Appendix D: Clinical evidence tables

Study	**ATACH-2 trial: Qureshi 2016[41]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=1000)
Countries and setting	Conducted in Multiple countries; Setting: ED, secondary care
Line of therapy	1st line
Duration of study	Intervention + follow up: Intervention 24 hours, follow-up at 90 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: CT
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Spontaneous intracerebral hemorrhage who had a systolic blood pressure of 150 to 220 mm Hg within 6 hours after symptom onset. At least one reading of systolic blood pressure of 180 mm Hg or more between symptom onset and the initiation of intravenous antihypertensive treatment
Exclusion criteria	Ischaemic stroke
Recruitment/selection of patients	ED
Age, gender and ethnicity	Age - Other: Mean 61.9 years. Gender (M:F): 38.0%/62%. Ethnicity: 56.2% Asian

Further population details	1. Age <80 vs >/=80 years: Not applicable 2. Lobar vs deep haematoma location: Not stated / Unclear 3. NIHSS: Not applicable 4. Volume of haemorrhage: Not applicable
Indirectness of population	No indirectness
Interventions	(n=500) Intervention 1: Intensive therapy. Reduce and maintain the hourly minimum systolic blood pressure in range of 110 to 139 mmHg. Duration 24 hours. Concurrent medication/care: Standard therapy. Indirectness: No indirectness Further details: 1. Time to treatment (within 6 hours vs >6 hours): Within 6 hours (n=500) Intervention 2: Conservative therapy. Reduce and maintain the hourly minimum systolic blood pressure in range of 140 to 179 mmHg. Duration 24 hour. Concurrent medication/care: Standard care. Indirectness: No indirectness Further details: 1. Time to treatment (within 6 hours vs >6 hours): Within 6 hours
Funding	Academic or government funding (National Institute of Neurological Disorders and Stroke, Intramural Research Fund for Cardiovascular Diseases of the National Cerebral and Cardiovascular Center. National Institute of Neurological Disorders and Stroke and by a grant (H23-4-3, to Dr. Toyoda) from the Intramural Research Fund for Cardiovascular Diseases of the National Cerebral and Cardiovascular Center.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTENSIVE THERAPY versus CONSERVATIVE THERAPY

Protocol outcome 1: Mortality at 90 days
- Actual outcome: Mortality at 90 days; Group 1: 33/481, Group 2: 34/480
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - ; Indirectness of outcome: No indirectness ; Baseline details: Systolic BP at presentation in ED Mean (SD) intensive 200 (27.1), conservative 201 (26.9); Group 1 Number missing: 19; Group 2 Number missing: 20

Protocol outcome 2: EQ-5D utility index score at 90 days
- Actual outcome: EQ-5D utility index score at 90 days; Group 1: median (IQR): 0.7 (-0.1 to 1.0); group 2: median (IQR): 0.7 (0 to 1.0).

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Systolic BP at presentation in ED Mean (SD) intensive 200 (27.1), conservative 201 (26.9); Group 1 Number missing: 19; Group 2 Number missing: 20 Protocol outcome 3: EQ-5D visual analogue scale at 90 days - Actual outcome: EQ-5D visual analogue scale at 90 days; ; Group 1: median (IQR): 62.5 (0 to 100); group 2: median (IQR): 70 (0 to 100). Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Systolic BP at presentation in ED Mean (SD) intensive 200 (27.1), conservative 201 (26.9); Group 1 Number missing: 19; Group 2 Number missing: 20 Protocol outcome 4: Neurological decline at 24 hours - Actual outcome: Neurological decline at 90 days; Group 1: 55/500, Group 2: 40/500 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Systolic BP at presentation in ED Mean (SD) intensive 200 (27.1), conservative 201 (26.9); Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 5: Haematoma growth at 24 hours - Actual outcome: Haematoma growth at 90 days; Group 1: 85/450, Group 2: 104/426 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Systolic BP at presentation in ED Mean (SD) intensive 200 (27.1), conservative 201 (26.9); Group 1 Number missing: 19, Reason: No CT; Group 2 Number missing: 20, Reason: No CT	
Protocol outcomes not reported by the study	Mortality at 24 hours; mRS score at 90 days; Recurrent and /or extended stroke at 24 hours; Recurrent and /or extended stroke at 90 days; Adverse events at 24 hours; Adverse events at 90 days; Quality of life at 90 days; Quality of life at 24 hours; mRS score at 90 days; mRS score 0-2 vs 3-6 at 90 days; mRS score 0-3 vs 4-6 at 90 days; Renal failure at 90 days; Myocardial infarction at 90 days; Neurological decline at 90 days; Barthel index at 90 days; mRS score at 1 year; EQ-5D at 90 days

