**Table 1.** Disclosures of the working group members

| Author | Discipline and affiliation | Intellectual and financial disclosures |
|---|---|---|
| Else Charlotte Sandset | Neurologist, Stroke Unit, Department of Neurology, Oslo University Hospital, Oslo, Norway<br><br>Senior Researcher,The Norwegian Air Ambulance, Oslo, Norway | Intellectual disclosures:<br><br>Trial Manager of the SCAST trial<br>International Advisory Board of the RIGHT2 trial<br>International Advisory Board of the INTERACT4 trial<br>Secretary General of the European Stroke Organisation<br>Financial disclosures: None |
| Craig S. Anderson | Professor of Neurology<br>The George Institute for Global Health, Faculty of Medicine, University of New South Wales, Sydney, NSW, Australia<br>Executive Director<br>The George Institute China at Peking University Health Science Center, Beijing, PR China | Intellectual disclosures:<br><br>Principle Investigator for INTERACT, ENCHANTED and TRIDENT studies<br><br>Financial disclosures: Research grants from Takeda China |
| Philip M. Bath, | Stroke Physician, Stroke Trials Unit, Division Clinical Neuroscience, University of Nottingham, Nottingham NG7 2UH UK | Intellectual disclosures:<br><br>CI ENOS, RIGHT, RIGHT-2<br><br>Member Trial Steering Committees/Advisory Committees: SCAST, INTERACT-1/2, ENCHANTED<br><br>Financial disclosures: |

| | | |
|---|---|---|
| | | Member advisory Boards - DiaMedica, Moleac, Phagenesis (none relevant to this topic) |
| Hanne Christensen | Professor of Neurology and Consultant Neurologist<br>Department of Neurology, Bispebjerg Hospital & University of Copenhagen, Copenhagen, Denmark. | Intellectual disclosures: Member Trial Steering Committee ENOS<br>Financial disclosures:<br>Speaker honoraria: Bayer. Daiichi-Sankyo, BMS og Boerhinger.<br>National Coordinating Investigator: Portola and Bayer |
| Urs Fischer | Prof. for Acute Neurology and Stroke; Co-Chairman Stroke Centre Bern<br>Deputy-Director Clinical Trial Unit Bern<br>University of Bern<br>Switzerland | Intellectual disclosures:<br>Steering Committee Member of the TRIDENT trial<br>Financial disclosures:<br>Consultant for Medtronic, Stryker and CSL Behring (none relevant for this topic) |
| Dariusz Gąsecki | Neurologist, Stroke Unit,<br>Department of Adult Neurology, Medical Univeristy of Gdańsk, Gdańsk, Poland | Intellectual disclosures:<br>Trial Participant of the SCAST trial<br>Past-President of the European Society of Hypertension Working Group on Hypertension and the Brain<br>Financial disclosures:none |
| Avtar Lal | Guidelines Methodologist, European Stroke Organisation, Basel, Switzerland | Intellectual disclosures: None<br>Financial disclosures: None |

| | | |
|---|---|---|
| Lisa S. Manning | Stroke Physician, Department of Stroke Medicine, University Hospitals of Leicester NHS Trust, UK | Intellectual disclosures: None<br><br>Financial disclosures: None |
| Simona Sacco | Neurologist Department of Biotechnological and Applied Clinical Sciences andBiotechnology, University of L'Aquila, Italy | Intellectual disclosures: Co-chair of the Guideline Board of the European Stroke Organization<br><br>Financial disclosures: Personal fees as speaker or advisor: Abbott, Allergan, AstraZeneca, Eli Lilly, Novartis, Teva. Research grants: Allergan, Novartis.<br><br>Non-financial support: Abbott, Allergan, Bayer, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly, Medtronic, Novartis, Pfizer, Starmed, Teva. Fees for CME/education: Medscape |
| Thorsten Steiner | Neurologist, Neurointensivist, ead, Department of Neurology, Frankfurt Hoechst Hospital, Frankfurt, Germany<br><br>Scientific co-worker, lecturer, Department of Neurology, Heidelberg University Hospital, Heidelberg, Germany | Intellectual disclosures:<br><br>ATACH-2,<br><br>Financial disclosures:<br><br>Personal fees: Bayer, Boehringer, BMS-Pfizer, Daiichy Sankyo, Alexion |
| Georgios Tsivgoulis | Professor of Neurology, 'Attikon' UniversityHospital, Second Department of Neurology,School of Medicine, National and KapodistrianUniversity of Athens, Athens, Greece&Department of | Intellectual disclosures:<br><br>- Section Editor: "Stroke" journal<br><br>- Associate Editor: "Therapeutics advances in Neurological Disorders" journal |

| | | |
|---|---|---|
| | Neurology, University of Tennessee Health Science Center, Memphis, Tennessee, USA | -Chair of European Stroke Organization Industry Roundtable<br><br>Financial disclosures:<br><br>- Participation in advisory meetings & satellite symposia for Boehringer-Ingelheim; Novartis, Sanofi, Biogen, Genesis Pharma, Teva, Merck-Serono, Bayer, Daichii-Sankyo, Allergan, Specifar, Actavis, Shire, Medtronic, CSL Behring, Abbvie, Abbott, Takeda, Biomarin.<br><br>- Unrestricted research grants from Novartis, Genesis Pharma, Teva, Shire, Merck-Serono, Medtronic, Boehringer-Ingelheim, Allergan, Abbott |

**PICO 1: In patients with suspected acute stroke, does pre-hospital blood pressure lowering with any vasodepressor drug compared to no drug improve outcome?**

**Figure 1** Effect of pre-hospital blood pressure lowering by any vasopressor drug compared to no drug on mortality at three months following symptom onset

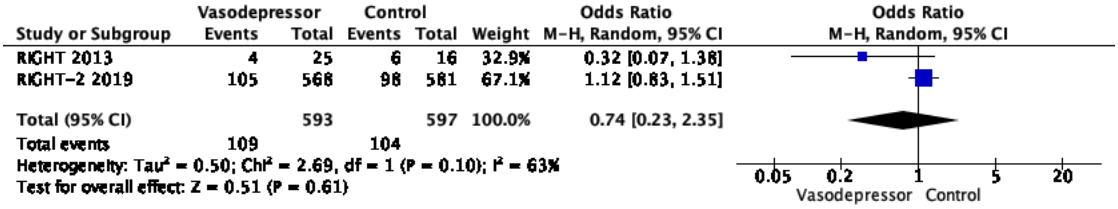



**Figure 2** Effect of pre-hospital blood pressure lowering by any vasopressor drug compared to no drug on good functional outcome (mRS-scores 0-2) at three months following symptom onset

