

70° CONGRESSO  
NAZIONALE

**SIGG**

LIBERI E LONGEVI

*Università degli Studi di  
Napoli Federico II*  
Polo Didattico di **SCAMPIA**  
Dicembre 17-20, 2025

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***SIMPOSIO SIGG-GIMSI***  
**UNA TERAPIA PER OGNI PAZIENTE  
CON SINCOPE**

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***Terapia del fenotipo ipotensivo  
nel paziente iperteso***

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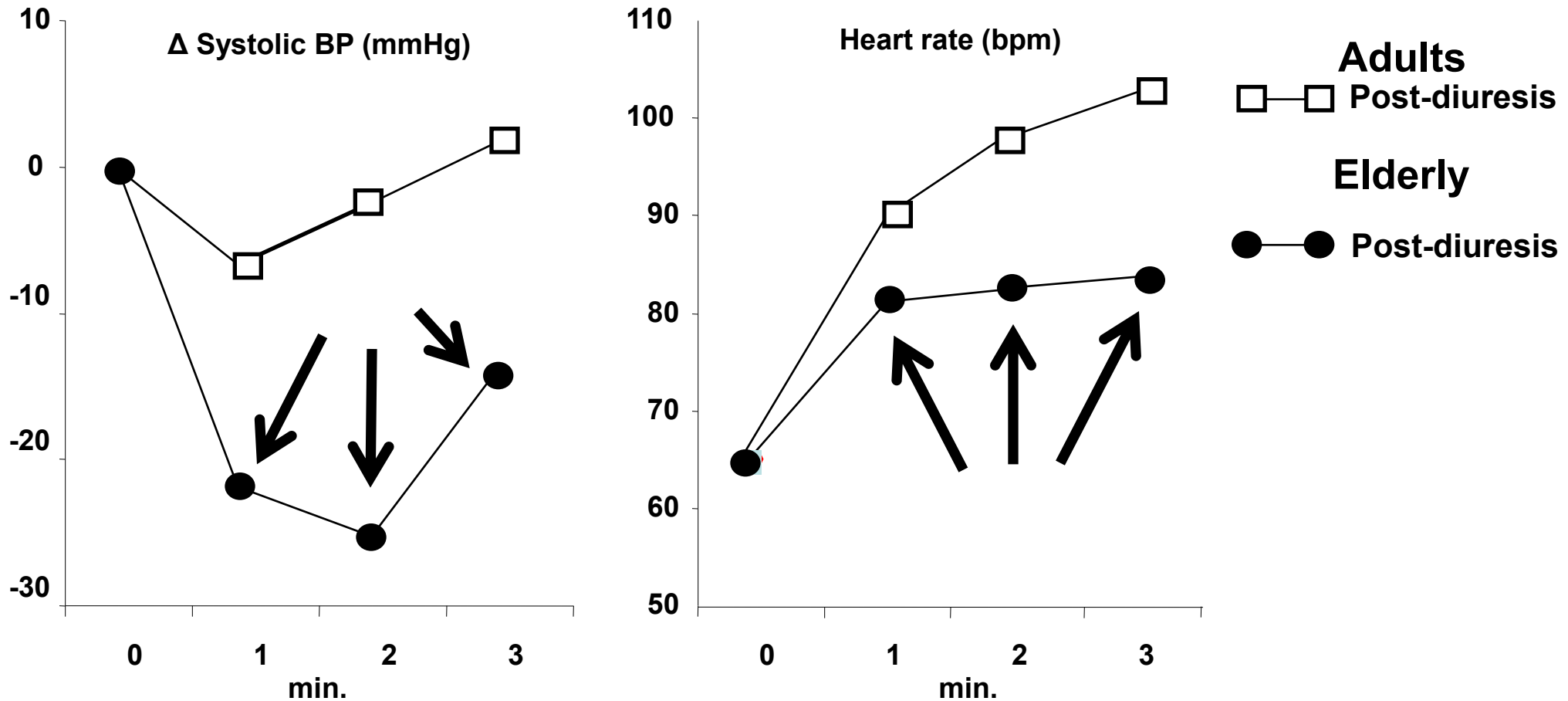


Prof. P. Abete  
Dipartimento di Scienze Mediche Traslazionali  
Università di Napoli Federico II

# Negative ORTHOSTATISM

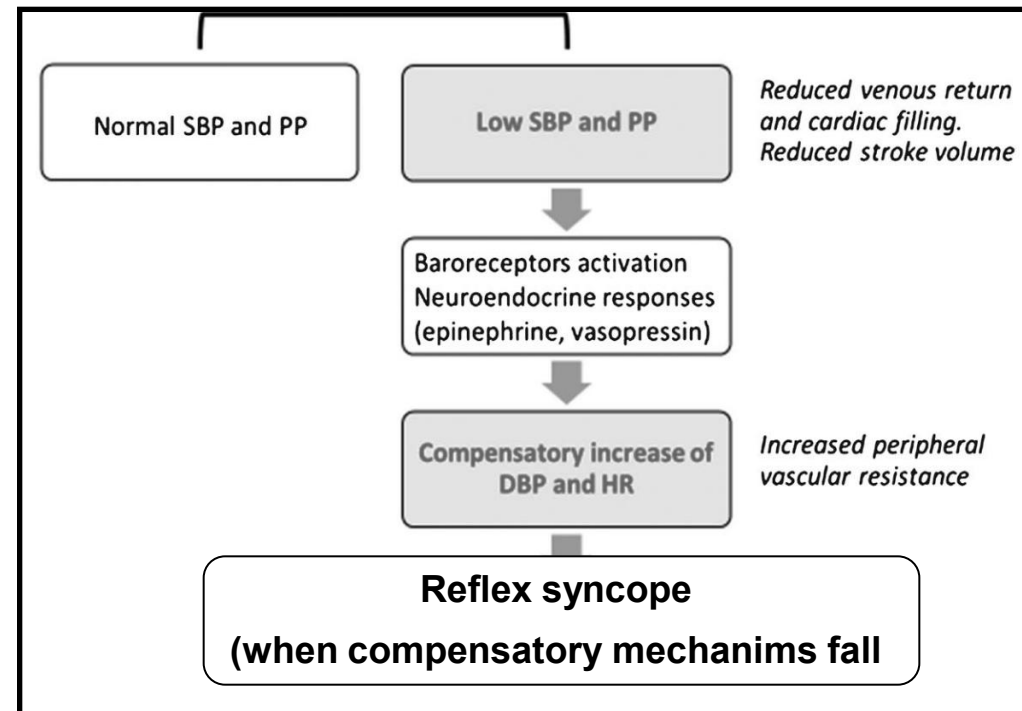
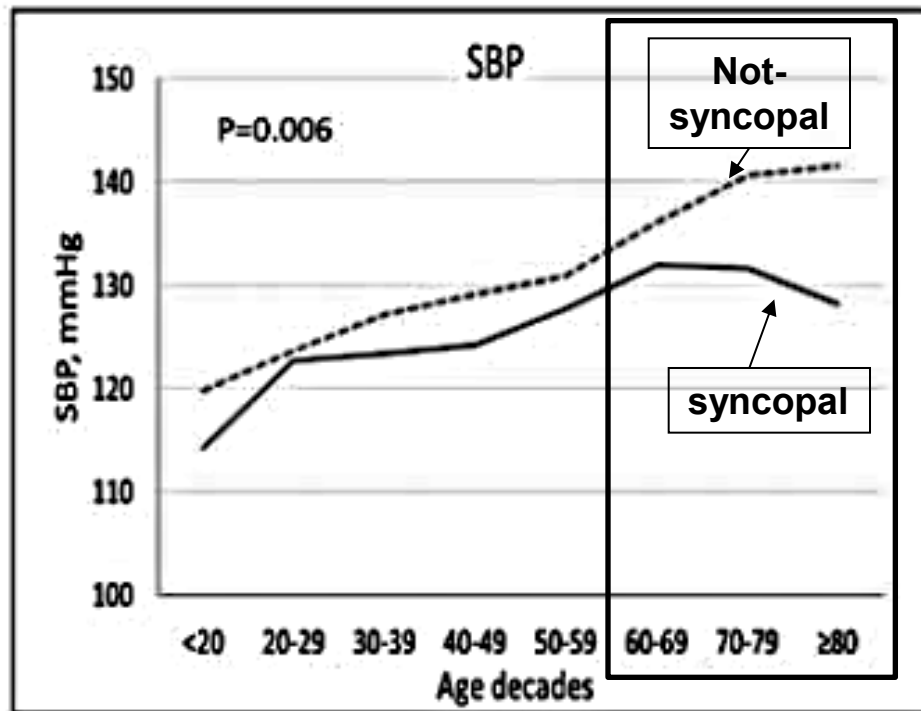
## *age-related VULNERABILITY*

*Effects of “age” and “sodium depletion”*  
**REDUCTION OF INTRINSIC CAPACITY**



- 
- **Hypotensive phenotype in older adults**
  - HYP-HYP phenomenon
  - Hypertension therapy and orthostatic hypotension
  - Therapy in elderly hypotensive phenotype
  - Take home messages
-

# Low-blood pressure phenotype underpins the tendency to reflex syncope



# Low blood pressure and dementia in elderly people: the Kungsholmen project

Zhenchao Guo, Matti Viitanen, Laura Fratiglioni, Bengt Winblad

Number (percentage) of elderly subjects with dementia by blood pressure

1642 subjects  
aged 75-101 years

**Blood pressure (mm Hg) All dementias**

Systolic:

≤ 120 (n=142)

46 (32.4)

**People with systolic pressure 140 mmHg were more often diagnosed as demented than those with systolic pressure > 140 mmHg.**

≤ 65 (n=186)

43 (23.1)

66-75 (n=380)

62 (16.3)

76-85 (n=623)

60 (9.6)

86-95 (n=346)

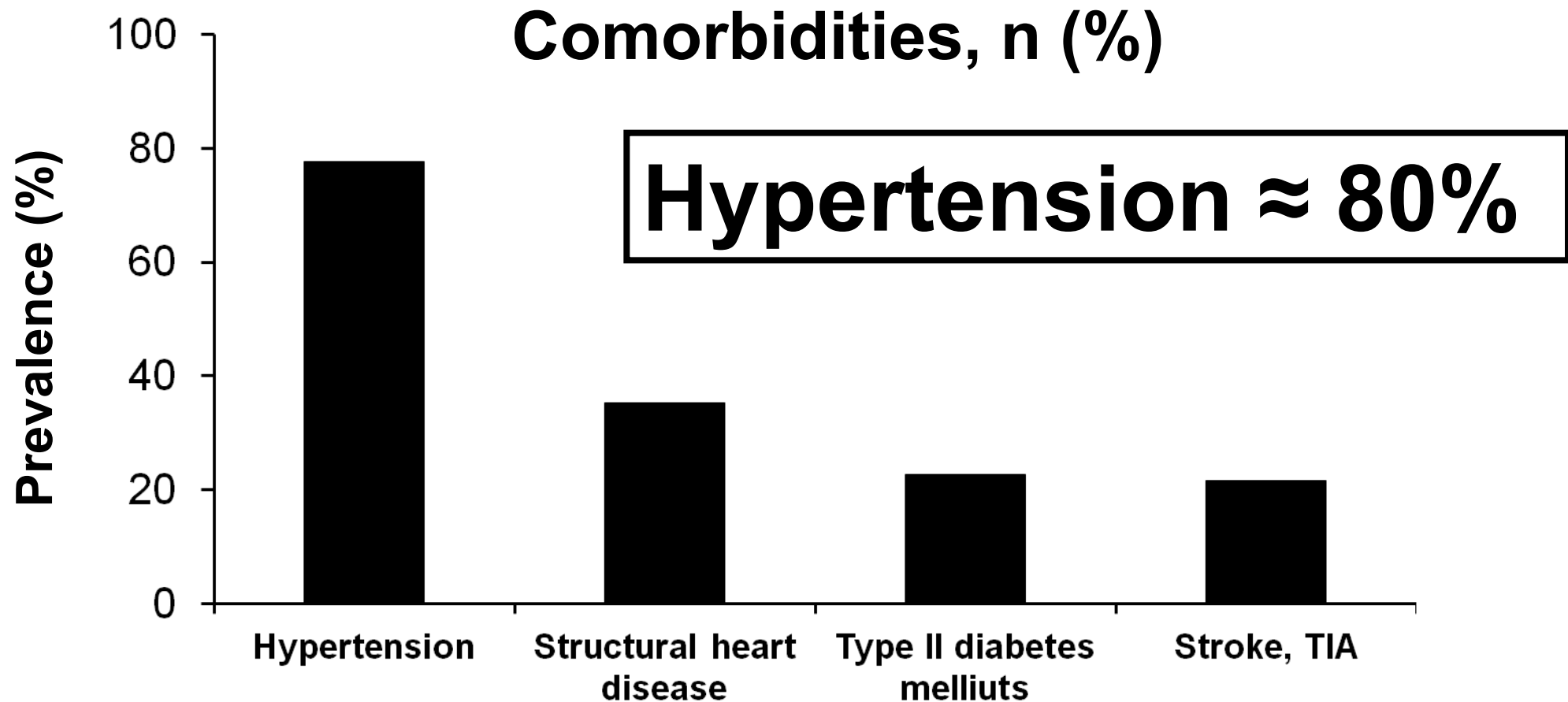
27 (7.8)

> 95 (n=107)

10 (9.3)

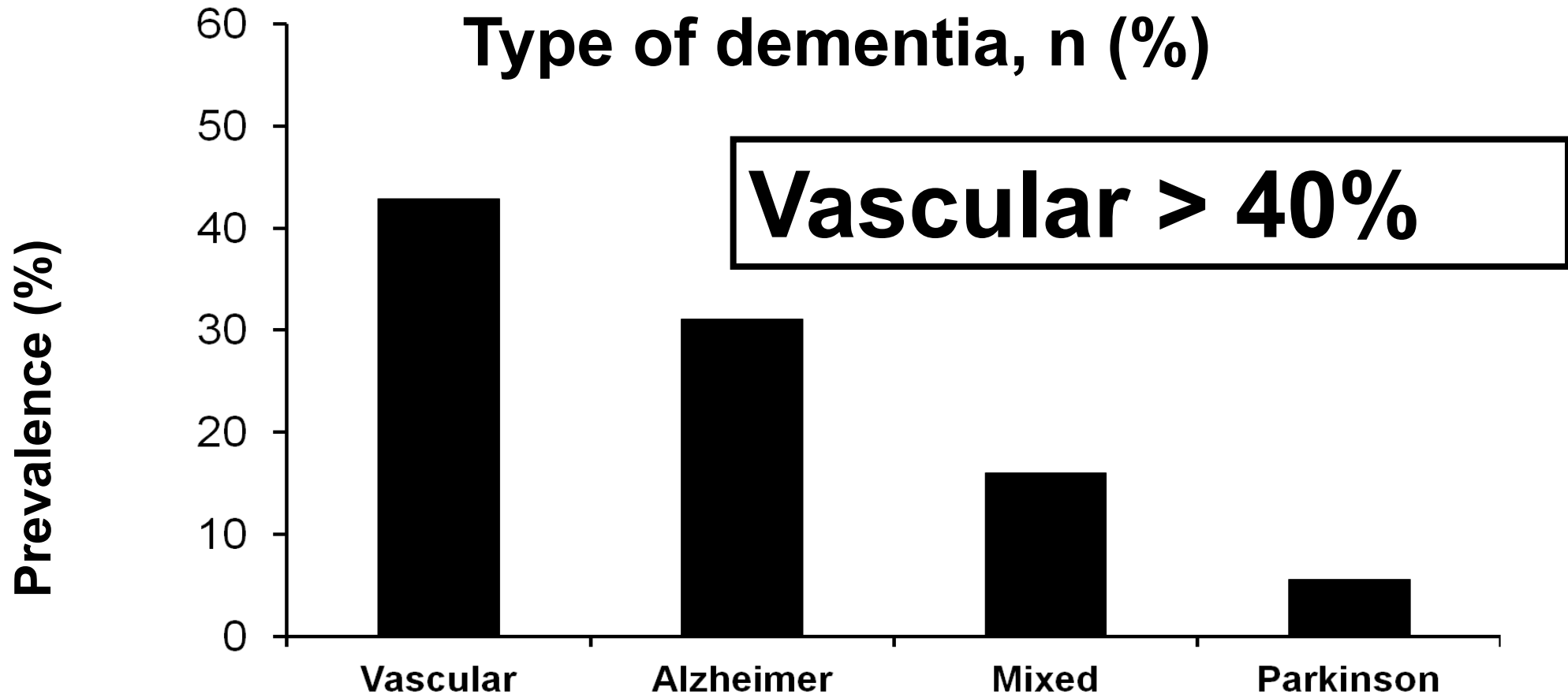
# Etiology of Syncope and Unexplained Falls in Elderly Adults with Dementia: Syncope and Dementia (SYD) Study

