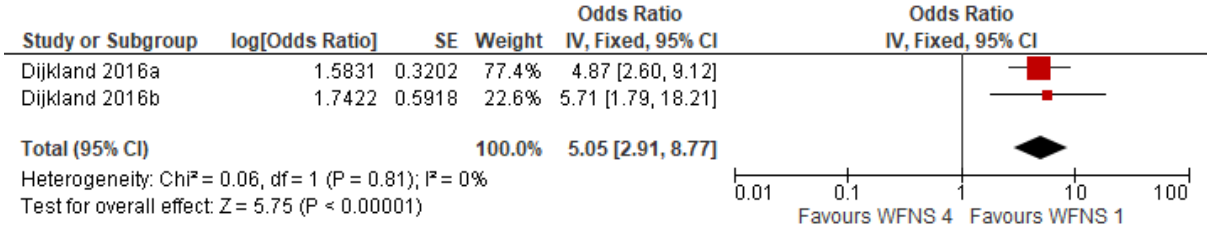


Figure 48: Mortality (90 days)

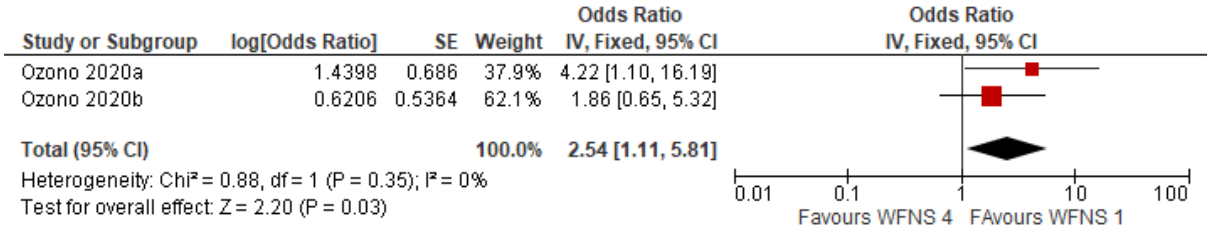


Figure 49: Mortality (12 months)

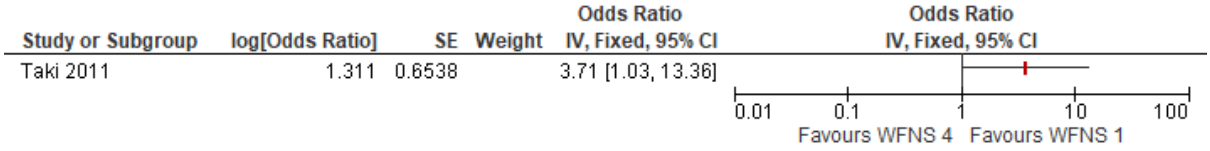


Figure 50: mRS 3-6 (12 months). Scale 0-6; high score represents poorer outcome.

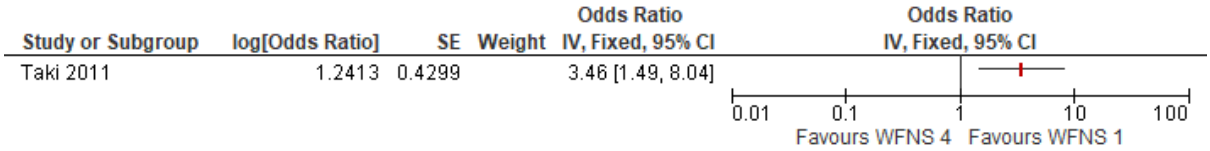


Figure 51: mRS 0 – 2 (6 months). Scale 0-6; high score represents poorer outcome.

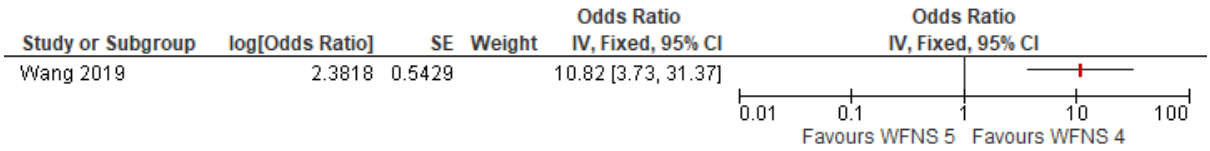
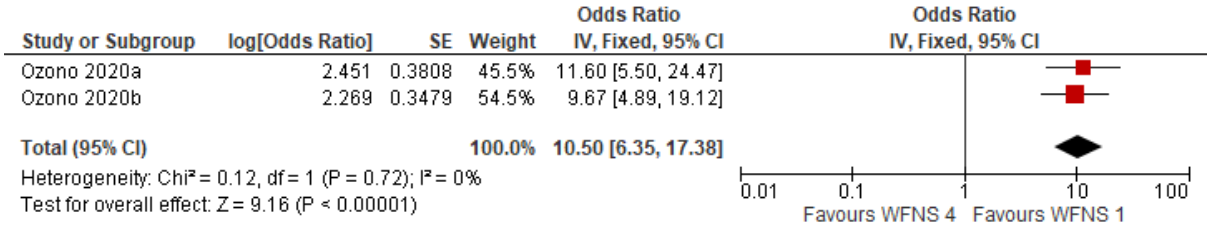
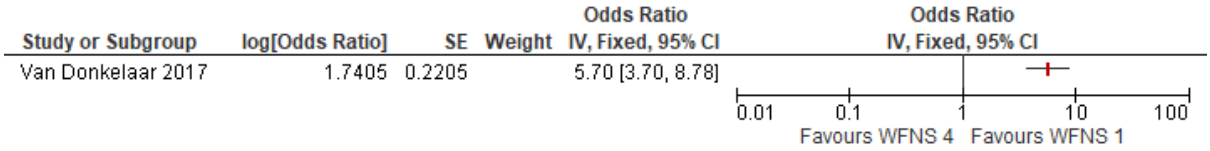


Figure 52: mRS ≥3 (3 months). Scale 0-6; high score represents poorer outcome.



1

Figure 53: mRS 4 – 6 (2 months). Scale 0-6; high score represents poorer outcome.



2

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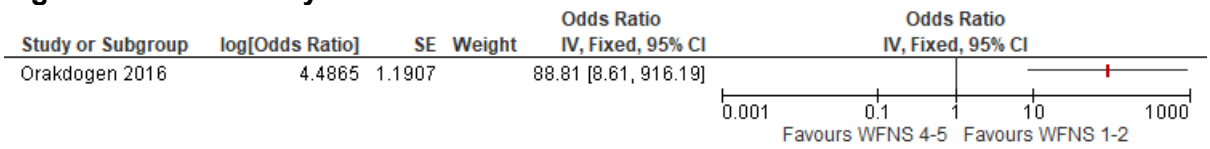
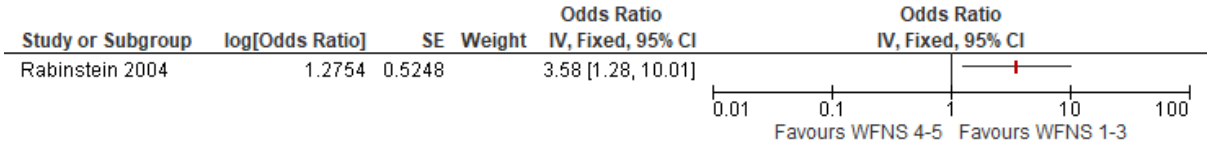
Figure 54: Mortality



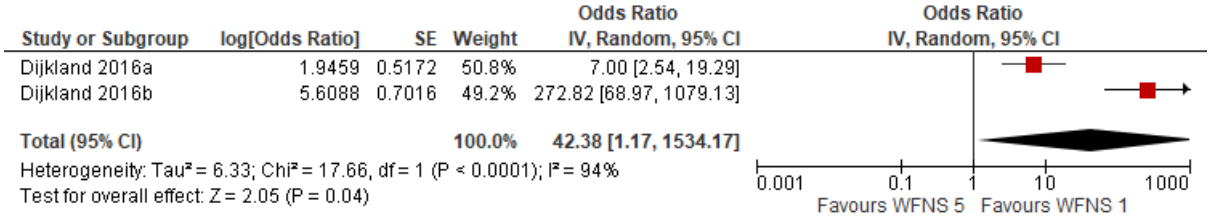
4

Figure 55: mRS >2 (3 months). Scale 0-6; high score represents poorer outcome.



