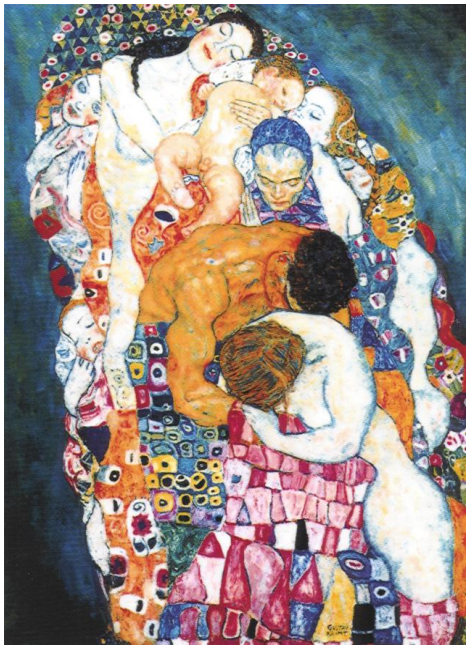
Le linee guida e l'anziano iperteso



Claudio Borghi
Cattedra di Medicina Interna
Dipartimento di Scienze Mediche e Chirurgiche
Università degli Studi di Bologna

"May not the elevation of systemic blood pressure be ***a natural response to guarantee a normal circulation to the heart, brain and kidneys ("essential" hypertension)****.*

Overzealous attempts to lower the pressure may do no good and often do harm. Many cases of ***essential hypertension not only do not need any treatment but are much better off without it****."*

Scott RW. Clinical blood pressure. In: Tice F. Practice of Medicine. Hagerstown, MD: W.F. Prior Co/Harper & Row; 1946: 93–114

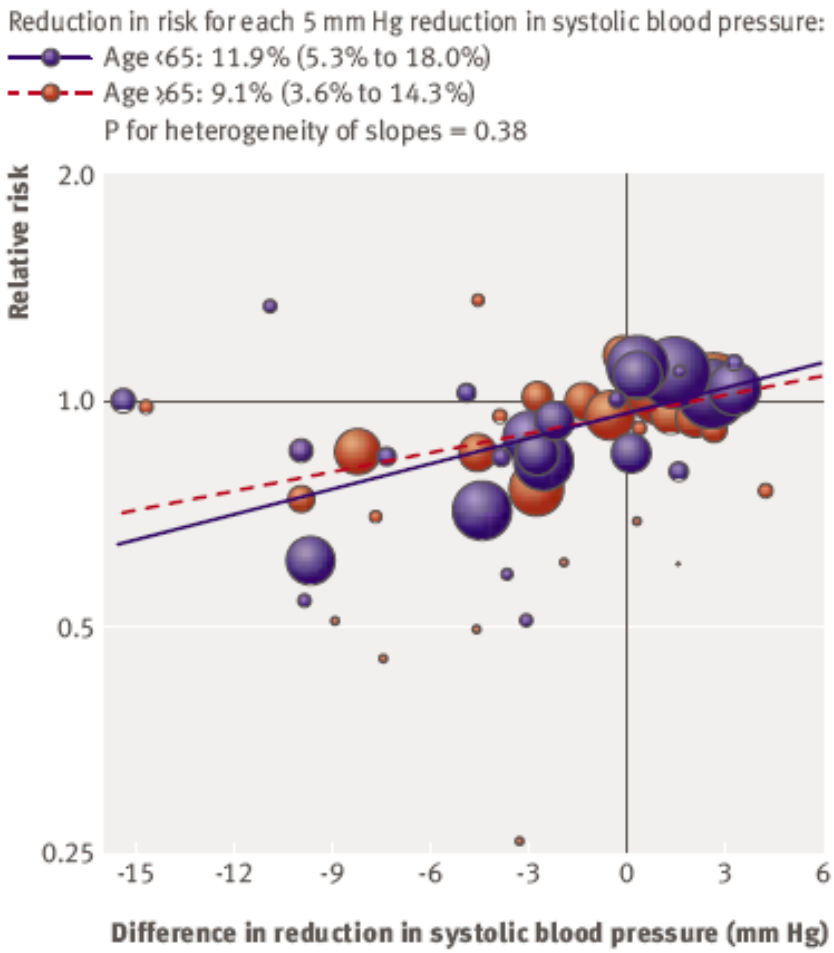
BMJ

RESEARCH

Effects of different regimens to lower blood pressure on major cardiovascular events in older and younger adults: meta-analysis of randomised trials

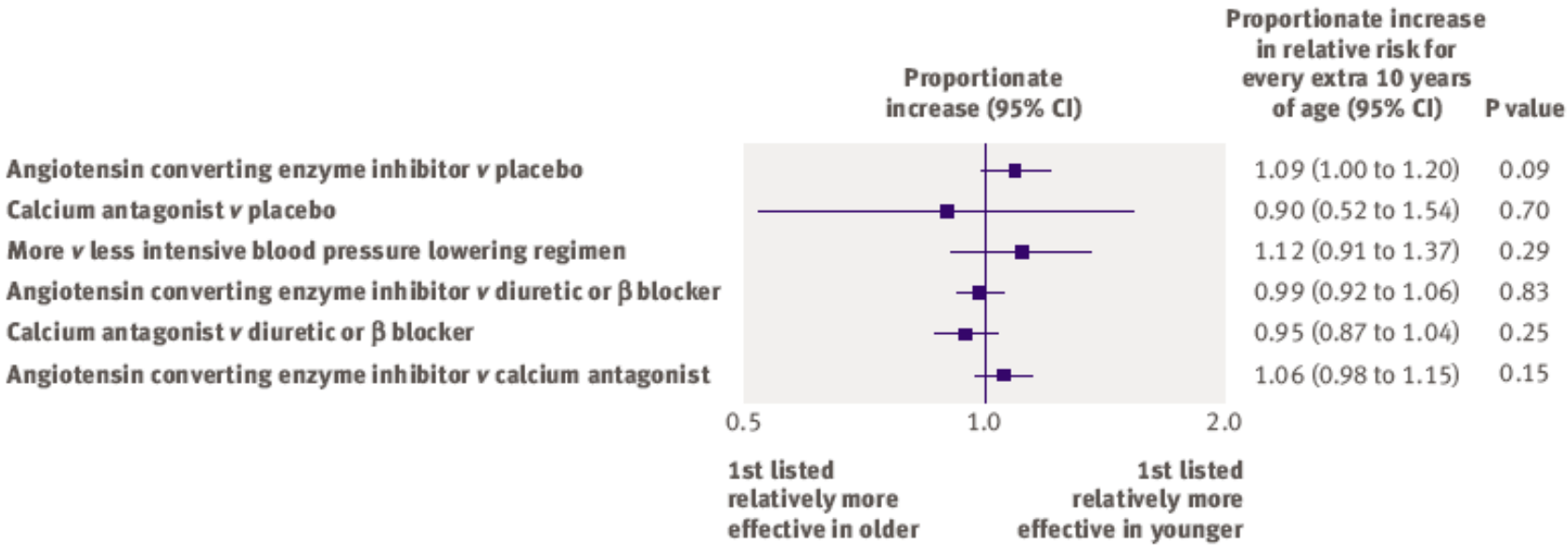
Blood Pressure Lowering Treatment Trialists' Collaboration