Andrea Ungar, MD, PhD,<sup>a</sup> Chiara Mussi, MD, PhD,<sup>b</sup> Alice Ceccofiglio, MD,<sup>a</sup> Giuseppe Bellelli, MD, PhD,<sup>c,d,e</sup> Franco Nicosia, MD,<sup>f</sup> Mario Bo, MD,<sup>g</sup> Daniela Riccio, MD,<sup>b</sup> Anna Maria Martone, MD,<sup>i</sup> Livia Guadagno, MD,<sup>j</sup> Gabriele Noro, MD,<sup>k</sup> Giulia Ghidoni, MD,<sup>b</sup> Martina Rafanelli, MD,<sup>a</sup> Niccolò Marchionni, MD,<sup>a</sup> and Pasquale Abete, MD, PhD<sup>j</sup>



# Etiology of Syncope and Unexplained Falls in Elderly Adults with Dementia: Syncope and Dementia (SYD) Study

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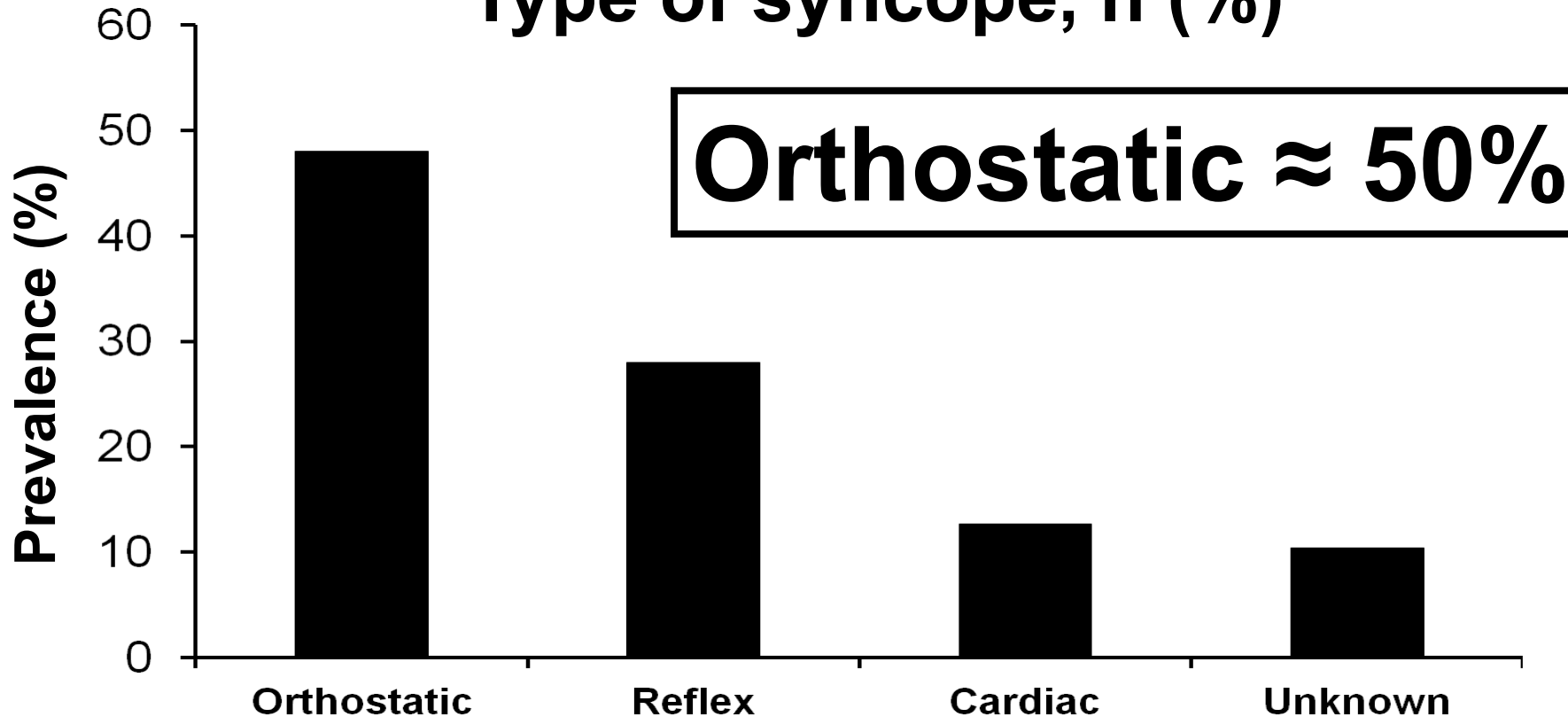


# Etiology of Syncope and Unexplained Falls in Elderly Adults with Dementia: Syncope and Dementia (SYD) Study

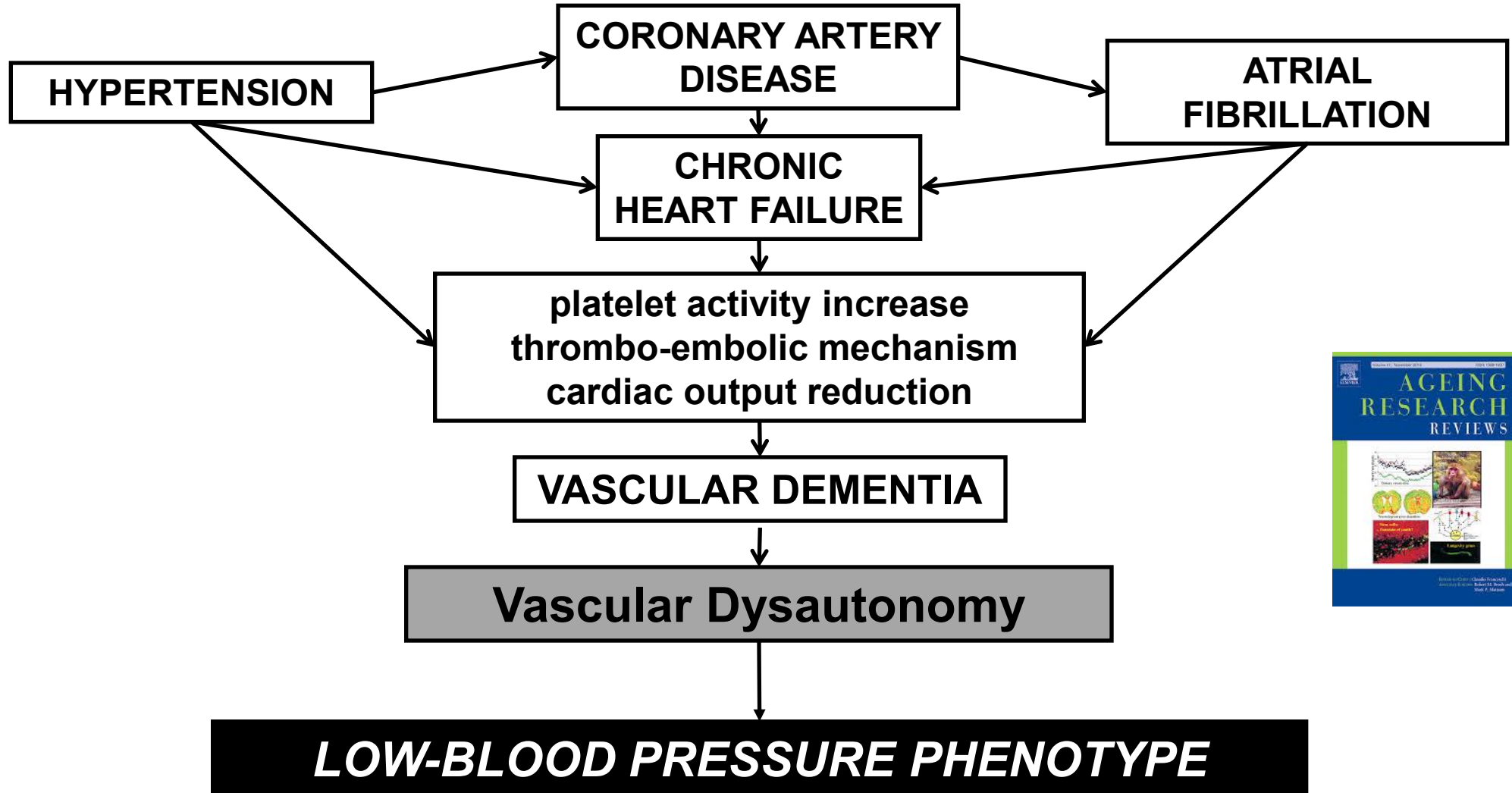
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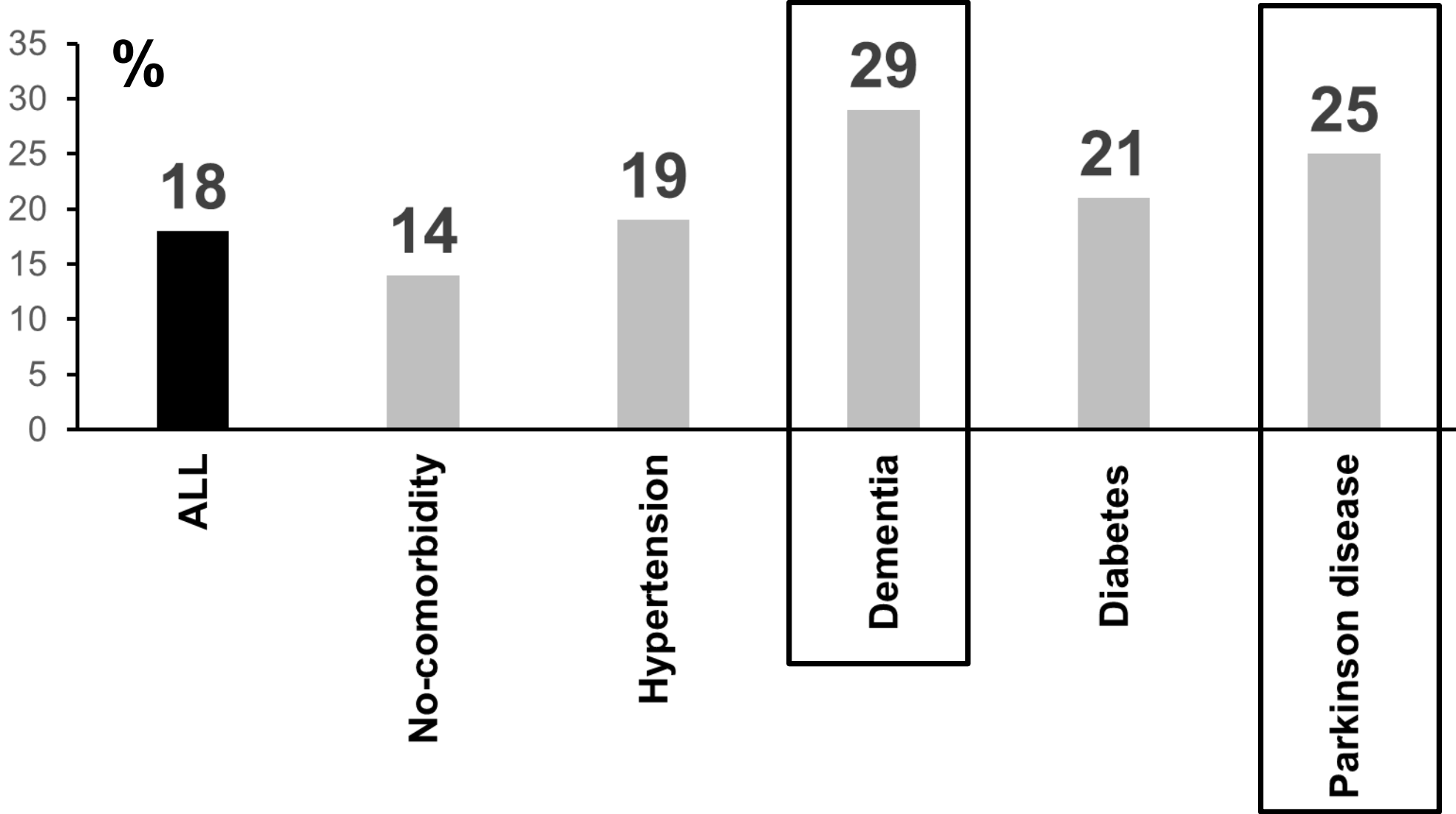
## Type of syncope, n (%)