E.205 WFNS 5

Figure 56: Mortality (60 days)



6
7 **Figure 57: Mortality (90 days)**
8

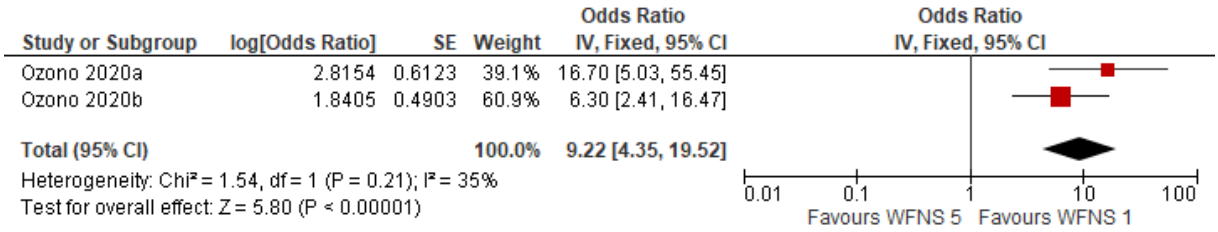


Figure 58: Mortality (12 months)

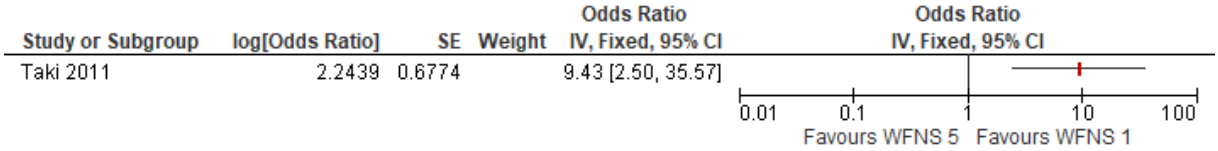


Figure 59: mRS 3-6 (12 months). Scale 0-6; high score represents poorer outcome.

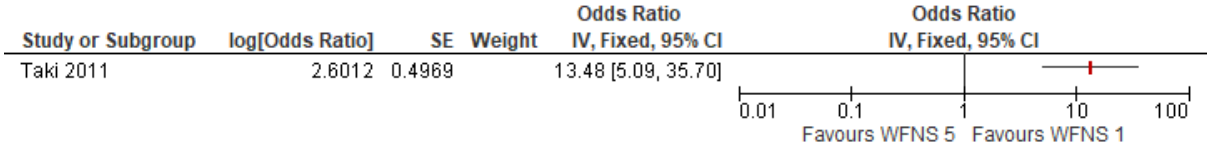


Figure 60:mRS ≥3 (3 months). Scale 0-6; high score represents poorer outcome.

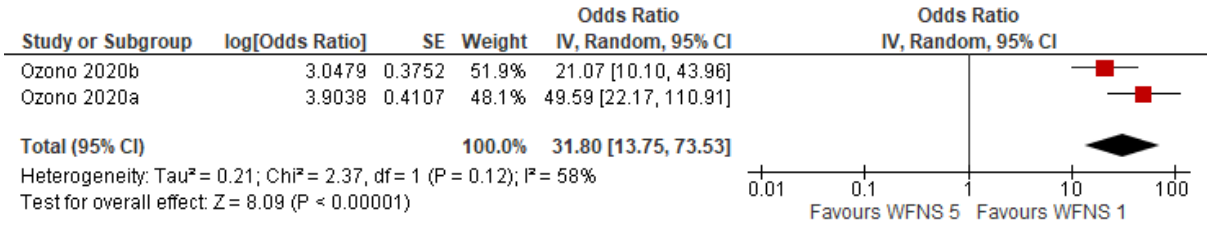


Figure 61: mRS 4 – 6 (2 months). Scale 0-6; high score represents poorer outcome.

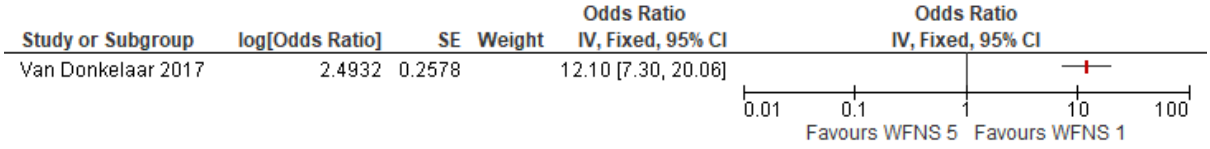


Figure 62: mRS 4 – 6 (12 months). Scale 0-6; high score represents poorer outcome.

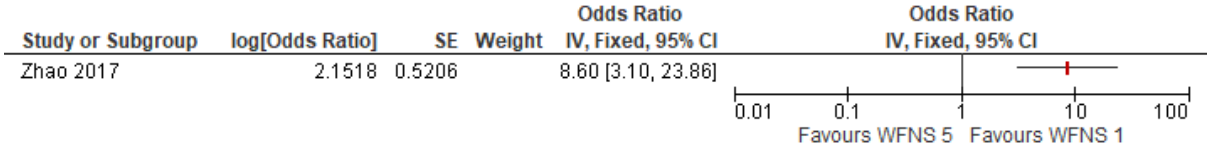
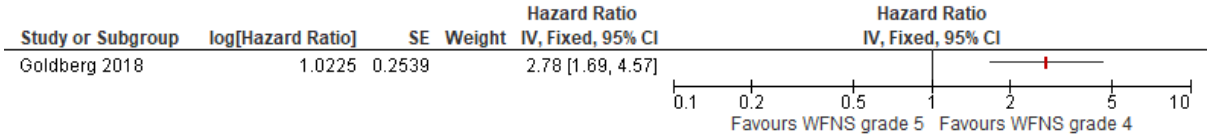
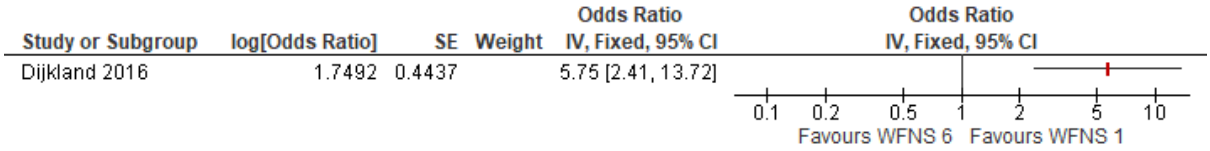


Figure 63: Survival analyses (23.5 months)



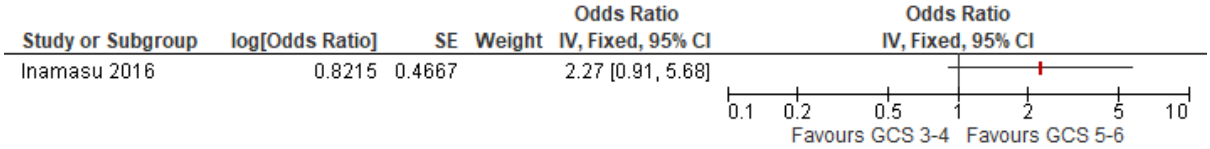
E.211 WFNS 6

Figure 64: Mortality (60 days)



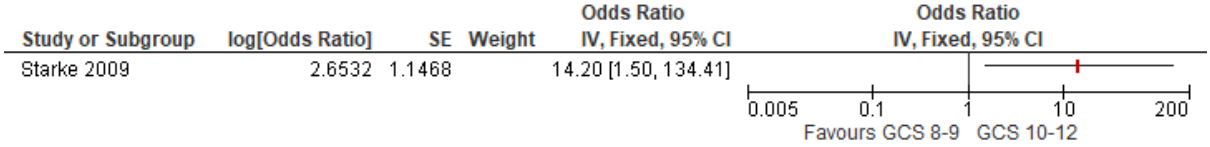
E.222 Glasgow Coma Scale 3 – 4

Figure 65: In-hospital mortality



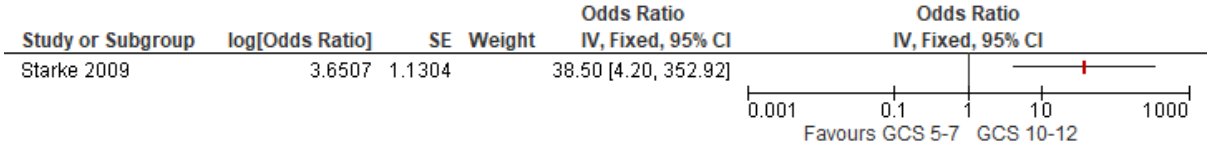
E.233 Glasgow Coma Scale 8 – 9

Figure 66: mRS 4 – 6 (1 year). Scale 0-6; high score represents poorer outcome.