Study	ENOS-ICH trial: Krishnan 2016[33]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=629)
Countries and setting	Conducted in Multiple countries; Setting: ED, Secondary care
Line of therapy	1st line
Duration of study	Intervention + follow up: 7 days, 90 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: CT / MRI
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Systolic blood pressure between 150 and 220 mm Hg, no definite indication for or contraindication to blood-pressure–lowering treatment that could be commenced within 6 hours after the onset of spontaneous intracranial hemorrhage
Exclusion criteria	Structural cerebral cause for the intracerebral hemorrhage, deep coma (defined as a score of 3 to 5 on the Glasgow Coma Scale in which scores range from 3 to 15, with lower scores indicating reduced levels of consciousness), massive hematoma with a poor prognosis, or if early surgery to evacuate the hematoma was planned
Recruitment/selection of patients	ED
Age, gender and ethnicity	Age - Mean (SD): 67.0 (12.4(. Gender (M:F): 66% make. Ethnicity: Not stated
Further population details	1. Age <80 vs >/=80 years: Not applicable 2. Lobar vs deep haematoma location: Not stated / Unclear 3. NIHSS: Not applicable 4. Volume of haemorrhage: Not applicable
Indirectness of population	No indirectness

Interventions	(n=310) Intervention 1: Intensive therapy - Intravenous or transdermal glyceryl trinitrate (GTN). 5 mg/day. Duration 7 days. Concurrent medication/care: Standard care. Indirectness: No indirectness Further details: 1. Time to treatment (within 6 hours vs >6 hours): Not stated / Unclear (n=319) Intervention 2: Standard care. No GTN. Duration 7 days. Concurrent medication/care: Standard care. Indirectness: No indirectness Further details: 1. Time to treatment (within 6 hours vs >6 hours):
Funding	Other (Bupa UK Foundation and Medical Research Council (G0501797). Agency for Science, Technology and Research (Singapore), Hypertension Trust (United Kingdom), Queen Elizabeth II Health Sciences Centre Research Fund (Canada), and Reichstadt family (United Kingdom))

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTRAVENOUS OR TRANSDERMAL GLYCERYL TRINITRATE (GTN) versus STANDARD CARE

Protocol outcome 1: Mortality at 90 days
- Actual outcome: Mortality at 90 days; Group 1: 42/310, Group 2: 47/319
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Systolic blood pressure mmHg, mean (SD) intensive 172.1 (19.4) versus conservative 172.3 (19.9), diastolic blood pressure mmHg, mean (SD) intensive 93.4 (13.9) versus conservative 94.0 (13.1), Treated hypertension intensive 40.2% versus 39.0%; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: mRS score at 90 days
- Actual outcome: mRS score at 90 days; ; Adjusted common OR: 1.04 (0.78 to 1.38), p=0.81;
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Systolic blood pressure mmHg, mean (SD) intensive 172.1 (19.4) versus conservative 172.3 (19.9), diastolic blood pressure mmHg, mean (SD) intensive 93.4 (13.9) versus conservative 94.0 (13.1), Treated hypertension intensive 40.2% versus 39.0%; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Myocardial infarction at 90 days
- Actual outcome: Myocardial infarction at 90 days; Group 1: 1/310, Group 2: 2/319
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Systolic blood pressure mmHg, mean (SD) intensive 172.1 (19.4) versus conservative 172.3 (19.9), diastolic blood pressure mmHg, mean (SD) intensive 93.4 (13.9) versus conservative 94.0 (13.1), Treated hypertension intensive 40.2% versus 39.0%; Group 1 Number missing: ;

Group 2 Number missing: Protocol outcome 4: Barthel index at 90 days - Actual outcome: mRS score at 90 days; Group 1: mean 62.3 (SD 38.1); n=310, Group 2: mean 61.4 (SD 39.7); n=319 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Systolic blood pressure mmHg, mean (SD) intensive 172.1 (19.4) versus conservative 172.3 (19.9), diastolic blood pressure mmHg, mean (SD) intensive 93.4 (13.9) versus conservative 94.0 (13.1), Treated hypertension intensive 40.2% versus 39.0%; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Recurrent stroke at 90 days - Actual outcome: Recurrent stroke at 90 days; Group 1: 7/304, Group 2: 7/318 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Systolic blood pressure mmHg, mean (SD) intensive 172.1 (19.4) versus conservative 172.3 (19.9), diastolic blood pressure mmHg, mean (SD) intensive 93.4 (13.9) versus conservative 94.0 (13.1), Treated hypertension intensive 40.2% versus 39.0%; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Mortality at 24 hours; Recurrent and /or extended stroke at 24 hours; Recurrent and /or extended stroke at 90 days; Adverse events at 24 hours; Adverse events at 90 days; Quality of life at 90 days; Quality of life at 24 hours; EQ-5D utility index score at 90 days; EQ-5D visual analogue scale at 90 days; mRS score at 90 days; mRS score 0-2 vs 3-6 at 90 days; mRS score 0-3 vs 4-6 at 90 days; Renal failure at 90 days; Neurological decline at 24 hours; Neurological decline at 90 days; Haematoma growth at 24 hours; mRS score at 1 year; EQ-5D at 90 days