Meta-regression analysis of the effects of antihypertensive drugs in different age groups



Blood Pressure Lowering Treatment Trialists' Collaboration BMJ, 2008

Relative risk of major CV events and the the effects of antihypertensive drugs in different age groups



Blood Pressure Lowering Treatment Trialists' Collaboration BMJ, 2008

2007 Guidelines for the Management of Arterial Hypertension

European Society of Hypertension
European Society of Cardiology

Journal of Hypertension 2007;25:1105-1187

Antihypertensive Treatment in the Elderly

- **Randomized trials** in patients with systolic-diastolic or isolated systolic hypertension aged ≥60 years have shown that a **marked reduction in cardiovascular morbidity and mortality** can be achieved with antihypertensive treatment

- **Drug treatment can be initiated** with thiazide diuretics, calcium antagonists, angiotensin receptor antagonists, ACE inhibitors and β-blockers, **in line with general guidelines**.

- Trials specifically addressing treatment of **isolated systolic hypertension** have shown the benefit of **thiazide and calcium antagonists** but subanalysis of other trials also show efficacy of **angiotensin receptor antagonists**

- **Initial doses and subsequent dose titration should be more gradual** because of a greater chance of undesirable effects, especially in very old and frail subjects

Journal of Hypertension 2007;25:1105-1187

Antihypertensive Treatment in the Elderly

- **Drug treatment should be tailored** to the risk factors, target organ damage and associated cardiovascular and non-cardiovascular conditions that are frequent in the elderly.
- Because of the **increased risk of postural hypertension**, BP should always be measured also in the erect posture
- *In subjects **aged 80 years and over**, evidence for benefits of antihypertensive treatment is as yet inconclusive, however, there is no reason for interrupting a successful and well tolerated therapy when a patient reaches 80 years of age (HYVET Study scheduled May, 2008)*
- ***BP goal is the same as in younger patients**, i.e. <140/90 mmHg or below, if tolerated. Many elderly patients need two or more drugs to control blood pressure.*

Journal of Hypertension 2007;25:1105-1187

The NEW ENGLAND JOURNAL of MEDICINE

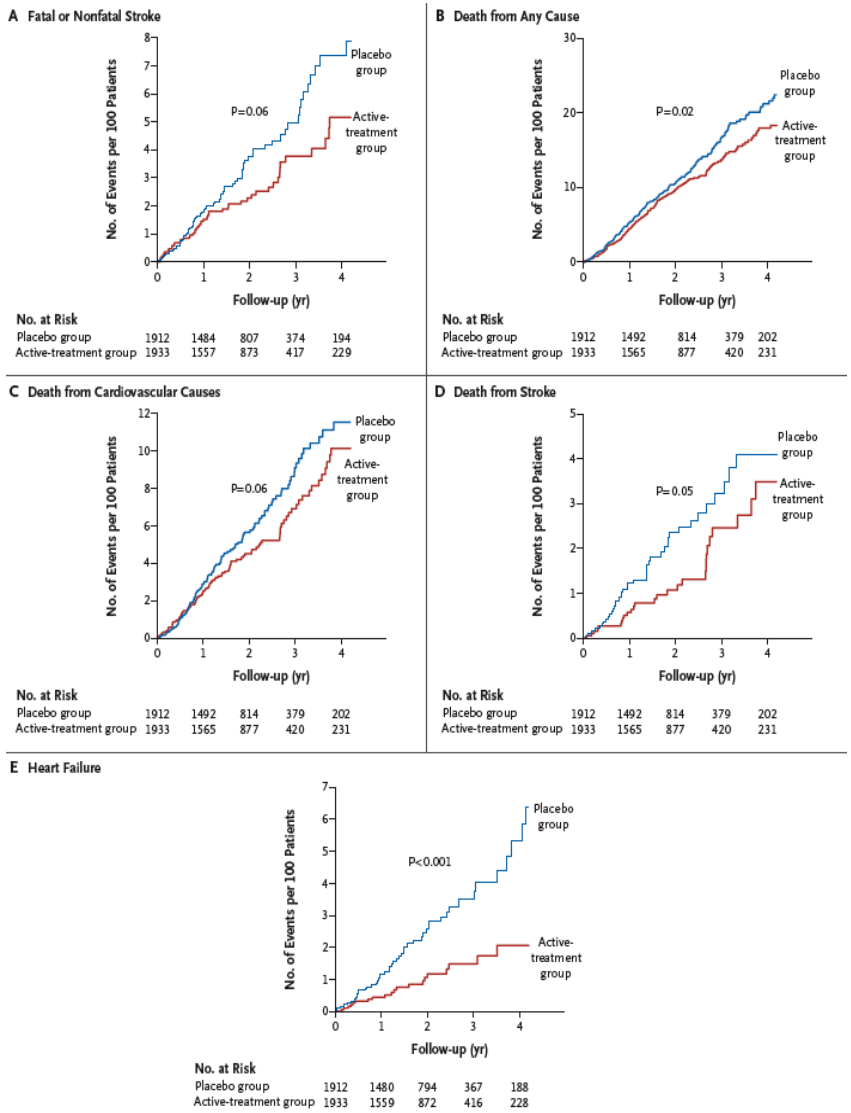
ESTABLISHED IN 1812 MAY 1, 2008 VOL. 358 NO. 18

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*

N Engl J Med 2008;358:1887-98.

