Supplemental Online Content

Hsu CY, Saver JL, Ovbiagele B, Wu YL, Cheng CY, Lee M. Association between magnitude of differential blood pressure reduction and secondary stroke prevention: a meta-analysis and meta-regression. *JAMA Neurol*. Published online March 20, 2023. doi:10.1001/jamaneurol.2023.0218

- eFigure 1. Study selection
- eFigure 2. Risk of bias
- eFigure 3. Major cardiovascular events
- eFigure 4. Recurrent ischemic stroke
- eFigure 5. Hemorrhagic stroke
- eFigure 6. Fatal or disabling stroke
- eFigure 7. Myocardial infarction
- eFigure 8. Death from cardiovascular causes
- eFigure 9. Death from any cause
- eFigure 10. Heart failure
- eFigure 11. Sensitivity testing
- eFigure 12. Time interval from index stroke to randomization
- eFigure 13. Study duration
- eFigure 14. Ethnicity
- eFigure 15. Antihypertensive drugs used in more intensive treated group
- eFigure 16. Mean baseline SBP
- eFigure 17. Achieved SBP in more intensive treated group
- eFigure 18. Achieved SBP in less intensive treated group
- eFigure 19. Entry event
- eFigure 20. Sample size
- eFigure 21. Study design
- eFigure 22. Definition of differential blood pressure reduction
- eFigure 23. Publication bias

eTable. Grading of Recommendations, Assessment, Development and Evaluations (GRADE)

eReferences

This supplemental material has been provided by the authors to give readers additional information about their work.

eTable. Grading of Recommendations, Assessment, Development and Evaluations (GRADE)

Legends: Summary of the quality assessments and summary finding for the primary and secondary outcomes

							Summary o	f findings			
Quality assess	sment						Event, No./	Fotal, No.	Effect		
Outcomes, No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Publication bias	More intensive	Less intensive	Relative (95% Cl)	Absolute	Quality
Recurrent stroke, n=10	RCT	No serious limitations	some inconsistency	No serious indirectness	No serious imprecision	Undetected	1704/20344	2061/20366	0.83 (0.78- 0.88)	17 fewer per 1000 (12-22)	High
Major cardiovascular events, n=9	RCT	No serious limitations	some inconsistency	No serious indirectness	No serious imprecision	Undetected	2348/19582	2679/19608	0.88 (0.83- 0.92)	16 fewer per 1000 (11-23)	High
Ischemic stroke, n=6	RCT	No serious limitations	some inconsistency	No serious indirectness	some imprecision	Undetected	1217/16134	1403/16189	0.87 (0.81- 0.94)	11 fewer per 1000 (5-17)	Moderate
Hemorrhagic stroke, n=6	RCT	No serious limitations	some inconsistency	No serious indirectness	some imprecision	Undetected	114/16134	212/16189	0.54 (0.43-	6 fewer per 1000 (4-7)	Moderate

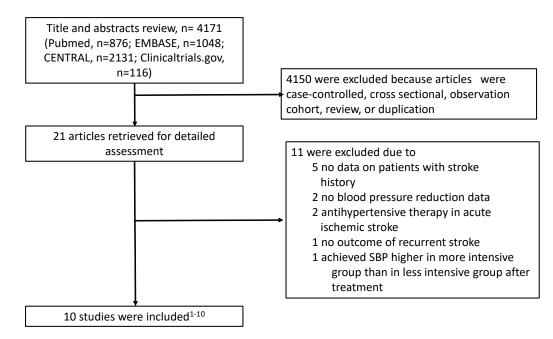
									0.68)		
Fatal or disabling stroke, n=6	RCT	No serious limitations	some inconsistency	No serious indirectness	some imprecision	Undetected	253/8537	334/8539	0.76 (0.64- 0.89)	9 fewer per 1000 (4-14)	Moderate
Myocardial infarction, n=9	RCT	No serious limitations	Serious inconsistency	No serious indirectness	Serious imprecision	Undetected	365/20344		0.89 (0.78- 1.03)	Not significant	Moderate
Death from cardiovascular causes, n=9	RCT	No serious limitations	No serious inconsistency	No serious indirectness	some imprecision	Undetected	629/19711	728/19736	0.86 (0.78- 0.96)	5 fewer per 1000 (1-8)	Moderate
Death from any cause, n=10	RCT	No serious limitations	Some inconsistency	No serious indirectness	some imprecision	Undetected	1511/20344	1554/20366	0.97 (0.91- 1.04)	Not significant	Moderate
Heart failure, n=2	RCT	No serious limitations	Serious inconsistency	No serious indirectness	Serious imprecision	Undetected	126/10779		1.05 (0.82- 1.35)	Not significant	Low

RCT: randomized clinical trial

© 2023 Hsu CY et al. JAMA Neurology.