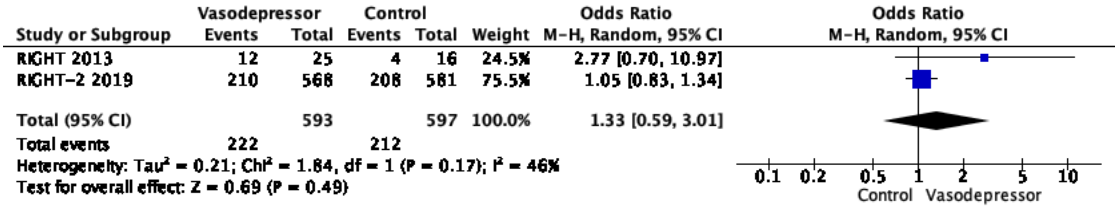


**Table 2**.Evidence profile table for pre-hospital blood pressure lowering with any vasodepressor drug compared to no drug in patients suspected stroke

| Certainty assessment | | | | | | | № of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | PICO 1a: Pre-hospital blood pressure lowering | control | Relative (95% CI) | Absolute (95% CI) | | |
| **3months mortality** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious | not serious | very serious [a] | publication bias strongly suspected [b] | 109/593 (18.4%) | 104/597 (17.4%) | **OR 0.74** (0.23 to 2.35) | **39 fewer per 1,000** (from 128 fewer to 157 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **3 months good functional outcome (mRS scores 0-2)** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious | not serious | very serious [a] | publication bias strongly suspected [b] | 222/593 (37.4%) | 212/597 (35.5%) | **OR 1.33** (0.59 to 3.01) | **68 more per 1,000** (from 110 fewer to 269 more) | ⨁◯◯◯ VERY LOW | CRITICAL |

**CI:** Confidence interval; **OR:** Odds ratio

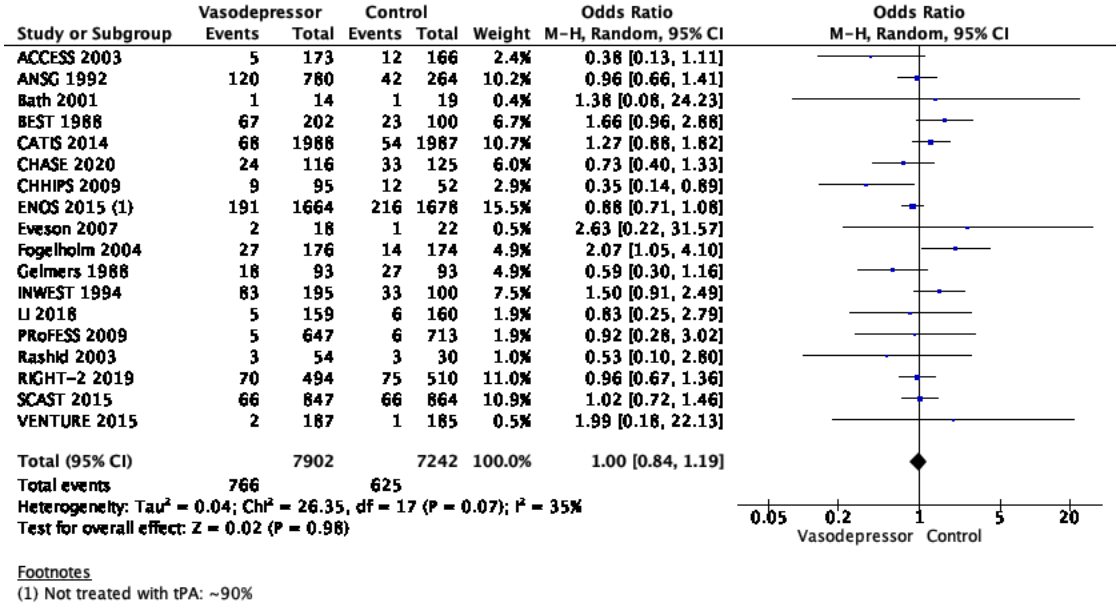
**Explanations**

a. Very wide confidence intervals

b. Two studies reported this outcome

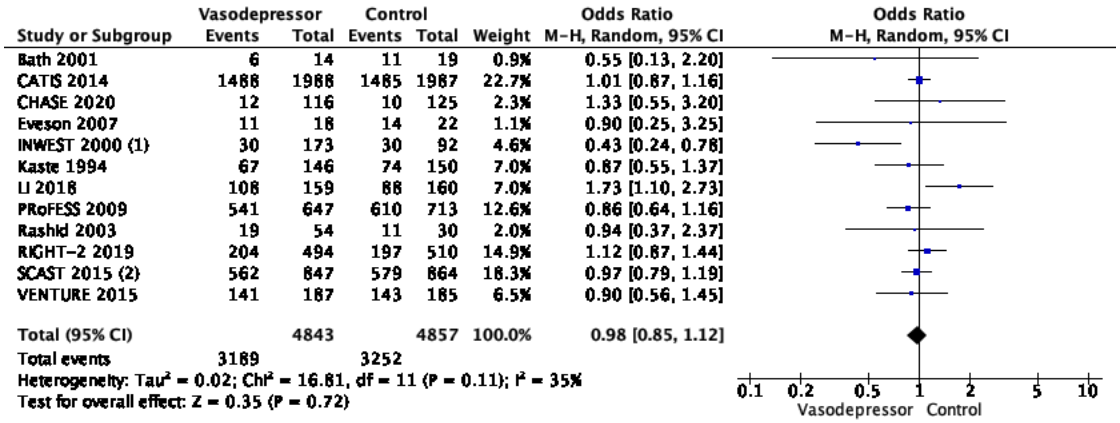
**PICO 2: In hospitalised patients with acute ischaemic stroke not treated with reperfusion therapies (intravenous thrombolysis or mechanical thrombectomy), does blood pressure lowering with any vasodepressor drug compared to no drug improve outcome?**

**Figure 3:** The effect of blood pressure lowering with any vasodepressor drug compared with no drug on mortality at three to six months following symptom onset in patients with acute ischaemic stroke not treated with for reperfusion therapies




Footnotes
(1) Not treated with tPA: ~90%

**Figure 4** The effect of blood pressure lowering with any vasodepressor drug compared with no drug on good functional outcome (mRS scores 0-2) at three to six months following symptom onset in patients with acute ischaemic stroke not treated with reperfusion therapies




Footnotes
(1) Barthel index score of <60 at 21 days
(2) Not treated with tPA: ~85%

**Table 3.** Evidence profile table for blood pressure lowering with any vasodepressor drug compared to no drug in patients with acute ischaemic stroke not treated with reperfusion therapies

| Certainty assessment | | | | | | | № of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | PICO 3 Blood pressure lowering with Vasodepressor | Control | Relative (95% CI) | Absolute (95% CI) | | |
| **3-6 months mortality** | | | | | | | | | | | | |
| 18 | randomised trials | not serious | not serious | not serious | serious [a] | none | 766/7902 (9.7%) | 625/7242 (8.6%) | **OR 1.00** (0.84 to 1.19) | **0 fewer per 1,000** (from 13 fewer to 15 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **3 - 6 months good functional outcome (mRS scores 0-2)** | | | | | | | | | | | | |
| 12 | randomised trials | not serious | not serious | not serious | serious [a] | none | 3189/4843 (65.8%) | 3252/4857 (67.0%) | **OR 0.98** (0.85 to 1.12) | **4 fewer per 1,000** (from 37 fewer to 25 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |

**CI:** Confidence interval; **OR:** Odds ratio;

## Explanations

a. Wide confidence intervals

**PICO 3: In hospitalised patients with acute ischaemic stroke and undergoing intravenous thrombolysis (with or without mechanical thrombectomy), does blood lowering therapies compared to control improve outcome?**

Table 4. Evidence profile table for safety and efficacy of intensive systolic blood pressure lowering (target 130–140 mmHg within 1 hour) compared to guideline-recommended systolic blood pressure levels (<180mmHg) over 72 hours following symptom onset in acute ischaemic stroke patients receiving intravenous thrombolysis

| Certainty assessment | | | | | | | № of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Experimental arm | Control arm | Relative (95% CI) | Absolute (95% CI) | | |
| **3 months mortality** | | | | | | | | | | | | |
| 1 | randomised trial | Unclear | N/A | not serious | very serious | N/A | 102/1081 (9.4%) | 88/1115 (7.9%) | **OR 1.22** (0.90 to 1.64) | **16 more per 1,000** (from 7 fewer to 44 more) | ⊕◯◯◯ VERY LOW | CRITICAL |
| **3 months good functional outcome (mRS scores 0-2)** | | | | | | | | | | | | |
| 1 | randomised trial | Unclear | N/A | not serious | very serious | N/A | 712/1072 (66.4%) | 734/1108 (66.4%) | **OR 1.00** (0.83 to 1.20) | **0 fewer per 1,000** (from 38 fewer to 42 more) | ⊕◯◯◯ VERY LOW | CRITICAL |
| **3 months improved mRS scores (shift analysis)** | | | | | | | | | | | | |
| 1 | randomised trial | Unclear | N/A | not serious | very serious | N/A | - | - | **common OR 1.01** (0.87 to 1.17) | - | ⊕◯◯◯ VERY LOW | CRITICAL |

**CI:** Confidence interval; **OR:** Odds ratio;

**PICO 4: In patients with acute ischaemic stroke caused by large vessel occlusion and undergoing mechanical thrombectomy (with or without intravenous thrombolysis), does blood pressure lowering with any vasodepressor drug compared to no drug improve outcome?**

Table 5. Randomized controlled clinical trials evaluating different blood pressures targets **following mechanical thrombectomy** in acute ischaemic stroke patients with large vessel occlusion receiving endovascular therapies.

| Study | Location | N patients | Experimental targets | Standard target | Randomization | Period of intervention | Termination date |
|---|---|---|---|---|---|---|---|
| BEST-II (**109**) | USA (Cincinnati & Nashville) | 120 | **140-160 mmHg*** **110-140 mmHg**** | 160-180mmHg | N/A | 24 hours | March 2023 |
| DETECT(**111**) | Canada (Hamilton) | 30 | <140 mmHg | <180mmHg | 1 hour | 48 hours | June 2022 |
| ENCHANTED2(**110**) | International | 2236 | <120 mmHg | 140-180mmHg | 3 hours | 72 hours | February, 2023 |
| **OPTIMAL BP** (**112**) | **Korea (multicenter)** | **644** | **<140 mmHg** | **<180mmHg** | **0.5-1 hour** | **24 hours** | **December 2023** |
| BP-TARGET (**113,114**) | France (multicenter) | 320 | <130 mmHg | <185mmHg | 1 hour | 24-36 hours | Completed<br>No differences in clinical or imaging endpoints between the two randomization arms |

*** first active comparator arm of BEST-II; ** second active comparator arm of BEST-II**

**Table 6.** Evidence profile for reducing systolic blood pressure <130mmHg in anterior circulation large vessel occlusion during the first 24 hours following successful mechanical thrombectomy. The following outcomes were evaluated: (i) 3-moth functional improvement (defined as 1-point decrease across all mRS-scores); (ii) 3-month mortality; (iii) any Intracranial Hemorrhage (ICH)

| Certainty assessment | | | | | | | № of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Experimental arm | Control arm | Relative (95% CI) | Absolute (95% CI) | | |
| **3 months mortality** | | | | | | | | | | | | |
| 1 | randomised trial | Unclear | N/A | Not serious | serious | N/A | 29/152 (19.1%) | 21/153 (13.7%) | **OR 1.48** (0.80 to 2.74) | **53 more per 1,000** (from 24 fewer to 166 more) | ⊕◯◯◯ VERY LOW | CRITICAL |
| **3 months good functional outcome (mRS scores 0-2)** | | | | | | | | | | | | |
| 1 | randomised trial | Unclear | N/A | Not serious | serious | N/A | 67/152 (44.1%) | 69/153 (45.1%) | **OR 0.96** (0.61 to 1.51) | **10 fewer per 1,000** (from 117 fewer to 103 more) | ⊕◯◯◯ VERY LOW- | CRITICAL |
| **3 months improved mRS scores (shift analysis)** | | | | | | | | | | | | |
| 1 | randomised trial | Unclear | N/A | Not serious | serious | N/A | - | - | **common OR 0.86** (0.57 to 1.28) | - | ⊕◯◯◯ VERY LOW | CRITICAL |
| **Any ICH** | | | | | | | | | | | | |

| Certainty assessment | | | | | | | № of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Experimental arm | Control arm | Relative (95% CI) | Absolute (95% CI) | | |
| 1 | randomised trial | Unclear | N/A | Not serious | serious | none | 65/154 (42.2%) | 68/157 (43.3%) | **OR 0.96** (0.60 to 1.51) | **10 fewer per 1,000** (from 115 fewer to 101 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |

**CI:** Confidence interval;**OR:** Odds ratio

**PICO 5: In patients with acute ischaemic stroke not treated with reperfusion therapies (intravenous thrombolysis or mechanical thrombectomy) and with clinical deterioration, does induced hypertension by any vasopressor drug compared to no drug improve outcome?**

**Table 7** Evidence profile for the safety and efficacy of blood pressure elevation using any vasopressor drug compared to no vasopressor drug in patients acute ischaemic stroke and clinical deterioration not treated with reperfusion therapies

| Certainty assessment | | | | | | | № of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | blood pressure elevation with vasopressor | Control | Relative (95% CI) | Absolute (95% CI) | | |
| **3 months mortality** | | | | | | | | | | | | |
| 1 | randomised trial | not serious | not serious | not serious | very serious [a] | publication bias strongly suspected [b] | 1/76 (1.3%) | 0/77 (0.0%) | **OR 3.08** (0.12 to 76.79) | **0 fewer per 1,000** (from 0 fewer to 0 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **3 months good functional outcome (mRS scores 0-2)** | | | | | | | | | | | | |
| 1 | randomised trial | not serious | not serious | not serious | serious [c] | publication bias strongly suspected [b] | 57/76 (75.0%) | 49/77 (63.6%) | **OR 1.71** (0.85 to 3.44) | **113 more per 1,000** (from 38 fewer to 221 more) | ⨁⨁◯◯ LOW | CRITICAL |