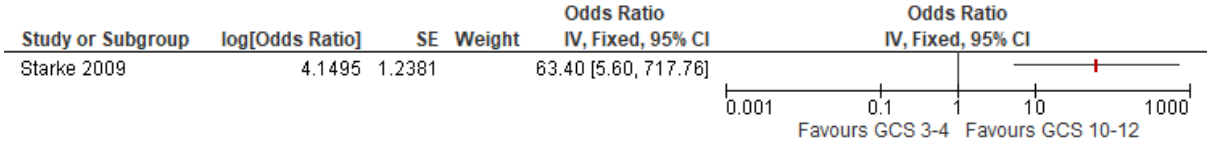
E.244 Glasgow Coma Scale 5 – 7

Figure 67: mRS 4 – 6 (1 year). Scale 0-6; high score represents poorer outcome.



E.251 Glasgow Coma Scale 3 – 4

Figure 68: mRS 4 – 6 (1 year). Scale 0-6; high score represents poorer outcome.



2

Appendix F: GRADE tables

Table 33: Clinical evidence profile: Hunt & Hess grade (per grade increase)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hunt & Hess grade	Control	Relative (95% CI)	Absolute		
mRS 4 - 6 (3 months)												
1	observational studies	no serious risk of bias	no serious inconsistency	Serious[1]	no serious imprecision	none	-	-	OR 1.8 (1.3 to 2.49)	-	⊕⊕⊕O MODERATE	CRITICAL
										-		
mRS 3 - 6 (6 months)												
1	observational studies	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	-	-	OR 2.03 (1.13 to 3.65)	-	⊕⊕⊕O MODERATE	CRITICAL
							-	-		-		

[1]The majority of the evidence had indirect outcomes (outcome per grade increase) and population (non aneurysmal SAH)
[2]Downgraded by 1 increment if the confidence interval crossed the null line

Table 34: Clinical evidence profile: Hunt & Hess grade two

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hunt & Hess grade 2	Control	Relative (95% CI)	Absolute		
Hunt and Hess grade 1 as reference												

Mortality (1-3 days)												
1	observational studies	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	- -	- -	OR 0.6 (0.1 to 3.6)	- -	⊕⊕OO LOW	CRITICAL
Mortality (4 - 30 days)												
1	observational studies	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	- -	- -	OR 1.4 (0.4 to 4.9)	- -	⊕⊕OO LOW	CRITICAL
Mortality (1 - 12 months)												
1	observational studies	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	- -	- -	OR 0.6 (0.2 to 1.8)	- -	⊕⊕OO LOW	CRITICAL
mRS 3 – 6 (follow up 6 months)												
1	observational studies	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	- -	- -	OR 1.19 (0.13 to 10.89)	- -	⊕⊕OO LOW	CRITICAL

[1] Downgraded by 1 increment if the confidence interval crossed the null line
[2] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Table 35: Clinical evidence profile: Hunt & Hess grade three

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Hunt & Hess grade 3**	**Control**	**Relative (95% CI)**	**Absolute**		

Hunt and Hess grade 1 as reference												
Mortality (1 - 3 days)												
1	observational studies	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	- -	- -	OR 1.1 (0.2 to 6.05)	- -	⊕⊕OO LOW	CRITICAL
Mortality (4 - 30 days)												
1	observational studies	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	- -	- -	OR 3.3 (1 to 10.89)	- -	⊕⊕⊕O MODERATE	CRITICAL
Mortality (1 - 12 months)												
1	observational studies	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	- -	- -	OR 2.8 (0.8 to 9.8)	- -	⊕⊕OO LOW	CRITICAL
mRS 3 – 6												
1	observational studies	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	- -	- -	OR 1.43 (0.13 to 15.73)	- -	⊕⊕OO LOW	CRITICAL

[1] Downgraded by 1 increment if the confidence interval crossed the null line
[2] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Table 36: Clinical evidence profile: Hunt & Hess grade four

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hunt & Hess grade 4	Control	Relative (95% CI)	Absolute		
Hunt and Hess grade 1-3 as reference												
In-hospital mortality												
2	observational studies	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 5.11 (2.67 to 9.77)	-	⊕⊕⊕O MODERATE	CRITICAL
							-	-		-		
Hunt and Hess grade 1 as reference												
Mortality (1-3 days)												
1	observational studies	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 6 (1.3 to 27.69)	-	⊕⊕⊕O MODERATE	CRITICAL
							-	-		-		
Mortality (4-30 days)												
1	observational studies	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 10 (3 to 33.33)	-	⊕⊕⊕O MODERATE	CRITICAL
							-	-		-		
Mortality (1-12 months)												
1	observational studies	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 3.4 (1 to 11.56)	-	⊕⊕⊕O MODERATE	CRITICAL
							-	-		-		
mRS 3 - 6 (6 months)												
1		serious[2]			serious[1]	none	-	-		-		CRITICAL

	observational studies		no serious inconsistency	no serious indirectness			-	-	OR 6.07 (0.6 to 61.41)	-	⊕⊕OO LOW	
mRS 4 - 6 (12 months)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	- -	- -	OR 1.1 (0.21 to 5.87)	- -	⊕⊕OO LOW	CRITICAL

[1] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MID
[2] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Table 37: Clinical evidence profile: Hunt & Hess grade five

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Hunt & Hess grade 5**	**Control**	**Relative (95% CI)**	**Absolute**		
Hunt and Hess grade 1-3 as reference												
In-hospital mortality												
2	observational studies	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	- -	- -	OR 42.02 (22.01 to 80.24)	- -	⊕⊕⊕O MODERATE	CRITICAL
Hunt and Hess grade 1 as reference												
Mortality (1-3 days)												
1	observational studies	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	- -	- -	OR 92 (21 to 403.04)	- -	⊕⊕⊕O MODERATE	CRITICAL

Mortality (4-30 days)												
1	observational studies	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 43 (11 to 168.1)	-	⊕⊕⊕O MODERATE	CRITICAL
							-	-		-		
Mortality (1-12 months)												
1	observational studies	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 12 (1.8 to 79.99)	-	⊕⊕⊕O MODERATE	CRITICAL
							-	-		-		
mRS 4 - 6 (12 months)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	-	-	OR 3.83 (0.61 to 24.01)	-	⊕⊕⊕O MODERATE	CRITICAL
							-	-		-		

[1] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MID
[2] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Table 38: Clinical evidence profile: Hunt & Hess grade four to five

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Hunt & Hess 4 - 5**	**Control**	**Relative (95% CI)**	**Absolute**		
Hunt and Hess grade 1-3 as reference												
mRS >3 (12 months)												
1				serious[1]	serious[2]	none	-	-		-		CRITICAL

	observational studies	no serious risk of bias	no serious inconsistency				-	-	OR 1.76 (1.13 to 2.73)	-	⊕⊕OO LOW	

[1] The majority of the evidence had indirect outcomes (outcome included multiple scores – grade 4 and 5)
[2] Downgraded by 1 increment if the confidence interval crossed the null line

Table 39: Clinical evidence profile: Fisher score (per grade increase)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Fisher grade 1**	**Control**	**Relative (95% CI)**	**Absolute**		
mRS 4 - 6 (12 months)												
1	observational studies	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	-	-	OR 2.3 (1.5 to 3.53)	-	⊕⊕⊕O MODERATE	CRITICAL
							-	-		-		

[1] The majority of the evidence had indirect outcomes (outcome per grade increase)

Table 40: Clinical evidence profile: Fisher score one

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Fisher grade 1**	**Control**	**Relative (95% CI)**	**Absolute**		
Fisher grade 4 as reference												

Mortality (60 days)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	- -	- -	OR 0.36 (0.09 to 1.44)	- -	⊕⊕OO LOW	CRITICAL
Fisher grade 0 as reference												
mRS 4 - 6 (2 months)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	- -	- -	OR 0.8 (0.3 to 2.13)	- -	⊕⊕⊕O MODERATE	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed the null line

Table 41: Clinical evidence profile: Fisher score one – two

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Fisher grade 2**	**Control**	**Relative (95% CI)**	**Absolute**		
Fisher grade 3-4 as reference												
mRS 0-2												
1		serious[1]				none	-	-		-		CRITICAL

	observational studies		no serious inconsistency	serious indirectness[2]	no serious imprecision		-	-	OR 12.10 (2.10 to 69.72)	-	⊕⊕⊕O MODERATE	

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[2] The majority of the evidence had indirect outcomes (outcome included multiple scores – grade 1 and 2)