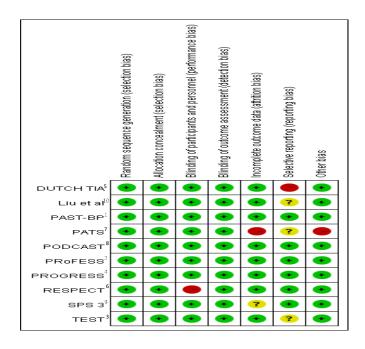
eFigure 1. Study selection

Legends: Flow of study selection.



eFigure 2. Risk of bias

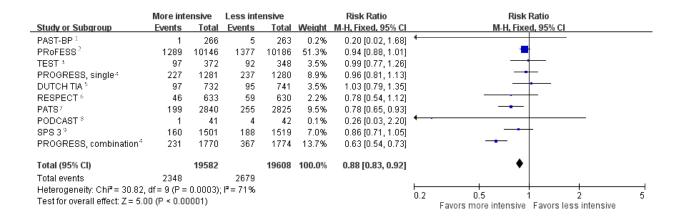
Legends: Risk of bias for included trials.



eFigure 3: Major cardiovascular events

Legends: Relative risk with 95% confidence interval of major cardiovascular events in more intensive vs less

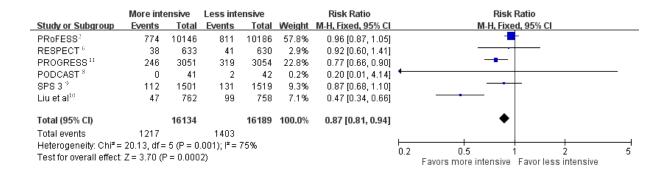
intensive blood pressure lowering in patients with stroke or transient ischemic attack.



eFigure 4. Recurrent ischemic stroke

Legends: Relative risk with 95% confidence interval of recurrent ischemic stroke in more intensive vs less intensive

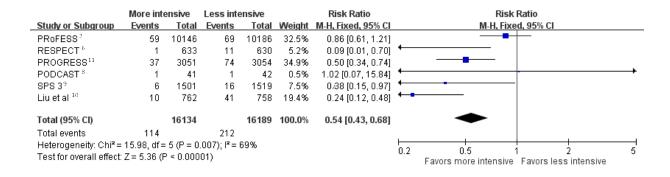
blood pressure lowering in patients with stroke or transient ischemic attack.



eFigure 5. Hemorrhagic stroke

Legends: Relative risk with 95% confidence interval of hemorrhagic stroke in more intensive vs less intensive blood

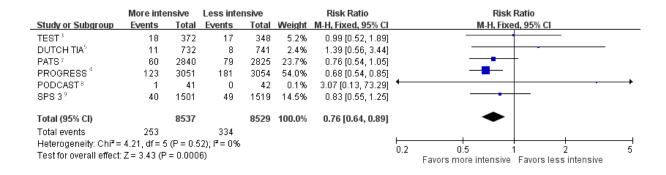
pressure lowering in patients with stroke or transient ischemic attack.



eFigure 6. Fatal or disabling stroke

Legends: Relative risk with 95% confidence interval of fatal or disabling stroke in more intensive vs less intensive

blood pressure lowering in patients with stroke or transient ischemic attack.



eFigure 7. Myocardial infarction

Legends: Relative risk with 95% confidence interval of myocardial infarction in more intensive vs less intensive blood

pressure lowering in patients with stroke or transient ischemic attack.

	More inte	ensive	Less inte	ensive		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
PAST-BP ¹	1	266	1	263	0.2%	0.99 [0.06, 15.72]	←
PRoFESS ²	168	10146	169	10186	41.2%	1.00 [0.81, 1.23]	_ _
TEST 3	13	372	14	348	3.5%	0.87 [0.41, 1.82]	
DUTCH TIA ^s	45	732	40	741	9.7%	1.14 [0.75, 1.72]	
RESPECT 6	5	633	4	630	1.0%	1.24 [0.34, 4.61]	
PATS ⁷	26	2840	23	2825	5.6%	1.12 [0.64, 1.97]	
PROGRESS ⁴	60	3051	96	3054	23.4%	0.63 [0.45, 0.86]	
PODCAST ⁸	0	41	1	42	0.4%	0.34 [0.01, 8.14]	<pre></pre>
SPS 3 ⁹	36	1501	40	1519	9.7%	0.91 [0.58, 1.42]	
Liu et al ¹⁰	11	762	21	758	5.1%	0.52 [0.25, 1.07]	
Total (95% CI)		20344		20366	100.0%	0.89 [0.78, 1.03]	•
Total events	365		409				
Heterogeneity: Chi ² =	10.58, df=	9 (P = 0	.31); I ^z = 1:	5%			
Test for overall effect:	Z = 1.58 (F	P = 0.11)					0.2 0.5 1 2 5 Favors more intensive Favors less intensive

