



**Ιατρική Σχολή - Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών**

**Πρόγραμμα Μεταπτυχιακών Σπουδών «Καρδιομεταβολική Ιατρική»**

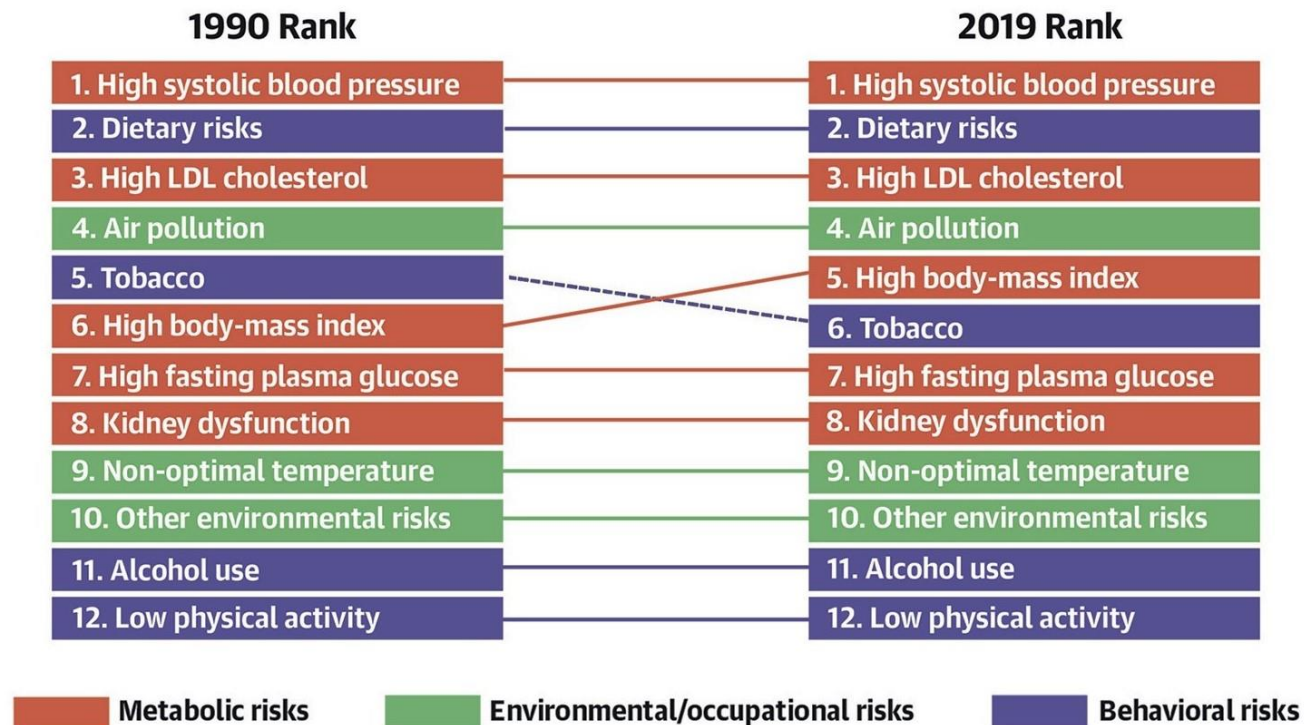
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Παθολόγος**

**Επιμελήτης Β' ΓΝΑ Αλεξάνδρα  
ESH Hypertension Specialist**

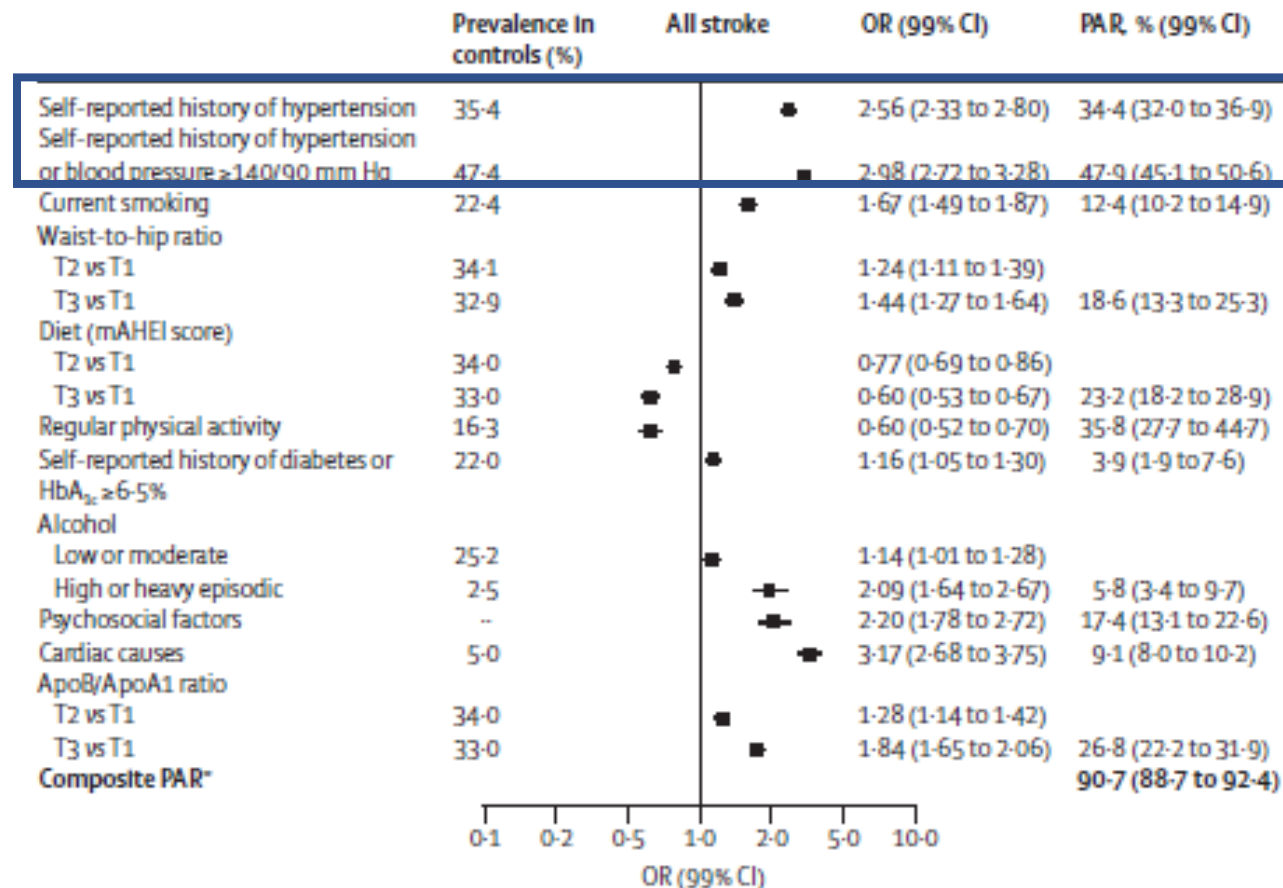
**Αγγειακά Εγκεφαλικά Επεισόδια και Αρτηριακή Υπέρταση:  
Θεραπευτική Αντιμετώπιση στην Οξεία Φάση και τη Δευτερογενή Πρόληψη**

- 1,1 εκατ. άτομα στην Ευρώπη πάσχουν από ένα αγγειακό εγκεφαλικό επεισόδιο (ΑΕΕ)/ έτος
- 15 εκατ. άτομα παγκοσμίως πάσχουν από ΑΕΕ/ έτος
- 5 εκατ. άτομα πεθαίνουν από ΑΕΕ/ 3<sup>η</sup> αιτία θνησιμότητας σε ανεπτυγμένες χώρες
- 5 εκατ. άτομα με αναπηρία
  
- **Ποσοστό υποτροπής** ενός ισχαιμικού ΑΕΕ: **9-15%** μετά από 1 έτος, **27-40%** στα 10 έτη
- Άτομα με ΑΕΕ μεγάλου αγγείου: 22% πιθανότητα οξέος στεφανιαίου επεισοδίου εντός 10 ετών

## CVD Burden Attributable to Modifiable Risk Factors



Αρτηριακή υπέρταση: ο σημαντικότερος τροποποιήσιμος παράγοντας κινδύνου για ΑΕΕ- μελέτη INTERSTROKE 2



Επίπτωση της μείωσης της ΑΠ στον κίνδυνο εμφάνισης ΑΕΕ και στεφανιαίας νόσου σε άτομα με ιστορικό ΑΕΕ

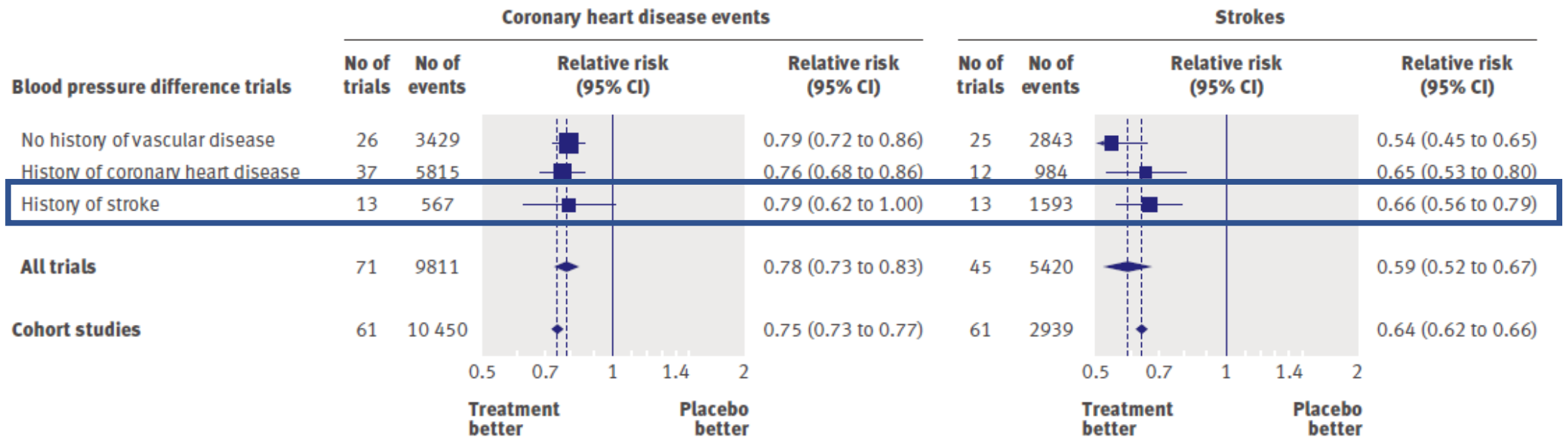
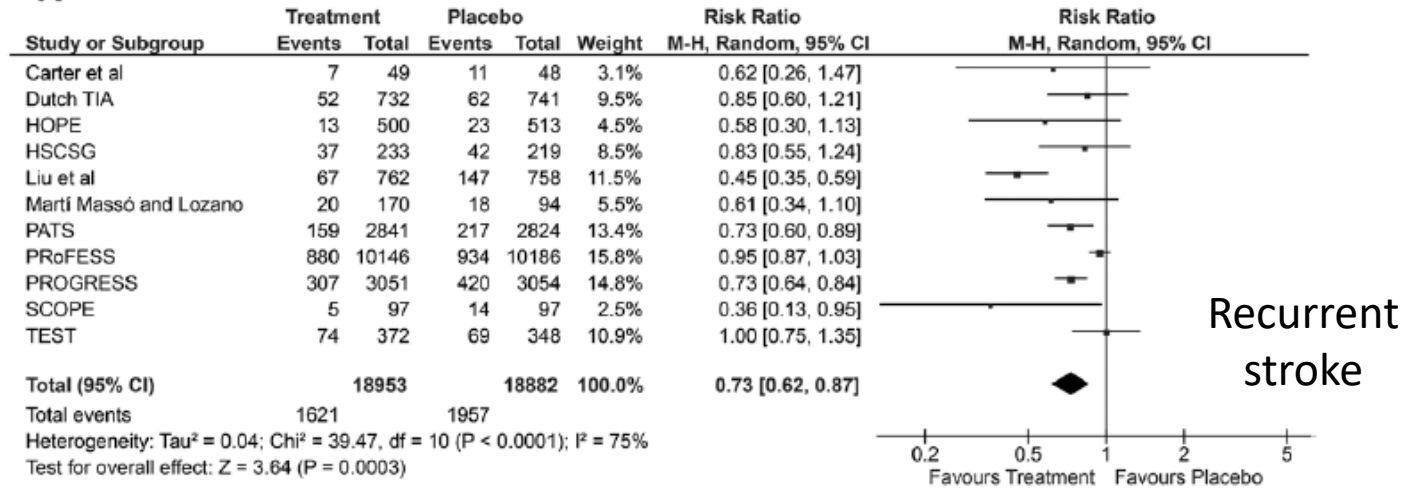


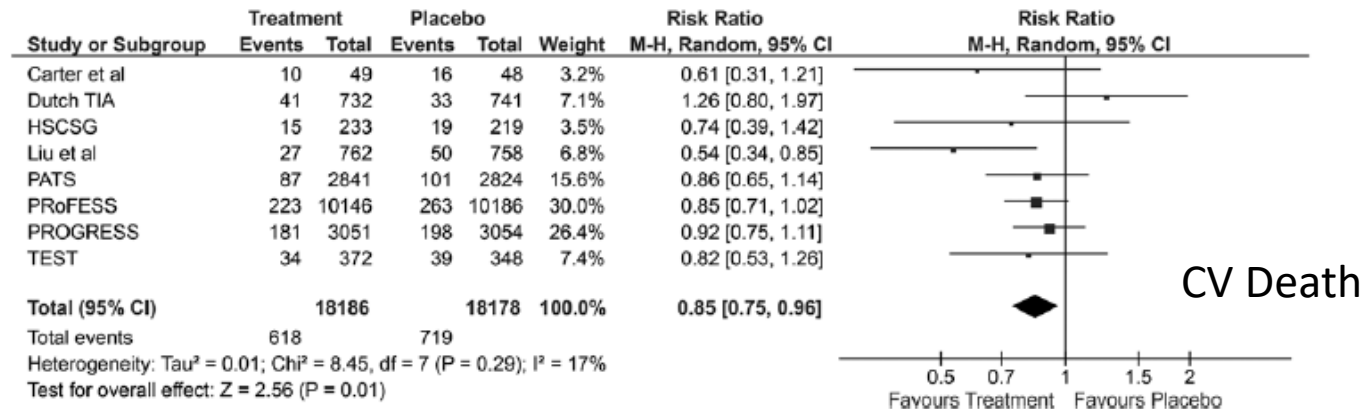
Fig 2| Relative risk estimates of coronary heart disease events and stroke for a blood pressure reduction of 10 mm Hg systolic or 5 mm Hg diastolic in the blood pressure difference trials and in epidemiological cohort studies. (Total number of trials is fewer than the sum of the three categories as five included participants with and without vascular disease; see web extra figures 2a-f for individual trial results and summary estimates)