# Cognitive impairment and cardiovascular diseases in the elderly....*A heart-brain continuum hypothesis*

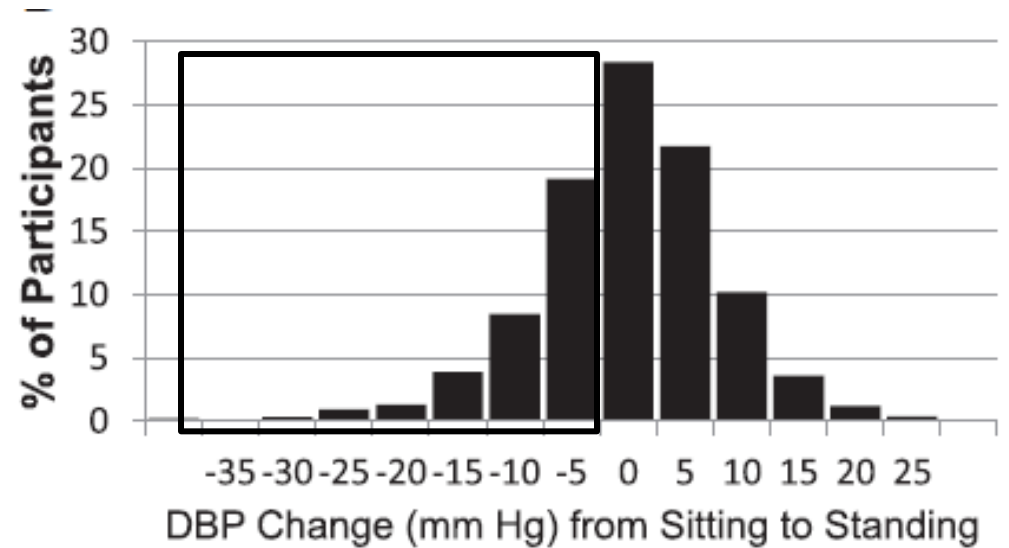
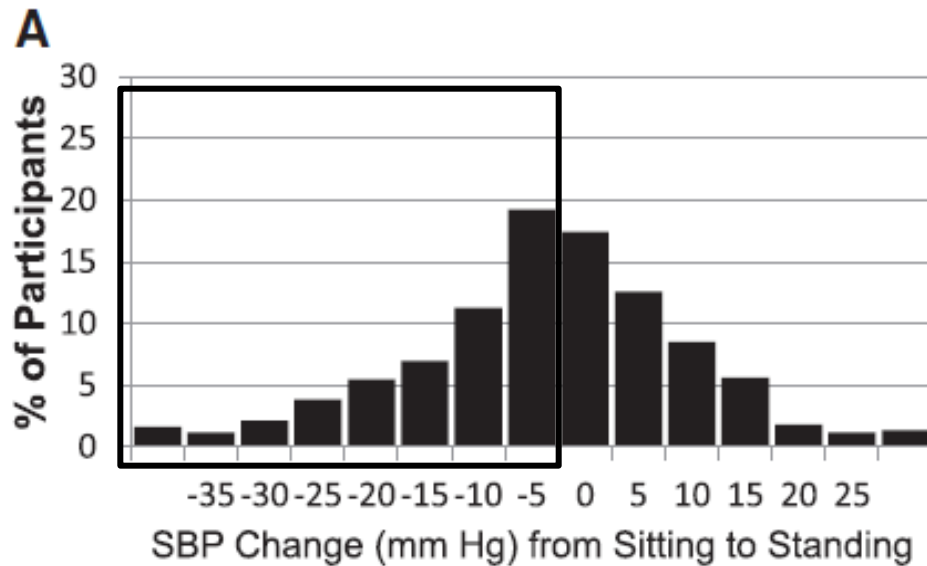


# Prevalence of ORTHOSATIC HYPOTENSION according to the consensus definition across disease subgroups.



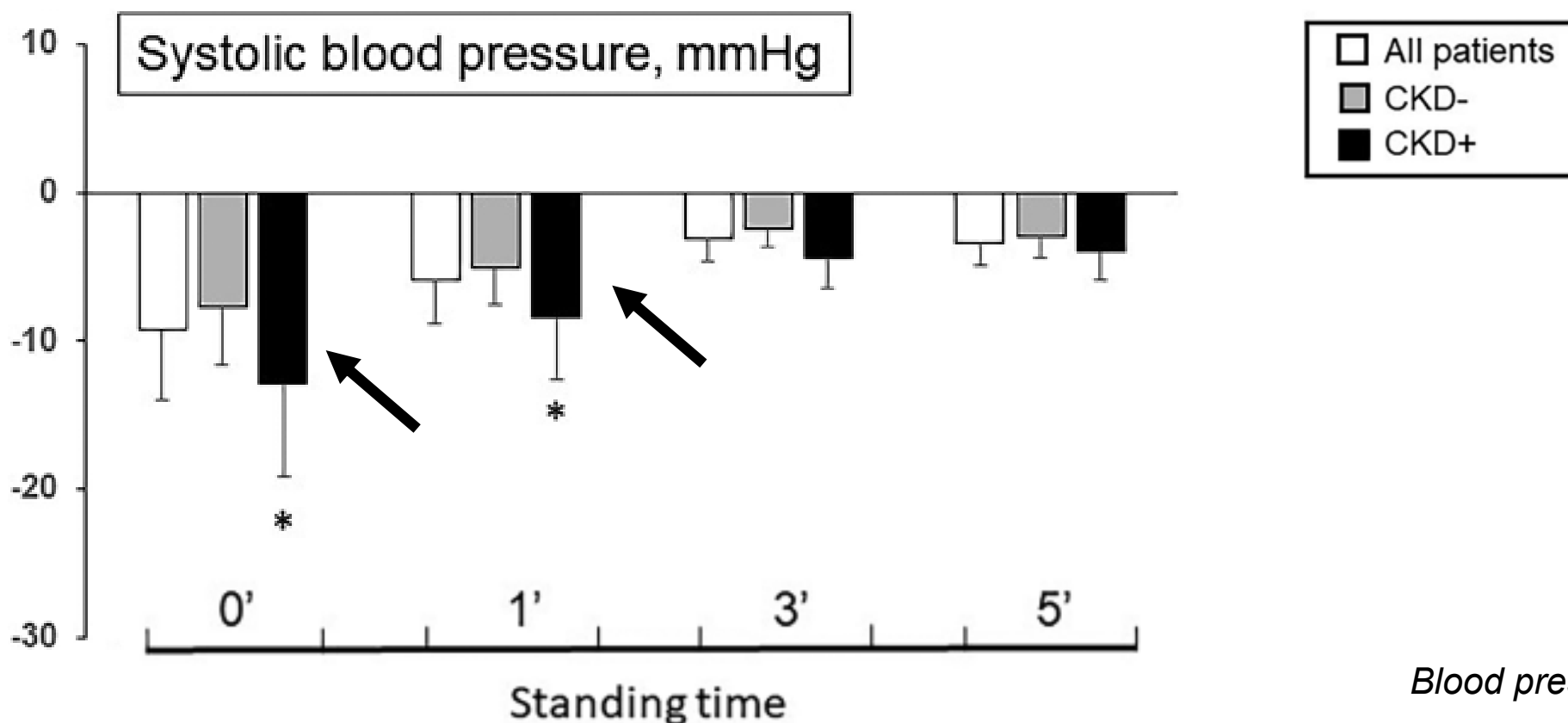
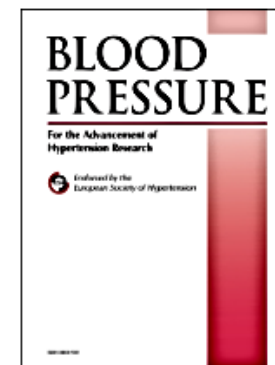
# Histograms showing distribution of orthostatic change in systolic (SBP) and diastolic (SBD) blood pressure at baseline.

## *ACCORD (Action to Control Cardiovascular Risk in DIABETES) Blood Pressure Trial*



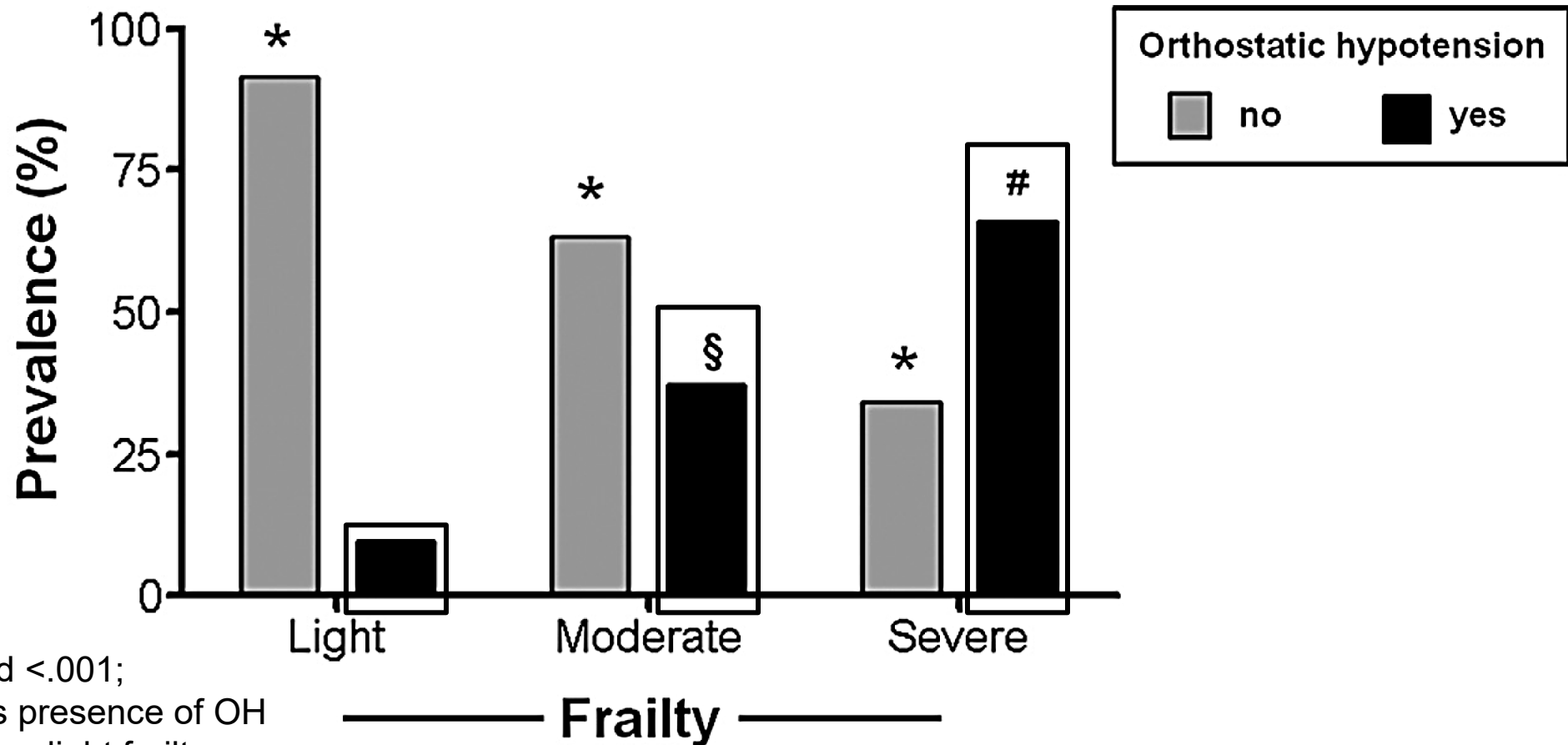
# Chronic kidney disease and orthostatic hypotension in hospitalised older adults

Francesco Curcio, Rosaria Chiappetti, Mattia De Furio, Veronica Flocco, David Della Morte, Gianluca Testa, Gaetano Gargiulo, Francesco Cacciatore, Pasquale Abete, Gianluigi Galizia & on behalf of the European Union - NextGenerationEU - AGE-It Spoke 3



# Orthostatic Hypotension in the Elderly: A Marker of Clinical Frailty?

Ilaria Liguori MD<sup>a</sup>, Gennaro Russo MD<sup>a</sup>, Vincenzo Coscia MD<sup>a</sup>, Luisa Aran MD<sup>a</sup>,  
Giulia Bulli MD<sup>a</sup>, Francesco Curcio MD<sup>a</sup>, David Della-Morte MD, PhD<sup>b,c</sup>,  
Gaetano Gargiulo MD<sup>d</sup>, Gianluca Testa MD, PhD<sup>a,e</sup>, Francesco Cacciatore MD, PhD<sup>a,f</sup>,  
Domenico Bonaduce MD<sup>a</sup>, Pasquale Abete MD, PhD<sup>a,\*</sup>



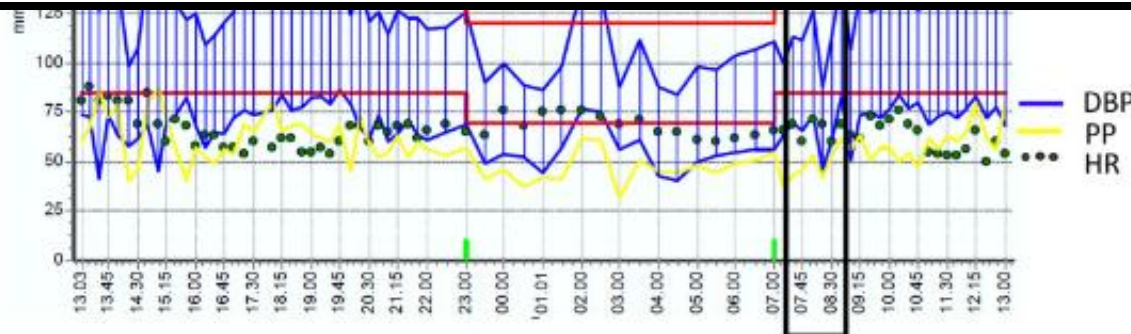
p for trend <.001;  
p<0.01 vs presence of OH  
# p<0.01 vs light frailty,  
§ p<.05 vs moderate frailty).

# Association between hypotension during 24 h ambulatory blood pressure monitoring and reflex syncope: the SynABPM 1 study

Twenty-four hour ambulatory blood pressure monitoring report of a patient with reflex syncope, showing a systolic blood pressure drop (88/46 mmHg) at 8.15 am

	Systolic BP	Diastolic BP	Mean BP	Pulse Pressure	Heart Rate
7:45	112	66	81	46	60
8:00	127	74	91	53	71
8:15	88	46	60	42	69

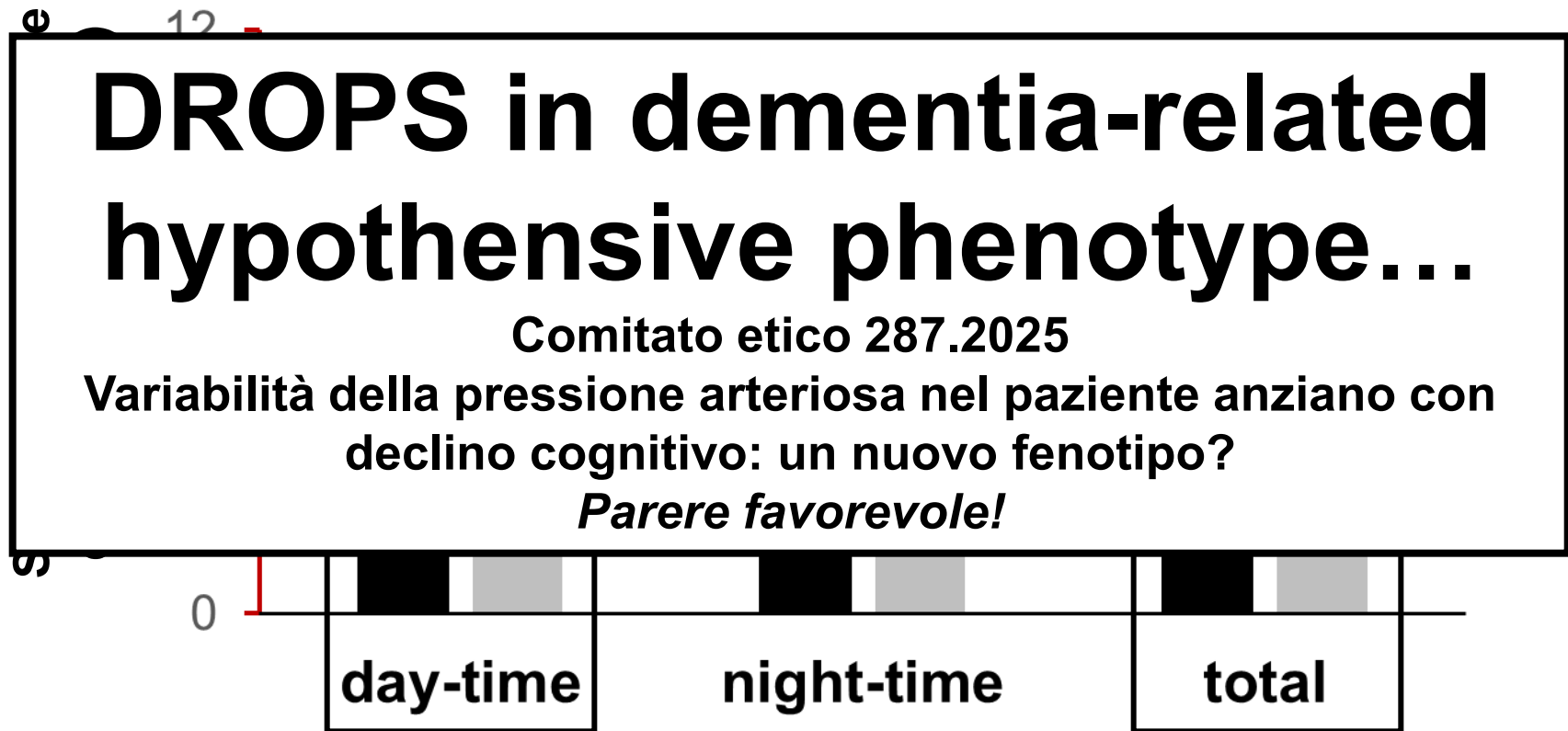
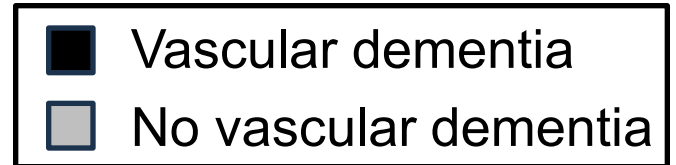
**One or more daytime DROPS <90 mmHg achieved 91% specificity and 32% sensitivity [odds ratio (OR) 4.6, P < 0.001]**



consisting of 11 or 22 single SBP measures <110, <100, <90 and <80 mmHg were recorded.