eFigure 8. Death from cardiovascular causes

Legends: Relative risk with 95% confidence interval of death from cardiovascular causes in more intensive vs less

intensive blood pressure lowering in patients with stroke or transient ischemic attack.

	More inte	ensive	Less inte	ensive		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
PAST-BP ¹	0	266	1	263	0.2%	0.33 [0.01, 8.05]	+ · · · · · · · · · · · · · · · · · · ·
PRoFESS ²	223	10146	263	10186	36.0%	0.85 [0.71, 1.02]	
TEST 3	34	372	39	348	5.5%	0.82 [0.53, 1.26]	
DUTCH TIA ^S	41	732	33	741	4.5%	1.26 [0.80, 1.97]	
PATS ⁷	86	2840	102	2825	14.0%	0.84 [0.63, 1.11]	
PROGRESS 4	181	3051	198	3054	27.1%	0.92 [0.75, 1.11]	
PODCAST ⁸	1	41	1	42	0.1%	1.02 [0.07, 15.84]	← →
SPS 3 ⁹	36	1501	41	1519	5.6%	0.89 [0.57, 1.38]	
Liu et al ¹⁰	27	762	50	758	6.9%	0.54 [0.34, 0.85]	
Total (95% CI)		19711		19736	100.0%	0.86 [0.78, 0.96]	•
Total events	629		728				
Heterogeneity: Chi ² =	7.71, df = 3	8 (P = 0.4	l6); l² = 0%	,			
Test for overall effect:	Z = 2.77 (F	= 0.006)				0.2 0.5 1 2 5 Favors more intensive Favors less intensive
							avora more miteriaive in avora leas miteriaive

eFigure 9. Death from any cause

Legends: Relative risk with 95% confidence interval of death from any cause in more intensive vs less intensive

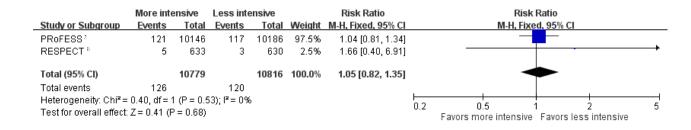
blood pressure lowering in patients with stroke or transient ischemic attack.

	More inte	ensive	Less inte	ensive		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
PAST-BP ¹	2	266	1	263	0.1%	1.98 [0.18, 21.68]	· · · · · ·
PRoFESS ²	755	10146	740	10186	47.5%	1.02 [0.93, 1.13]	+
TEST ³	51	372	60	348	4.0%	0.80 [0.56, 1.12]	
DUTCH TIA ^S	64	732	58	741	3.7%	1.12 [0.79, 1.57]	
RESPECT 6	30	633	37	630	2.4%	0.81 [0.50, 1.29]	
PATS 7	145	2840	161	2825	10.4%	0.90 [0.72, 1.11]	
PROGRESS ⁴	306	3051	319	3054	20.5%	0.96 [0.83, 1.11]	
PODCAST ⁸	4	41	3	42	0.2%	1.37 [0.33, 5.73]	
SPS 39	106	1501	101	1519	6.5%	1.06 [0.82, 1.38]	-
Liu et al ¹⁰	48	762	74	758	4.8%	0.65 [0.46, 0.91]	
Total (95% CI)		20344		20366	100.0%	0.97 [0.91, 1.04]	•
Total events	1511		1554				
Heterogeneity: Chi ² =	10.51, df=	9 (P = 0	.31); P = 1	4%			
Test for overall effect:							0.2 0.5 1 2 5 Favors more intensive Favors less intensive

eFigure 10. Heart failure

Legends: Relative risk with 95% confidence interval of heart failure in more intensive vs less intensive blood pressure

lowering in patients with stroke or transient ischemic attack.

