

SINCOPE 2023

11° Convegno Nazionale GIMSI



*Centro Congressi dell'Università degli
Studi di Napoli Federico II
16-18 gennaio 2023*

Valutazione rischio/beneficio della terapia vasoattiva nel paziente con sincope



Prof. P. Abete

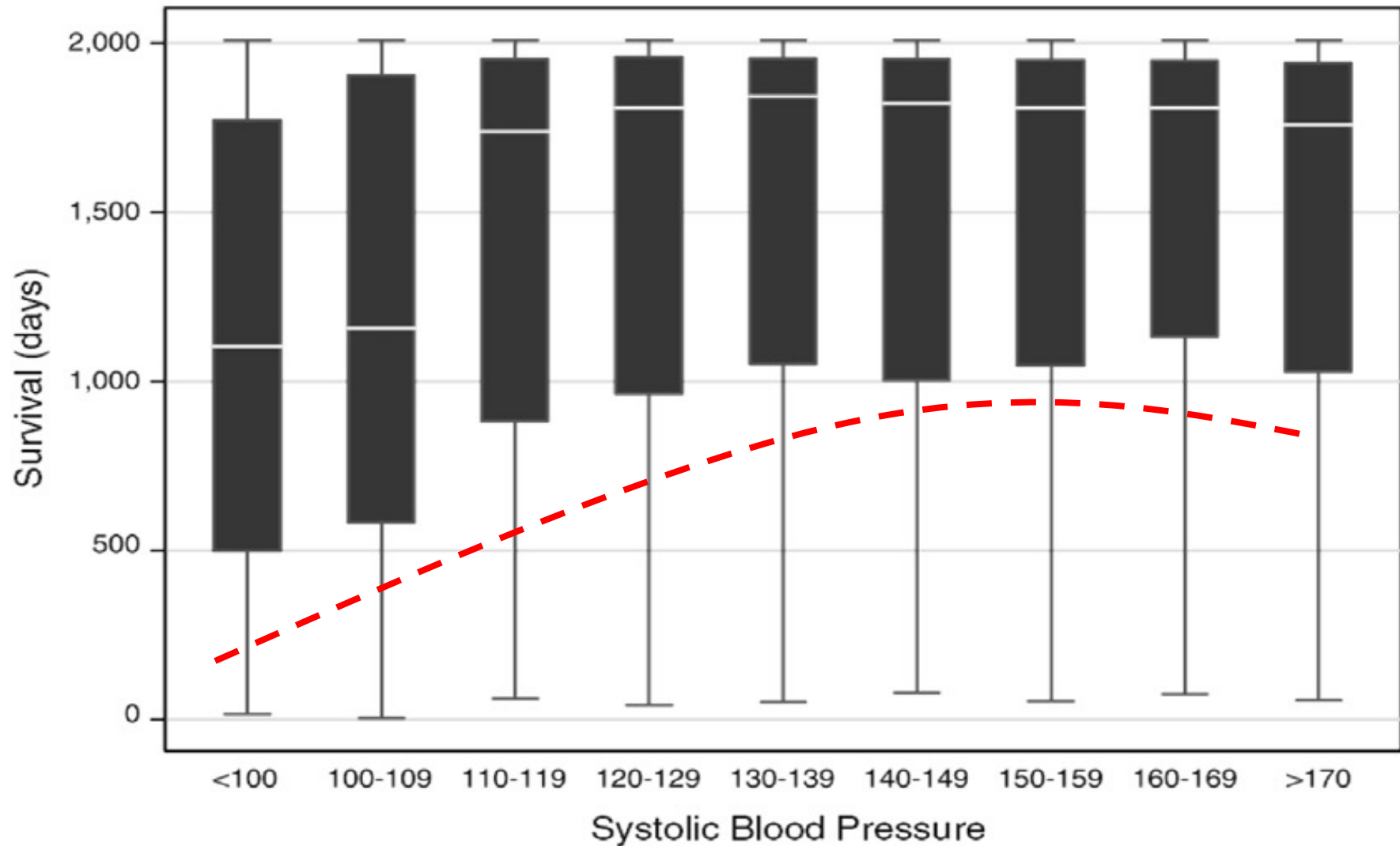
Dipartimento di Scienze Mediche Traslazionali
Università di Napoli Federico II



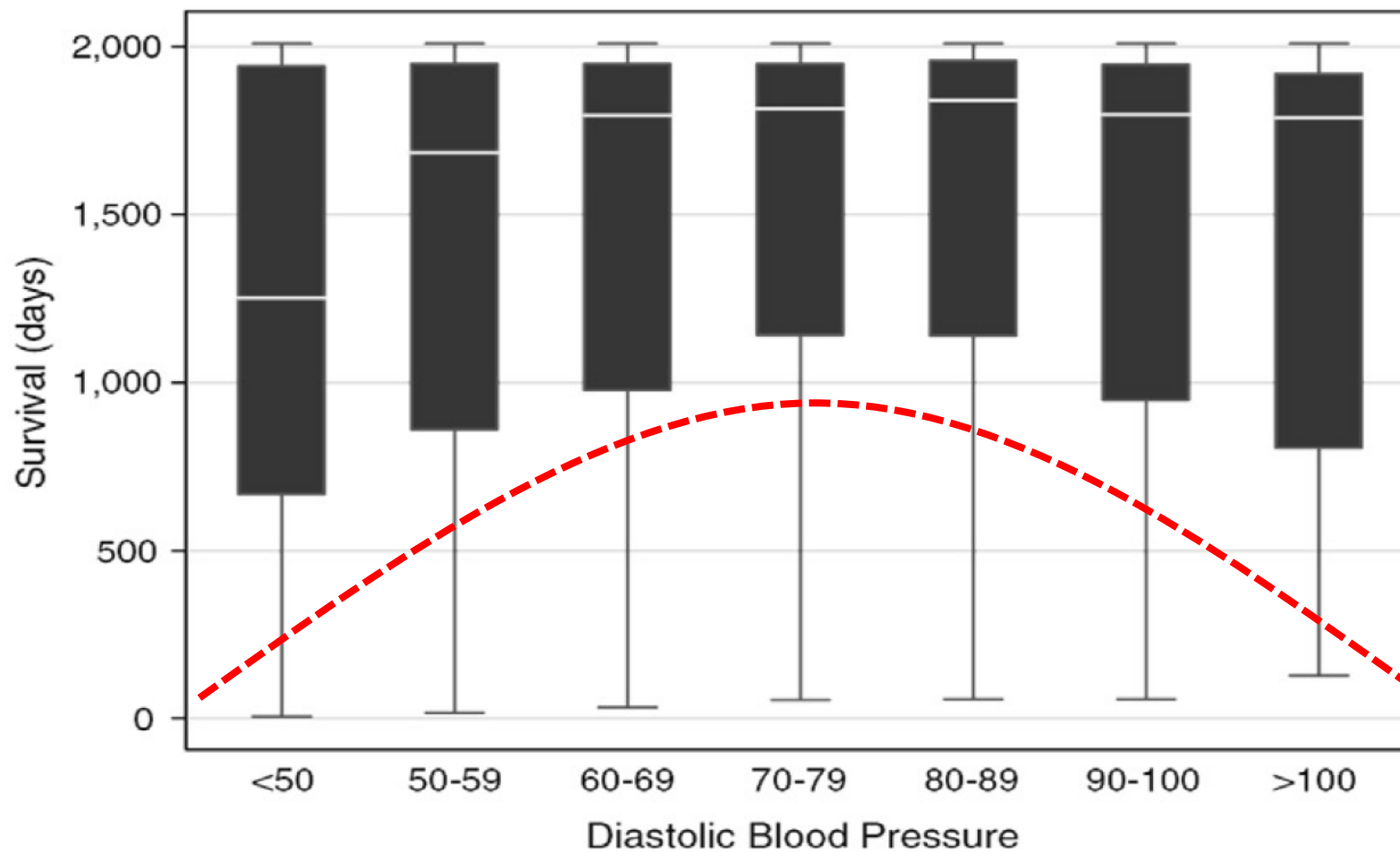
*Centro Congressi dell'Università degli
Studi di Napoli Federico II
16-18 febbraio 2023*

- **Clinical evidences**
- Intensive treatment in the “frail” patient
- Stop/reduce vasoactive drugs: the “SYD-study”
- Hyp-hyp phenomenon
- Clinical approaches

Systolic blood pressure and survival in the oldest-old

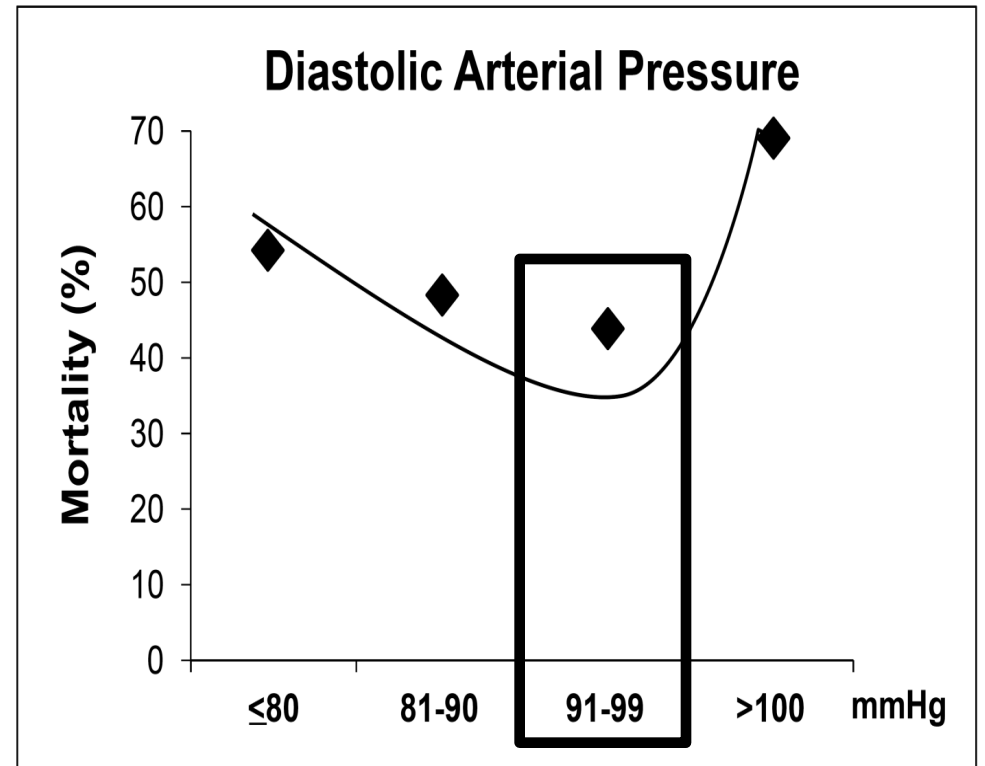
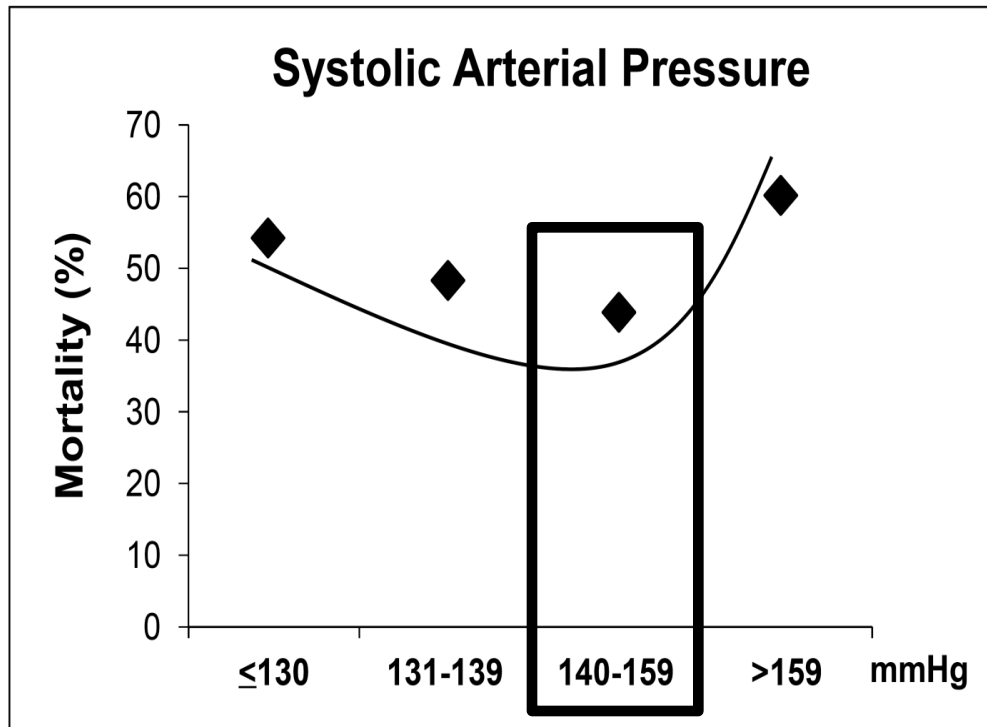