## Μείωση της ΑΠ και δευτερογενής πρόληψη ΑΕΕ

**A**



**B**



## Αγγειακό εγκεφαλικό επεισόδιο / παθοφυσιολογική ταξινόμηση & συχνότητα

Ισχαιμικό ΑΕΕ - 80%

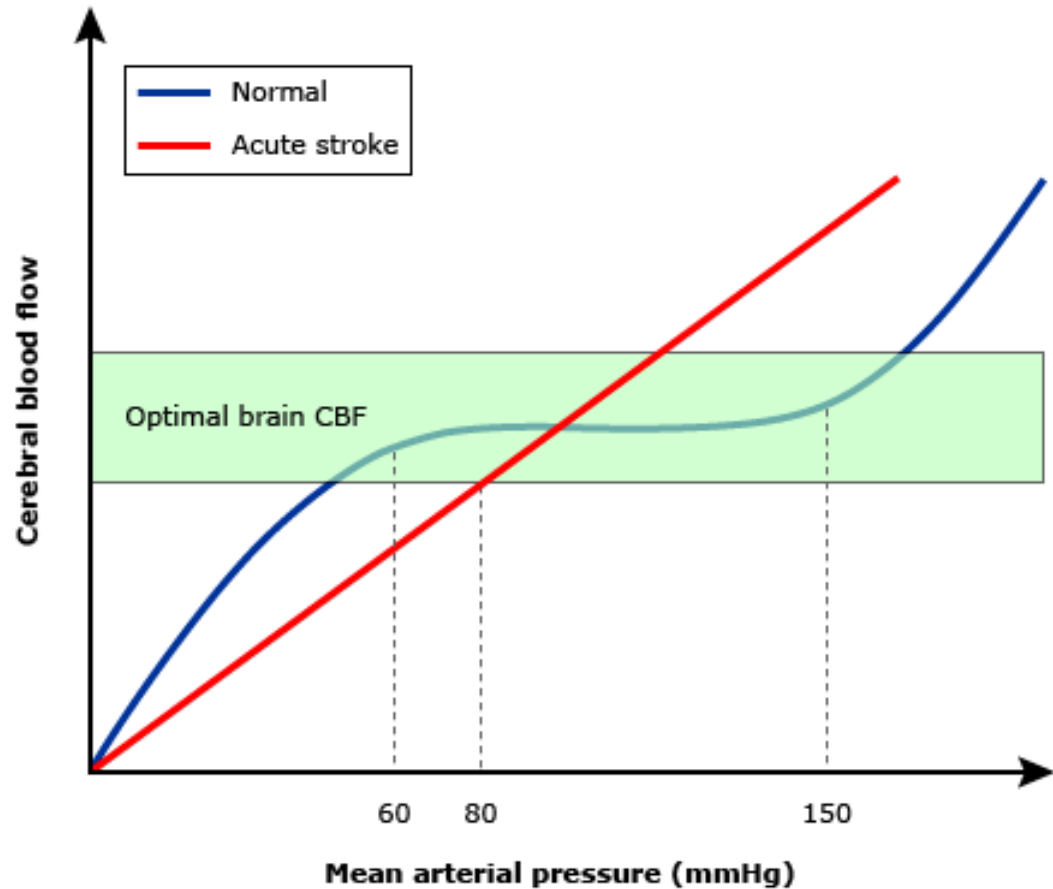
- Αθηρωμάτωση - atheromatosis (15-35 %)
- Καρδιοεμβολικά - cardioembolic (18-33 %)
- Κενοτοπιώδη - lacunar (17-25 %)
- Κρυπτογενή - undetermined etiology (12-37 %)
- Διάφορα αίτια - other determined etiology (5 %)

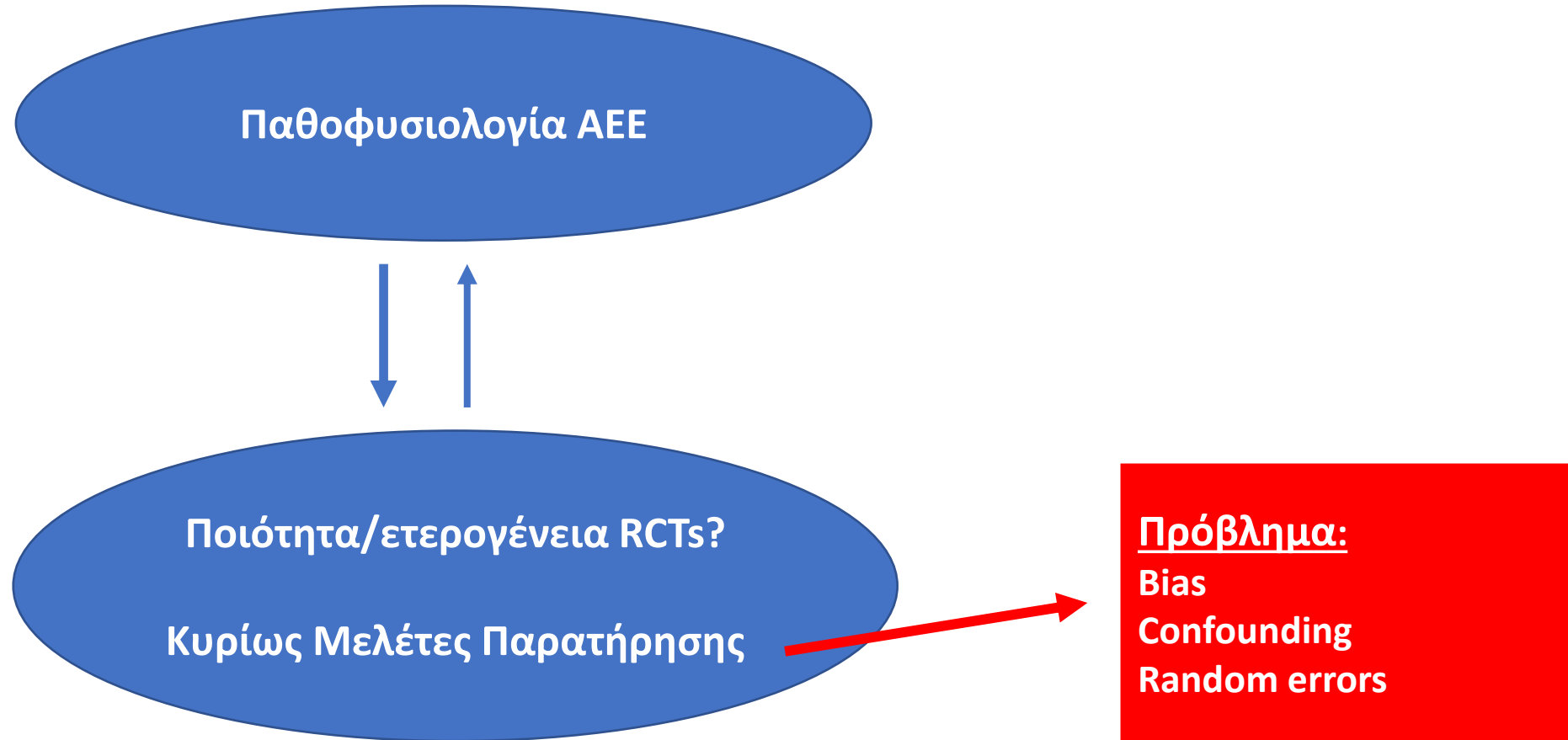
Αιμορραγικό ΑΕΕ - 20%

- Υποαραχνοειδής α. - subarachnoid (5-7 %)
- Ενδοεγκεφαλική α. - intracerebral (15 %)



## Αγγειακό εγκεφαλικό επεισόδιο/ αυτορρύθμιση εγκεφαλικής κυκλοφορίας





**Σε ασθενή με οξύ ΑΕΕ:**

- **Πότε ξεκινώ αντιυπερτασική αγωγή;**
- **Ποιος είναι ο στόχος της αρτηριακής πίεσης;**
- **Ποια αντιυπερτασικά φάρμακα να χρησιμοποιήσω;**

2023 ESH Guidelines for the management of  
arterial hypertension

*The Task Force for the management of arterial hypertension  
of the European Society of Hypertension*

Endorsed by the International Society of Hypertension (ISH) and the European  
Renal Association (ERA)

Guideline

## European Stroke Organisation (ESO) guidelines on blood pressure management in acute ischaemic stroke and intracerebral haemorrhage

**Else Charlotte Sandset**<sup>1,2</sup> , **Craig S Anderson**<sup>3,4</sup> ,  
**Philip M Bath**<sup>5</sup>, **Hanne Christensen**<sup>6</sup>, **Urs Fischer**<sup>7</sup>,  
**Dariusz Gąsecki**<sup>8</sup>, **Avtar Lal**<sup>9</sup>, **Lisa S Manning**<sup>10</sup>,  
**Simona Sacco**<sup>11</sup> , **Thorsten Steiner**<sup>12,13</sup>  and  
**Georgios Tsivgoulis**<sup>14,15</sup>

**EUROPEAN  
STROKE JOURNAL**

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*Guideline*

# European Stroke Organisation (ESO) guideline on pharmacological interventions for long-term secondary prevention after ischaemic stroke or transient ischaemic attack

Jesse Dawson<sup>1</sup> , Yannick Béjot<sup>2,3</sup>, Louisa M Christensen<sup>4</sup> , Gian Marco De Marchis<sup>5</sup> , Martin Dichgans<sup>6,7</sup>, Guri Hagberg<sup>8,9</sup>, Mirjam R Heldner<sup>10</sup>, Haralampos Milionis<sup>11</sup>, Linxin Li<sup>12</sup> , Francesca Romana Pezzella<sup>13</sup>, Martin Taylor Rowan<sup>1</sup>, Cristina Tiu<sup>14,15</sup>  and Alastair Webb<sup>12</sup> 

**EUROPEAN  
STROKE JOURNAL**

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Οξεία Φάση

«Υποξεία» Φάση

Χρόνια Φάση

«Υπερ»-Οξεία Φάση

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

Χορήγηση TTS glyceryl trinitrate / SBP>140 ή 120 mmHg

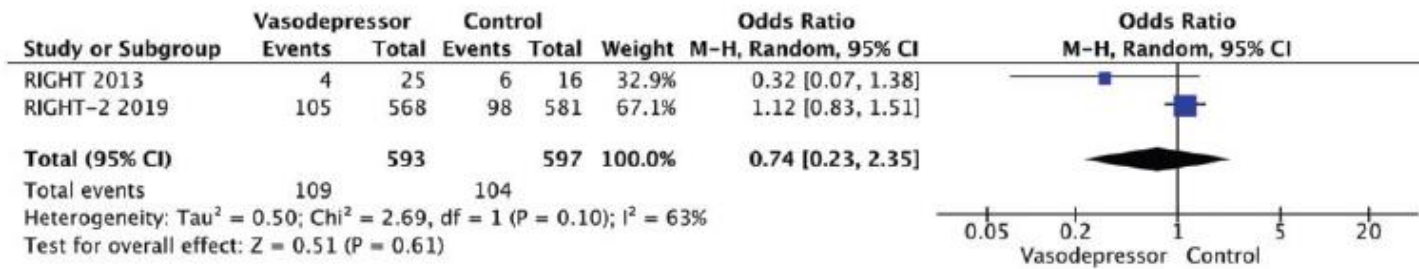


Figure 1. Effect of pre-hospital blood pressure lowering by any vasopressor drug compared to no drug on mortality at three months following symptom onset.

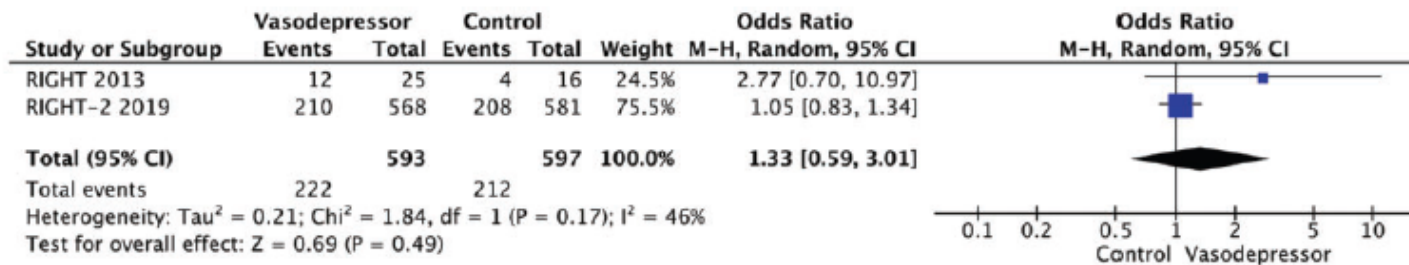


Figure 2. Effect of pre-hospital blood pressure lowering by any vasopressor drug compared to no drug on good functional outcome (mRS scores 0-2) at three months following symptom onset.



«Υπερ»-Οξεία Φάση

ESO guidelines, 2021

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

**Recommendation**

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** ↓?

**Expert consensus statement**

Due to the potential harm in patients with intracerebral haemorrhage prehospital treatment with glyceryl trinitrate should be avoided. Vote 9 of 10.