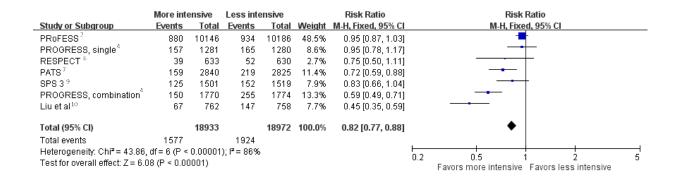


eFigure 11. Sensitivity testing

Legends: Relative risk with 95% confidence interval of recurrent stroke in more intensive vs less intensive blood

pressure lowering in patients with stroke or transient ischemic attack among trials with recurrent stroke being the

primary outcome in the original trial design.

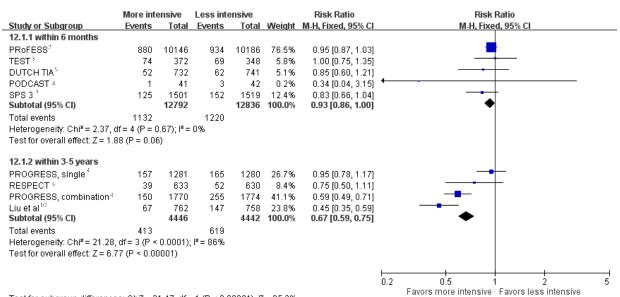


eFigure 12. Time interval from index stroke to randomization

Legends: Relative risk with 95% confidence interval of recurrent stroke in more intensive vs less intensive blood

pressure lowering in patients with stroke or transient ischemic attack with randomization within 6 months from stroke

vs within 3-5 years from stroke.

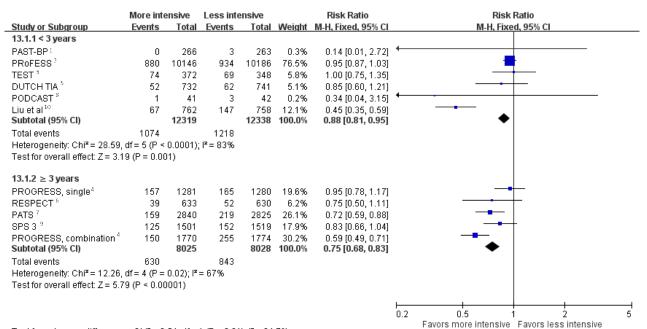


Test for subgroup differences: $Chi^2 = 21.47$ df = 1 (P < 0.00001) I² = 95.3%

eFigure 13. Study duration

Legends: Relative risk with 95% confidence interval of recurrent stroke in more intensive vs less intensive blood

pressure lowering in patients with stroke or transient ischemic attack with study duration < 3 years vs \ge 3 years.

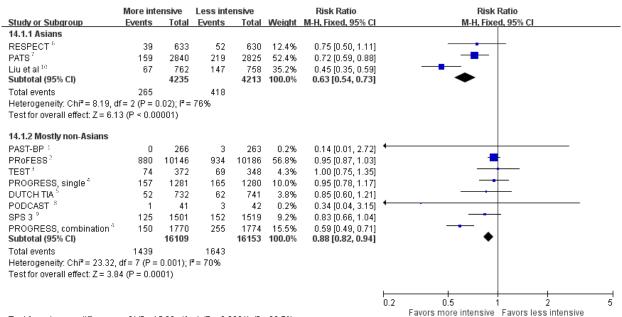


Test for subgroup differences: $Chi^2 = 6.54$ df = 1 (P = 0.01) $I^2 = 84.7\%$

eFigure 14. Ethnicity

Legends: Relative risk with 95% confidence interval of recurrent stroke in more intensive vs less intensive blood

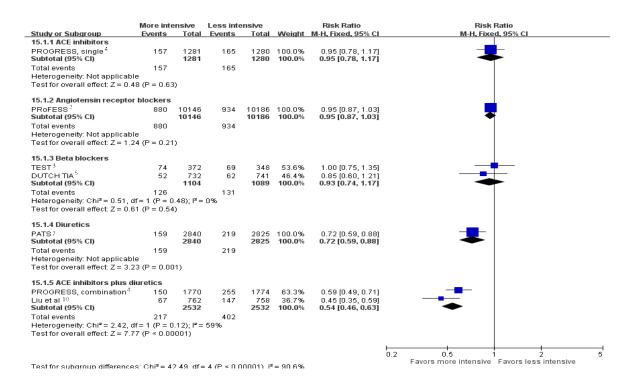
pressure lowering in patients with stroke or transient ischemic attack in Asians vs mostly non-Asians.



