Conoscere e Curare il Cuore 2018

VENERDI' 16 MARZO

IPERTENSIONE NELL'ANZIANO. QUALI SONO I LIMITI PRESSORI?

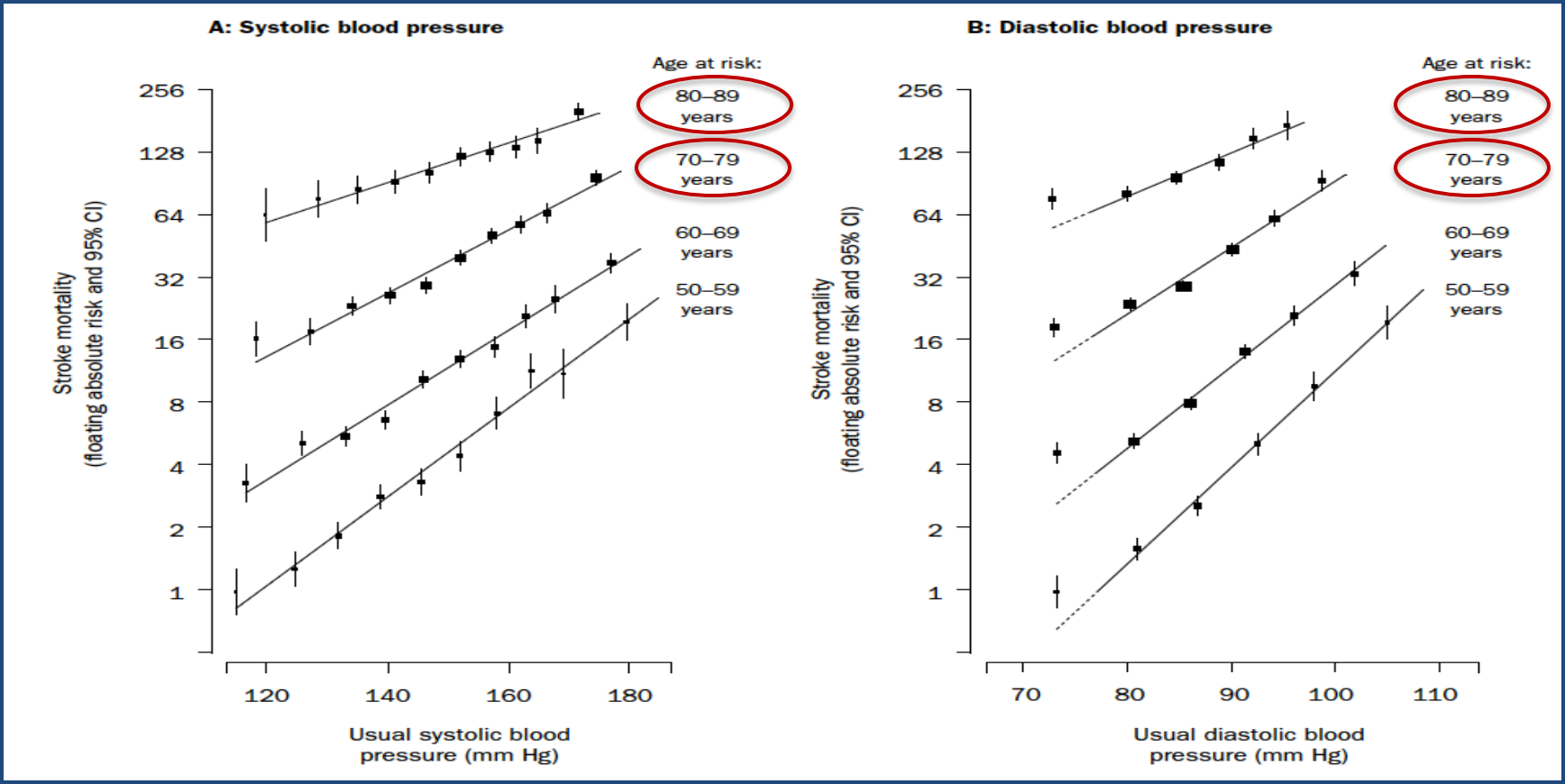
Massimo Volpe

Cattedra ed Unità Complessa di Cardiologia
Dipartimento di Medicina Clinica e Molecolare
Università degli Studi "La Sapienza" di Roma
A. O. Sant'Andrea, Roma

HYPERTENSION MANAGEMENT IN THE ELDERLY

Cattedra di Cardiologia, Dipartimento di Medicina Clinica e Molecolare, Facoltà di Medicina, Università di Roma "Sapienza", Azienda Ospedaliera Sant 'Andrea, Roma, Italia.
E-mail:massim.volpe@uniroma1.it

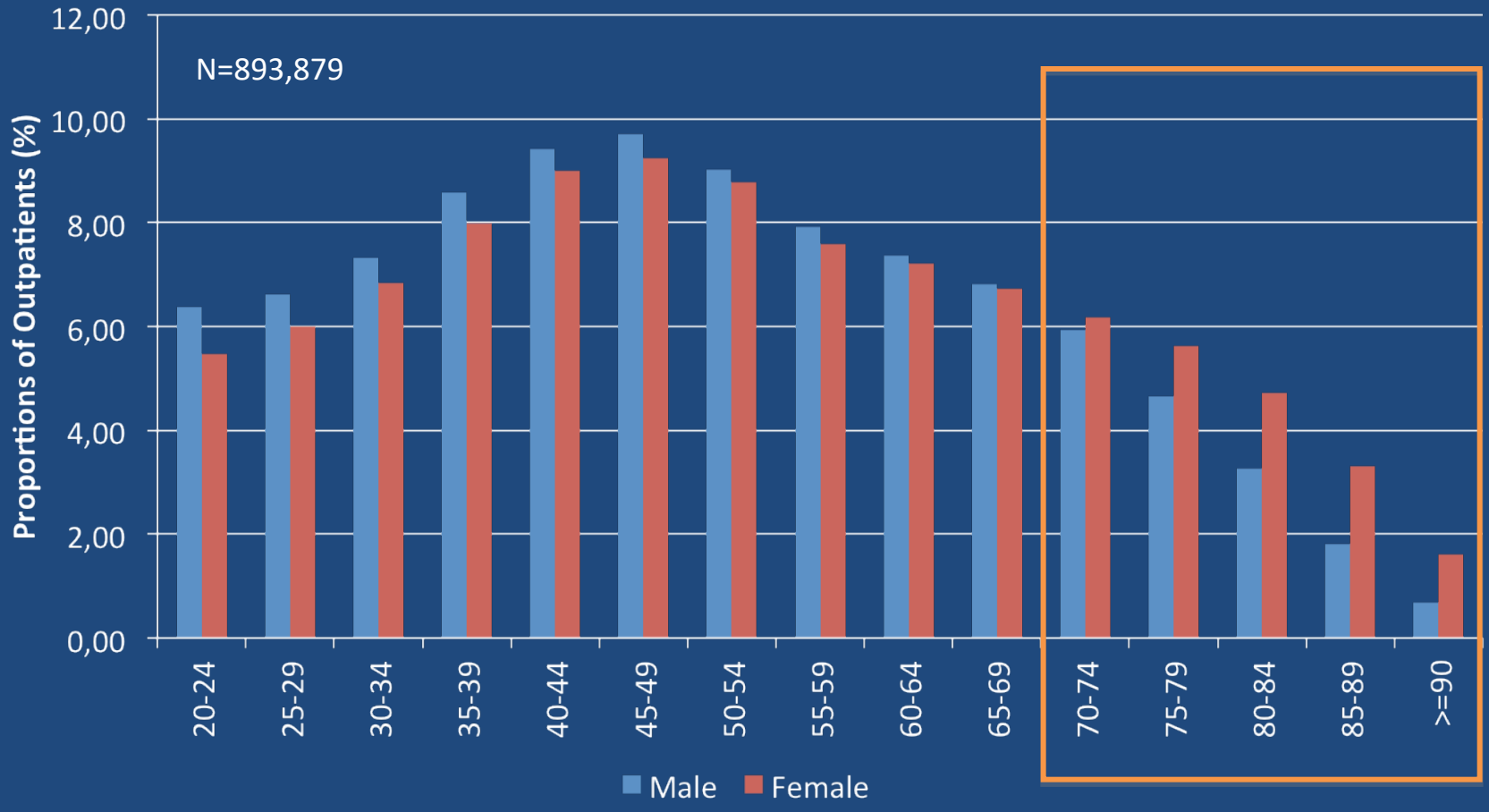
Stroke mortality rate in each decade of age versus usual BP at the start of that decade



