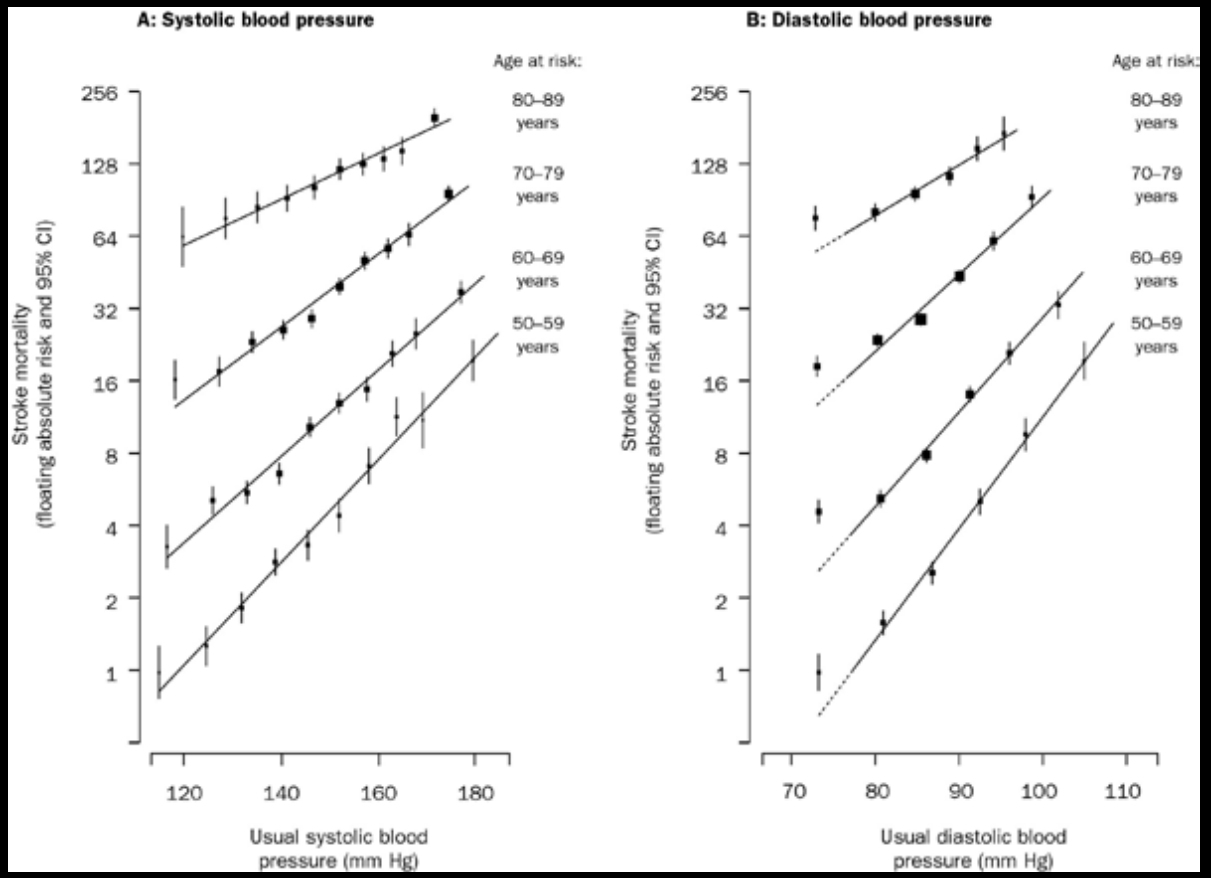
OLMESARTAN: Central Blood Pressure and Cardiovascular Risk

Professor John Cockcroft
Professor of Cardiology
Wales Heart Research Institute
Cardiff