Test for subgroup differences: $Chi^2 = 15.90$, df = 1 (P < 0.0001), $l^2 = 93.7\%$

eFigure 15. Antihypertensive drugs used in more intensive treated group

Legends: Relative risk with 95% confidence interval of recurrent stroke in more intensive vs less intensive blood pressure lowering in patients with stroke or transient ischemic attack for antihypertensive drugs used in the more intensive treated arm (angiotensin-converting enzyme [ACE] inhibitors vs angiotensin receptor blockers vs beta blockers vs diuretics vs ACI inhibitors plus diuretics).



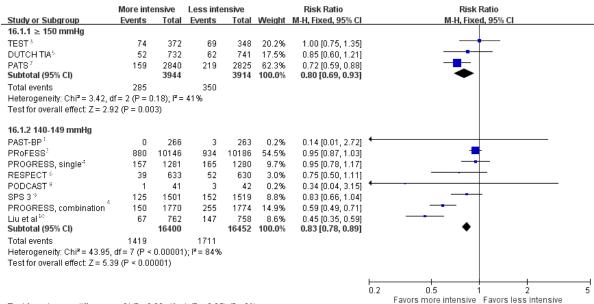
eFigure 16. Mean baseline SBP

Legends: Relative risk with 95% confidence interval of recurrent stroke in more intensive vs less intensive blood

pressure lowering in patients with stroke or transient ischemic attack with mean baseline SBP levels ≥ 150 mmHg vs

140-149 mmHg.

SBP: systolic blood pressure



Test for subaroup differences: $Chi^2 = 0.20$, df = 1 (P = 0.65), $l^2 = 0.56$.

eFigure 17. Achieved SBP in more intensive treated group

Legends: Relative risk with 95% confidence interval of recurrent stroke in more intensive vs less intensive blood

pressure lowering in patients with stroke or transient ischemic attack with achieved SBP levels in the more intensive

blood pressure lowering group (≥ 140 mmHg vs 130 to < 140 mmHg vs < 130 mmHg).

SBP: systolic blood pressure

	More inte	ensive	Less inte	ensive		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixed, 95% Cl
17.1.1 ≥ 140 mmHg								
TEST 3	74	372	69	348	13.8%	1.00 [0.75, 1.35]		+
PROGRESS, single ⁴	157	1281	165	1280	31.9%	0.95 [0.78, 1.17]		
DUTCH TIA ^S	52	732	62	741	11.9%	0.85 [0.60, 1.21]		
PATS 7	159	2840	219	2825	42.4%	0.72 [0.59, 0.88]		
Subtotal (95% CI)		5225		5194	100.0%	0.85 [0.75, 0.96]		•
Total events	442		515					
Heterogeneity: Chi ^z = 5.00, d	if = 3 (P = 0).17); I ² =	40%					
Test for overall effect: Z = 2.6	67 (P = 0.00)8)						
17.1.2 130 to < 140 mmHg								
PRoFESS ²	880	10146	934	10186	78.3%	0.95 [0.87, 1.03]		
PODCAST ^S	1	41	3	42	0.2%	0.34 [0.04, 3.15]	•	
PROGRESS, combination ⁴	150	1770	255	1774	21.4%	0.59 [0.49, 0.71]		
Subtotal (95% CI)		11957			100.0%	0.87 [0.80, 0.94]		◆
Total events	1031		1192					
Heterogeneity: Chi ^z = 20.17,	df = 2 (P <	0.0001);	I² = 90%					
Test for overall effect: Z = 3.4	19 (P = 0.00	005)						
17.1.3 < 130 mmHg								
PAST-BP ¹	0	266	3	263	1.7%	0.14 [0.01, 2.72]	←	
RESPECT 6	39	633	52	630	25.2%	0.75 [0.50, 1.11]		
SPS 3 9	125	1501	152	1519	73.1%	0.83 [0.66, 1.04]		
Subtotal (95% CI)		2400		2412	100.0%	0.80 [0.66, 0.97]		◆
Total events	164		207					
Heterogeneity: Chi ² = 1.55, d	if = 2 (P = 0).46); I ^z =	0%					
Test for overall effect: Z = 2.2	25 (P = 0.02	2)						
							0.2	0.5 1 2
								Favors more intensive Favors less intensive

Test for subaroun differences: $Chi^2 = 0.62$ df = 2 (P = 0.73) $I^2 = 0.%$

eFigure 18. Achieved SBP in less intensive treated group

Legends: Relative risk with 95% confidence interval of recurrent stroke in more intensive vs less intensive blood

pressure lowering in patients with stroke or transient ischemic attack with achieved SBP levels in the less intensive

blood pressure lowering group (≥ 140 mmHg vs 130 to < 140 mmHg vs < 130 mmHg).