Kaplan-Meier estimate of the CV end-points in the HYVET study



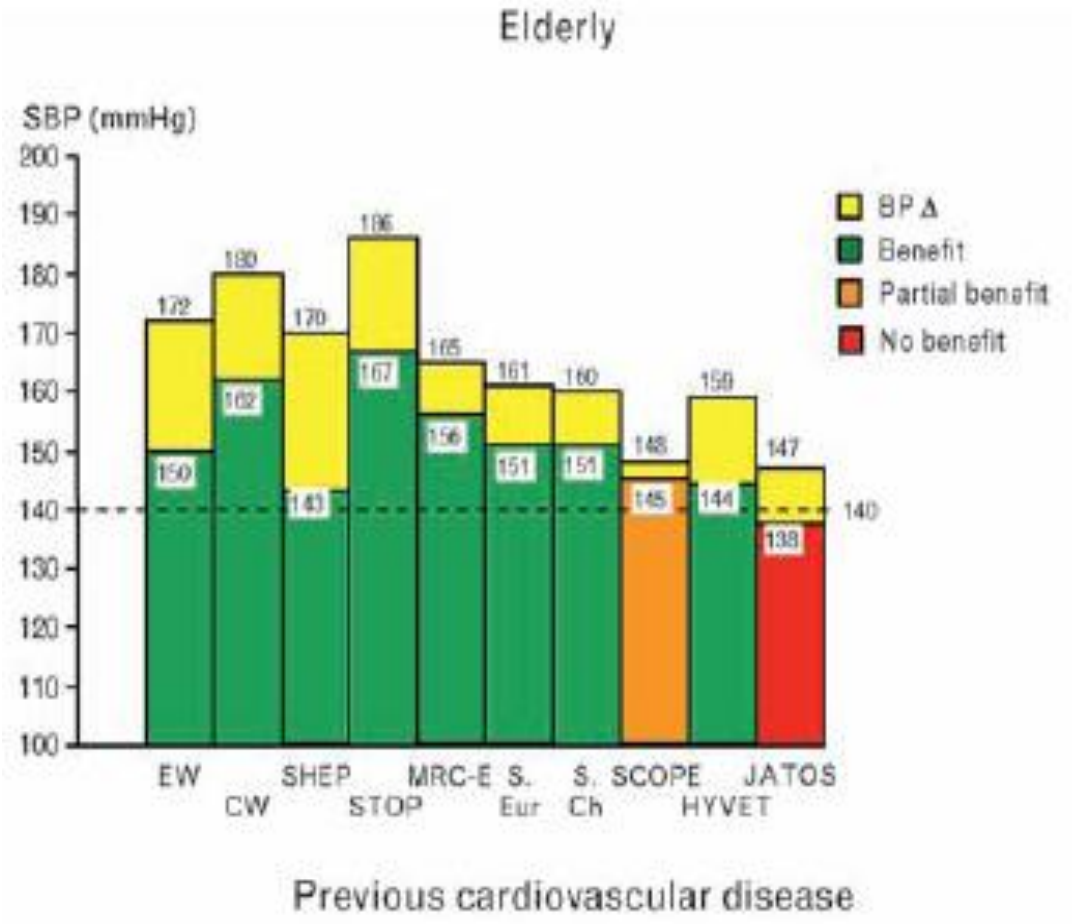
Beckett NS et al, N Engl J Med 2008

Baseline chracteristics of the population in the HYVET study

Characteristic	Active Treatment (N=1933)	Placebo (N=1912)
Age — yr	83.6±3.2	83.5±3.1
Female sex — no. (%)	1174 (60.7)	1152 (60.3)
Blood pressure — mm Hg		
While sitting	173.0±8.4/90.8±8.5	173.0±8.6/90.8±8.5
While standing	168.0±11.0/88.7±9.3	167.9±11.1/88.6±9.3
Orthostatic hypotension — no. (%)†	152 (7.9)	169 (8.8)
Isolated systolic hypertension — no. (%)	625 (32.3)	623 (32.6)
Heart rate — beats/min	74.5±9.1	74.5±9.3
Cardiovascular history		
Cardiovascular disease — no. (%)	223 (11.5)	229 (12.0)
Hypertension — no. (%)	1737 (89.9)	1718 (89.9)
Antihypertensive treatment — no. (%)	1241 (64.2)	1245 (65.1)
Stroke — no. (%)	130 (6.7)	131 (6.9)
Myocardial infarction — no. (%)	59 (3.1)	62 (3.2)
Heart failure — no. (%)	56 (2.9)	55 (2.9)
Cardiovascular risk factors		
Current smoker — no. (%)	123 (6.4)	127 (6.6)
Diabetes — no. (%)‡	132 (6.8)	131 (6.9)
Total cholesterol — mmol/liter	5.3±1.1	5.3±1.1
High-density lipoprotein cholesterol — mmol/liter	1.35±0.38	1.35±0.37
Serum creatinine — μmol/liter	88.6±20.5	89.2±20.5
Uric acid — μmol/liter	280.4±79.3	279.0±81.3
Body-mass index§	24.7±3.8	24.7±3.5

Beckett NS et al, N Engl J Med 2008

Achieved SBP in patients randomized to a more active or less active treatment in clinical trials in hypertension



Mancia G et al, J Hypertens 2009

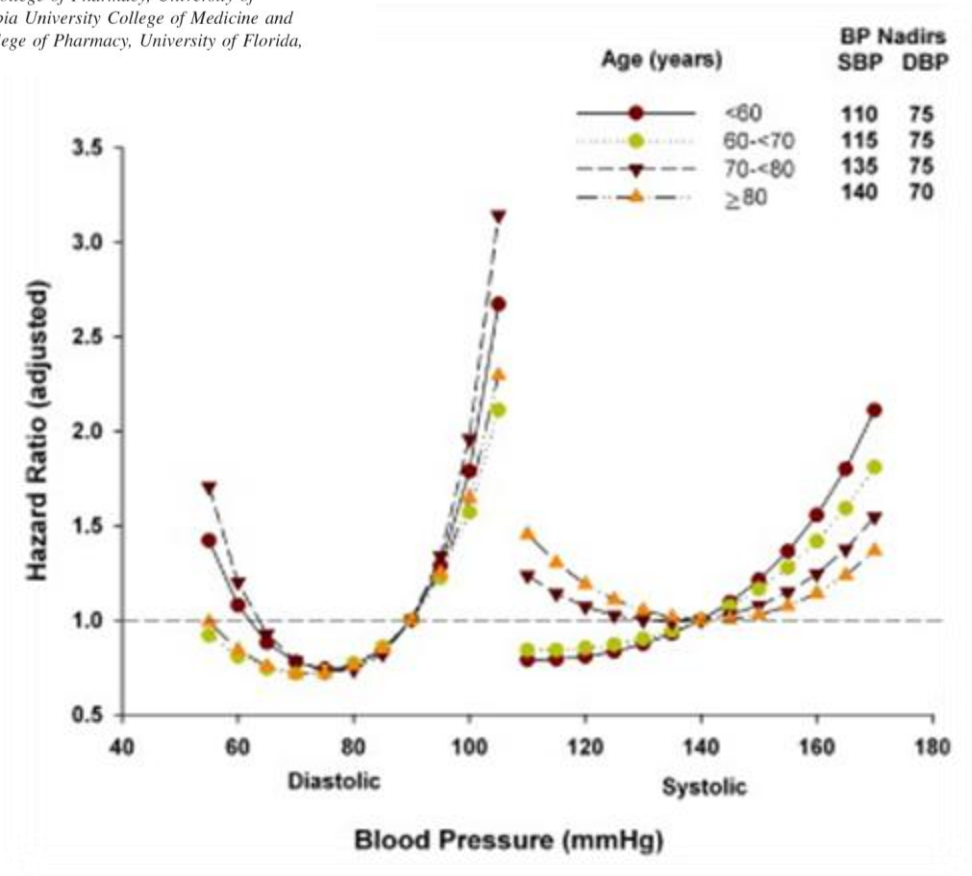
CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

