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 Table 1. Disclosures of the working group members

		Member advisory Boards - DiaMedica, Moleac, Phagenesis (none relevant to this topic)
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	Department of Neurology, Bispedierg Hospital & University	Speaker honoraria: Bayer. Daiichi-Sankyo, BMS og Boerhinger.
	of Copenhagen, Copenhagen, Denmark.	National Coordinating Investigator: Portola and Bayer
Urs Fischer	Prof. for Acute Neurology and	Intellectual disclosures:
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	Deputy-Director Clinical Trial Unit	Financial disclosures:
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	University of Bern	this topic)
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Dariusz Gąsecki	Neurologist, Stroke Unit,	Intellectual disclosures:
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		Financial disclosures:none
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Simona Sacco	Neurologist Department of Biotechnological and Applied Clinical Sciences andBiotechnology, University of	Intellectual disclosures: Co-chair of the Guideline Board of the European Stroke OrganizationFinancial disclosures: Personal fees as speaker or advisor: Abbott, Allergan, AstraZeneca, Eli Lilly, Novartis, Teva. Research grants:					
	L'Aquila, italy	Allergan, Novartis.					
		Non-financial support: Abbott, Allergan, Bayer, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly, Medtronic, Novartis, Pfizer, Starmed, Teva. Fees for CME/education: Medscape					
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Neurology, University of Tennessee Health Science Center, Memphis, Tennessee, USA	-Chair of European Stroke Organization Industry Roundtable
Mempilis, Telliessee, USA	Financial disclosures:
	- 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.
	- 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

	Vasodepre	essor	Cont	rol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
RIGHT 2013	12	25	4	16	24.5%	2.77 [0.70, 10.97]	
RIGHT-2 2019	210	568	208	581	75.5%	1.05 [0.83, 1.34]	-
Total (95% CI)		593		597	100.0%	1.33 [0.59, 3.01]	
Total events	222		212				
Heterogeneity: Tau ² =	0.21; Chl ²						
Test for overall effects	Z = 0.69 (P	9 = 0.49))))				Control Vasodepressor

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

			Certainty ass	essment	№ of patients		Ef	fect				
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PICO 1a: Pre-hospital blood pressure lowering	control	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance

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

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

	Vasodepr	essor	Cont	rol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M–H, Random, 95% Cl
ACCESS 2003	5	173	12	166	2.4%	0.38 [0.13, 1.11]	
ANSG 1992	120	760	42	264	10.2%	0.96 [0.66, 1.41]	-4-
Bath 2001	1	14	1	19	0.4%	1.38 [0.08, 24.23]	
BEST 1988	67	202	23	100	6.7%	1.66 [0.96, 2.88]	— •—
CATIS 2014	66	1966	54	1987	10.7%	1.27 [0.66, 1.62]	+
CHASE 2020	24	116	33	125	6.0%	0.73 [0.40, 1.33]	
CHHIPS 2009	9	95	12	52	2.9%	0.35 [0.14, 0.69]	
ENOS 2015 (1)	191	1664	216	1678	15.5%	0.66 [0.71, 1.06]	
Eveson 2007	2	16	1	22	0.5%	2.63 [0.22, 31.57]	
Fogelholm 2004	27	176	14	174	4.9%	2.07 [1.05, 4.10]	
Geimers 1988	16	93	27	93	4.9X	0.59 [0.30, 1.16]	
INWEST 1994	63	195	33	100	7.5%	1.50 [0.91, 2.49]	
LI 2018	5	159	6	160	1.9%	0.83 [0.25, 2.79]	
PRoFESS 2009	5	647	6	713	1.9%	0.92 [0.28, 3.02]	
Rashid 2003	3	54	3	30	1.0%	0.53 [0.10, 2.80]	
RIGHT-2 2019	70	494	75	510	11.0%	0.96 [0.67, 1.36]	-+-
SCAST 2015	66	647	66	864	10.9%	1.02 [0.72, 1.46]	_ _
VENTURE 2015	2	187	1	185	0.5%	1.99 [0.18, 22.13]	
Total (95% CI)		7902		7242	100.0%	1.00 [0.84, 1.19]	•
Total events	766		625				
Heterogeneity: Tau ² =	0.04; Chl ²	= 26.35	5, df = 1	7 (P = (0.07); 🗗	- 35%	0.05 0.2 1 5 20
Test for overall effect:	Z = 0.02 (P = 0.96	8)				Vasodepressor Control
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

