

## 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

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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

Quality assessment							Summary of findings				Quality
							Event, No./Total, No.		Effect		
Outcomes, No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Publication bias	More intensive	Less intensive	Relative (95% CI)	Absolute	
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

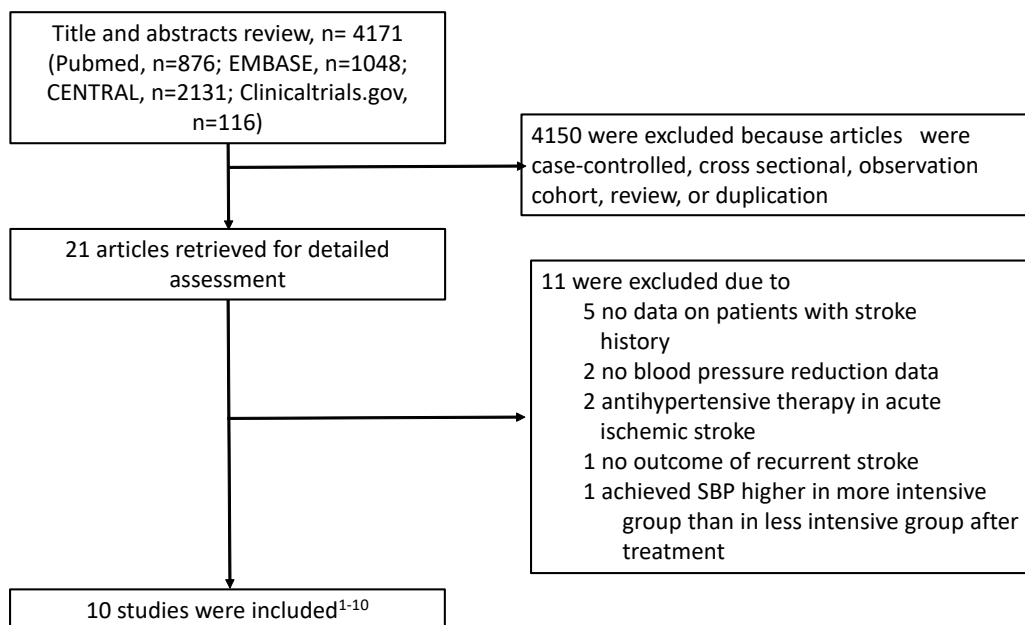
									0.68)		
Fatal or disabling stroke, n=6	RCT	No serious limitations	some inconsistency	No serious indirectness	some imprecision	Undetected	253/8537	334/8539	0.76 (0.64-0.89)	9 fewer per 1000 (4-14)	Moderate
Myocardial infarction, n=9	RCT	No serious limitations	Serious inconsistency	No serious indirectness	Serious imprecision	Undetected	365/20344	409/20366	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	120/10816	1.05 (0.82-1.35)	Not significant	Low

RCT: randomized clinical trial



## eFigure 1. Study selection

Legends: Flow of study selection.



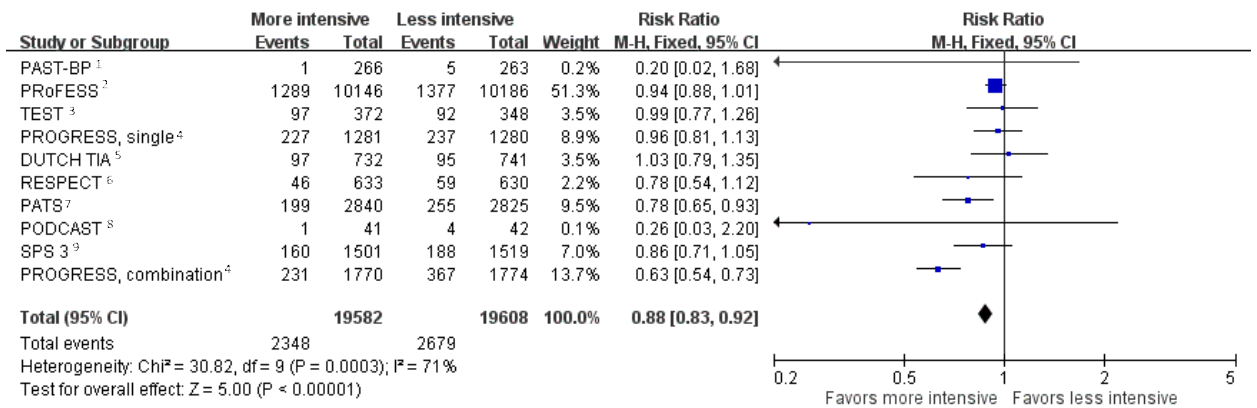
## eFigure 2. Risk of bias

Legends: Risk of bias for included trials.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
DUTCH TIA <sup>5</sup>							
Liu et al <sup>10</sup>							
PAST-BP <sup>1</sup>							
PATS <sup>7</sup>							
PODCAST <sup>8</sup>							
PRoFESS <sup>3</sup>							
PROGRESS <sup>4</sup>							
RESPECT <sup>6</sup>							
SPS <sup>3</sup>							
TEST <sup>3</sup>							

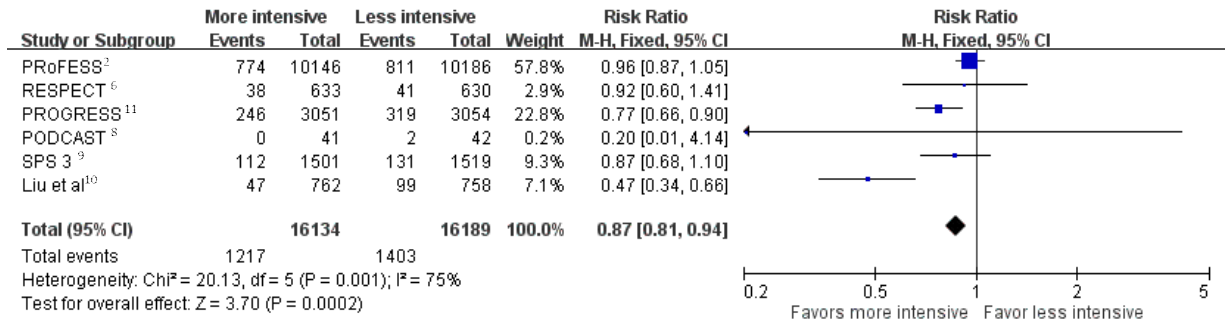
### eFigure 3: Major cardiovascular events