Rates are plotted on a floating absolute scale, and each square has area inversely proportional to the effective variance of the log mortality rate. For diastolic BP, each age-specific regression line ignores the left-hand point (ie, at slightly less than 75 mm Hg), for which the risk lies significantly above the fitted regression line (as indicated by the broken line below 75 mmHg).

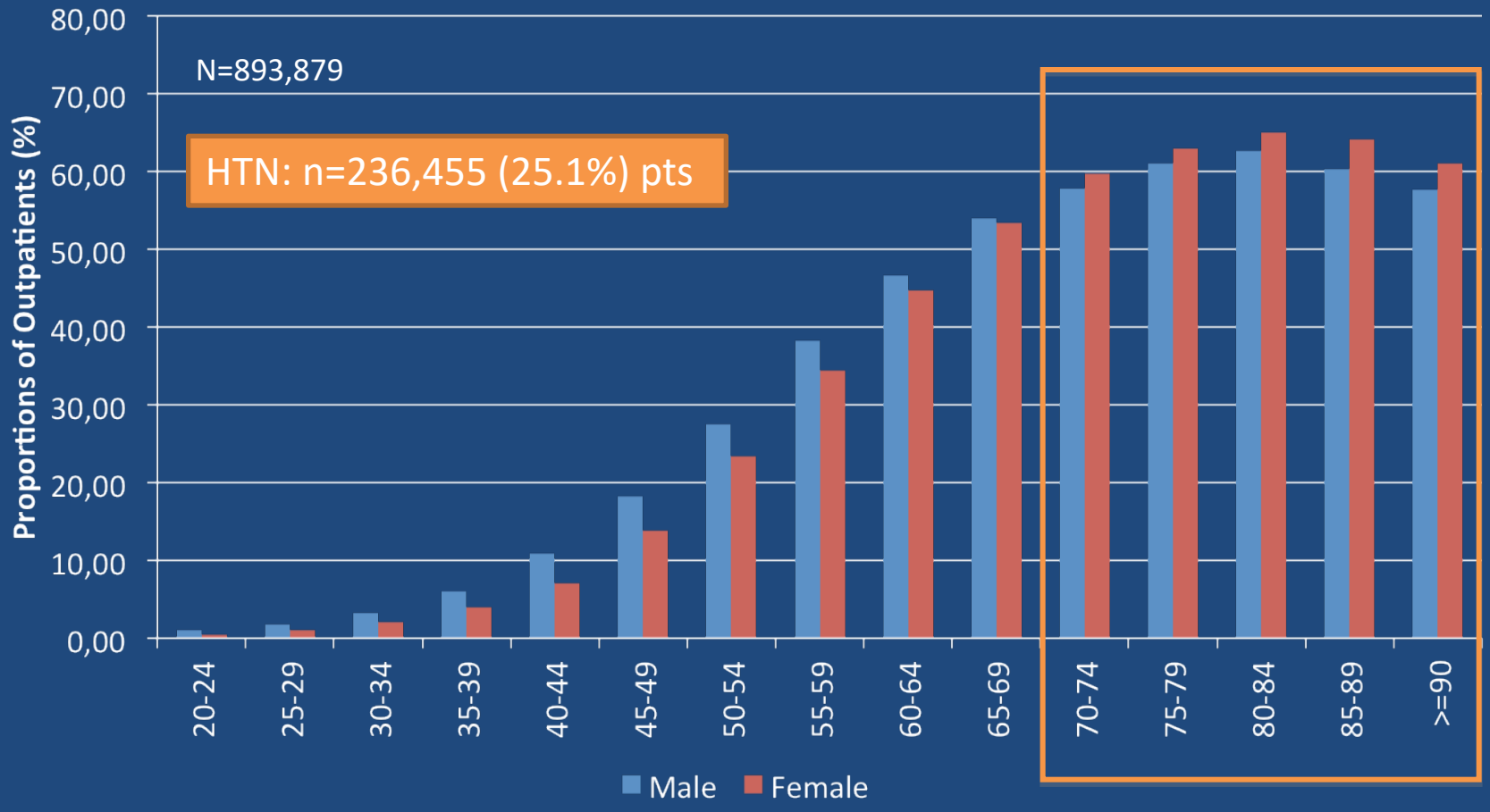
Perspective Studies Collaboration. Lancet 2002;360:1903–13

Analysis from large database of GPs (year 2013): Gender Distribution



Tocci G, Borghi C, Volpe M, et al. J Human Hypertension 2016; first revision

Analysis from large database of GPs (year 2013): Prevalence of Hypertension according to Gender Groups



Tocci G, Borghi C, Volpe M, et al. J Human Hypertension 2016; first revision

The challenge of lowering BP in elderly: Prospective data from mega-trials

	N. pazienti	Età (anni)	Pressione arteriosa (mmHg)	Trattamento farmacologico	
				Step I	Step II
SHEP[4]	4736	71.6	170/77	Clortalidone	Atenololo
Syst-Eur[5]	4695	70.2	174/85	Nitrendipina	Enalapril
Syst-China[6]	2394	66.5	171/86	Nitrendipina	Captopril
EWPHE[7]	840	72.0	182/101	Idroclorotiazide + triamterene	Alfa-metildopa
STOP-Hypertension[8]	1627	76.0	195/102	iuretico o betabloccante	Diuretico o betabloccante
Coope e Warrender[9]	884	68.7	196/99	Atenololo	Diuretico
MRC[10]	4396	70.0	185/91	tico o betabloccante	Diuretico o betabloccante
STONE[11]	1632	66.0	168/100	Nifedipina	Captopril