	Vasodepr	ressor	Cont	rol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M–H, Random, 95% CI
Bath 2001	6	14	11	19	0.9%	0.55 [0.13, 2.20]	
CATIS 2014	1466	1966	1485	1987	22.7%	1.01 [0.87, 1.16]	+
CHASE 2020	12	116	10	125	2.3%	1.33 [0.55, 3.20]	
Eveson 2007	11	16	14	22	1.1%	0.90 [0.25, 3.25]	
INWEST 2000 (1)	30	173	30	92	4.6%	0.43 [0.24, 0.78]	
Kaste 1994	67	146	74	150	7.0%	0.87 [0.55, 1.37]	+
LI 2016	106	159	66	160	7.0%	1.73 [1.10, 2.73]	 →→
PRoFESS 2009	541	647	610	713	12.6%	0.86 [0.64, 1.16]	
Rashid 2003	19	54	11	30	2.0%	0.94 [0.37, 2.37]	
RIGHT-2 2019	204	494	197	510	14.9X	1.12 [0.87, 1.44]	- -
SCAST 2015 (2)	562	647	579	864	16.3%	0.97 [0.79, 1.19]	
VENTURE 2015	141	187	143	185	6.5%	0.90 [0.56, 1.45]	
Total (95% CI)		4843		4857	100.0%	0.98 [0.85, 1.12]	
Total events	3169		3252				
Heterogeneity: Tau ² =	0.02; Chl ²	= 16.83	1, df = 1	1 (P = (0.11); ř •	= 35 %	
Test for overall effect:	Z = 0.35 (V.1 V.2 V.5 I 2 5 10 Vasodepressor Control					

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 asse	essment		№ of patie	Ef	fect					
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PICO 3 Blood pressure lowering with Vasodepressor	Control	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance

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)		CRITICAL
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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)	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 a	issessment			№ of p	patients	Effec	t	Containty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Experimental arm	Control arm	Relative (95% Cl)	Absolute (95% Cl)	Gertainty	importance

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
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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
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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*	160- 180mmHg	N/A	24 hours	March 2023
			110-140 mmHg**				
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	644	<140 mmHg	<180mmHg	0.5-1 hour	24 hours	December
	(multicenter)						2023
BP-TARGET (113 114)	France (multicenter)	320	<130 mmHg	<185mmHg	1 hour	24-36 hours	Completed
(113,114)	(matterner)						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 a	ssessment			№ of p	atients	Effect	:	Contrainty	lanantonoo
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Experimental arm	Control arm	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance

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
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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 a	issessment			Nº of p	atients	Effec	t	Contractory.	luurateese
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Experimental arm	Control arm	Relative (95% Cl)	Absolute (95% Cl)	Certainty	ітропапсе
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 a	ssessment			Nº of p	atients	Effect	:		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	blood pressure elevation with vasopressor	Control	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance

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)	CRITICAL

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

l r	randomised trial	not serious	not serious	not serious	serious °	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)	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

	Continue	Stop	Odds Ratio	Odds Ratio
Study or Subgroup	Events Total Ev	ents Total Weigh	t M-H, Random, 95% Cl	M-H, Random, 95% CI
COSSACS 2010	109 220	99 198 19.9	6 0.98 [0.67, 1.44]	
ENOS 2015	325 925	329 902 80.1	6 0.94 [0.78, 1.14]	
Total (95% CI)	1145	1100 100.05	6 0.95 [0.80, 1.13]	
Total events Heterogeneity: Tau ² = Test for overall effect	434 • 0.00; Chl ² = 0.03, • Z = 0.58 (P = 0.56	426 , df = 1 (P = 0.85); 6)	2 - 0%	0.7 0.85 1 1.2 1.5 Continue Stop

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

	Certainty assessment							atients	Effect	:		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Continuing	Stopping previous antihypertensive therapy	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance

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)	CRITICAL

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

2	randomised not serious trials *	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)		CRITICAL
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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).