Age range 48-75 years

# Unexplained falls in elderly patients with vascular cognitive impairment: role of blood pressure variability

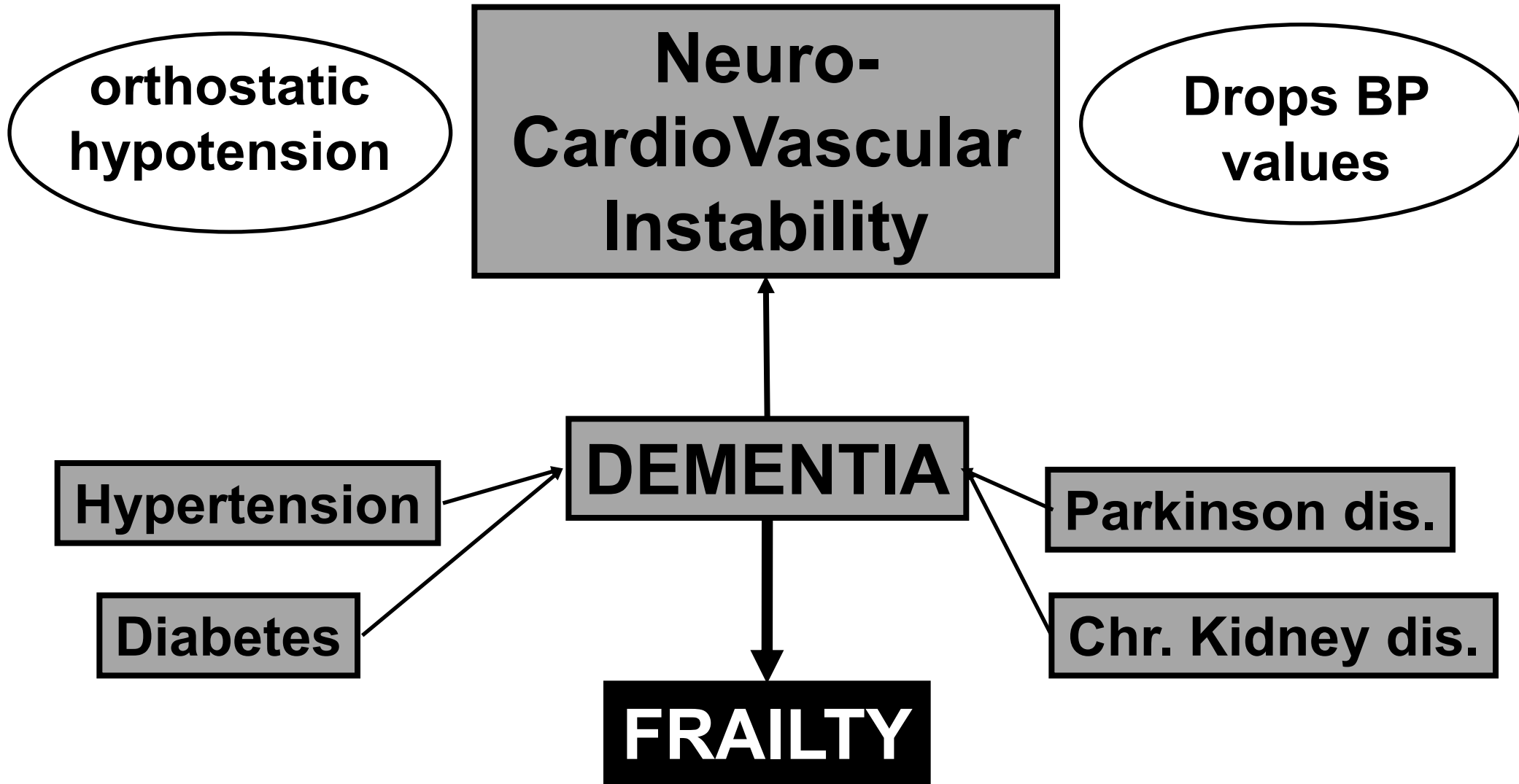


\*p<0.05 vs no vascular dementia

Curcio F et al., 2025 in progress

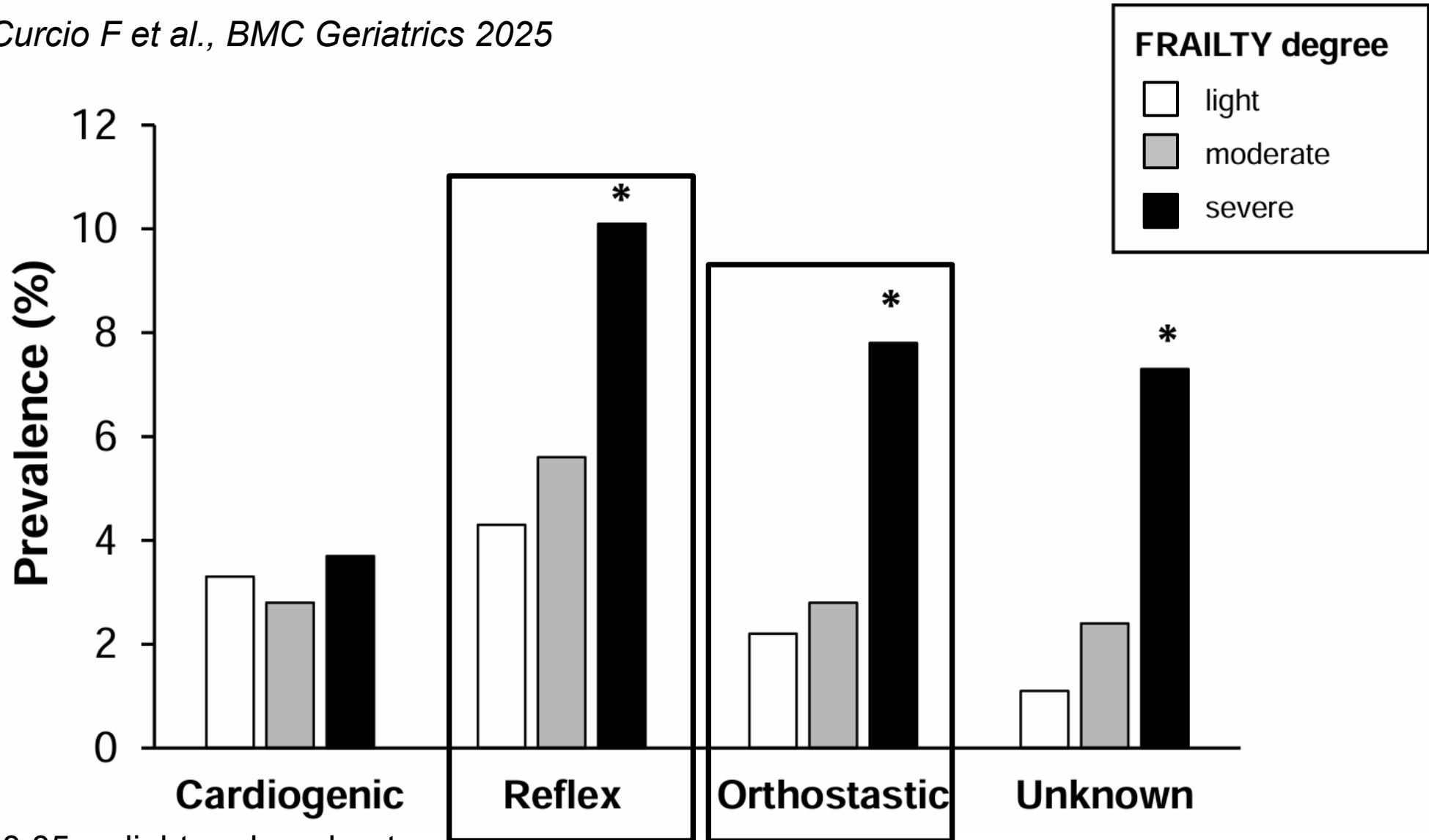
# Low-blood pressure phenotype in the elderly

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# Prevalence of different types of syncope in older adults stratified by multidimensional frailty

Curcio F et al., BMC Geriatrics 2025



- 
- Hypotensive phenotype in older adults
  - **HYP-HYP phenomenon**
  - Hypertension therapy and orthostatic hypotension
  - Anti-hypertensive therapy in hypotensive phenotype
  - Take home messages
-

## Review

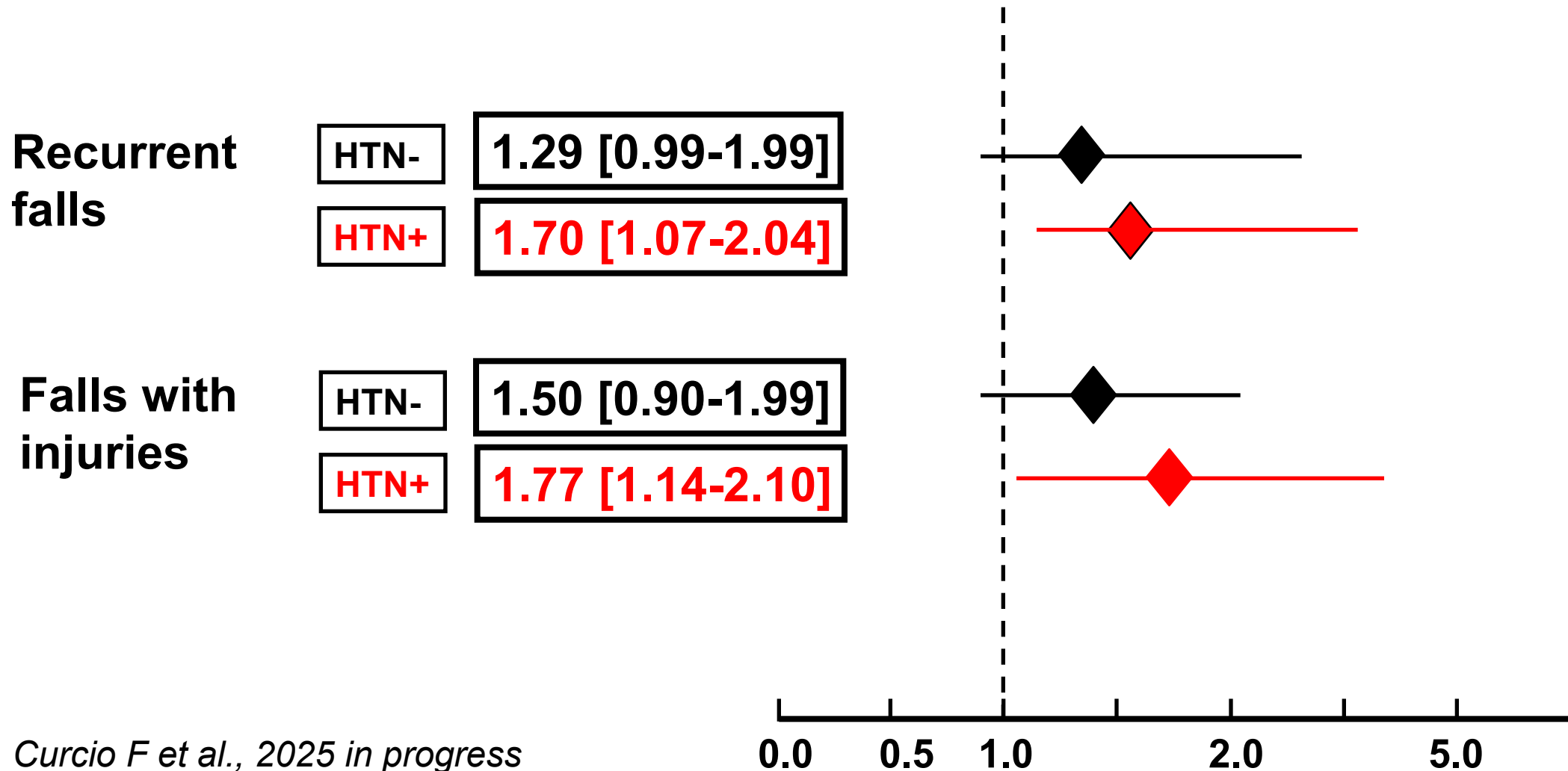
# Clinostatic Hypertension and Orthostatic Hypotension