	Pressione arteriosa (mmHg)			Ictus (%)	Eventi (%)		Mortalità (%)	
	Gruppo placebo	Gruppo trattato con farmaci attivi	Δ		Coronarici	Cardiovascolari	Cardiovascolare	Totale
SHEP[4]	155/71	144/68	-11/-3		-27	-32*	-20	-13
Syst-Eur[5]	161/83	151/78	-10/-5		-26*	-31*	-27	-14
Syst-China[6]	159/84	151/81	-9/-3	-38*	-37	-37*	-39*	-39*
EWPHE[7]	167/90	148/85	-19/-5	-32	-47*	-38*	-27*	-9
STOP-Hypertension[8]	186/96	167/87	-19/-8	-47*	-13	-40*	ND	-43
Coope e Warrender[9]	180/89	162/78	-18/-11	-42*	+3	ND	-22	-3
MRC[10]	168/85	152/76	-16/-9	-25*	-19	-17*	-9	-3
STONE[11]	156/90	146/87	-9/-5	-57*	-6	-60*	-26	-45*

Leonetti G, et al.G Ital Cardiol 2001;11:1161-1169

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 1, 2008 VOL. 358 NO. 18

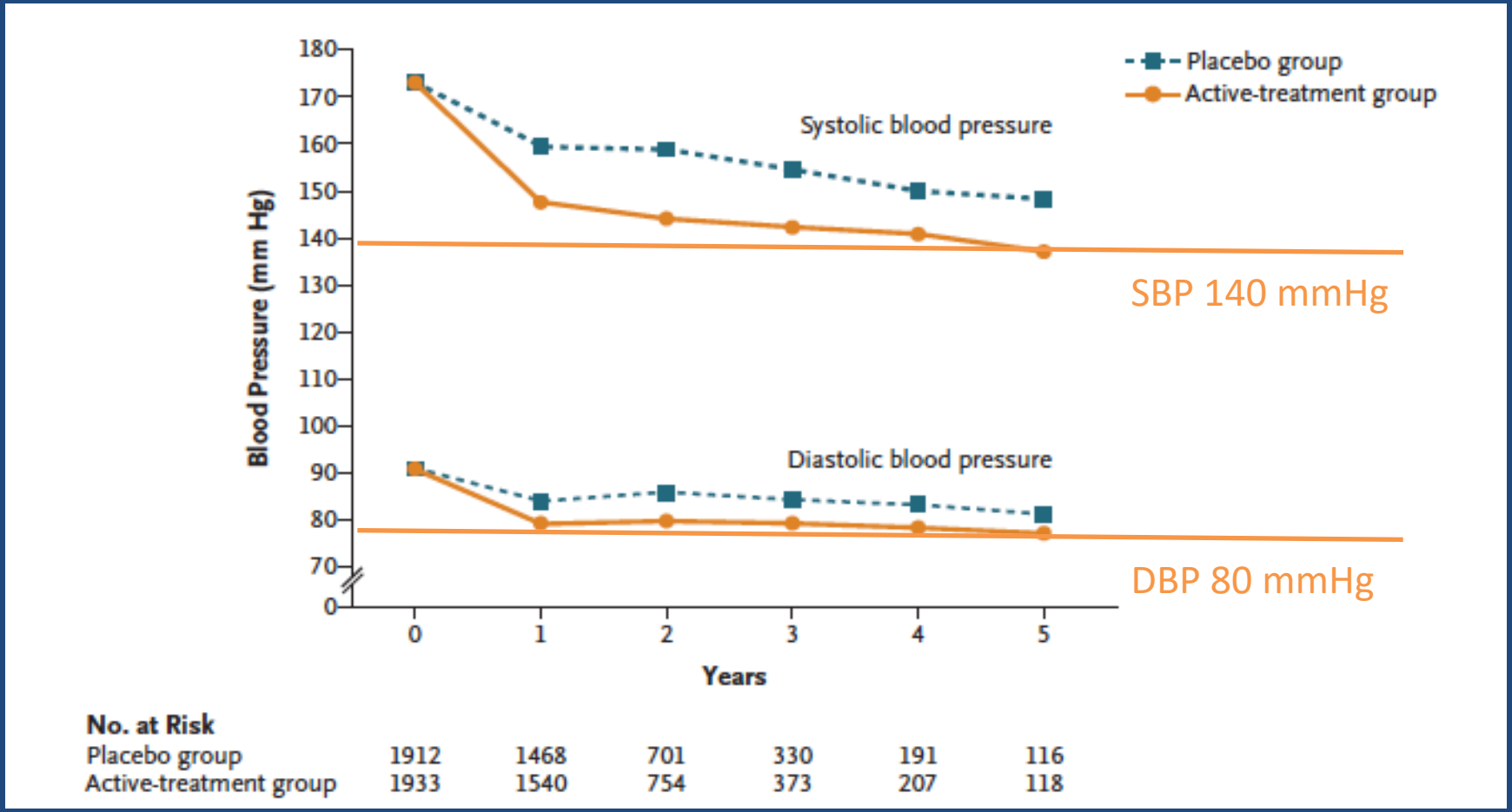
Treatment of Hypertension in Patients 80 Years of Age or Older

Nigel S. Beckett, M.B., Ch.B., Ruth Peters, Ph.D., Astrid E. Fletcher, Ph.D., Jan A. Staessen, M.D., Ph.D., Lisheng Liu, M.D., Dan Dumitrascu, M.D., Vassil Stoyanovsky, M.D., Riitta L. Antikainen, M.D., Ph.D., Yuri Nikitin, M.D., Craig Anderson, M.D., Ph.D., Alli Belhani, M.D., Françoise Forette, M.D., Chakravarthi Rajkumar, M.D., Ph.D., Lutgarde Thijs, M.Sc., Winston Banya, M.Sc., and Christopher J. Bulpitt, M.D., for the HYVET Study Group*

After randomization, patients received either indapamide (sustained release, 1.5 mg) or matching placebo alone. At each visit (or at the discretion of the investigator), if needed to reach the target BP, perindopril (2 mg or 4 mg) or matching placebo could be added.

