Il management dell'ipertensione arteriosa nel paziente anziano

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Il sottoscritto

ai sensi dell’art. 76, comma 4 dell’Accordo Stato-Regioni del 2 febbraio 2017 e del paragrafo 4.5. del Manuale nazionale di accreditamento per l'erogazione di eventi ECM

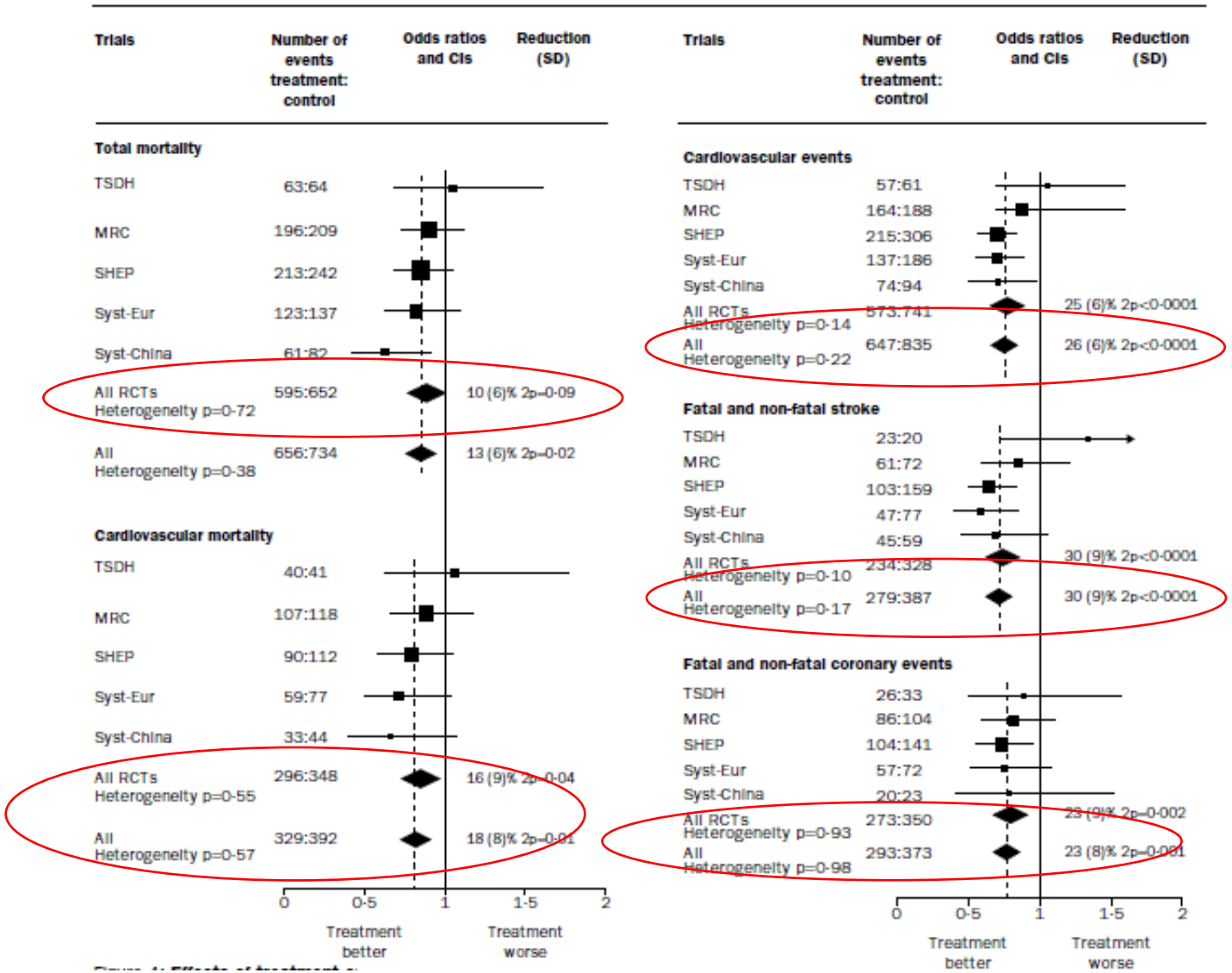
dichiara che

negli ultimi due anni ha avuto rapporti con i seguenti soggetti portatori di interessi commerciali in ambito sanitario:

- Berlin Chemie Menarini
- Recordati

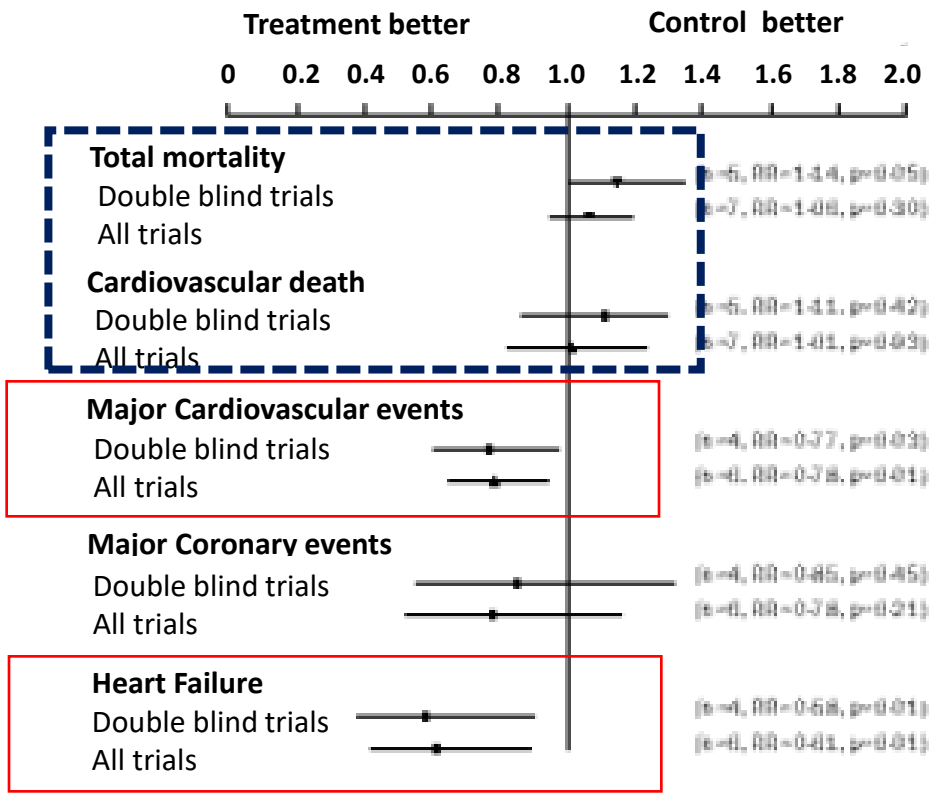
Ridurre la PA nell'anziano iperteso porta benefici: effetto su mortalità e morbidità CV

Effetto della terapia antiipertensiva nell'anziano (>60 anni)
PAS > 160 mHg; PAD < 95 mmHg



Staessen JA et al, Lancet 2000

Effetto della terapia antiipertensiva nel grande anziano (>80 anni)



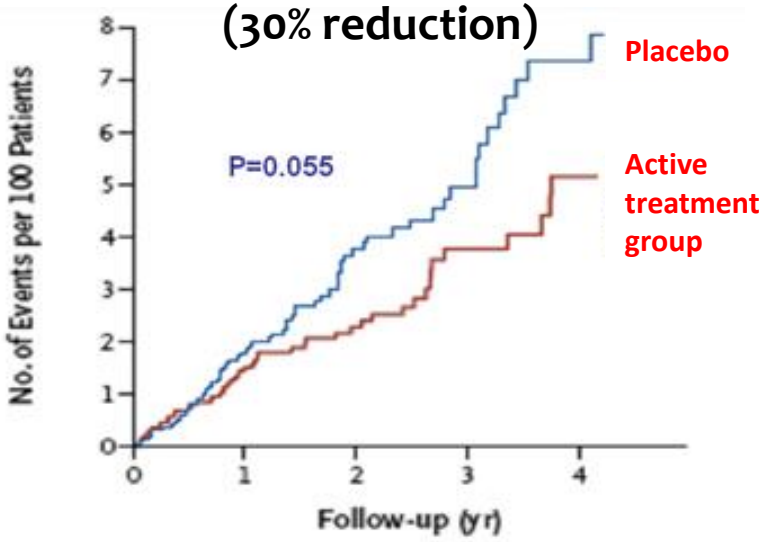
Gueyffier F et al, Lancet 1999

Treatment of hypertension in patients 80 yrs of age or older: The HYVET study

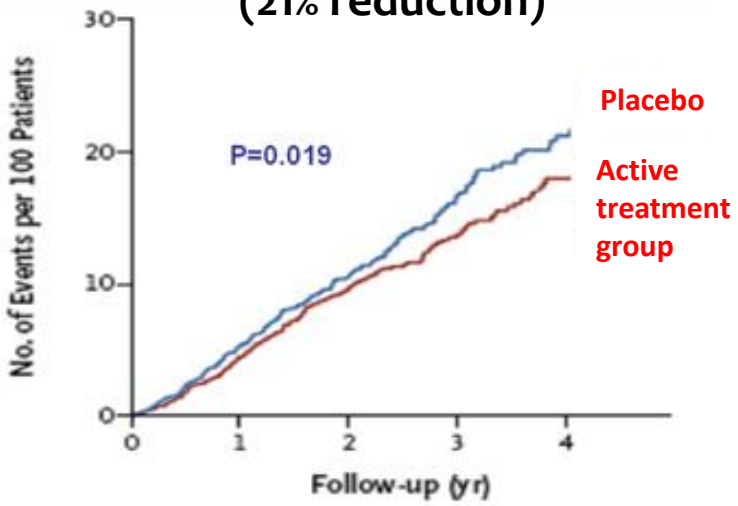
The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 MAY 1, 2008 VOL. 358 NO. 18

Initial BP: 161/84 mmHg
Final BP: 144/78 mmHg

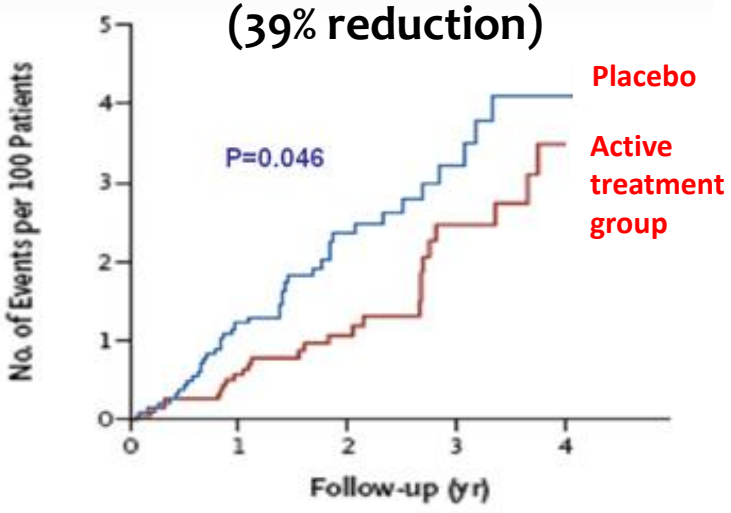
All Stroke (30% reduction)



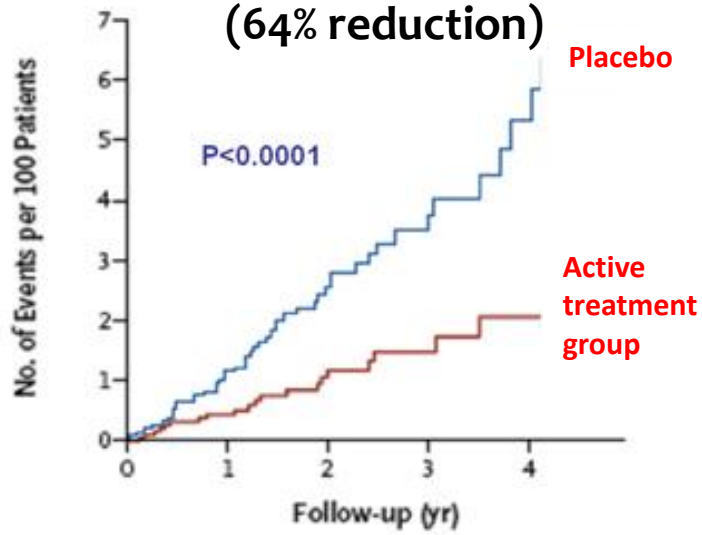
Total mortality (21% reduction)