SBP: systolic blood pressure

	More inte	ensive	Less inte	ensive		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
18.1.1 ≥ 140 mmHg							
TEST 3	74	372	69	348	13.8%	1.00 [0.75, 1.35]	
PROGRESS, single 4	157	1281	165	1280	31.9%	0.95 [0.78, 1.17]	— —
DUTCH TIA ^S	52	732	62	741	11.9%	0.85 [0.60, 1.21]	
PATS 7	159	2840	219	2825	42.4%	0.72 [0.59, 0.88]	
Subtotal (95% CI)		5225		5194	100.0 %	0.85 [0.75, 0.96]	•
Total events	442		515				
Heterogeneity: Chi ² = 5.00, d	f= 3 (P = 0).17); l² =	40%				
Test for overall effect: Z = 2.6	7 (P = 0.00	08)					
18.1.2 130 to < 140 mmHg							
PRoFESS 2	880	10146	934	10186	66.9%	0.95 [0.87, 1.03]	
RESPECT ⁶	39	633	52	630	3.7%	0.75 [0.50, 1.11]	
PODCAST ⁸	1	41	3	42	0.2%	0.34 [0.04, 3.15]	• • • • • • • • • • • • • • • • • • • •
SPS 3 ⁹	125	1501	152	1519	10.8%	0.83 [0.66, 1.04]	
PROGRESS, combination ⁴	150	1770	255	1774	18.3%	0.59 [0.49, 0.71]	_ _
Subtotal (95% CI)		14091		14151	100.0%	0.86 [0.80, 0.93]	•
Total events	1195		1396				
Heterogeneity: Chi ² = 20.80,	df = 4 (P =	0.0003);	I ² = 81%				
Test for overall effect: Z = 4.0	3 (P < 0.00	001)					
18.1.3 < 130 mmHg							
PAST-BP 1	0	266	3	263	100.0%	0.14 [0.01, 2.72]	•
Subtotal (95% CI)		266		263	100.0%	0.14 [0.01, 2.72]	
Total events	0		3				
Heterogeneity: Not applicabl	е						
Test for overall effect: Z = 1.3	0 (P = 0.19	3)					
							0.2 0.5 1 2
T							Favors more intensive Favors less intensive

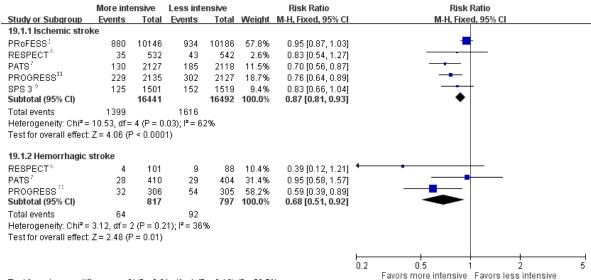
Test for subaroun differences: $Chi^2 = 1.46$ df = 2 (P = 0.48) $I^2 = 0.\%$

eFigure 19. Entry event

Legends: Relative risk with 95% confidence interval of recurrent stroke in more intensive vs less intensive blood

pressure lowering in patients with stroke or transient ischemic attack with ischemic stroke vs hemorrhagic stroke as

an entry event



Test for subaroun differences: $Chi^2 = 2.31$, df = 1 (P = 0.13), $l^2 = 56.7\%$

eFigure 20. Sample size

Legends: Relative risk with 95% confidence interval of recurrent stroke in more intensive vs less intensive blood

pressure lowering in patients with stroke or transient ischemic attack with sample size < 3000 vs ≥ 3000 patients.