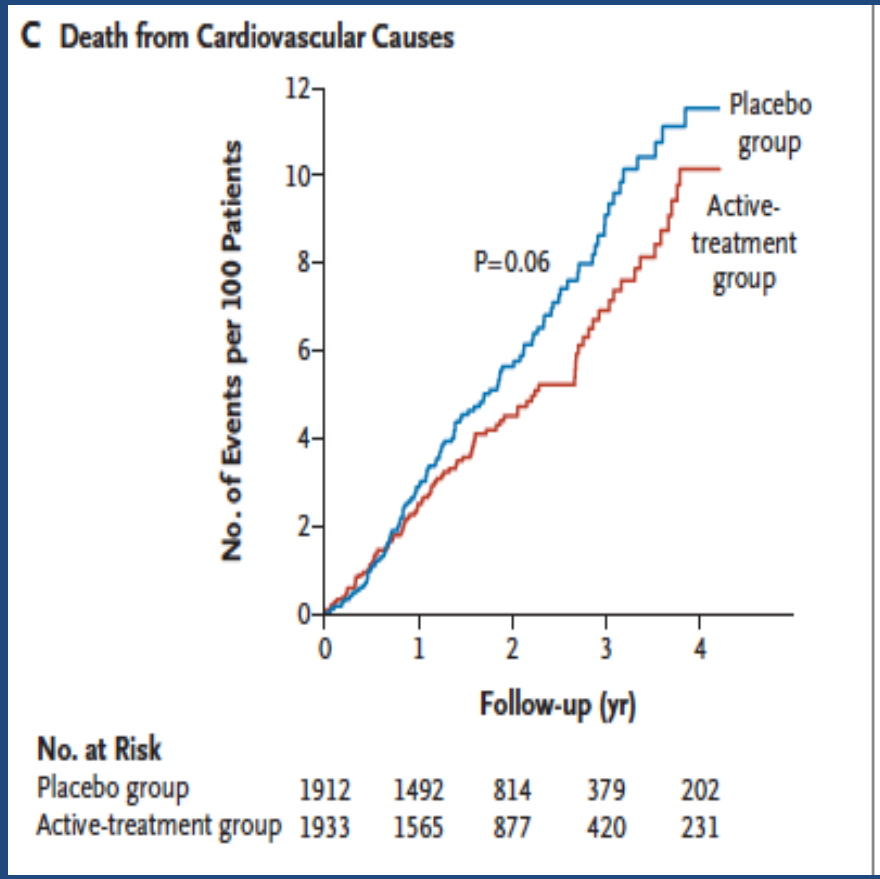
Beckett NS, et al. N Engl J Med 2008;358:1887-98

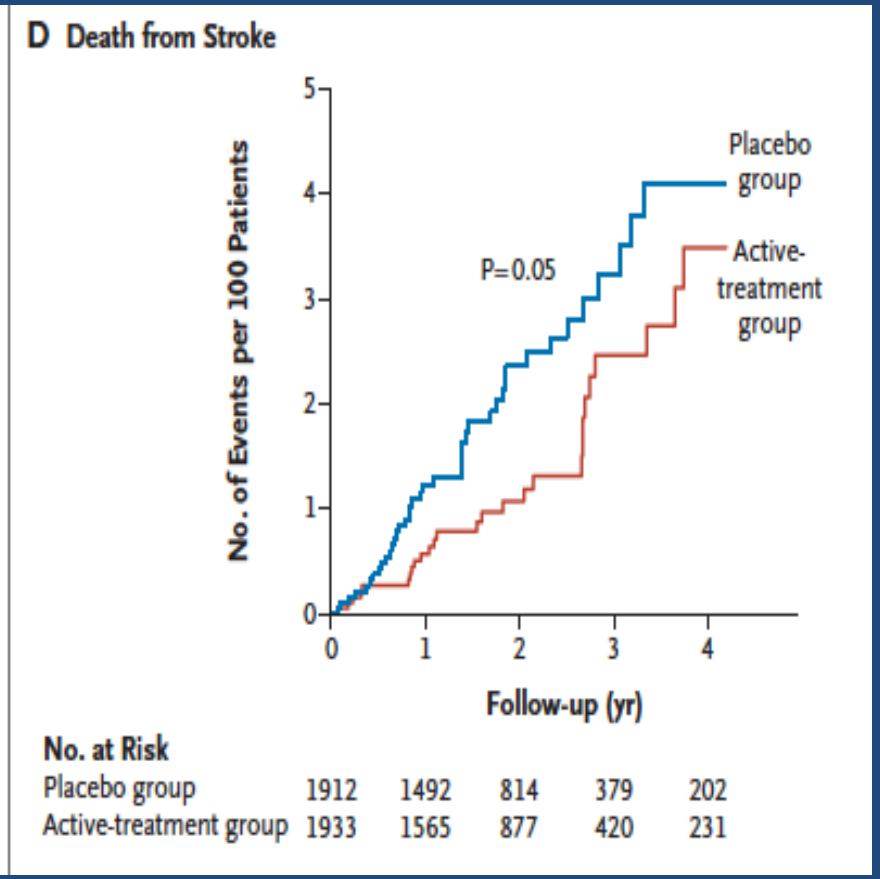
Mean Blood Pressure, Measured while Patients Were Seated, in the Intention-to-Treat Population, According to Study Group



Beckett NS, et al. N Engl J Med 2008;358:1887-98

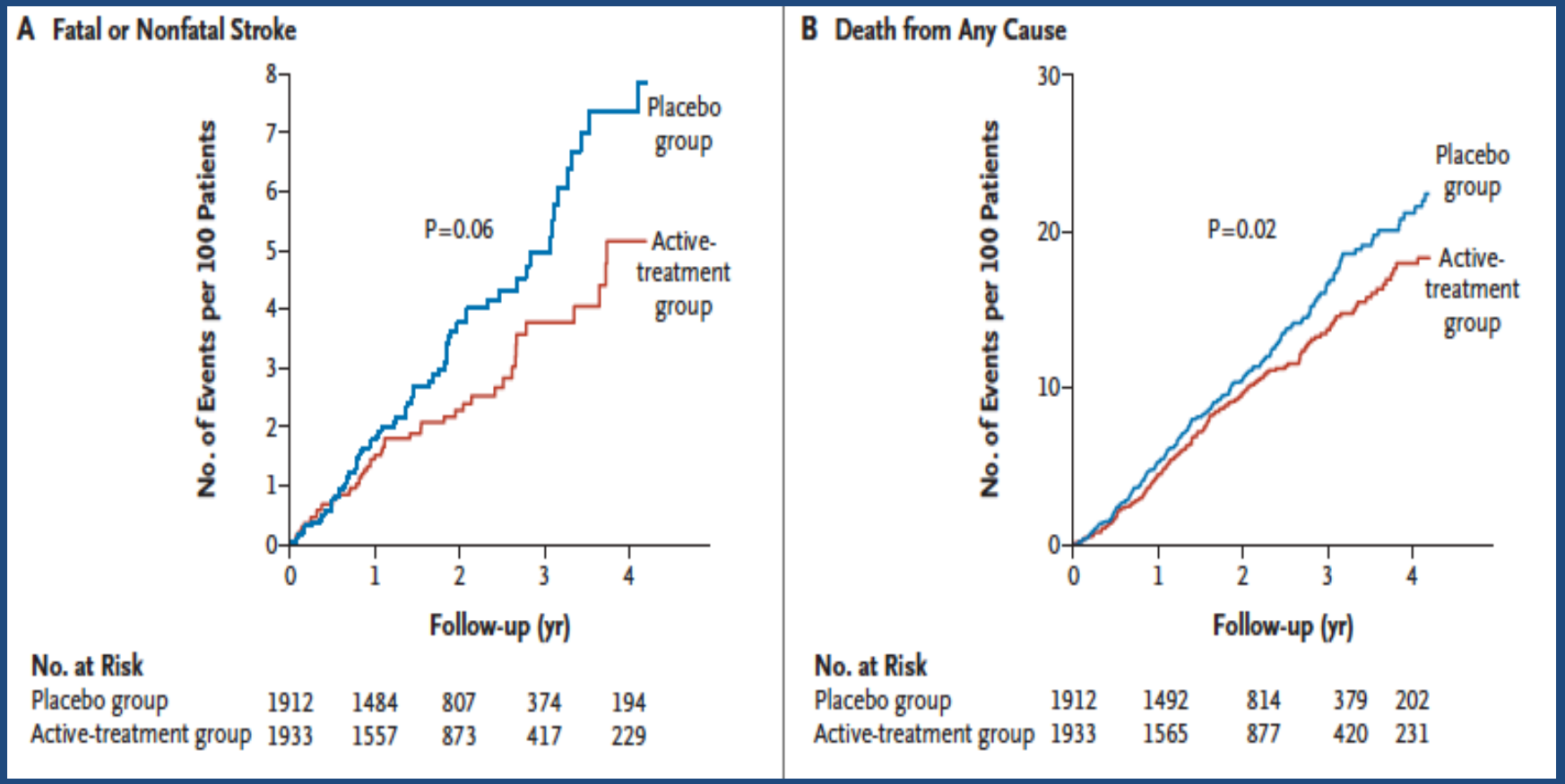
Kaplan-Meier Curves for the Incidence of Secondary Endpoints (1/2)