Diastolic blood pressure and survival in the oldest-old

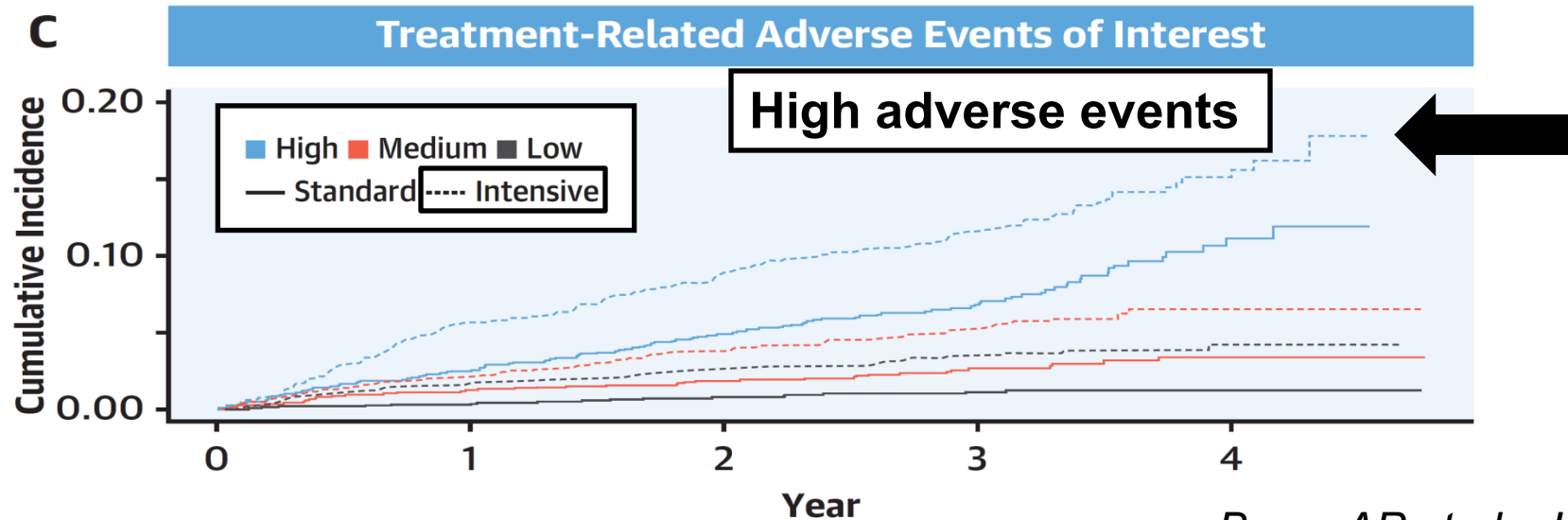
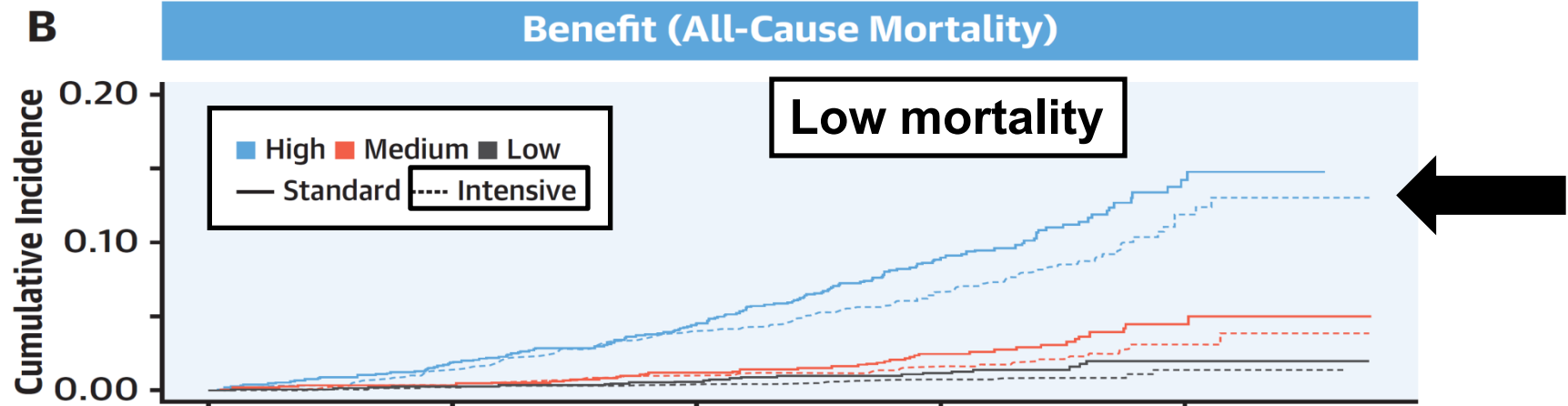


Mortality and Blood Pressure in Elderly People

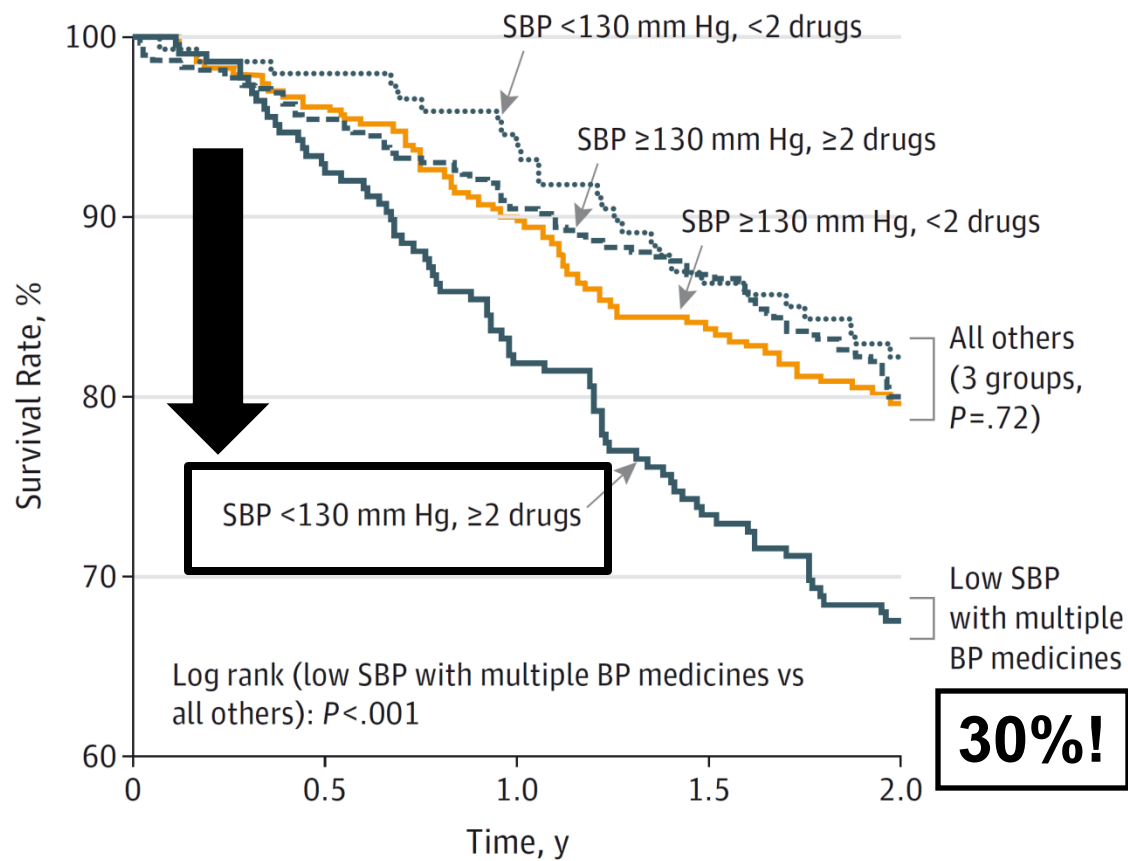
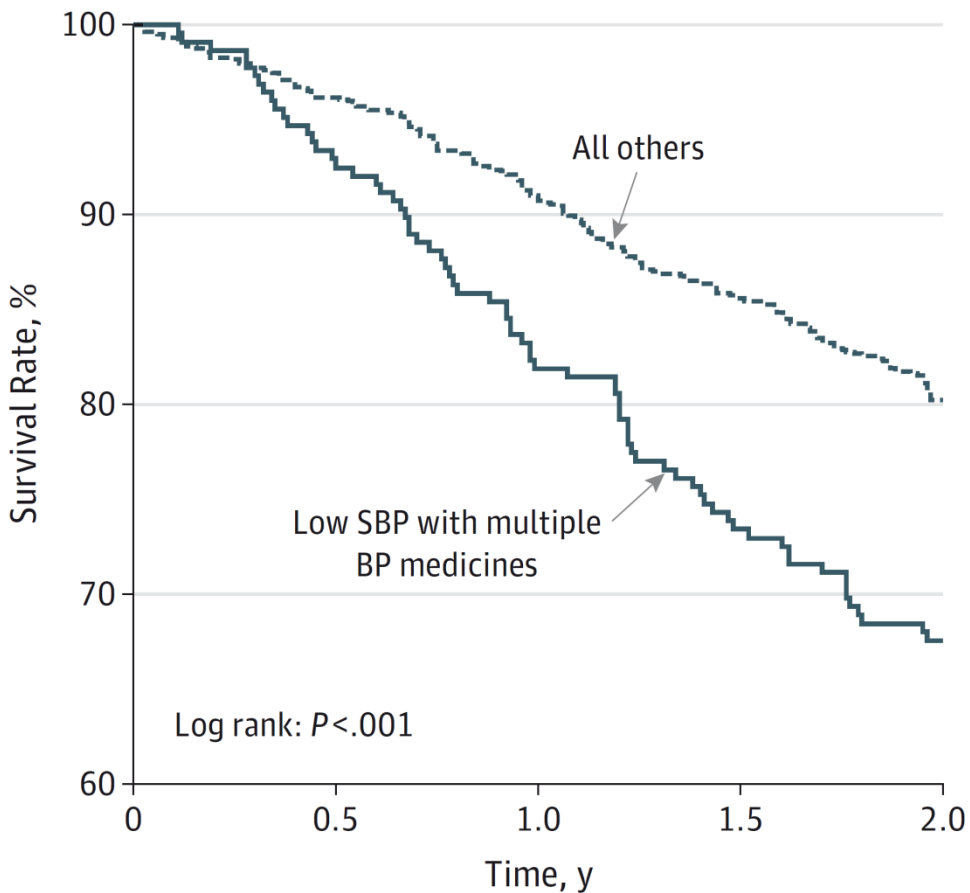
Osservatorio Geriatrico Campano



All-cause mortality and treatment-related adverse events for intensive versus standard systolic blood pressure treatment (SPRINT study)



Kaplan-Meier Survival Curves in patients with low systolic blood pressure (SBP) receiving multiple BP medicines and all other groups



Older Nursing Home Residents
The PARTAGE Study

Benetos A et al., JAMA Intern Med 2015

Serious FALL injury events among relevant subgroups according to anti-hypertensive intensity in older adults with hypertension

Fall in past year

No (n = 4621)

Moderate intensity

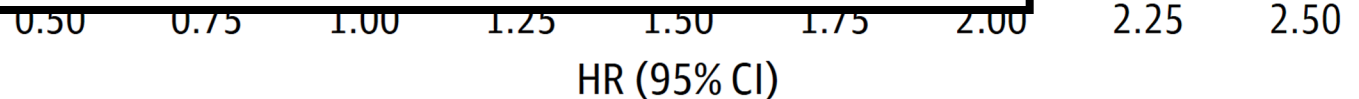
High intensity

Yes (n = 503)

Moderate intensity

High intensity

anti-hypertensive therapy
moderate intensity
2.17 (95%CI, 0.98-4.80)
high intensity
2.31 (1.01-5.29)



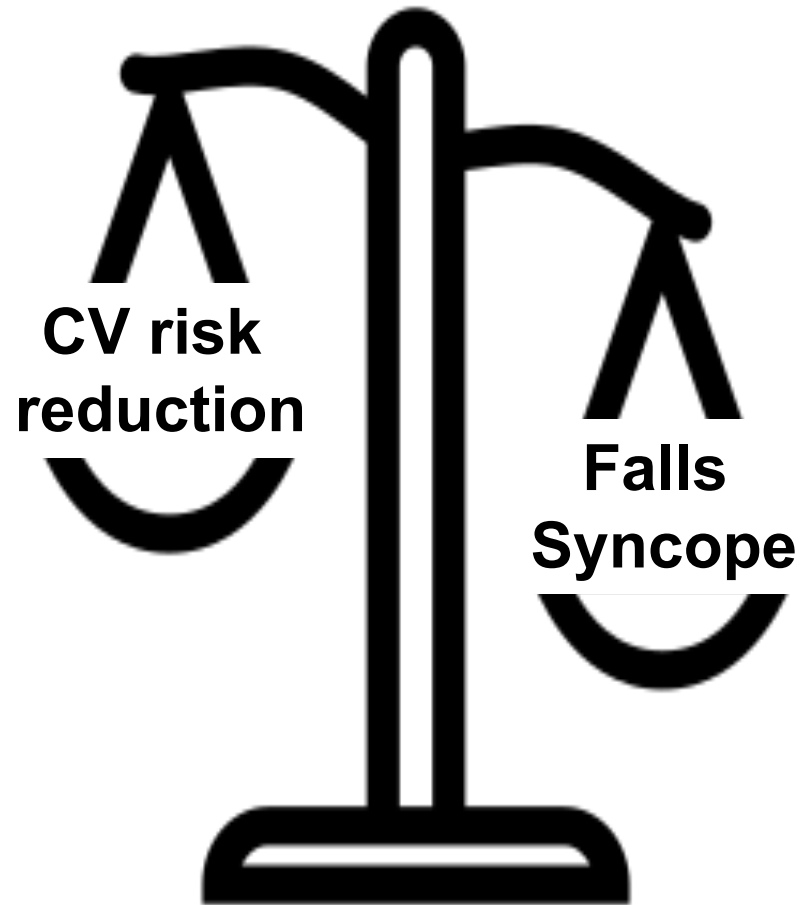
4961 community-living adults older than 70 years with hypertension - Medicare Current Beneficiary Survey

Number of Serious Fall Injuries and Syncope by Systolic Blood Pressure (SBP)

SBP	Syncope	
	<65 years, OR (95% CI)	≥65 years, OR (95% CI)
Minimum SBP		
≥110	1	1
<110	3.11 (2.85, 3.40)	2.33 (2.22, 2.45)
Mean SBP		
≥110	1	1
<110	2.05 (1.72, 2.43)	1.74 (1.56, 1.93)

A cross-sectional study among medically treated hypertensive individuals within the Kaiser Permanente Southern California health system (2014-2015)

Anti-hypertensive therapy

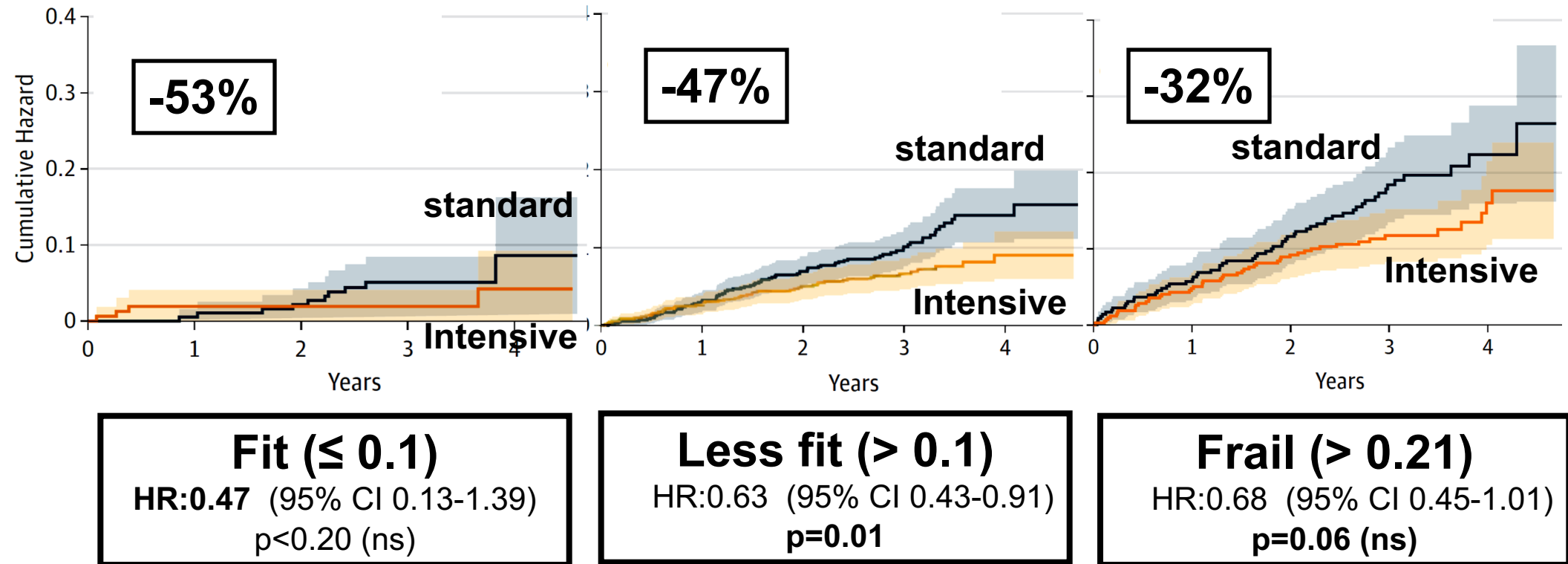


...especially in advancing age!