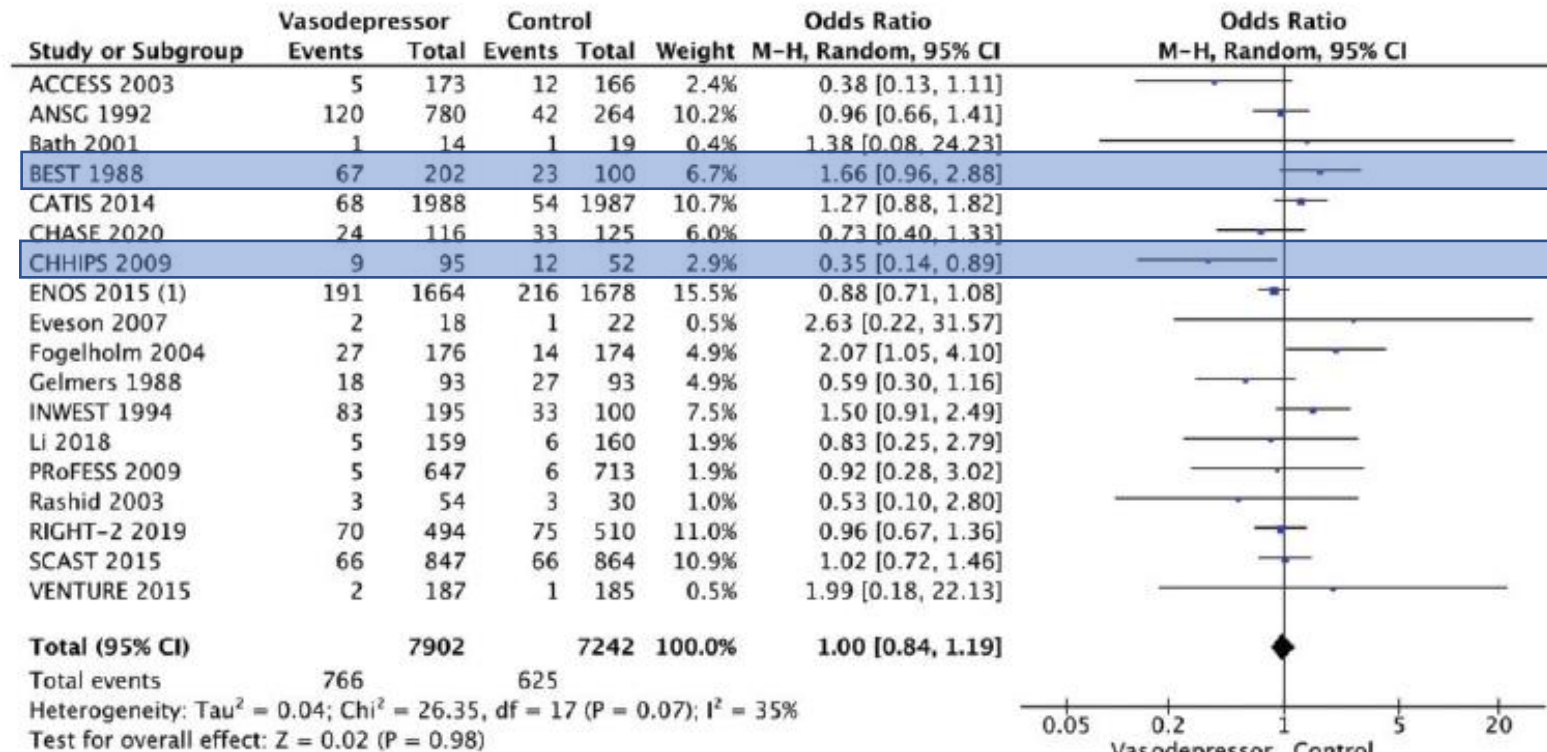
**Οξεία Φάση**

In hospitalized patients with AIS **not treated** with reperfusion therapies (intravenous thrombolysis or mechanical thrombectomy), does BP lowering with any vasodepressor drug compared to no drug improve outcome?

**Σε άτομα χωρίς άλλες επείγουσες καταστάσεις που να απαιτούν πτώση της αρτηριακής πίεσης**

**Οξεία Φάση**

Hospitalized patients with AIS not treated with reperfusion therapies



Propranolol

Lisinopril  
or  
labetalol

- Μετα-ανάλυση 18 RCTs
- 15.144 άτομα
- Θνητότητα 3-6 μήνες μετά το ΑΕΕ

Footnotes

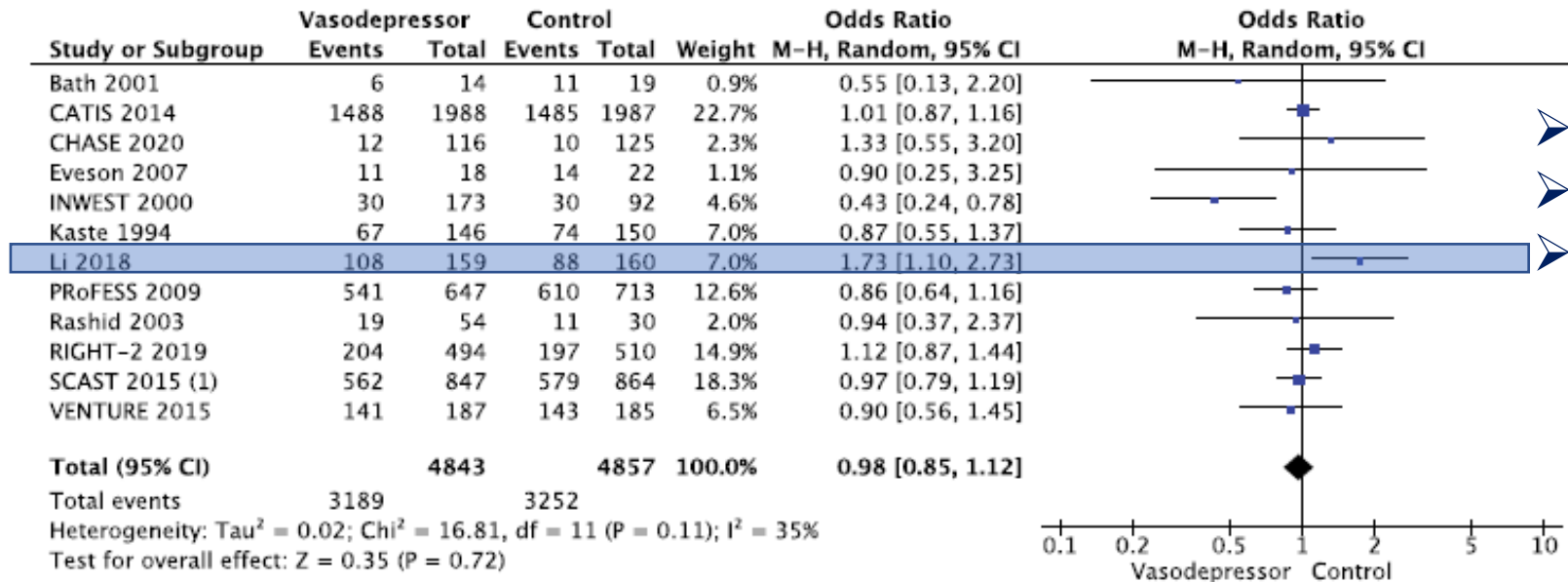
(1) Not treated with tPA: ~90%

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 reperfusion therapies.

**Οξεία Φάση**

Hospitalized patients with AIS not treated with reperfusion therapies

iv Nimodipine



- Μετα-ανάλυση 12 RCTs
- 9.340 άτομα
- Λειτουργική κατάσταση στους 3-6 μήνες (mRS 0-2)

Footnotes

(1) Not treated with tPA: ~85%

**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.

**Οξεία Φάση**

Hospitalized patients with AIS **not treated** with reperfusion therapies

**Recommendations**

In hospitalised patients with acute ischaemic stroke and blood pressure < 220/110 mm Hg 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** ⊕⊕⊕

Strength of recommendation: **Weak** ↓?

**Συγχυτικοί παράγοντες**

- Κατηγορία αντιυπερτασικού φαρμάκου
- Στόχος ΑΠ
- Στιγμή έναρξης αγωγής (<4 hr έως 5 ημ.)
- Αιτιολογία ΑΕΕ
- Πρότερα επίπεδα ΑΠ (αποκλεισμός από RCTs ατόμων με ΣΑΠ>220)
- Ρυθμός και μέγεθος πτώσης της ΑΠ

**Οξεία Φάση**

Hospitalized patients with AIS **not treated** with reperfusion therapies

**Expert consensus statement**

In patients with acute ischaemic stroke not treated with intravenous thrombolysis or mechanical thrombectomy and blood pressure  $>220/120$  mm Hg, careful blood pressure reduction ( $<15\%$  systolic blood pressure reduction in 24 hours) is reasonable and likely to be safe. No specific blood pressure lowering agent can be recommended. Vote 10 of 10.

## Οξεία Φάση

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
In patients with acute intracerebral haemorrhage: <ul style="list-style-type: none"> <li>● Immediate BP lowering is not recommended for patients with SBP &lt;220 mmHg.<sup>509–513</sup></li> <li>● In patients with SBP ≥220 mmHg, careful acute BP lowering with i.v. therapy to &lt;180 mmHg should be considered.<sup>509–513</sup></li> </ul>	III	A
	IIa	B
In acute ischaemic stroke, routine BP lowering with antihypertensive therapy is not recommended, <sup>516,517</sup> with the exceptions: <ul style="list-style-type: none"> <li>● In patients with acute ischaemic stroke who are eligible for i.v. thrombolysis, BP should be carefully lowered and maintained at &lt;180/105 mmHg for at least the first 24 h after thrombolysis.<sup>514,515</sup></li> <li>● In patients with markedly elevated BP who do not receive fibrinolysis, drug therapy may be considered, based on clinical judgement, to reduce BP by 15% during the first 24 h after the stroke onset.</li> </ul>	III	A
	IIa	B
	IIb	C
In hypertensive patients with an acute cerebrovascular event, antihypertensive treatment is recommended: <ul style="list-style-type: none"> <li>● Immediately for TIA.<sup>526</sup></li> <li>● After several days in ischaemic stroke.<sup>526</sup></li> </ul>	I	A
	I	A
In all hypertensive patients with ischaemic stroke or TIA, an SBP target range of 120–130 mmHg should be considered. <sup>244,524,526</sup>	IIa	B
The recommended antihypertensive drug treatment strategy for stroke prevention is a RAS blocker plus a CCB or a thiazide-like diuretic. <sup>338</sup>	I	A



Οξεία Φάση

In patients with acute ischaemic stroke **not treated** with reperfusion therapies and with clinical deterioration, does induced hypertension by any vasopressor drug compared to no drug improve outcome?

In patients with acute ischaemic stroke not treated with reperfusion therapies who experience clinical deterioration, we suggest **against the routine use of vasopressor drugs to increase blood pressure.**

Quality of evidence: **Very low** ⊕

Strength of recommendation: **Weak** ↓↓

Οξεία Φάση

**Expert Consensus Statement**

In patients with acute ischaemic stroke **not treated** with reperfusion therapies and with clinical deterioration where a haemodynamic mechanism is 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.

Οξεία Φάση

Hospitalized patients with AIS **treated** with reperfusion therapies (intravenous thrombolysis with or without mechanical thrombectomy), does blood pressure lowering therapies compared to control improve outcome?

We suggest maintaining BP below **185/110 mmHg** before bolus and below **180/105 mmHg** 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** ↑?

No RCTs suggest this cut-off

Evidence only from non-randomized real world data

Οξεία Φάση

Hospitalized patients with AIS **treated** with reperfusion therapies

In patients with AIS 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 ↓?

Οξεία Φάση

Hospitalized patients with AIS **treated** with reperfusion therapies

Intensive blood pressure reduction with intravenous thrombolysis therapy for acute ischaemic stroke (ENCHANTED): an international, randomised, open-label, blinded-endpoint, phase 3 trial

2227 patients  
Intensive arm SBP 130-140 mmHg  
VS  
SBP <180 mmHg

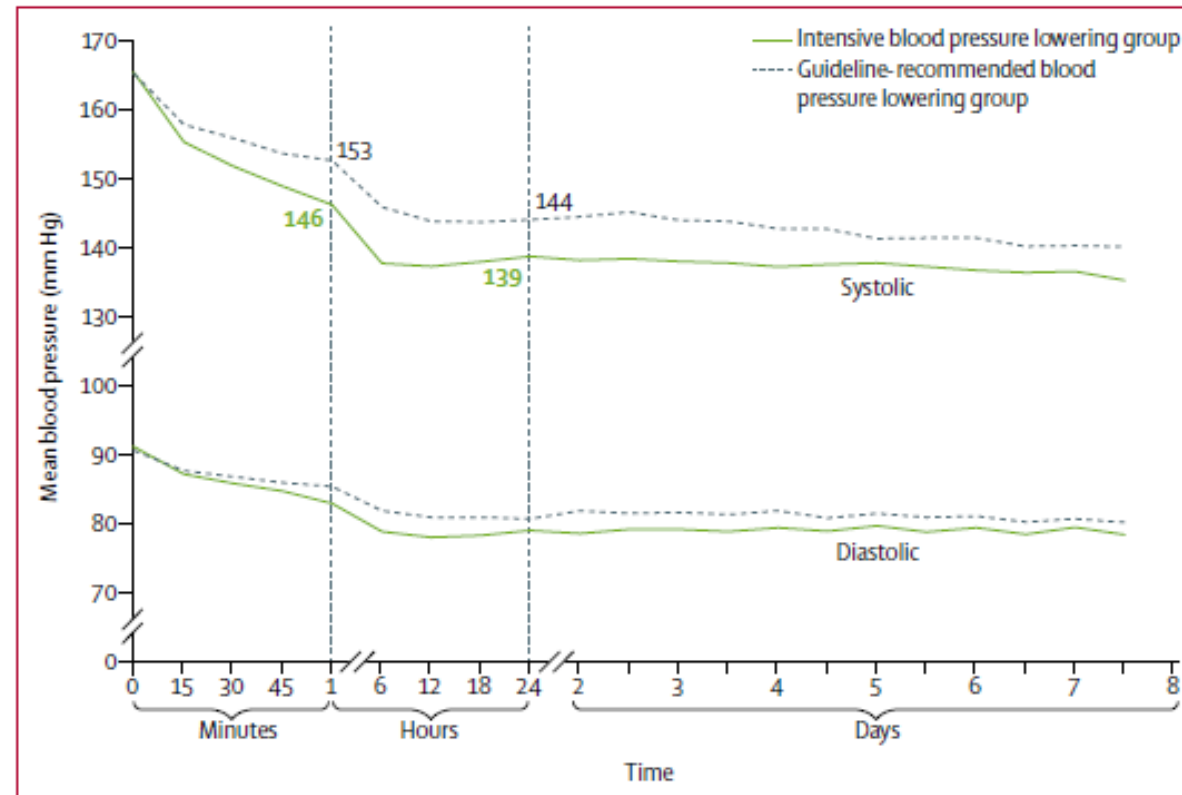


Figure 2: Mean systolic and diastolic blood pressure from randomisation to day 7

Blood pressure values are shown for intensive and guideline-recommended blood pressure lowering groups based on recordings at 15-min intervals for the first hour after randomisation (time 0), hourly from hours 1 to 6, 6-hourly until 24 h, and twice daily until day 7. Mean between-group difference in systolic blood pressure over 24 h was 5.5 mm Hg (95% CI 4.5–6.4).