	More inte	ensive	Less inte	ensive		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl	
20.1.1 < 3000								
PAST-BP ¹	0	266	3	263	0.7%	0.14 [0.01, 2.72]	•	
TEST 3	74	372	69	348	14.1%	1.00 [0.75, 1.35]		
PROGRESS, single ⁴	157	1281	165	1280	32.8%	0.95 [0.78, 1.17]		
DUTCH TIA ⁵	52	732	62	741	12.2%	0.85 [0.60, 1.21]		
RESPECT ⁶	39	633	52	630	10.3%	0.75 [0.50, 1.11]		
PODCAST ⁸	1	41	3	42	0.6%	0.34 [0.04, 3.15]	• • •	
Liu et al ¹⁰	67	762	147	758	29.2%	0.45 [0.35, 0.59]		
Subtotal (95% Cl)		4087		4062	100.0 %	0.77 [0.68, 0.87]	•	
Total events	390		501					
Test for overall effect: Z = 4.1	4 (1 - 0.00	,01,						
20.1.2 ≥ 3000								
PRoFESS ²	880	10146	934	10186	59.8%	0.95 [0.87, 1.03]	-	
	880 159	10146 2840	934 219	10186 2825	59.8% 14.1%	0.95 [0.87, 1.03] 0.72 [0.59, 0.88]	=	
PRoFESS ²								
PRoFESS ² PATS ⁷	159	2840	219	2825	14.1% 9.7% 16.4%	0.72 [0.59, 0.88]		
PRoFESS ² PATS ⁷ SPS 3 ⁹ PROGRESS, combination ⁴	159 125	2840 1501 1770	219 152	2825 1519 1774	14.1% 9.7% 16.4%	0.72 [0.59, 0.88] 0.83 [0.66, 1.04] 0.59 [0.49, 0.71]		
PRoFESS ² PATS ⁷ SPS 3 ⁹ PROGRESS, combination ⁴ Subtotal (95% CI)	159 125 150 1314	2840 1501 1770 16257	219 152 255 1560	2825 1519 1774	14.1% 9.7% 16.4%	0.72 [0.59, 0.88] 0.83 [0.66, 1.04] 0.59 [0.49, 0.71]		
PRoFESS ² PATS ⁷ SPS 3 ³ PROGRESS, combination ⁴ Subtotal (95% CI) Total events	159 125 150 1314 df= 3 (P <	2840 1501 1770 16257 0.0001);	219 152 255 1560	2825 1519 1774	14.1% 9.7% 16.4%	0.72 [0.59, 0.88] 0.83 [0.66, 1.04] 0.59 [0.49, 0.71]	•	
PRoFESS ² PATS ⁷ SPS 3 ⁹ PROGRESS, combination ⁴ Subtotal (95% CI) Total events Heterogeneity: Chi ² = 22.47,	159 125 150 1314 df= 3 (P <	2840 1501 1770 16257 0.0001);	219 152 255 1560	2825 1519 1774	14.1% 9.7% 16.4%	0.72 [0.59, 0.88] 0.83 [0.66, 1.04] 0.59 [0.49, 0.71]		

Test for subgroup differences: $Chi^2 = 1.64$ df = 1 (P = 0.20) $I^2 = 39.1\%$

eFigure 21. Study design

Legends: Relative risk with 95% confidence interval of recurrent stroke in more intensive vs less intensive blood

pressure lowering in patients with stroke or transient ischemic attack, antihypertensive drugs vs placebo and a lower

blood pressure target vs a higher blood pressure target.

	More inte	ensive	Less inte	ensive		Risk Ratio		Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixed, 95% Cl	
21.1.1 Antihypertensive dru	ugs vs Plac	ebo							
PRoFESS ²	880	10146	934	10186	50.3%	0.95 [0.87, 1.03]			
TEST ³	74	372	69	348	3.9%	1.00 [0.75, 1.35]			
PROGRESS, single ⁴	157	1281	165	1280	8.9%	0.95 [0.78, 1.17]			
DUTCH TIA ^S	52	732	62	741	3.3%	0.85 [0.60, 1.21]			
PATS 7	159	2840	219	2825	11.9%	0.72 [0.59, 0.88]		_ 	
PROGRESS, combination	150	1770	255	1774	13.8%	0.59 [0.49, 0.71]		_	
Liu et al ¹⁰	67	762	147	758	8.0%	0.45 [0.35, 0.59]			
Subtotal (95% CI)		17903		17912	100.0%	0.83 [0.78, 0.89]		•	
Total events	1539		1851						
Heterogeneity: Chi ² = 45.23	, df = 6 (P <	0.00001); l² = 87%						
Test for overall effect: Z = 5.	67 (P < 0.00	0001)							
21.1.2 A lower BP target vs	A higher E	3P target							
PAST-BP ¹	0	266	3	263	1.7%	0.14 [0.01, 2.72]	←		
RESPECT 6	39	633	52	630	24.9%	0.75 [0.50, 1.11]			
PODCAST ⁸	1	41	3	42	1.4%	0.34 [0.04, 3.15]	•		
SPS 3 ⁹	125	1501	152	1519	72.1%	0.83 [0.66, 1.04]			
Subtotal (95% CI)		2441		2454	100.0%	0.79 [0.65, 0.96]		◆	
Total events	165		210						
Heterogeneity: Chi ² = 2.12, i	df = 3 (P = 0).55); I ² =	0%						
Test for overall effect: $Z = 2.3$	34 (P = 0.0)	2)							
							⊢		
							0.2	0.5 1 2	(
To all four and an and all four and								Favors more intensive Favors less intensive	