Beckett NS, et al. N Engl J Med 2008;358:1887-98

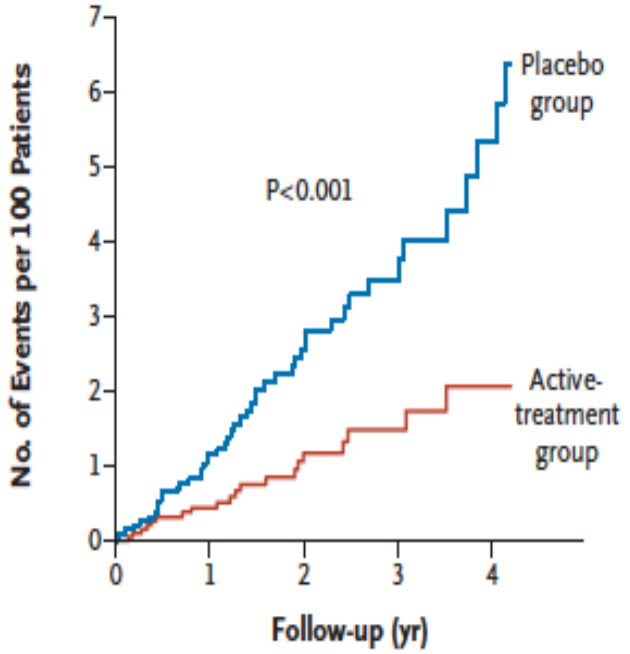
Kaplan-Meier Curves for the Incidence of Primary Endpoints (2/2)



Beckett NS, et al. N Engl J Med 2008;358:1887-98

Kaplan-Meier Curves for the Incidence of Secondary Endpoints (2/2)

E Heart Failure



No. at Risk

Placebo group	1912	1480	794	367	188
Active-treatment group	1933	1559	872	416	228

Beckett NS, et al. N Engl J Med 2008;358:1887-98

BP goals in hypertensive patients

Recommendations	Class	Level
A SBP goal <140 mmHg:		
a) is recommended in patients at low–moderate CV risk;	I	B
b) is recommended in patients with diabetes;	I	A
c) should be considered in patients with previous stroke or TIA;	IIa	B
d) should be considered in patients with CHD;	IIa	B
e) should be considered in patients with diabetic or non-diabetic CKD.	IIa	B
In elderly hypertensives less than 80 years old with SBP ≥160 mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A
In fit elderly patients less than 80 years old SBP values <140 mmHg may be considered, whereas in the fragile elderly population SBP goals should be adapted to individual tolerability.	IIb	C
In individuals older than 80 years and with initial SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg provided they are in good physical and mental conditions.	I	B
A DBP target of <90 mmHg is always recommended, except in patients with diabetes, in whom values <85 mmHg are recommended. It should nevertheless be considered that DBP values between 80 and 85 mmHg are safe and well tolerated.	I	A

Mancia G, et al. Eur Heart J 2013 Jul;34(28):2159-219

Drugs to be preferred in specific conditions

Condition	Drug
Asymptomatic organ damage	
• LVH	ACE inhibitor, calcium antagonist, ARB
• Asymptomatic atherosclerosis	Calcium antagonist, ACE inhibitor
• Microalbuminuria	ACE inhibitor, ARB
• Renal dysfunction	ACE inhibitor, ARB
Clinical CV event	
• Previous stroke	Any agent effectively lowering BP
• Previous myocardial infarction	BB, ACE inhibitor, ARB
• Angina pectoris	BB, calcium antagonist
• Heart failure	Diuretic, BB, ACE inhibitor, ARB, mineralocorticoid receptor antagonists
• Aortic aneurysm	BB
• Atrial fibrillation, prevention	Consider ARB, ACE inhibitor, BB or mineralocorticoid receptor antagonist
• Atrial fibrillation, ventricular rate control	BB, non-dihydropyridine calcium antagonist
• ESRD/proteinuria	ACE inhibitor, ARB
• Peripheral artery disease	ACE inhibitor, calcium antagonist
Other conditions	
• **ISH (elderly)**	**Diuretic, calcium antagonist**
• Metabolic syndrome	ACE inhibitor, ARB, calcium antagonist
• Diabetes mellitus	ACE inhibitor, ARB
• Pregnancy	Methyldopa, BB, calcium antagonist
• Blacks	Diuretic, calcium antagonist