**CI:** Confidence interval; **OR:** Odds ratio

**Explanations**

a. Very wide confidence intervals b. One study reported this outcome

**PICO 6: In patients with acute ischaemic stroke, does continuing versus temporarily stopping previous oral blood pressure lowering therapy improve outcome?**

**Figure 5** The effect of continuing versus temporarily stopping previous blood pressure lowering therapy on mortality at three to six months following symptom onset in patients with acute ischemic stroke

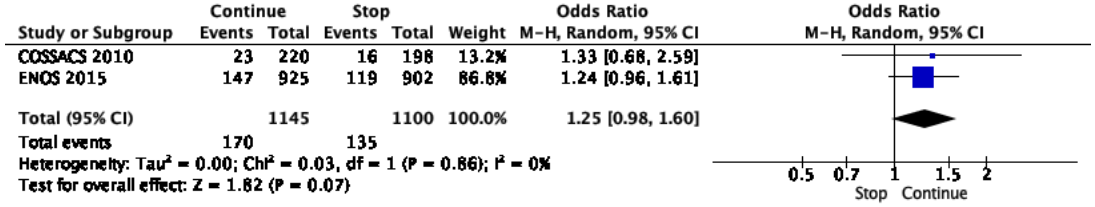



**Figure 6** The effect of continuing versus temporarily stopping previous blood pressure lowering therapy on good functional outcome (defined as mRS scores 0-2) at three to six months following symptom onset in patients with acute ischemic stroke

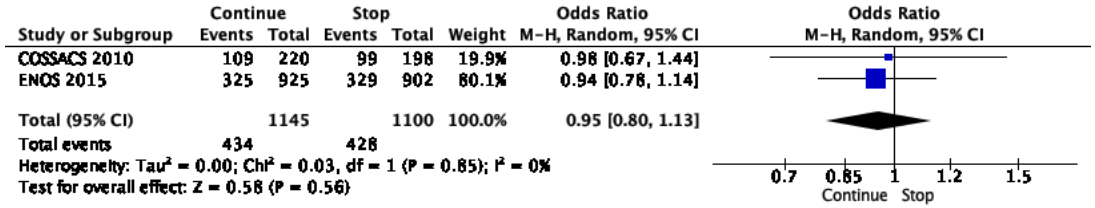


**Table 8** Evidence profile table for continuing versus temporarily stopping previous blood-pressure lowering therapy in patients with acute ischemic stroke

| Certainty assessment | | | | | | | № of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Continuing | Stopping previous antihypertensive therapy | Relative (95% CI) | Absolute (95% CI) | | |
| **3-6 months mortality** | | | | | | | | | | | | |
| 2 | randomised trials * | not serious | not serious | not serious | serious [a] | publication bias strongly suspected [b] | 170/1145 (14.8%) | 135/1100 (12.3%) | **OR 1.25** (0.98 to 1.60) | **26 more per 1,000** (from 2 fewer to 60 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **3-6 months good functional outcome (mRS scores 0-2)** | | | | | | | | | | | | |
| 2 | randomised trials * | not serious | not serious | not serious | serious [a] | publication bias strongly suspected [b] | 434/1145 (37.9%) | 428/1100 (38.9%) | **OR 0.95** (0.80 to 1.13) | **12 fewer per 1,000** (from 52 fewer to 29 more) | ⨁⨁◯◯ LOW | CRITICAL |

**CI:** Confidence interval; **OR:** Odds ratio

**Explanations**

a. Wide confidence intervals b. Two studies reported this outcome

**PICO 7: In patients with acute intracerebral haemorrhage, does intensive blood pressure lowering with any vasodepressor drug compared to control improve outcome?**

**Figure 7** The effect of intensive blood pressure lowering with any vasodepressor drug compared to control on mortality at three to six months following symptom onset in patients with acute intracerebral haemorrhage

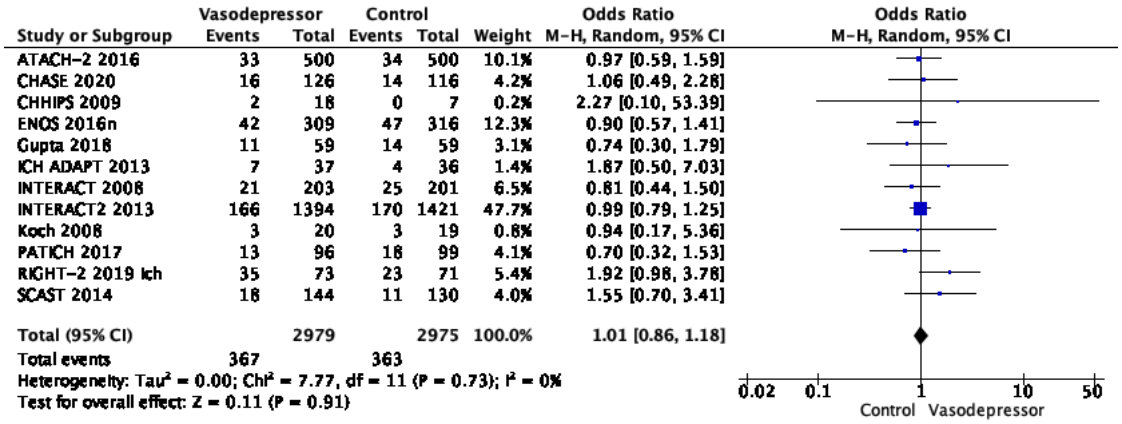



**Figure 8** The effect of intensive blood pressure lowering with any vasodepressor drug compared to control on mortality at three to six months following symptom onset in in subgroups stratified by time to treatment (trials enrolling patients within **6 hours**, trials enrolling patients within 24 hours after exclusion of trials enrolling patients within 6 hours, and trials enrolling patients within 72 hours after excluding trials enrolling within 24 hours).