Table 42: Clinical evidence profile: Fisher score two

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Fisher grade 2**	**Control**	**Relative (95% CI)**	**Absolute**		
Fisher grade 4 as reference												
Mortality (60 days)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 0.52 (0.27 to 1)	-	⊕⊕⊕O MODERATE	CRITICAL
							-	-		-		
Fisher grade 0 as reference												
mRS 4 - 6 (2 months)												
1	observational studies	No serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	-	-	OR 1.1 (0.4 to 3.02)	-	⊕⊕⊕O MODERATE	CRITICAL
							-	-		-		

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[2] Downgraded by 1 increment if the confidence interval crossed the null line

1 **Table 43: Clinical evidence profile: Fisher score three**

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fisher grade 3	Control	Relative (95% CI)	Absolute		
Fisher grade 4 as reference												
Mortality (60 days)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	-	-	OR 0.97 (0.7 to 1.34)	-	⊕⊕OO LOW	CRITICAL
							-	-		-		
							-	-		-		
Fisher grade 1 as reference												
mRS >2 (6 months)												
1	observational studies	serious[1]	no serious inconsistency	serious[3]	serious[2]	none	-	-	OR 0.49 (0.25 to 0.96)	-	⊕OOO VERY LOW	CRITICAL
							-	-		-		
mRS 4 - 6 (12 months)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	-	-	OR 1.41 (0.44 to 4.51)	-	⊕⊕⊕O MODERATE	CRITICAL
							-	-		-		
Fisher grade 0 as reference												
mRS 4 - 6 (2 months)												

1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	-	-	OR 1.6 (0.4 to 6.4)	-	⊕⊕⊕O MODERATE	CRITICAL
							-	-		-		

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed the null line
[3] The majority of the evidence had indirect population (Patients with aneurysms of carotid bifurcation and posterior communicating artery)

Table 44: Clinical evidence profile: Fisher score three to four

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Fisher score 3 - 4**	**Control**	**Relative (95% CI)**	**Absolute**		
Fisher grade 1-2 as reference												
mRS >3 (12 months)												
1	observational studies	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	-	-	OR 3.23 (2.43 to 4.3)	-	⊕⊕⊕O MODERATE	CRITICAL
							-	-		-		

[1] The majority of the evidence had indirect outcomes (outcome included multiple scores – grade 3 and 4)

Table 45: Clinical evidence profile: Fisher score four

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Fisher grade 4**	**Control**	**Relative (95% CI)**	**Absolute**		

Fisher grade 0 as reference												
mRS 4 - 6 (2 months)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	- -	- -	OR 4.1 (1.7 to 9.89)	- -	⊕⊕⊕⊕ HIGH	CRITICAL
Fisher grade 1 as reference												
mRS 4 - 6 (12 months)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	- -	- -	OR 1.09 (0.33 to 3.58)	- -	⊕⊕⊕O MODERATE	CRITICAL

[1] Downgraded by 1 increment if the confidence interval crossed the null line

Table 46: Clinical evidence profile: WFNS (per grade increase)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**WFNS 1 - 5**	**Control**	**Relative (95% CI)**	**Absolute**		
GOS 1 – 3 (at discharge)												
1	observational studies	serious[1]	no serious inconsistency	serious indirectness[2]	no serious imprecision	none	-	-	OR 2.06 (1.91 to 2.22)	-	⊕⊕OO LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[2] The majority of the evidence had indirect outcomes (outcome per grade increase)

Table 47: Clinical evidence profile: WFNS 1 – 3

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	WFNS 1 - 3	Control	Relative (95% CI)	Absolute		
WFNS grade 4-5 as reference												
mRS >2 (6 months)												
1	observational studies	serious[1]	no serious inconsistency	serious indirectness[2]	no serious imprecision	none	-	-	OR 9.6 (4.9 to 18.81)	-	⊕⊕OO LOW	CRITICAL
							-	-		-		

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] The majority of the evidence had indirect outcomes (outcome included multiple scores – grade 1 to 3)

Table 48: Clinical evidence profile: WFNS 2

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	WFNS 2	Control	Relative (95% CI)	Absolute		
WFNS grade 1 as reference												
Mortality (60 days)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 1.94 (1.3 to 2.87)	-	⊕⊕⊕O MODERATE	CRITICAL
							-	-		-		

							-	-		-		
Mortality (90 days)												
1	observational studies	No serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	-	-	OR 2.07 (0.87 – 4.9)	-	⊕⊕⊕O MODERATE	CRITICAL
mRS ≥3 (90 days)												
1	observational studies	No serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	-	-	OR 1.64 (0.93 to 2.92)	-	⊕⊕⊕O MODERATE	
mRS 4 - 6 (2 months)												
1	observational studies	No serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 1.6 (1.1 to 2.33)	-	⊕⊕⊕⊕ HIGH	CRITICAL
							-	-		-		

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed the null line

Table 49: Clinical evidence profile: WFNS 3

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**WFNS 3**	**Control**	**Relative (95% CI)**	**Absolute**		
WFNS grade 1 as reference												
Mortality (60 days)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	-	-	OR 1.82 (0.95 to 3.47)	-	⊕⊕OO LOW	CRITICAL
							-	-		-		

Mortality (90 days)												
1	observational studies	No serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	-	-	OR 2.26 (0.8 to 6.34)	-	⊕⊕⊕O MODERATE	CRITICAL
mRS ≥3 (90 days)												
1	observational studies	No serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none			OR 4.35 (2.29 to 8.27)		⊕⊕⊕⊕ HIGH	CRITICAL
mRS 4 - 6 (2 months)												
1	observational studies	No serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 3.2 (1.4 to 7.31)	-	⊕⊕⊕⊕ HIGH	CRITICAL
							-	-		-		

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed the null line

Table 50: Clinical evidence profile: WFNS 4

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**WFNS 4**	**Control**	**Relative (95% CI)**	**Absolute**		
WFNS grade 1 as reference												
Mortality (60 days)												

1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	- - -	- - -	OR 5.05 (2.91 to 8.77)	- - -	⊕⊕⊕O MODERATE	CRITICAL
Mortality (12 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	- -	- -	OR 3.71 (1.03 to 13.36)	- -	⊕⊕⊕O MODERATE	CRITICAL
Mortality (90 days)												
1	observational studies	No serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 2.54 (1.11 to 5.81)	-	⊕⊕⊕⊕ HIGH	CRITICAL
mRS 3-6 (12 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	- -	- -	OR 3.46 (1.49 to 8.04)	- -	⊕⊕⊕O MODERATE	CRITICAL
mRS ≥3 (90 days)												
1	observational studies	No serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 10.50 (6.35 to 17.38)	-	⊕⊕⊕⊕ HIGH	CRITICAL
mRS 4 - 6 (2 months)												
1	observational studies	No serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	- -	- -	OR 5.7 (3.7 to 8.78)	- -	⊕⊕⊕⊕ HIGH	CRITICAL
WFNS grade 5 as reference												

mRS 0 - 2												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	- -	- -	OR 10.82 (3.73 to 31.37)	- -	⊕⊕⊕O MODERATE	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed the null line

Table 51: Clinical evidence profile: WFNS 4 - 5

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**WFNS 4 - 5**	**Control**	**Relative (95% CI)**	**Absolute**		
WFNS grade 1-3 as reference												
Mortality												
1	observational studies	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	- -	- -	OR 88.81 (8.61 to 916.19)	- -	⊕⊕OO LOW	CRITICAL
mRS >2												
1	observational studies	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	- -	- -	OR 3.58 (1.28 to 10.01)	- -	⊕⊕OO LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] The majority of the evidence had indirect outcomes (outcome included multiple scores – grade 4 and 5)

1 **Table 52: Clinical evidence profile: WFNS 5**

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	WFNS 5	Control	Relative (95% CI)	Absolute		
WFNS grade 1 as reference												
Mortality (60 days)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious imprecision[2]	none	-	-	OR 42.38 (1.17 to 1534.17)	-	⊕⊕OO LOW	CRITICAL
							-	-		-		
Mortality (90 days)												
1	observational studies	No serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 9.22 (4.35 to 19.52)	-	⊕⊕⊕⊕ HIGH	CRITICAL
Mortality (12 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 9.43 (2.5 to 35.57)	-	⊕⊕⊕O MODERATE	CRITICAL
mRS 3-6 (12 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 13.48 (5.09 to 35.7)	-	⊕⊕⊕O MODERATE	CRITICAL
							-	-		-		
mRS ≥3 (90 days)												

1	observational studies	No serious risk of bias	no serious inconsistency	no serious indirectness	serious imprecision[2]	none	-	-	OR 31.80 (13.75 to 73.53)	-	⊕⊕⊕O MODERATE	CRITICAL
mRS 4 - 6 (2 months)												
1	observational studies	No serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 12.1 (7.3 to 20.06)	-	⊕⊕⊕⊕ HIGH	CRITICAL
							-	-		-		
mRS 4 - 6 (12 months)												
1	observational studies	No serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	OR 8.6 (3.1 to 23.86)	-	⊕⊕⊕⊕ HIGH	CRITICAL
							-	-		-		
WFNS grade 4 as reference												
Survival Analyses (23.5 months)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	HR 2.78 (1.69 to 4.57)	-	⊕⊕⊕O MODERATE	IMPORTANT
							-	-		-		

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 or 2 increments because of heterogeneity, I2>50%, p>0.04, subgroup analysis not possible; <2 studies per subgroup.