Alfonso Lagi, MD and Simona Spini, MD, PhD

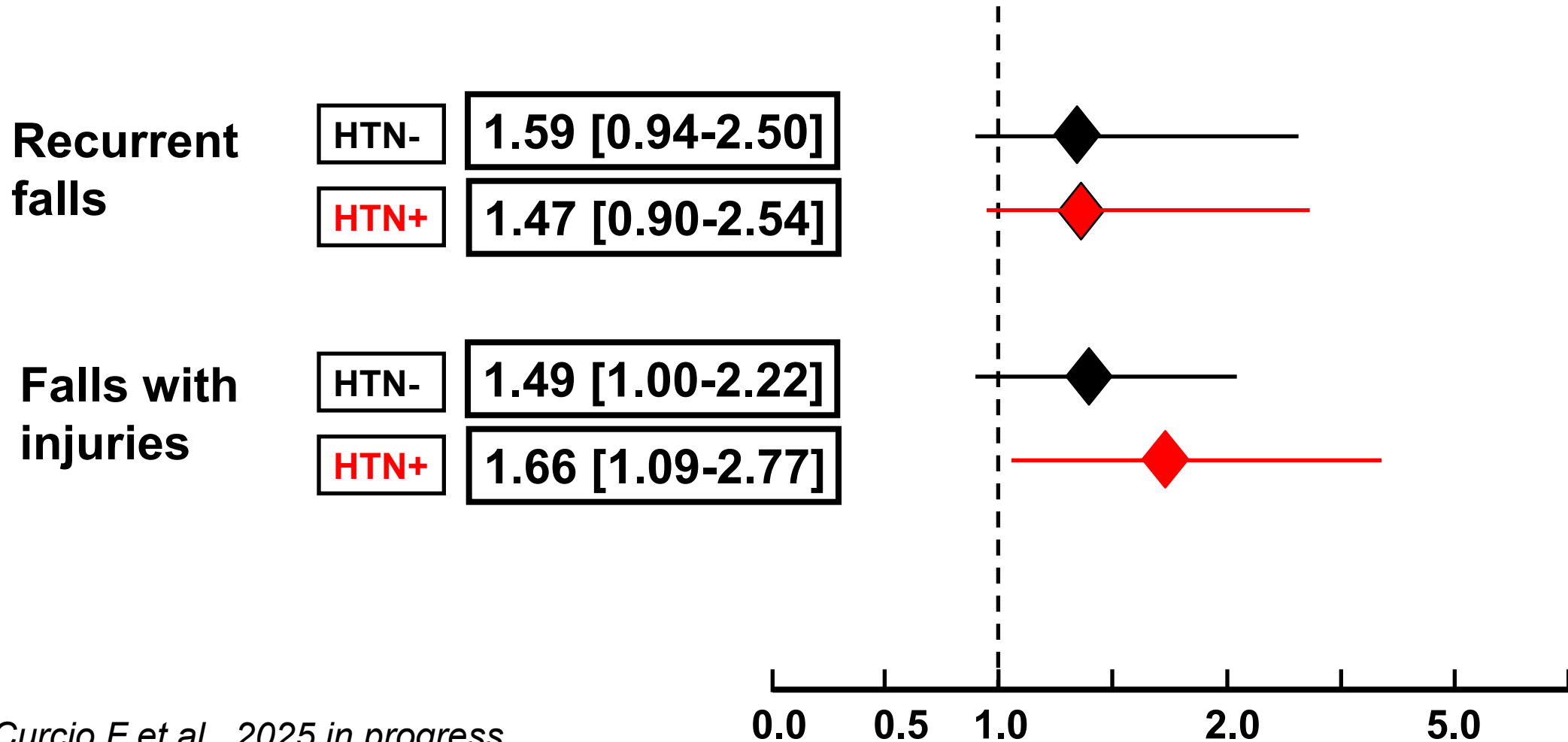
Emergency and Accident Department, Medicine Unit – Syncope and Autonomic Unit,  
Ospedale S. Maria Nuova, Florence, Italy

*The association of clinostatic hypertension (CH) and orthostatic hypotension (OH) is described as the “Hyp-Hyp phenomenon,” **and it has been found in about 5.5% of hypertensive patients and in up to 50% of patients with OH.** The importance of CH/OH in clinical practice is mainly due to the presence of troublesome symptoms, end-organ damage, **and difficulties in its clinical management.***

# Multivariate analysis in pts with ORTHOSTATIC HYPOTENSION “at 1 min” in presence (HTN+) and absence (HTN-) of CLINOSTATIC HYPERTENSION



# Multivariate analysis in pts with ORTHOSTATIC HYPOTENSION “at 3 min” in presence (HTN+) and absence (HTN-) of CLINOSTATIC HYPERTENSION



- 
- Hypotensive phenotype in older adults
  - HYP-HYP phenomenon
  - **Hypertension therapy and orthostatic hypotension**
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-

# Association between orthostatic hypotension after standing for 1 or 3 minutes and being a faller in subjects with controlled and uncontrolled hypertension

Hazard Ratio\* (95% Confidence Interval)

Predictor	Controlled Hypertension	Uncontrolled Hypertension
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*Uncontrolled Hypertension*

SBP  $\geq$  20 mmHg after 1 min standing

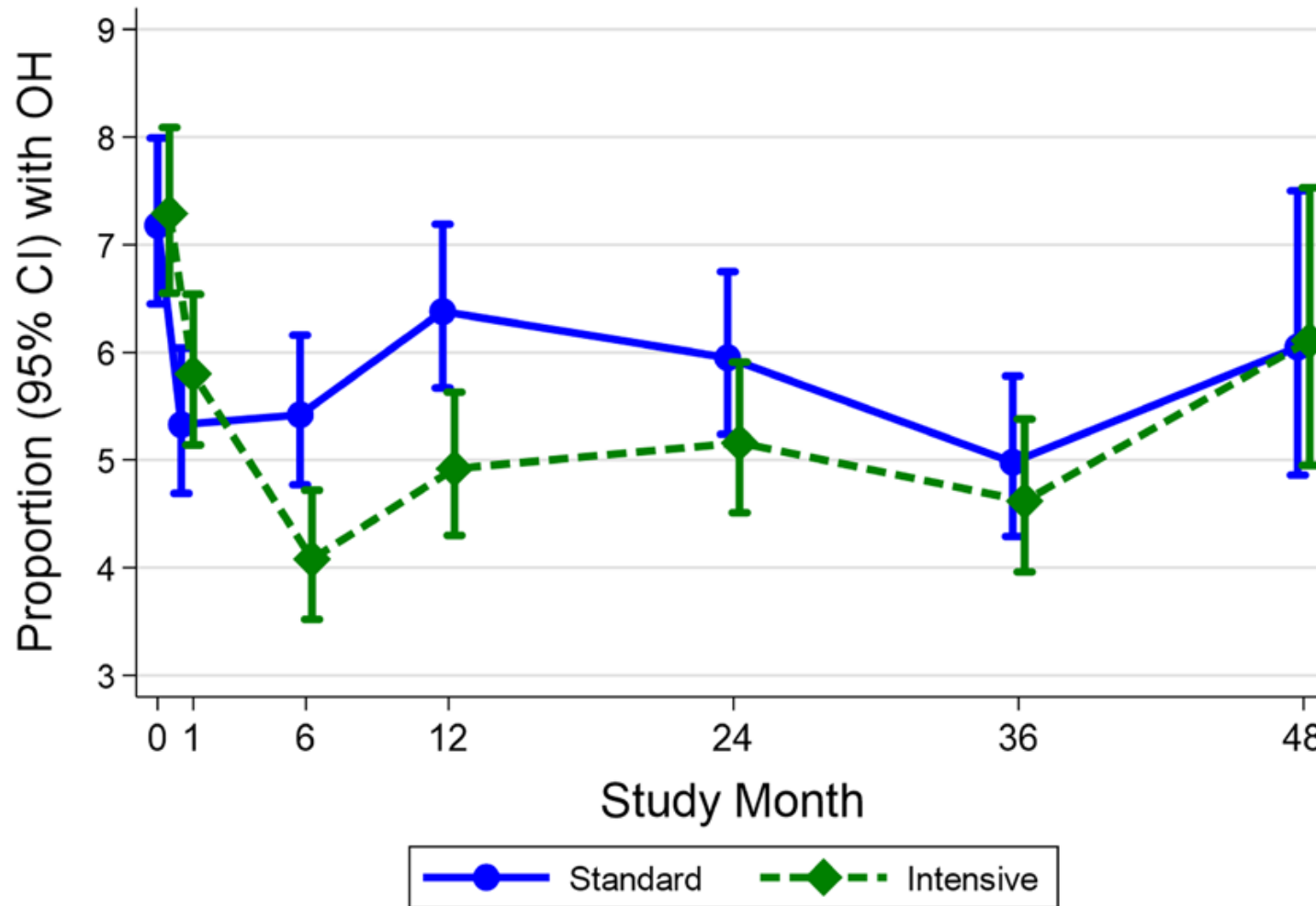
**HR 2.54 CI 95% (1.27-5.09)**

Drop in DBP $\geq$ 10 mmHg after 3 minute standing	1.22 (0.16–9.17)	0.71 (0.17–2.9)
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\*Models were adjusted for age, sex, race, education, stroke, diabetes, receiving hypertension medication. Mini Mental State Examination score. hem-

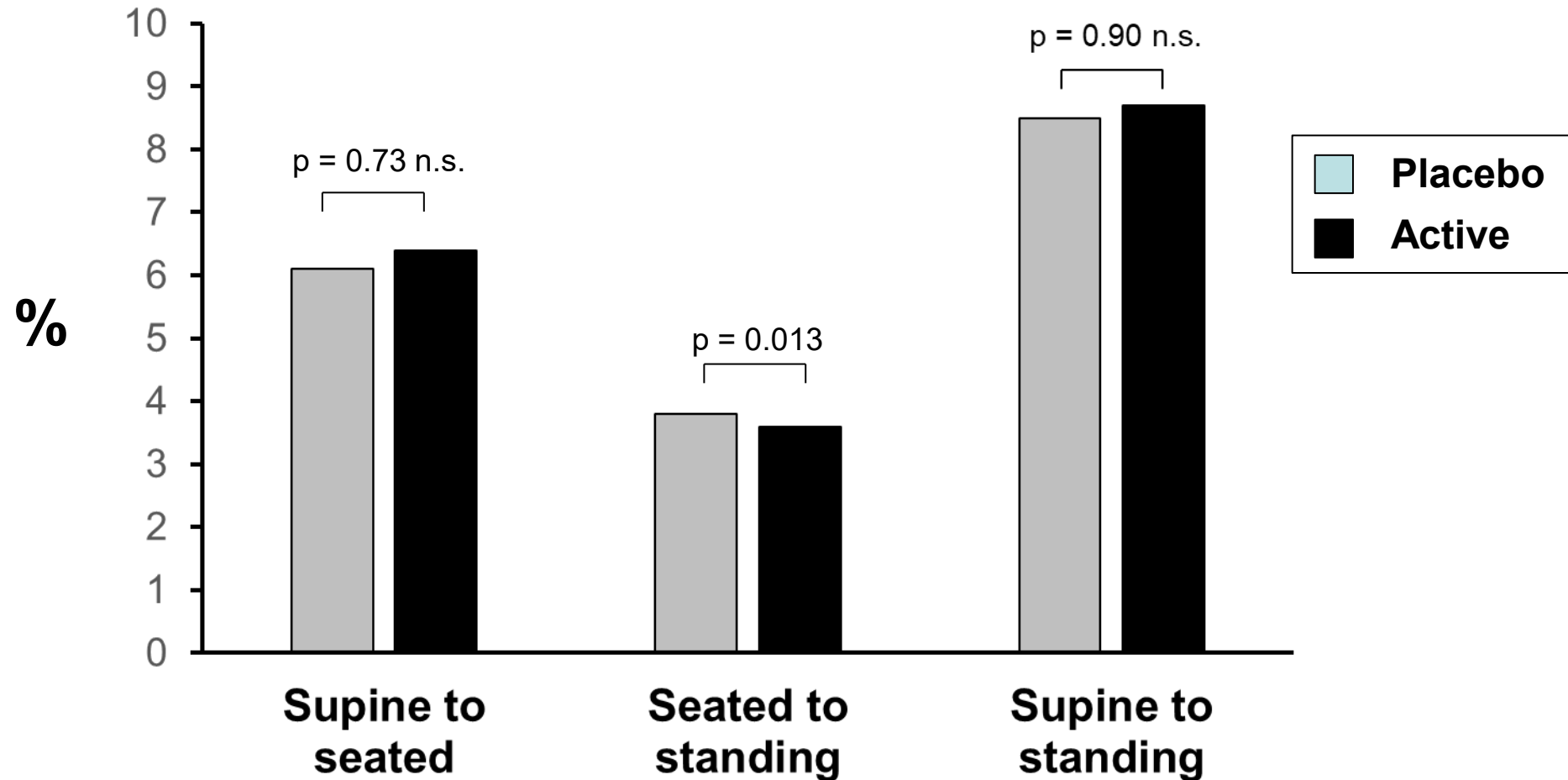
# The proportion with orthostatic hypotension (OH) by treatment assignment

## *Results From SPRINT study*

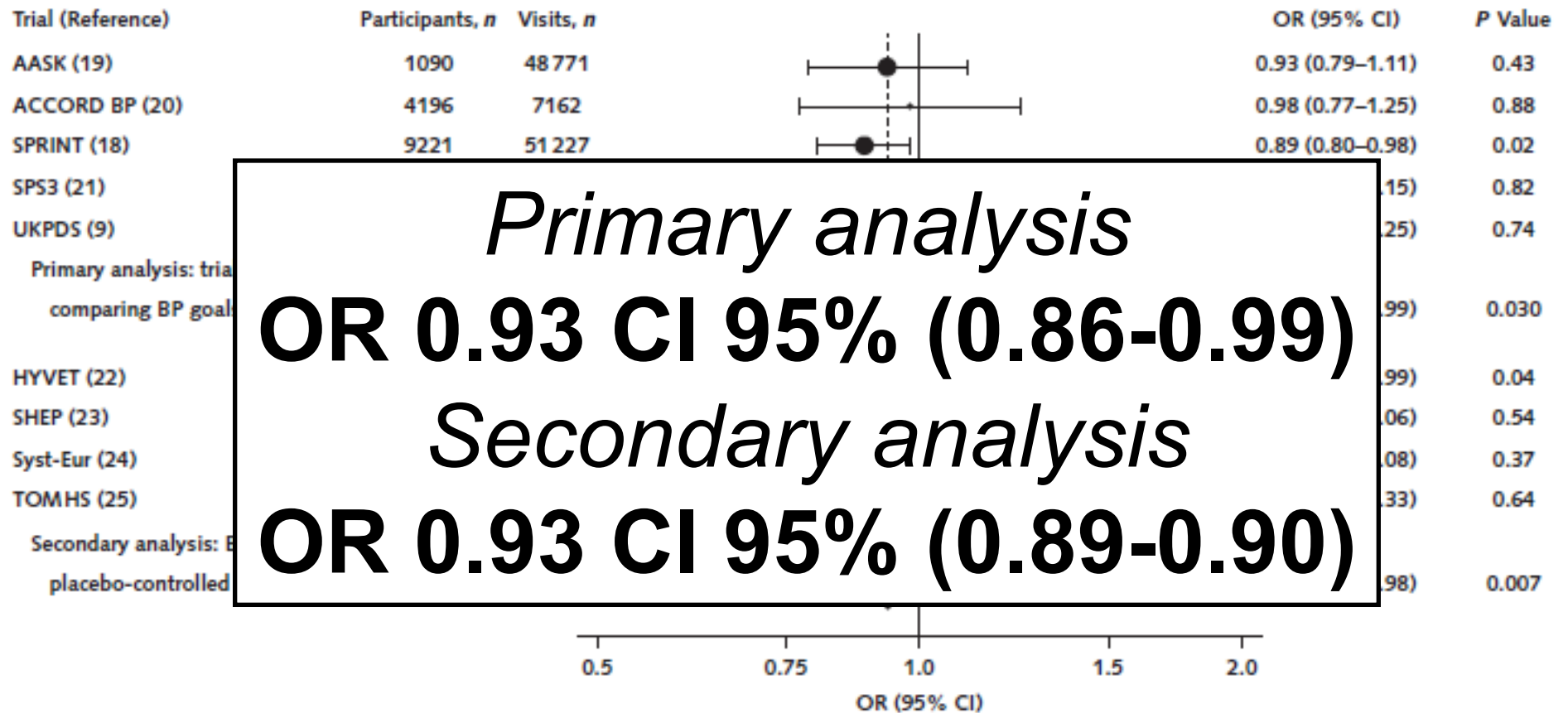


# Effects of Active Treatment on Orthostatic Hypotension at follow-up

(*n=4694 participants with 53335 measures*)