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

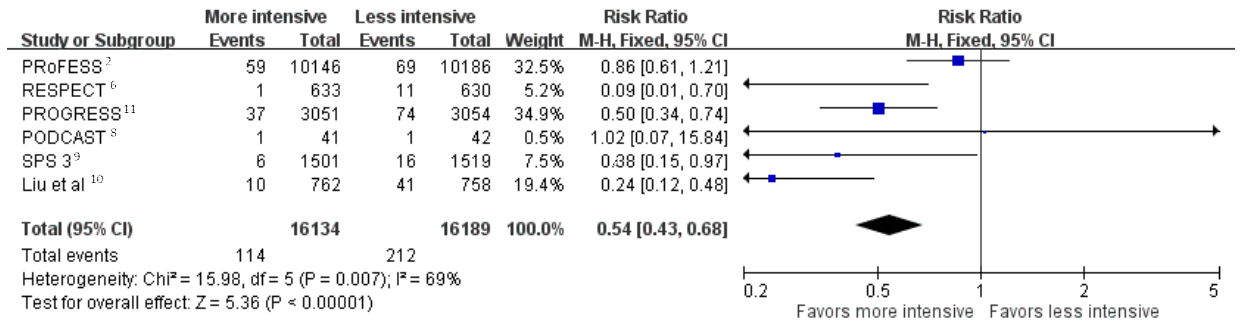
Legends: Relative risk with 95% confidence interval of recurrent ischemic stroke in more intensive vs less intensive blood pressure lowering in patients with stroke or transient ischemic attack.





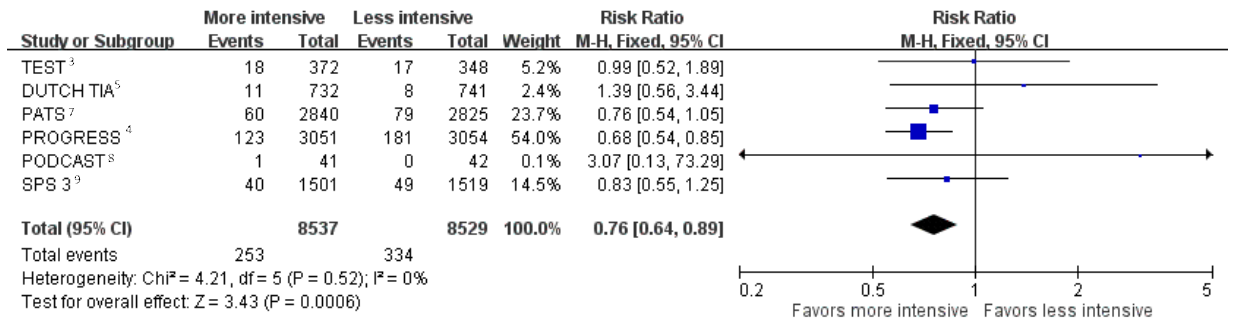
## eFigure 5. Hemorrhagic stroke

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.



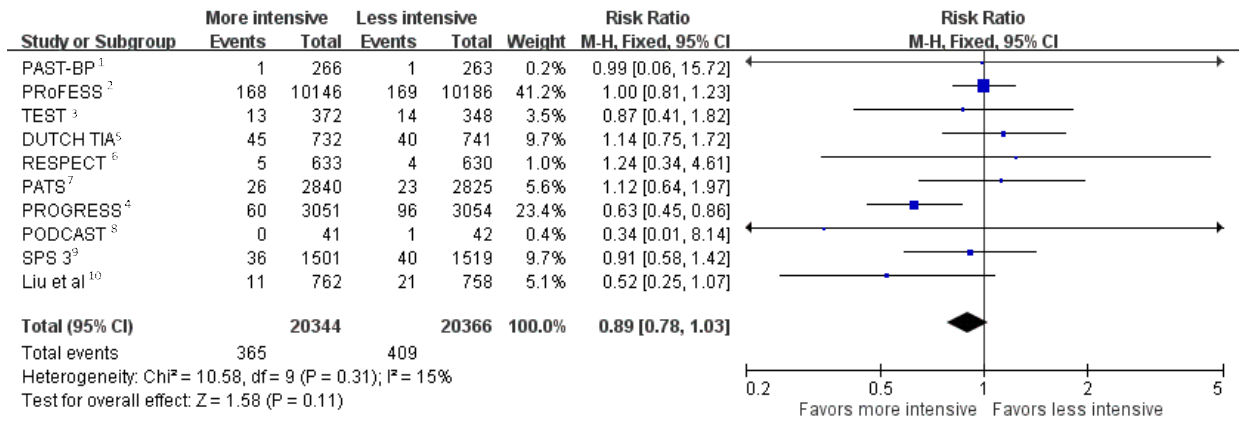
## eFigure 6. Fatal or disabling stroke

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.



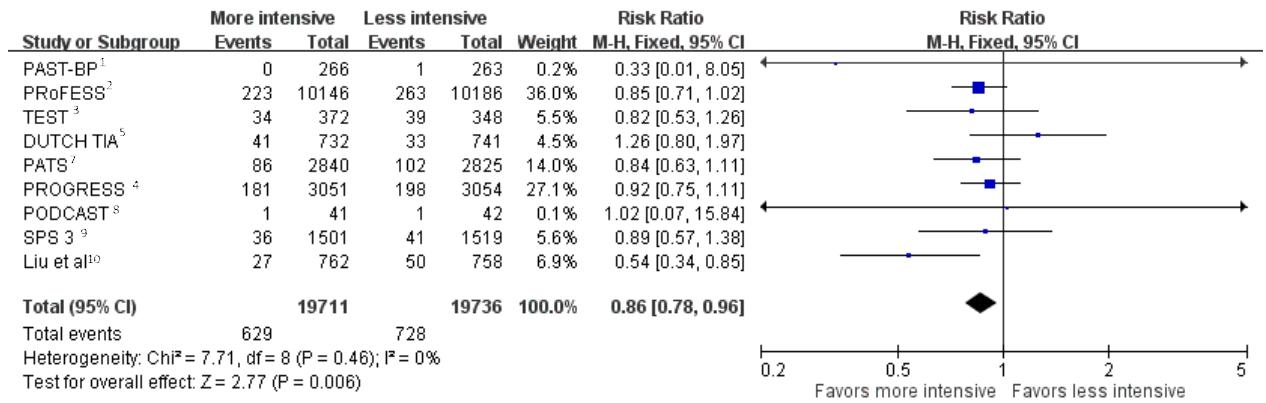
## eFigure 7. Myocardial infarction

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.