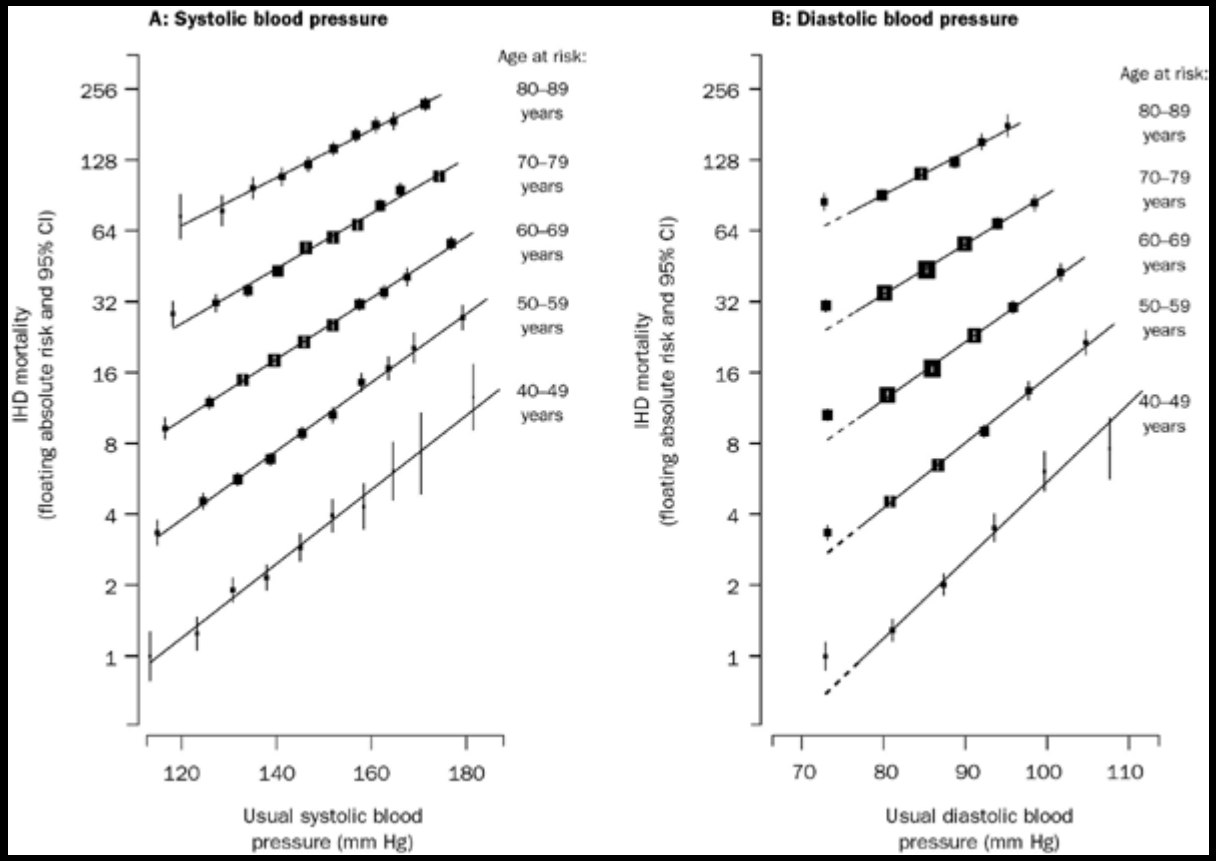
British Heart Foundation

Relationship Between Blood Pressure and Stroke in over 1 Million Subjects



Lancet 2002; **360:** 1903-13

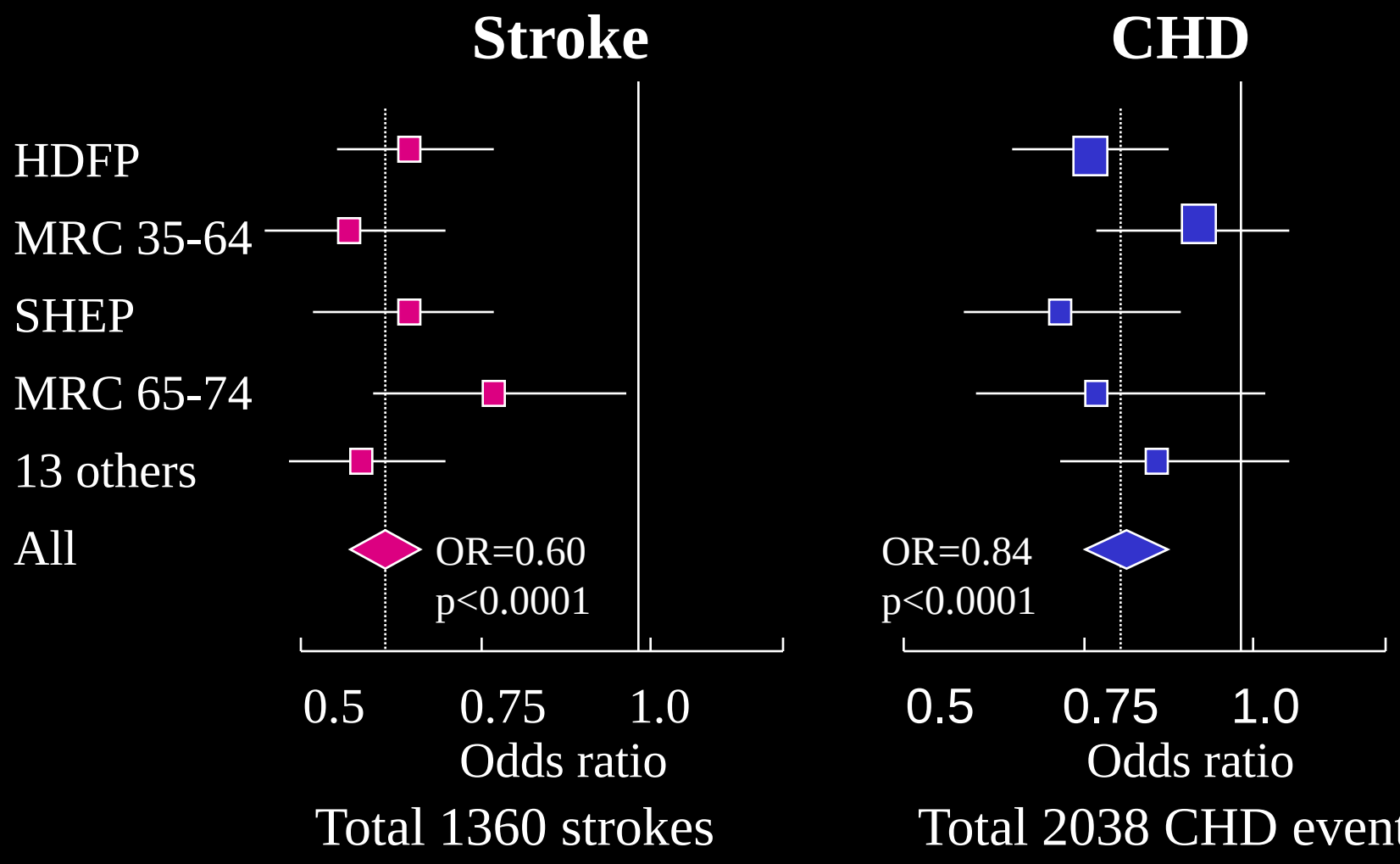
Relationship Between Blood Pressure and MI in over 1 Million Subjects



Lancet 2002; **360:** 1903-13

Pooled Results of Randomised Trials of BP Lowering

47,500 patients in 17 trials. About 5 years of Treatment, DBP Reduced by 6mmHg, SBP approx 12mmHg. Diuretics and Beta blockers.