Study	ICH-ADAPT trial: Butcher 2013[15]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=78)
Countries and setting	Conducted in Canada; Setting: ED, Secondary care
Line of therapy	1st line
Duration of study	Intervention + follow up: 24 hours, follow-up 90 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: CT
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	≥18 years of age, with spontaneous cerebral haemorrhage diagnosed on noncontrast computed tomography (CT) <24 hours after onset. SBP was ≥150 mm Hg (≥2 readings ≥5 minutes apart)
Exclusion criteria	evidence of secondary cerebral haemorrhage (vascular malformation), planned surgical resection, or contraindications to CT perfusion (CTP; eg, contrast allergy or renal impairment)
Recruitment/selection of patients	ED
Age, gender and ethnicity	Age - Mean (SD): Intensive 70.7 (12.5), conservative therapy 68.7 (11.1). Gender (M:F): Intensive 67% male, conservative therapy 78%. Ethnicity: Not reported
Further population details	1. Age <80 vs >/=80 years: Not applicable 2. Lobar vs deep haematoma location: Not stated / Unclear 3. NIHSS: Not applicable 4. Volume of haemorrhage: Not applicable
Indirectness of population	No indirectness

Interventions	(n=39) Intervention 1: Intensive therapy. Intensive therapy. Duration 24 hours. Concurrent medication/care: Standard care. Indirectness: No indirectness Further details: 1. Time to treatment (within 6 hours vs >6 hours): Not applicable (n=36) Intervention 2: Conservative therapy. Conservative care. Duration 24 hours. Concurrent medication/care: Standard care. Indirectness: No indirectness Further details: 1. Time to treatment (within 6 hours vs >6 hours): Not applicable
Funding	Academic or government funding (Alberta Innovates Health Solutions, Heart and Stroke Foundation of Canada)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTENSIVE THERAPY versus CONSERVATIVE THERAPY

Protocol outcome 1: Mortality at 90 days
- Actual outcome: Mortality at 90 days; Group 1: 7/37, Group 2: 4/39
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Very serious indirectness, Comments: Mortality at 30 days not 90 days; Baseline details: Systolic BP mmHg, mean (SD) intensive 182 (20), conservative 184 (25), diastolic , BP mmHg, mean (SD) intensive 93 (19), conservative 97 (23), Prior hypertension intensive 67%, conservative 27%; Group 1 Number missing: 2, Reason: Not stated; Group 2 Number missing: 0, Reason: Not stated

Protocol outcome 2: mRS score at 90 days
- Actual outcome: mRS score at 90 days; 0 to 6 Top=High is poor outcome;
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Systolic BP mmHg, mean (SD) intensive 182 (20), conservative 184 (25), diastolic , BP mmHg, mean (SD) intensive 93 (19), conservative 97 (23), Prior hypertension intensive 67%, conservative 27%; Group 1 Number missing: 2, Reason: Not stated; Group 2 Number missing: 0, Reason: Not stated

Protocol outcome 3: Neurological decline at 24 hours
- Actual outcome: Neurological decline at 2 hours; Group 1: 3/37, Group 2: 2/36
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness, Comments: Decline at 2 hours not 24 hours; Baseline details: Systolic BP mmHg, mean (SD) intensive 182 (20), conservative 184 (25), diastolic , BP mmHg, mean (SD) intensive 93 (19), conservative 97 (23), Prior hypertension intensive 67%, conservative 27%; Group 1 Number missing: 2, Reason: Not stated; Group 2 Number missing: 0, Reason: Not stated