*Centro Congressi dell'Università degli
Studi di Napoli Federico II
16-18 febbraio 2023*

- Clinical evidences
- **Intensive treatment in the “frail” patient (SPRINT)**
- Stop/reduce vasoactive drugs: the “SYD-study”
- Hyp-hyp phenomenon
- Clinical approaches

Kaplan-Meier curves for the primary cardiovascular disease outcome in Systolic blood PRessure INtervention Trial (SPRINT) in participants aged 75 years or older by baseline frailty status



Impact of SPRINT results on hypertension guidelines: implications for “frail” elderly patients

Gennaro Russo¹ · Ilaria Liguori¹ · Luisa Aran¹ · Giulia Bulli¹ · Francesco Curcio¹ · Gianluigi Galizia² · Gaetano Gargiulo³ · Gianluca Testa^{1,4} · Andrea Ungar⁵ · Francesco Cacciatore^{1,6} · Domenico Bonaduce¹ · Pasquale Abete¹

Received: 22 March 2018 / Revised: 12 June 2018 / Accepted: 18 June 2018

© Macmillan Publishers Limited, part of Springer Nature 2018

The logo for the Journal of Human Hypertension, featuring the journal title in white serif font inside a dark red circular background.

Journal of
Human
Hypertension

Frailty's degree in SPRINT elderly

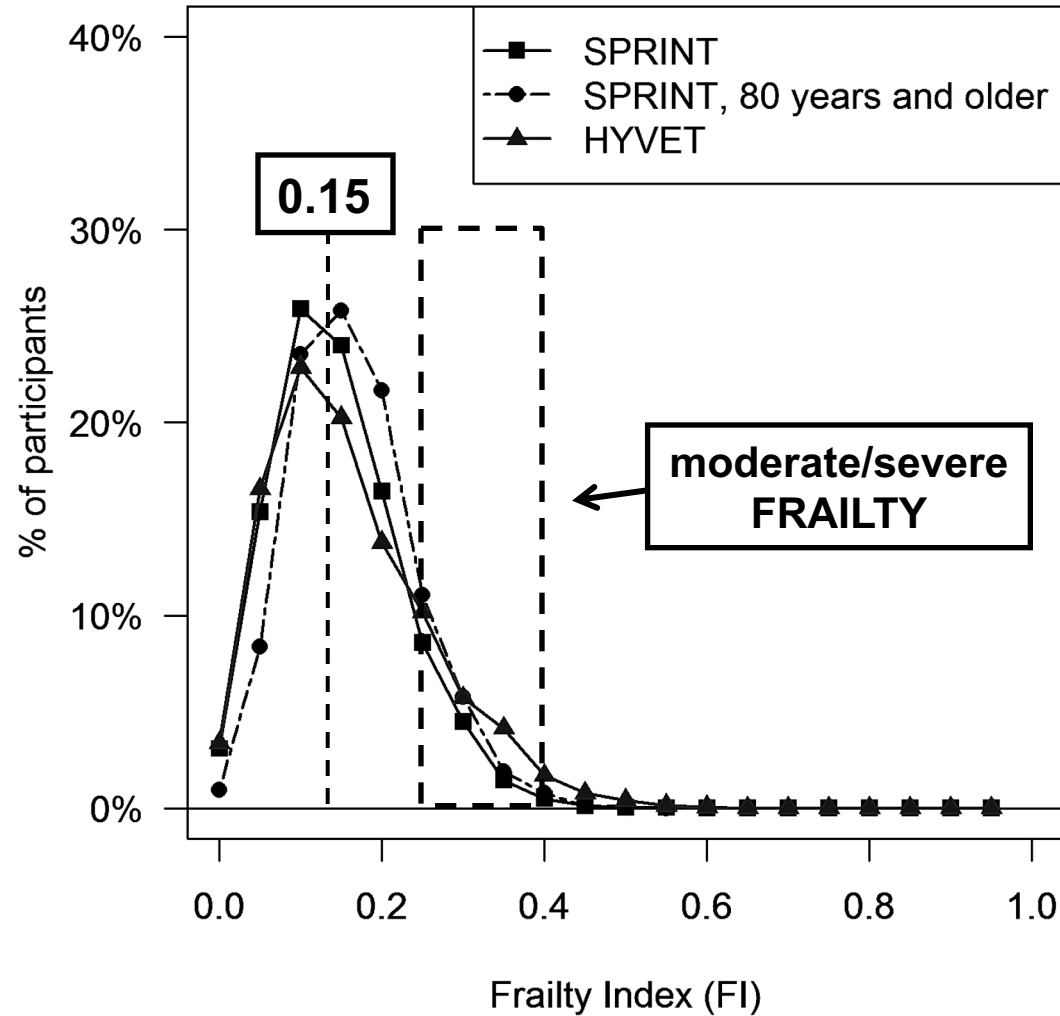
Frailty index (37 items)

0.18 (0.13-0.23); 7 item (5-9)
intensive treatment

0.17 (0.12-0.22); 6 item (4-8)
standard treatment

The higher frailty degree = 0.23
Items lost = 9/37 !!

Characterizing Frailty Status in the Systolic Blood Pressure Intervention Trial (SPRINT)



Aging Clin Exp Res

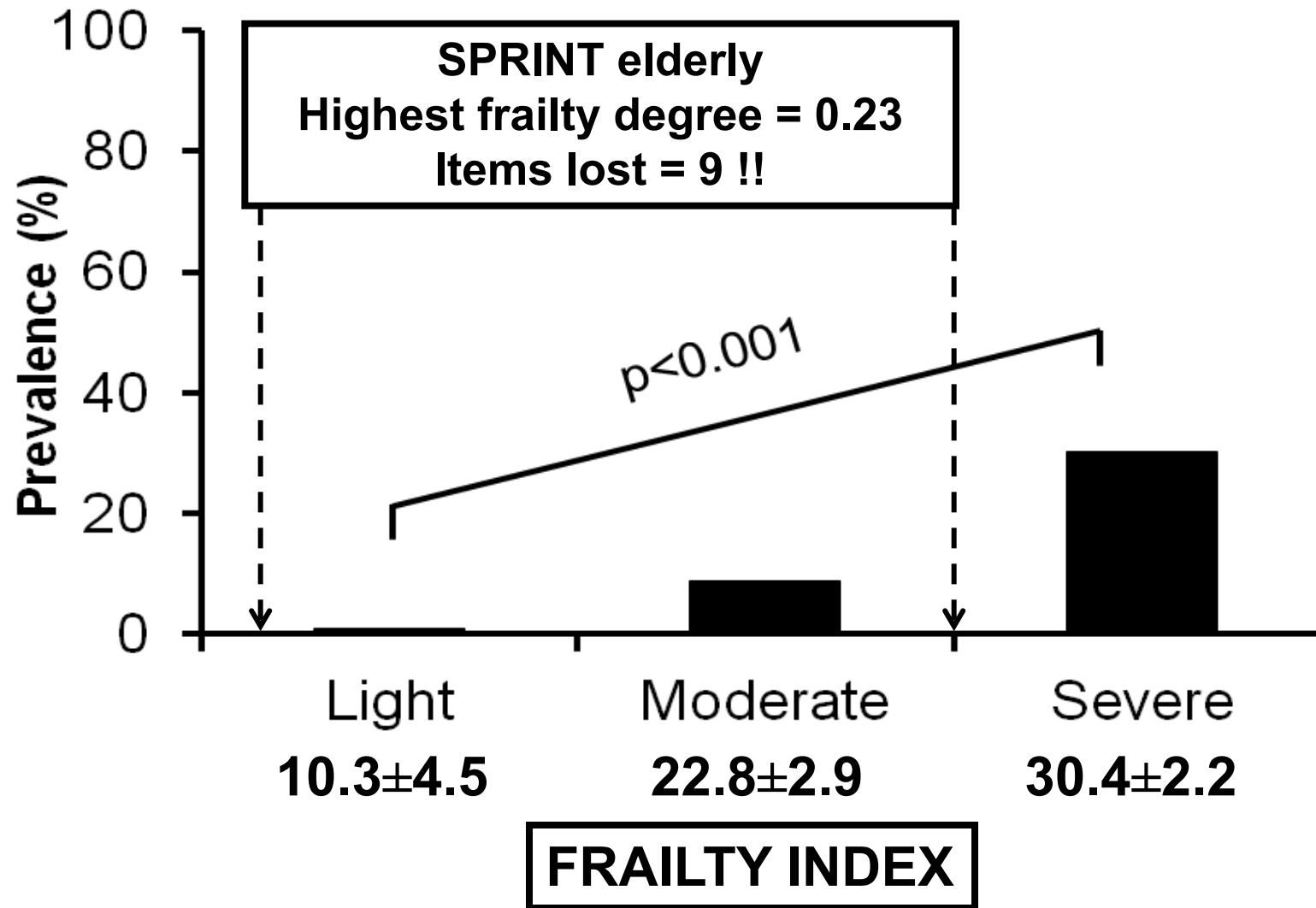
DOI 10.1007/s40520-016-0639-x

ORIGINAL ARTICLE

The Italian version of the “frailty index” based on deficits in health: a validation study

**Pasquale Abete¹ · Claudia Basile¹ · Giulia Bulli¹ · Francesco Curcio¹ ·
Ilaria Liguori¹ · David Della-Morte^{2,3} · Gaetano Gargiulo^{1,4} · Assunta Langellotto^{1,5} ·
Gianluca Testa^{1,6} · Gianluigi Galizia^{1,7} · Domenico Bonaduce¹ · Francesco Cacciatore¹**

Mortality at 24 months stratified by Frailty index





ELSEVIER

JAMDA

journal homepage: www.jamda.com



Original Study

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

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

^a Department of Translational Medical Sciences, University of Naples-Federico II, Naples, Italy

^b Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy

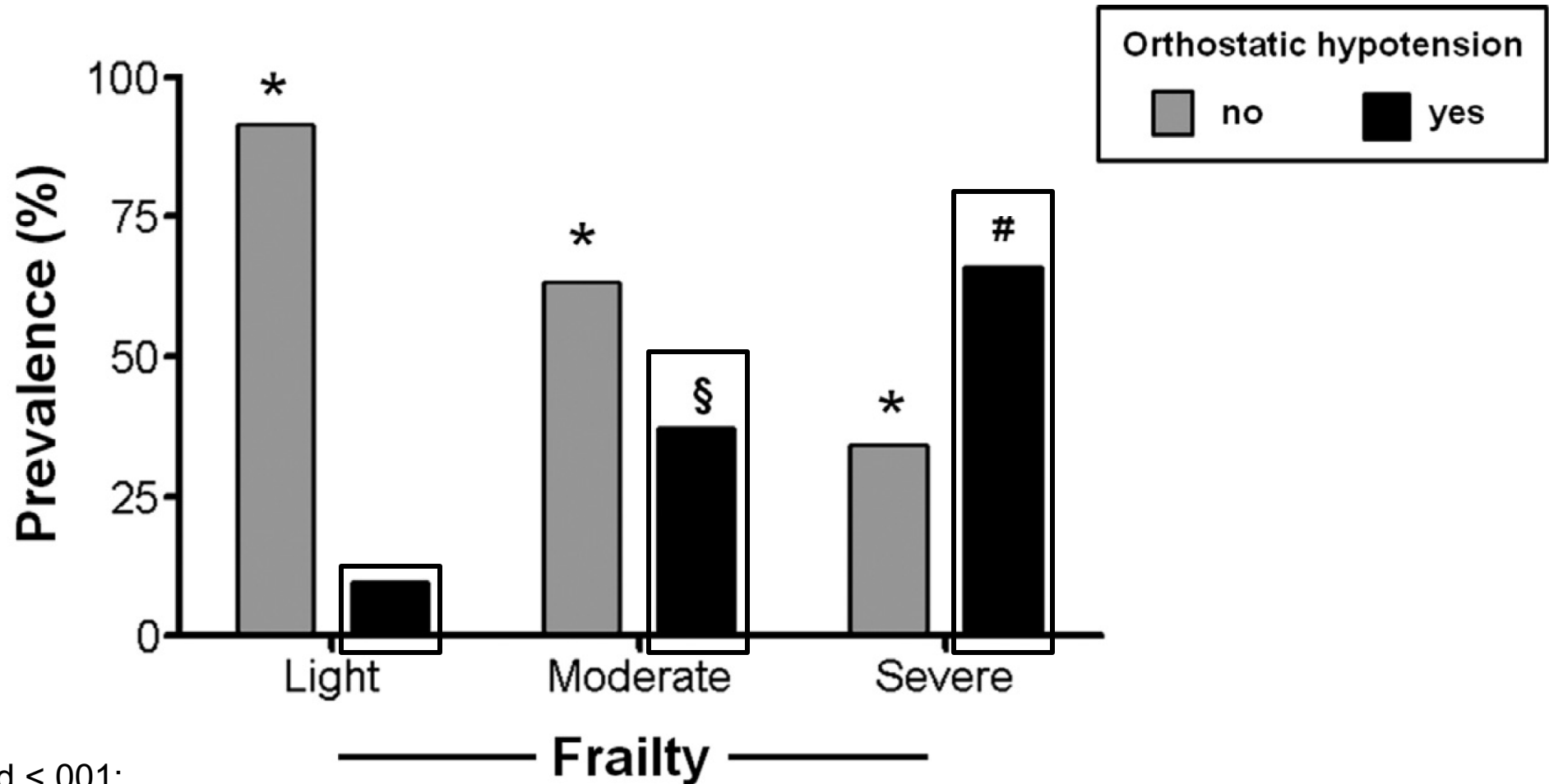
^c San Raffaele Roma Open University, Rome, Italy

^d Division of Internal Medicine, AOU San Giovanni University of Naples-Federico II, di Dio e Ruggi di Aragona, Salerno, Italy

^e Department of Medicine and Health Sciences, University of Molise, Campobasso, Italy