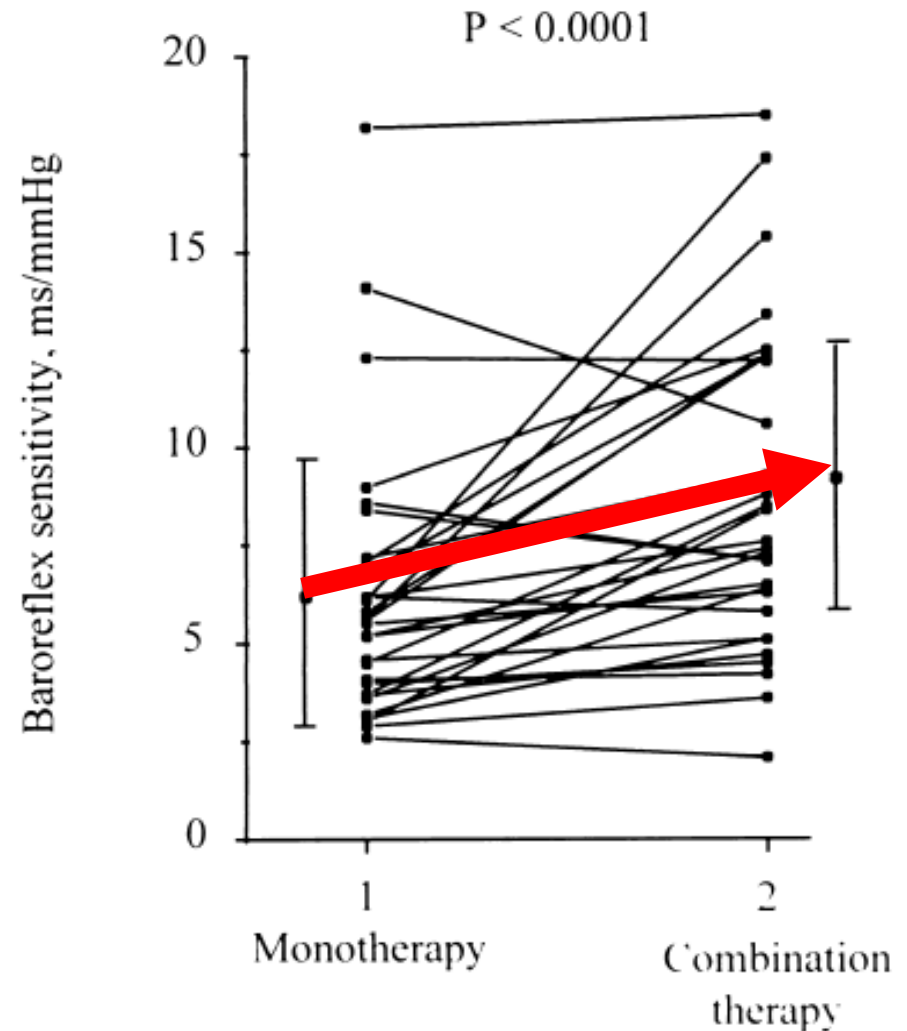
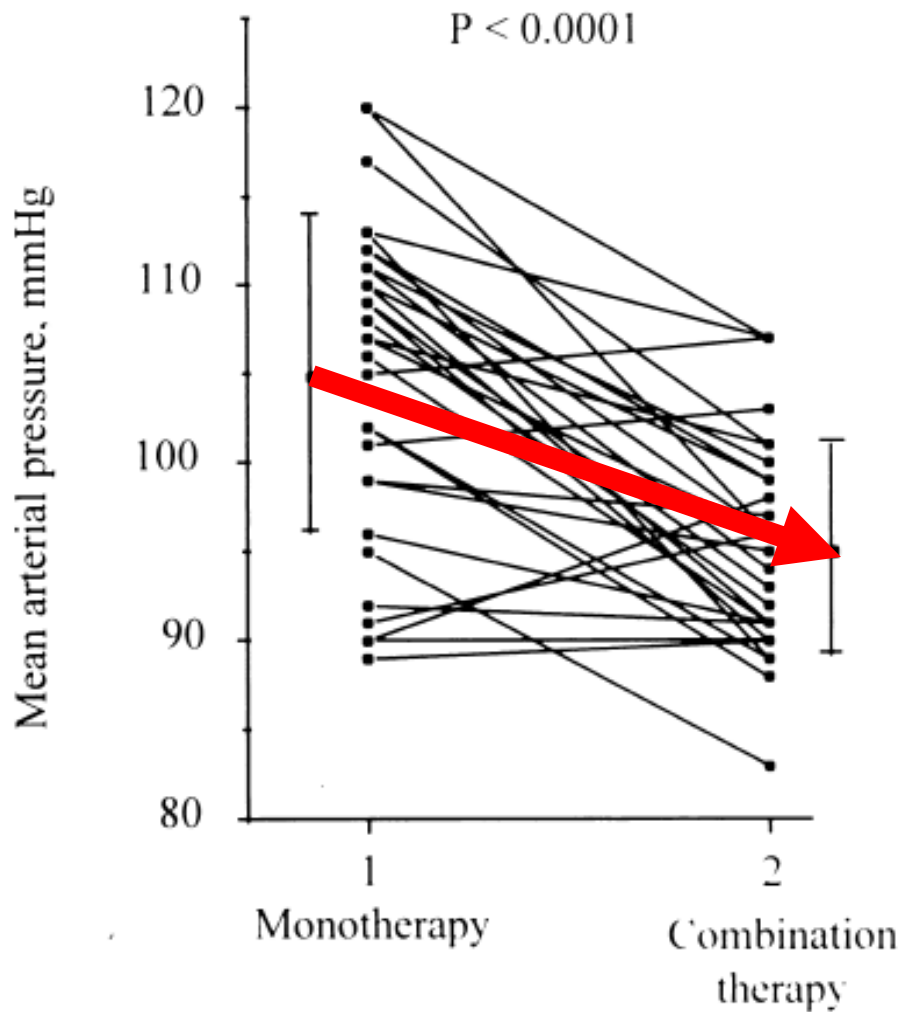


# Effects of BP treatment on risk for orthostatic hypotension, by study



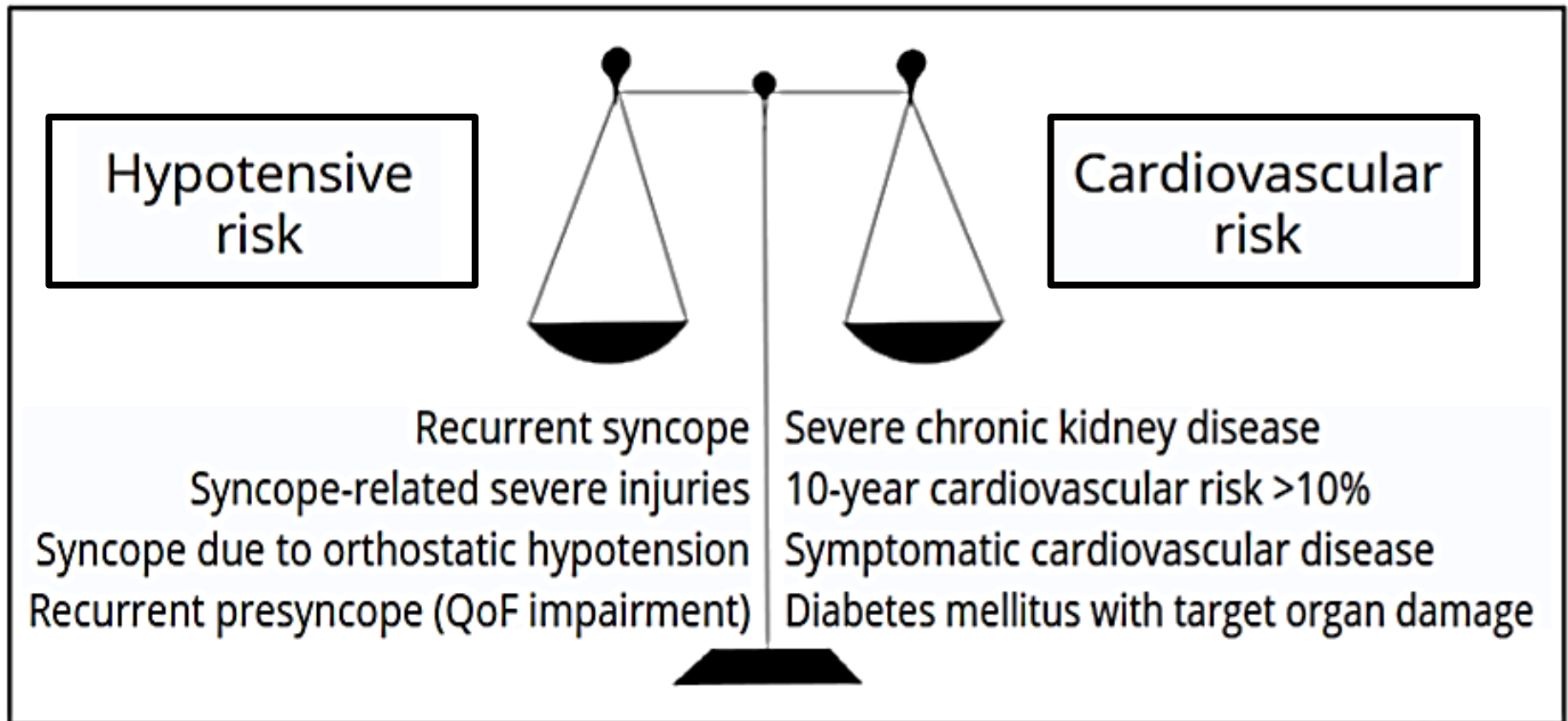
Pooled effects are organized by the 5 primary studies (primary effect) and with the 4 additional trials identified through our search. The size of each point estimate is weighted by the number of follow-up visits with orthostatic hypotension assessments. AASK = African American Study of Kidney Disease and Hypertension; ACCORD BP = Action to Control Cardiovascular Risk in Diabetes: Blood Pressure; BP = blood pressure; SPRINT = Systolic Blood Pressure Intervention Trial; SPS3 = Secondary Prevention of Small Subcortical Strokes; UKPDS = U.K. Prospective Diabetes Study; HYVET = Hypertension in the Very Elderly Trial; OR = odds ratio; SHEP = Systolic Hypertension in the Elderly Program; Syst-Eur = Systolic Hypertension in Europe; TOMHS = Treatment of Mild Hypertension Study.

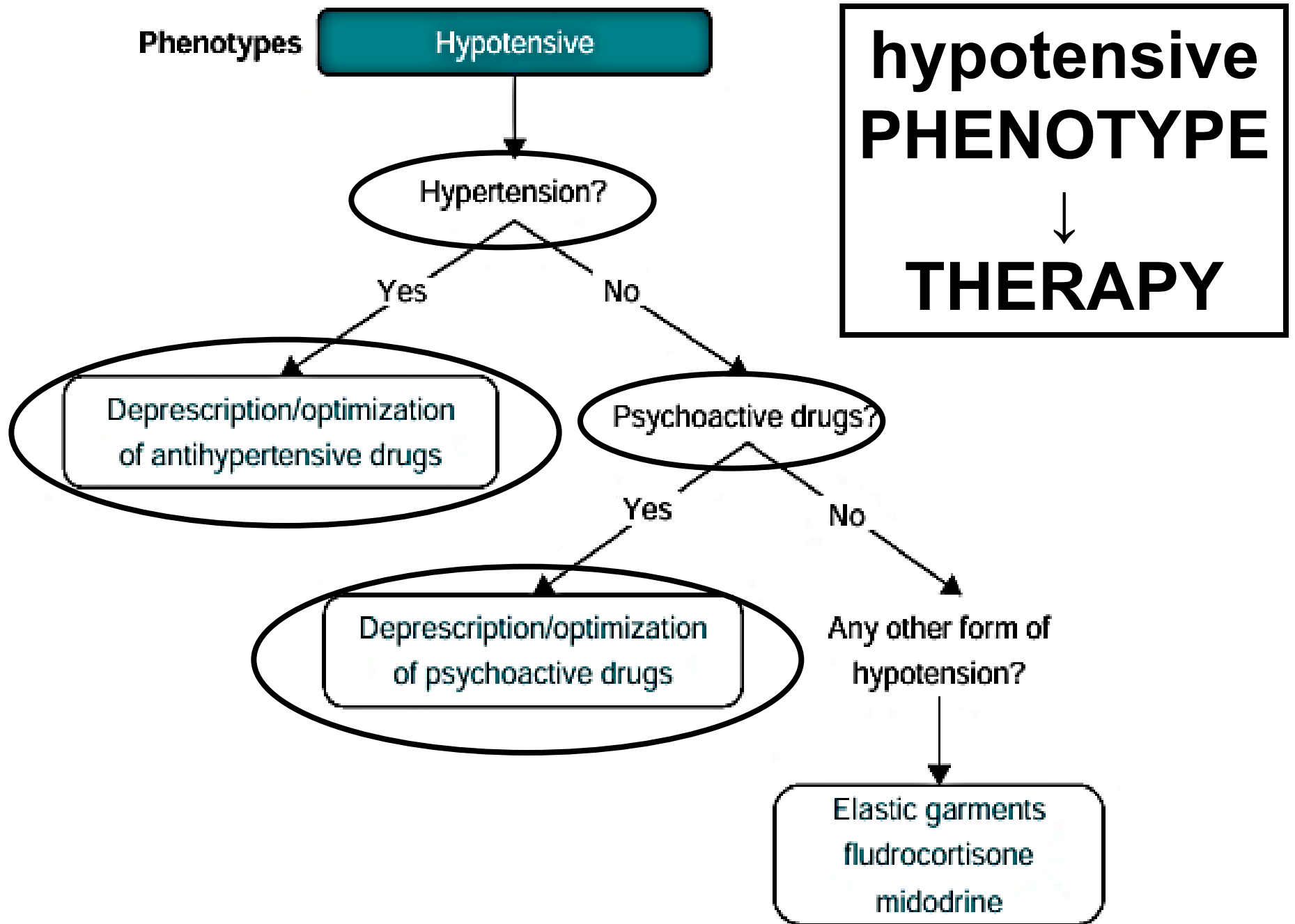
# Effects of Combination Antihypertensive Therapy on Baroreflex Sensitivity and Heart Rate Variability in Systemic Hypertension



- 
- Hypotensive phenotype in older adults
  - HYP-HYP phenomenon
  - Hypertension therapy and orthostatic hypotension
  - **Anti-hypertensive therapy in hypotensive phenotype**
  - Take home messages
-