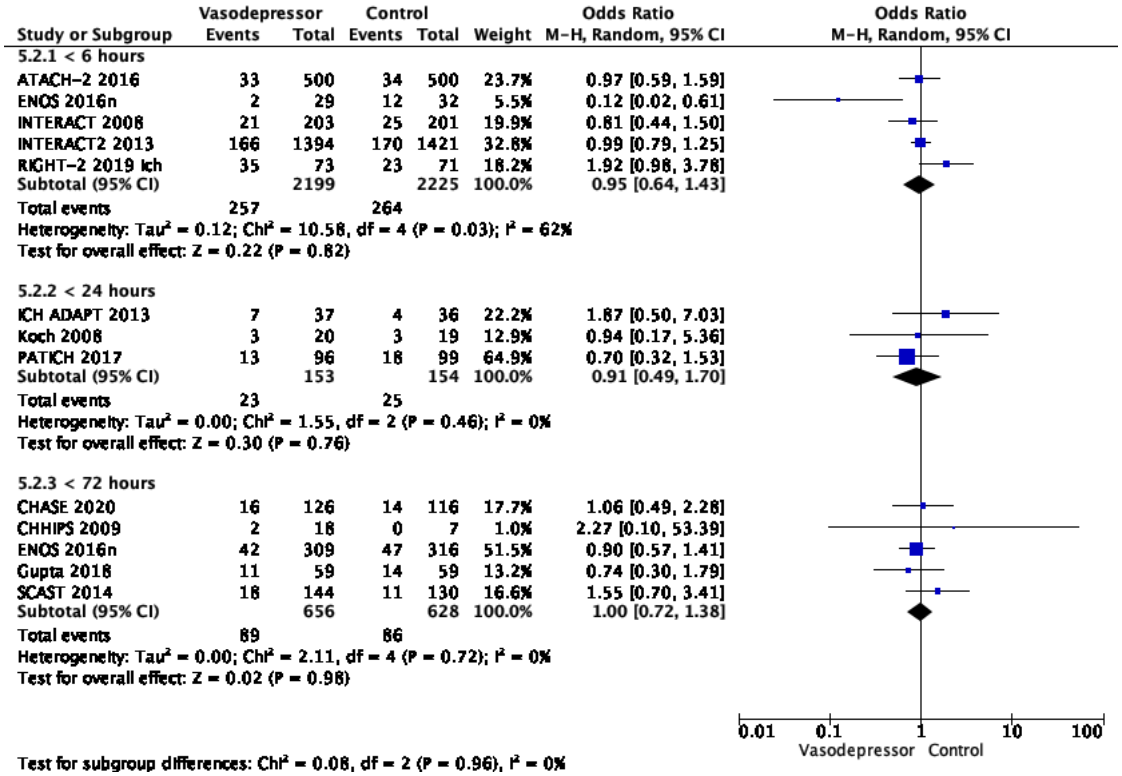


**Figure 9** The effect of intensive blood pressure lowering with any vasodepressor drug compared to control on good functional outcome (defined as mRS scores 0-2 at three to six months following symptom onset) in patients with acute intracerebral haemorrhage

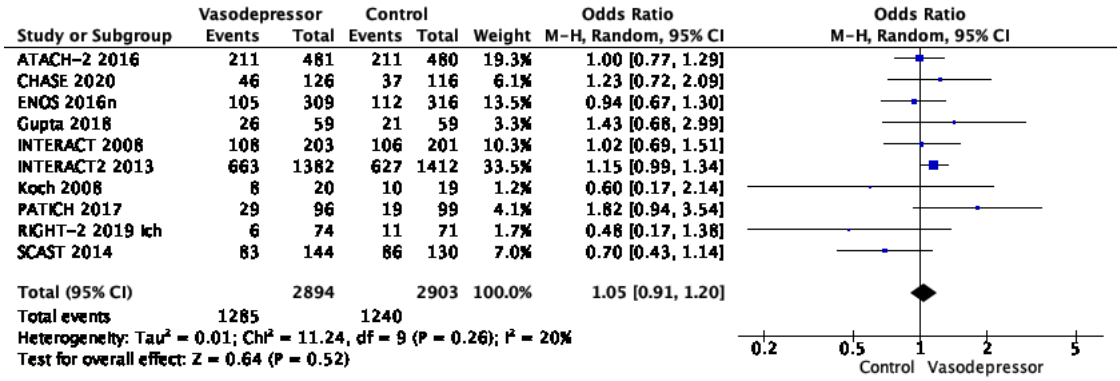



**Figure 10** The effect of intensive blood pressure lowering with any vasodepressor drug compared to control on good functional outcome (defined as mRS scores 0-2 at three to six months following symptom onset) in subgroups stratified by time to treatment (trials enrolling patients within **6 hours**, trials enrolling patients within 24 hours after exclusion of trials enrolling patients within 6 hours, and trials enrolling patients within 72 hours after excluding trials enrolling within 24 hours).

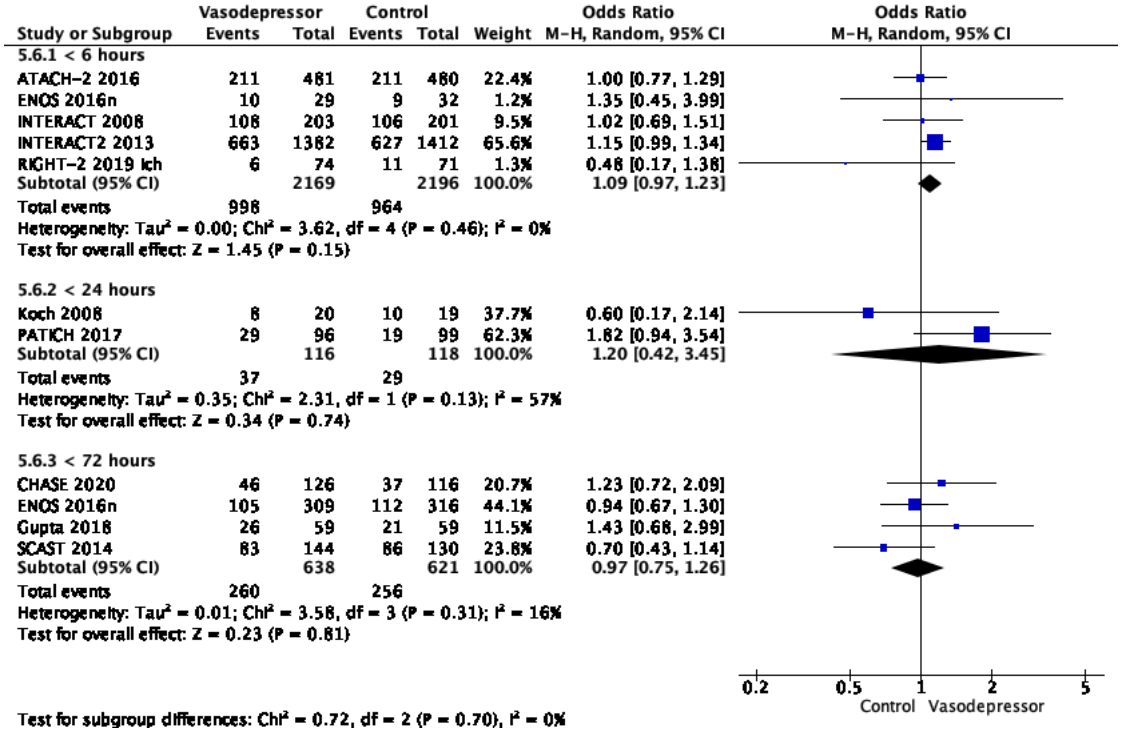


**Figure 11** The effect of intensive blood pressure lowering with any vasodepressor drug compared to control on haematoma expansion