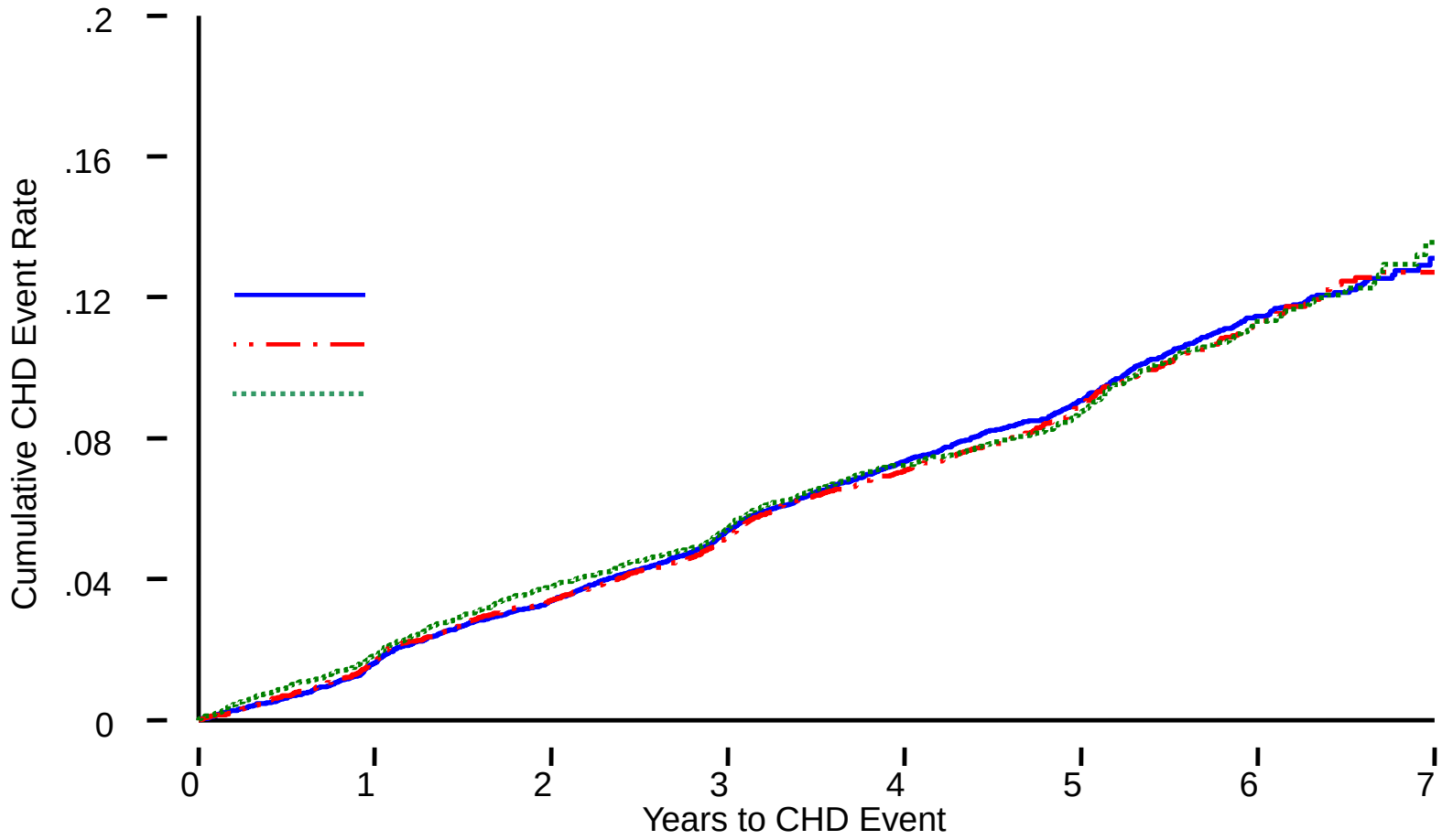


Effective Drug Therapy for Hypertension

- 1940s Sympathetic blockers
- 1950s Thiazide diuretics
- 1960s β-blockers
- 1970s Calcium channel blockers
- 1980s ACE inhibitors
- 1990s AT_1 blockers
- 2000s Direct renin inhibitors

Is it the drug you use or blood pressure reduction per se……?