## eFigure 8. Death from cardiovascular causes

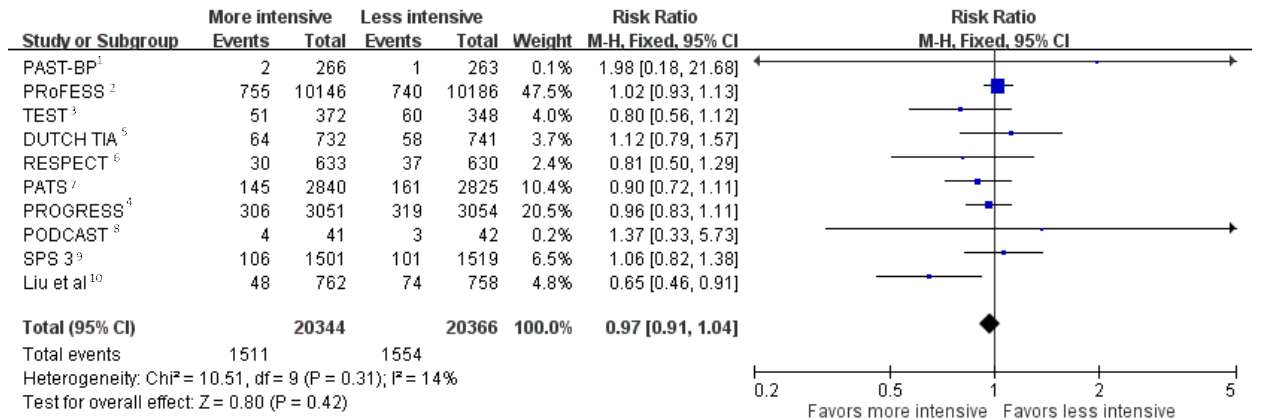
Legends: Relative risk with 95% confidence interval of death from cardiovascular causes in more intensive vs less intensive blood pressure lowering in patients with stroke or transient ischemic attack.



## eFigure 9. Death from any cause

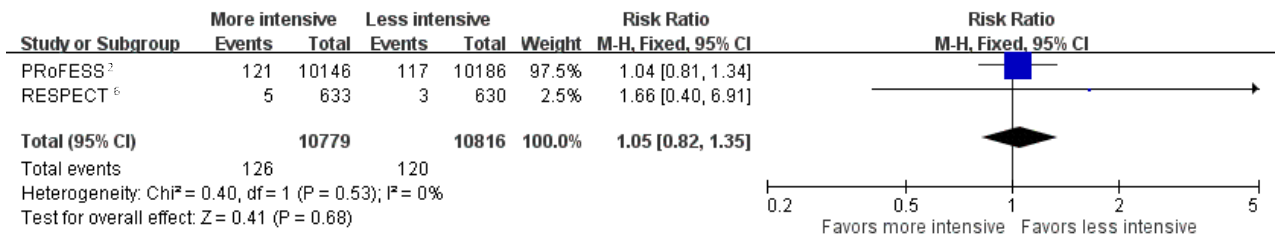
Legends: Relative risk with 95% confidence interval of death from any cause in more intensive vs less intensive

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



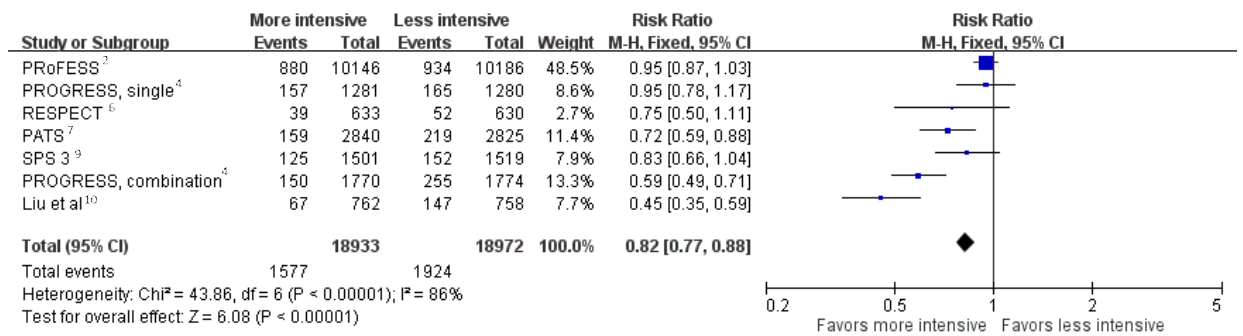
## eFigure 10. Heart failure

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.