Fatal Stroke (39% reduction)



Heart Failure (64% reduction)



NS Beckett et al, NEJM 2008

Original Investigation

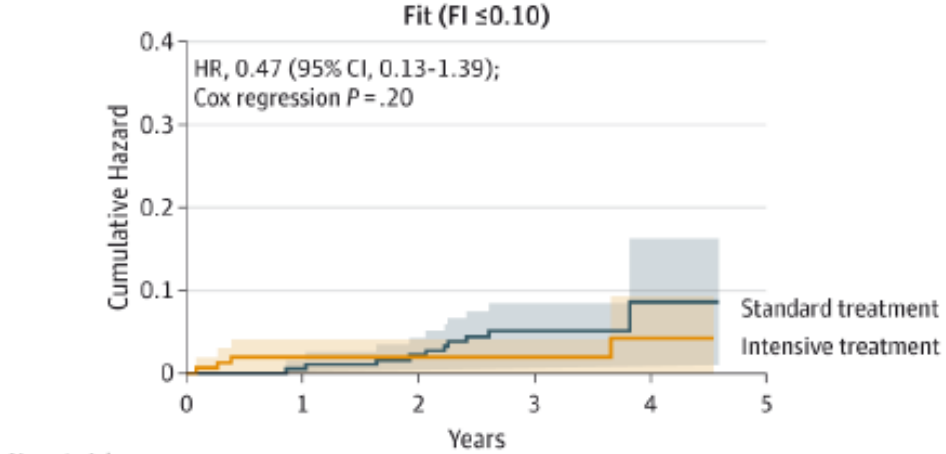
Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged ≥75 Years
A Randomized Clinical Trial

Jeff D. Williamson, MD, MHS; Mark A. Supiano, MD; William B. Applegate, MD, MPH; Dan R. Berlowitz, MD; Ruth C. Campbell, MD, MSPH; Glenn M. Chertow, MD; Larry J. Fine, MD; William E. Haley, MD; Amret T. Hawfield, MD; Joachim H. Ix, MD, MAS; Dalane W. Kitzman, MD; John B. Kostis, MD; Marie A. Krousel-Wood, MD; Lenore J. Launer, PhD; Suzanne Oparil, MD; Carlos J. Rodriguez, MD, MPH; Christianne L. Roumie, MD, MPH; Ronald I. Shorr, MD, MS; Kaycee M. Sink, MD, MAS; Virginia G. Wadley, PhD; Paul K. Whelton, MD; Jeffrey Whittle, MD; Nancy F. Woolard; Jackson T. Wright Jr, MD, PhD; Nicholas M. Pajewski, PhD; for the SPRINT Research Group

CONCLUSIONS AND RELEVANCE Among ambulatory adults aged 75 years or older, treating to an SBP target of less than 120 mm Hg compared with an SBP target of less than 140 mm Hg resulted in significantly lower rates of fatal and nonfatal major cardiovascular events and death from any cause.

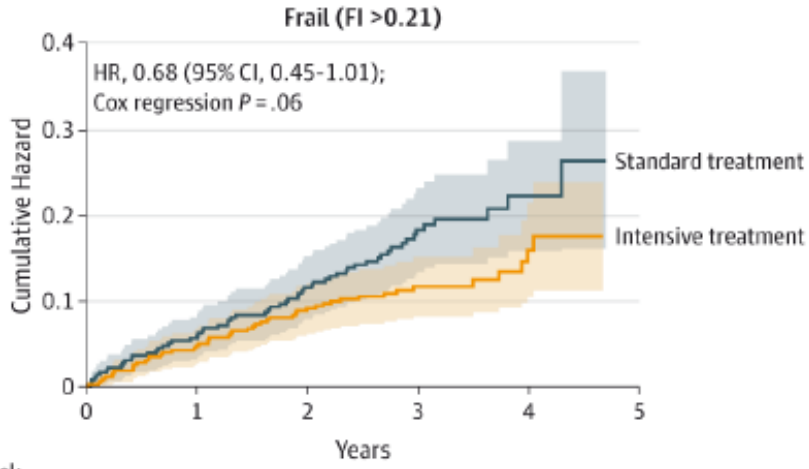
Williamson JD et al. JAMA. doi:10.1001/jama.2016.7050 Published online May 19, 2016.

SPRINT trial



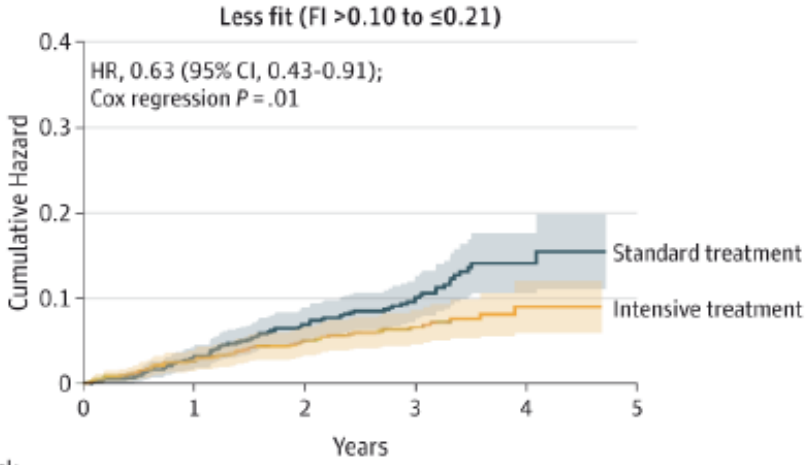
No. at risk

Type of treatment					
Standard	190	186	182	94	19
Intensive	159	151	150	107	16



No. at risk

Type of treatment					
Standard	375	338	305	177	49
Intensive	440	398	371	223	71



No. at risk

Type of treatment					
Standard	745	697	653	390	91
Intensive	711	677	644	378	93

Beckett et al, *JAMA 2016*

ORIGINAL ARTICLE

Trial of Intensive Blood-Pressure Control in Older Patients with Hypertension

- Multicenter, randomized, controlled trial: Chinese patients 60-80 yrs
- Mean **age 66.2** [4.8] years with hypertension
- SBP target of 110 to less than 130 mm Hg (**intensive treatment**) or
- SBP target of 130 to less than 150 mm Hg (**standard treatment**).
- Intensive treatment resulted in a **lower incidence of CV events**.
- **Beneficial effects of intensive treatment NOT CONFIRMED in those aged 70-80 yrs, in women and in those with diabetes**

Zhang W et al. For the **STEP** Study Group. N Engl J Med 2021;385:1268-79

Clinical Trials vs Real World

(Some) exclusion criteria from clinical trials

HYVET

- Heart failure requiring treatment
- Serum creatinine >1.7 mg/dl
- Dementia
- Requirement of nursing care
- SBP < 160 mmHg

Beckett NS et al, NEJM 2008

SPRINT

- Symptomatic heart failure
- 1' SBP < 110 mm Hg
- Diabetes
- eGFR < 20 ml/min or ESRD
- Survival less than 3 years
- Nursing home residents
- Dementia
- Unintentional weight loss >10% in last 6 months

Wright JT et al, NEJM 2015

STEP

- Previous stroke
- Recent MI or decompensated Heart Failure
- Atrial fibrillation
- Valvular disease
- Dilated or hypertrophic cardiomyopathy
- Severe cognitive impairment
- Uncontrolled Diabetes

Zhang W et al. NEJM 2021

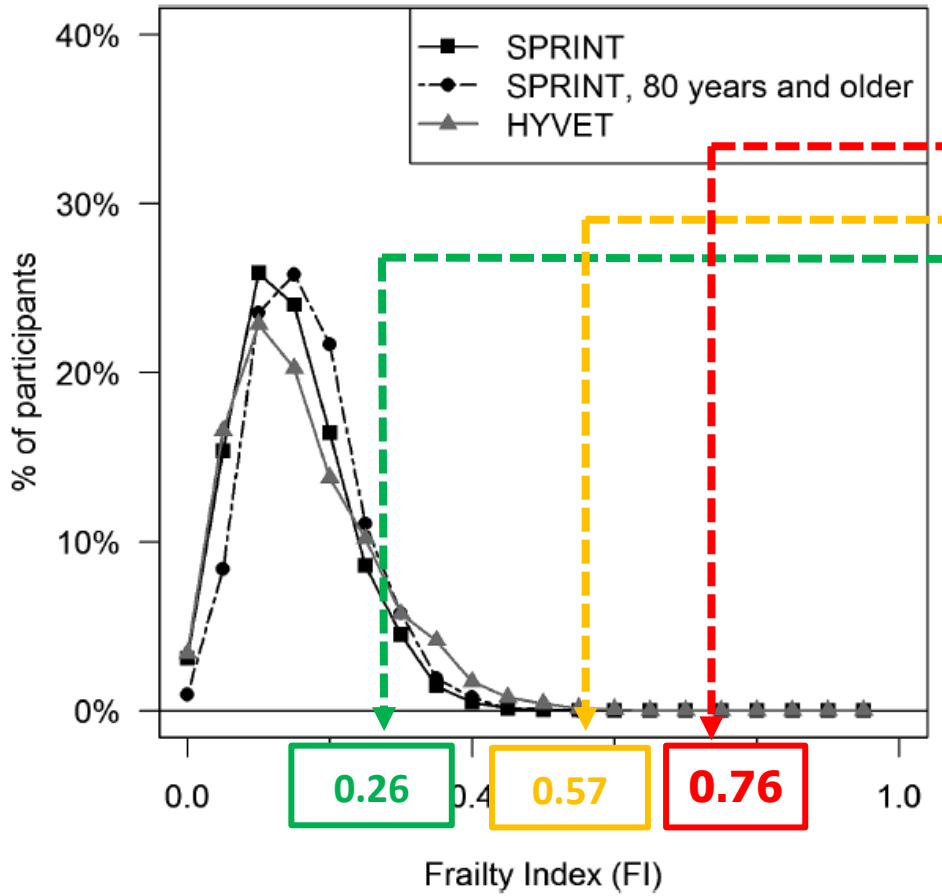
Baseline Characteristics of Participants Aged 75 Years or Older: SPRINT trial

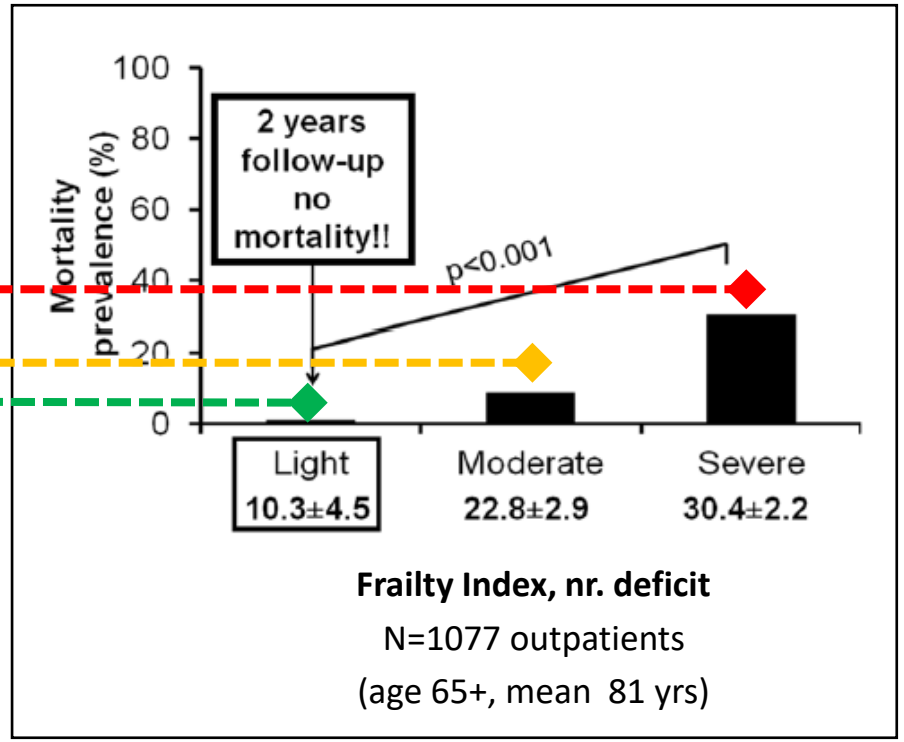
	Intensive Treatment (n = 1317)	Standard Treatment (n = 1319)
Gait speed		
Median (IQR), m/s	0.90 (0.77-1.05)	0.92 (0.77-1.06)
Speed <0.8 m/s, No. (%)	371 (28.2)	369 (28.0)
Frailty index, median (IQR)[c]	0.18 (0.13-0.23)	0.17 (0.12-0.22)
Frailty status, No. (%)		
Fit (frailty index ≤0.10)	159 (12.1)	190 (14.4)
Less fit (frailty index >0.10 to ≤0.21)	711 (54.0)	745 (56.5)
Frail (frailty index >0.21)	440 (33.4)	375 (28.4)

Williamson JD et al. JAMA 2016

Degrees of FI associated with mortality rate

Frailty Index distribution





Pajewski NM, et al. J Gerontol A Biol Sci Med Sci 2016

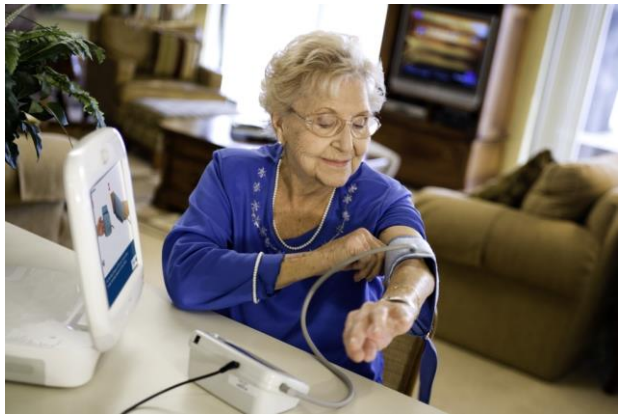
Modified from Russo G, et al. J Hum Hypertens 2018

ORIGINAL ARTICLE

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group*

Goals of antihypertensive treatment in the frail.