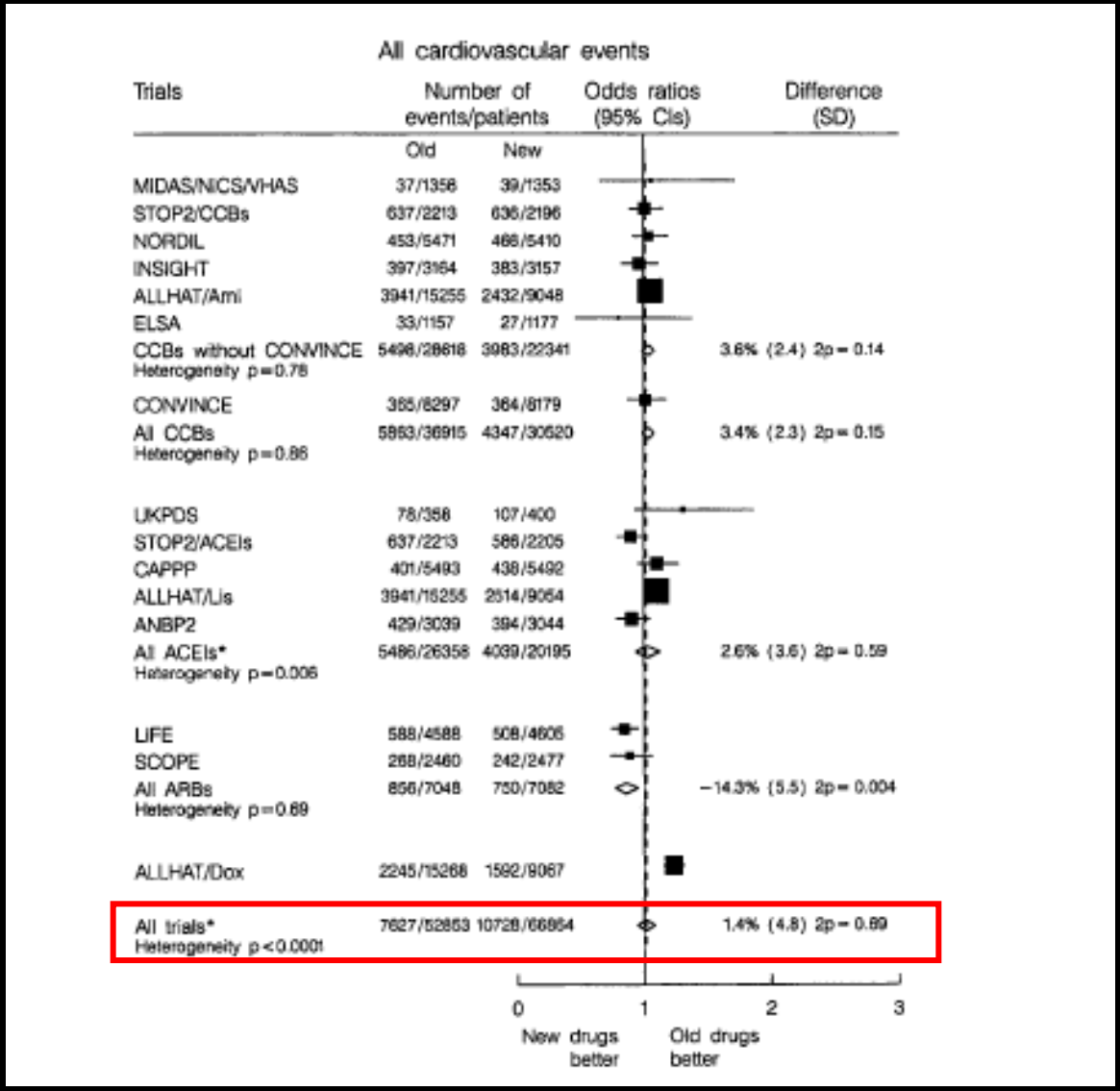
Cumulative Event Rates for the Primary Outcome (Fatal CHD or Nonfatal MI) by ALLHAT Treatment Group