Table 53: Clinical evidence profile: WFNS 6

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**WFNS 6**	**Control**	**Relative (95% CI)**	**Absolute**		
WFNS grade 1 as reference												

Mortality (60 days)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	- -	- -	OR 5.75 (2.41 to 13.72)	- -	⊕⊕⊕O MODERATE	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Table 54: Clinical evidence profile: Glasgow coma scale GCS 3 - 4

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Glasgow Coma Scale**	**Control**	**Relative (95% CI)**	**Absolute**		
GCS grade 5-6 as reference												
In-hospital mortality												
1	observational studies	serious[1]	No serious inconsistency	serious indirectness[3]	serious[2]	none	- -	- -	OR 2.27 (0.91 to 5.68)	- -	⊕⊕OO LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed the null line
[3] The majority of the evidence had indirect outcomes (outcome included multiple scores – GCS 3 – 4)

Table 55: Clinical evidence profile: Glasgow coma scale 8 – 9

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Glasgow Coma Scale 8 - 9	Control	Relative (95% CI)	Absolute		
GCS grade 10-12 as reference												
mRS 4 – 6 (1 year)												
1	observational studies	serious[1]	no serious inconsistency	serious indirectness[2]	no serious imprecision	none	-	-	OR 14.2 (1.5 to 134.41)	-	⊕⊕OO LOW	CRITICAL
							-	-		-		

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] The majority of the evidence had indirect outcomes (outcome included multiple scores – GCS 8 – 9)

Table 56: Clinical evidence profile: Glasgow coma scale 5 – 7

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Glasgow Coma Scale 5 - 7**	**Control**	**Relative (95% CI)**	**Absolute**		
GCS grade 10-12 as reference												
mRS 4 – 6 (1 year)												
1	observational studies	serious[1]	no serious inconsistency	serious indirectness[2]	no serious imprecision	none	-	-	OR 38.5 (4.2 to 352.92)	-	⊕⊕OO LOW	CRITICAL
							-	-		-		

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] The majority of the evidence had indirect outcomes (outcome included multiple scores – GCS 5 – 7)

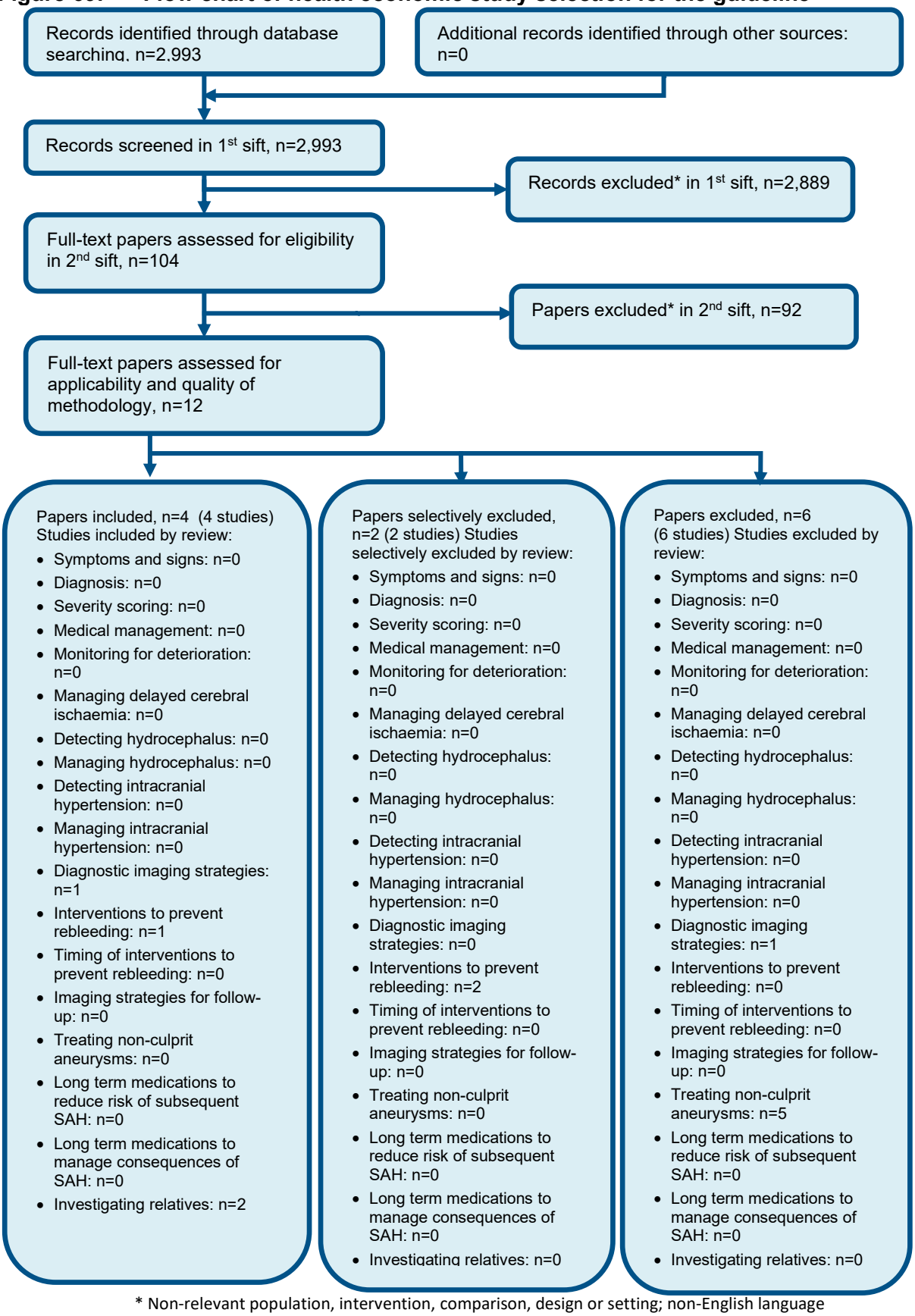
Table 57: Clinical evidence profile: Glasgow coma scale 3 – 4

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Glasgow Coma Scale 3 - 4	Control	Relative (95% CI)	Absolute		
GCS grade 10-12 as reference												
mRS 4 – 6 (1 year)												
1	observational studies	serious[1]	no serious inconsistency	serious indirectness[2]	no serious imprecision	none	-	-	OR 63.4 (5.6 to 717.76)	-	⊕⊕OO LOW	CRITICAL
							-	-		-		

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] The majority of the evidence had indirect outcomes (outcome included multiple scores – GCS 3 – 4)

Appendix G: Health economic evidence selection

Figure 69: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language

1

Appendix H: Health economic evidence tables

None.