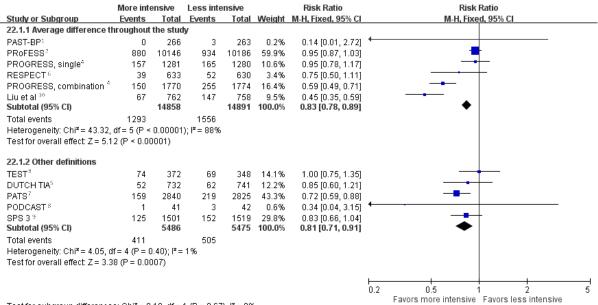
Test for subgroup differences: $Chi^2 = 0.20$, df = 1 (P = 0.65), $l^2 = 0.%$

eFigure 22. Definition of differential blood pressure reduction

Legends: Relative risk with 95% confidence interval of recurrent stroke in more intensive vs less intensive blood

pressure lowering in patients with stroke or transient ischemic attack with, average difference throughout the studies

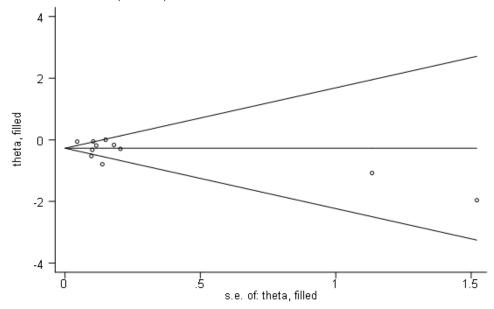
vs other definitions.



Test for subgroup differences: $Chi^2 = 0.18$ df = 1 (P = 0.67) $I^2 = 0.%$

eFigure 23. Publication bias

Legends: Trim-and-fill analysis for included trials to explore potential publication bias



Filled funnel plot with pseudo 95% confidence limits

eReferences

- Mant J, McManus RJ, Roalfe A, et al. Different systolic blood pressure targets for people with history of stroke or transient ischaemic attack: PAST-BP (Prevention After Stroke--Blood Pressure) randomised controlled trial. BMJ. 2016;352:i708.
- 2. Yusuf S, Diener HC, Sacco RL, et al. Telmisartan to prevent recurrent stroke and cardiovascular events. N Engl J Med. 2008;359(12):1225-1237.
- Eriksson S, Olofsson B, Wesley P, the TEST study group. Atenolol in Secondary Prevention after Stroke. Cerebrovascular Diseases. 1995;5:21-25.
- PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6105 individuals with previous stroke or transient ischaemic attack. The Lancet. 2001;358(9287):1033-1041.
- 5. The Dutch TIA Trial Study Group. Trial of secondary prevention with atenolol after transient ischemic attack or nondisabling ischemic stroke. Stroke. 1993;24(4):543-548.
- Kitagawa K, Yamamoto Y, Arima H, et al. Effect of Standard vs Intensive Blood Pressure Control on the Risk of Recurrent Stroke: A Randomized Clinical Trial and Meta-analysis. JAMA Neurol. 2019;76(11):1309-1318.
- Liu L, Wang Z, Gong L, et al. Blood pressure reduction for the secondary prevention of stroke: a Chinese trial and a systematic review of the literature. Hypertens Res. 2009;32(11):1032-1040.
- Bath PM, Scutt P, Blackburn DJ, et al. Intensive versus Guideline Blood Pressure and Lipid Lowering in Patients with Previous Stroke: Main Results from the Pilot "Prevention of Decline in Cognition after Stroke Trial" (PODCAST) Randomised Controlled Trial. PLoS One. 2017;12(1):e0164608.
- The SPS3 Study Group. Blood-pressure targets in patients with recent lacunar stroke: the SPS3 randomised trial. The Lancet. 2013;382(9891):507-515.
- 10. Liu LS, Gong LS, Wang W, Blood Pressure Lowering to Prevent Recurrent Stroke Study G. Effects of blood pressure lowering treatment on stroke recurrence in patients with cerebrovascular diseases- a large-scale, randomized, placebo controlled trial. Zhonghua Xin Xue Guan Bing Za Zhi. 2005;33(7):613-617.
- 11. Chapman N, Huxley R, Anderson C, et al. Effects of a perindopril-based blood pressure-lowering regimen on the risk of recurrent stroke according

to stroke subtype and medical history: the PROGRESS Trial. Stroke. 2004;35(1):116-121.