	Vasodepr	essor	Cont	rol		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M–H, Random, 95% CI
5.2.1 < 6 hours								
ATACH-2 2016	33	500	34	500	23.7%	0.97 [0.59, 1.59]		_ _
ENOS 2016n	2	29	12	32	5.5%	0.12 [0.02, 0.61]	_	
INTERACT 2008	21	203	25	201	19.9%	0.81 [0.44, 1.50]		_
INTERACT2 2013	166	1394	170	1421	32.6%	0.99 [0.79, 1.25]		+
RIGHT-2 2019 ich	35	73	23	71	18.2%	1.92 [0.98, 3.78]		—
Subtotal (95% CI)		2199		2225	100.0%	0.95 [0.64, 1.43]		•
Total events	257		264					
Heterogeneity: Tau ² =	0.12; Chr2	= 10.51	8, df = 4	$\langle \mathbf{P} = 0 \rangle$.03); 1² =	62%		
Test for overall effect:	Z = 0.22 (P = 0.82	2)					
5.2.2 < 24 hours								
ICH ADAPT 2013	7	37	4	36	22.2%	1.87 (0.50, 7.03)		
Koch 2008	3	20	3	19	12.9%	0.94 [0.17. 5.36]		
PATICH 2017	13	96	18	99	64.9X	0.70 [0.32, 1.53]		_
Subtotal (95% CI)		153		154	100.0%	0.91 [0.49, 1.70]		
Total events	23		25					-
Heterogeneity: Tau ² =	0.00; Chl ²	= 1.55,	df = 2 (P = 0.4	(6); i ² = 0)%		
Test for overall effect:	z = 0.30 (P = 0.76	i)					
5.2.3 < 72 hours								
CHASE 2020	16	126	14	116	17.7%	1 06 0 49 2 281		
CHHIPS 2009	2	18	17	7	1.0%	2 27 10 10 53 301		
ENOS 2016n	42	309	47	316	51 58	0 90 10 57 1 411		
Gunta 2018	11	59	14	59	13.2%	0 74 [0 30 1 79]		_
SCAST 2014	18	144	11	130	16.6%	1 55 10 70 3 411		
Subtotal (95% CI)	-•	656		628	100.0%	1.00 [0.72, 1.38]		
Total events	89		86					
Heterogeneity: Tau ² =	0.00; Chf ²	= 2.11,	df = 4 (P = 0.7	'2); i ² = 0)%		
Test for overall effect:	Z = 0.02 (P = 0.98	3)					
							0.01	0.1 1 10 100
						A-1		Vasodepressor Control

Test for subgroup differences: $Cht^2 = 0.08$, df = 2 (P = 0.96), $t^2 = 0\%$

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

	Vasodepr	essor	Cont	rol		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Random, 95% Cl
ATACH-2 2016	211	481	211	460	19.3%	1.00 [0.77, 1.29]		_ + _
CHASE 2020	46	126	37	116	6.1%	1.23 [0.72, 2.09]		
ENOS 2016n	105	309	112	316	13.5%	0.94 [0.67, 1.30]		- _
Gupta 2018	26	59	21	59	3.3%	1.43 [0.66, 2.99]		
INTERACT 2008	108	203	106	201	10.3%	1.02 [0.69, 1.51]		_
INTERACT2 2013	663	1362	627	1412	33.5%	1.15 [0.99, 1.34]		
Koch 2008	6	20	10	19	1.2%	0.60 [0.17, 2.14]		
PATICH 2017	29	96	19	99	4.1%	1.82 [0.94, 3.54]		
RIGHT-2 2019 Ich	6	74	11	71	1.7%	0.46 [0.17, 1.36]		
SCAST 2014	63	144	66	130	7.0%	0.70 [0.43, 1.14]		
Total (95% CI)		2894		2903	100.0%	1.05 [0.91, 1.20]		•
Total events	1285		1240					-
Heterogeneity: Tau ² =	0.01; Chl ²	= 11.24	1, df = 9	$\langle \mathbf{P} = 0 \rangle$.26); l ² =	20%	-	
Test for overall effect:	Z = 0.64 (P = 0.52	2)	-			Ų.2	Control Vasodepressor

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).