Protocol outcome 4: Haematoma growth at 24 hours - Actual outcome: Haematoma growth at 2 hours; Group 1: 9/37, Group 2: 4/36 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness, Comments: Growth at 2 hours not 24 hours; Baseline details: Systolic BP mmHg, mean (SD) intensive 182 (20), conservative 184 (25), diastolic , BP mmHg, mean (SD) intensive 93 (19), conservative 97 (23), Prior hypertension intensive 67%, conservative 27%; Group 1 Number missing: 2, Reason: Not stated; Group 2 Number missing: 0, Reason: Not stated	
Protocol outcomes not reported by the study	Mortality at 24 hours; Recurrent and /or extended stroke at 24 hours; Recurrent and /or extended stroke at 90 days; Adverse events at 24 hours; Adverse events at 90 days; Quality of life at 90 days; Quality of life at 24 hours; EQ-5D utility index score at 90 days; EQ-5D visual analogue scale at 90 days; mRS score at 90 days; mRS score 0-2 vs 3-6 at 90 days; mRS score 0-3 vs 4-6 at 90 days; Renal failure at 90 days; Myocardial infarction at 90 days; Neurological decline at 90 days; Barthel index at 90 days; mRS score at 1 year; EQ-5D at 90 days

Study	INTERACT-2 trial: Anderson 2013[1]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=2839)
Countries and setting	Conducted in Multiple countries; Setting: ED, Secondary care
Line of therapy	1st line
Duration of study	Intervention + follow up: Intervention 7 days, follow-up 90 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: CT
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Intracerebral haemorrhage within previous 6 hours, structural cerebral cause for the intracerebral hemorrhage, if they were in a deep coma (defined as a score of 3 to 5 on the Glasgow Coma Scale in which scores range from 3 to 15, with lower scores indicating reduced levels of consciousness), if they had a massive hematoma with a poor prognosis, or if early surgery to evacuate the hematoma was planned, age ≥18 years, at least 2 systolic BP measurements of ≥150 and ≤220 mmHg, recorded 2 or more minutes apart. Patients with initial systolic BP levels outside of this range (<150 or >220 mmHg) may be randomised should the BP levels fulfill entry criteria on re- checking up to 6 hours after the onset of ICH., patients with an initial systolic BP >220 at least 2 systolic BP measurements of ≥150 and ≤220 mmHg, recorded 2 or more minutes apart. Patients with initial systolic BP levels outside of this range (<150 or >220 mmHg) may be randomised should the BP levels fulfill entry criteria on re- checking up to 6 hours after the onset of ICH. Patients with an initial systolic BP >220 at least 2 systolic BP measurements of ≥150 and ≤220 mmHg, recorded 2 or more minutes apart. Patients with initial systolic BP levels outside of this range (<150 or >220 mmHg) may be randomised should the BP levels fulfill entry criteria on re- checking up to 6 hours after the onset if intracerebral haemorrhage
Exclusion criteria	Structural cerebral cause for the structural cerebral cause for the intracerebral hemorrhage, if they were in a deep coma (defined as a score of 3 to 5 on the Glasgow Coma Scale) in which scores range from 3 to 15, with lower scores indicating reduced levels of consciousness), if they had a massive hematoma with a poor prognosis, or if early surgery

	to evacuate the hematoma was planned if they were in a deep coma (defined as a score of 3 to 5 on the Glasgow Coma Scale in which scores range from 3 to 15, with lower scores indicating reduced levels of consciousness), if they had a massive hematoma with a poor prognosis, or if early surgery to evacuate the hematoma was planned
Recruitment/selection of patients	ED
Age, gender and ethnicity	Age - Mean (SD): Intensive therapy 63.0 (13.1), conservative therapy 64.1 (12.6) years. Gender (M:F): Intensive therapy 898/501, conservative therapy 882/548. Ethnicity: Not reported
Further population details	1. Age <80 vs >/=80 years: Not applicable 2. Lobar vs deep haematoma location: Not stated / Unclear 3. NIHSS: Not stated / Unclear 4. Volume of haemorrhage: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=1399) Intervention 1: Intensive therapy. Intensive therapy. Duration 7 days. Concurrent medication/care: Standard care. Indirectness: No indirectness Further details: 1. Time to treatment (within 6 hours vs >6 hours): Within 6 hours (n=1430) Intervention 2: Conservative therapy. Conservative therapy. Duration 7 days. Concurrent medication/care: Standard care. Indirectness: No indirectness Further details: 1. Time to treatment (within 6 hours vs >6 hours): Within 6 hours
Funding	Academic or government funding (National Health and Medical Research Council of Australia)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTENSIVE THERAPY versus CONSERVATIVE THERAPY Protocol outcome 1: Mortality at 90 days - Actual outcome: Mortality at 90 days; Group 1: 166/1394, Group 2: 170/1421 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - ; Indirectness of outcome: No indirectness ; Baseline details: Systolic blood pressure mean (SD) intensive 19 (17), conservative 179 (17), diastolic blood pressure mean (SD) intensive 101 (15), conservative 101 (15), history of hypertension intensive 72.4% conservative 72.5%; Group 1 Number missing: 5, Reason: Not stated; Group 2 Number missing: 9, Reason: Not stated	