SPRINT study (as well as HYVET and STEP) are not applicable to frail pts

Cosa dicono le LG?

2023 ESH Guidelines for the management of arterial hypertension

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

"The present guidelines strongly support the concept that **age should be no barrier to antihypertensive drug treatment …**

Soglie di trattamento

In patients **18 to 79 years**, the recommended office threshold for initiation of drug treatment is 140 mmHg for SBP and/or 90 mmHg for DBP (IA)

Target di trattamento

The primary goal of treatment is to lower BP to <140/80 mmHg (IA)
Lowering BP to below 130/80 mmHg can be considered if treatment is well tolerated (IB)

In patients with ISH, the primary goal of treatment is to lower SBP in the 140 to 150 mmHg range (IA)

2023 ESH Guidelines for the management of arterial hypertension

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

Patients aged >80 years: "Evidence on the BP threshold for treatment is much more scant…

Soglie di trattamento

The recommended office SBP threshold for initiation of drug treatment is 160 mmHg (I B)

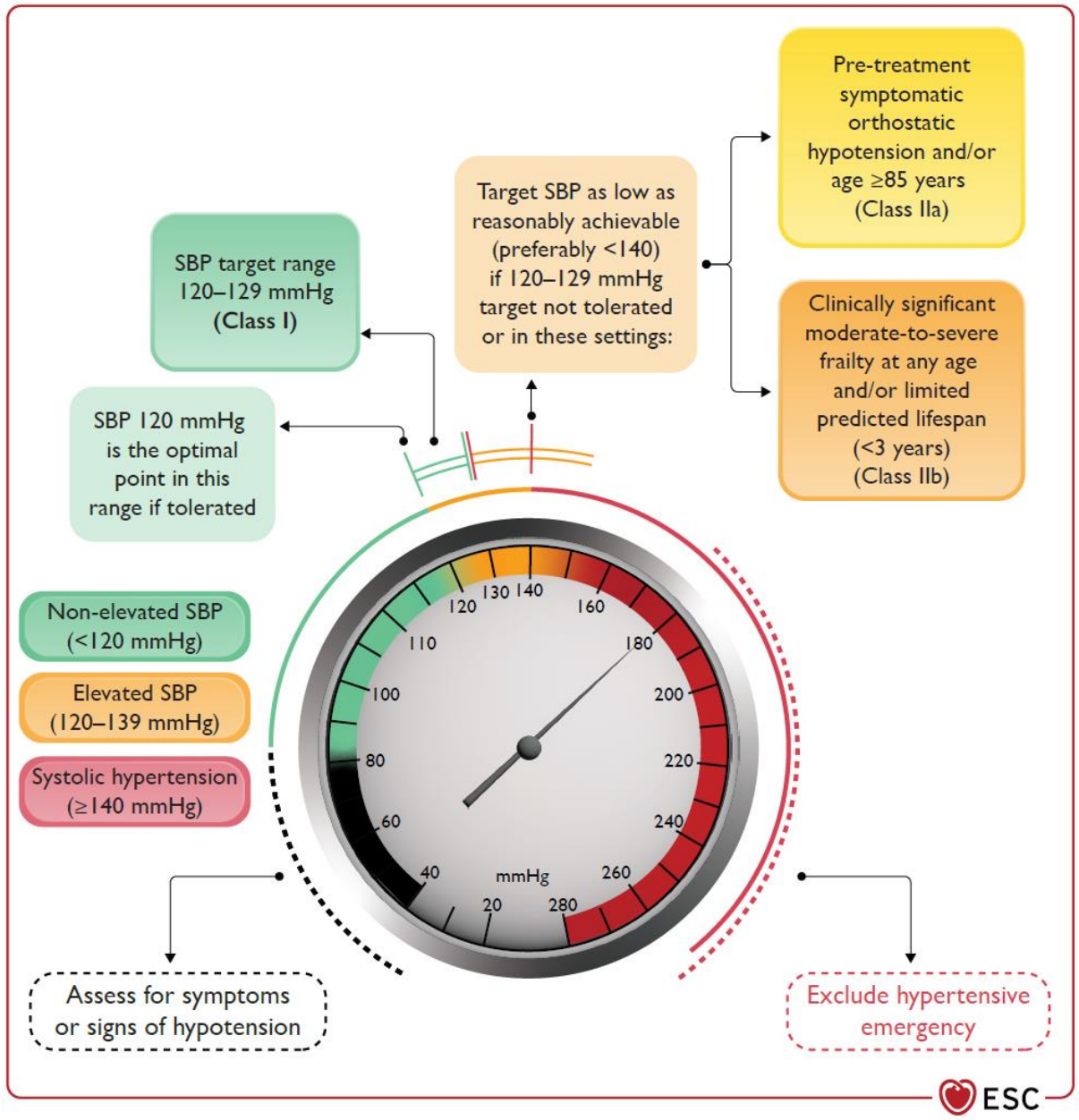
However, a lower SBP threshold in the range 140 – 160 mmHg may be considered (II C)

Target di trattamento

Office BP should be lowered to a SBP in the 140-150 mmHg range and to a DBP <80mmHg(IA)

However, reduction of office SBP between 130-139 mmHg may be considered if well tolerated, albeit cautiously if DBP is already below 70 mmHg (IIB)

Reduction of treatment can be considered in patients aged 80 years or older with a low SBP (< 120 mmHg) or in the presence of severe orthostatic hypotension or a high frailty level (IIIC)



ESC European Society of Cardiology
European Heart Journal (2024) 00, 1–107
https://doi.org/10.1093/eurheartj/ehae178
ESC GUIDELINES

2024 ESC Guidelines for the management of elevated blood pressure and hypertension

- **Treatment target is always 120–129/70–79 mmHg**
- (if treatment is tolerated and with certain exceptions)
- **Data** supporting this target among adults **>85 years are inconclusive.**
- **Personalized BP-lowering treatment** should be instituted in people aged ≥85 years and/or with significant frailty.

Recommendations for blood pressure targets with treatment

ESC European Society of Cardiology
European Heart Journal (2024) **00**, 1–107
https://doi.org/10.1093/eurheartj/ehae178
ESC GUIDELINES

2024 ESC Guidelines for the management of elevated blood pressure and hypertension

Because the CVD benefit of an on-treatment systolic BP target of 120–129 mmHg may not generalize to the following specific settings, personalized and more lenient BP targets (e.g. <140 mmHg) should be considered among patients meeting the following criteria: pre-treatment symptomatic orthostatic hypotension, and/or age ≥85 years.[131]	IIa	C
Because the CVD benefit of an on-treatment systolic BP target of 120–129 mmHg may not generalize to the following specific settings, personalized and more lenient BP targets (e.g. <140/90 mmHg) may be considered among patients meeting the following criteria: clinically significant moderate-to-severe frailty at any age, and/or limited predicted lifespan (<3 years).	IIb	C

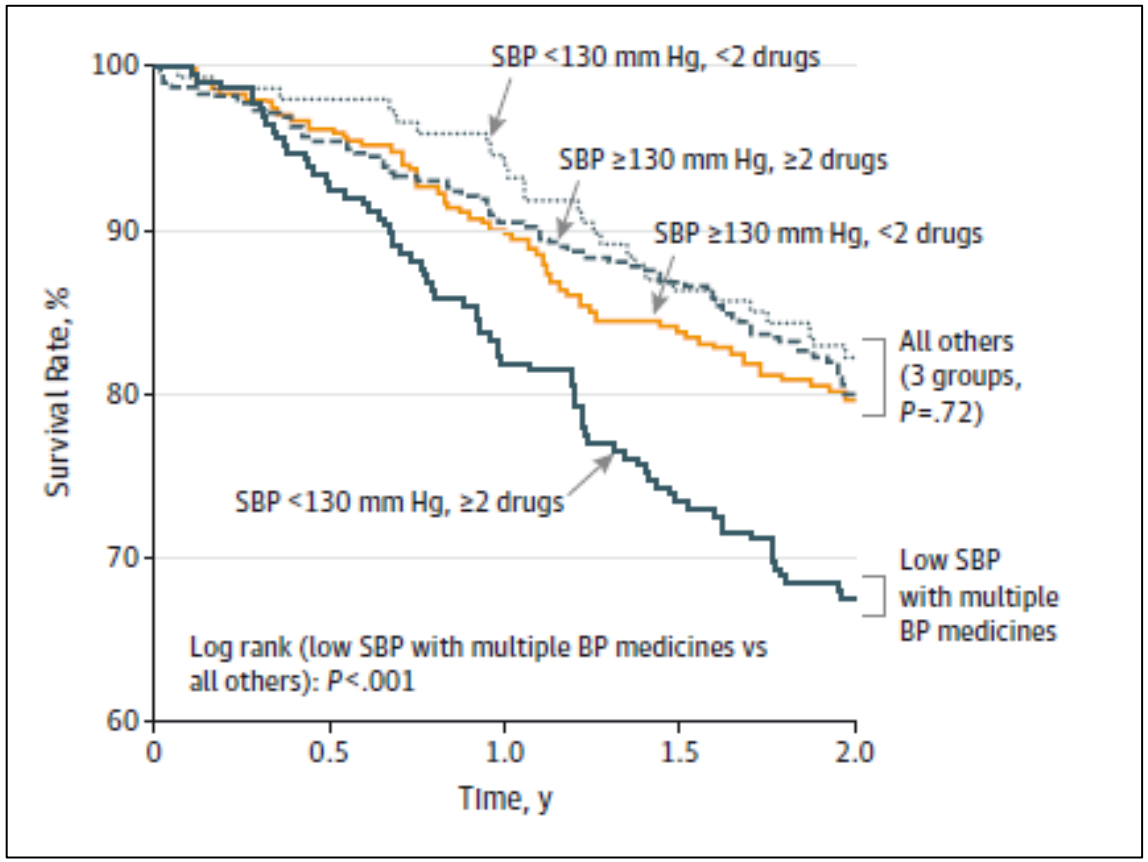
More lenient BP targets (e.g. <140/90 mmHg mmHg)

- Age ≥85
- Symptomatic OH
- Moderate-severe frailty
- Life expectancy <3 y

Original Investigation

Treatment With Multiple Blood Pressure Medications, Achieved Blood Pressure, and Mortality in Older Nursing Home Residents