	Vasodepr	essor	Cont	rol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M–H, Random, 95% CI
5.6.1 < 6 hours							
ATACH-2 2016	211	481	211	480	22.4%	1.00 [0.77, 1.29]	+
ENOS 2016n	10	29	9	32	1.2%	1.35 [0.45, 3.99]	
INTERACT 2008	108	203	106	201	9.5%	1.02 [0.69, 1.51]	_
INTERACT2 2013	663	1382	627	1412	65.6%	1.15 [0.99, 1.34]	
RIGHT-2 2019 ich	6	74	11	71	1.3%	0.48 [0.17, 1.38]	
Subtotal (95% CI)		2169		2196	100.0%	1.09 [0.97, 1.23]	◆
Total events	996		964				
Heterogeneity: Tau ² =	• 0.00; Chl ²	= 3.62,	df = 4 (P = 0.4	l6); l ² = 0	%	
Test for overall effect:	: Z = 1.45 (P = 0.19	i)				
5.6.2 < 24 hours							
Koch 2008	6	20	10	19	37.7%	0.60 [0.17, 2.14]	_
PATICH 2017	29	96	19	99	62.3%	1.82 [0.94, 3.54]	
Subtotal (95% CI)		116		118	100.0%	1.20 [0.42, 3.45]	
Total events	37		29				
Heterogeneity: Tau ² =	• 0.35; Chl ²	= 2.31,	df = 1 (P = 0.1	.3); i ² = 5	7%	
Test for overall effect:	: Z = 0.34 (P = 0.74	•)				
5.6.3 < 72 hours							
CHASE 2020	46	126	37	116	20.7%	1.23 [0.72, 2.09]	_
ENOS 2016n	105	309	112	316	44.1%	0.94 [0.67, 1.30]	_ _
Gupta 2018	26	59	21	59	11.5%	1.43 [0.68, 2.99]	
SCAST 2014	83	144	86	130	23.8%	0.70 [0.43, 1.14]	
Subtotal (95% CI)		638		621	100.0%	0.97 [0.75, 1.26]	•
Total events	260		256				
Heterogeneity: Tau ² =	• 0.01; Chl ²	= 3.58.	df = 3 ($\mathbf{P} = 0.3$	(1); $f^2 = 1$	6%	
Test for overall effect:	: Z = 0.23 (P = 0.81	l) .				
							U.2 U.S I Z

Test for subgroup differences: $Cht^2 = 0.72$, df = 2 (P = 0.70), $t^2 = 0\%$

Figure 11	The effect	of intensive bloc	od pressure	lowering wit	h any	vasodepressor	drug
compared	to control o	on haematoma ex	pansion				

	Vasodepr	ressor	Cont	rol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M–H, Random, 95% CI
ATACH-2 2016	85	450	104	426	33.6%	0.72 [0.52, 1.00]	
ICH ADAPT 2013	9	37	4	36	5.0%	2.57 [0.71, 9.27]	
INTERACT 2008	26	174	40	172	19.6%	0.58 [0.34, 1.00]	
INTERACT2 2013	128	491	125	473	36.8%	0.98 [0.74, 1.31]	
Koch 2008	6	21	6	21	4.7%	1.00 [0.26, 3.81]	
Total (95% CI)		1173		1128	100.0%	0.84 [0.62, 1.13]	•
Total events	254		279				-
Heterogeneity: Tau ² -	= 0.04; Chl ²	= 6.75.	df = 4 (P = 0.1	.5); i ² = 4	1%	
Test for overall effect	: Z = 1.15 (P = 0.25	5)			-	0.1 0.2 0.5 1 2 5 10 Vasodepressor Control

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).