# Balancing cardiovascular and hypotensive risk in hypertensive patients hypotension



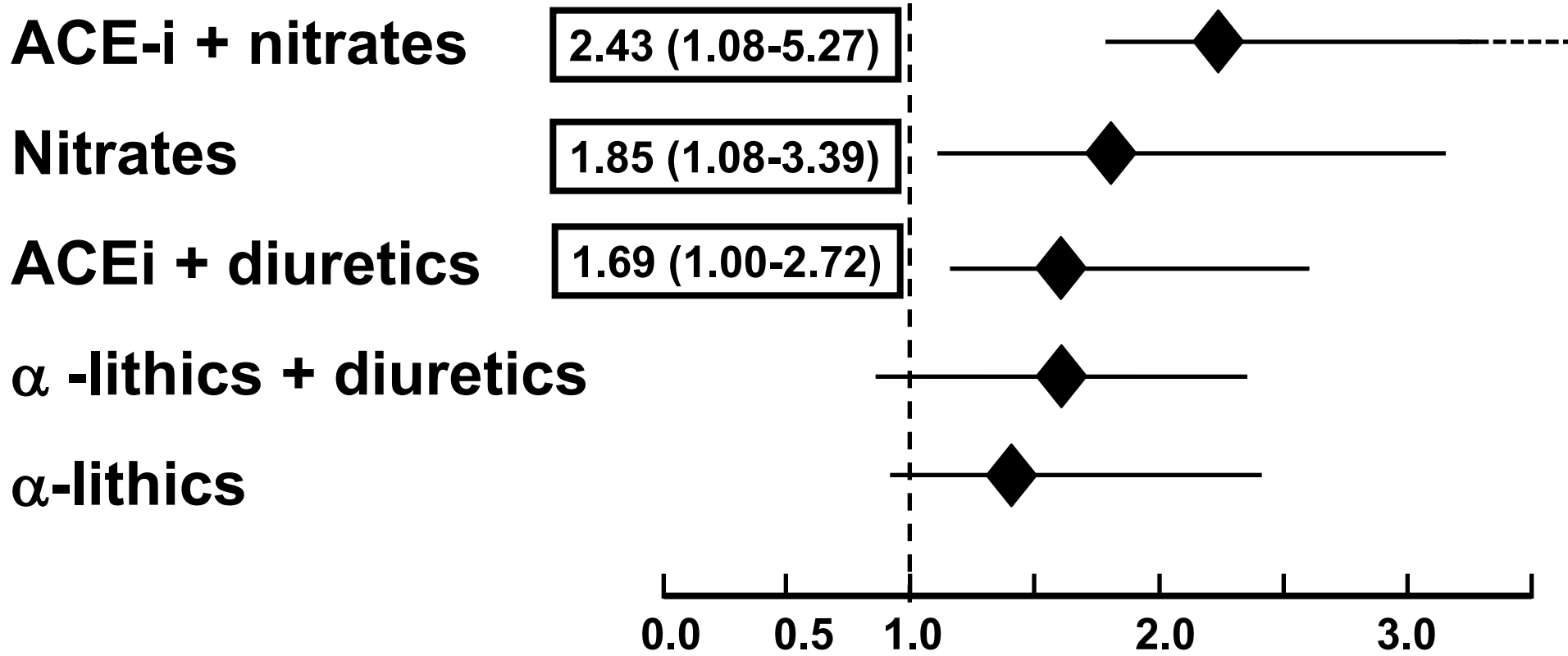


# Hypothensive drugs and their combinations are associated with “orthostatic syncope” in patients with dementia

*Results from SYD study*

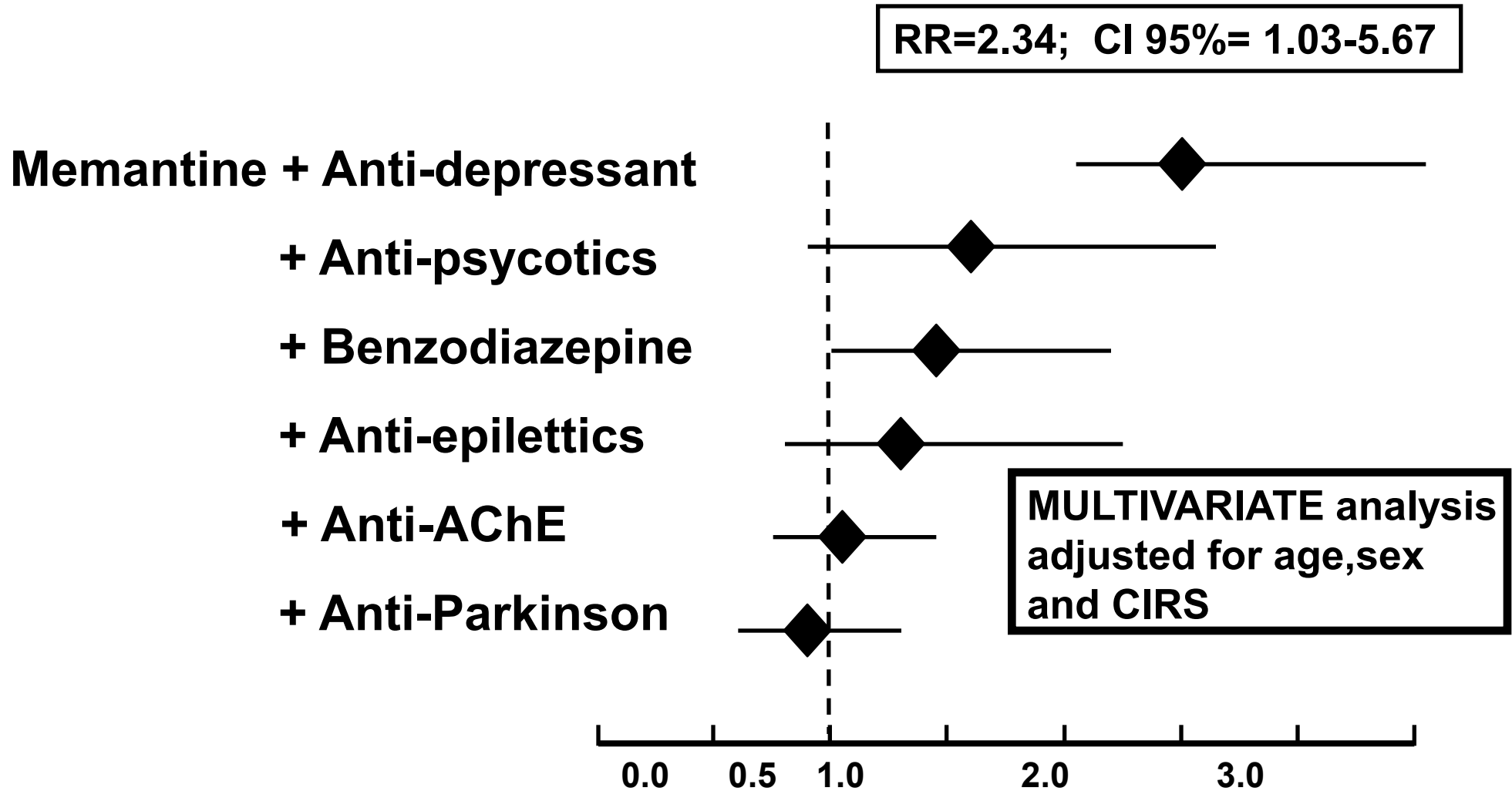
**MULTIVARIATE analysis  
adjusted for age,sex and CIRS**

*Testa G et et al, 2018 JAGS 2018*

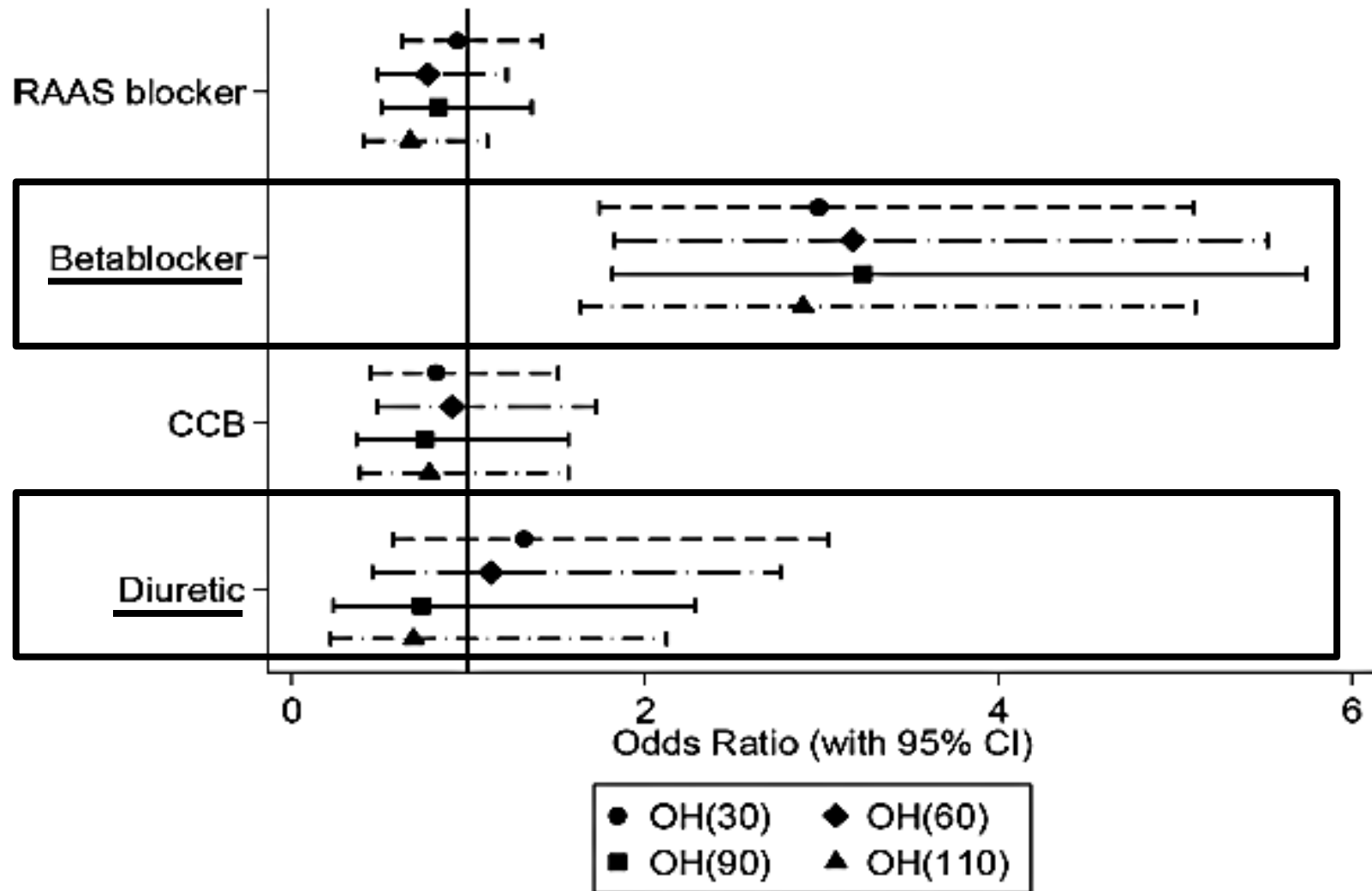


# Psychotropic drugs and their combinations and “reflex syncope” in patients with dementia

## *Results from SYD study*



# Odds ratios (with 95% confidence interval) of orthostatic hypotension (OH) at 30, 60, 90 and 110 seconds post-active stand for each antihypertensive agent.

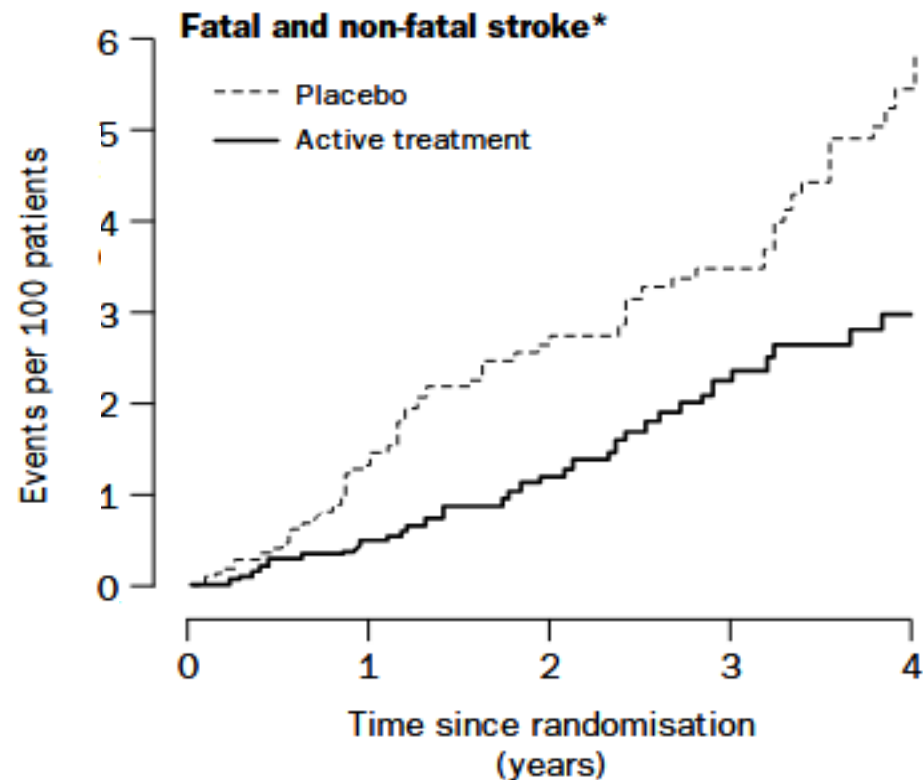


# Cumulative rates of fatal and non-fatal stroke and myocardial infarction by treatment group

## Syst-Eur

Syst-Eur, a multicentre trial designed to test the antihypertensive treatment of elderly patients with isolated systolic hypertension results in a significant change in stroke morbidity and mortality.

The study, which was supposed to last 5 years, was interrupted after about 2 years due to the significant reduction in the rate of cardiovascular complications in the group treated with a CALCIUM CHANNEL BLOCKER (NITRENDIPINE) compared to the placebo.



# Dihydropyridine Calcium antagonists and Blood–Brain Barrier Penetration

Drug	Blood–Brain Barrier Penetration	Notes
Nimodipine	High	The calcium antagonist with the best CNS penetration.
<b>Nitrendipine</b>	<b>Moderate</b>	Moderately lipophilic but strongly extruded by P-gp.
Nicardipine	Moderate	Partial CNS penetration; used in hypertensive emergencies.
Isradipine	Low–Moderate	Some experimental interest in Parkinson's disease.
Nifedipine	Very Low	Minimal lipophilicity; negligible CNS penetration.
Amlodipine	Very Low	Polar and long-acting; clinically irrelevant BBB penetration.
Felodipine	Very Low	Poor CNS penetration.
Lacidipine	Very Low	Negligible penetration.