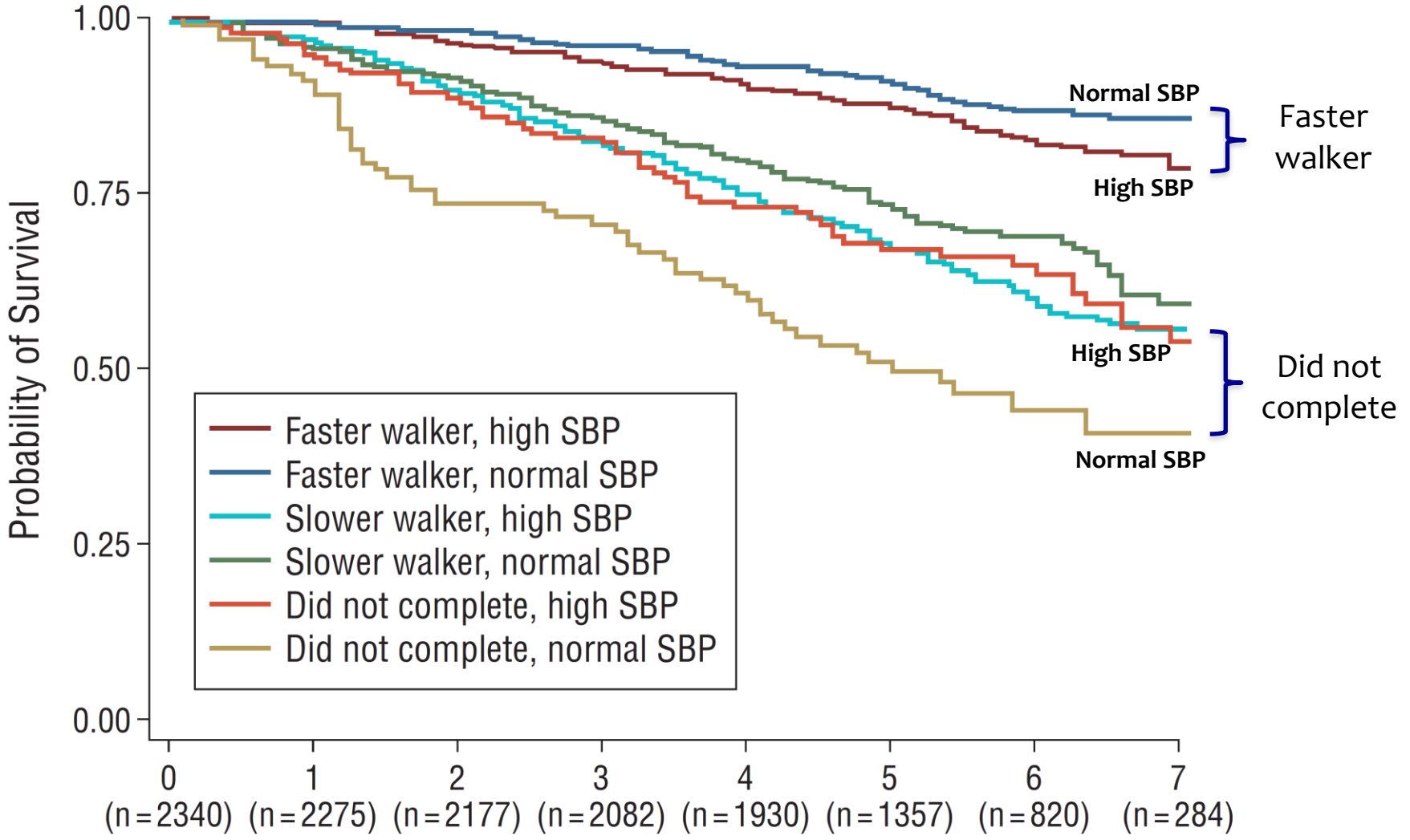
The PARTAGE Study



Association between BP and risk of death in the institutionalized elderly

Benetos A et al. JAMA Int Med 2015

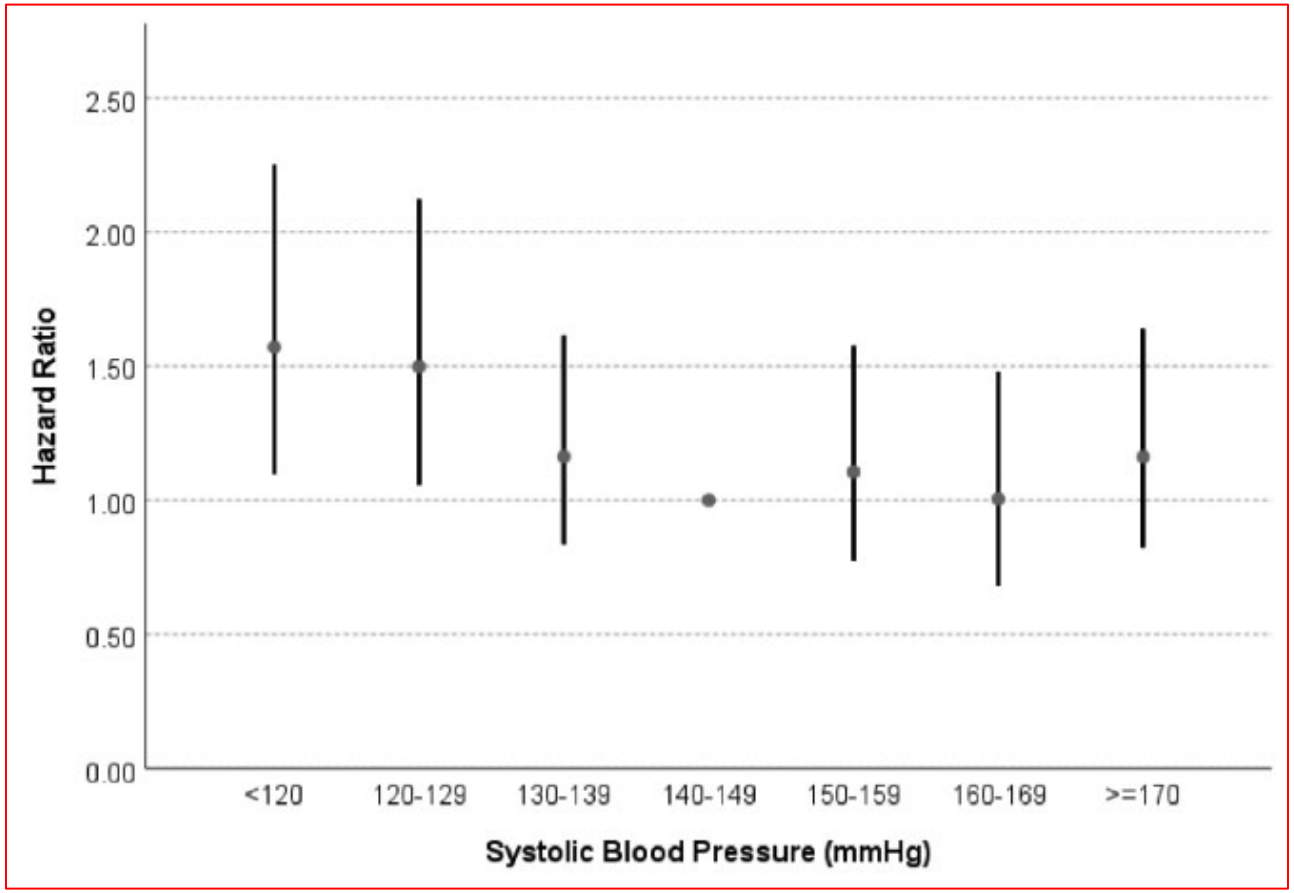
Association of elevated SBP and mortality, stratified by walking speed, in NHANES Survey participants 65 years and older (1999-2002)



Odden MC et al. Arch Intern Med. 2012;172(15):1162-1168.

Control of blood pressure and risk of mortality in a cohort of older adults: the Berlin Initiative Study

Association of SBP with the risk of all-cause mortality in community-dwelling older adults.



Increased risks were observed in

- ✓ patients ≥ 80 years (HR 1.40; [CI 1.12–1.74]
- ✓ previous CV events (HR 1.61; [CI 1.14–2.27]

- ✓ not in those aged 70–79 years
- ✓ Not in those without previous CV events

Douros A et al. Eur Heart J 2019

JAMA Internal Medicine | Original Investigation | LESS IS MORE

Antihypertensive Medication and Fracture Risk in Older Veterans Health Administration Nursing Home Residents

Chintan V. Dave, PharmD, PhD; Yongmei Li, PhD; Michael A. Steinman, MD; Sei J. Lee, MD, MAS; Xiaojuan Liu, MS; Bocheng Jing, MS; Laura A. Graham, PhD; Zachary A. Marcum, PharmD, PhD; Kathy Z. Fung, MS; Michelle C. Odden, PhD

JAMA Intern Med. doi:10.1001/jamainternmed.2024.0507
Published online April 22, 2024.

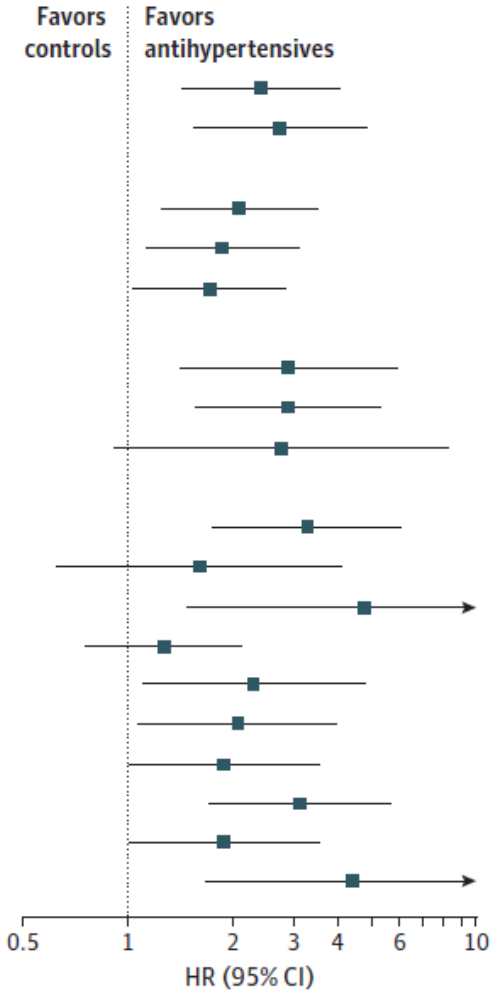
29 648 older long-term care nursing home residents in the Veterans Health Administration (01/01/2006, - 31/10/2019

Endpoint

nontraumatic fracture of the humerus, hip, pelvis, radius, or ulna within 30 days of antihypertensive medication initiation

Adjusted Risk of Fracture Among Nursing Home Residents Initiating Antihypertensive Medication:
Sensitivity and Subgroup Analyses

Analysis	HR (95% CI)
Primary	2.42 (1.43-4.08)
ITT	2.74 (1.55-4.85)
Length of follow-up	
45 d	2.09 (1.25-3.49)
60 d	1.87 (1.13-3.07)
90 d	1.72 (1.04-2.85)
Sensitivity	
12-wk Washout	2.89 (1.41-5.94)
Exclusion of loop diuretics	2.89 (1.58-5.28)
Inclusion of facility-level measures	2.76 (0.91-8.32)
Subgroup	
Residents with dementia	3.28 (1.76-6.10)
Residents without dementia	1.61 (0.63-4.11)
No prior use of antihypertensives	4.77 (1.49-15.32)
Prior use of antihypertensives	1.27 (0.76-2.12)
Age <80 y	2.29 (1.10-4.79)
Age ≥80 y	2.07 (1.08-3.95)
SBP <140 mm Hg	1.89 (1.01-3.53)
SBP ≥140 mm Hg	3.12 (1.71-5.69)
DBP <80 mm Hg	1.89 (1.01-3.53)
DBP ≥80 mm Hg	4.41 (1.67-11.68)



JAMA Internal Medicine | Original Investigation | LESS IS MORE

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Risk of Fall-Related Events Among Nursing Home Residents Initiating Antihypertensive Medication