Protocol outcome 2: Recurrent and /or extended stroke at 90 days
- Actual outcome: Recurrent stroke at 90 days; Group 1: 12/1399, Group 2: 12/1430
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Systolic blood pressure mean (SD) intensive 19 (17), conservative 179 (17), diastolic blood pressure mean (SD) intensive 101 (15), conservative 101 (15), history of hypertension intensive 72.4 %, conservative 72.5%; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: EQ-5D at 90 days
- Actual outcome: EQ-5D at 90 days; Group 1: mean 0.6 (SD 0.39); n=1394, Group 2: mean 0.55 (SD 0.4); n=1421
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Systolic blood pressure mean (SD) intensive 19 (17), conservative 179 (17), diastolic blood pressure mean (SD) intensive 101 (15), conservative 101 (15), history of hypertension intensive 72.4 %, conservative 72.5%; Group 1 Number missing: 5, Reason: Not stated; Group 2 Number missing: 9, Reason: Not stated

Protocol outcome 4: mRS score 0-2 vs 3-6 at 90 days
- Actual outcome: mRS score 0-2 vs 3-6 at 90 days; Group 1: 663/1382, Group 2: 627/1412; ordinal analysis: pooled OR: 0.87 (0.77 to 1.00)

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - ; Indirectness of outcome: No indirectness ; Baseline details: Systolic blood pressure mean (SD) intensive 19 (17), conservative 179 (17), diastolic blood pressure mean (SD) intensive 101 (15), conservative 101 (15), history of hypertension intensive 72.4 %, conservative 77.5%; Group 1 Number missing: 5, Reason: Not stated; Group 2 Number missing: 9, Reason: Not stated

Protocol outcome 5: mRS score 0-3 vs 4-6 at 90 days
- Actual outcome: mRS score 0-3 vs 4-6 at 90 days; Group 1: 883/1382, Group 2: 861/1412
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - ; Indirectness of outcome: No indirectness ; Baseline details: Systolic blood pressure mean (SD) intensive 19 (17), conservative 179 (17), diastolic blood pressure mean (SD) intensive 101 (15), conservative 101 (15), history of hypertension intensive 72.4 %, conservative 77.5%; Group 1 Number missing: 5, Reason: Not stated; Group 2 Number missing: 9, Reason: Not stated

Protocol outcome 6: Neurological decline at 24 hours
- Actual outcome: Neurological decline at 90 days; Group 1: 198/1369, Group 2: 211/1395
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - ; Indirectness of outcome: No indirectness ; Baseline details: Systolic blood pressure mean (SD) intensive 19 (17), conservative 179 (17), diastolic blood pressure mean (SD) intensive 101 (15), conservative 101 (15), history of hypertension intensive 72.4 %, conservative 77.5%; Group 1 Number missing: 5, Reason: Not stated; Group 2 Number missing: 9, Reason: Not stated

Protocol outcome 7: Haematoma growth at 24 hours

- Actual outcome: Haematoma growth at 90 days; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - ; Indirectness of outcome: No indirectness ; Baseline details: Systolic blood pressure mean (SD) intensive 19 (17), conservative 179 (17), diastolic blood pressure mean (SD) intensive 101 (15), conservative 101 (15), history of hypertension intensive 72.4 %, conservative 77.5%; Group 1 Number missing: 5, Reason: Not stated; Group 2 Number missing: 9, Reason: Not stated	
Protocol outcomes not reported by the study	Mortality at 24 hours; mRS score at 90 days; Recurrent and /or extended stroke at 24 hours; Adverse events at 24 hours; Adverse events at 90 days; Quality of life at 90 days; Quality of life at 24 hours; EQ-5D visual analogue scale at 90 days; mRS score at 90 days; Renal failure at 90 days; Myocardial infarction at 90 days; Neurological decline at 90 days; Barthel index at 90 days; mRS score at 1 year; EQ-5D utility index score at 90 days