Blood Pressure and Outcomes in Very Old Hypertensive Coronary Artery Disease Patients: An INVEST Substudy

Scott J. Denardo, MD,[a] Yan Gong, PhD,[b] Wilmer W. Nichols, PhD,[a] Franz H. Messerli, MD,[c] Anthony A. Bavry, MD, MPH,[a] Rhonda M. Cooper-DeHoff, PharmD,[a,d] Eileen M. Handberg, PhD,[a] Annette Champion, MBA,[e] Carl J. Pepine, MD[a]

[a]Division of Cardiovascular Medicine, College of Medicine, [b]Center for Pharmacogenomics, College of Pharmacy, University of Florida, Gainesville; [c]Division of Cardiology, St Luke's-Roosevelt Hospital Center and Columbia University College of Medicine and Physicians, New York, NY; [d]Department of Pharmacotherapy and Translational Research, College of Pharmacy, University of Florida, Gainesville; [e]Abbott Laboratory, Abbott Park, Ill.



Denardo S et al, Am J Med 2010

Reappraisal of treatment of hypertension

Blood pressure in the elderly

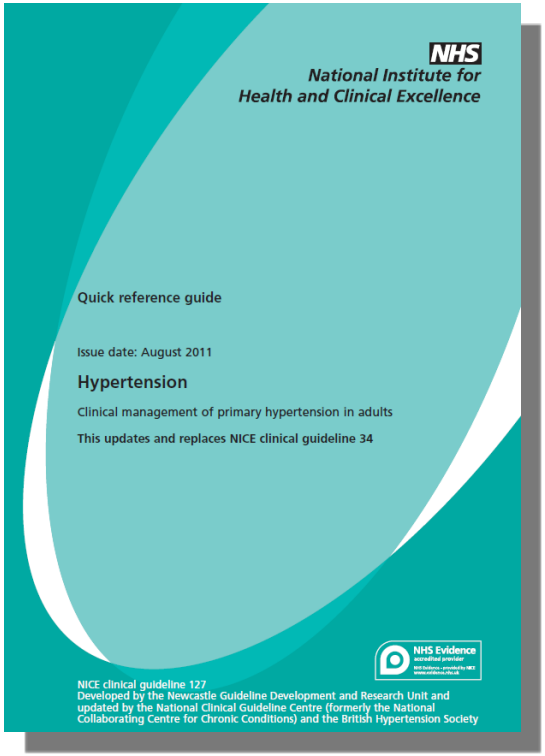
(1) In the elderly patients antihypertensive treatment is highly beneficial.

(1) SBP should be lowered below 140 mmHg (and DBP below 90mmHg) in all hypertensive patients. *Evidence is only missing in the elderly hypertensive patients, in whom the benefit of lowering SBP below 140 mmHg has never been tested in randomized trials.*

(1) Antihypertensive treatment has benefits also in patients aged >80 years (HYVET trial). *Because HYVET patients were generally in good conditions, the extent to which HYVET data can be extrapolated to more fragile octogenarians is uncertain.*

(2) Common sense considerations suggest that also in the elderly drug treatment ***can be initiated when SBP is >140 mmHg, and that SBP can be brought to below 140 mmHg****, provided treatment is conducted with particular* ***attention to adverse responses, potentially more frequent in the elderly.***

Mancia G et al, J Hypertens 2009



NICE-BHS Guideliens
Monitoring drug treatment (1)

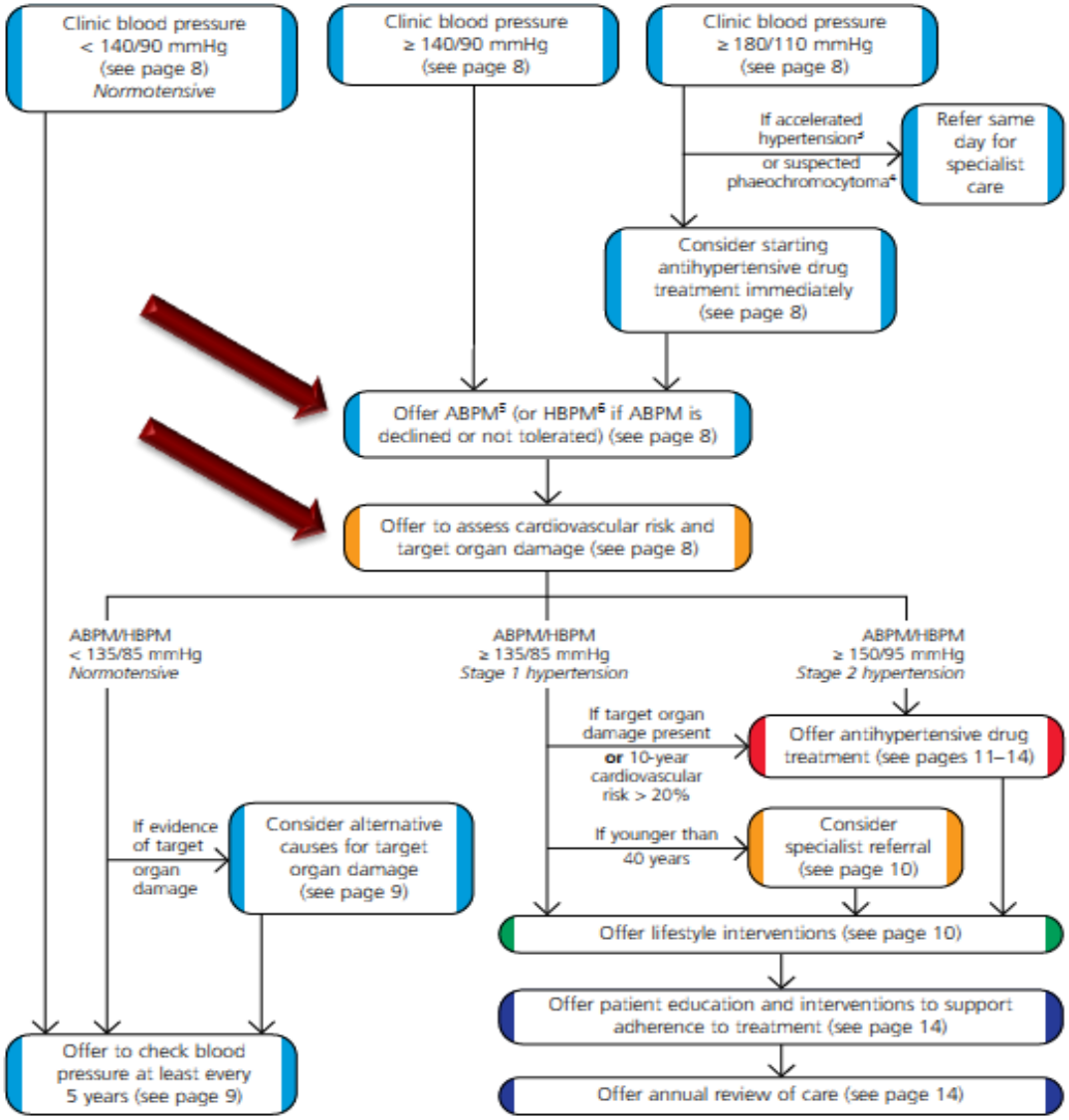
Use clinic blood pressure measurements to monitor response to treatment. Aim for target blood pressure below:

- 140/90 mmHg in people aged under 80
- 150/90 mmHg in people aged 80 and over

Care pathway for hypertension

BHS British Hypertension Society

NHS National Institute for Health and Clinical Excellence



[3] Signs of papilloedema or retinal haemorrhage.
[4] Labile or postural hypotension, headache, palpitations, pallor and diaphoresis.
[5] Ambulatory blood pressure monitoring.
[6] Home blood pressure monitoring.

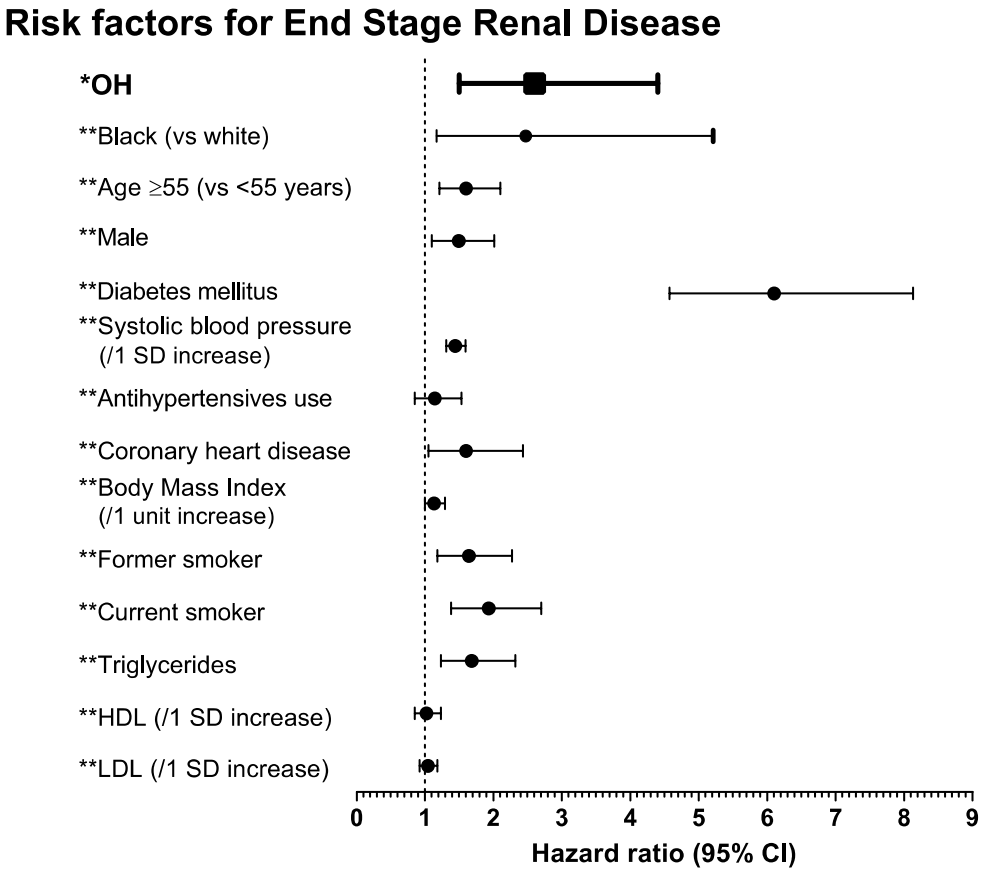
HBP in the elderly:
possible clinical features

- Postural (orthostatic) hypotension
- Post-prandial hypotension

Editorial Commentary

Orthostatic Hypotension and Cardiovascular Risk

Cyndya Shibao, Italo Biaggioni



Hypertension , 2010

Original Article

Meal-induced blood pressure variation and cardiovascular mortality in ambulatory hypertensive elderly patients: preliminary results

Andrea Zanasi[a], Enrico Tincani[b], Valeria Evandri[a], Paolo Giovanardi[c], Marco Bertolotti[a], and Giuseppe Rioli[a]