**Οξεία Φάση**

Hospitalized patients with AIS **treated** with reperfusion therapies

Intensive blood pressure reduction with intravenous thrombolysis therapy for acute ischaemic stroke (ENCHANTED): an international, randomised, open-label, blinded-endpoint, phase 3 trial

**2227 patients**  
**Intensive arm SBP 130-140 mmHg**  
**VS**  
**SBP <180 mmHg**

	Intensive blood pressure lowering group	Guideline-recommended blood pressure lowering group	Treatment effect	p value
Improvement in mRS according to category* at day 90	..	..	<u>1.01 (0.87-1.17)†, 0.97 (0.83-1.13)†‡</u>	<u>0.8702†, 0.7171†‡</u>
0	307/1072 (28.6%)	312/1108 (28.2%)	..	..
1	267/1072 (24.9%)	264/1108 (23.8%)	..	..
2	138/1072 (12.9%)	160/1108 (14.4%)	..	..
3	110/1072 (10.3%)	120/1108 (10.8%)	..	..
4	98/1072 (9.1%)	104/1108 (9.4%)	..	..
5	50/1072 (4.7%)	60/1108 (5.4%)	..	..
6	102/1072 (9.5%)	88/1108 (7.9%)	..	..
<b>Death or disability (mRS score 2-6) within 90 days</b>				
Intention-to-treat analysis				
Unadjusted	498/1072 (46.5%)	532/1108 (48.0%)	<u>0.94 (0.79-1.11)</u>	<u>0.4660</u>
Adjusted	498/1072 (46.5%)	531/1106 (48.0%)	<u>0.94 (0.78-1.14)‡</u>	<u>0.5508</u>
Per-protocol analysis				
Unadjusted	451/958 (47.1%)	499/1028 (48.5%)	<u>0.94 (0.79-1.12)</u>	<u>0.5141</u>
Adjusted	451/958 (47.1%)	498/1026 (48.5%)	<u>0.96 (0.79-1.16)‡</u>	<u>0.6595</u>

**Οξεία Φάση**

Hospitalized patients with AIS **treated** with reperfusion therapies

Intensive blood pressure reduction with intravenous thrombolysis therapy for acute ischaemic stroke (ENCHANTED): an international, randomised, open-label, blinded-endpoint, phase 3 trial

**2227 patients**  
Intensive arm SBP 130-140 mmHg  
vs  
SBP <180 mmHg

	Intensive blood pressure lowering group	Guideline-recommended blood pressure lowering group	Treatment effect	p value
Any intracranial haemorrhage*	160/1081 (14.8%)	209/1115 (18.7%)	<u>0.75 (0.60-0.94)</u>	<u>0.0137</u>
Any intracranial haemorrhage reported as a serious adverse event	59/1081 (5.5%)	100/1115 (9.0%)	<u>0.59 (0.42-0.82)</u>	<u>0.0017</u>

Table 3: Safety outcomes at day 90

**However! In a post-hoc analysis:  
Intensive BP lowering increased 3 month mortality vs guideline BP lowering**

**Οξεία Φάση**

In patients with AIS caused by large vessel occlusion and undergoing mechanical thrombectomy (with or without thrombolysis), does BP lowering with any vasodepressor drug compared to no drug improve outcome?

We suggest keeping blood pressure **below 180/105 mmHg** 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** ↑?

**Thresholds have been arbitrarily adopted based on evidence regarding BP management in the setting of IVT for AIS.**

**The rationale of this recommendation is to avoid reperfusion hemorrhages associated with elevated blood pressure**



Οξεία Φάση

In patients with acute ischaemic stroke due to large vessel occlusion we suggest against actively reducing systolic BP <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 thrombolysis) systolic BP drops should be avoided.

Quality of evidence: **Very low** ⊕

Strength of recommendation: **Strong** ↓↓

**Οξεία Φάση**

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

**Expert consensus statement**

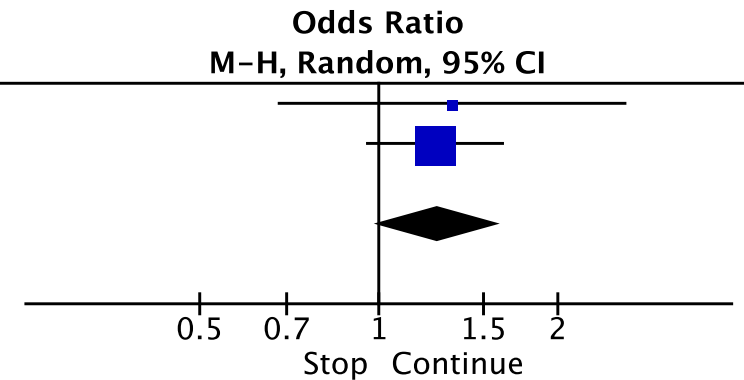
In patients with acute ischaemic stroke we suggest stopping previous oral BP lowering therapy in patients with dysphagia until swallowing is restored or a nasogastric tube is in place.

**Οξεία Φάση**

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

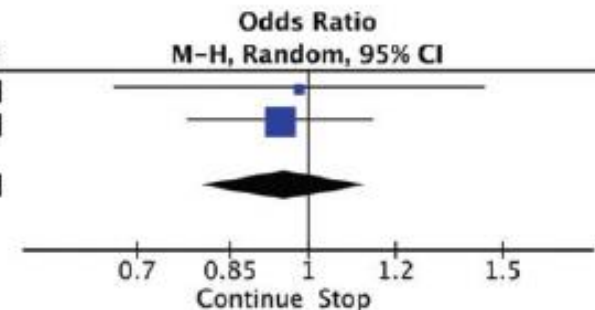
Continuing versus stopping previous antihypertensive drugs in acute ischaemic stroke and mortality

Study or Subgroup	Continue		Stop		Weight	Odds Ratio M-H, Random, 95% CI
	Events	Total	Events	Total		
COSSACS 2010	23	220	16	198	13.2%	1.33 [0.68, 2.59]
ENOS 2015	147	925	119	902	86.8%	1.24 [0.96, 1.61]
<b>Total (95% CI)</b>		<b>1145</b>		<b>1100</b>	<b>100.0%</b>	<b>1.25 [0.98, 1.60]</b>
Total events	170		135			
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.03, df = 1 (P = 0.86); I <sup>2</sup> = 0%						
Test for overall effect: Z = 1.82 (P = 0.07)						



Continuing versus stopping previous antihypertensive drugs in acute ischaemic stroke and mRS 0-2

Study or Subgroup	Continue		Stop		Weight	Odds Ratio M-H, Random, 95% CI
	Events	Total	Events	Total		
COSSACS 2010	109	220	99	198	19.9%	0.98 [0.67, 1.44]
ENOS 2015	325	925	329	902	80.1%	0.94 [0.78, 1.14]
<b>Total (95% CI)</b>		<b>1145</b>		<b>1100</b>	<b>100.0%</b>	<b>0.95 [0.80, 1.13]</b>
Total events	434		428			
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.03, df = 1 (P = 0.85); I <sup>2</sup> = 0%						
Test for overall effect: Z = 0.58 (P = 0.56)						



Οξεία Φάση

## Blood pressure lowering agents

COR IIb	LOE C-E0
Patient otherwise eligible for emergency reperfusion therapy except that BP is >185/110 mm Hg:	
Labetalol 10–20 mg IV over 1–2 min, may repeat 1 time; or	
Nicardipine 5 mg/h IV, titrate up by 2.5 mg/h every 5–15 min, maximum 15 mg/h; when desired BP reached, adjust to maintain proper BP limits; or	
Clevidipine 1–2 mg/h IV, titrate by doubling the dose every 2–5 min until desired BP reached; maximum 21 mg/h	
Other agents (eg, hydralazine, enalaprilat) may also be considered	
If BP is not maintained $\leq$ 185/110 mm Hg, do not administer alteplase	
Management of BP during and after alteplase or other emergency reperfusion therapy to maintain BP $\leq$ 180/105 mm Hg:	
Monitor BP every 15 min for 2 h from the start of alteplase therapy, then every 30 min for 6 h, and then every hour for 16 h	
If systolic BP >180–230 mm Hg or diastolic BP >105–120 mm Hg:	
Labetalol 10 mg IV followed by continuous IV infusion 2–8 mg/min; or	
Nicardipine 5 mg/h IV, titrate up to desired effect by 2.5 mg/h every 5–15 min, maximum 15 mg/h; or	
Clevidipine 1–2 mg/h IV, titrate by doubling the dose every 2–5 min until desired BP reached; maximum 21 mg/h	
If BP not controlled or diastolic BP >140 mm Hg, consider IV sodium nitroprusside	

Οξεία Φάση



**Cochrane**  
**Library**

Cochrane Database of Systematic Reviews

**Interventions for deliberately altering blood pressure in acute stroke (Review)**

Bath PMW, Krishnan K

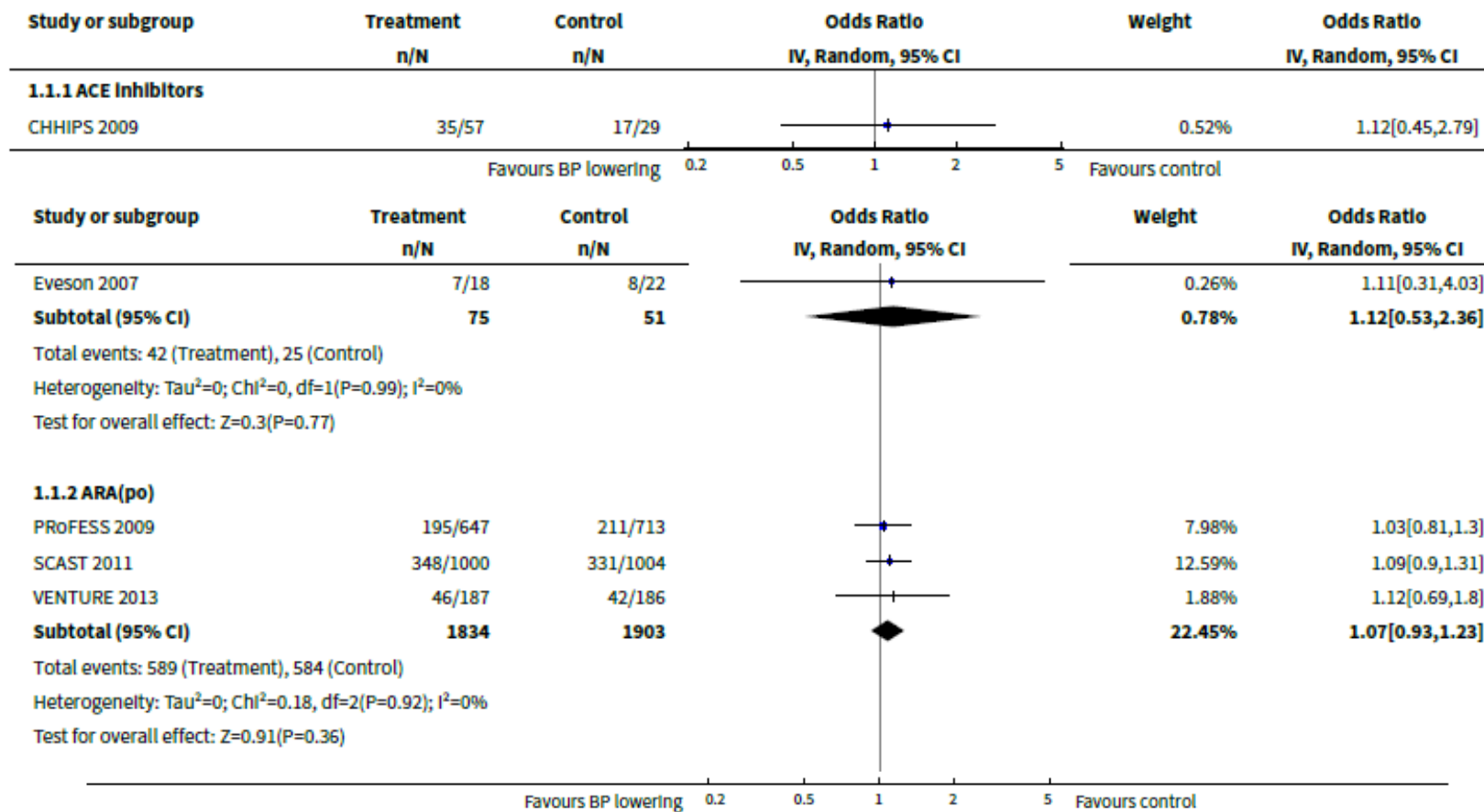
Οξεία Φάση

Twenty-one trials provided data on one or more outcomes relating to treatment with:

- ACE-I (lisinopril): (Eveson 2007; CHHIPS 2009; PIL-FAST 2013);
- ARA (candesartan, telmisartan): (ACCESS 2003; PRoFESS 2009; SCAST 2011; TAST 2013; VENTURE 2013);
- β-RA (labetalol): (CHHIPS 2009);
- CCB (nimodipine): (Uzuner 1995);
- NO donor (glyceryl trinitrate): (Bath 2000; Rashid 2003 5 mg/Rashid 2003 5/10 mg/Rashid 2003 10 mg; Willmot 2006; RIGHT 2013; ENOS 2014);