Study	INTERACT trial: Anderson 2008[3]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=404)
Countries and setting	Conducted in Multiple countries; Setting: ED, Secondary care
Line of therapy	1st line
Duration of study	Intervention + follow up: 7 days intervention, 90 days follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: CT
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Eligible patients were at least 18 years of age, had spontaneous ICH confirmed by CT and elevated systolic blood pressure (≥2 measurements of 150–220 mm Hg, recorded ≥2 min apart), and were able to commence the randomly assigned treatment within 6 hours of ICH onset
Exclusion criteria	Clear indication for intensive lowering of blood pressure (eg, systolic blood pressure >220 mm Hg or hypertensive encephalopathy); a clear contraindication to intensive lowering of blood pressure, clear evidence that the ICH was secondary to a structural cerebral abnormality, or the use of a thrombolytic agent, an ischaemic stroke within 30 days, a score of 3–5 on the Glasgow coma scale (GCS) indicating deep coma, significant prestroke disability or medical illness; or early planned decompressive neurosurgical intervention
Recruitment/selection of patients	ED
Age, gender and ethnicity	Age - Mean (SD): Intervention 62 (13), control 63 (12) years. Gender (M:F): Intensive 63% make, conservative 62% male. Ethnicity: Not reported

Further population details	1. Age <80 vs >/=80 years: Not applicable 2. Lobar vs deep haematoma location: Not stated / Unclear 3. NIHSS: Not applicable 4. Volume of haemorrhage: Not applicable
Indirectness of population	No indirectness
Interventions	(n=201) Intervention 1: Conservative therapy. Conservative therapy. Duration 7 days. Concurrent medication/care: Standard care. Indirectness: No indirectness Further details: 1. Time to treatment (within 6 hours vs >6 hours): Not applicable (n=203) Intervention 2: Intensive therapy. Intensive therapy. Duration 7 days. Concurrent medication/care: Standard care. Indirectness: No indirectness Further details: 1. Time to treatment (within 6 hours vs >6 hours): Within 6 hours
Funding	Academic or government funding (National Health and Medical Research Council of Australia)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTENSIVE THERAPY versus CONSERVATIVE THERAPY

Protocol outcome 1: Recurrent and /or extended stroke at 90 days
- Actual outcome: Recurrent stroke at 90 days; Group 1: 2/203, Group 2: 3/201
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Previous ischaemic stroke intensive versus conservative: 13% vs 19%, Previous ICH intensive versus conservative: 9% vs 13%, hypertension intensive versus conservative: 74% vs 74%; Group 1 Number missing: 1, Reason: Loss to follow-up; Group 2 Number missing: 1, Reason: Loss to follow-up

Protocol outcome 2: mRS score at 90 days
- Actual outcome: mRS score at 90 days; 0 to 6 Top=High is poor outcome; median (IQR) Group 1: 2 (1-4); group 2: 2 (1-4)
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Previous ischaemic stroke intensive versus conservative: 13% vs 19%, Previous ICH intensive versus conservative: 9% vs 13%, hypertension intensive versus conservative: 74% vs 74%; Group 1 Number missing: 1, Reason: Loss to follow-up; Group 2 Number missing: 1, Reason: Loss to follow-up

Protocol outcome 2: EQ-5D at 90 days
- Actual outcome: EQ-5D at 90 days; OR; Median (range) intensive: 0.75 (0.52 to 1.00), conservative: 0.78 (0.59 to 1.00);
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Baseline details: Previous ischaemic stroke intensive versus conservative: 13% vs 19%, Previous ICH intensive versus conservative: 9% vs 13%, hypertension intensive versus conservative: 74% vs 74%; Group 1 Number missing: 1, Reason: Loss to follow-up; Group 2 Number missing: 1, Reason: Loss to follow-up

Protocol outcome 3: Mortality at 90 days
- Actual outcome: Mortality at 90 days; Group 1: 21/202, Group 2: 25/200
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Baseline details: Previous ischaemic stroke intensive versus conservative: 13% vs 19%, Previous ICH intensive versus conservative: 9% vs 13%, hypertension intensive versus conservative: 74% vs 74%; Group 1 Number missing: 1, Reason: Loss to follow-up; Group 2 Number missing: 1, Reason: Loss to follow-up

Protocol outcome 4: Renal failure at 90 days
- Actual outcome: Renal failure at 90 days; Group 1: 4/203, Group 2: 2/201
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Baseline details: Previous ischaemic stroke intensive versus conservative: 13% vs 19%, Previous ICH intensive versus conservative: 9% vs 13%, hypertension intensive versus conservative: 74% vs 74%; Group 1 Number missing: 1, Reason: Loss to follow-up; Group 2 Number missing: 1, Reason: Loss to follow-up