Test for subgroup differences: $Chl^2 = 2.25$, df = 1 (P = 0.13), $l^2 = 55.6\%$

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

			Certainty asse	ssment			№ of patie	Ef	fect			
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Blood pressure lowering with Vasodepressor	Control	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance

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)		CRITICAL
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3-6 months mortality< 6 hours

5	randomised trials	not serious	serious °	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)		CRITICAL
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3-6 months mortality \leq 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)	CRITICAL

				№ of patie	ents	Ef	fect					
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Blood pressure lowering with Vasodepressor	Control	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance

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)		CRITICAL
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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)		CRITICAL
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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)		CRITICAL
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3-6 months good functional outcome (mRS scores 0-2)- \leq 24 hours

2	randomised trials	not serious	not serious	not serious	very serious °	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)	CRITICAL

			Certainty asse	ssment			№ of patio	ents	Ef	fect		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Blood pressure lowering with Vasodepressor	Control	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance

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)	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)	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)		CRITICAL
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Hematoma expansion - \leq 24 hours

2	randomised trials	not serious	not serious	not serious	very serious °	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)		CRITICAL
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Certainty assessment						№ of patients		Effect				
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Blood pressure lowering with Vasodepressor	Control	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance

Acute Renal injury

4 ra	randomised trials	not serious	not serious	not serious	very serious •	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)		IMPORTANT
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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

	Continue	Stop		Odds Ratio	Odds Ratio
Study or Subgroup	Events Tota	Events Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
COSSACS 2010	5 16	3 15	14.3%	1.54 [0.30, 7.87]	
ENOS 2016	19 119	23 126	85.7%	0.85 [0.44, 1.66]	
Total (95% CI)	137	141	100.0%	0.93 [0.50, 1.72]	
Total events	24	26			
Heterogeneity: Tau ² = Test for overall effect:	0.00; Chl ² = 0 Z = 0.24 (P =	.43, df = 1 (P = 0.61)	0.51); ř	- 0%	0.1 0.2 0.5 1 2 5 10 Continue Stop

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

	Contin	nue	Sto	р		Odds Ratio			Odds Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H	l, Random, 95	5% CI	
COSSACS 2010	5	18	2	15	8.6%	2.50 [0.41, 15.29]			•		
ENOS 2016	35	119	35	126	91.4%	1.08 [0.62, 1.89]					
Total (95% CI)		137		141	100.0%	1.16 [0.68, 1.98]			•		
Total events	40		37								
Heterogeneity: Tau ² = Test for overall effect:	• 0.00; Cl : Z = 0.56	nt² = 0. i (P = (75, df =).57)	1 (P =	0.39); ř	- 0%	0.01	0.1	1 Stop Contin	10 nue	100

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					
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Continuing	Stopping previous antihypertensive therapy	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance

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)	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)		CRITICAL
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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. Quality of evidence: Moderate⊕⊕⊕ 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. Quality of evidence: Moderate $\oplus \oplus \oplus$ Strength of recommendation: Weak \downarrow ?	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. Quality of evidence: Very low⊕ Strength of recommendation: Weak ↑? 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. Quality of evidence: Moderate⊕⊕⊕ 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. Quality of evidence: Very low⊕ Strength of recommendation: Weak ↑? 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 Quality of evidence: Moderate⊕⊕⊕ Strength of recommendation: Weak ↓? In patients with acute ischaemic stroke due to large vessel occlusion undergoing treatment with mechanical thrombectomy (with or without intravenous	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
	thrombolysis) systolic blood pressure drops should be avoided. Quality of evidence: Very low⊕ Strength of recommendation: Strong ↓↓	
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. Quality of evidence: Very low ⊕ Strength of recommendation: Weak ↓↓ 	 suspected or shown to be directly responsible for the deterioration, we suggest: stopping existing blood pressure lowering therapy, administering intravenous fluids and introducing non-pharmacological procedures to raise blood pressure before considering 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. Quality of evidence: Moderate⊕⊕⊕ 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. Quality of evidence: Moderate⊕⊕⊕ Strength of recommendation: - 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. 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 ⊕⊕ 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. Quality of evidence: Moderate⊕⊕⊕ 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. 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.