Mancia G, et al. Eur Heart J 2013 Jul;34(28):2159-219

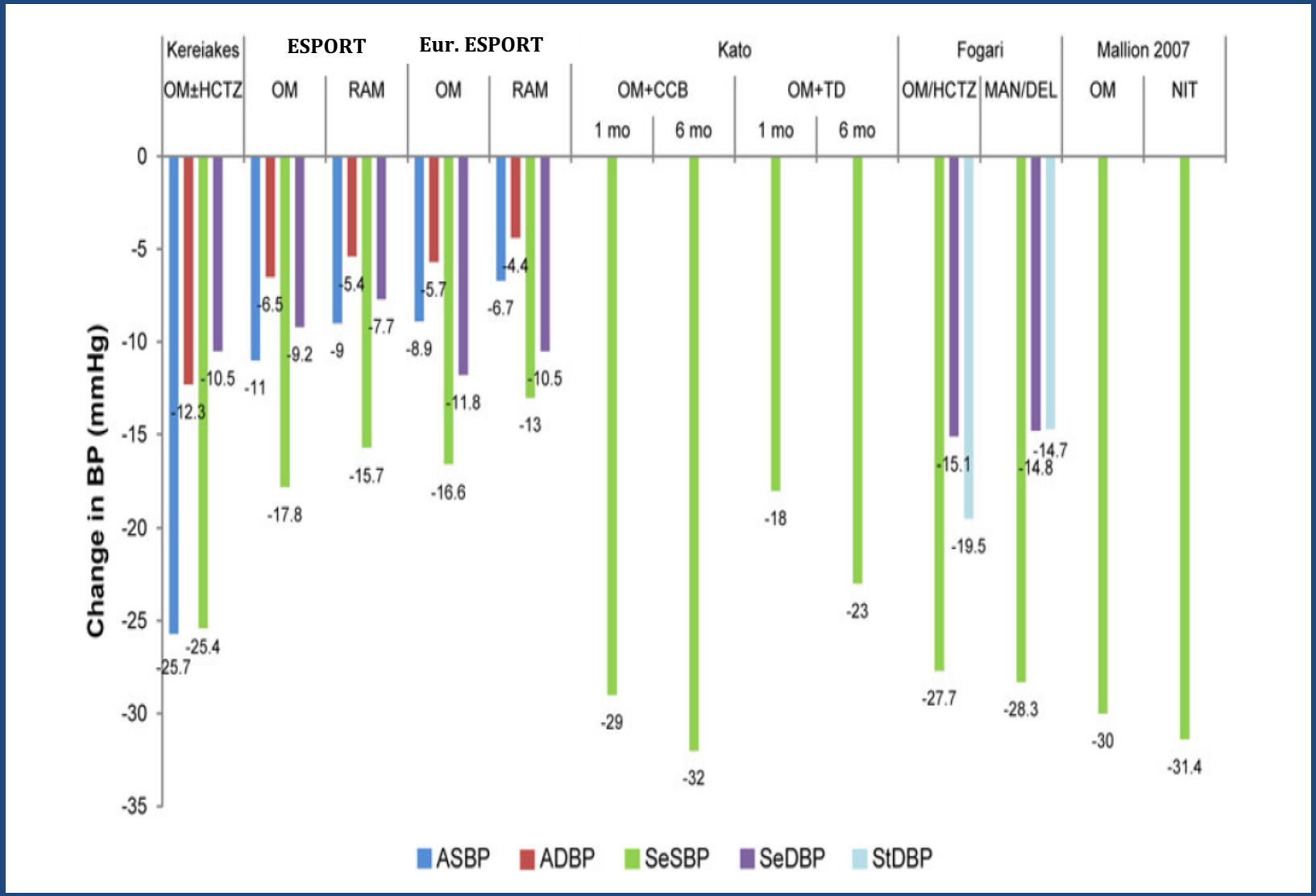
Antihypertensive efficacy and safety of olmesartan medoxomil and ramipril in elderly patients with mild to moderate essential hypertension: the ESPORT study

Ettore Malacco[a], Stefano Omboni[b], Massimo Volpe[c], Alberto Auteri[d] and Alberto Zanchetti[e], on behalf of the ESPORT Study Group

- After a 2-week placebo wash-out 1453 elderly hypertensive patients (65–89 years; sitting office DBP 90–109 mmHg and/or sitting office SBP 140–179 mmHg) were randomized to a 12-week double-blind treatment with olmesartan medoxomil 10 mg or ramipril 2.5 mg once-daily, up-titrated (20 and 40 mg olmesartan medoxomil; 5 and 10mg ramipril) after 2 and 6 weeks in patients without normalized office BP.
- To assess the antihypertensive efficacy of olmesartan medoxomil and ramipril on 24-h ambulatory blood pressure (ABP) in elderly hypertensive patients by pooled data analysis of two studies with identical designs.

Malacco E, Volpe M, et al. J Hypertens 2010;28:2342–2350

Clinical trials with ARB based therapy in hypertension in the elderly



Volpe M, Tocci G. Drugs Aging. 2013;30(12):987-98

Safety reports

Reference	Design (duration)	Treatments	Patients (*n*)	Age range (years [mean ± SD])	DR-TEAEs (% of patients)	Most common DR-TEAEs and other tolerability results
Kereiakes et al. [24]	R, O, MC, BEP (12 weeks)	OM 20/40 mg/day ± HCTZ 12.5/25 mg/day	176; newly diagnosed/uncontrolled HT (SeSBP/SeDBP ≥140/90 mmHg)	65–86 [71.9 ± 5.2]	11.8 %	Dizziness (3.4 %), hypotension (2.2 %), headache (1.1 %)
Malacco et al. [19]	R, DB, PG (12 weeks)	OM 10 mg/day vs RAM 2.5 mg/day	1,102; treated or untreated HT (AMBP *n* = 630)	65–89 [72 ± 5]	3.6 % OM, 3.6 % RAM	Cough (RAM 13 vs OM 2 episodes), dizziness or vertigo, asthenia, hypertensive crisis or hypotension
Mallion et al. [39]	R, DB, MC, PG (12 weeks)	OM 10 mg/day, RAM 2.5 mg/day	351; HT (SeSBP/SeDBP 140–179/90–109 mmHg) (AMBP *n* = 85)	65–89 [OM 72 ± 5; RAM 71 ± 5]	4.0 % OM, 4.5 % RAM	Cough (only with RAM), dizziness, headache and GI side-effects (diarrhoea, nausea, stomach pain)
Kato et al. [37]	R, O, MC (6 months)	OM + D-CCB (AZL, AML or BEN) vs OM + TD (TCM or IND) (mean OM doses: 22.1 mg/day with CCB and 21.2 mg/day with TD)	58; HT >140/90 mmHg on treatment or >160/100 mmHg if treatment naive	65–85 [+CCB 72.6 ± 6.1; +TD 73.3 ± 5.9]	NR	Cr and eGFR unchanged with OM + CCB but Cr elevated and eGFR and HDL-C reduced with OM + TD (all $p < 0.05$)
Fogari et al. [36]	R, O, BEP (48 weeks)	OM 20 mg/day/HCTZ 12.5 mg/day vs MAN 10 mg/day/DEL 30 mg/day	158; essential HT (SeSBP/SeDBP 130–179/80–99 mmHg) with T2DM	66–74 [MAN/DEL 69.5 ± 3.2; OM/HCTZ 70.2 ± 3.5]	NR	No changes in metabolic parameters with MAN/DEL; increased HbA_{1c} (+0.7 %, $p < 0.05$), uric acid (+0.4 mg/dL, $p < 0.05$) and TG (+41.3 mg/dL, $p < 0.05$) and decreased serum K+ (−0.3 mmol/L, $p < 0.05$) and HDL-C (−3.4 mg/dL, $p < 0.05$) with OM/HCTZ
Mallion et al. [38]	R, DB, stepped (24 weeks)	OM 20/40 mg/day vs NIT 10/20 mg bid (both + HCTZ as required 12.5/25 mg/day)	382; ISH	65–94, split into 65–74 and ≥75 groups [OM 74.0 ± 6.1; NIT 73.5 ± 5.8]	Any AE: OM 38.7 %; NIT 45.2 %	Headache, peripheral oedema, dizziness, nasopharyngitis and vertigo