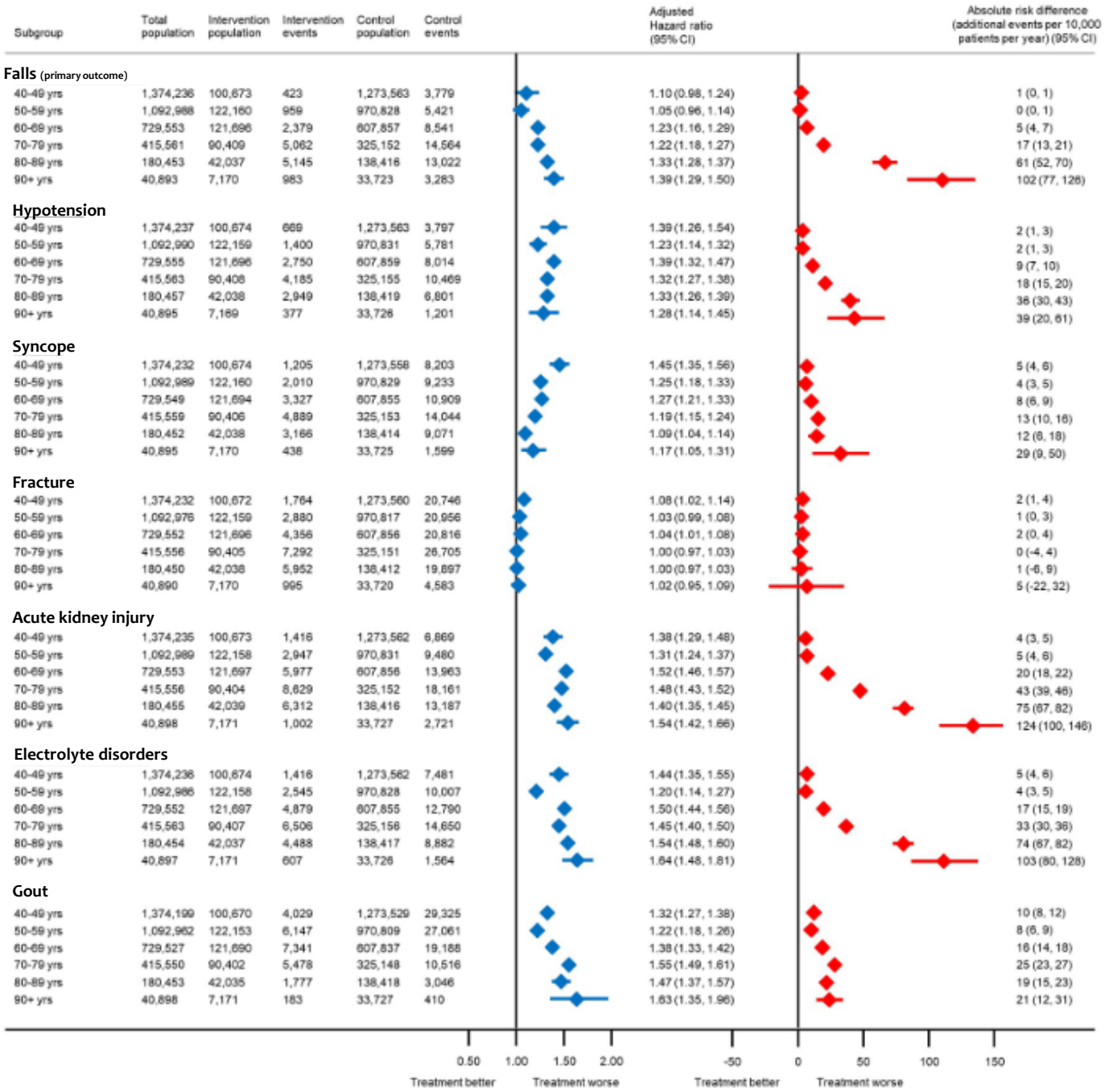
	Pooled analysis		
	No. of events (IR)[a]		
Event	Treated (n = 12 942)	Control (n = 51 768)	HR (95% CI)
Fracture[b]	46 (5.4)	56 (2.2)	2.42 (1.43-4.08)
Severe fall	246 (28.8)	386 (15.5)	1.80 (1.53-2.13)
Syncope	135 (15.8)	231 (9.3)	1.69 (1.30-2.19)
Expanded outcome definition[b]	52 (6.1)	66 (2.6)	2.30 (1.44-3.69)

Short-term Risk of Serious Fall Injuries in Older Adults Initiating and Intensifying Treatment with Antihypertensive Medication

Table 3. Short-Term Odds Ratios for a Serious Fall Injury Associated With Initiation, Adding a New Drug Class, and Antihypertensive Medication Titration

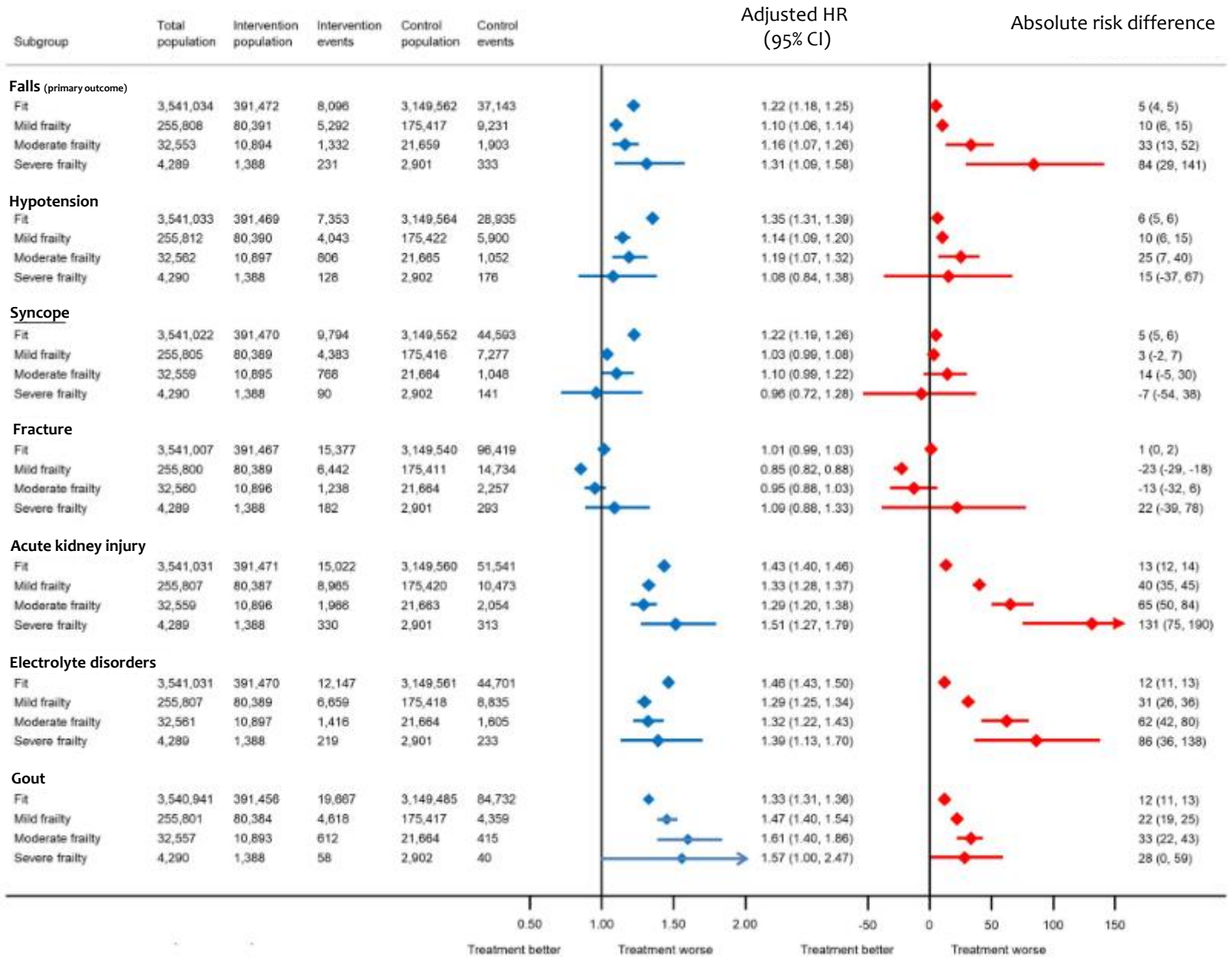
	Overall (n=90 127 Serious Fall Injuries)			Previous Hypertension Diagnosis* (n=90 127 Serious Fall Injuries)			No Recent Hospitalization† (n=60 211 Serious Fall Injuries)		
	Case Period n (%)‡	Control Periods n (%)§	OR (95% CI)	Case Period n (%)‡	Control Periods n (%)§	OR (95% CI)	Case Period n (%)‡	Control Periods n (%)§	OR (95% CI)
Initiation	272 (0.30)	1201 (0.22)	1.36 (1.19–1.55)	159 (0.18)	701 (0.13)	1.36 (1.15–1.62)	146 (0.24)	635 (0.18)	1.38 (1.15–1.65)
Addition of new class	1508 (1.67)	7820 (1.45)	1.16 (1.10–1.23)	1276 (1.42)	6664 (1.23)	1.15 (1.09–1.23)	687 (1.14)	3450 (0.95)	1.20 (1.10–1.30)
Titration	3113 (3.45)	16 714 (3.09)	1.13 (1.08–1.18)	2696 (2.99)	14 542 (2.69)	1.12 (1.08–1.17)	1432 (2.38)	7662 (2.12)	1.13 (1.07–1.20)

Shimbo et al,
Circ Cardiovasc Qual Outcomes 2016



The association between antihypertensive treatment and serious adverse events by age and frailty: A cohort study

Sheppard JP et al Plos Med 2023



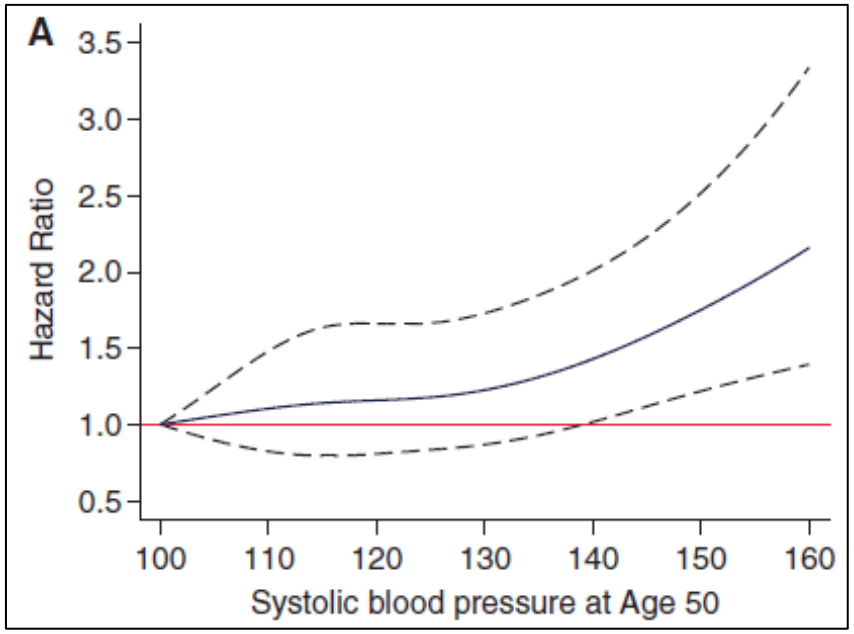
The association between antihypertensive treatment and serious adverse events by age and frailty: A cohort study

Sheppard JP et al Plos Med 2023

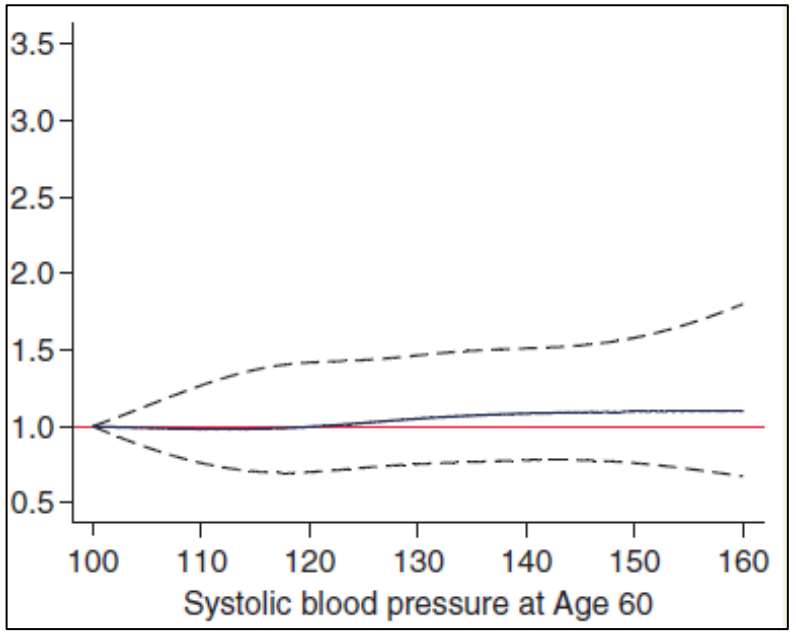
Association between SBP and dementia in the Whitehall II cohort study: role of age, duration, and threshold used to define hypertension

Threshold: association of SBP with dementia at:

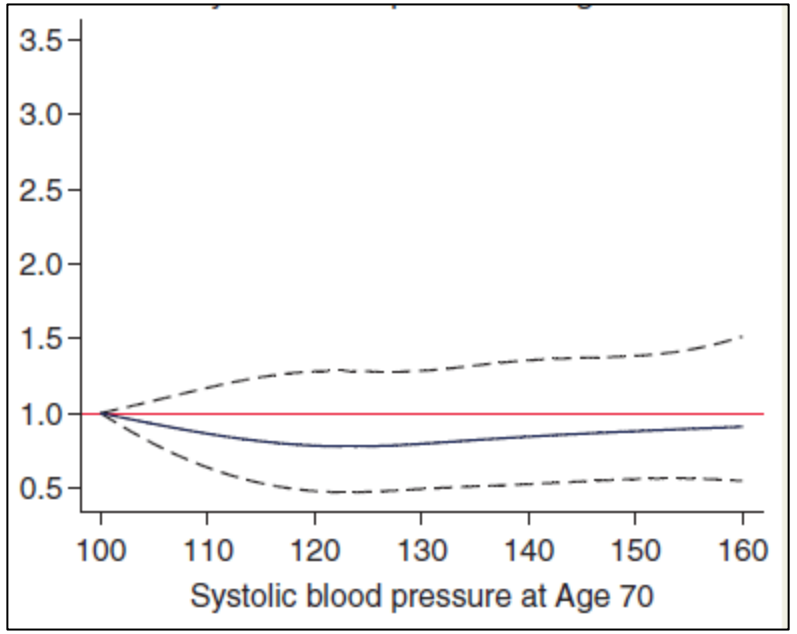
Age 50 yrs



Age 60 yrs



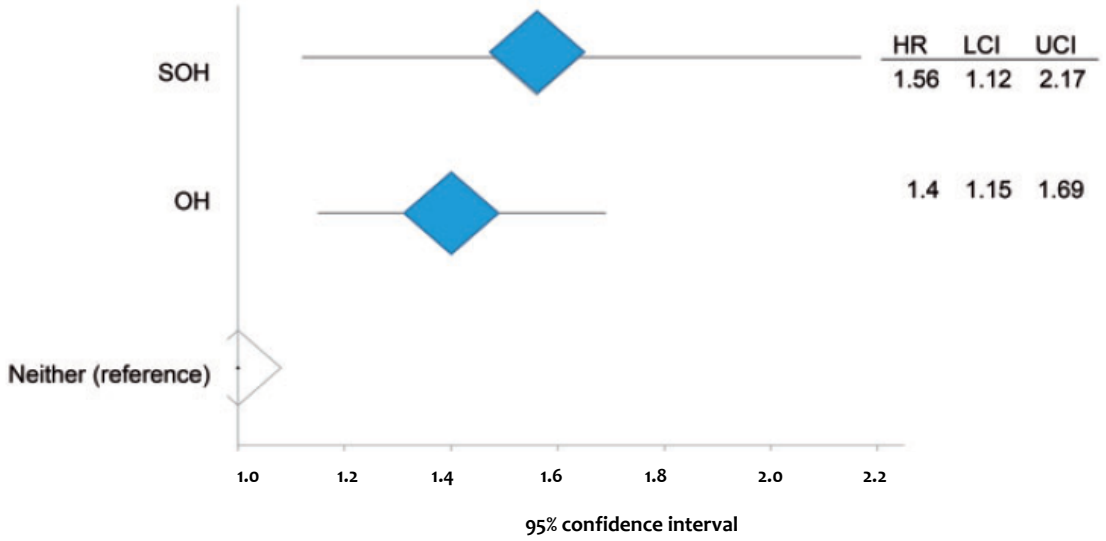
Age 70 yrs



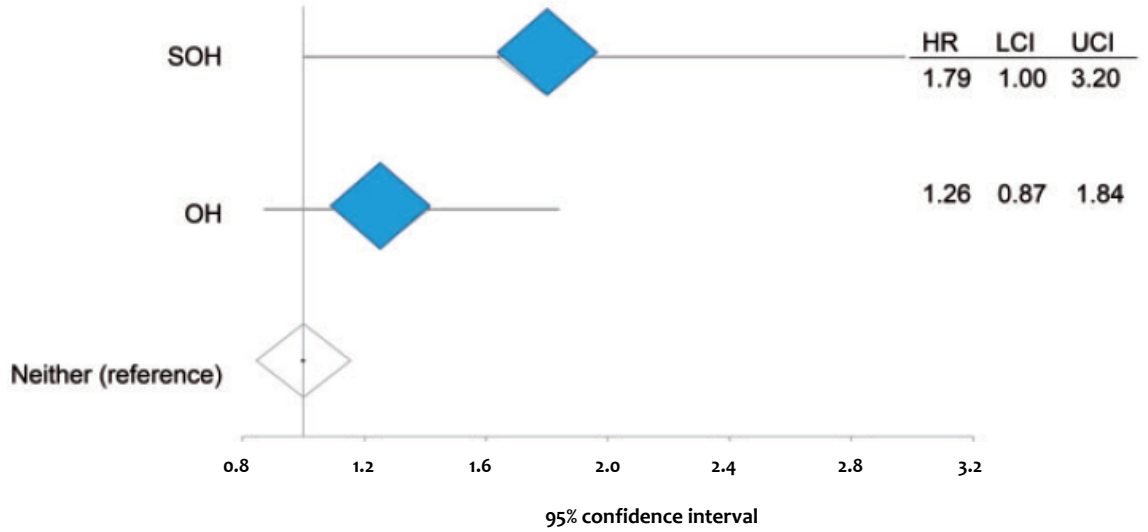
Abell JG et al, Eur Heart J 2018

Orthostatic hypotension (OH) and symptomatic OH increase risk of cognitive impairment: an integrated evidence review and analysis of a large older hypertensive (HYVET) cohort

Risk of cognitive decline



Risk of dementia

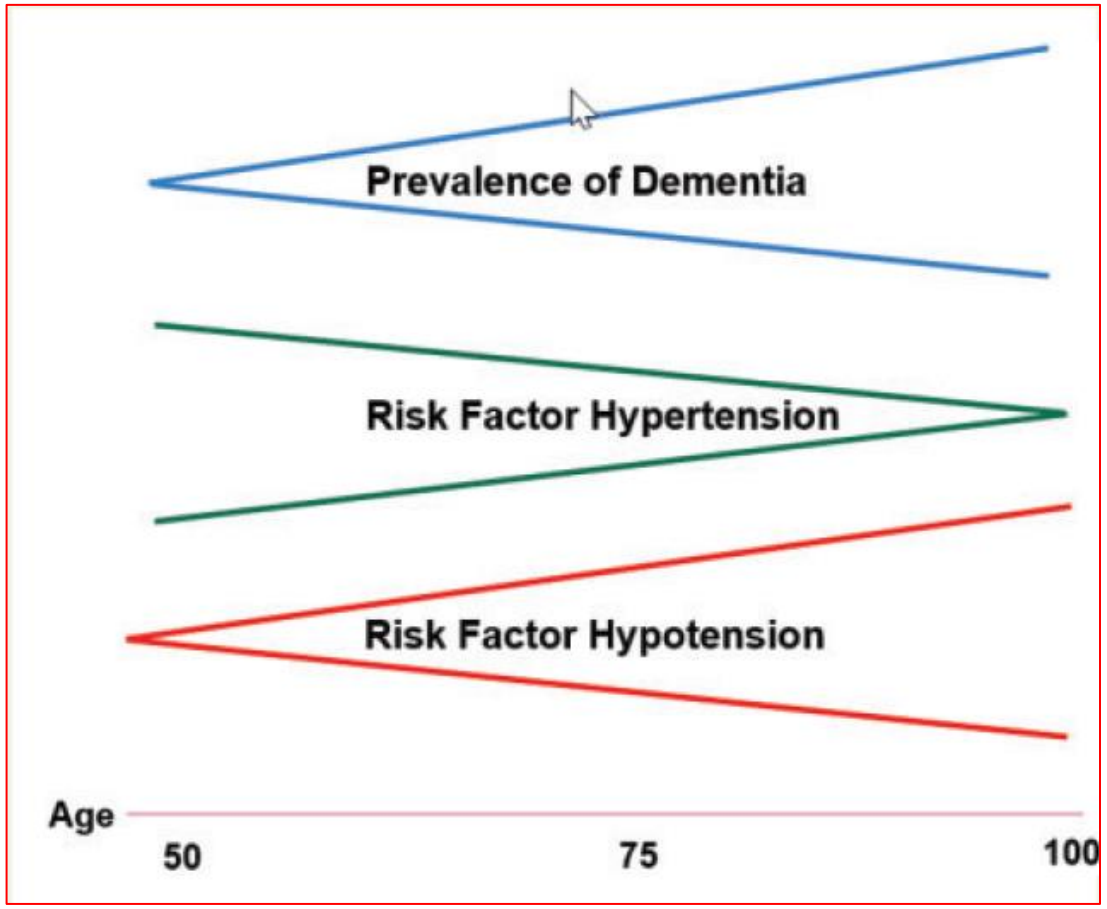


Peters R et al. Eur Heart J 2018; 39, 3135-3143

ESC European Society of Cardiology
European Heart Journal (2018) **39**, 3144–3146
doi:10.1093/eurheartj/ehy525

EDITORIAL

The oldest old: does hypertension become essential again?



"The older the patient, the less important a risk factor hypertension becomes.

In older patients, elevated BP progressively becomes less of a risk factor for dementia and too low a BP increasingly becomes the principle haemodynamic culprit."

Messerli FH et al. Eur Heart J 2018

- ✓ Hypotension
- ✓ Syncope, falls
- ✓ Electrolyte disorders
- ✓ Dehydration
- ✓ Acute kidney injury
- ✓ Fatigue, dizziness
- ✓ Confusion

→

- ✓ Activity restriction, anxiety
- ✓ Functional decline
- ✓ Unplanned hospitalization complicated by:
  - bed rest, sarcopenia,
  - nosocomial infections, falls,
  - delirium and cognitive decline

↙

Impaired life trajectory at old age
20 to 300-fold increased risk of disability and/or institutionalization

Hospitalization, Restricted Activity, and the Development of Disability Among Older Persons

Prospective cohort study, conducted in the general community, of people ≥ 70 years. Individuals not disabled (ie, required no personal assistance) in 4 essential activities of daily living: bathing, dressing, walking inside the house, and transferring from a chair.

Table 2. Exposure to Intervening Events per 100 Months According to Disability Status*

	Any Disability			Persistent Disability			Disability With Nursing Home Admission		
Intervening Event	Present (n = 417)	Absent (n = 337)	*P* Value	Present (n = 278)	Absent (n = 476)	*P* Value	Present (n = 199)	Absent (n = 555)	*P* Value
Hospitalization	3.0 (0-8.3)	0 (0-2.0)	<.001	3.8 (0-9.1)	0 (0-3.4)	<.001	7.0 (3.7-13)	1.7 (0-3.7)	<.001
Restricted activity only	14 (2.4-33)	7.8 (3.7-16)	<.001	14 (2.6-33)	8.9 (3.8-19)	<.001	13 (2.6-28)	10 (3.9-20)	.16

*Values represent the median number of months (interquartile range) of the exposure. The exposure period includes the time to onset of the relevant disability outcome or to a censoring event for participants who did not develop the relevant disability outcome. *P* values were calculated using the Wilcoxon rank test.

Gill TM et al. JAMA. 2004;292(17):2115-2124.