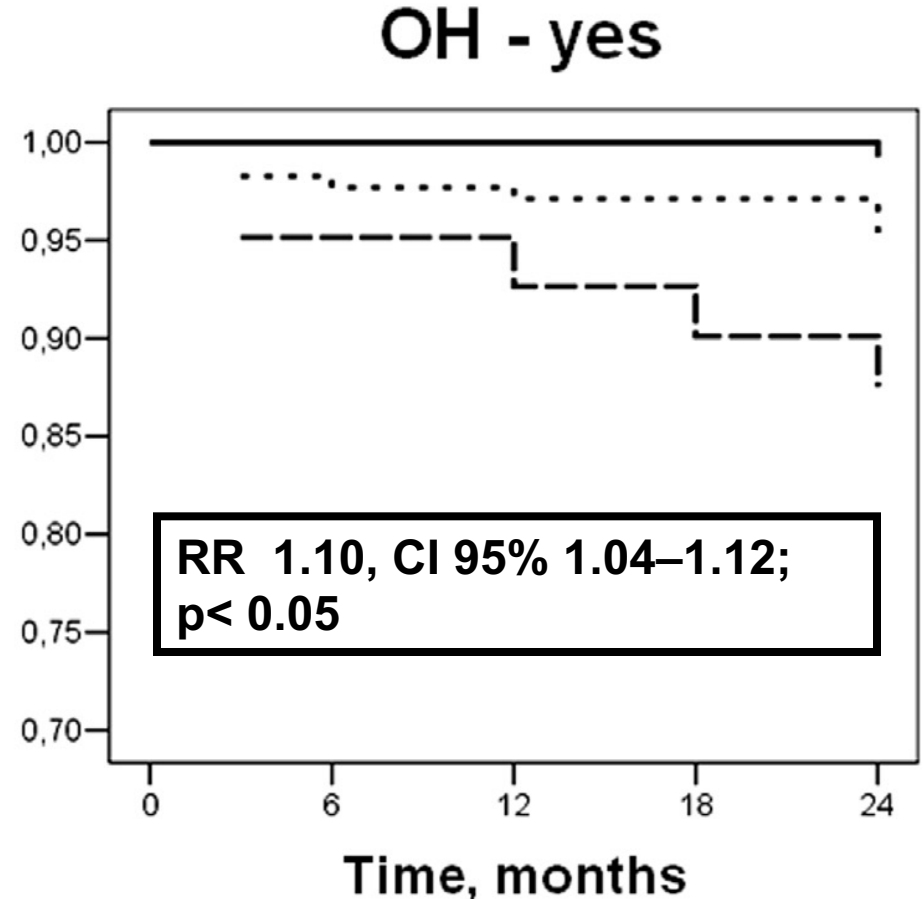
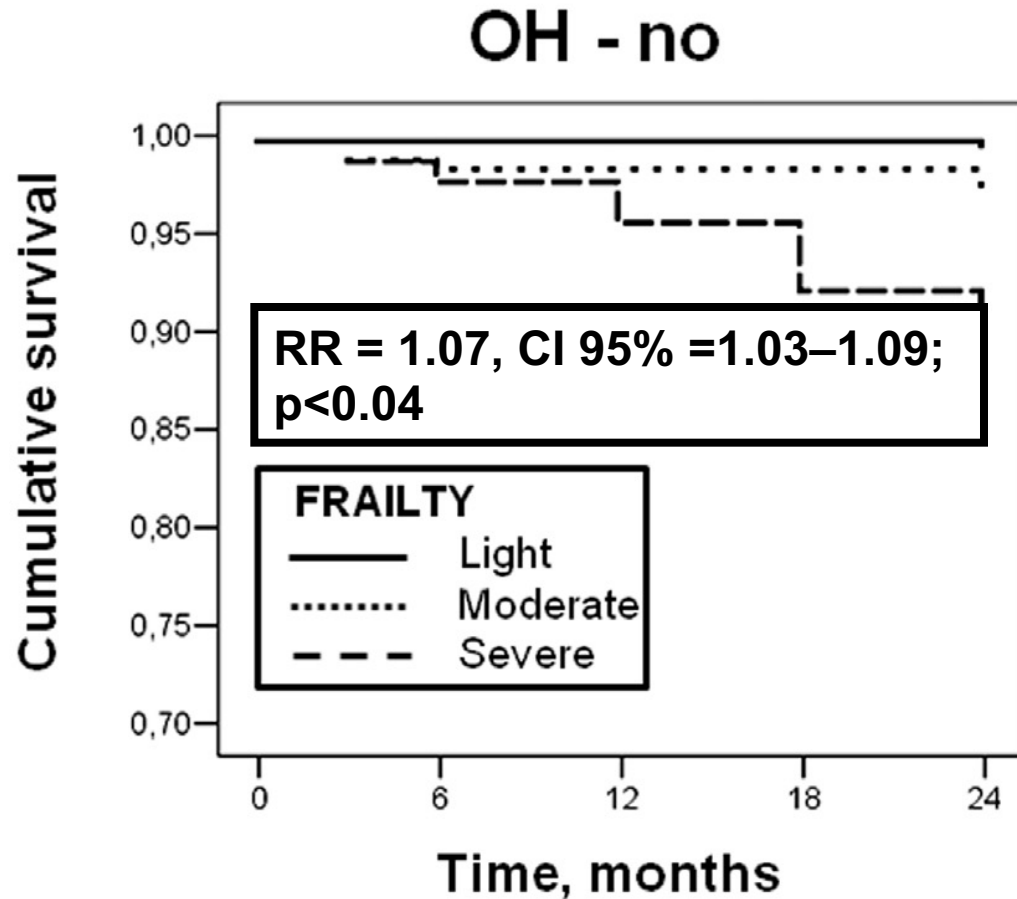
^f Azienda Ospedaliera dei Colli, Heart Transplantation Unit, Monaldi Hospital, Naples, Italy

Prevalence of orthostatic hypotension in different frailty



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

Cox regression analysis on MORTALITY stratified by degree of FRAILITY in the presence or absence of orthostatic hypotension (OH)



PERSPECTIVE



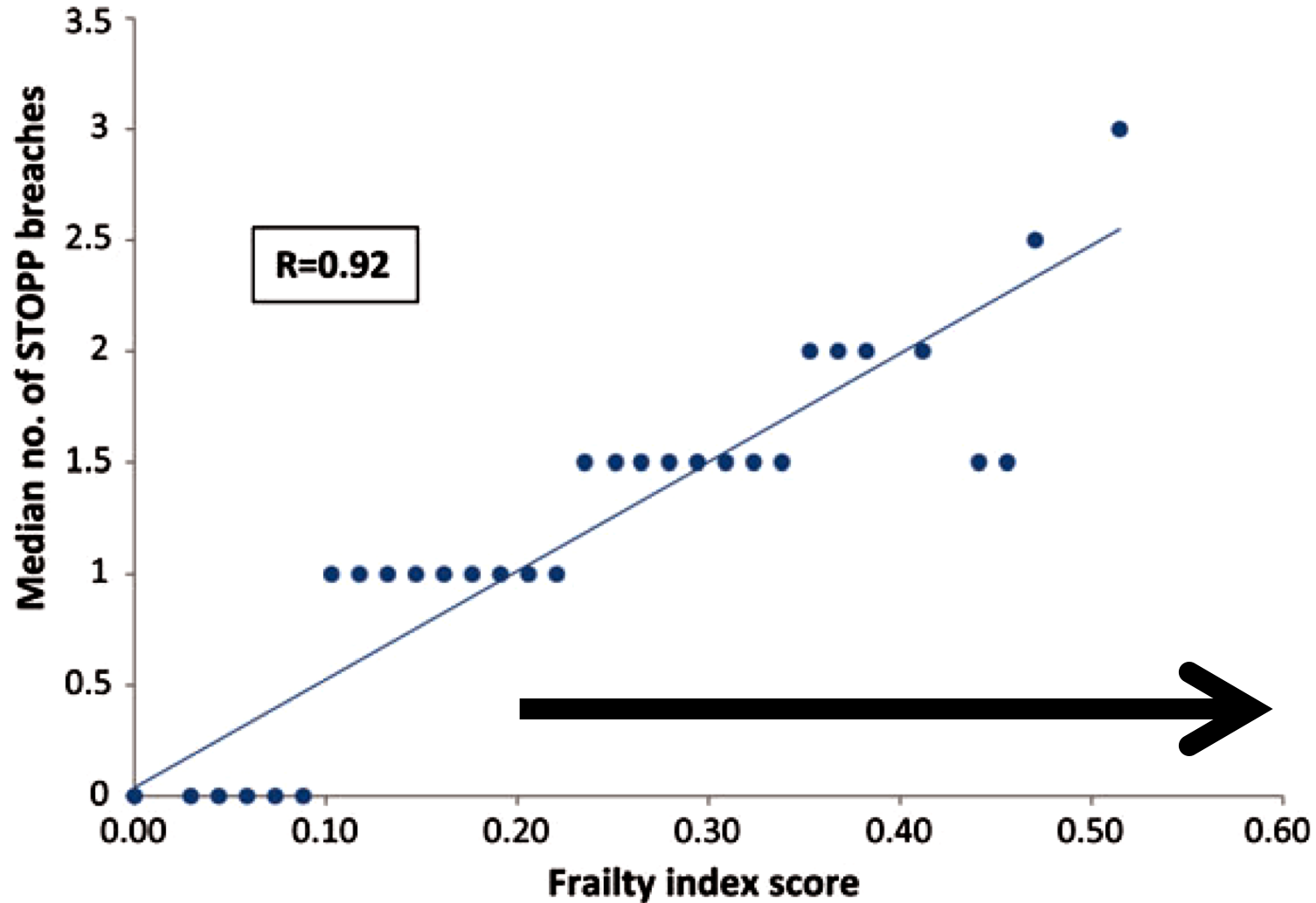
STOPP/START criteria for potentially inappropriate medications/potential prescribing omissions in older people: origin and progress

Denis O'Mahony

Department of Medicine, University College Cork, Ireland & consultant geriatrician, Cork University Hospital, Cork, Ireland

- Inappropriate prescribing (IP) is highly prevalent among older people in all clinical settings who experience **multi-morbid illness** which inevitably leads to polypharmacy.
- **STOPP/START** explicit IP criteria are designed to detect common and/ or **important potentially inappropriate medications** (PIMs – STOPP criteria) and **potential prescribing omissions** (PPOs – START criteria).

Frailty index score plotted against median number of breaches of the STOPP criteria.



*Centro Congressi dell'Università degli
Studi di Napoli Federico II
16-18 febbraio 2023*

- Clinical evidences
- Intensive treatment in the “frail” patient (SPRINT)
- **Stop/reduce vasoactive drugs: the “SYD-study”**
- Hyp-hyp phenomenon
- Clinical approaches

Syncope due to orthostatic hypotension

**Stop/reduce
vasoactive drugs
(Class IIa)**

**Counter-pressure
manoeuvres
(Class IIa)**

**Compression
garments
(Class IIa)**

**Head-up tilt
sleeping
(Class IIa)**

**Midodrine
(Class IIa)**

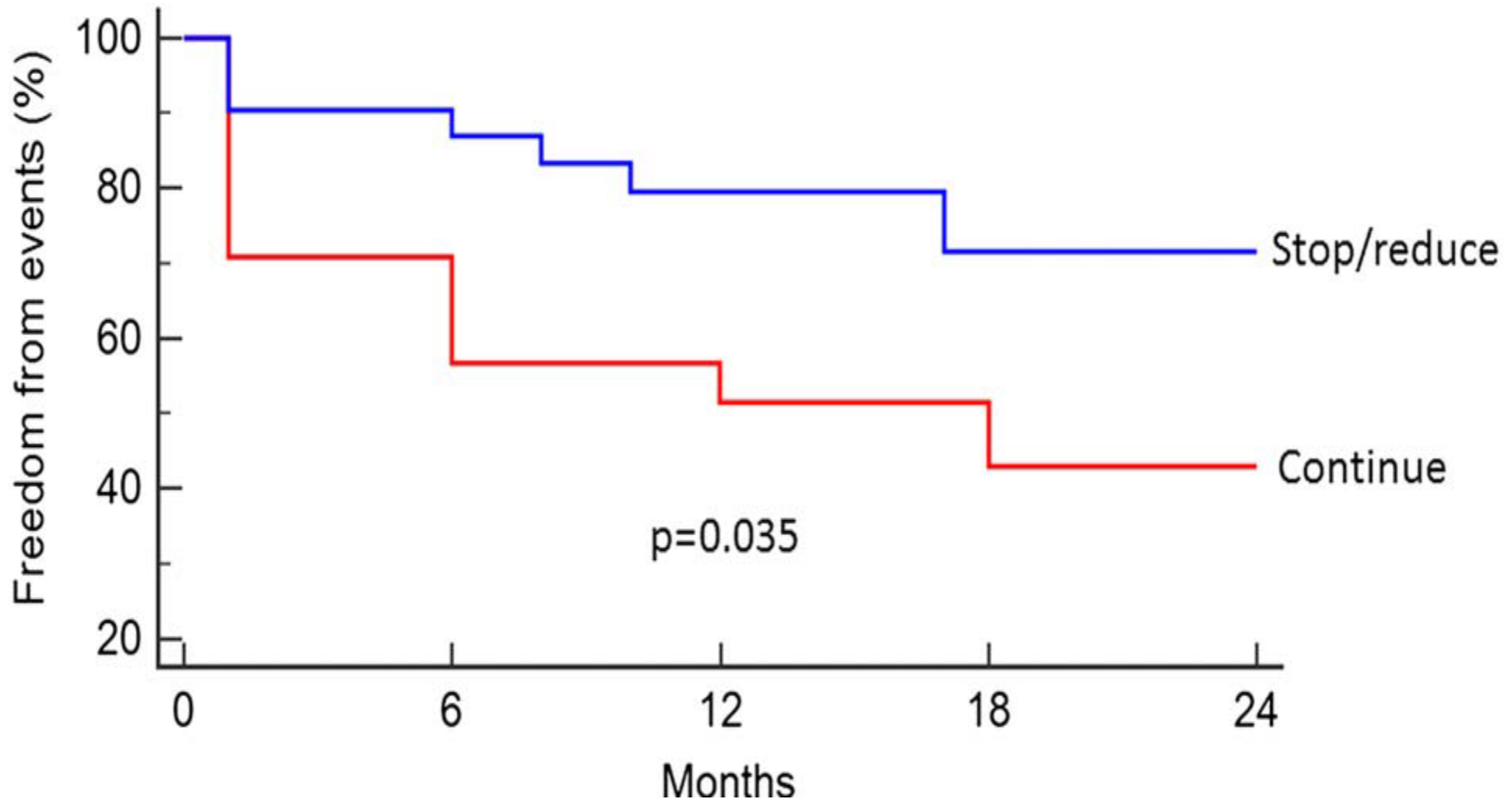
**Fludrocortisone
(Class IIa)**

Stop vasodepressor drugs in reflex syncope: a randomised controlled trial

	Stop/reduce therapy (n=31)	Continue therapy (n=24)	p value
Age, years	75±12	73±11	0.54
number of vasoactive drugs	2.4±1.1	2.5±0.9	0.77
Class of drug (number of patients)			
ACE inhibitor or ARB	27 (87%)	23 (96%)	0.37
Diuretic	12 (39%)	11 (46%)	0.79
Calcium channel blocker	12 (39%)	6 (25%)	0.39
β-Blocker	7 (23%)	5 (21%)	1.00
α-Antagonist	5 (16%)	5 (21%)	0.73
Neuroleptic antidepressant	5 (16%)	5 (21%)	0.73
L-dopa antagonist	2 (6%)	1 (4%)	1.00
Others	2 (6%)	2 (8%)	1.00