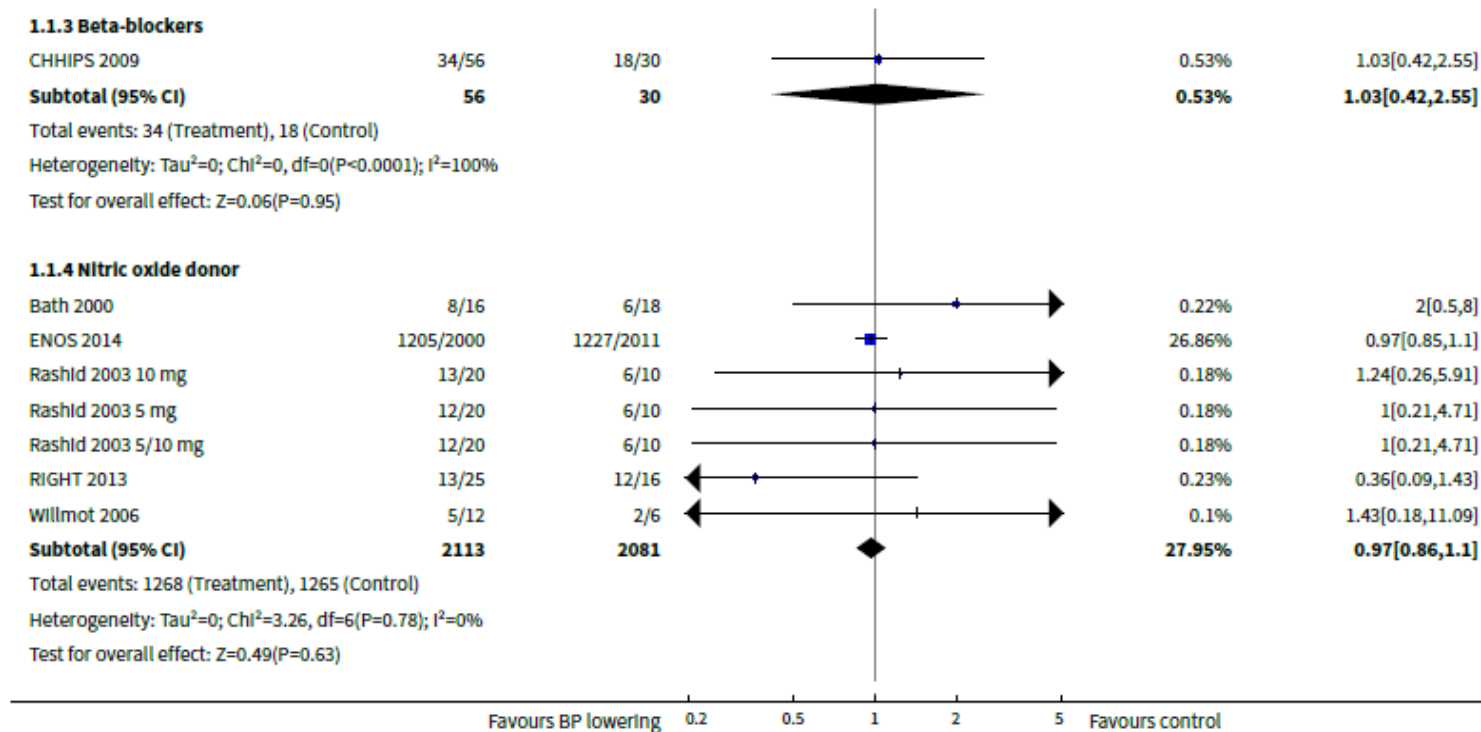
## Οξεία Φάση

**Analysis 1.1. Comparison 1 Blood pressure lowering therapy in acute stroke, Outcome 1 Death or dependency, end of trial by intervention.**



## Οξεία Φάση

**Analysis 1.1. Comparison 1 Blood pressure lowering therapy in acute stroke, Outcome 1 Death or dependency, end of trial by intervention.**





Χρόνια Φάση

**Διαχείριση Αρτηριακής Πίεσης στη δευτερογενή πρόληψη ΑΕΕ**

- **Πότε ξεκινώ αντιυπερτασική αγωγή;**
- **Ποιος είναι ο στόχος της αρτηριακής πίεσης;**
- **Ποια αντιυπερτασικά φάρμακα να χρησιμοποιήσω;**

Χρόνια Φάση

Post – stroke antihypertensive treatment - PATS study

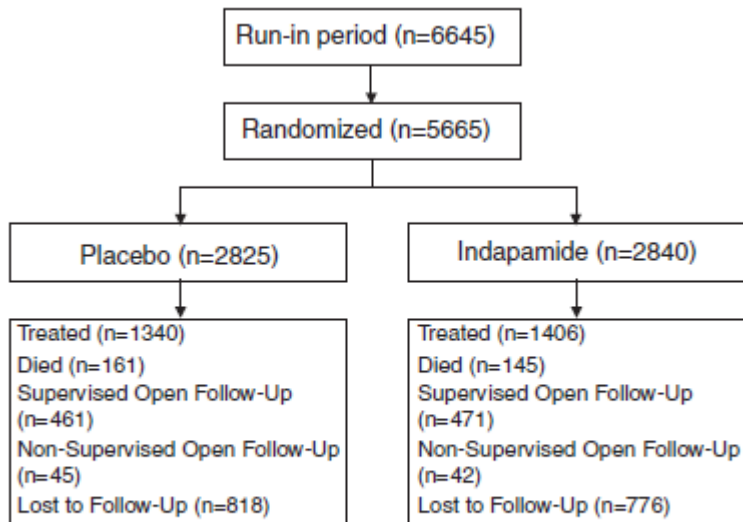


Figure 1 Profile of the Post-stroke Antihypertensive Treatment Study.

$\Delta$ \_BP: 7/4 mm Hg

Table 3 Nonfatal and fatal combined with nonfatal end points by treatment group

End point	Rate per 1000 patient-years (no. of deaths)		Difference <sup>a</sup>	
	Placebo (n=2825)	Indapamide (n=2840)	% Rate (95% CI)	P-value
<i>Nonfatal endpoints</i>				
Stroke	28.8 (143)	20.0 (103)	-31 (-46 to -11)	0.005
Myocardial infarction	2.0 (10)	1.9 (10)	-3 (-60 to 133)	0.94
Other cardiovascular	2.6 (13)	1.0 (5)	-63 (-87 to -5)	0.049
All cardiovascular	33.1 (164)	22.9 (118)	-31 (-45 to -12)	0.002
<i>Fatal plus nonfatal endpoints</i>				
Stroke	44.1 (219)	30.9 (159)	-30 (-43 to -14)	<0.001
Myocardial infarction	4.5 (23)	4.9 (26)	10 (-38 to 92)	0.76
Other cardiovascular	4.5 (23)	2.7 (14)	-41 (-70 to 15)	0.11
All cardiovascular	52.1 (258)	38.7 (199)	-25 (-38 to -11)	0.002

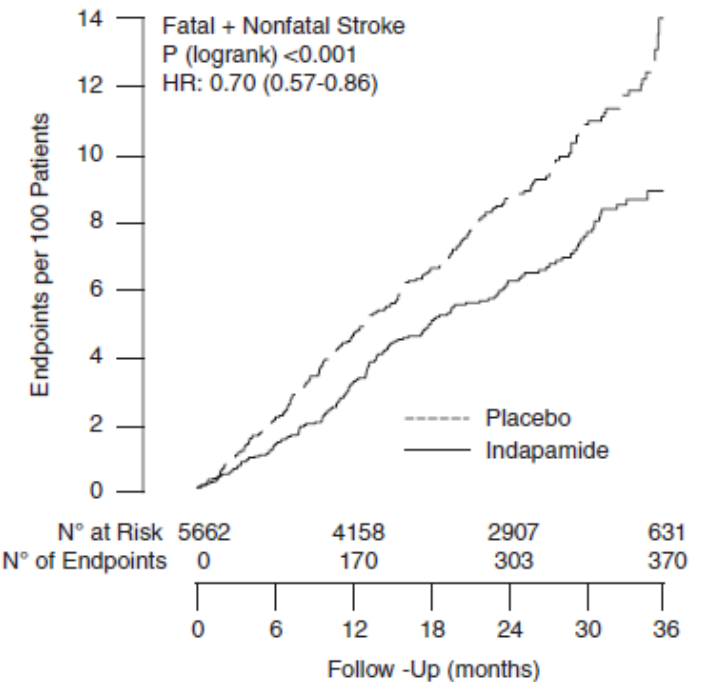
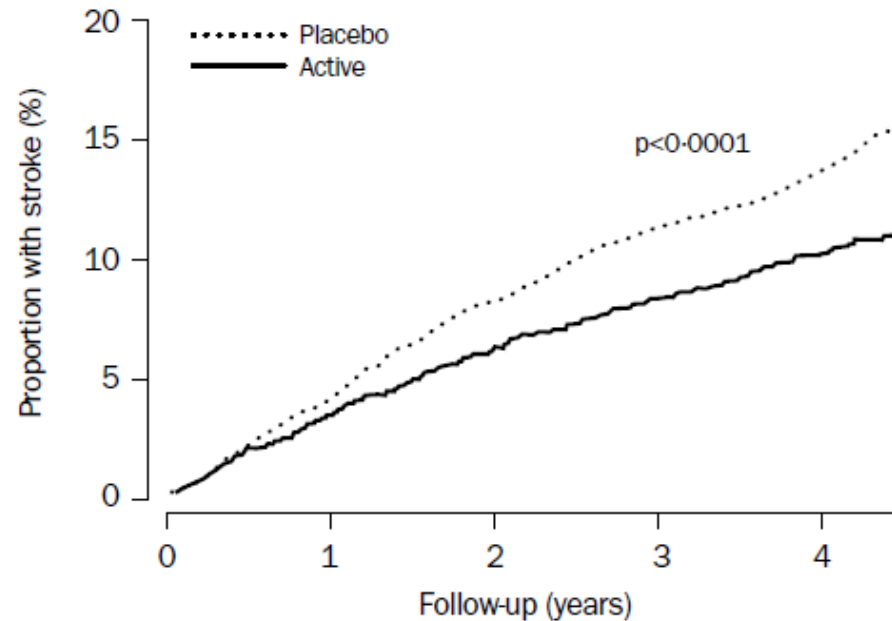


Figure 3 Cumulative incidence of fatal and nonfatal stroke recurrence by treatment group in the Post-stroke Antihypertensive Treatment Study.

## Χρόνια Φάση

- RCT placebo controlled
- 6105 άτομα με ιστορικό ΑΕΕ
- Perindopril +/- indapamide  
vs  
placebo
- 4 έτη παρακολούθηση
- Καταληκτικό σημείο: Νέο ΑΕΕ



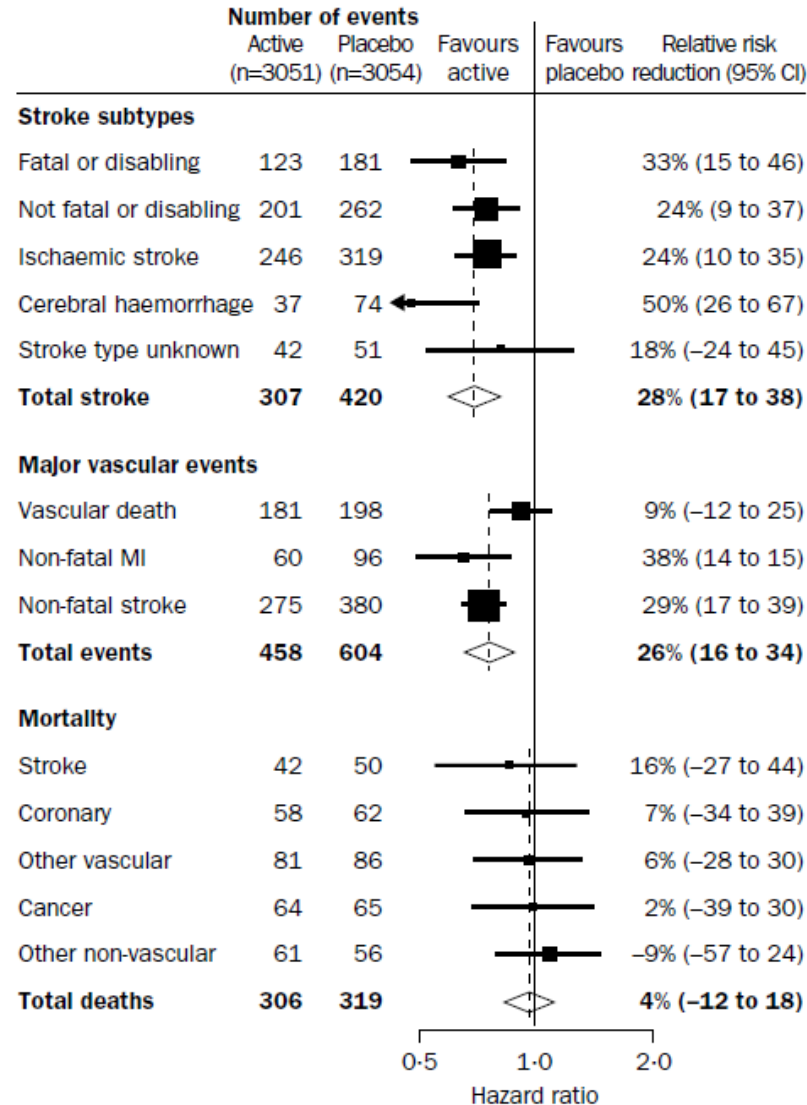
### Numbers at risk

Active	3051	2902	2765	2634	1595
Placebo	3054	2880	2707	2551	1533

Figure 3: Cumulative incidence of stroke among participants assigned active treatment and those assigned placebo

- 9/4 mm Hg

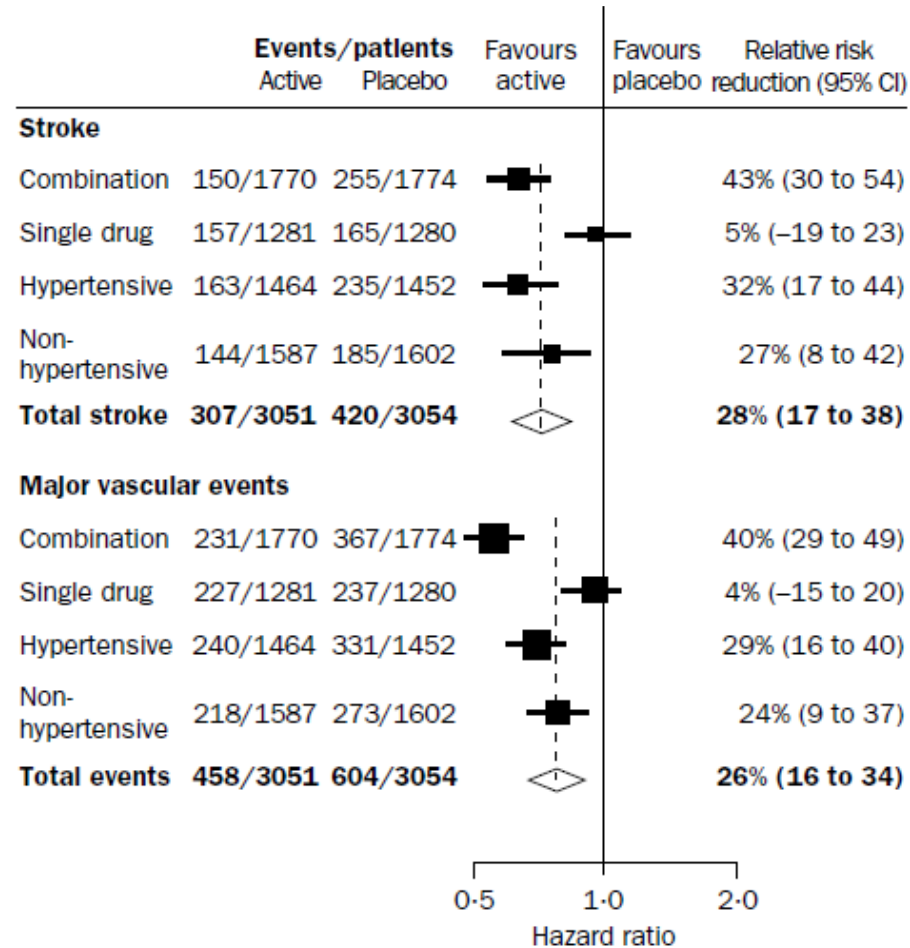
Χρόνια Φάση



- 9/4 mm Hg

Figure 4: Effects of study treatment on stroke subtypes, major vascular events, and deaths