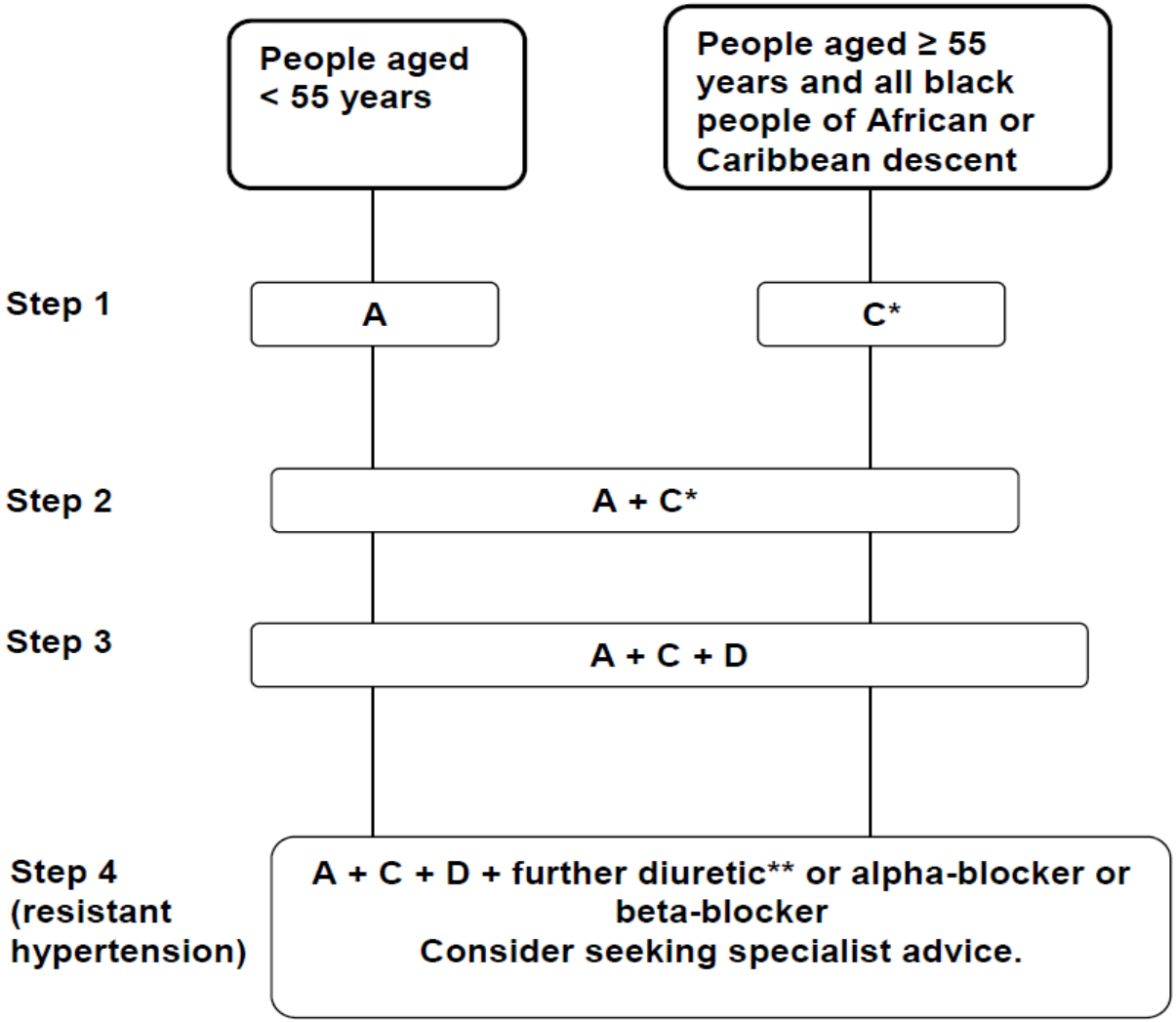
Clinical characteristics in patients decreased or alive at follow-up

	Alive, $n = 333$ (83%)	Dead for cardiovascular causes, $n = 34$ (8.5%)	P
Male	155 (46.5%)	9 (26.5%)	0.018
Age (years)	76 ± 11	85 ± 6	<0.001
BMI (kg/m^2)	26.5 ± 3.6	25 ± 4	0.05
Smoking habit	48 (14.4%)	4 (11%)	0.56
Dyslipidemia	80 (24%)	5 (15%)	0.74
Clinic BP			
SBP (mmHg)	148 ± 18	145 ± 24	0.09
DBP (mmHg)	82 ± 13	77 ± 13	0.74
Postprandial hypotension and meal-induced BP variation			
One or more episode of PPH during the day	264 (79.2%)	28 (82.4%)	0.23
PPH after breakfast	92 (25.1%)	18 (52.9%)	0.001
Breakfast BPV (mmHg)	8.4 ± 18.2	21.4 ± 21.9	<0.001
PPH after lunch	164 (44.7%)	15 (44.1%)	0.99
Lunch BPV (mmHg)	20.8 ± 14.8	17.3 ± 15.1	0.57
PPH after dinner	141 (38.4%)	17 (50%)	0.20
Dinner BPV (mmHg)	17.3 ± 15.1	21.2 ± 17.3	0.14

PPH=post-prandial hypotension

Journal of Hypertension. 30(11):2125-2132,

Antihypertensive Drug Treatment: NICE-BHS 2011



Key:

A = ACE inhibitor or ARB

C = CCB

D = Thiazide-like diuretic such as chlorthalidone (12.5 mg–25 mg once daily) or indapamide (2.5 mg or SR 1.5 mg once daily) rather than thiazide diuretic such as bendroflumethiazide or hydrochlorothiazide.

C* = CCB preferred but consider thiazide-like diuretics in people with oedema or a high risk of heart failure
Further diuretic** = low-dose spironolactone or higher doses of a thiazide-like diuretic

Editorial

The Cardiovascular World Is Definitely Not Flat

P. Kaul, PhD; E.D. Peterson, MD, MPH

What Guidelines still do not say……

1. How to manage complex pharmacotherapy?
2. It is reasonable to start treatment soon?
3. Are there preferred drugs among the recommended?
4. Is there a room for the newest drugs?

Examination of multiple medication use among TRICARE beneficiari

Age Group, Years	Mean (SE) Rx*			P Value	Mean (SE) Therapeutic Categories†			P Value
	Total (N=126,682)	Men (n=58,338)	Women (n=68,344)		Total (N=126,682)	Men (n=58,338)	Women (n=68,344)	
65-69	5.65 (±4.01)	5.25 (±3.82)	5.98 (±4.20)	0.000	3.58 (±2.06)	3.26 (±1.92)	3.86 (±2.13)	0.000
70-74	6.00 (±4.04)	5.68 (±4.02)	6.30 (±4.14)	0.000	3.78 (±2.09)	3.51 (±2.02)	4.04 (±2.13)	0.000
75-79	6.24 (±3.99)	6.01 (±3.98)	6.43 (±4.07)	0.000	3.93 (±2.08)	3.72 (±2.03)	4.10 (±2.10)	0.000
80-84	6.34 (±3.97)	6.07 (±4.00)	6.54 (±4.02)	0.000	4.02 (±2.07)	3.80 (±2.03)	4.19 (±2.08)	0.000
85+	6.25 (±3.90)	6.02 (±4.09)	6.45 (±3.91)	0.000	4.00 (±2.05)	3.84 (±2.07)	4.14 (±2.03)	0.000
Total	6.01 (±4.01)	5.69 (±3.97)	6.28 (±4.12)	0.000	3.80 (±2.08)	3.54 (±2.01)	4.03 (±2.11)	0.000
P value	0.000	0.000	0.000		0.000	0.000	0.000	

** Mean and standard error for number of medications obtained across all level 1, AHFS therapeutic category .*

† Mean and standard error for number of level 1 AHFS therapeutic categories used.

AHFS=American Hospital Formulary System; Rx=prescription.