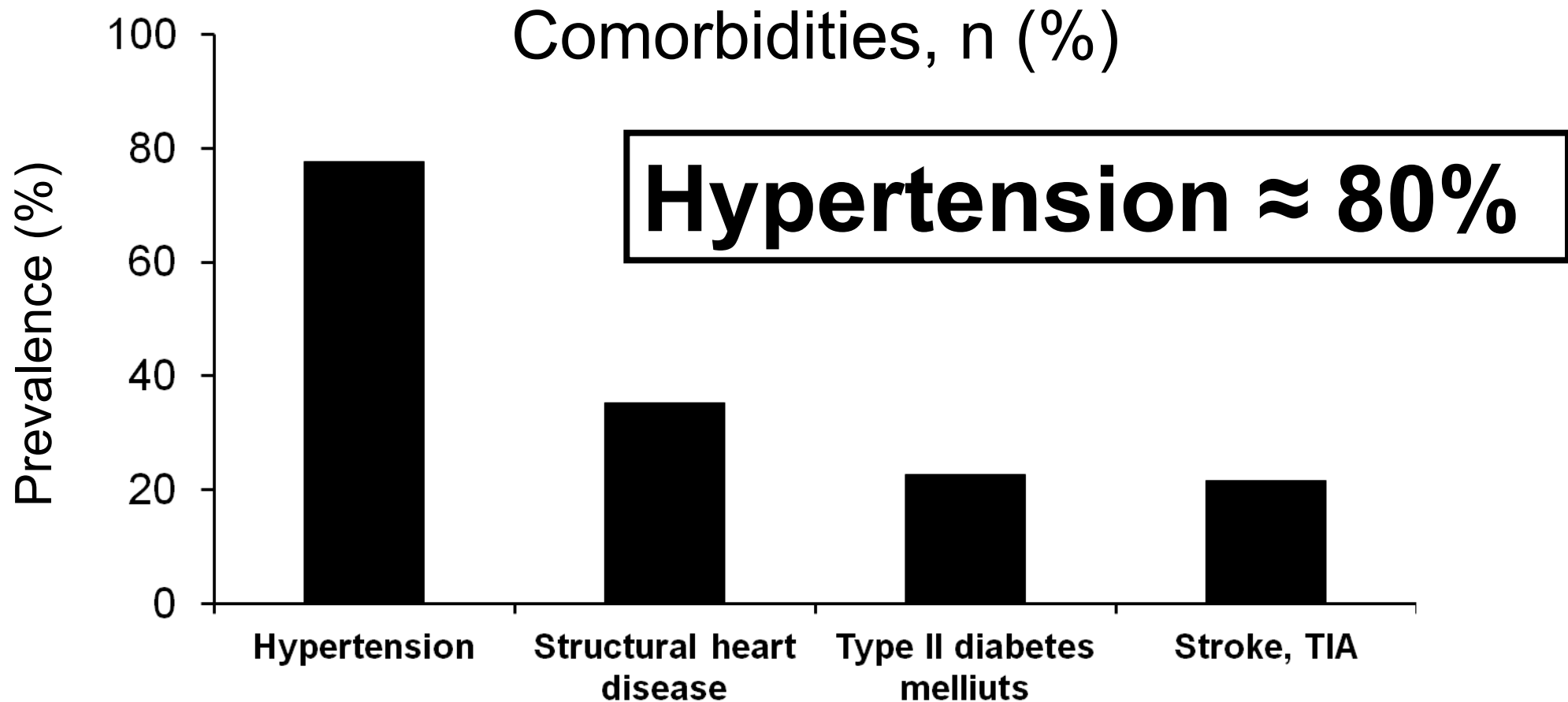
Stop vasodepressor drugs in reflex syncope: a randomised controlled trial

Combined end point of syncope and presyncope



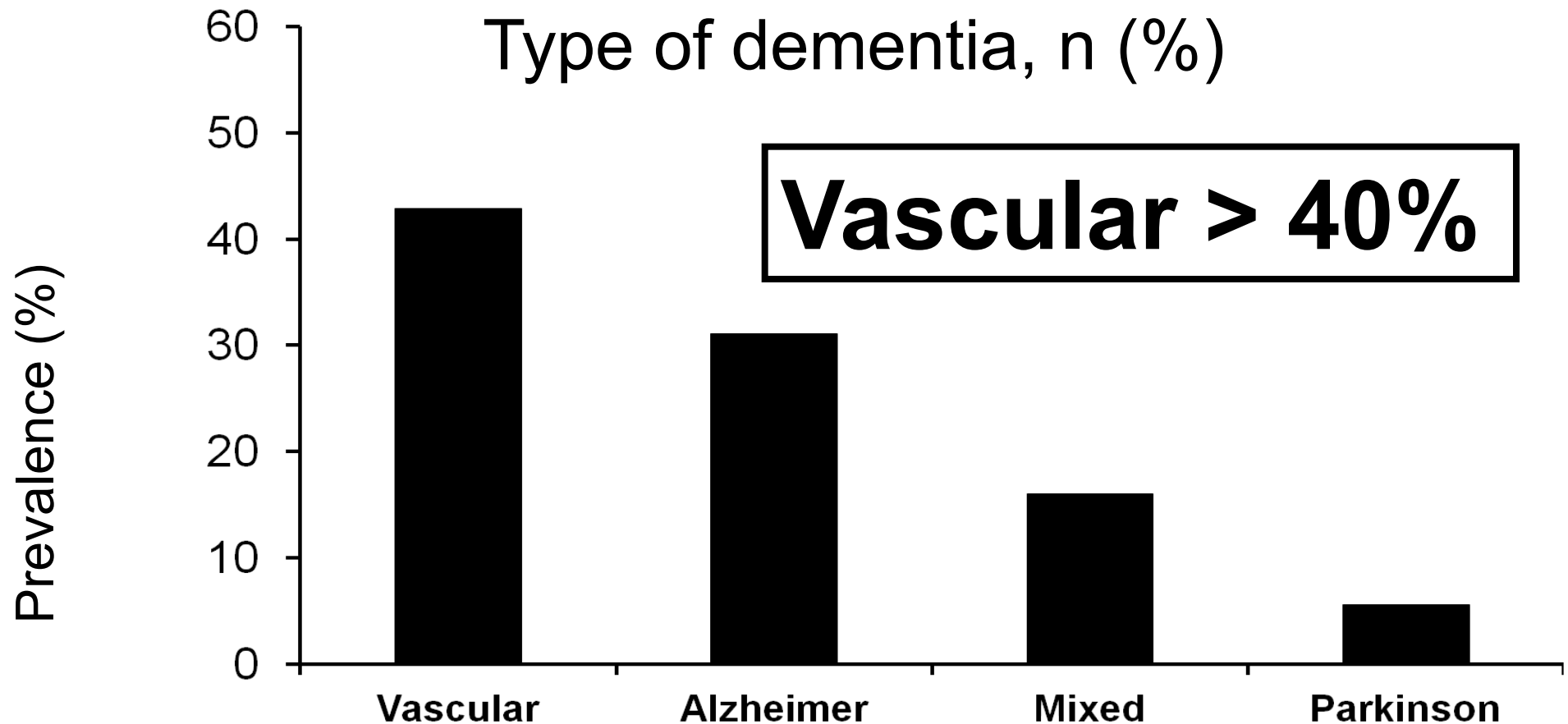
Etiology of Syncope and Unexplained Falls in Elderly Adults with Dementia: Syncope and Dementia (SYD) Study

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



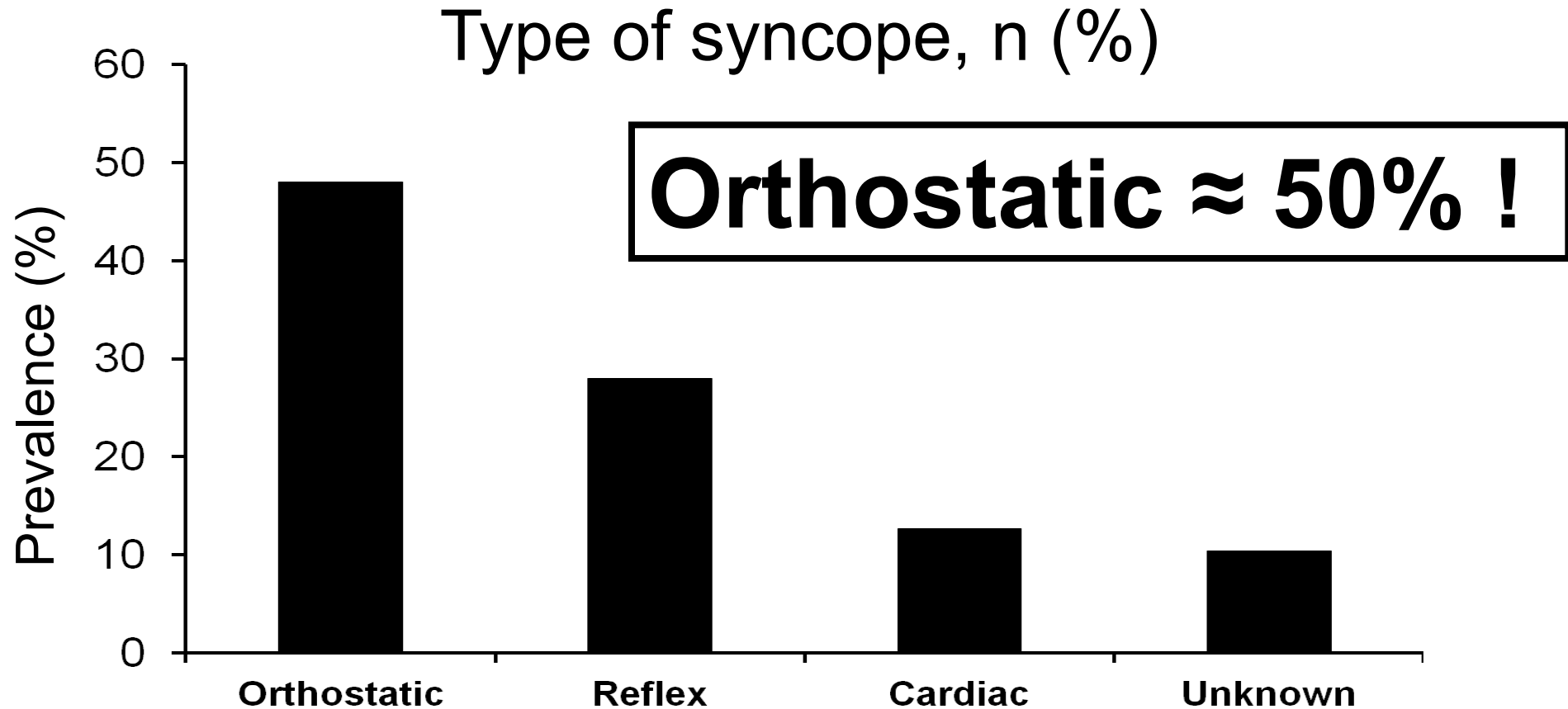
Etiology of Syncope and Unexplained Falls in Elderly Adults with Dementia: Syncope and Dementia (SYD) Study

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



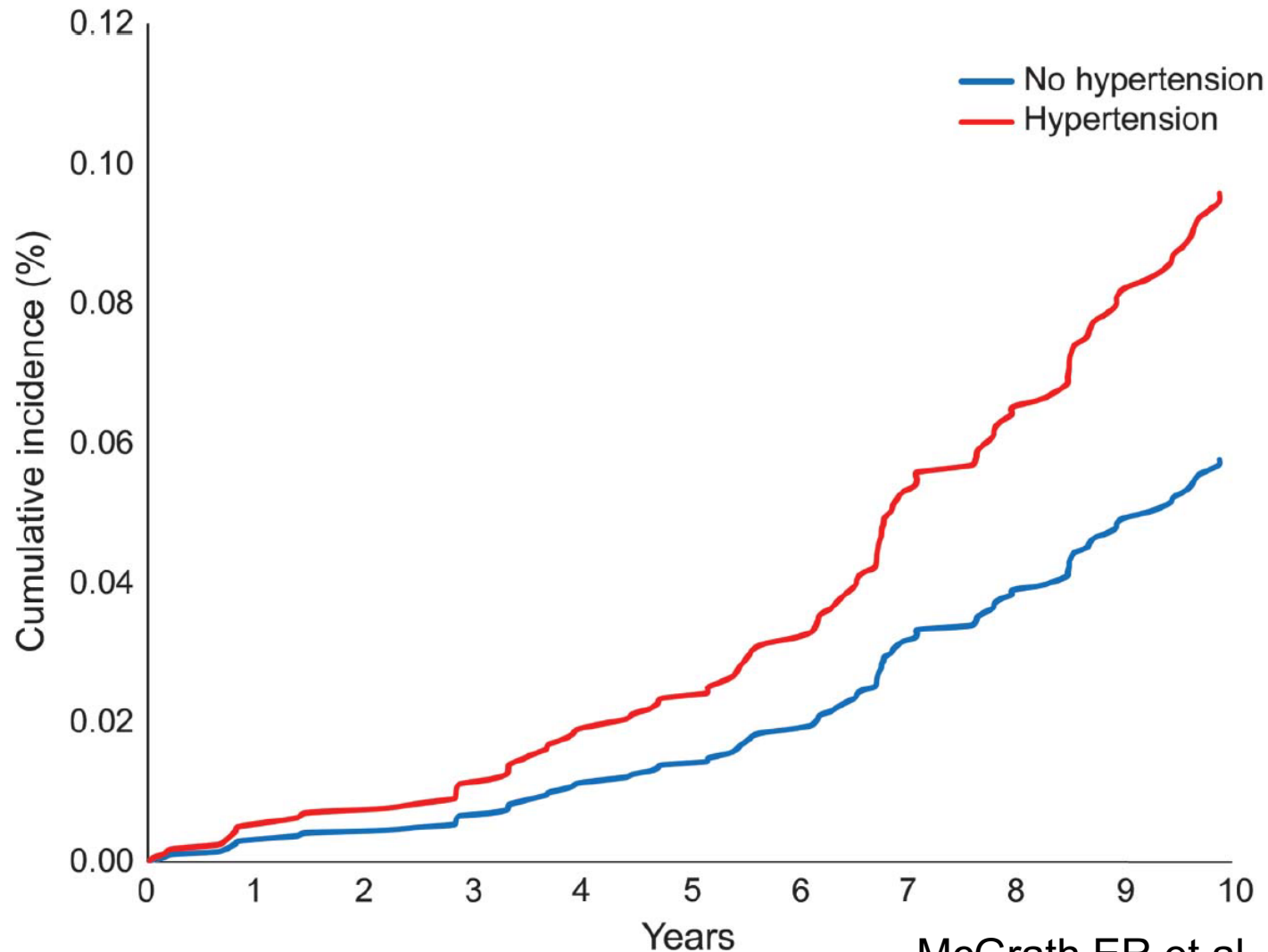
Etiology of Syncope and Unexplained Falls in Elderly Adults with Dementia: Syncope and Dementia (SYD) Study