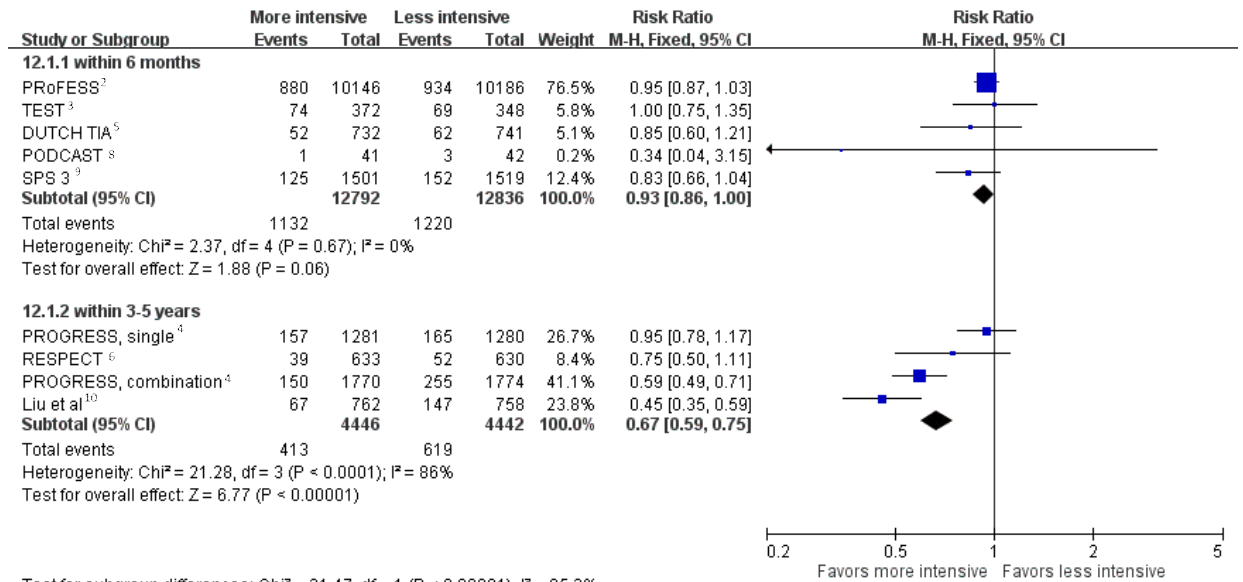
## eFigure 11. Sensitivity testing

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

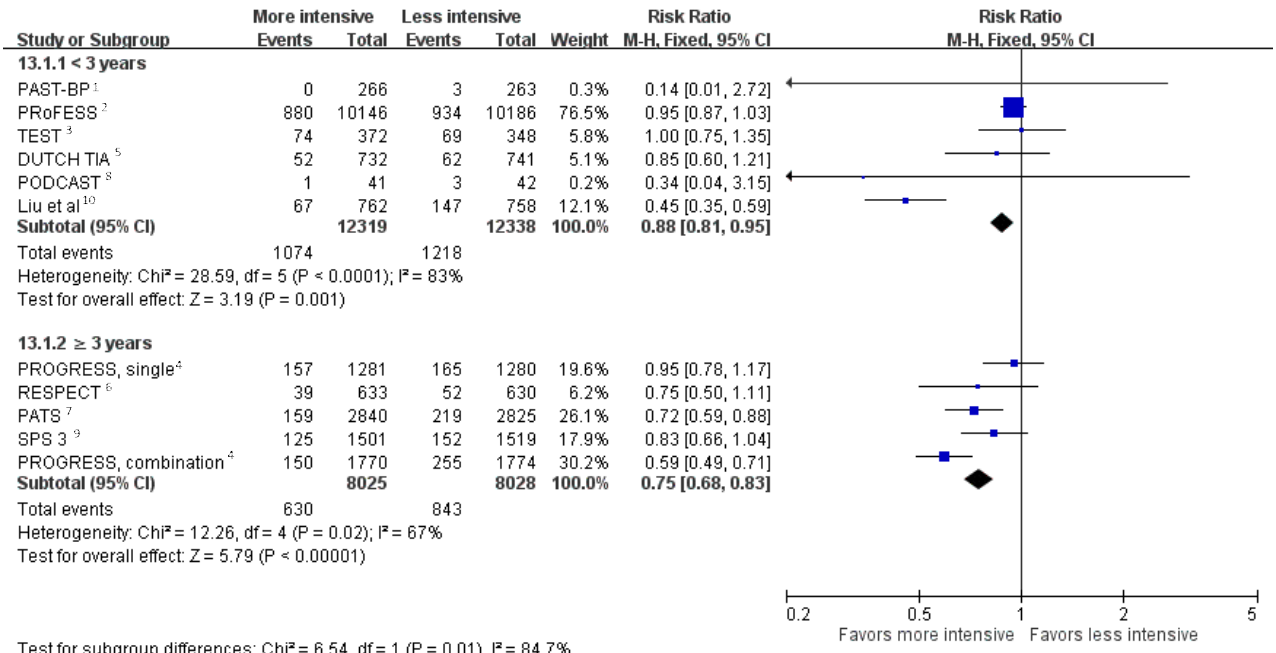
Legends: Relative risk with 95% confidence interval of recurrent stroke in more intensive vs less intensive blood pressure lowering in patients with stroke or transient ischemic attack with randomization within 6 months from stroke vs within 3-5 years from stroke.





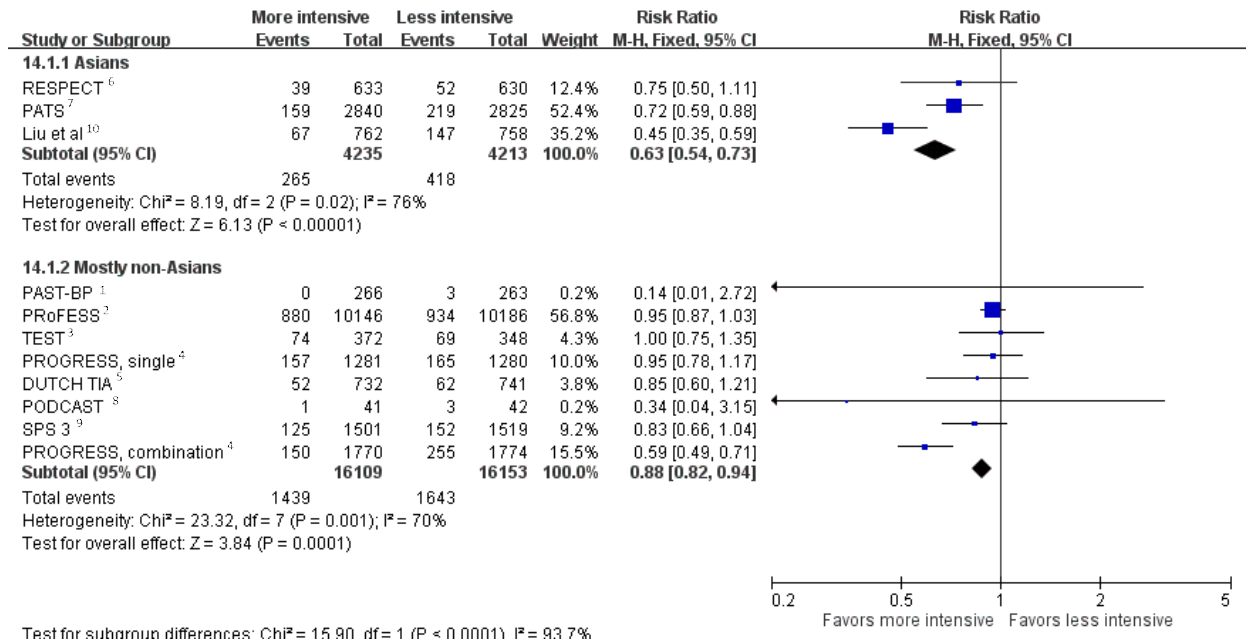
## eFigure 13. Study duration

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 ≥ 3 years.