Protocol outcome 5: Neurological decline at 24 hours
- Actual outcome: Neurological decline at 72 hours; Group 1: 31/203, Group 2: 30/201
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: Serious indirectness, Comments: 72 hours not 24 hours; Baseline details: Previous ischaemic stroke intensive versus conservative: 13% vs 19%, Previous ICH intensive versus conservative: 9% vs 13%, hypertension intensive versus conservative: 74% vs 74%; Group 1 Number missing: 1, Reason: Loss to follow-up; Group 2 Number missing: 1, Reason: Loss to follow-up

Protocol outcome 6: Haematoma growth at 24 hours
- Actual outcome: Haematoma growth at 24 hours; Group 1: 26/174, Group 2: 40/172
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness ; Baseline details: Previous ischaemic stroke intensive versus conservative: 13% vs 19%, Previous ICH intensive versus conservative: 9% vs 13%, hypertension intensive versus conservative: 74% vs 74%; Group 1 Number missing: 27, Reason: Loss to follow-up; Group 2 Number missing: 29, Reason: Loss to follow-up

Protocol outcomes not reported by the study	Mortality at 24 hours; Mortality at 90 days; mRS score at 90 days; Recurrent and /or extended stroke at 24 hours; Adverse events at 24 hours; Adverse events at 90 days; Quality of life at 90 days; Quality of life at 24 hours; EQ-5D visual analogue scale at 90 days; mRS score 0-2 vs 3-6 at 90 days; mRS score 0-3 vs 4-6 at 90 days; Myocardial infarction at 90 days; Neurological decline at 90 days; Barthel index at 90 days; mRS score at 1 year; EQ-5D utility index score at 90 days

Study	Koch 2008[32]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=42)
Countries and setting	Conducted in USA; Setting: ED, Secondary care
Line of therapy	1st line
Duration of study	Intervention + follow up: 48 hours, 90 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: CT
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Radiologically confirmed acute spontaneous intracerebral haemorrhage within 8 hours of symptom onset, age ≥18 years
Exclusion criteria	History of head trauma, coma, coagulopathy, MAP <100 mmHg, arteriovenous malformations, trauma aneurysms or other secondary causes, surgical haematoma evacuation, inability to give consent
Recruitment/selection of patients	ED
Age, gender and ethnicity	Age - Mean (SD): intensive 60 (11), conservative 62 (13). Gender (M:F): Intensive 43% male, conservative 67%. Ethnicity: African descent 57%, Hispanic 41%
Further population details	1. Age <80 vs >/=80 years: Not stated / Unclear 2. Lobar vs deep haematoma location: Not stated / Unclear 3. NIHSS: Not stated / Unclear 4. Volume of haemorrhage: Not stated / Unclear
Indirectness of population	No indirectness

Interventions	(n=21) Intervention 1: Intensive therapy. Intensive therapy. Duration 48 hours. Concurrent medication/care: Standard care. Indirectness: No indirectness Further details: 1. Time to treatment (within 6 hours vs >6 hours): >6 hours (Within 8 hours). (n=21) Intervention 2: Conservative therapy. Conservative therapy. Duration 48 hours. Concurrent medication/care: Standard care. Indirectness: No indirectness Further details: 1. Time to treatment (within 6 hours vs >6 hours): >6 hours (Within 8 hours).
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTENSIVE THERAPY versus CONSERVATIVE THERAPY

Protocol outcome 1: Mortality at 90 days
- Actual outcome: Mortality at 90 days; Group 1: 3/21, Group 2: 3/21
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Arrival MAP mmHg mean (SD) intensive 144.3 (15.8), conservative 150.7 (20.1), Prior hypertension intensive 18%, conservative 19%; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: mRS score at 90 days
- Actual outcome: mRS score at 90 days; Group 1: 10/21, Group 2: 8/21
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Arrival MAP mmHg mean (SD) intensive 144.3 (15.8), conservative 150.7 (20.1), Prior hypertension intensive 18%, conservative 19%; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: Renal failure at 90 days
- Actual outcome: Renal failure at 90 days; Group 1: 1/21, Group 2: 1/21
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Arrival MAP mmHg mean (SD) intensive 144.3 (15.8), conservative 150.7 (20.1), Prior hypertension intensive 18%, conservative 19%; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 4: Neurological decline at 90 days
- Actual outcome: Neurological decline at 48 hours; Group 1: 2/21, Group 2: 1/21
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;