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

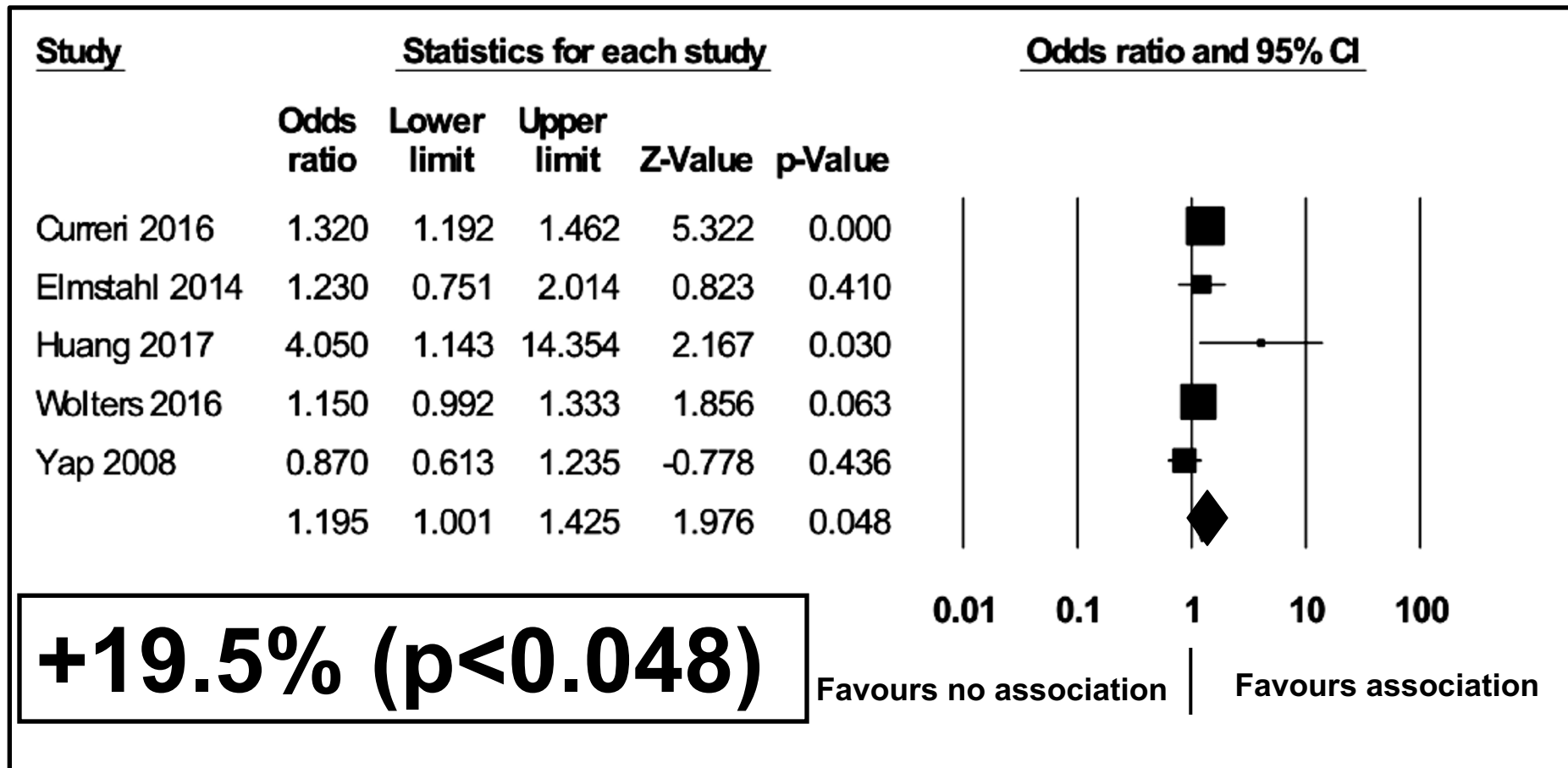


Blood pressure from mid- (40-64 years old) to late life (≥ 65 years old) and risk of “INCIDENT DEMENTIA”

This study included 1,440 (758 women, mean age 69 ± 6 years (Framingham Participants)

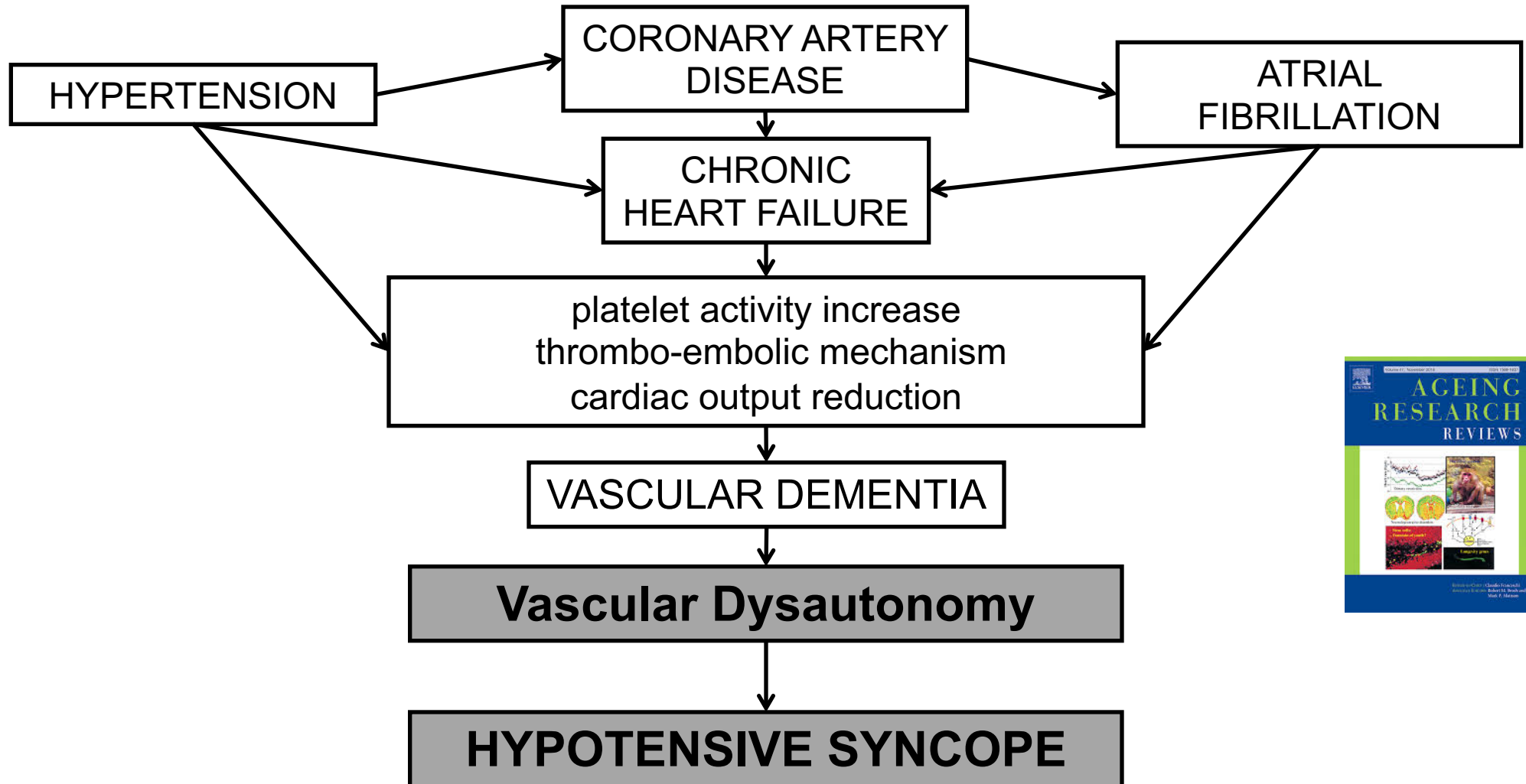


Orthostatic hypotension and cognition in older adults: A systematic review and meta-analysis

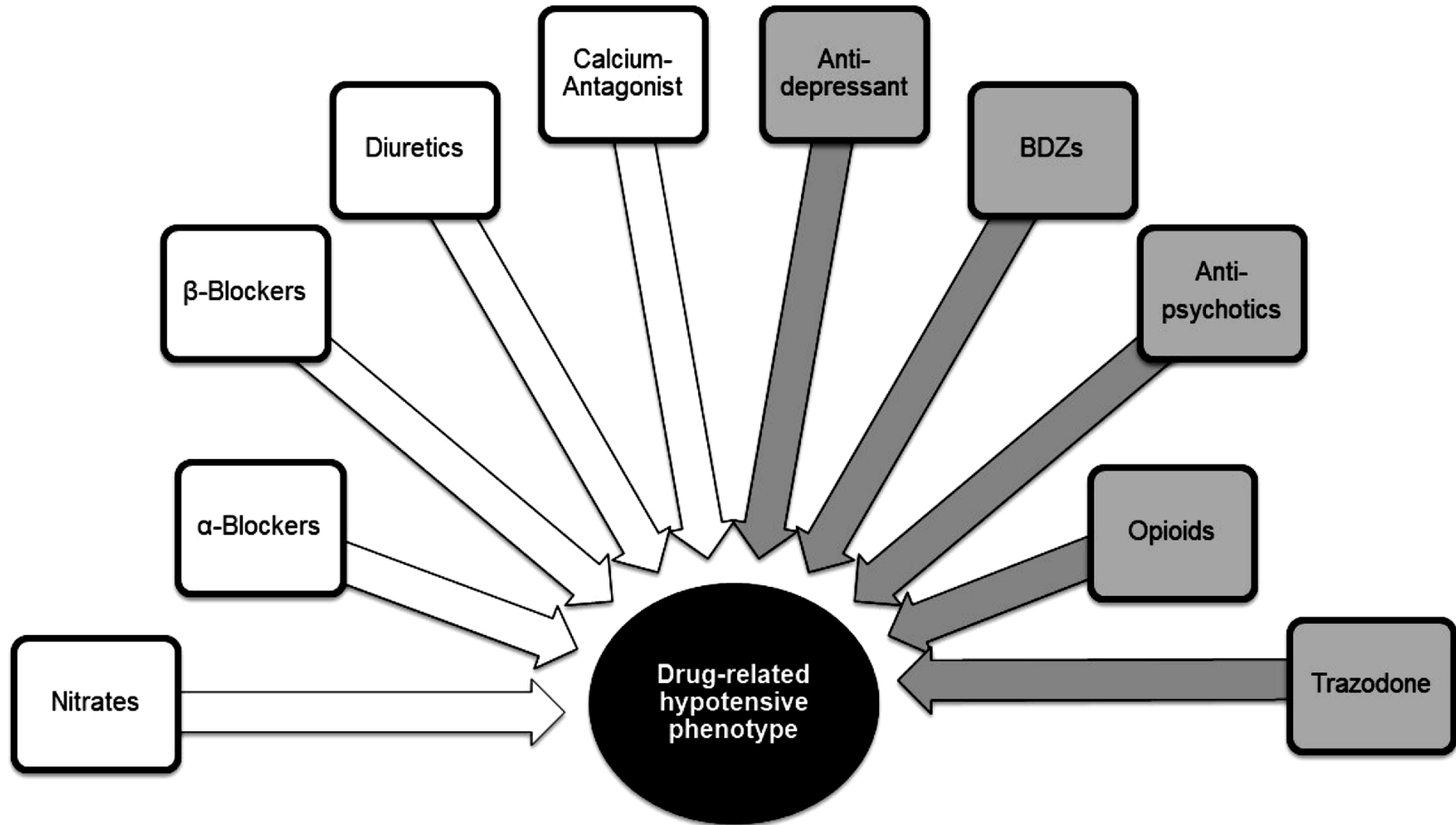


Cognitive impairment and cardiovascular diseases in the elderly.

A heart-brain continuum hypothesis

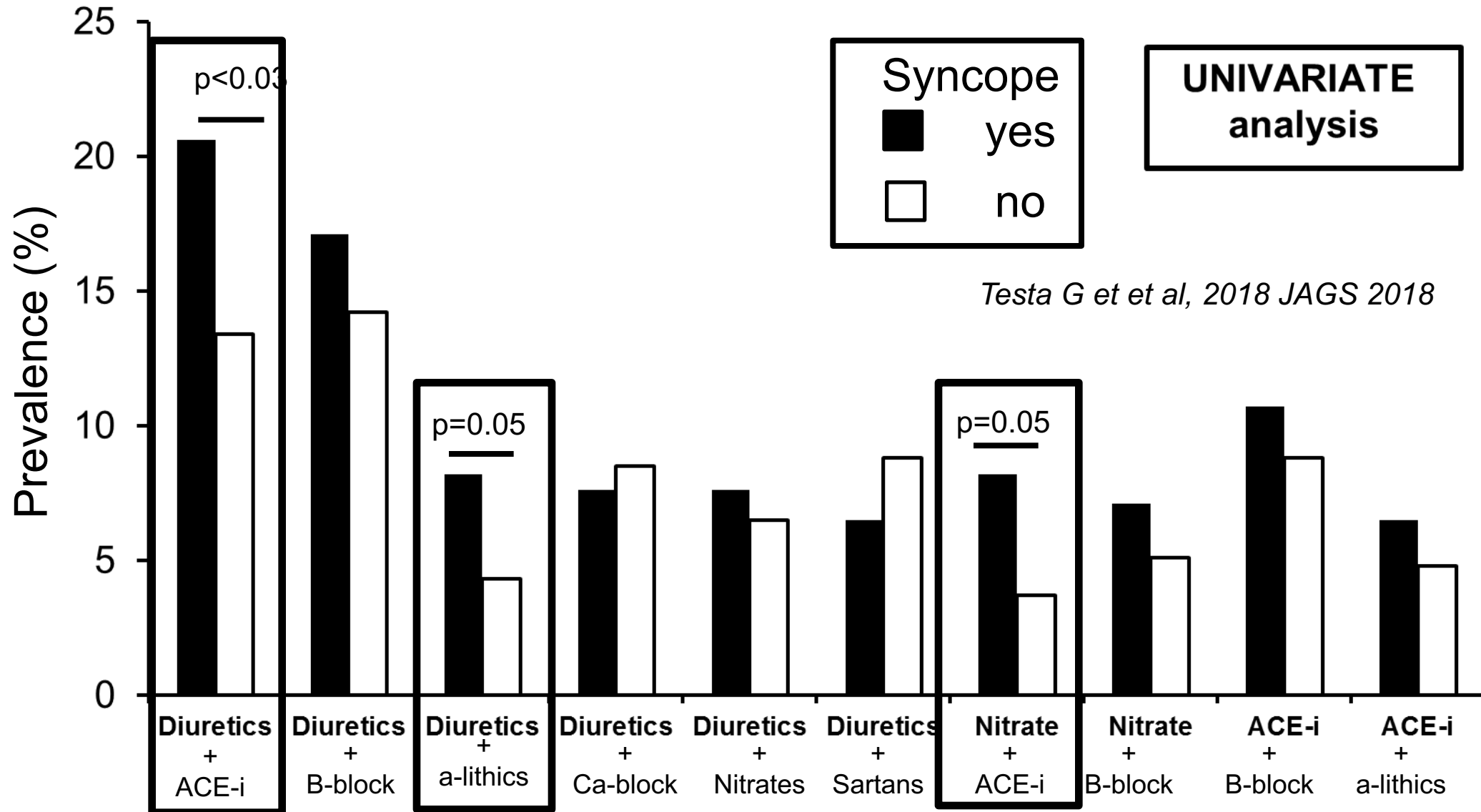


Drug-related “Hypotensive phenotype”