1 Appendix I: Excluded studies

I.1 2 Excluded clinical studies

3 **Table 58: Studies excluded from the clinical review**

Reference	Reason for exclusion
Aggarwal 2018[2]	Inappropriate study design – Multivariate analysis did not consider key confounders
Ahn 2018[3]	Inappropriate study design – Proposed model – unclear analysis within new scoring system
Albertine 2016[4]	Inappropriate study design – Multivariate analysis did not consider key confounders
Allen 2018[5]	Inappropriate study design – Multivariate analysis did not consider key confounders
Anonymous 2018[6]	Duplicate study
Asano 2007[7]	Inappropriate study design – Multivariate analysis uses unvalidated scale (Japan Coma Scale)
Badalyan 2018[8]	Inappropriate study design – No multivariate analysis
Basile-Filho 2018[9]	Inappropriate study design – Multivariate analysis did not consider key confounders
Baumann 2008[10]	Inappropriate study design – No multivariate analysis
Bavinzski 1999[11]	Inappropriate study design – Multivariate analysis did not consider key confounders
Benes 2017[12]	Inappropriate study design – Multivariate analysis did not consider key confounders
Bian 2015[13]	Inappropriate study design – Multivariate analysis did not consider key confounders
Bidzinski 1990[14]	Inappropriate study design – No multivariate analysis
Bijlenga 2017[15]	Inappropriate study design – Multivariate analysis did not consider key confounders
Boerboom 2016[16]	Inappropriate study design – Multivariate analysis did not consider key confounders
Bohnstedt 2013[17]	Inappropriate study design – Multivariate analysis did not consider key confounders
Braun 2005[18]	Inappropriate study design – Multivariate analysis did not consider key confounders
Bretz 2017[19]	Inappropriate study design – Multivariate analysis did not consider key confounders
Cedzich 2005[20]	Inappropriate study design – No multivariate analysis
Cellerini 2008[21]	Inappropriate study design – Multivariate analysis did not consider key confounders
Chalouhi 2013[22]	Inappropriate study design – Multivariate analysis did not consider key confounders
Chalouhi 2015[23]	Inappropriate study design – No multivariate analysis
Chan 2014[24]	Inappropriate comparison – HASBLED score
Cherian 2011[25]	Inappropriate study design – Multivariate analysis did not consider key confounders
Cheung 2003[26]	Inappropriate study design – Proposed scale – Intracerebral Haemorrhage score

Reference	Reason for exclusion
Chiang 2000[27]	Inappropriate study design – Multivariate analysis did not consider key confounders
Choi 2017[28]	Inappropriate study design – Multivariate analysis groups severity score as a single outcome (odds ratio of severity score overall, not individualized grades of scoring system)
Chotai 2013[29]	Inappropriate study design – Multivariate analysis did not consider key confounders
Claassen 2001[30]	Inappropriate study design – Multivariate analysis did not consider key confounders
Cui 2018[32]	Inappropriate study design – Multivariate analysis did not consider key confounders
Czorlich 2015[33]	Inappropriate study design – Multivariate analysis did not consider key confounders
Czorlich 2015[34]	Inappropriate study design – Multivariate analysis did not consider key confounders
Dabilgou 2019[35]	Inappropriate study design – no multivariate analysis
Dapaah 2019[36]	Inappropriate study design – abstract
Darflinger 2016[37]	Inappropriate study design – Multivariate analysis did not consider key confounders
Daverat 1991[38]	Inappropriate study design – Multivariate analysis did not consider key confounders
De Marchis 2014[39]	Inappropriate study design – Multivariate analysis groups severity score as a single outcome (odds ratio of severity score overall, not individualized grades of scoring system)
de Oliveira Manoel 2016[40]	Systematic review – references reviewed
De Santis 2007[41]	Inappropriate study design – Multivariate analysis did not consider key confounders
De Santis 1998[42]	Inappropriate study design – Multivariate analysis did not consider key confounders
Dehdashti 2004[43]	Inappropriate study design – Multivariate analysis did not consider key confounders
Delgado Almandoz 2012[44]	Inappropriate study design – Multivariate analysis did not consider key confounders
Delgado Almandoz 2010[45]	Inappropriate study design / population – Multivariate did not consider key confounders / mixed pathologies
Dengler 2017[46]	Inappropriate study design – Multivariate analysis groups severity score as a single outcome (odds ratio of severity score overall, not individualized grades of scoring system)
Dengler 2018[47]	Inappropriate study design – Multivariate analysis did not consider key confounders
Deruty 1995[48]	Inappropriate study design – No multivariate analysis
Diaz 2011[49]	Inappropriate study design – No multivariate analysis
Diesing 2018[50]	Inappropriate Population – shunt dependent hydrocephalus
Dilvesi 2016[52]	Inappropriate study design – Validation of severity scoring system – no multivariate analysis
Dinc 2017[53]	Inappropriate study design – Multivariate analysis did not consider key confounders
Diringer 1997[54]	Inappropriate study design – No multivariate analysis
Dreier 2007[55]	Inappropriate Population– migraine compared to no migraine in delayed neurological ischemic deficit (DNID)

Reference	Reason for exclusion
Duan 2017[56]	Inappropriate study design – Multivariate analysis did not consider key confounders
Dunham 2004[58]	Inappropriate Population – traumatic brain injury
Eagles 2018[59]	Inappropriate study design – No multivariate analysis
Egashira 2013[60]	Inappropriate Population– Haematoma growth
Eide 2006[61]	Inappropriate intervention – intracranial pressure monitoring post SAH; no multivariate analysis
Elliott 1996[62]	Inappropriate comparison – predicting length of stay and cost of stay by aneurysm grade
Elsayed 2019[63]	Inappropriate study design – Abstract
Elwatidy 2003[64]	Inappropriate study design – Multivariate analysis did not consider key confounders
Fauchier 2016[65]	Inappropriate Population – risk scoring in atrial fibrillation
Fernandez Perez 2019[66]	Inappropriate study design – Abstract
Fiehler 2008[67]	Inappropriate population – monitoring of cerebral aneurysm therapy
Flores 2020[68]	Inappropriate comparison – no relevant outcomes
Foreman 2018[69]	Inappropriate study design – Multivariate analysis did not consider key confounders
Fountas 2008[70]	Inappropriate study design – Multivariate did not consider key confounders
Franke 1992[71]	Inappropriate study design – unclear analysis (unclear of severity score and outcome measure)
Friedman 2002[72]	Inappropriate comparison – model to predict vasospasm
Frontera 2006[73]	Inappropriate comparison – predicting vasospasm; Multivariate did not consider key confounders
Gallas 2005[75]	Inappropriate comparison – durability of Gugliemi coils
Garbossa 2012[76]	Inappropriate study design – Multivariate analysis did not consider key confounders
Gerber 1993[77]	Inappropriate study design – no multivariate analysis
Ghelmez 2013[79]	Inappropriate study design / population– Multivariate analysis did not consider key confounders / hypertension in relation to haemorrhage
Ghosh 2012[80]	Inappropriate comparison – correlation of glucose levels to severity scores
Gilsbach 1989[81]	Inappropriate study design – Multivariate analysis did not consider key confounders
Giraldo 2012[82]	Inappropriate study design – Multivariate analysis did not consider key confounders
Goldberg 2018[83]	Duplicate paper
Greving 2014[84]	Inappropriate study design – Proposed score – development of PHASES score; Multivariate analysis did not consider key confounders
Gruber 1998[85]	Inappropriate study design – No multivariate analysis
Grunwald 2012[86]	Inappropriate comparison – scale for evaluation of intracranial aneurysms treated with flow diverters
Guresir 2008[87]	Inappropriate comparison – incidence and impact of intracerebral haematoma on aneurysmal subarachnoid haemorrhage
Ha 2011[88]	Inappropriate comparison – surgical factors affecting outcomes of MCA aneurysms
Hamid 2010[89]	Inappropriate study design – technical success of coiling aneurysms

Reference	Reason for exclusion
Hanel 2002[90]	Systematic review – references reviewed
Haug 2010[91]	Inappropriate study design – Multivariate analysis did not consider key confounders
Haupt 1995[92]	Inappropriate study design – no relevant outcomes
Heeley 2015[93]	Inappropriate comparison – modified severity scoring systems for ICH
Hellawell 1999[94]	Inappropriate study design – Multivariate analysis did not consider key confounders
Hemphill 2001[95]	Inappropriate study design – Multivariate analysis groups severity score as a single outcome (odds ratio of severity score overall, not individualized grades of scoring system)
Heuer 2004[96]	Inappropriate study design – Multivariate analysis did not consider key confounders
Hijdra 1988[97]	Inappropriate study design – Multivariate analysis did not consider key confounders
Hilditch 2018[98]	Paper not available
Hong 2016[99]	Inappropriate study design – Multivariate analysis did not consider key confounders
Hostettler 2018[100]	Inappropriate study design – Multivariate analysis did not consider key confounders
Huang 1994[101]	Inappropriate population – stroke / TIA
Hutchinson 2000[102]	Inappropriate study design – Multivariate analysis did not consider key confounders
Hutter 2001[103]	Inappropriate study design – Multivariate analysis did not consider key confounders
Ikawa 2004[104]	Inappropriate comparison – No relevant outcomes
Inagawa 2018[105]	Inappropriate study design – Multivariate analysis did not consider key confounders
Iosif 2014[107]	Inappropriate study design – Multivariate analysis did not consider key confounders
Ironside 2019[108]	Inappropriate study design – multivariate analysis for severity scores overall (not individualised)
Jabbarli 2015[109]	Inappropriate study design – Multivariate analysis groups severity score as a single outcome (odds ratio of severity score overall, not individualized grades of scoring system)
Jain 2004[111]	Inappropriate study design – Multivariate analysis did not consider key confounders
Jaja 2013[112]	Systematic review – references reviewed
Jaja 2018[113]	Inappropriate study design – Multivariate analysis groups severity score as a single outcome (odds ratio of severity score overall, not individualized grades of scoring system)
Jamil 2008[114]	Inappropriate study design – Multivariate analysis did not consider key confounders
Jamjoom 1993[115]	Inappropriate study design – Multivariate analysis did not consider key confounders
Juvela 1992[116]	Inappropriate study design – no relevant outcomes
Katsuki 2019[118]	Inappropriate comparison – no relevant outcomes
Kazumata 2006[119]	Inappropriate study design – Outcomes unclear
Khandelwal 2005[120]	Inappropriate study design – Multivariate analysis did not consider key confounders