Volpe M, Tocci G. Drugs Aging. 2013;30(12):987-98

Antihypertensive strategies with ARB-based therapy combined with either HCTZ or CCB (or both) according to Individual Global CV Risk Stratification (1/2)

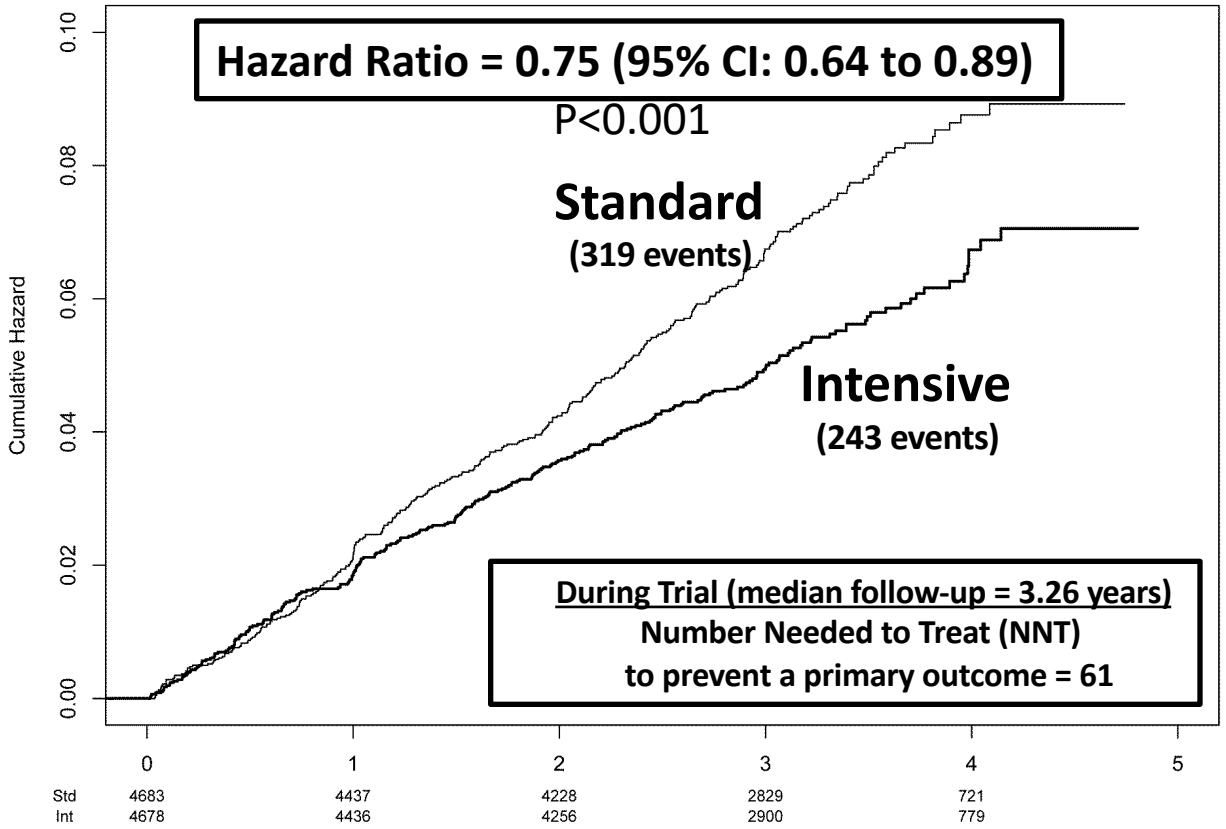
Clinical conditions	Grade 1 HT (SBP 140–159 mmHg or DBP 90–99 mmHg)	Grade 2 HT (SBP 160–179 mmHg or DBP 100–109 mmHg)	Grade 3 HT (SBP ≥180 mmHg or DBP ≥110 mmHg)
No risk factors	OLM 10–20 mg If not at target, →	OLM/AML 20/5 mg If not at target, *→	OLM/AML 20–40/10 mg*
		OLM/HCTZ 20/12.5 mg If not at target, *→	OLM/HCTZ 20–40/25 mg*
Dyslipidaemia, obesity, hyperuricemia, metabolic syndrome	OLM 10–20 mg If not at target, →	OLM/AML 20/5 mg If not at target, *→	OLM/AML 20–40/5–10 mg*
Fit elderly, <80 years	OLM 10–20 mg If not at target, →	OLM/HCTZ 20/12.5 mg If not at target, *→	OLM/HCTZ 20–40/25 mg*
Frail elderly, >80 years, SBP ≥160 mmHg	OLM 10–20 mg If not at target, →	OLM/HCTZ 10–20/12.5 mg If not at target, *→	OLM/HCTZ 20–40/25 mg*
Atherosclerosis, arteriosclerosis, PAD	OLM 10–20 mg If not at target, →	OLM/AML 20–40/5 mg If not at target, →	OLM/AML 20–40/10 mg
LV hypertrophy	OLM 20–40 mg If not at target, →	OLM/HCTZ 20–40/12.5 mg If not at target, *→	OLM/HCTZ 20–40/25 mg*
MAU or proteinuria (CKD ≤3 stage)	OLM 20–40 mg If not at target, →	OLM/AML 40/5 mg If not at target, →	OLM/AML 40/10 mg
Diabetes	OLM 20–40 mg If not at target, →	OLM/AML 40/5 mg If not at target, *→	OLM/AML 40/10 mg*