Combination of “*hypotensive drugs*” are associated with “orthostatic syncope” in patients with dementia

Results from SYD study

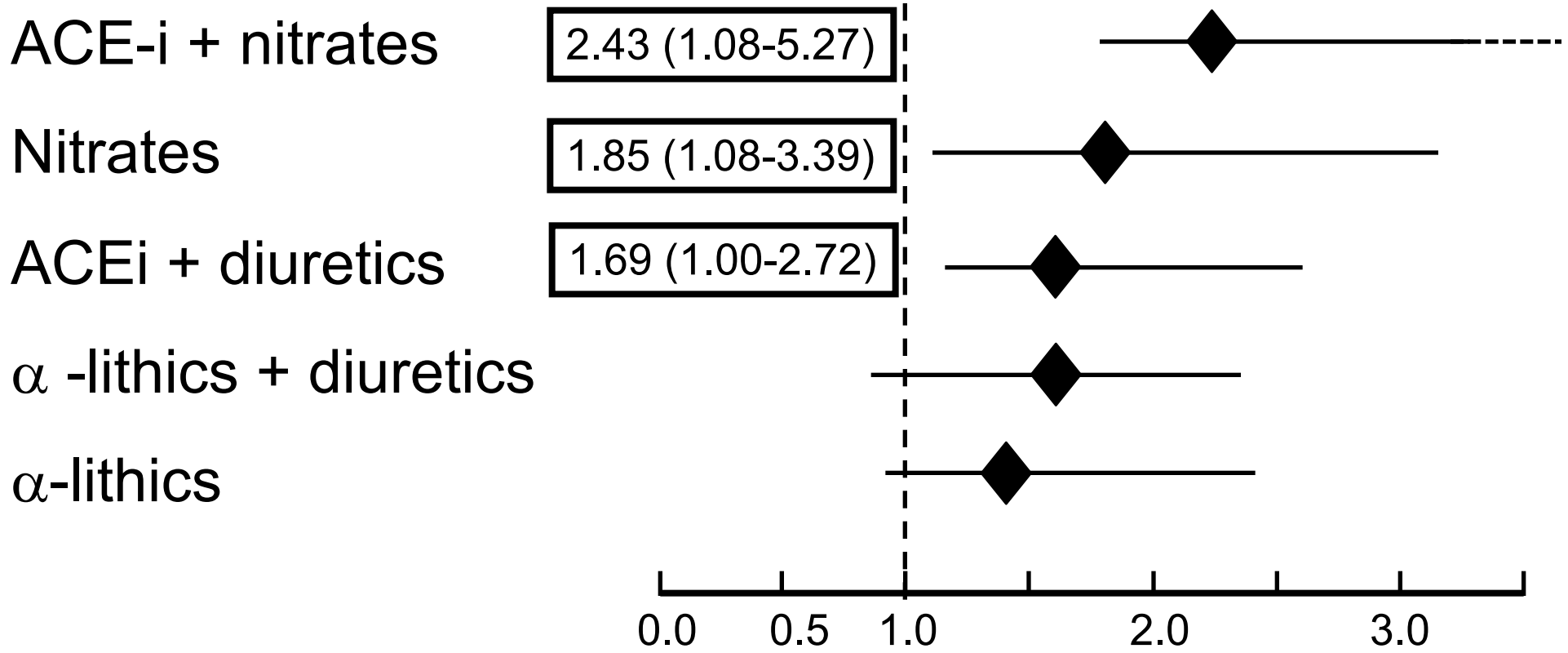


Hypothensive drugs and their combinations are associated with “orthostatic syncope” in patients with dementia

Results from SYD study

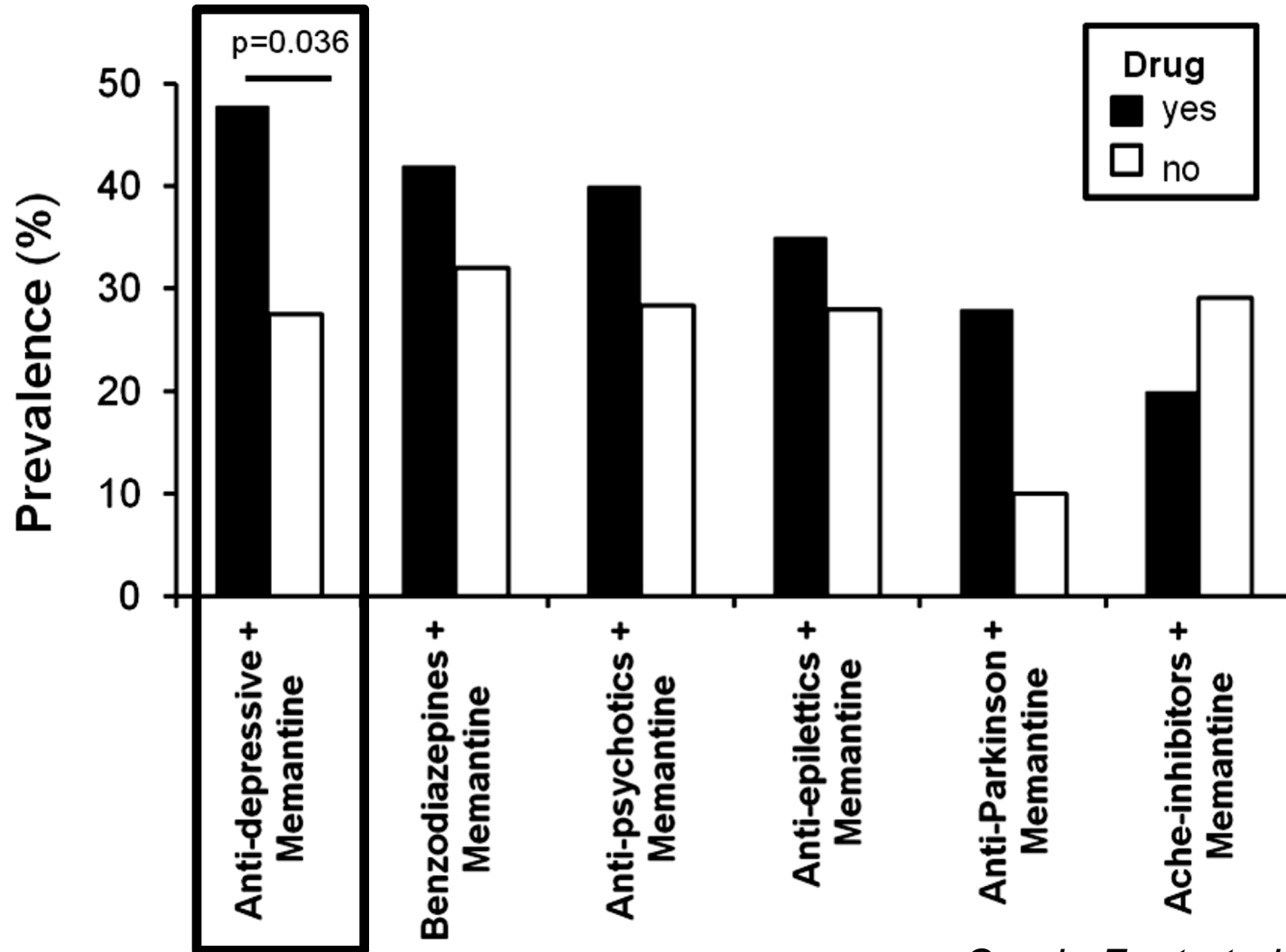
MULTIVARIATE analysis
adjusted for age,sex and CIRS

Testa G et et al, 2018 JAGS 2018



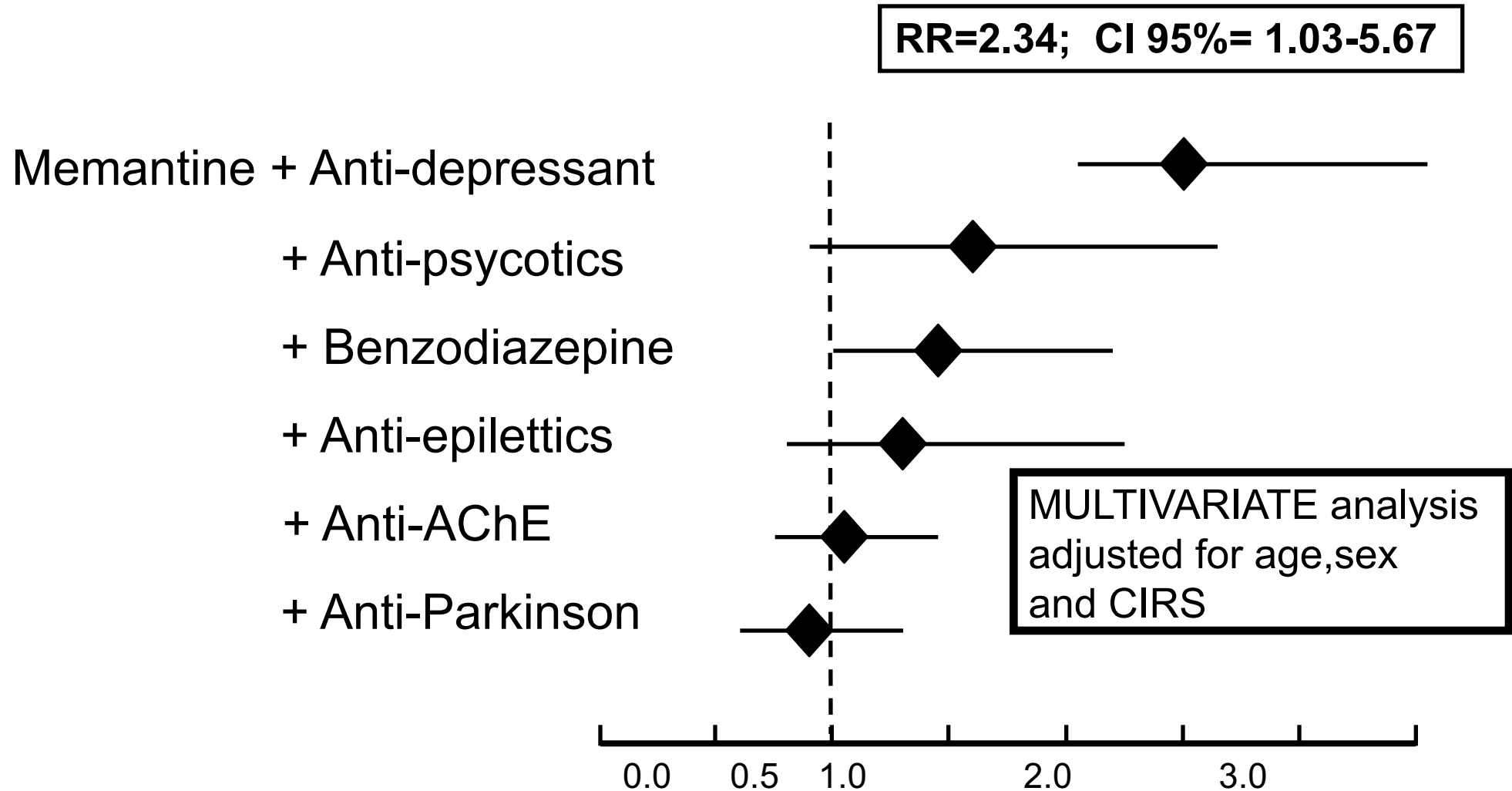
Combinations of “*psychotropic drugs*” and reflex syncope in patients with dementia

Results from SYD study



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

Results from SYD study



*Centro Congressi dell'Università degli
Studi di Napoli Federico II
16-18 febbraio 2023*

- Clinical evidences
- Intensive treatment in the “frail” patient (SPRINT)
- Stop/reduce vasoactive drugs: the “SYD-study”
- **Hyp-hyp phenomenon**
- Clinical approaches

Orthostatic Hypotension in the Hypertensive Patient

Italo Biaggioni

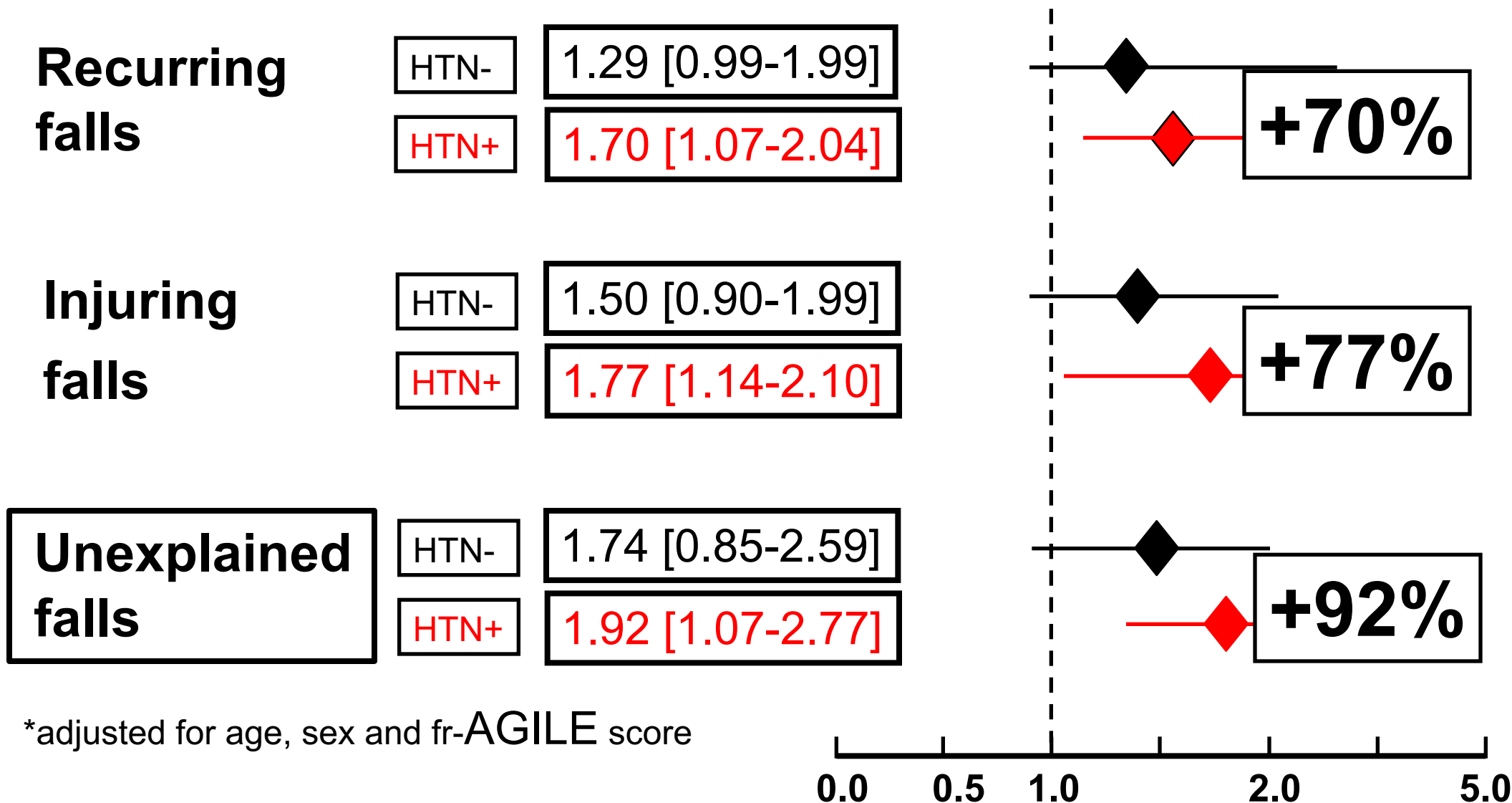
Hypertension is among the most common comorbidities associated with OH, and its presence complicates the management of these patients because treatment of one can worsen the other...