**The drug is not easy to find....**

# Orthostatic Hypotension in the Hypertensive Patient

Italo Biaggioni

Orthostatic hypotension (OH) is an important and common medical condition that can be exacerbated by certain medications, such as alpha-blockers and acarbose, respectively, without the need to increase baseline

**In patients with isolated orthostatic hypertension and orthostatic hypotension:**

- **Avoid supine position during the day**
- **Prefer short-acting anti-hypertensives dosed at night**

can worsen OH, including ones that are easily overlooked, such as tamsulosin, tizanidine, sildenafil, trazodone, and carvedilol. OH and postprandial hypotension can be prevented with abdominal binders

*Keywords:* autonomic nervous system, blood pressure, hypertension, orthostatic hypotension; sympathetic nervous system.

doi:10.1093/ajh/hpy089

# Hypertension and orthostatic hypotension in the elderly: a challenging balance

Julia Wiersinga,<sup>a,h\*</sup> Sofie Jansen,<sup>a</sup> Mike J. L. Peters,<sup>c</sup> Hanneke F. M. Rhodius-Meester,<sup>d,e</sup> Marjke C. Trappenburg,<sup>f</sup> Jurgen A. H. R. Claassen,<sup>g,h</sup> and Majan Muller<sup>a,b</sup>

The Lancet Regional  
Health - Europe  
2025;48: 101154  
Published Online 3  
December 2024  
<https://doi.org/10.1016/j.lanpe.2024.101154>

## Patient A:

**Patient characteristics:** male, 83 years

**Referral reason:** recurrent falls

**Medical history:** transient ischemic attack, hypertension, benign prostate hyperplasia, osteoarthritis.

**Medication:** Clopidogrel, enalapril, simvastatin, tamsulosin, paracetamol, calcium-cholecalciferol.

**Clinical frailty scale:** 4, living with mild frailty (1).

### Blood pressure measurement:

- Supine : 165/90 mmHg, pulse (p) 65 beats per minute (bpm).
- 1 minute : 135/80mmHg, p85 bpm
- 3 minute : 130/75mmHg, p83bpm



## Patient A - Recommendations:

### OH recommendation:

Information, counter maneuvers instruction. Ensure fluid repletion.

### Hypertension treatment:

Target values: SBP <140mmHg, >110mmHg

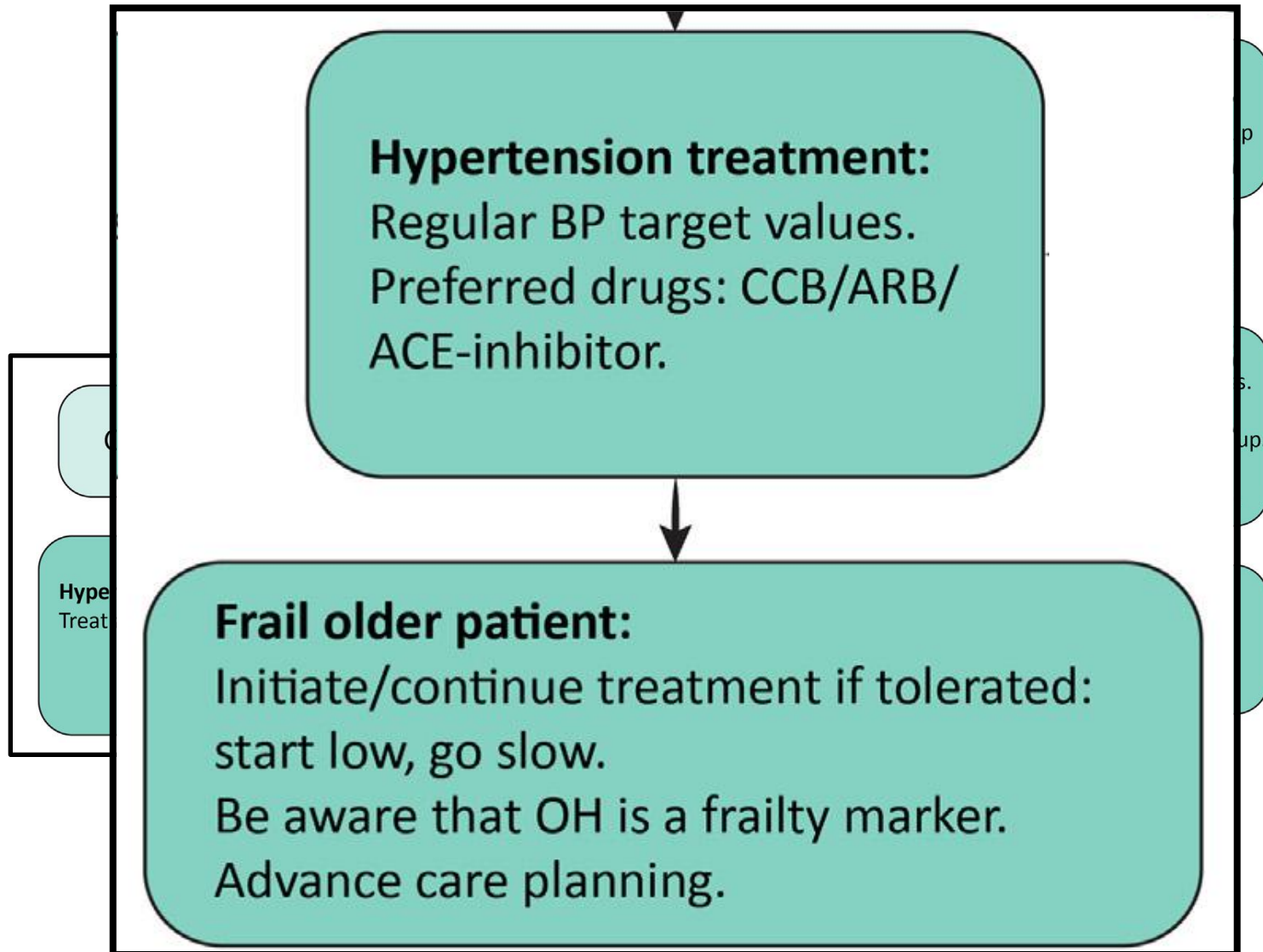
Preferred antihypertensive drug: Calcium channel blocker

### Additional recommendation:

Replacing tamsulosin with a 5-alpha-reductase-inhibitor



# OH Assessment and treatment in older patients with hypertension.



# Targets for deprescribing in patients with hypertension and reflex syncope

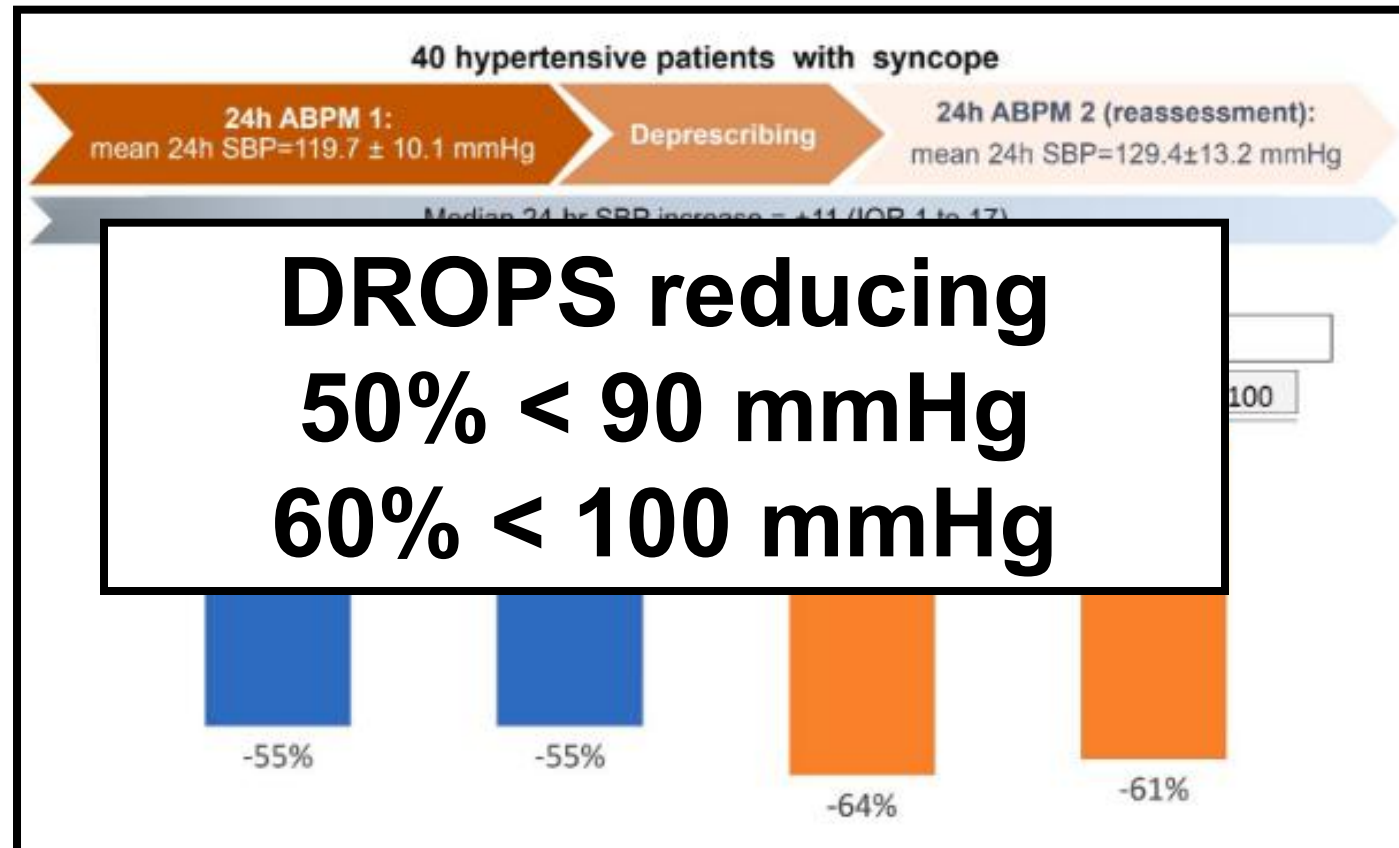
SBP drops consisted of  $\geq 1$  SBP measures  $<100$  or  $<90$  mmHg

	ABPM 1	ABPM 2		
		Withdrawal	Dose reduction	Unchanged
Total number of hypotensive drugs	98	44 (45 %)	16 (16 %)	38 (39 %)
Median number per patient (SD)	2 (1 to 2)		1 (0 to 2)	
-ACE-inhibitors	0	0	0	0
-ARBs	0	0	0	0
-Beta-blockers	3	3	0	0
-Ca-antagonists	2	2	0	0
-Alpha-blockers	3	3	0	0
-Diuretics	17	12	3	2
-Benzodiazepines	4	1	1	2
-Antidepressants	4	1	0	3
-SSRI/SNRI	3	0	0	2
-Opioids	1	0	0	1
-Trazodone	1	1	0	0
-Levo-Dopa	1	0	0	1

**deprescribing  
DIURETICS  $\approx 70\%$**

# Targets for deprescribing in patients with hypertension and reflex syncope

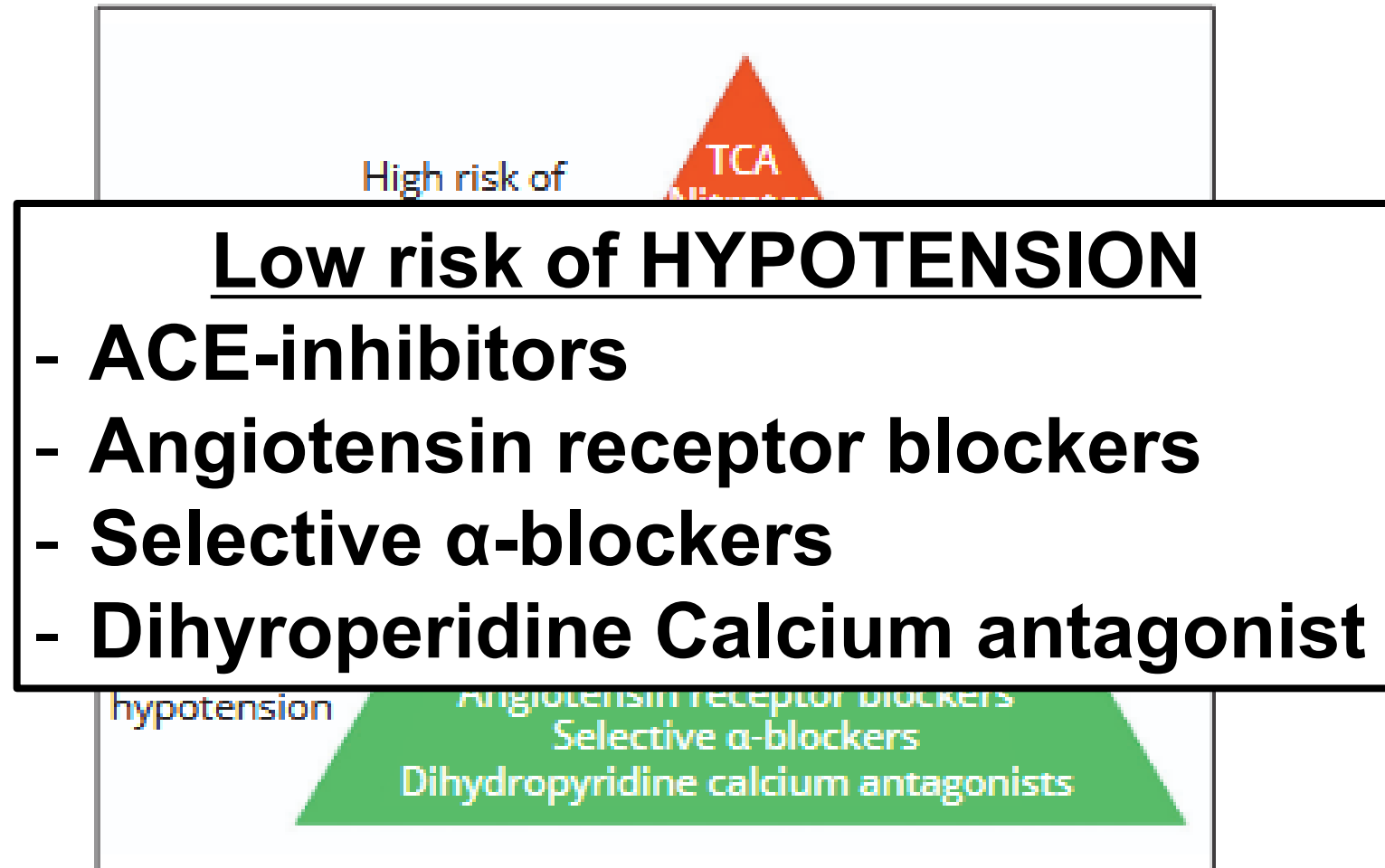
SBP drops consisted of  $\geq 1$  SBP measures  $< 100$  or  $< 90$  mmHg



# Recommendations for managing hypertension in patients with orthostatic hypotension

Recommendation	Class	Level
<b><u>Before starting or intensifying BP-lowering medication</u></b> , it is recommended to test for orthostatic hypotension, by first having the patient sit or lie for 5 min and then measuring BP 1 and/or 3 min after standing	I	B

# Drug-related hypotension: risk profile of major antihypertensive and psychoactive drug classes



Tca: tricyclic antidepressants;  
SSri: Serotonin-selective reuptake inhibitors;  
SNri: serotonin-norepinephrine reuptake inhibitors.

- 
- Hypotensive phenotype in older adults
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-

# TAKE HOME MESSAGES

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- The hypotensive phenotype in older adults is characterized by orthostatic hypotension and blood pressure drops. It is strongly influenced by vascular dysautonomia secondary to dementia.
- This phenotype includes the 'HYP-HYP' phenomenon (clinostatic hypertension-orthostatic hypertension) and serves as a strong predictor of adverse outcomes.
- Anti-hypertensive therapy, except for beta-blockers and diuretics, does not exacerbate orthostatic hypotension.
- Deprescribing hypotensive and psychoactive drugs is crucial for managing blood pressure drops and negative orthostatic responses in the elderly.
- However, dihydropyridine calcium channel antagonists and RAAS blockers remain the preferred options for treating hypertension in elderly patients with a hypotensive phenotype.