* Consider single-pill triple combination Tx, if BP not at target

Volpe et al. High Blood Press Cardiovasc Prev 2014;21:137–47

SPRINT Primary Outcome

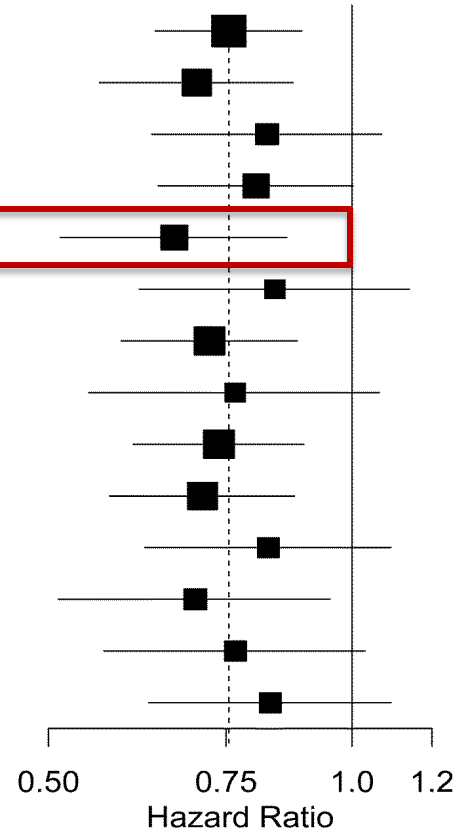
Cumulative Hazard



Primary Outcome in the Pre-specified Subgroups

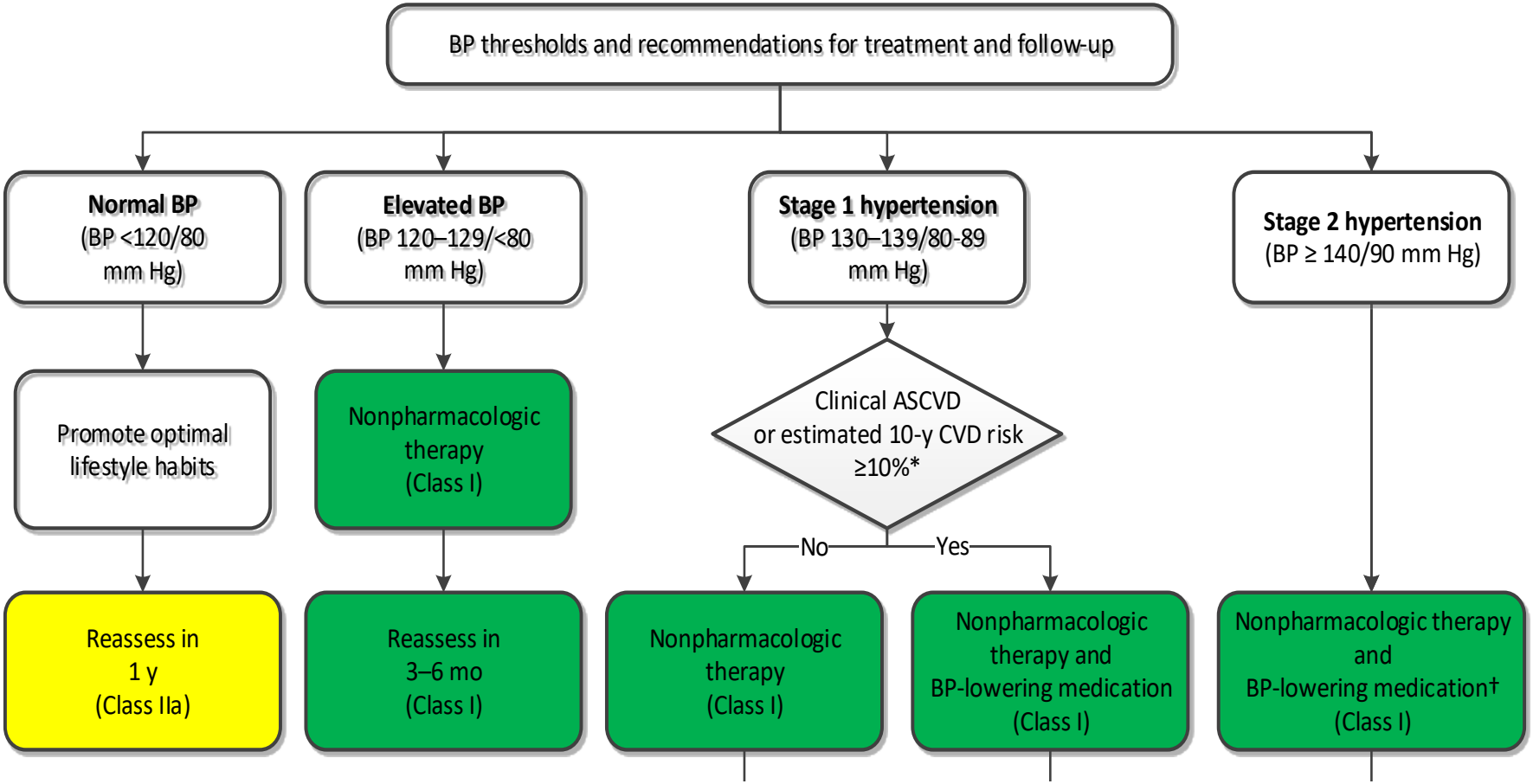
Subgroup	HR	P*
Overall	0.75 (0.64,0.89)	
No Prior CKD	0.70 (0.56,0.87)	0.36
Prior CKD	0.82 (0.63,1.07)	
Age < 75	0.80 (0.64,1.00)	0.32
Age ≥ 75	0.67 (0.51,0.86)	
Female	0.84 (0.62,1.14)	0.45
Male	0.72 (0.59,0.88)	
African−American	0.77 (0.55,1.06)	0.83
Non African−American	0.74 (0.61,0.90)	
No Prior CVD	0.71 (0.57,0.88)	0.39
Prior CVD	0.83 (0.62,1.09)	
SBP ≤ 132	0.70 (0.51,0.95)	0.77
132 < SBP < 145	0.77 (0.57,1.03)	
SBP ≥ 145	0.83 (0.63,1.09)	

*Treatment by subgroup interaction
*Unadjusted for multiplicity



SPRINT
Systolic Blood Pressure Intervention Trial

Blood Pressure (BP) Thresholds and Recommendations for Treatment and Follow-Up (continued on next slide)



AMERICAN COLLEGE of CARDIOLOGY

American Heart Association®

life is why™

Managing Hypertension in Elderly: Take-Home Messages (1/2)

- BP reduction, mostly systolic BP, in elderly hypertensive patients is difficult to achieve and maintain over time.

- BP reductions towards 140/90 mmHg have demonstrated to be beneficial in fit elderly individuals with isolated systolic hypertension and relatively low-moderate CV risk profile.

- BP reduction below 140/90 mmHg are not supported by scientific evidence, thus they might be achieved, but they are currently not recommended in elderly hypertensive patients.

Managing Hypertension in Elderly: Take-Home Messages (2/2)

- Although 2013 European guidelines still recommended an antihypertensive strategy based on diuretics and calcium-channel blockers, modern pharmacological approach should always include RAS blocking agents (i.e. ACE inhibitors or ARBs) at medium dose.

- Patients whose BP was >140/90 mmHg after 6-8 weeks can be uptitrated to the maximum tolerated dose or added to diuretic (HCTZ or indapamide).

- Fixed combination therapies should be always preferred to reduce the pill burden in elderly hypertensive patients.

Practical suggestions for the management of hypertension in the elderly based on the current evidence

Lifestyle intervention and drug treatment should be started when SBP is >160 mmHg in fit older patients, even aged >80 years
Lifestyle intervention and pharmacological therapy should be started in grade 1 (SBP 140-159 mmHg) hypertensive fit elderly, aged between 65 and 80 years, if treatment is well tolerated
In older patients who receive drug treatment, BP should be lowered to <140/80 mmHg, but not below a SBP of 130 mmHg
Antihypertensive treatment may be administered also to frail older patients, if well tolerated
Antihypertensive treatment should not be withdrawn in patients aged ≥80 years, if well tolerated

Volpe M 2018

Thank You for Your attention!

E: massimo.volpe@uniroma1.it