Linton A et al, J Manag Care Pharm 20

BMJ

BMJ 2012;344:d7541 doi: 10.1136/bmj.d7541 (Published 4 January 2012)

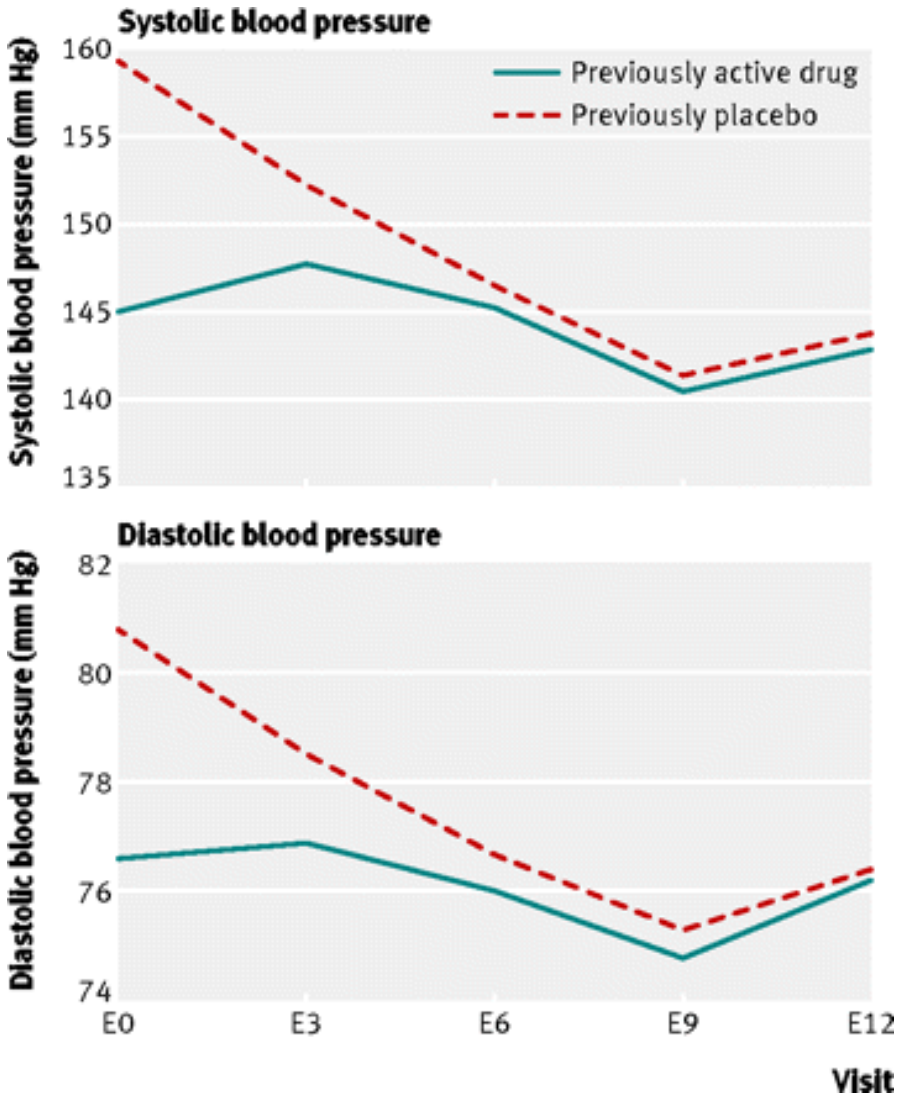
RESEARCH

Immediate and late benefits of treating very elderly people with hypertension: results from active treatment extension to Hypertension in the Very Elderly randomised controlled trial

N Beckett *honorary clinical senior lecturer*[1], R Peters *science and business development manager*[2], J Tuomilehto *professor of public health*[3 4], C Swift *professor of health care of the elderly*[5], P Sever *professor of clinical pharmacology and therapeutics*[6], J Potter *professor of ageing and stroke medicine*[7], T McCormack *general practitioner*[8], F Forette *professor of internal medicine and geriatrics*[9], B Gil-Extremera *professor for internal medicine*[10], D Dumitrascu *professor of medicine*[11], J A Staessen *head of Studies Coordinating Centre*[12], L Thijs *statistician*[13], A Fletcher *professor of epidemiology of ageing*[14], C Bulpitt *emeritus professor of geriatric and cardiovascular medicine*[1], for the HYVET Study Group

[1]Department of Medicine, Imperial College London, London SW7 2AZ, UK; [2]Clinical Trials Unit, Imperial College London; [3]Department of Public Health, University of Helsinki, Helsinki, Finland; [4]South Ostrobothnia Central Hospital, Seinäjoki, Finland; [5]Clinical Age Research Unit, Department of Clinical Gerontology, Kings College London, London; [6]International Centre for Circulatory Health, Imperial College London; [7]School of Medicine, Health Policy and Practice, University of East Anglia, Norfolk, UK; [8]Whitby Group Practice, Spring Vale Medical Centre, Whitby, UK; [9]Hôpital Broca, University Paris V, Paris, France; [10]FAC Medicina, Departmento Medicina Granada, Granada, Spain; [11]Spitalul Judetean Cluj, Clinica Medicală 2, Cluj, Romania; [12]Department of Epidemiology, Maastricht University, Netherlands; [13]Studies Coordinating Centre, Division of Hypertension and Cardiovascular Rehabilitation, Department of Cardiovascular Diseases, University of Leuven, Leuven, Belgium; [14]London School of Hygiene and Tropical Medicine, London