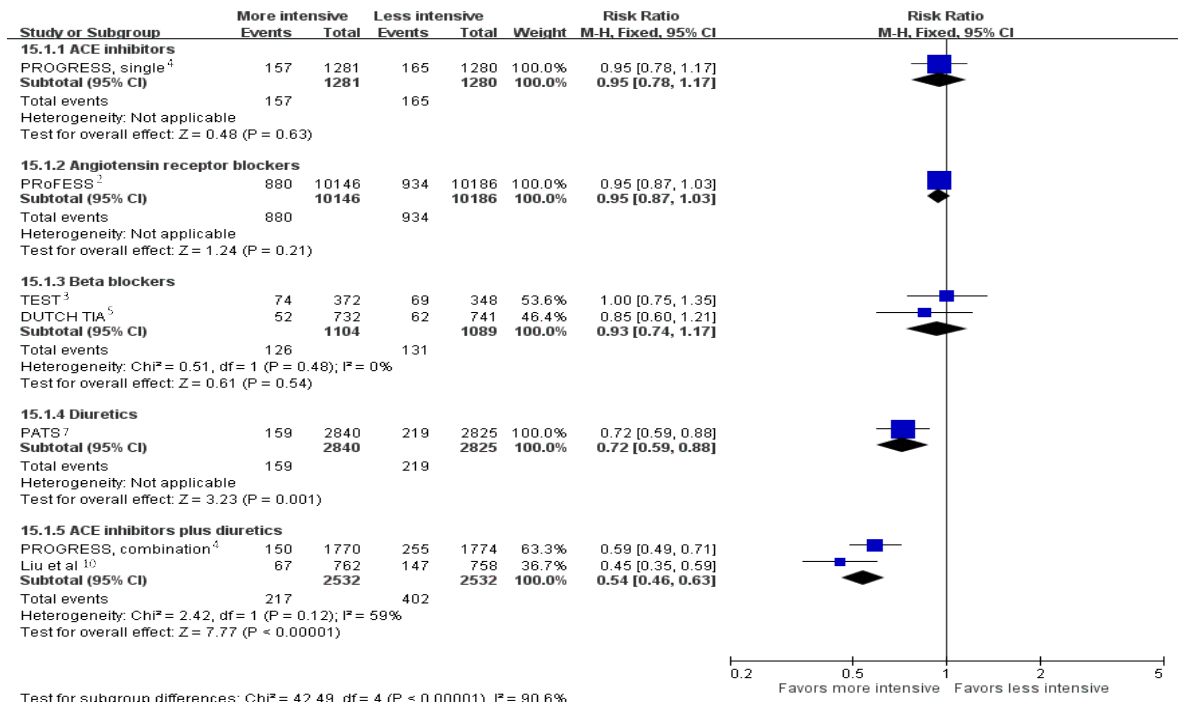
## eFigure 14. Ethnicity

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.



## eFigure 15. Antihypertensive drugs used in more intensive treated group

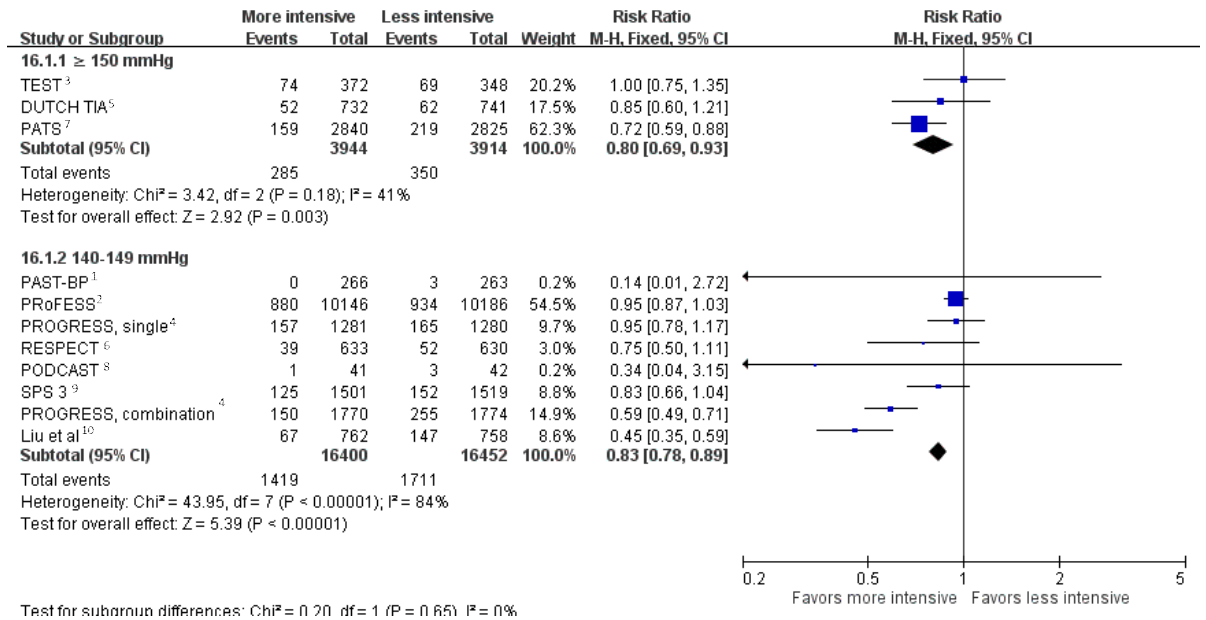
Legends: Relative risk with 95% confidence interval of recurrent stroke in more intensive vs less intensive blood pressure lowering in patients with stroke or transient ischemic attack for antihypertensive drugs used in the more intensive treated arm (angiotensin-converting enzyme [ACE] inhibitors vs angiotensin receptor blockers vs beta blockers vs diuretics vs ACE 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  $\geq 150$  mmHg vs 140-149 mmHg.