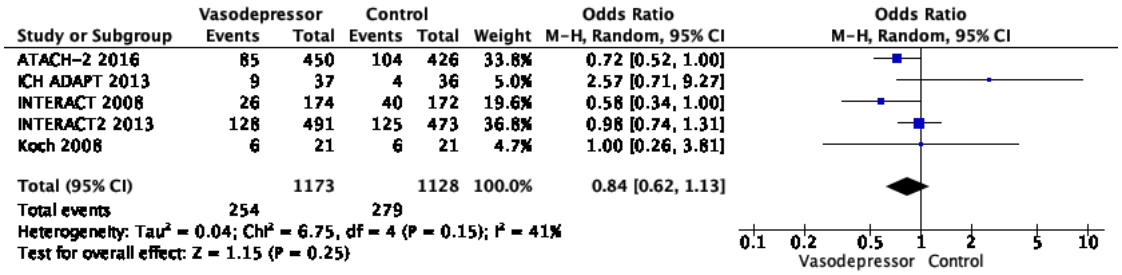



**Figure 12** The effect of intensive blood pressure lowering with any vasodepressor drug compared to control on haematoma expansion in subgroups stratified by time to treatment (trials enrolling patients within 6 hours, trials enrolling patients within 24 hours after exclusion of trials enrolling patients within 6 hours, and trials enrolling patients within 72 hours after excluding trials enrolling within 24 hours).

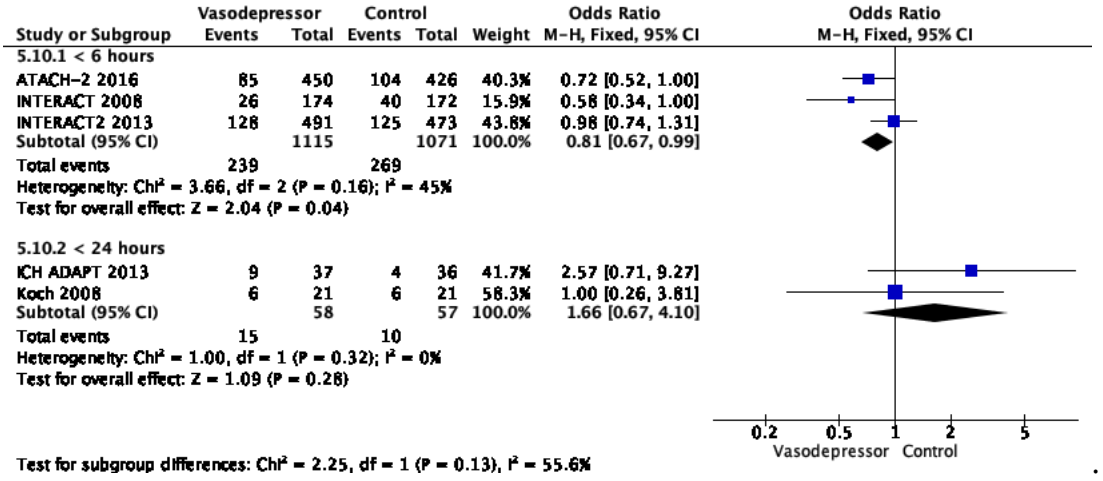


**Table 9** Evidence profile table for intensive blood pressure lowering with any vasodepressor drug in patients with acute intracerebral haemorrhage.

:

| Certainty assessment | | | | | | | № of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Blood pressure lowering with Vasodepressor | Control | Relative (95% CI) | Absolute (95% CI) | | |
| **3-6 months mortality** | | | | | | | | | | | | |
| 12 | randomised trials | not serious | not serious | not serious | serious [a] | publication bias strongly suspected [b] | 367/2979 (12.3%) | 363/2975 (12.2%) | **OR 1.01** (0.86 to 1.18) | **1 more per 1,000** (from 15 fewer to 19 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **3-6 months mortality< 6 hours** | | | | | | | | | | | | |
| 5 | randomised trials | not serious | serious [c] | not serious | serious [a] | publication bias strongly suspected [d] | 257/2199 (11.7%) | 264/2225 (11.9%) | **OR 0.95** (0.64 to 1.43) | **5 fewer per 1,000** (from 39 fewer to 43 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **3-6 months mortality ≤ 24 hours** | | | | | | | | | | | | |
| 3 | randomised trials | not serious | not serious | not serious | serious [a] | publication bias strongly suspected [d] | 23/153 (15.0%) | 25/154 (16.2%) | **OR 0.91** (0.49 to 1.70) | **12 fewer per 1,000** (from 76 fewer to 85 more) | ⨁⨁◯◯ LOW | CRITICAL |

| Certainty assessment | | | | | | | № of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Blood pressure lowering with Vasodepressor | Control | Relative (95% CI) | Absolute (95% CI) | | |

## 3-6 months mortality< 72 hours

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 5 | randomised trials | not serious | not serious | not serious | serious [a] | publication bias strongly suspected [d] | 89/656 (13.6%) | 86/628 (13.7%) | **OR 1.00** (0.72 to 1.38) | **0 fewer per 1,000** (from 34 fewer to 43 more) | ⨁⨁◯◯ LOW | CRITICAL |

## 3-6 months good functional outcome (mRS scores 0-2)

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 10 | randomised trials | not serious | not serious | not serious | serious [a] | none | 1285/2894 (44.4%) | 1240/2903 (42.7%) | **OR 1.05** (0.91 to 1.20) | **12 more per 1,000** (from 23 fewer to 45 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |

## 3-6 months good functional outcome (mRS scores 0-2)- < 6 hours

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 5 | randomised trials | not serious | not serious | not serious | serious [a] | publication bias strongly suspected [d] | 998/2169 (46.0%) | 964/2196 (43.9%) | **OR 1.09** (0.97 to 1.23) | **21 more per 1,000** (from 7 fewer to 51 more) | ⨁⨁◯◯ LOW | CRITICAL |