Mean sitting SBP and DBP by group in the extension of the HYVET Study

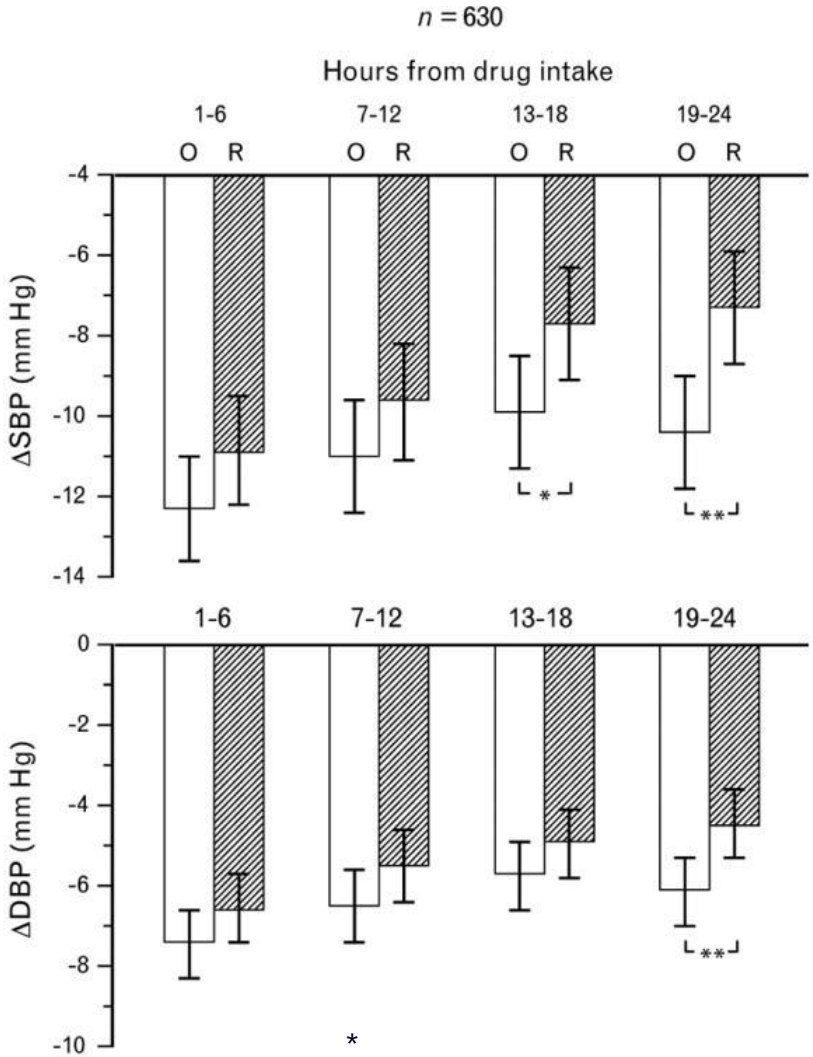


Beckett N et al, BMJ 2012

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

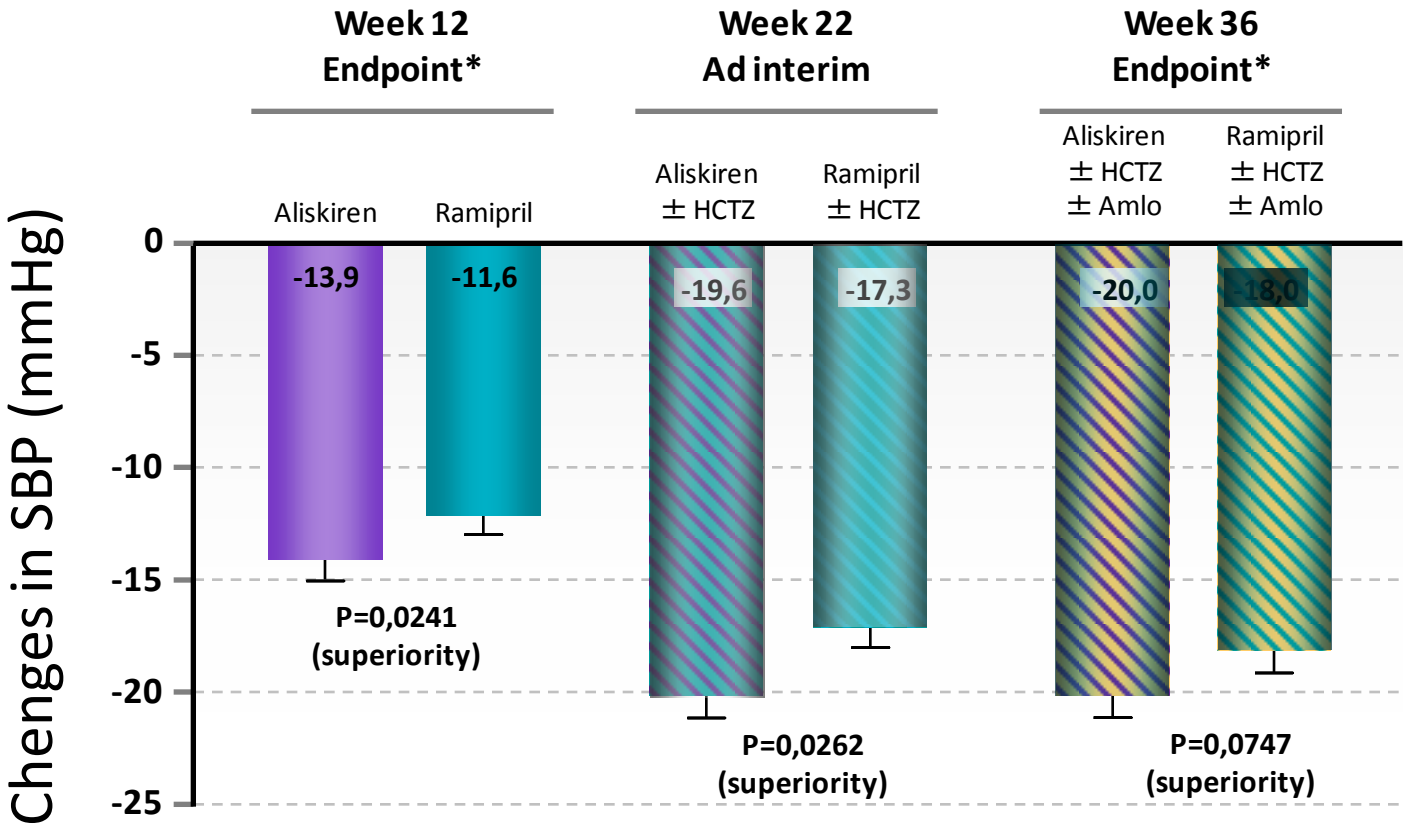
Malacco Ettore; Omboni Stefano; Volpe Massimo; Auteri Alberto; Zanchetti Alberto

Journal of Hypertension. 28(11):2342-2350, November 2010.



ABPM

AGELESS Study: Effects of aliskiren and ramipril on seated SBP after 12,22 and 36 weeks of treatment



All the comparisons are significant at p<0.001 for non-inferiority

Duprez et al; Journal of Human Hypertension 2009

Summary of recommendations on antihypertensive strategies in the elderly

6.3.1 Summary of recommendations on antihypertensive treatment strategies in the elderly

Recommendations	Class[a]	Level[b]	Grade	Ref.[c]
The recommendation of lowering systolic BP <150 mmHg in elderly individuals with systolic BP ≥160 mmHg is strongly evidence-based.	I	A	Strong	8,134,247
In elderly individuals younger than 80 years, antihypertensive treatment may be considered at systolic BP values >140 mmHg and aimed at values <140 mmHg, if the individuals are fit and treatment is well tolerated.	IIb	C	Weak	252
It is also recommended that hypertensive individuals older than 80 years be given antihypertensive treatment if their initial systolic BP is >160 mmHg, and that their systolic BP be reduced to <150 mmHg provided that they are in good physical and mental condition.	I	B	Weak	263
In frail elderly patients decisions on antihypertensive therapy should be left to the treating physician and based on monitoring the clinical effects of treatment.	I	C	Weak	
There is no obvious reason why well-tolerated antihypertensive treatment should be interrupted or reduced when a treated individual becomes octogenarian.	IIa	C		
All hypertensive agents can be used in the elderly, although diuretics and calcium antagonists may be preferred in isolated systolic hypertension.	I	A	Strong	398

Eur Heart J, 2013 (in press)