Indirectness of outcome: Serious indirectness, Comments: Decline at 48 hours not 24 hours; Baseline details: Arrival MAP mmHg mean (SD) intensive 144.3 (15.8), conservative 150.7 (20.1), Prior hypertension intensive 18%, conservative 19%; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 5: Haematoma growth at 24 hours - Actual outcome: Haematoma growth at 24 hours; Group 1: 6/21, Group 2: 6/21 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Arrival MAP mmHg mean (SD) intensive 144.3 (15.8), conservative 150.7 (20.1), Prior hypertension intensive 18%, conservative 19%; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Mortality at 24 hours; Recurrent and /or extended stroke at 24 hours; Recurrent and /or extended stroke at 90 days; Adverse events at 24 hours; Adverse events at 90 days; Quality of life at 90 days; Quality of life at 24 hours; EQ-5D utility index score at 90 days; EQ-5D visual analogue scale at 90 days; mRS score at 90 days; mRS score 0-2 vs 3-6 at 90 days; mRS score 0-3 vs 4-6 at 90 days; Myocardial infarction at 90 days; Neurological decline at 24 hours; Barthel index at 90 days; mRS score at 1 year; EQ-5D at 90 days

Study	PATICH trial: Zheng 2017[63]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=201)
Countries and setting	Conducted in China; Setting: ED, Secondary care
Line of therapy	1st line
Duration of study	Intervention + follow up: 7 days + 90 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: CT / MRI
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged ≥18 years, had computed tomography- or magnetic resonance imaging–confirmed sICH with elevated systolic BP between 150 and 220 mm Hg (at least 2 measurements) and were able to receive surgery within 24 hours after ictus
Exclusion criteria	Definite indication or contraindications to antihypertensives, secondary intracerebral hemorrhage, a Glasgow Coma Scale score between 3 and 5, a definite contraindication to operation, advanced dementia or disability before ICH onset, or comorbidities that would interfere with the outcome assessment and follow-up.
Recruitment/selection of patients	ED
Age, gender and ethnicity	Age - Mean (SD): Intensive 54 (14), conservative 55 (12). Gender (M:F): Male sex intensive 75%, conservative 69%. Ethnicity: Chinese
Further population details	1. Age <80 vs >/=80 years: Not applicable 2. Lobar vs deep haematoma location: Not stated / Unclear 3. NIHSS: Not stated / Unclear 4. Volume of haemorrhage: Not stated / Unclear

Indirectness of population	No indirectness
Interventions	(n=101) Intervention 1: Intensive therapy. Intensive therapy. Duration 7 days. Concurrent medication/care: Standard care. Indirectness: No indirectness Further details: 1. Time to treatment (within 6 hours vs >6 hours): Within 6 hours (n=101) Intervention 2: Conservative therapy. Conservative care. Duration 7 days. Concurrent medication/care: Standard care. Indirectness: No indirectness Further details: 1. Time to treatment (within 6 hours vs >6 hours): Not applicable
Funding	Academic or government funding (The National Key Technology R&D Program for the 12th Five-year Plan of P.R. China)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTENSIVE THERAPY versus CONSERVATIVE THERAPY

Protocol outcome 1: Mortality at 90 days
- Actual outcome: Mortality at 90 days; Group 1: 13/96, Group 2: 18/99
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Systolic blood pressure mmHg, mean (SD), intensive 181 (16), conservative 183 (19), diastolic blood pressure mmHg, mean (SD) intensive 103 (12), conservative 104 (13), Prior hypertension intensive 51% conservative 59%; Group 1 Number missing: 5, Reason: Not stated; Group 2 Number missing: 2, Reason: Not stated

Protocol outcome 2: EQ-5D utility index score at 90 days
- Actual outcome: EQ-5D utility score at 90 days; Group 1: mean 0.54 (SD 0.23); n=96, Group 2: mean 0.56 (SD 0.23); n=99
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Systolic blood pressure mmHg, mean (SD), intensive 181 (16), conservative 183 (19), diastolic blood pressure mmHg, mean (SD) intensive 103 (12), conservative 104 (13), Prior hypertension intensive 51% conservative 59%; Group 1 Number missing: 5, Reason: Not stated; Group 2 Number missing: 2, Reason: Not stated

Protocol outcomes not reported by the study	Mortality at 24 hours; mRS score at 90 days; Recurrent and /or extended stroke at 24 hours; Recurrent and /or extended stroke at 90 days; Adverse events at 24 hours; Adverse events at 90 days; Quality of life at 90 days; Quality of life at 24 hours; EQ-5D visual analogue scale at 90 days; mRS score at 90 days; mRS score 0-2 vs 3-6 at 90 days; mRS

score 0-3 vs 4-6 at 90 days; Renal failure at 90 days; Myocardial infarction at 90 days; Neurological decline at 24 hours; Neurological decline at 90 days; Barthel index at 90 days; mRS score at 1 year; EQ-5D at 90 days