## 3-6 months good functional outcome (mRS scores 0-2)- ≤ 24 hours

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2 | randomised trials | not serious | not serious | not serious | very serious [e] | publication bias strongly suspected [d] | 37/116 (31.9%) | 29/118 (24.6%) | **OR 1.20** (0.42 to 3.45) | **35 more per 1,000** (from 125 fewer to 283 more) | ⨁◯◯◯ VERY LOW | CRITICAL |

| Certainty assessment | | | | | | | № of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Blood pressure lowering with Vasodepressor | Control | Relative (95% CI) | Absolute (95% CI) | | |
| **3-6 months good functional outcome (mRS scores 0-2)- <72 hours** | | | | | | | | | | | | |
| 4 | randomised trials | not serious | not serious | not serious | serious [a] | publication bias strongly suspected [d] | 260/638 (40.8%) | 256/621 (41.2%) | **OR 0.97** (0.75 to 1.26) | **7 fewer per 1,000** (from 68 fewer to 57 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **Haematoma expansion** | | | | | | | | | | | | |
| 5 | randomised trials | not serious | not serious | not serious | serious [a] | **publication bias strongly suspected** [d] | 254/1173 (21.7%) | 279/1128 (24.7%) | **OR 0.84** (0.62 to 1.13) | **31 fewer per 1,000** (from 78 fewer to 23 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Haematoma expansion - < 6 hours** | | | | | | | | | | | | |
| 3 | randomised trials | not serious | not serious | not serious | not serious | publication bias strongly suspected [d] | 239/1115 (21.4%) | 269/1071 (25.1%) | **OR 0.81** (0.67 to 0.99) | **38 fewer per 1,000** (from 68 fewer to 2 fewer) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Hematoma expansion - ≤ 24 hours** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious | not serious | very serious [e] | publication bias strongly suspected [d] | 15/58 (25.9%) | 10/57 (17.5%) | **OR 1.66** (0.67 to 4.10) | **86 more per 1,000** (from 51 fewer to 290 more) | ⨁◯◯◯ VERY LOW | CRITICAL |

| Certainty assessment | | | | | | | № of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Blood pressure lowering with Vasodepressor | Control | Relative (95% CI) | Absolute (95% CI) | | |
| **Acute Renal injury** | | | | | | | | | | | | |
| 4 | randomised trials | not serious | not serious | not serious | very serious [e] | publication bias strongly suspected [d] | 6/947 (0.6%) | 7/932 (0.8%) | **OR 0.87** (0.28 to 2.74) | **1 fewer per 1,000** (from 5 fewer to 13 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |

**CI:** Confidence interval; **OR:** Odds ratio

## Explanations

a. Wide confidence intervals

b. Five or less studies reporting this outcome

c. Significant heterogeneity, I2 $\geq$ 62%

d. Very wide confidence intervals

**PICO 8: In patients with acute intracerebral haemorrhage, does continuing versus temporarily stopping previous oral antihypertensive therapy improve outcome?**

**Figure 13** The effect of continuing versus temporarily stopping previous blood pressure lowering therapy on mortality at three to six months following symptom onset in patients with acute intracerebral hemorrhage

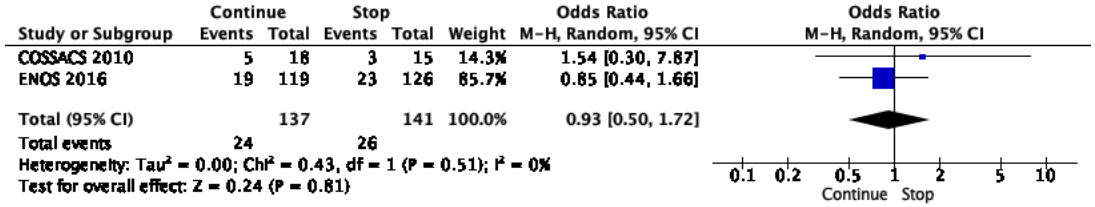



**Figure 14** The effect of continuing versus temporarily stopping previous blood pressure lowering therapy on good functional outcome (defined as mRS scores 0-2) at three to six months following symptom onset in patients with acute intracerebral hemorrhage

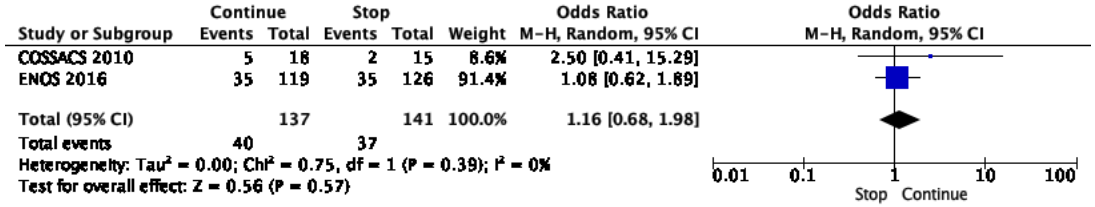


**Table 10.** Evidence profile table for continuing versus temporarily stopping previous blood-pressure lowering therapy in patients with acute intracerebral hemorrhage

| Certainty assessment | | | | | | | № of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Continuing | Stopping previous antihypertensive therapy | Relative (95% CI) | Absolute (95% CI) | | |
| **3-6 months mortality** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious | not serious | serious [a] | publication bias strongly suspected [b] | 24/137 (17.5%) | 26/141 (18.4%) | **OR 0.93** (0.50 to 1.72) | **11 fewer per 1,000** (from 83 fewer to 96 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **3-6 month good functional outcome (mRS scores 0-2)** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious | not serious | serious [a] | publication bias strongly suspected [b] | 40/137 (29.2%) | 37/141 (26.2%) | **OR 1.16** (0.68 to 1.98) | **30 more per 1,000** (from 68 fewer to 151 more) | ⨁⨁◯◯ LOW | CRITICAL |

**CI:** Confidence interval; **OR:** Odds ratio

**Explanations**

a. Wide confidence intervals b. Two studies reported this outcome

**Table 11**. Evidence table for ESO Guidelines on Blood Pressure Management in Acute Ischaemic Stroke and Intracerebral Haemorrhage

| PICO Question | Recommendations | Expert consensus statement |
|---|---|---|
| **PICO 1: In patients with suspected acute stroke, does pre-hospital blood pressure lowering with any vasodepressor drug compared to no drug improve outcome?** | In patients with suspected stroke we suggest against routine blood pressure lowering in the pre-hospital setting.<br>Quality of evidence: **Moderate**⨁⨁⨁<br>Strength of recommendation: Weak ↓? | Due to the potential harm in patients with intracerebral haemorrhage prehospital treatment with glyceryl trinitrate should be avoided. Vote 9 of 10. |
| **PICO 2: In hospitalised patients with acute ischaemic stroke not treated with reperfusion therapies (intravenous thrombolysis or mechanical thrombectomy), does blood pressure lowering with any vasodepressor drug compared to no drug improve outcome?** | In hospitalised patients with acute ischaemic stroke and blood pressure<220/110 mmHg not treated with intravenous thrombolysis or mechanical thrombectomy, we suggest against the routine use of blood pressure lowering agents **at least in first 24 hours following symptom onset**, unless this is necessary for a specific comorbid condition.<br>Quality of evidence: **Moderate**⨁⨁⨁<br>Strength of recommendation: Weak ↓? | In patients with acute ischaemic stroke not treated with intravenous thrombolysis or mechanical thrombectomy and blood pressure >220/120 mmHg, careful blood pressure reduction (<15% systolic blood reduction in 24 hours) is reasonable and likely to be safe. **No specific blood pressure lowering agent can be recommended.** Vote 10 of 10. |
| **PICO 3: In hospitalised patients with acute ischaemic stroke and undergoing intravenous thrombolysis (with or without mechanical thrombectomy), does blood lowering therapies compared to control improve outcome?** | In patients with acute ischaemic stroke undergoing treatment with intravenous thrombolysis (with or without mechanical thrombectomy) we suggest maintaining blood pressure below 185/110mmHg before bolus and below 180/105mmHg after bolus, and for 24 hours after alteplase infusion. No specific blood pressure-lowering agent can be recommended.<br>Quality of evidence: **Very low**⨁<br>Strength of recommendation: Weak ↑?<br>In patients with acute ischaemic stroke undergoing treatment with intravenous thrombolysis (with or without mechanical thrombectomy) we suggest against lowering systolic blood pressure to a target of 130-140mmHg | |