## Χρόνια Φάση



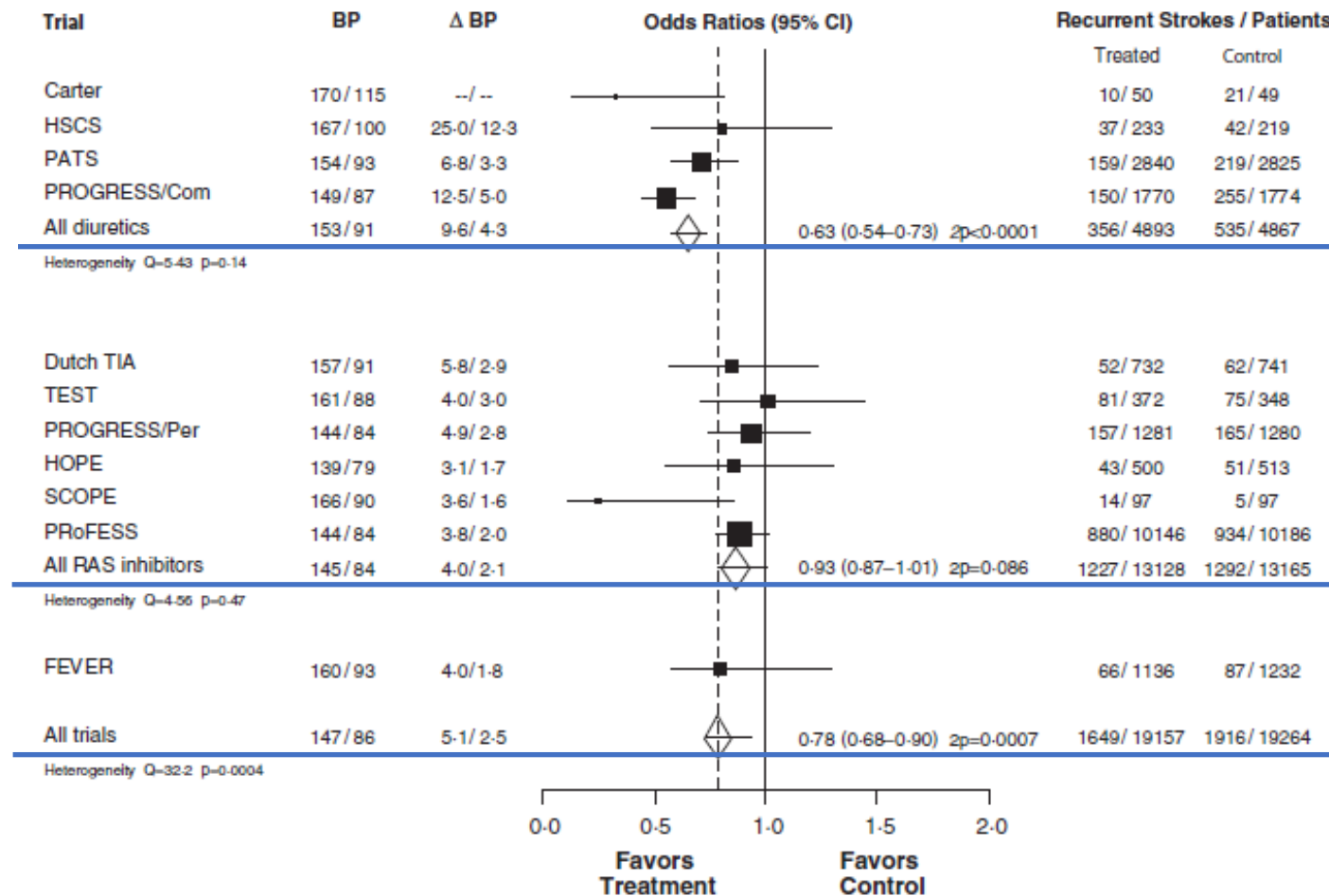
Comb: - 12/5 mm Hg  
Single: - 5/3 mmHg

Figure 5: **Effects of study treatment on stroke and major vascular events in subgroups of patients**

Hazard ratios (and 95% CIs) for hypertensive and non-hypertensive subgroups standardised to study-wide proportions of patients for whom combination or single drug therapy was planned. p values for

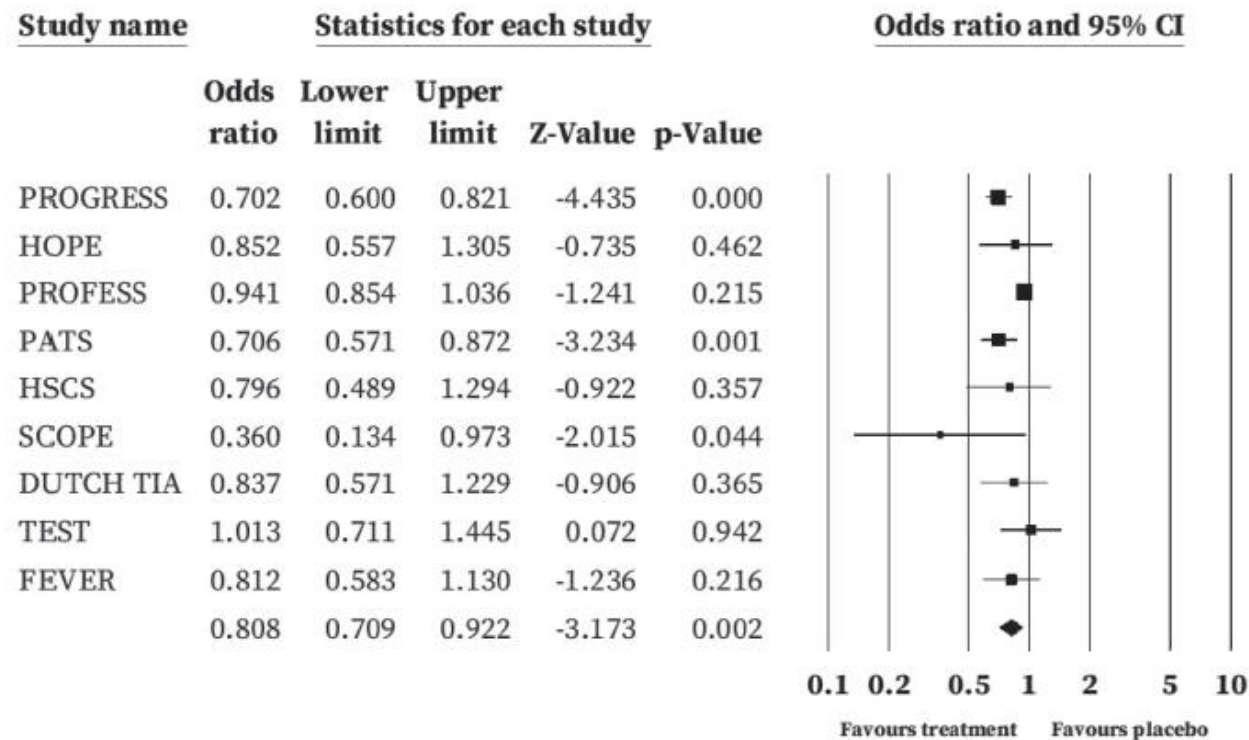
## Χρόνια Φάση

### Μετα-ανάλυση – αποτέλεσμα αντιυπερτασικής αγωγής ως προς την υποτροπή ΑΕΕ



Χρόνια Φάση

Μετα-ανάλυση – αποτέλεσμα αντιυπερτασικής αγωγής ως προς την υποτροπή ΑΕΕ



RCTs  
Treatment vs placebo

Figure 1. Forest plot for the risk of any stroke in randomised trials of antihypertensive medication versus placebo after stroke or TIA. Heterogeneity;  $I^2 = 53$ ,  $p = 0.03$ .

Χρόνια Φάση

In people with a history of ischaemic stroke or TIA, does BP lowering treatment compared to no treatment reduce the risk of any recurrent stroke?

ESO Guidelines, 2022

**Evidence-based recommendation**

In people with previous ischaemic stroke or TIA, we recommend blood pressure lowering treatment to reduce the risk of recurrent stroke.

Quality of evidence: **High** ⊕⊕⊕⊕

Strength of recommendation: **Strong for intervention** ↑↑

- Σε καμία μελέτη δεν έγινε έναρξη θεραπείας στην οξεία φάση του ΑΕΕ
- Δεν παρέχουν καμία ιδιαίτερη σύσταση για τη στιγμή έναρξης της αντιυπερτασικής αγωγής



## Χρόνια Φάση

Study	Stroke type	N	Mean time to randomization	Outcome
ACCESS <i>Stroke 2003</i>	I: 100% H: 0%	342	29.8 (<36h)	No diff in CV events
PRoFESS substudy <i>Stroke 2009</i>	I: 100% H: 0%	1360	58 (<72h)	No diff in mRS
SCAST <i>Lancet 2011</i>	I: 86% H: 14%	2029	18 (<30h)	No diff in mRS or stroke recurrence
CHHIPS <i>Lancet Neurol 2009</i>	I: 86% H: 14%	179	Treatment 19.8 Placebo 17.4 (<36h)	No diff in death, stroke recurrence or dependence
COSSACS <i>Lancet Neurol 2010</i>	I: 59% H: 5%	763	23.6 after stroke (<48h)	No diff in death or dependence
CATIS <i>JAMA 2014</i>	I: 100% H: 0%	4071	Treatment 15.3 Control 14.9 (<48h)	No diff in death or disability
ENOS <i>Lancet 2015</i>	I: 84% H: 14%	4011	26 (<48h)	No diff in functional outcome

Χρόνια Φάση

In people with a history of ischaemic stroke or TIA starting antihypertensive therapy, does use of out-of-office BP measurements compared to clinic measurements provide better long-term control of BP?

ESO Guidelines, 2022

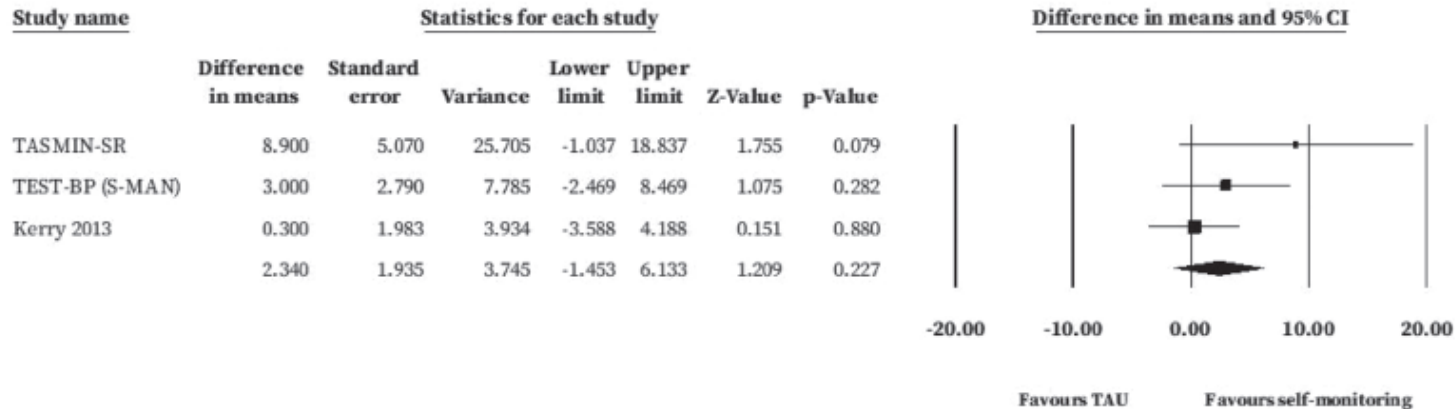


Figure 3. Forest plot for the difference in achieved mean blood pressure between ‘treatment as usual’ and introduction of home or remote blood pressure monitoring after stroke or TIA. Heterogeneity:  $I^2 = 0.000$ ;  $Q = 1.509$ ;  $p = 0.470$ .

**Expert consensus statement**

In people with previous ischaemic stroke or TIA, we support the use of out of office blood pressure measurements wherever feasible, to achieve better long-term control of blood pressure.

Χρόνια Φάση

In people with a history of ischaemic stroke or TIA starting or increasing antihypertensive therapy, does treating to a **more intensive (i.e. BP <130/80) versus less intensive (<140/90 mmHg)** target reduce the risk of recurrent stroke?