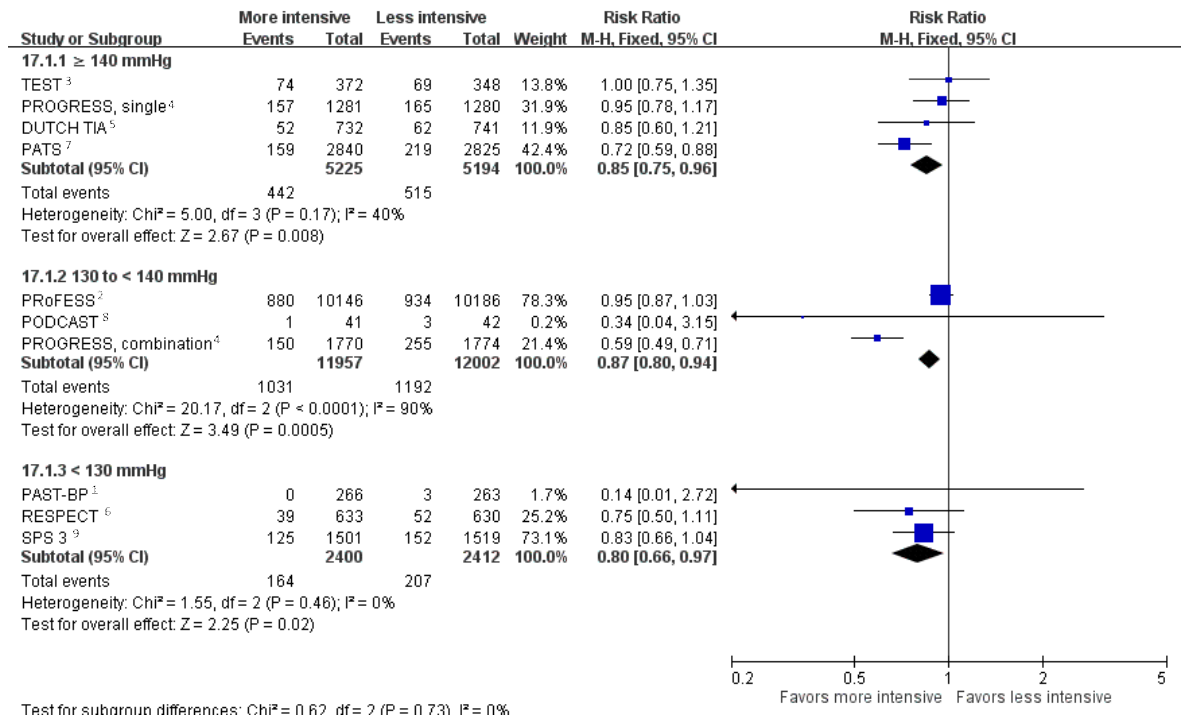
SBP: systolic blood pressure



## 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 ( $\geq 140$  mmHg vs 130 to  $< 140$  mmHg vs  $< 130$  mmHg).

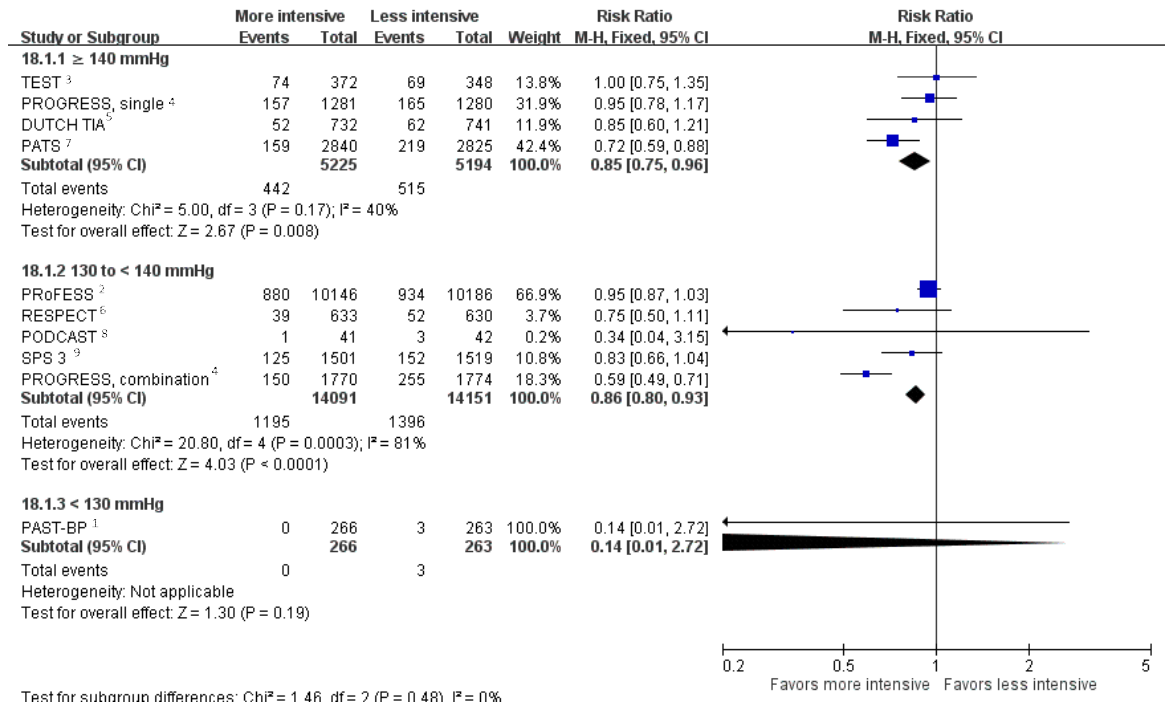
SBP: systolic blood pressure



## eFigure 18. Achieved SBP in less intensive treated group

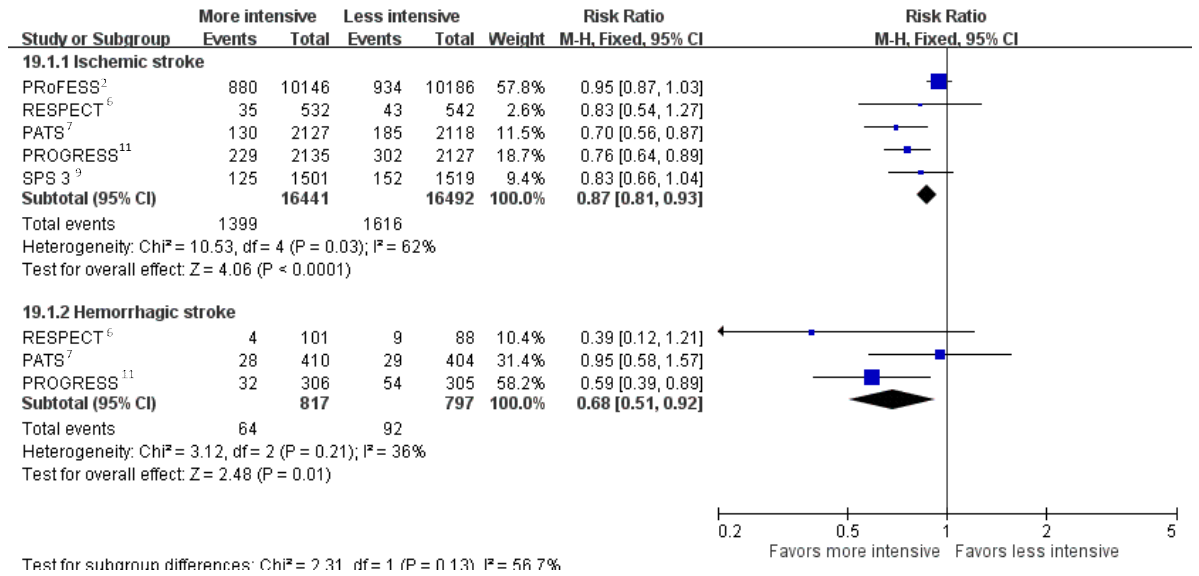
Legends: Relative risk with 95% confidence interval of recurrent stroke in more intensive vs less intensive blood pressure lowering in patients with stroke or transient ischemic attack with achieved SBP levels in the less intensive blood pressure lowering group ( $\geq 140$  mmHg vs 130 to  $< 140$  mmHg vs  $< 130$  mmHg).