Reference	Reason for exclusion
Kikkawa 2017[121]	Inappropriate study design – Multivariate analysis did not consider key confounders
Kilic 2017[122]	Inappropriate comparison – hydrocephalus in SAH
Koc 1997[123]	Inappropriate study design – Multivariate analysis did not consider key confounders
Kollegger 1989[124]	Inappropriate study design – No multivariate analysis
Kranthi 2016[127]	Inappropriate study design – Multivariate analysis did not consider key confounders
Kremer 2002[128]	Inappropriate study design – Multivariate analysis did not consider key confounders
Kulwin 2014[129]	Inappropriate study design – Multivariate analysis did not consider key confounders
Kumar 2010[130]	Paper not available
Kurtz 2019[131]	Inappropriate study design – abstract
Kusumi 2005[132]	Inappropriate comparison – cerebral aneurysms during angiography
Kutsuna 2018[133]	Inappropriate study design – Multivariate analysis did not consider key confounders
Lagares 2005[134]	Inappropriate comparison / study design - Comparison of different severity scores; Multivariate analysis did not consider key confounders
Lagares 2001[135]	Inappropriate comparison - Outcomes unclear
Laidlaw 2003[136]	Inappropriate study design – Multivariate analysis did not consider key confounders
Le Roux 1996[137]	Inappropriate study design – Multivariate analysis did not consider key confounders
Lee 2012[138]	Inappropriate study design – Multivariate analysis did not consider key confounders
Lee 1997[139]	Inappropriate comparison – No relevant outcomes
Leira 2007[141]	Inappropriate study design – Proposed modification to NIHSS score for SAH; Multivariate analysis does not match protocol
Leira 2006[142]	Inappropriate study design – Abstract only
Lerch 2006[143]	Inappropriate study design – Multivariate analysis did not consider key confounders
Liao 2013[144]	Inappropriate study design – Multivariate analysis did not consider key confounders
Liao 2020[145]	Inappropriate study design – no multivariate analysis
Lin 1998[146]	Inappropriate study design – no multivariate analysis
Lin 1999[148]	Inappropriate study design – no multivariate analysis
Lin 1999[147]	Inappropriate study design – no multivariate analysis
Lin 2016[149]	Inappropriate comparison – outcome post pipeline embolization
Lindvall 2009[150]	Inappropriate study design – Multivariate analysis did not consider key confounders
Lip 2013[151]	Inappropriate comparison - Comparison of bleeding risk scores
Lisk 1994[152]	Inappropriate comparison – No relevant outcomes
Liu 2013[153]	Inappropriate study design – Multivariate analysis did not consider key confounders
Lo 2016[155]	Inappropriate study design – Multivariate analysis did not consider key confounders
Lo 2016[154]	Inappropriate study design – Multivariate analysis did not consider key confounders

Reference	Reason for exclusion
Lo 2015[156]	Systematic review – references reviewed
Lo 2013[157]	Inappropriate comparison – Multivariate analysis does not include severity scores
Luo 2019[158]	Systematic review – references checked
Mader 1998[159]	Inappropriate comparison – development of a score to compare haemorrhagic stroke to ischemic stroke
Maragkos 2019[160]	Inappropriate study design – Multivariate analysis did not consider key confounders
Meling 2008[161]	Inappropriate study design – Multivariate analysis did not consider key confounders
Miyazawa 2002[162]	Inappropriate study design – no multivariate analysis
Mortimer 2014[164]	Inappropriate study design – Multivariate analysis did not consider key confounders
Mouchtouris 2020[165]	Inappropriate comparison – No relevant outcomes
Muengtaweepongsa 2015[166]	Inappropriate population – SEDAN score for stroke
Murphy 2018[167]	Inappropriate study design – Multivariate analysis did not consider key confounders
Mushtaq 2017[168]	Inappropriate study design – Descriptive review of patients
Myles 1996[169]	Inappropriate population – medically induced coma
Nakagawa 2013[170]	Inappropriate study design – Proposed new subgrouping of WFNS; Multivariate analysis did not consider key confounders
Nanda 2002[172]	Inappropriate study design – Multivariate analysis did not consider key confounders
Nanda 2003[171]	Inappropriate study design – Multivariate analysis did not consider key confounders
Nastasovic 2019[173]	Paper not available
Naval 2013[175]	Inappropriate study design – Multivariate analysis groups severity score as a single outcome (odds ratio of severity score overall, not individualized grades of scoring system)
Navalitloha 2000[176]	Inappropriate study design – Multivariate analysis did not consider key confounders
Neidert 2018[177]	Inappropriate study design – Multivariate analysis did not consider key confounders
Nemoto 2018[178]	Inappropriate study design – Multivariate analysis groups severity score as a single outcome (odds ratio of severity score overall, not individualized grades of scoring system)
Niemann 2003[179]	Inappropriate study design – Multivariate analysis did not consider key confounders
Nossek 2016[180]	Inappropriate study design – Proposed classification ; no clear prognostic data
O'Sullivan 1994[181]	Inappropriate study design – no multivariate analysis
O'Sullivan 1996[182]	Inappropriate study design – Multivariate analysis did not consider key confounders
Oder 1991[183]	Inappropriate study design – no multivariate analysis
Ogden 2019[184]	Inappropriate comparison – No relevant outcomes
Ogilvy 1998 [185]	Inappropriate study design – Adapted severity score used; unclear analysis
Ogilvy 2006[186]	Inappropriate comparison – Unclear outcomes
Oh 2012[187]	Inappropriate study design – Multivariate analysis did not consider key confounders

Reference	Reason for exclusion
Ois 2019[188]	Inappropriate study design – Multivariate analysis not clear whether per grade increase or overall score
Olsen 2019[189]	Inappropriate comparison – no relevant outcomes
Osawa 2001[191]	Inappropriate study design – no multivariate analysis
Oshiro 1997[192]	Inappropriate study design – Multivariate analysis did not consider key confounders
Ota 2019[193]	Inappropriate study design – Multivariate analysis did not include appropriate grading systems
Otani 2013[194]	Inappropriate study design – results post craniectomy; no multivariate analysis
Otani 2008[195]	Inappropriate study design – Multivariate analysis did not consider key confounders
Passier 2011[197]	Inappropriate study design – Multivariate analysis does not include severity scoring
Payner 2011[198]	Inappropriate study design – Multivariate analysis did not consider key confounders
Pereira 2007[199]	Inappropriate study design – Multivariate analysis did not consider key confounders
Pisters 2010[200]	Inappropriate study design – no multivariate analysis
Proust 2003[202]	Inappropriate study design – Multivariate analysis did not consider key confounders
Proust 2020[201]	Inappropriate comparison – no relevant outcomes
Raj 2019[204]	Inappropriate study design – No multivariate analysis
Ravindran 2018[205]	Inappropriate study design – no relevant outcomes
Reponen 2016[206]	Inappropriate study design – Multivariate analysis did not consider key confounders
Reponen 2014[207]	Systematic review – references reviewed
Risselada 2010[208]	Inappropriate study design – no multivariate analysis
Risselada 2010[209]	Inappropriate study design – no multivariate analysis
Rivero-Arias 2009[210]	Inappropriate comparison – investigating Ischemic neurological deficit
Roganovic 2002[211]	Inappropriate study design – Multivariate analysis did not consider key confounders
Ronne-Engstrom 2014[212]	Inappropriate study design – Multivariate analysis does not match protocol
Rosen 2004[213]	Inappropriate study design – Proposed unvalidated scoring system,
Rosen 2005[214]	Systematic review - references reviewed
Rosengart 2007[215]	Inappropriate study design – Multivariate analysis groups severity score as a single outcome (odds ratio of severity score overall, not individualized grades of scoring system)
Rubbert 2018[216]	Inappropriate comparison – No useable outcomes
Sacho 2013[217]	Inappropriate comparison – No useable outcomes
Salary 2007[218]	Multivariate analysis groups severity score as a single outcome (odds ratio of severity score overall, not individualized grades of scoring system)
Sandercock 1985[219]	Scoring system for stroke
Sano 2010[220]	Inappropriate comparison – No relevant outcomes
Sasahara 2016[221]	Inappropriate study design – Correction notification
Sasaki 2004[222]	Inappropriate study design – Multivariate analysis did not consider key confounders