In patients with isolated clinostatic hypertension and orthostatic hypotension:

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

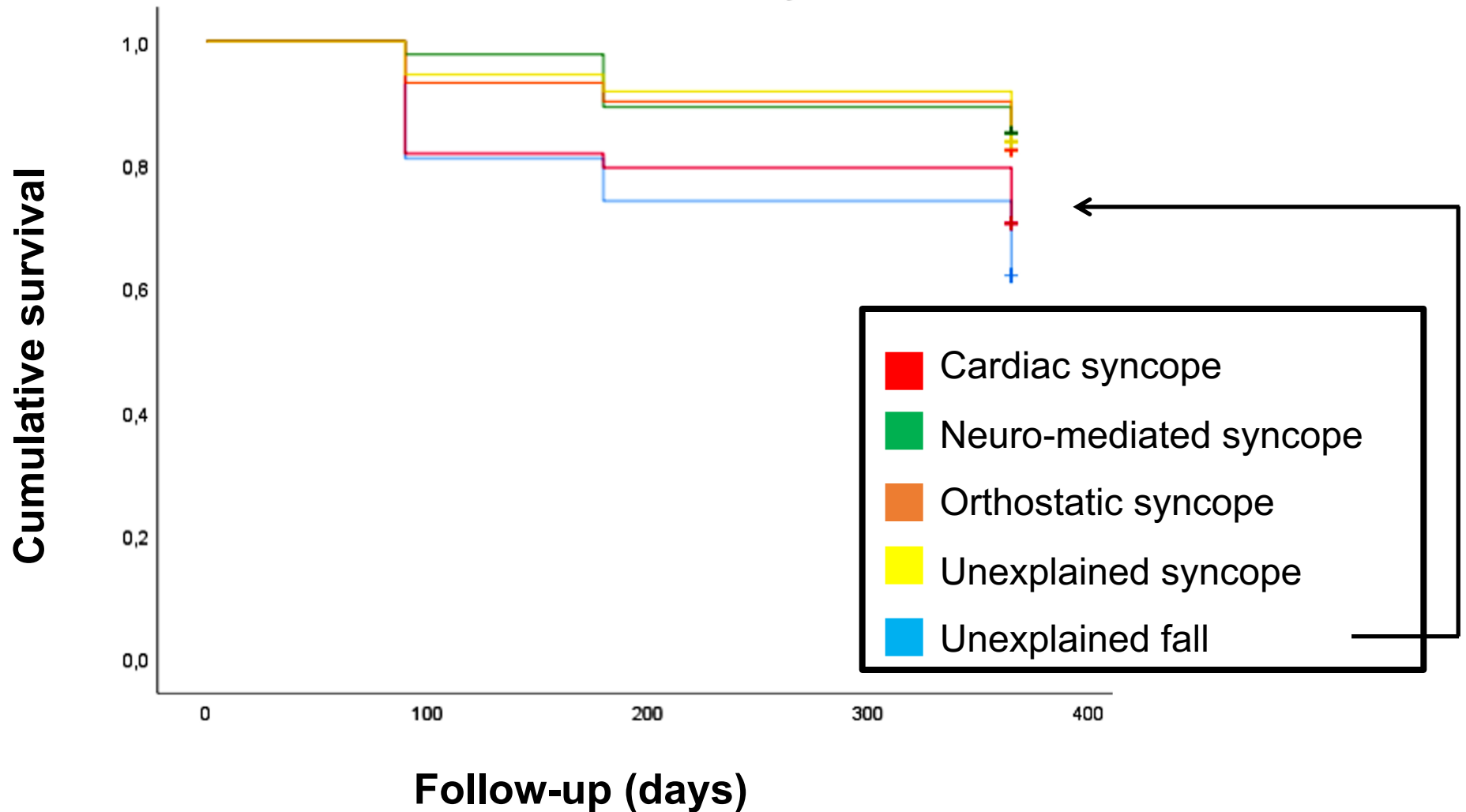
Orthostatic hypotension - Clinostatic hypertension (HTN)

*multivariate analysis**



MORTALITY

and etiologic causes of syncope and fall



*Centro Congressi dell'Università degli
Studi di Napoli Federico II
16-18 febbraio 2023*

- Clinical evidences
- Intensive treatment in the “frail” patient (SPRINT)
- Stop/reduce vasoactive drugs: the “SYD-study”
- Hyp-hyp phenomenon
- **Clinical approaches**

Blood pressure management in hypertensive patients with syncope: how to balance hypotensive and cardiovascular risk

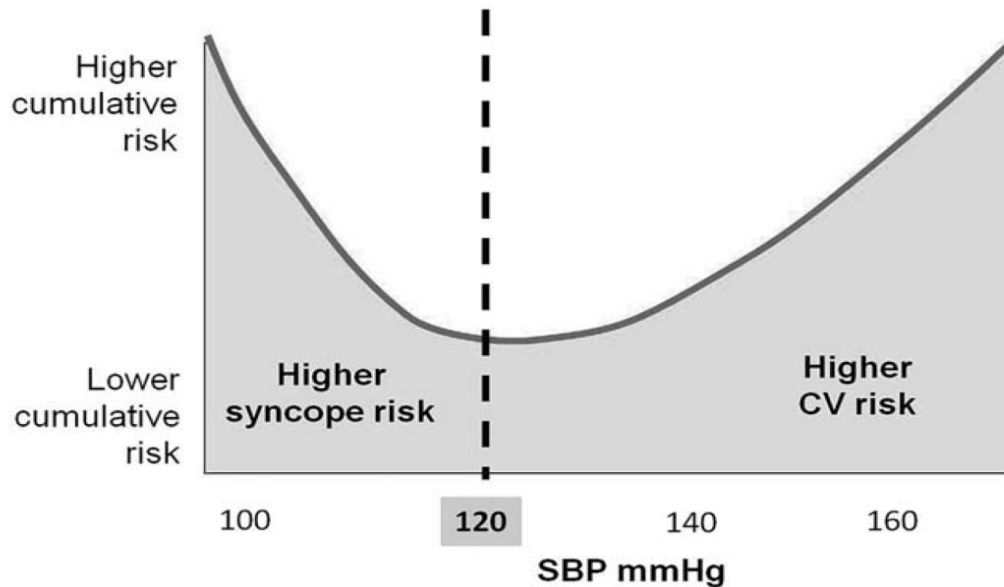
Giulia Rivasi^a, Michele Brignole^b, Martina Rafanelli^a, Grzegorz Bilo^b, Martino F. Pengo^b,
Andrea Ungar^a, and Gianfranco Parati^{b,c}

Journal of Hypertension 2020, 38:2356–2362

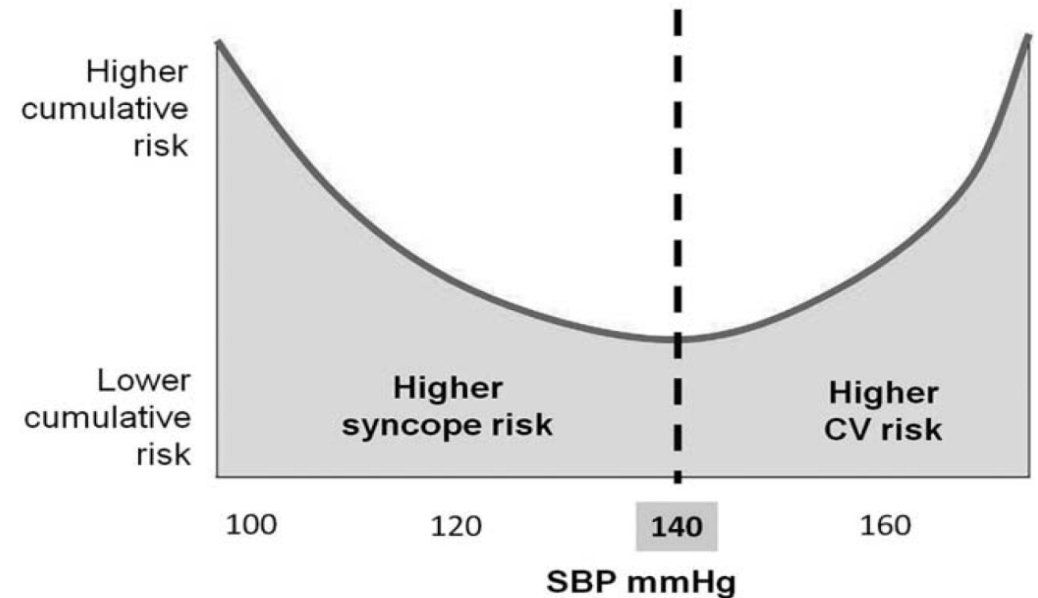


Cardiovascular and syncope risk according to Systolic Blood Pressure (SBP) values

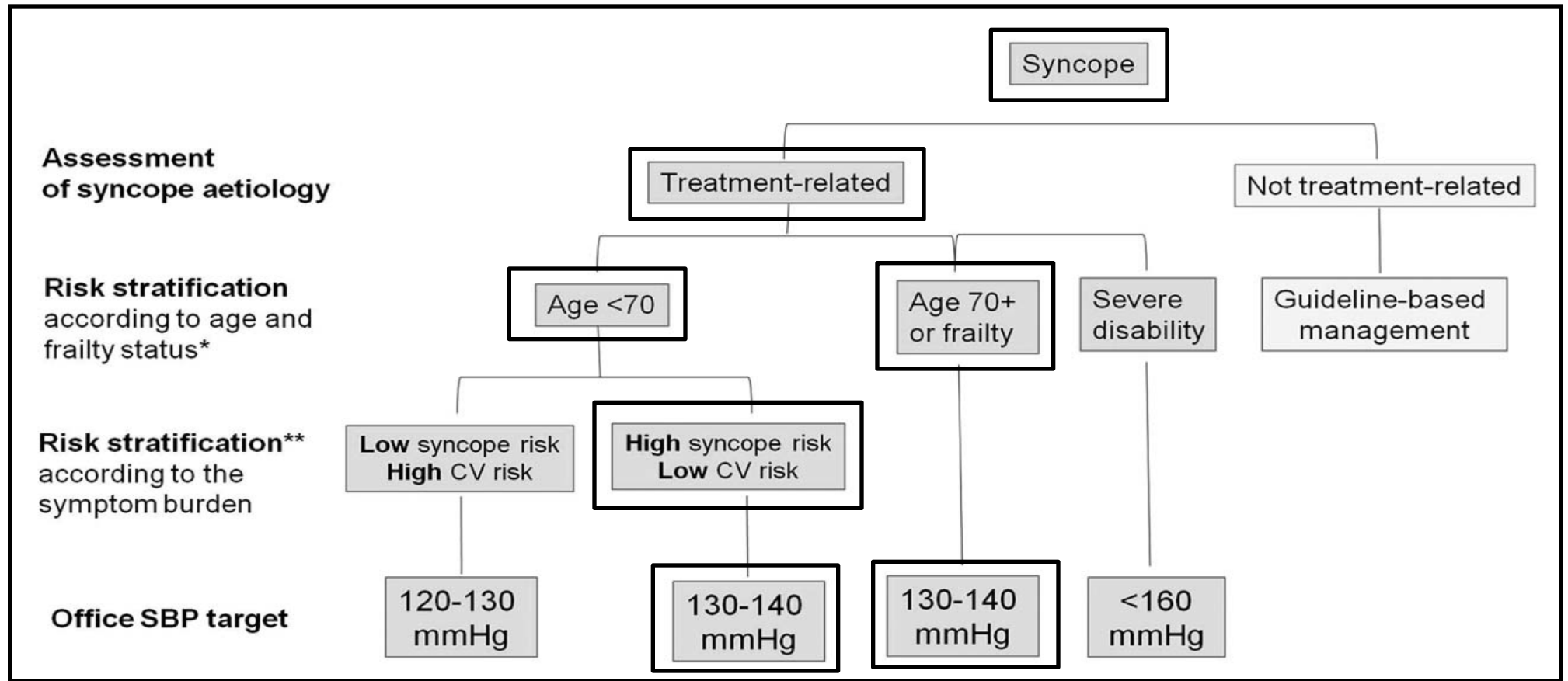
younger adults



older frail adults



Algorithm strategy to guide blood pressure management in patients with hypertension and syncope



TAKE HOME MESSAGES - 1

- The clinical evidence indicates that **intensive anti-hypertensive treatment increases the risk of syncope and falls** especially in elderly patients;
- In the elderly patient, **the identification and quantification of frailty** play a key role especially in deciding the level of intensity of treatment.
- The SYD study clearly demonstrated that a **history of hypertension can lead to dementia complicated in many cases in syncopal episodes** often attributable to the intensity of anti-hypertensive treatment.

TAKE HOME MESSAGES - 2

The supine hypertension/orthostatic hypotension phenotype (**hyp-hyp phenomenon**) and related adverse events represents an intriguing clinical entity.

- Thus, **the balance between intensive anti-hypertensive treatment and the risk of syncope/fall** must be carefully considered especially in advancing age.