| | | |
|---|---|---|
| | compared to <180mmHg during the first 72 hours following of symptom onset.<br>Quality of evidence: **Moderate**⊕⊕⊕<br>Strength of recommendation: Weak ↓? | |
| **PICO 4: In patients with acute ischaemic stroke caused by large vessel occlusion and undergoing mechanical thrombectomy (with or without intravenous thrombolysis), does blood pressure lowering with any vasodepressor drug compared to no drug improve outcome?** | In patients with acute ischaemic stroke **due to large vessel occlusion** undergoing mechanical thrombectomy (with or without intravenous thrombolysis) we suggest keeping blood pressure below 180/105mmHg during, and 24 hours after, mechanical thrombectomy. No specific blood pressure-lowering agent can be recommended.<br>Quality of evidence: **Very low**⊕<br>Strength of recommendation: Weak ↑?<br><br>In patients with acute ischaemic stroke due to large vessel occlusion we suggest against actively reducing systolic blood pressure <130mmHg during the first 24 hours following successful mechanical thrombectomy<br>Quality of evidence: **Moderate**⊕⊕⊕<br>Strength of recommendation: Weak ↓?<br><br>**In patients with acute ischaemic stroke due to large vessel occlusion undergoing** treatment with mechanical thrombectomy (with or without intravenous thrombolysis) systolic blood pressure drops should be avoided.<br>Quality of evidence: **Very low**⊕<br>Strength of recommendation: Strong ↓↓ | In patients with acute ischaemic stroke due to large vessel occlusion who achieve successful reperfusion defined as modified Thrombolysis in Cerebral Infarction grade of 3 following mechanical thrombectomy we suggest against induced hypertension. Vote 10 of 10 |
| **PICO 5: In patients with acute ischaemic stroke not treated with reperfusion therapies (intravenous thrombolysis or** | In patients with acute ischaemic stroke not **treated with** reperfusion **therapies** (intravenous thrombolysis or mechanical thrombectomy) who experience clinical | **In patients with acute ischaemic stroke not treated with reperfusion therapies (intravenous thrombolysis or mechanical thrombectomy) and with clinical deterioration where a haemodynamic mechanism is** |

| | | |
|---|---|---|
| **mechanical thrombectomy) and with clinical deterioration, does induced hypertension by any vasopressor drug compared to no drug improve outcome?** | deterioration, we suggest against the routine use of vasopressor drugs to increase blood pressure.<br><br>Quality of evidence: Very low ⊕<br>Strength of recommendation: Weak ↓↓ | **suspected or shown to be directly responsible for the deterioration, we suggest:**<br>• **stopping existing blood pressure lowering therapy,**<br>• **administering intravenous fluids and**<br>• **introducing non-pharmacological procedures to raise blood pressure**<br>**before considering**<br>• **careful use of vasopressor agents to increase blood pressure with close monitoring of blood pressure values**. Vote 10 of 10. |
| **PICO 6: In patients with acute ischaemic stroke, does continuing versus temporarily stopping previous oral blood pressure lowering therapy improve outcome?** | In patients with acute ischaemic stroke, there is continued uncertainty over the benefits and risks (advantages/disadvantages) of continuing versus temporarily stopping previous blood pressure lowering therapy.<br>Quality of evidence: **Moderate**⊕⊕⊕<br>Strength of recommendation: - | In patients with acute ischaemic stroke we suggest stopping previous oral blood pressure lowering therapy in patients with dysphagia until swallowing is restored or a nasogastric tube is in place. Vote 10 of 10 |
| **PICO 7: In patients with acute intracerebral haemorrhage, does intensive blood pressure lowering with any vasodepressor drug compared to control improve outcome?** | **In patients with acute (<24 hours) intracerebral haemorrhage there is continued uncertainty over the benefits and risks (advantages/disadvantages) of intensive blood pressure lowering on functional outcome.**<br>Quality of evidence: **Moderate**⊕⊕⊕<br>Strength of recommendation: -<br><br>In patients with hyperacute (<6 hours) intracerebral haemorrhage, we suggest lowering blood pressure to below 140 mmHg (and to keep it above 110 mmHg) to reduce haematoma expansion. | In patients with acute intracerebral haemorrhage, we suggest initiating antihypertensive treatment as early as possible and ideally within 2 hours of symptom onset. The decrease of systolic blood pressure should not exceed 90mmHg from baseline values. Vote 10 of 10.<br><br>In patients with acute intracerebral haemorrhage, we suggest lowering blood pressure according to recommended levels beyond 6 hours after onset of treatment for at least 24 hours **and up to 72 hours** to reduce haematoma expansion. Vote 10 of 10. |

| | | |
|---|---|---|
| | Quality of evidence: **Moderate**⨁⨁<br>Strength of recommendation: Weak ↑ | |
| **PICO 8: In patients with acute intracerebral haemorrhage, does continuing versus temporarily stopping previous oral antihypertensive therapy improve outcome?** | In patients with acute intracerebral haemorrhage there is continued uncertainty over the benefits and risks (advantages/disadvantages) of continuing versus temporarily stopping previous blood pressure lowering therapy.<br>Quality of evidence: **Moderate**⨁⨁⨁<br>Strength of recommendation: - | In patients acute intracerebral haemorrhage who need blood pressure lowering therapy to maintain blood pressure within the recommended range and who do not have swallowing problems, we suggest continuation of prior oral antihypertensive agents. Vote 10 of 10.<br><br>In patients with acute intracerebral haemorrhage who need blood pressure lowering therapy to maintain blood pressure within the recommended range and who have dysphagia or decreased level of consciousness, we suggest temporarily stopping previous oral hypertensive therapy and using intravenous antihypertensive agents until swallowing is restored or a nasogastric tube is in place. Vote 10 of 10. |