ESO Guidelines, 2022

Χρόνια Φάση

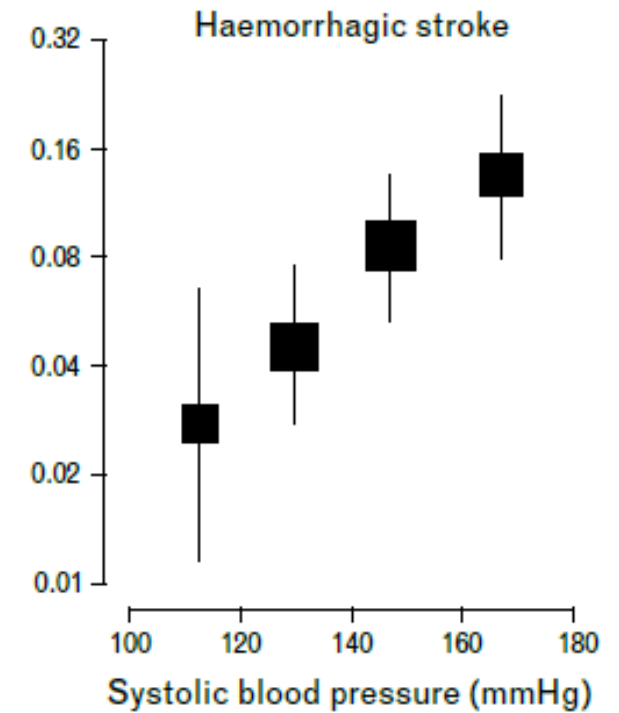
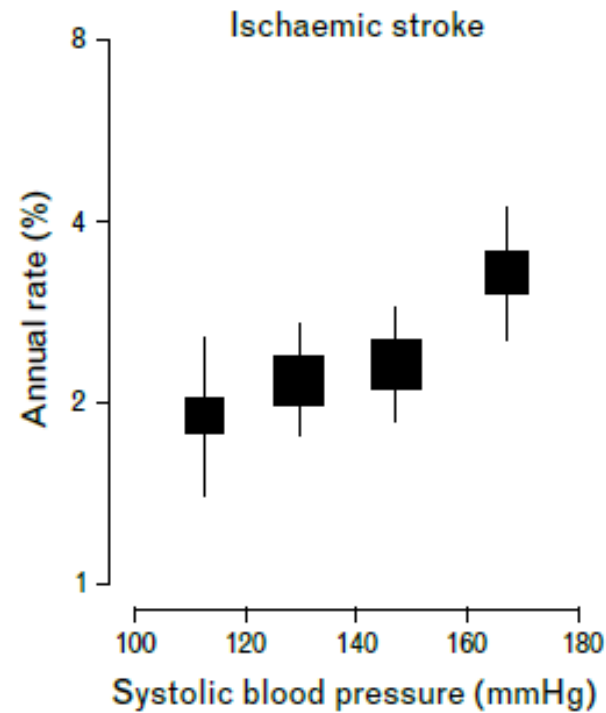
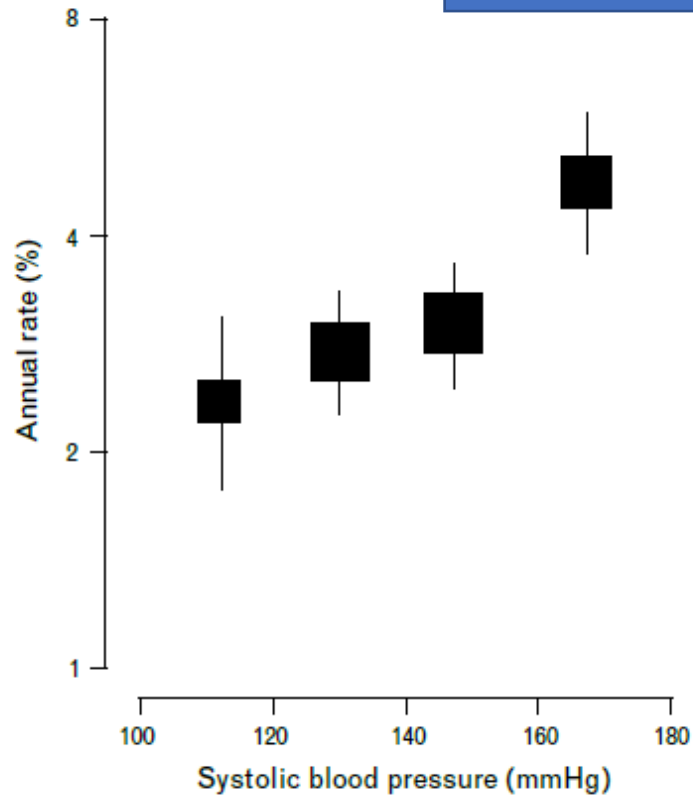
**Table 4.** Adjusted Risk of Clinical Outcomes by Mean Systolic Blood Pressure Level in 20 330 Patients With a Recent Ischemic Stroke

	Mean Systolic Blood Pressure Level, mm Hg				
	High-Normal (130-<140; n = 6004)	Very Low-Normal (<120; n = 1919)	Low-Normal (120-<130; n = 3982)	High (140-<150; n = 4520)	Very High (≥150; n = 3905)
AHR (95% CI)					
Stroke <sup>a</sup>	1 [Reference]	1.29 (1.07-1.56)	1.10 (0.95-1.28)	1.23 (1.07-1.41)	2.08 (1.83-2.37)
Stroke, MI, or vascular death <sup>b</sup>	1 [Reference]	1.31 (1.13-1.52)	1.16 (1.03-1.31)	1.24 (1.11-1.39)	1.94 (1.74-2.16)
Fatal stroke <sup>c</sup>	1 [Reference]	0.63 (0.26-1.49)	1.01 (0.64-1.89)	1.50 (0.94-2.40)	2.51 (1.62-3.09)

Abbreviations: AHR, adjusted hazard ratio; MI, myocardial infarction.

Χρόνια Φάση

Annual rates of stroke according to achieved follow-up SBP levels



Χρόνια Φάση

Benavente, SPS3, Lancet 2013

## SPS3 study

- Randomised open label study
- Lacunar strokes
- SBP 130-149 vs <130 mmHg
- 3020 patients
- 3.7 years

	Higher-target group (n=1519)		Lower-target group (n=1501)		Hazard ratio (95% CI)	p value
	Number of patients	Rate (% per patient-year)	Number of patients	Rate (% per patient-year)		
<b>Stroke</b>						
All stroke	152	2.77%	125	2.25%	0.81 (0.64-1.03)	0.08
Ischaemic stroke or unknown	131	2.4%	112	2.0%	0.84 (0.66-1.09)	0.19
<b>Intracranial haemorrhage</b>						
All	21*	0.38%	13†	0.23%	0.61 (0.31-1.22)	0.16
Intracerebral	16	0.29%	6	0.11%	0.37 (0.15-0.95)	0.03
Subdural or epidural	5	0.091%	6	0.11%	1.18 (0.36-3.88)	0.78
Other	2	0.036%	4	0.072%	1.97 (0.36-10.74)	0.43
Disabling or fatal stroke‡	49	0.89%	40	0.72%	0.81 (0.53-1.23)	0.32

No differences in adverse events

## Χρόνια Φάση

Kitagawa, JAMA Neurol 2019

JAMA Neurology | Original Investigation

## Effect of Standard vs Intensive Blood Pressure Control on the Risk of Recurrent Stroke

A Randomized Clinical Trial and Meta-analysis

### RESPECT study

- RCT
- BP <140/90 vs <120/80 mmHg
- 1263 patients
- Losartan/ARB, amlodipine, HCTZ, spironolactone
- 3.9 years

Table 2. Effects of Intensive Blood Pressure Treatment on Primary and Secondary Outcomes

Outcome	No. of Events (Annual Rate)		Hazard Ratio (95% CI)	P Value
	Standard Treatment (n = 630)	Intensive Treatment (n = 633)		
<b>Primary Outcome</b>				
Stroke <sup>a</sup>	52 (2.26)	39 (1.65)	0.73 (0.49-1.11)	.15
<b>Secondary Outcomes</b>				
Ischemic stroke	41 (1.76)	38 (1.60)	0.91 (0.59-1.42)	.69
Lacunar infarction	12 (0.50)	14 (0.58)	1.16 (0.54-2.52)	.70
Atherothrombotic infarction	9 (0.37)	4 (0.16)	0.44 (0.14-1.42)	.17
Cardiogenic embolism	5 (0.21)	4 (0.16)	0.79 (0.21-2.96)	.73
Other	16 (0.67)	19 (0.78)	1.17 (0.60-2.27)	.65
Intracerebral hemorrhage	11 (0.46)	1 (0.04)	0.09 (0.01-0.70) <sup>b</sup>	.02 <sup>b</sup>
Subarachnoid hemorrhage	0 (0)	1 (0.04)	Not calculable	
Transient ischemic attack	3 (0.12)	8 (0.33)	2.66 (0.71-10.02)	.15
Myocardial infarction	4 (0.17)	5 (0.20)	1.23 (0.33-4.59)	.75
Major vascular event <sup>c</sup>	59 (2.57)	46 (1.95)	0.76 (0.52-1.12)	.17
All-cause death	37 (1.52)	30 (1.22)	0.80 (0.49-1.29)	.36
Composite outcome <sup>d</sup>	86 (3.75)	68 (2.88)	0.77 (0.56-1.06)	.11

Χρόνια Φάση

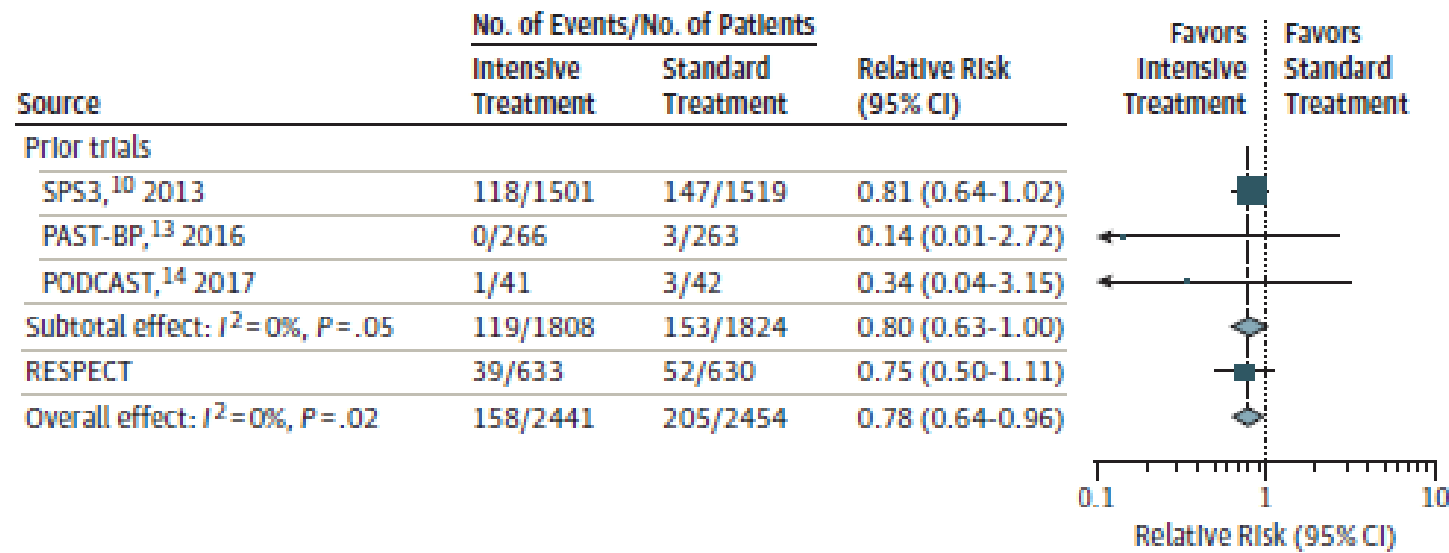
Kitagawa, JAMA Neurol 2019

JAMA Neurology | Original Investigation

Effect of Standard vs Intensive Blood Pressure Control on the Risk of Recurrent Stroke

A Randomized Clinical Trial and Meta-analysis

Figure 3. Effects of Intensive Blood Pressure Lowering on Recurrent Stroke in a Meta-analysis of Randomized Clinical Trials