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Before start…

Frailty assessment is mandatory

In old patients with hypertension there should always be an assessment of functional/autonomy status including cognitive function.	I	C
In patients with reduced functional/autonomy status and/or dementia treatment should be individualized.	I	C

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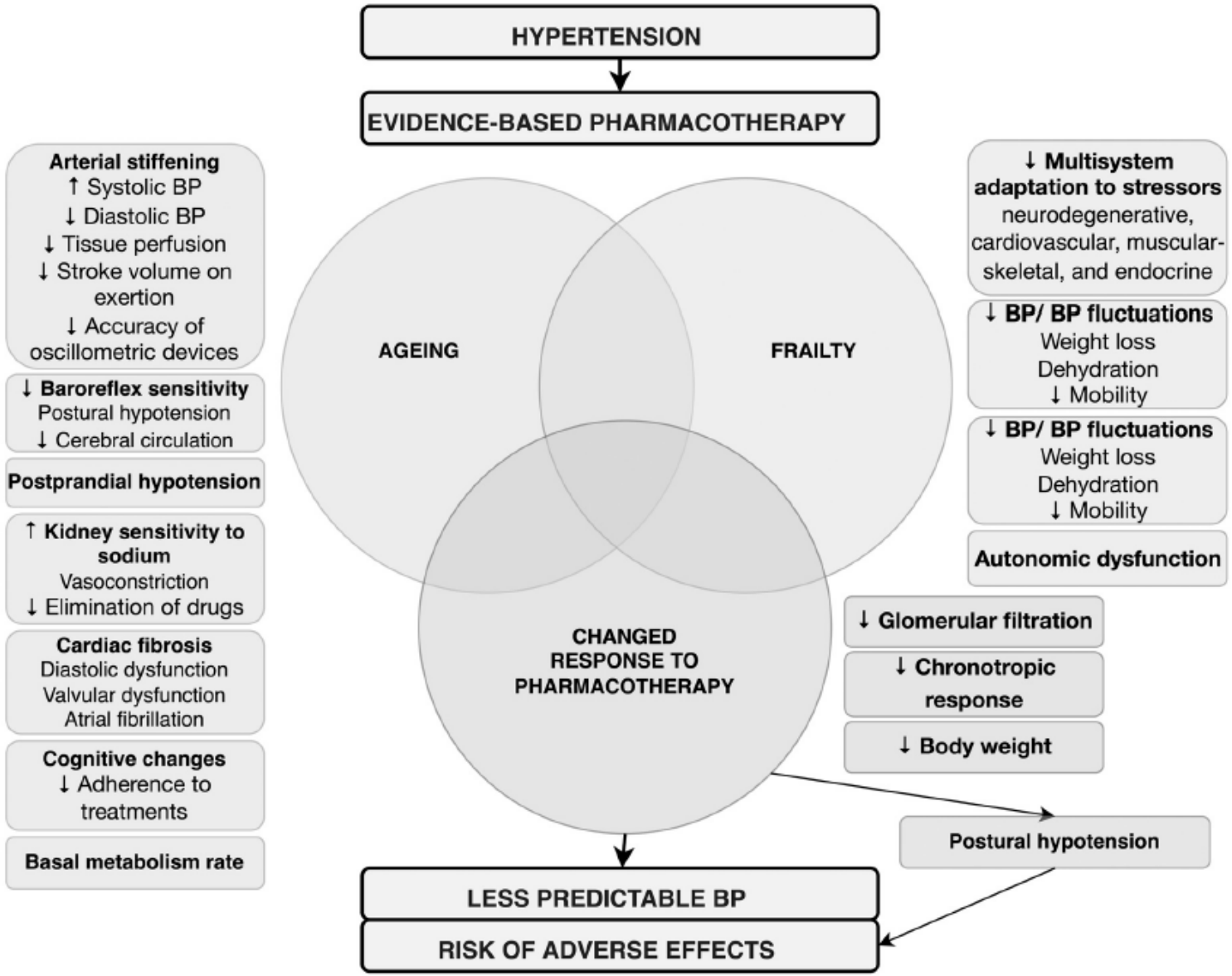
BP control and frailty

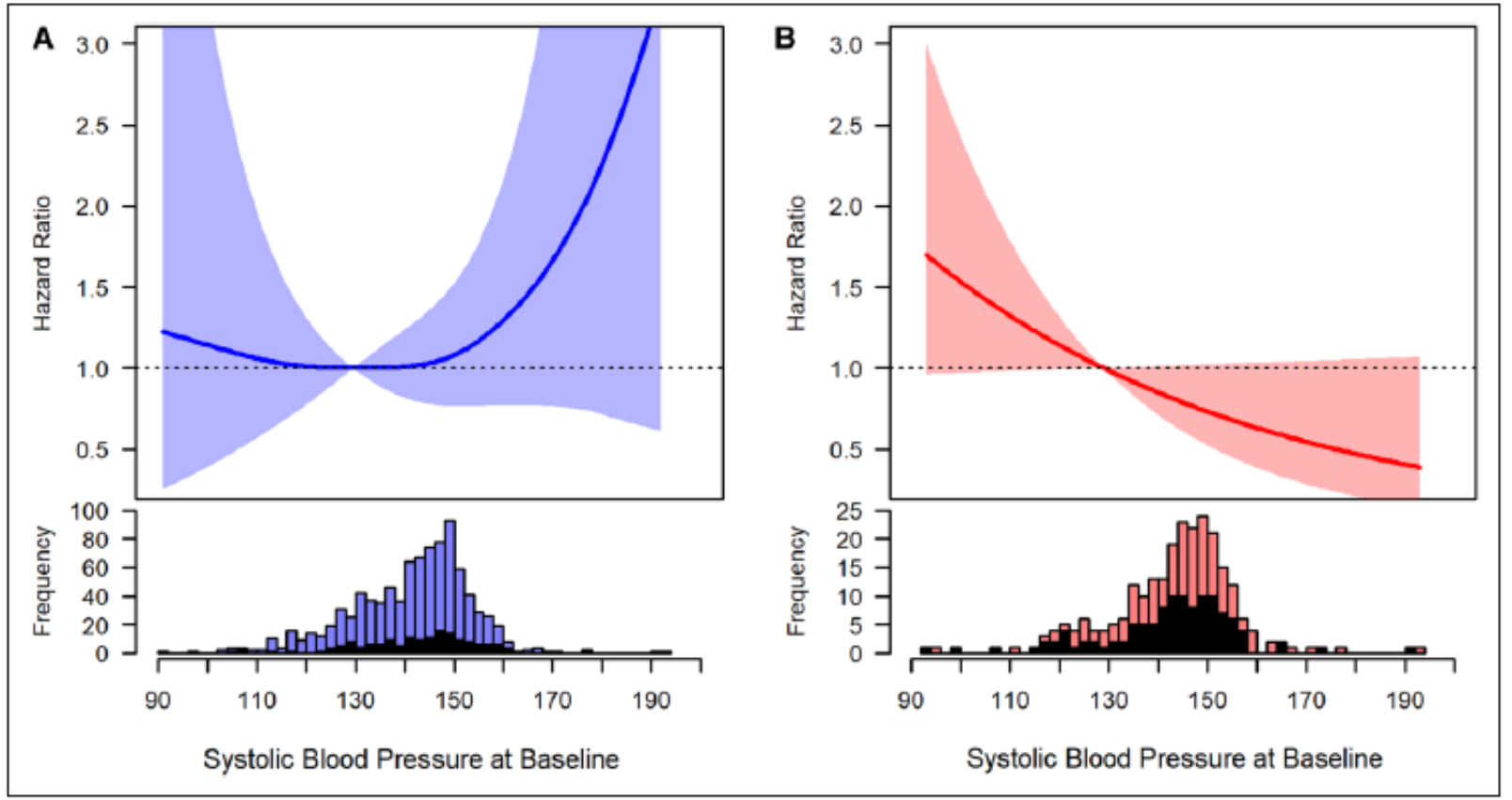


Shantsila et al, *J Hypertens 2023*

Systolic Blood Pressure and Mortality in Community-Dwelling Older Adults: Frailty as an Effect Modifier

Splines for the association between systolic blood pressure and 8-y all-cause-mortality stratified by frailty

Non frail



Frail

Kremer KM et al. Hypertension 2022; 79;24-32.

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Adapting BP-lowering strategies in pts older than 80 years according to functional/antonomy status

	Fit patients	Intermediate functional status	Severe loss of autonomy	
	• ADL score 5/6 • No dementia • Capacity of routine walking activities	• Partial loss of autonomy	• ADL 1-2/6 • Severe dementia • Chronic bedridden • End of life	
			Treatment **individually decided**	
threshold	**SBP 160 mmHg (IB)**	**SBP 160 mmHg (IB)**	**SBP 160 mmHg (IC)**	**threshold**
	SBP 140-159 mmHg may be considered (IIC)	**SBP 140-159 mmHg may be considered (IIC)**		
target	**SBP 140-150 mmHg and DBP < 80 mmHg (IA)**	**SBP 140-150 mmHg and DBP < 80 mmHg (IA)**	**SBP 140-150 mmHg (IC)**	**target**
	SBP 130-139 mmHg may be considered (IIB)	**SBP 130-139 mmHg may be considered (IIB)**	**Reduce treatment with SBP (< 120 mmHg) (IIC)**	

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How to start:

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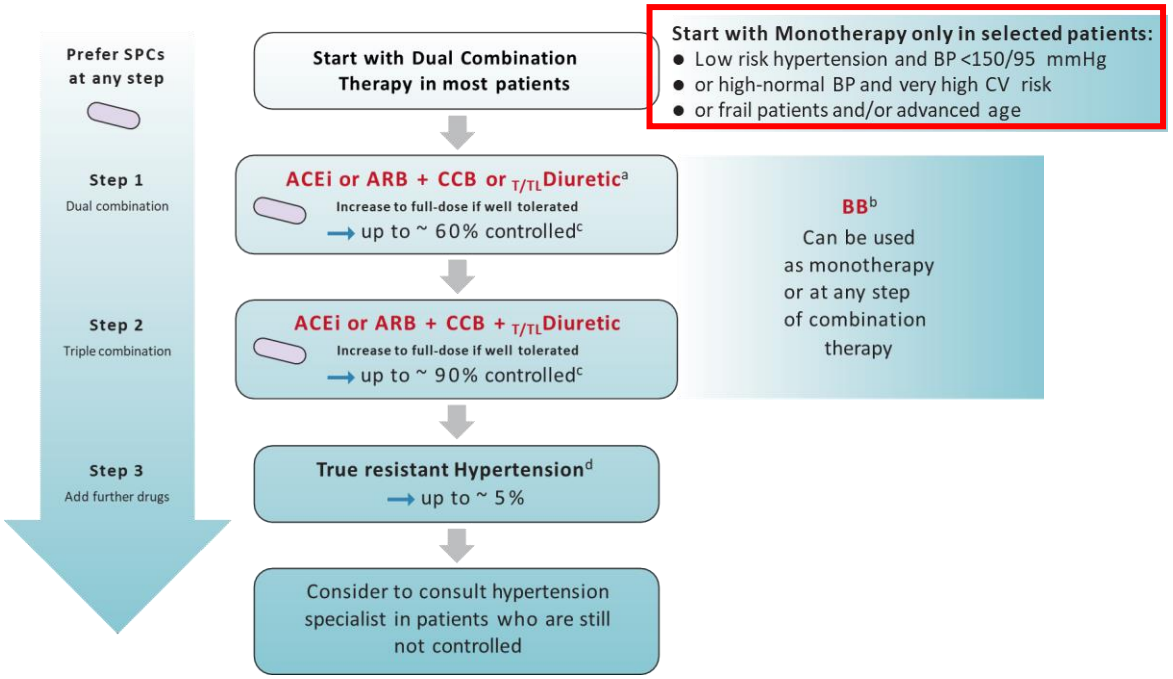
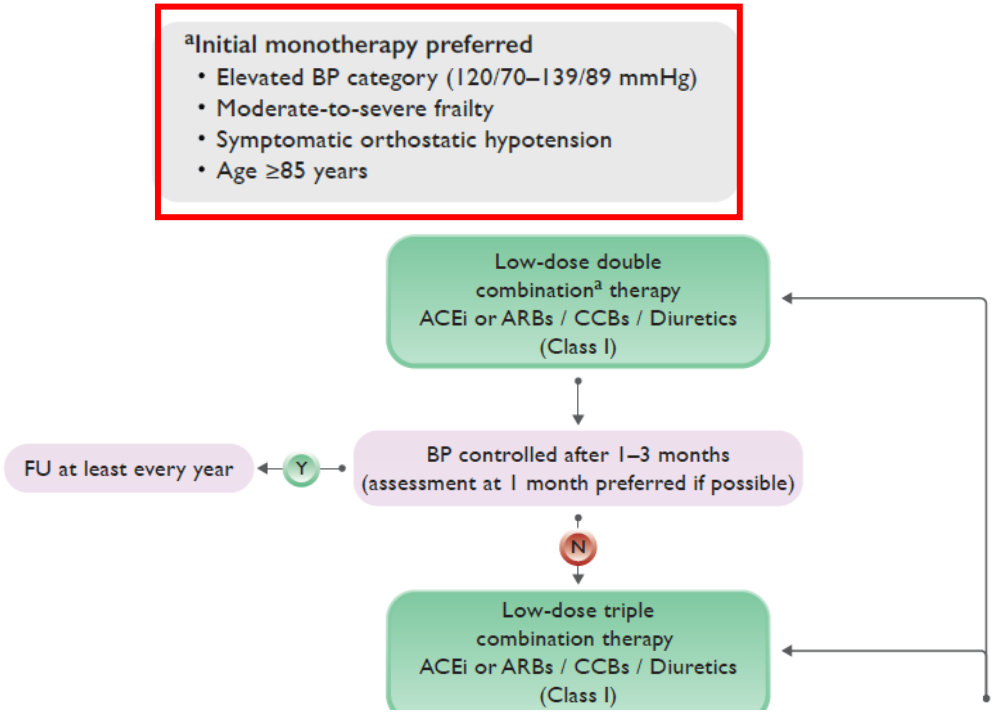