SBP: systolic blood pressure



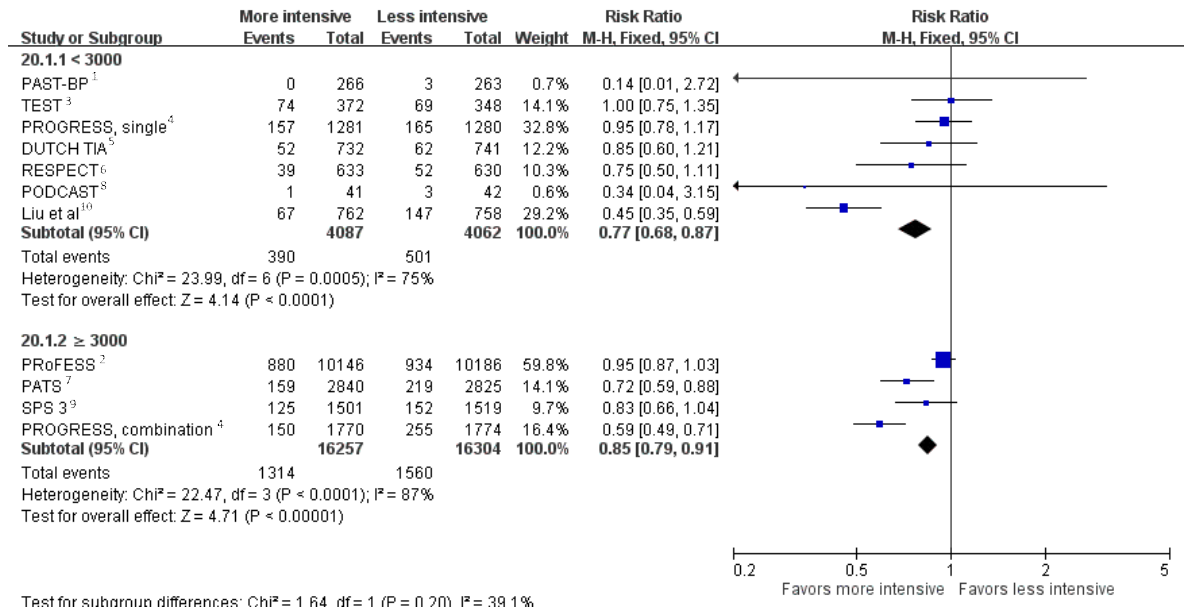
## eFigure 19. Entry event

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



## eFigure 20. Sample size

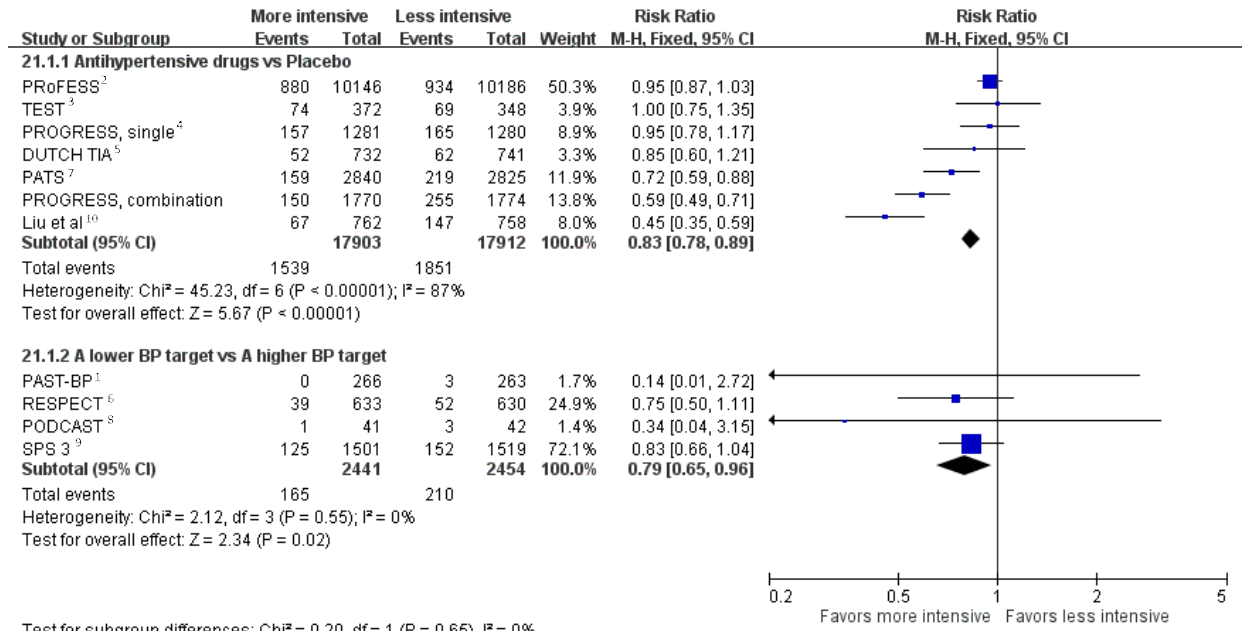
Legends: Relative risk with 95% confidence interval of recurrent stroke in more intensive vs less intensive blood pressure lowering in patients with stroke or transient ischemic attack with sample size < 3000 vs ≥ 3000 patients.