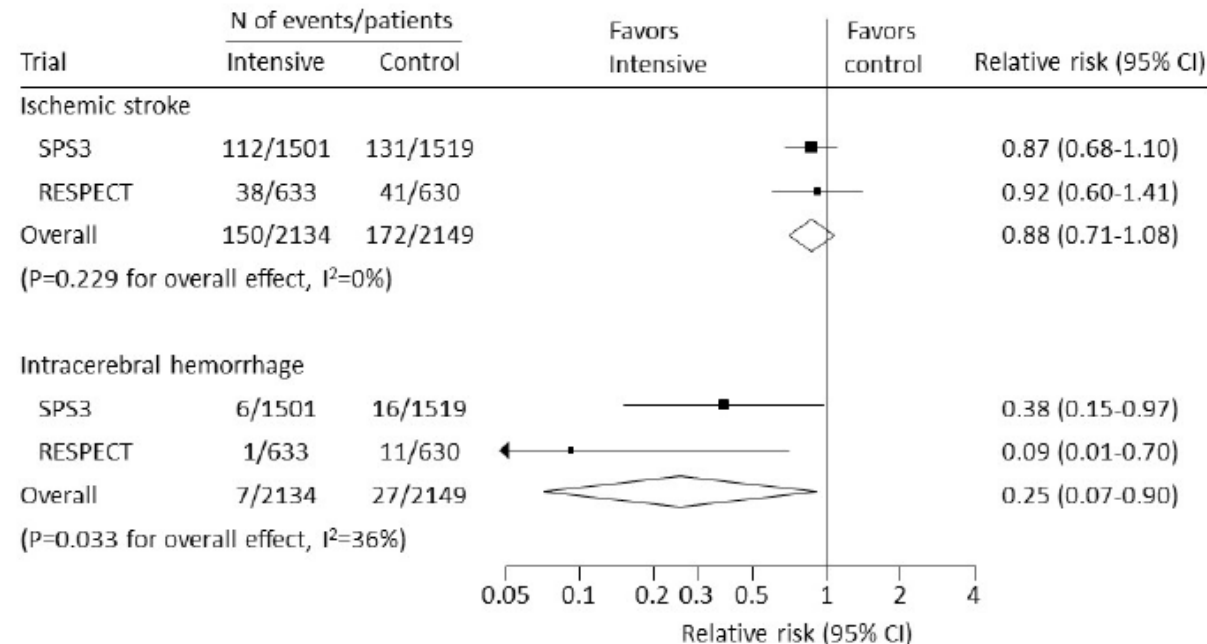
Χρόνια Φάση

Kitagawa, JAMA Neurol 2019

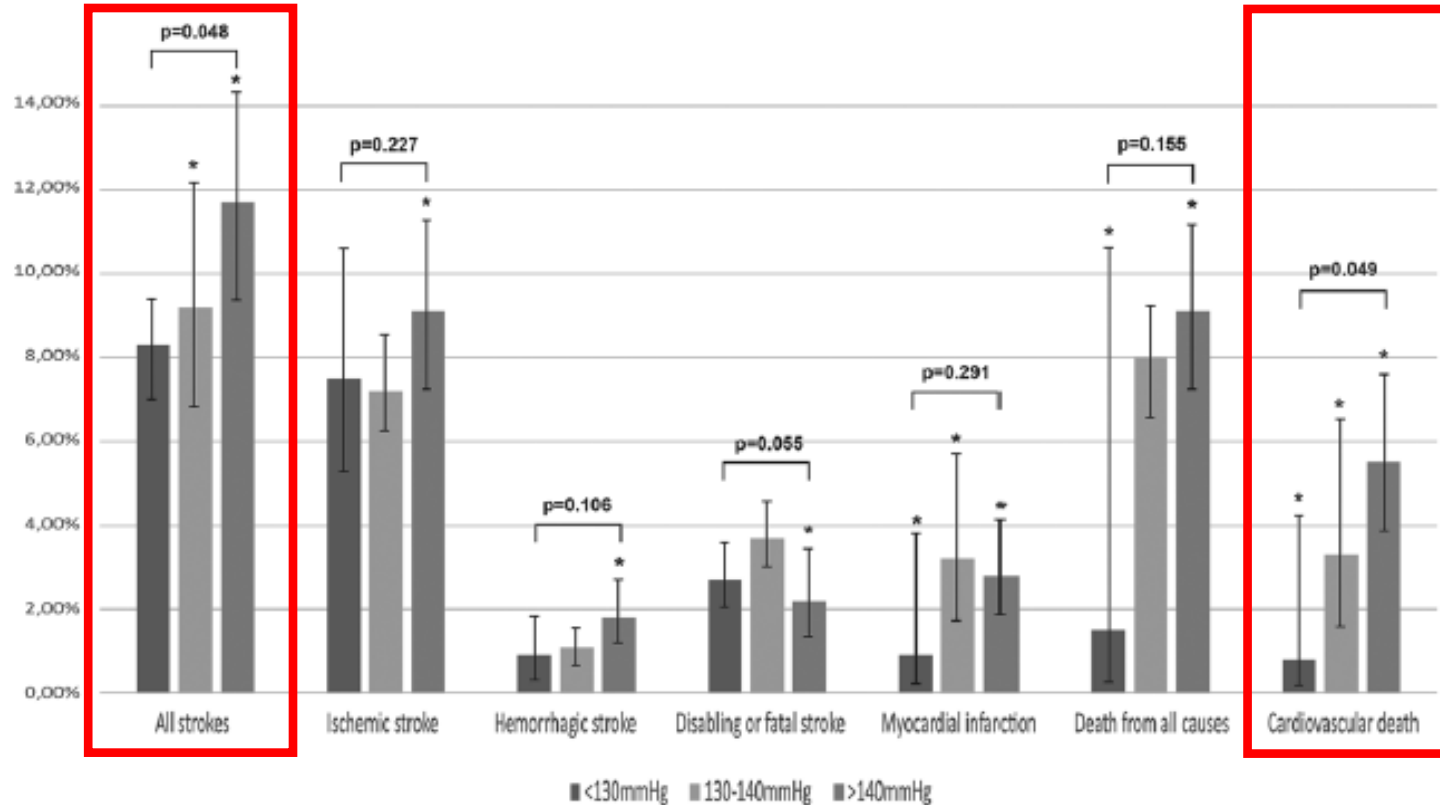
JAMA Neurology | Original Investigation

**Effect of Standard vs Intensive Blood Pressure Control on the Risk of Recurrent Stroke**  
A Randomized Clinical Trial and Meta-analysis

**eFigure 3.** Effects of Intensive Blood Pressure Lowering on Recurrent Ischemic Stroke and Intracerebral Hemorrhage: Meta-analysis of Randomized Controlled Trials



## Χρόνια Φάση



Χρόνια Φάση

In people with a history of ischaemic stroke or TIA starting or increasing antihypertensive therapy, does treating to a **more intensive (i.e. BP <130/80) versus less intensive (<140/90 mmHg)** target reduce the risk of recurrent stroke?

ESO Guidelines, 2022

**Evidence-based recommendation**

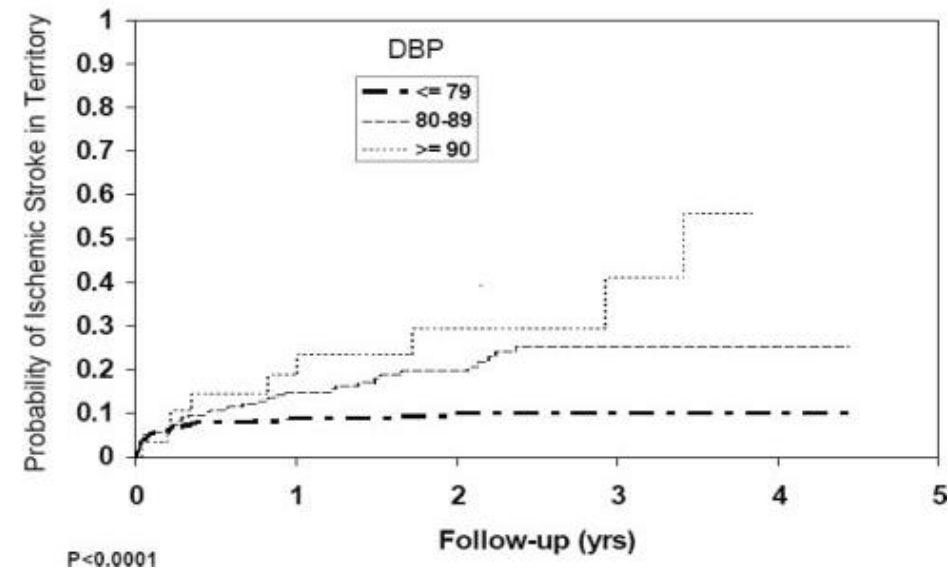
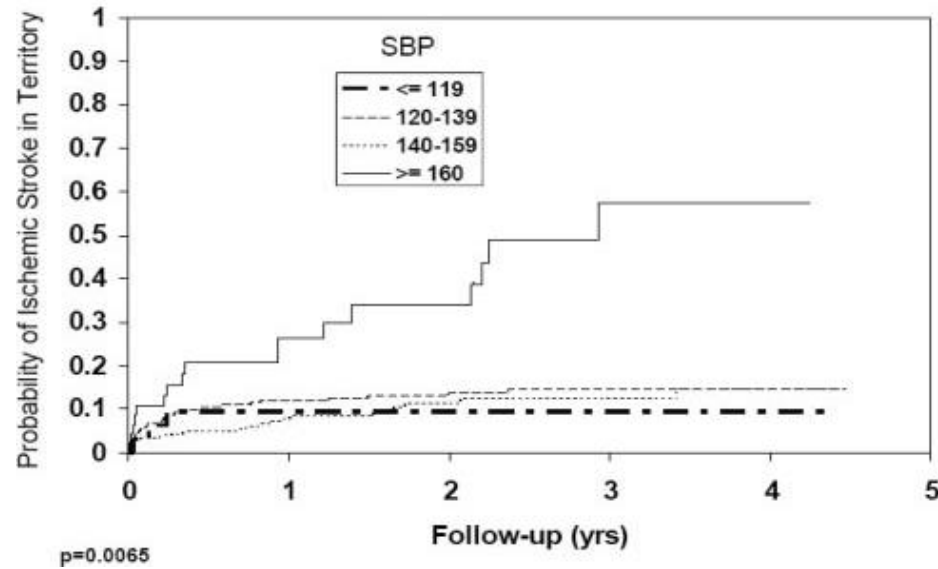
In people with previous ischaemic stroke or TIA, we suggest aiming for a blood pressure target of <130/80 mmHg to reduce the risk of recurrent stroke.

Quality of evidence: **Moderate** ⊕⊕⊕

Strength of recommendation: **Weak for intervention** ↑?

Χρόνια Φάση

### Blood Pressure and Stroke Recurrence in Patients With Intracranial Arterial Stenosis



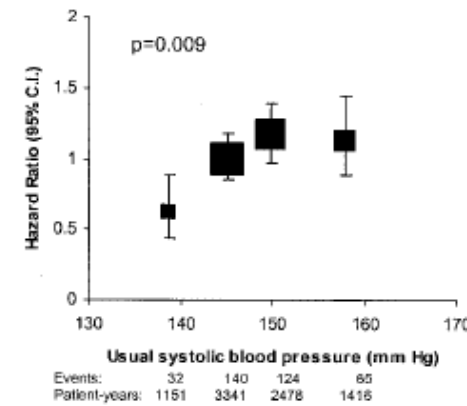
Χρόνια Φάση

**BP and stroke risk in patients with symptomatic carotid occlusive disease**

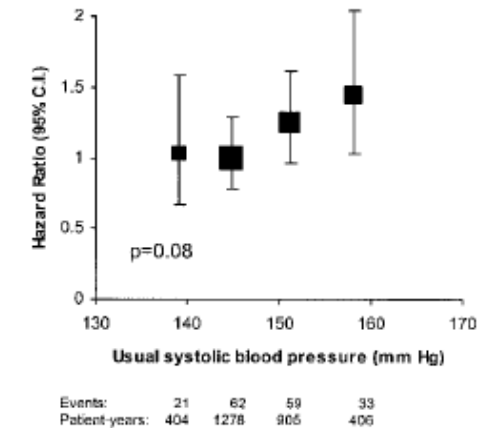
**HR for risk of stroke**

Stenosis Group	SBP, mm Hg			
	<130	130–149	150–169	≥170
Bilateral <70%	1 (0.69–1.44)	1 (0.84–1.19)	1 (0.83–1.20)	1 (0.78–1.29)
Unilateral ≥70%	1.90 (1.24–2.89)	1.18 (0.92–1.51)	1.27 (0.99–1.64)	1.64 (1.15–2.33)
<i>P</i>	0.025	0.30	0.13	0.03
Bilateral ≥70%	5.97 (2.43–14.68)	2.54 (1.47–4.39)	0.97 (0.4–2.35)	1.13 (0.50–2.54)
<i>P</i>	<0.001	0.001	0.95	0.77

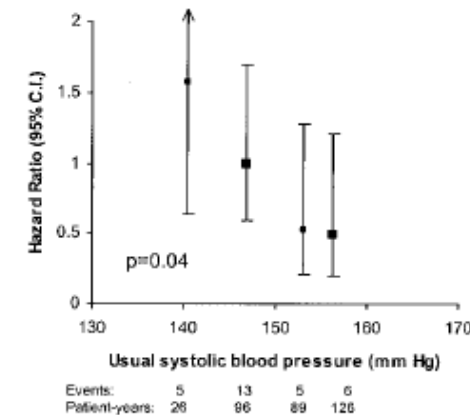
(a) Both stenoses <70%



(b) One stenosis ≥70%



(c) Both stenoses ≥70%



## Χρόνια Φάση

AHA/ACC Guidelines, Stroke 2021

COR	LOE	Recommendations
1	A	1. In patients with hypertension who experience a stroke or TIA, treatment with a thiazide diuretic, angiotensin-converting enzyme inhibitor, or angiotensin II receptor blockers is useful for lowering BP and reducing recurrent stroke risk. <sup>185-189</sup>
1	B-R	2. In patients with hypertension who experience a stroke or TIA, an office BP goal of <130/80 mm Hg is recommended for most patients to reduce the risk of recurrent stroke and vascular events. <sup>185,190-194</sup>
1	B-NR	3. In patients with hypertension who experience a stroke or TIA, individualized drug regimens that take into account patient comorbidities, agent pharmacological class, and patient preference are recommended to maximize drug efficacy. <sup>188,189,195,196</sup>
2a	B-R	4. In patients with no history of hypertension who experience a stroke or TIA and have an average office BP of $\geq 130/80$ mm Hg, antihypertensive medication treatment can be beneficial to reduce the risk of recurrent stroke, ICH, and other vascular events. <sup>190,191,193,197</sup>

## Χρόνια Φάση

**Table 23** Office blood pressure treatment target range

Age group	Office SBP treatment target ranges (mmHg)					Office DBP treatment target range (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke <sup>a</sup> /TIA	
18-65 years	Target to 130 <i>or lower if tolerated</i> Not <120	Target to 130 <i>or lower if tolerated</i> Not <120	Target to <140 to 130 if tolerated	Target to 130 <i>or lower if tolerated</i> Not <120	Target to 130 <i>or lower if tolerated</i> Not <120	70-79
65-79 years <sup>b</sup>	Target to 130-139 <i>if tolerated</i>	Target to 130-139 <i>if tolerated</i>	Target to 130-139 <i>if tolerated</i>	Target to 130-139 <i>if tolerated</i>	Target to 130-139 <i>if tolerated</i>	70-79
≥80 years <sup>b</sup>	Target to 130-139 <i>if tolerated</i>	Target to 130-139 <i>if tolerated</i>	Target to 130-139 <i>if tolerated</i>	Target to 130-139 <i>if tolerated</i>	Target to 130-139 <i>if tolerated</i>	70-79
Office DBP treatment target range (mmHg)	70-79	70-79	70-79	70-79	70-79	

©ESC/ESH 2018

In all hypertensive patients with ischaemic stroke or TIA, an SBP target range of 120–130 mmHg should be considered.<sup>244,524,526</sup>

The recommended antihypertensive drug treatment strategy for stroke prevention is a RAS blocker plus a CCB or a thiazide-like diuretic.<sup>338</sup>

IIa

B

I

A

## Συμπερασματικά

Υπάρχει μεγάλη ετερογένεια στους παθοφυσιολογικούς μηχανισμούς των ισχαιμικών ΑΕΕ

### Στο οξύ ΑΕΕ

Σε παρέμβαση επαναιμάτωσης: διατηρώ ΣΑΠ/ΔΑΠ < 180/105 mmHg και για 24 ώρες (όχι <140)

Σε μη παρέμβαση επαναιμάτωσης: δε μειώνω αν ΣΑΠ/ΔΑΠ < 220/110 mmHg, αν > 220/120 μειώνω κατά < 15% εντός 24ώρου

### Στη δευτερογενή πρόληψη

Θεραπεία με RAAS blocker, θειαζιδικό διουρητικό ή CCB

Συνήθως έναρξη < 48-72 ώρες δε μειώνει τη θνητότητα ή αναπηρία

Στόχος ΣΑΠ 130 mmHg ή και 120-130 mmHg εφόσον καλά ανεκτή



**Σας ευχαριστώ πολύ για την προσοχή**