ESC European Society of Cardiology
European Heart Journal (2024) 00, 1–107
https://doi.org/10.1093/eurheartj/ehae178
ESC GUIDELINES

2024 ESC Guidelines for the management of elevated blood pressure and hypertension

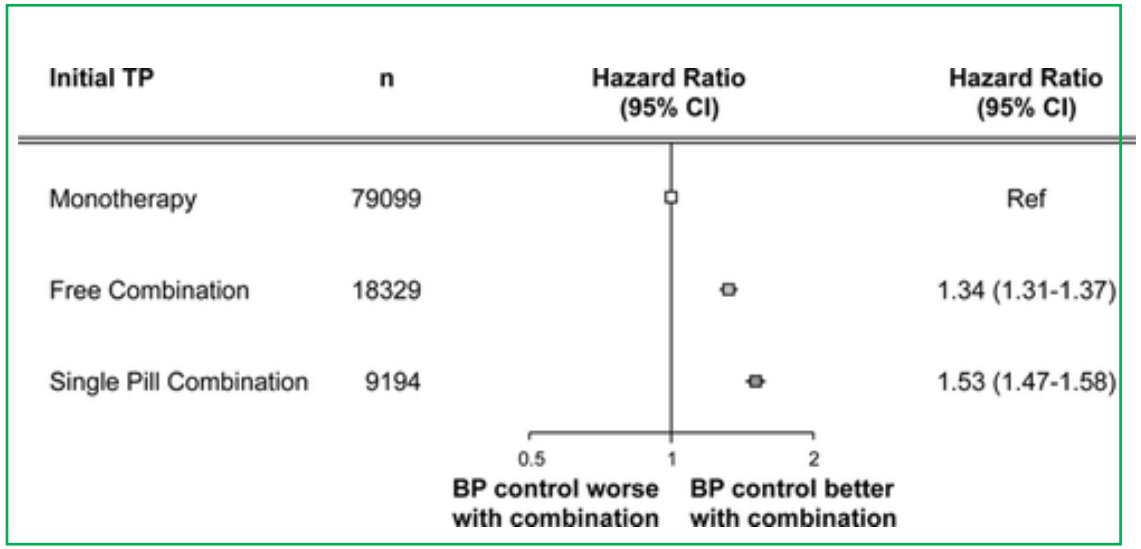


Practical tip: uptitrate…….. but at a lower pace

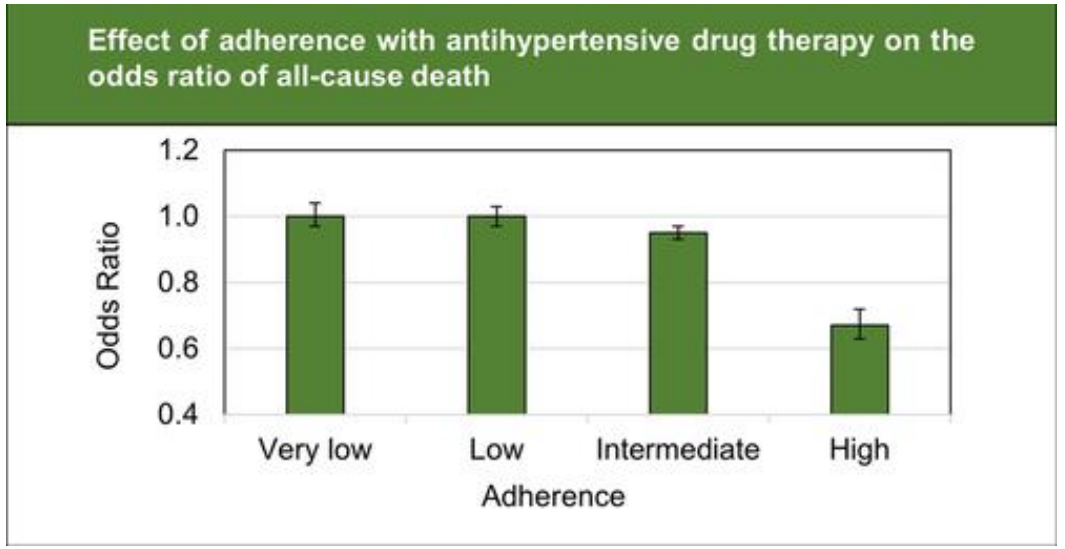
(avoid intolerance and side effects !)

Up-titration with a SPC treatment

- Less clinical inertia
- More adherence
- More CV prevention

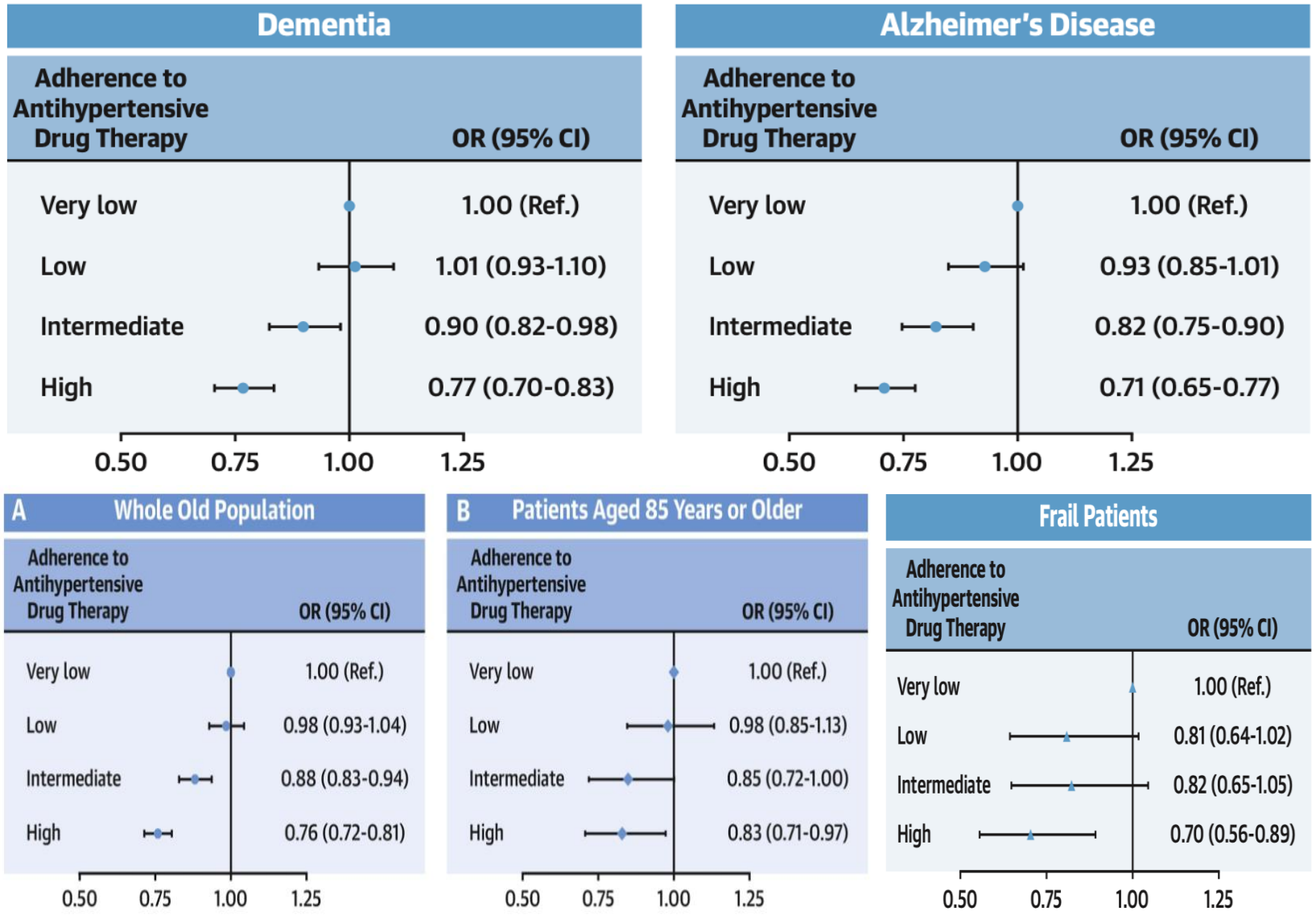


Mancia et al, *Circ Res 2019*



Rea et al, *Hypertension 2020*

Antihypertensive drugs and dementia – Nested case-control study – 215,547 patients ≥65 years - 13,812 patients (77.5±6.6 years; 40% men) developed dementia/AD during follow-up



Rea F et al J Am Coll Cardiol; 2024 Apr 2; 83 (13)1194-1203;

Come – Quali farmaci ?

"… **older patients may be more susceptible to side effects of drugs due to age by itself and health condition changes/comorbidities**" (Consensus document, ESH Working Group)

- Incontinenza urinaria (diuretici)
- Affaticabilità e disturbi del sonno (beta-bloccanti)
- **Ipotensione ortostatica** (vasodilatatori, diuretici, beta-bloccanti)

Intermediate Risk
Trazodone
Ca-antagonisti non DHP
BDZ
Antipsicotici

Low Risk
Ace-I/Sartani
α-litici uroselettivi
Ca-antagonisti DHP

High Risk
Diuretici
α-litici
ß-bloccanti
Nitrati
Antidepressivi triciclici

Adapted from Rivasi G et al, Minerva Medica 2022

Conclusioni

QUANDO?

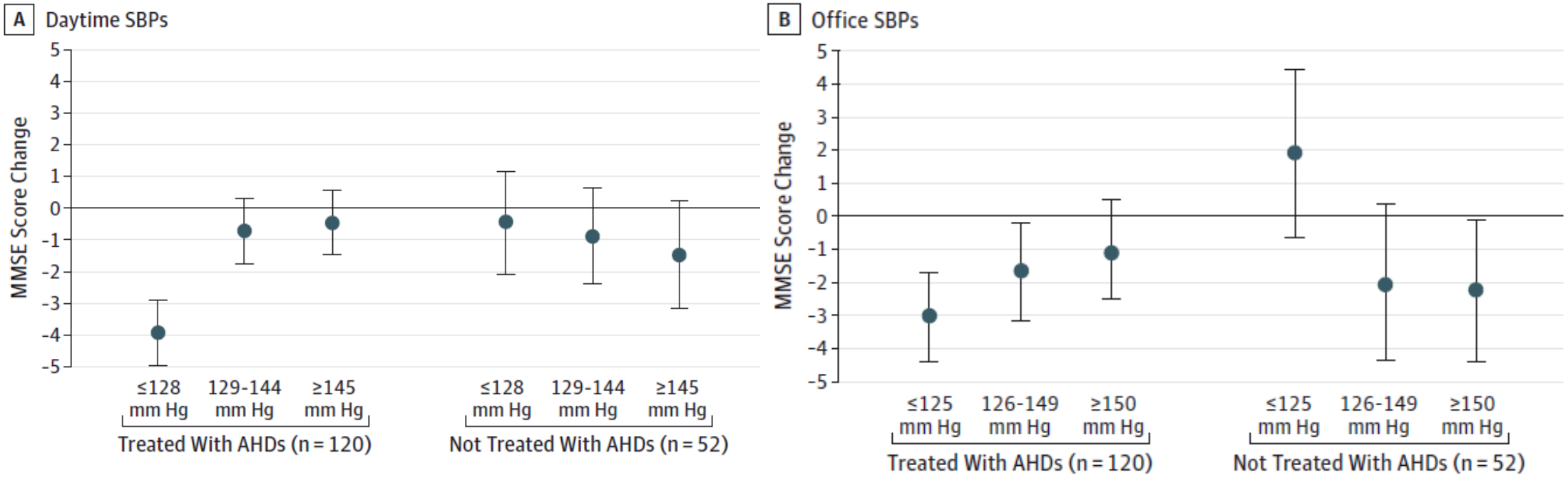
- Soglia e target **personalizzati in base al livello di autonomia e di fragilità** (approccio geriatrico)
- Considerare modalità di **misurazione out-of-office (white-coat effect)**
- Valutare eventuale presenza di ipotensione ortostatica

COME?

- Valutare monoterapia e titolazione **graduale**
- **Farmaci a più basso rischio ipotensivo**
- **Stretto monitoraggio** dei valori pressori e del livello di fragilità

Effects of low blood pressure in cognitively impaired elderly patients treated with antihypertensive drugs

N=172 patients with mild/moderate CI/dementia, mean age of 79, mean MMSE score of 22.1



Mossello E et al. JAMA Int Med 2015