Reference	Reason for exclusion
Saveland 1992[223]	Inappropriate study design – no multivariate analysis
Saveland 1993[224]	Inappropriate study design – no multivariate analysis
Saveland 1986[225]	Inappropriate study design – no multivariate analysis
Scharbrodt 2009[226]	Inappropriate population – comparison of SF 36 to healthy population
Scholler 2013[227]	Inappropriate study design – Multivariate analysis groups severity score as a single outcome (odds ratio of severity score overall, not individualized grades of scoring system)
Schuiling 2005[228]	Inappropriate study design – Multivariate analysis did not consider key confounders
Sharma 2016[229]	Inappropriate study design – no multivariate analysis
Shen 2019[230]	Inappropriate comparison – no relevant outcomes
Shimoda 1997[231]	Inappropriate study design – no relevant outcomes
Sloan 1998[232]	Inappropriate population – thrombolysis induced haemorrhage
Slusarz 2009[233]	Inappropriate study design – Multivariate analysis did not consider key confounders
Slusarz 2012[234]	Inappropriate study design – Multivariate analysis did not consider key confounders
Slusarz 2017[235]	Inappropriate study design – Severity scoring for levels of consciousness
Smith 2005[236]	Inappropriate study design – Multivariate analysis did not consider key confounders
Solaroglu 2003[237]	Inappropriate study design – Multivariate analysis did not consider key confounders
St Julien 2008[238]	Inappropriate study design – Multivariate analysis groups severity score as a single outcome (odds ratio of severity score overall, not individualized grades of scoring system)
Stapleton 2015[239]	Inappropriate study design – Multivariate analysis did not consider key confounders
Starke 2009[241]	Inappropriate study design – Multivariate analysis did not consider key confounders
Stienen 2015[242]	Inappropriate study design – Multivariate analysis did not consider key confounders
Suzuki 1990[243]	Inappropriate comparison – No relevant outcomes
Szklener 2015[244]	Inappropriate study design – no relevant outcomes
Szydelko 2008[245]	Inappropriate comparison – effect of rehabilitation after SAH
Tai 2019[246]	Inappropriate comparison – no relevant outcomes
Takagi 1999[247]	Inappropriate study design – Multivariate analysis did not consider key confounders
Takahashi 2017[248]	Inappropriate comparison – mean transit time to clinical outcomes
Tawk 2015[251]	Inappropriate study design – Unclear outcomes
Taylor 2011[252]	Inappropriate study design – Multivariate analysis did not consider key confounders
Tewari 2015[253]	Inappropriate study design – Multivariate analysis did not consider key confounders
Thomeer 1994[254]	Inappropriate study design – Multivariate analysis did not consider key confounders
Tjahjadi 2013[255]	Inappropriate study design – Multivariate analysis did not consider key confounders

Reference	Reason for exclusion
Tjahjadi 2016[256]	Inappropriate study design – Multivariate analysis did not consider key confounders
Tommasino 2018[257]	Inappropriate study design – Unclear statistical analysis
Towgood 2005[258]	Inappropriate population – unruptured aneurysms in comparison to controls
Ungersbock 1994[259]	Inappropriate study design – no multivariate analysis
van den Berg 2011[260]	Inappropriate study design – Multivariate analysis did not consider key confounders
van Heuven 2008[262]	Inappropriate study design – Multivariate analysis did not consider key confounders
Vannemreddy 2011[263]	Inappropriate comparison - No relevant outcomes
Vergouwen 2012[264]	Inappropriate population – stroke
Wang 2019[265]	Inappropriate comparison – no relevant outcomes
Wani 2007[267]	Inappropriate study design – no relevant outcomes
Washington 2014[268]	Inappropriate study design – Proposed prediction model; Multivariate analysis did not consider key confounders
Watcharasaksilp 2013[269]	Inappropriate study design – Multivariate analysis did not consider key confounders
Weir 2003[270]	Inappropriate study design – no multivariate analysis
White 2017[271]	Inappropriate study design – no multivariate analysis
Wilson 2012[272]	Inappropriate study design – Multivariate analysis did not consider key confounders
Witsch 2016[273]	Inappropriate study design – Development of FRESH score
Witsch 2019[274]	Inappropriate comparison – no relevant outcomes
Witsch 2019[275]	Inappropriate study design – Abstract
Woertgen 2003[276]	Inappropriate study design – Multivariate analysis did not consider key confounders
Wong 2013[277]	Inappropriate study design – Multivariate analysis did not consider key confounders
Wong 2015[278]	Inappropriate study design – Multivariate analysis did not consider key confounders
Wong 2004[279]	Inappropriate study design – Multivariate analysis did not consider key confounders
Wong 1999[280]	Inappropriate study design – Multivariate analysis did not consider key confounders
Wostrack 2013[281]	Inappropriate study design – Unclear outcomes
Xu 2011[282]	Inappropriate study design – no relevant outcomes
Yahia 2011[283]	Inappropriate comparison - No relevant outcomes
Yanaka 1993[284]	Inappropriate study design – Proposed model to predict outcome after subdural haematoma
Yang 2015[285]	Inappropriate study design – no multivariate analysis
Yilmaz 2017[286]	Inappropriate study design – demographic and clinical features of aneurysmal subarachnoid haemorrhage
Yousef 2019[287]	Paper not available
Zapata-Wainberg 2015[288]	Incorrect comparison – epidemiology of ICH with Vitamin K
Zeiler 2017[289]	Inappropriate study design – Multivariate analysis did not consider key confounders
Zhang 2016[290]	Inappropriate study design – no relevant outcomes
Zhao 2014[291]	Inappropriate study design – no relevant outcomes

Reference	Reason for exclusion
Zheng 2011[293]	Incorrect comparison – effects of hyponatraemia on aneurysmal subarachnoid haemorrhage
Zheng 2019[294]	Inappropriate study design – risk score development
Zijlmans 2018[295]	Inappropriate study design – no multivariate analysis
Zou 2020[296]	Inappropriate study design – no relevant outcomes

I.21 Excluded health economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2003 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

Table 59: Studies excluded from the health economic review

Reference	Reason for exclusion
None.	

Appendix J: Research recommendations

J.1 Prognostic factors

Research question: What variables predict death or disability for people with aneurysmal subarachnoid haemorrhage?

Why this is important:

Timely and reliable prediction of outcome is important in clinical practice for treatment decision-making and also for providing information to patients with aneurysmal subarachnoid haemorrhage and their relatives.

Criteria for selecting high-priority research recommendations:

PICO question	Population: Adults (16 or over) who have had aneurysmal subarachnoid haemorrhage. Exposure(s): any baseline factors/parameters that are thought to have prognostic value (either based on clinical experience or on previous evidence), for example gender, blood pressure/history of hypertension, smoking history, weight, alcohol consumption, family history, presenting symptoms, clinical findings including level of consciousness, CT findings, etc. Confounding factor(s): other characteristics that could affect the outcome, for example age. Outcome(s): Death or disability.
Importance to patients or the population	The ability to predict outcome following SAH would allow patients and their families to better understand the risk of mortality or long-term disability and may support associated decision making. Better understanding of the prognostic variables predicting poor outcome in people with aSAH would allow for the development of an accurate and useful risk prediction tool.
Relevance to NICE guidance	Factors that predict outcome and/or any predictive score will contribute to updates of this guideline.
Relevance to the NHS	The ability to predict outcome following SAH would assist clinicians in decision making and utilisation of resources.
National priorities	None
Current evidence base	Clinical condition at the time of presentation following SAH varies and several scoring systems based on conscious level and radiographic findings are used to assess severity. Studies have shown some association between these scoring systems and mortality/morbidity but have limited validity in contemporary practice due to the low quality and often small sample size. Larger studies to formally identify factors that predict outcome may inform the development and validation of an accurate prognostic tool.
Equality	None
Study design	Prognostic Prediction Modelling Study (TRIPOD) combining multiple variables to estimate the probability of a particular outcome occurring within a certain time period.
Timeframe	A minimum of 12 months post-discharge, ideally 3 years – it will take time to see outcomes.
Feasibility	This study is feasible and could be delivered in a reasonable timeframe.
Other comments	None
Importance	• High: the research is essential to inform future updates of key recommendations in the guideline.

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