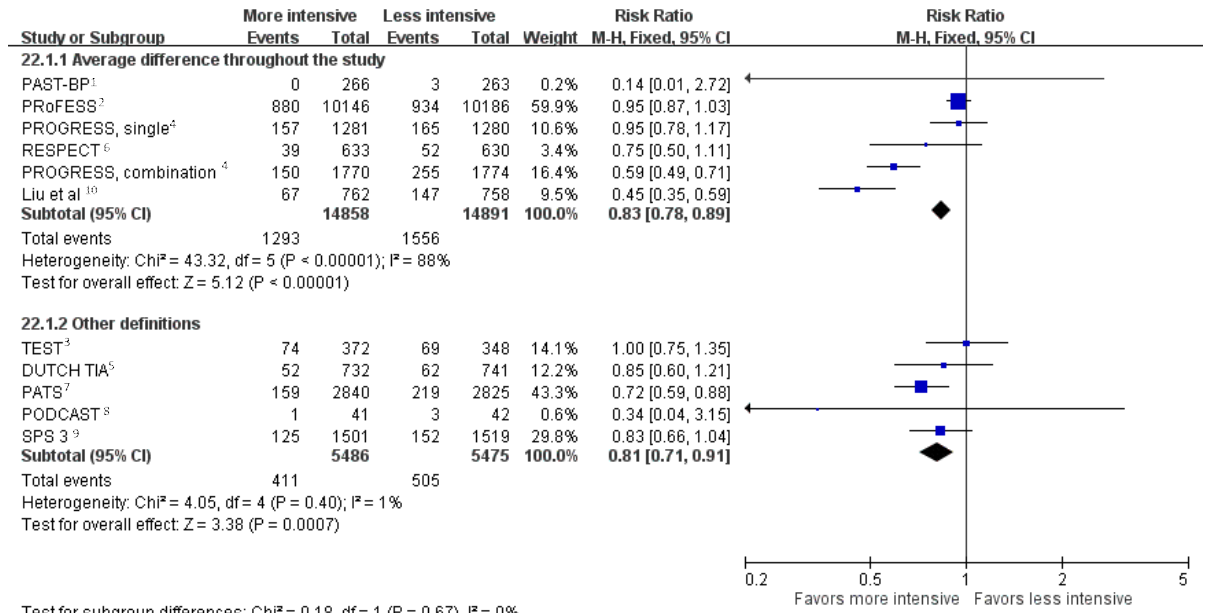
## eFigure 21. Study design

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.



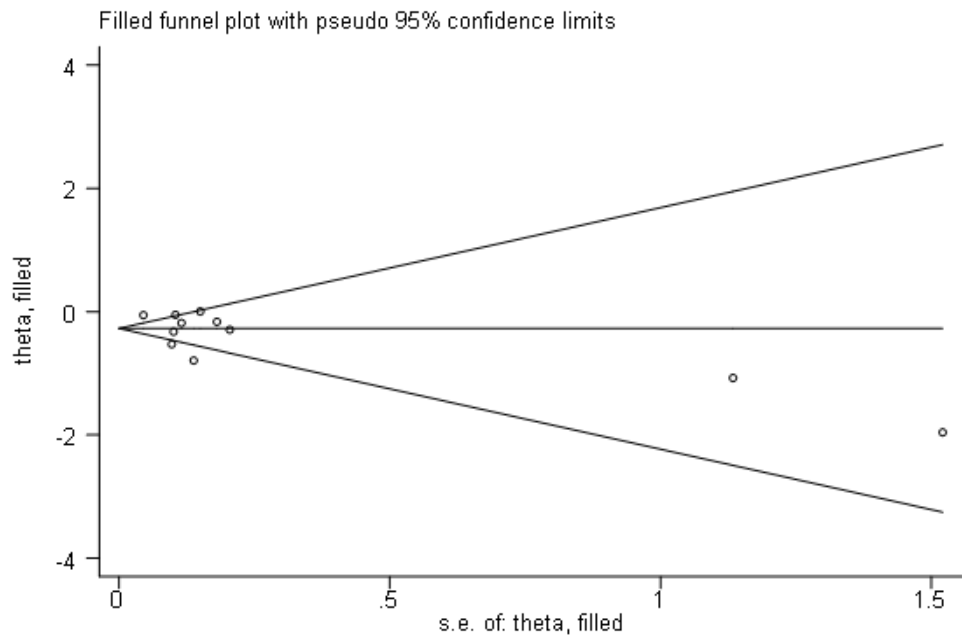
## eFigure 22. Definition of differential blood pressure reduction

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.



### eFigure 23. Publication bias

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



## eReferences

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