Number at Risk:								
Chlorthalidone	15,255	14,477	13,820	13,102	11,362	6,340	2,956	209
Amlodipine	9,048	8,576	8,218	7,843	6,824	3,870	1,878	215
Lisinopril	9,054	8,535	8,123	7,711	6,662	3,832	1,770	195

Blood Pressure Reduction and Cardiovascular Prevention

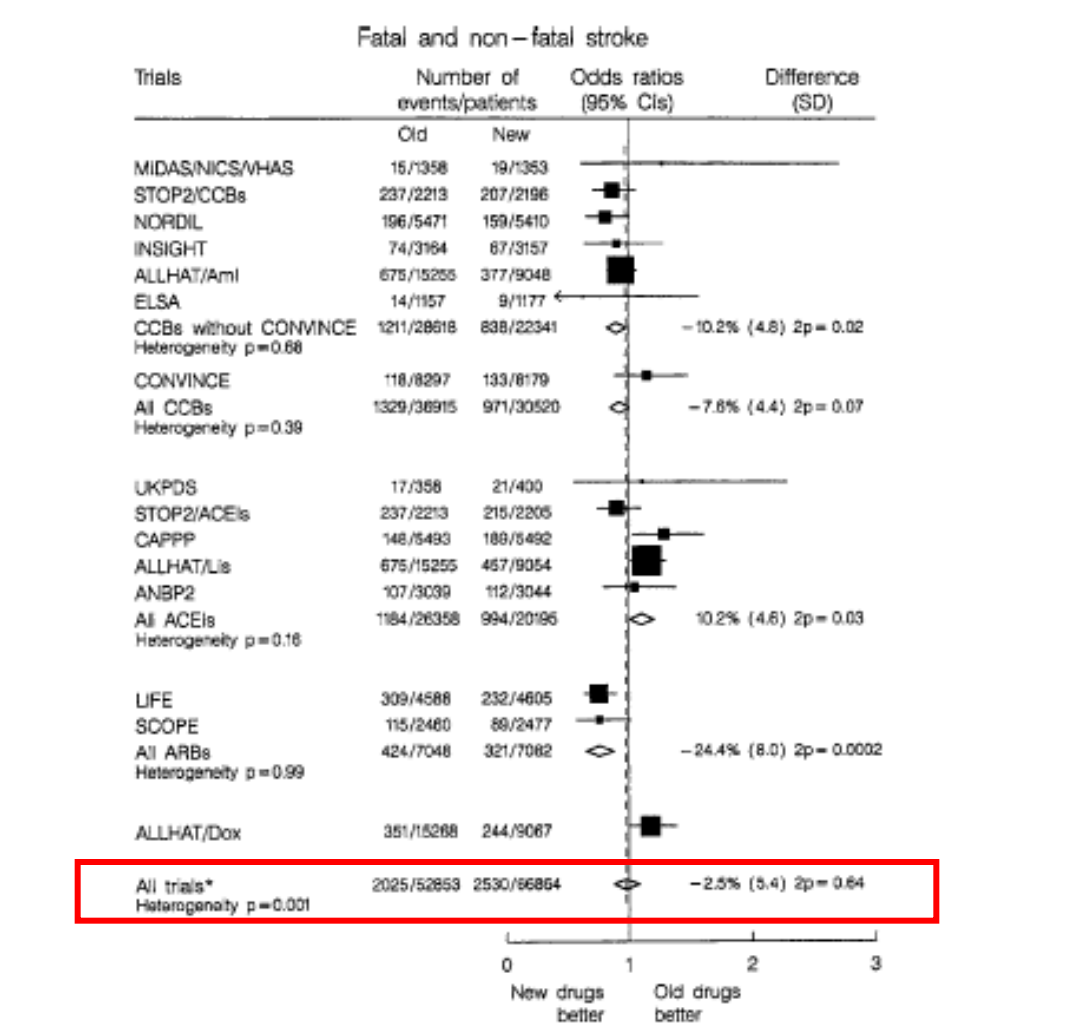
ALL CARDIOVASCULAR EVENTS



Staessen et al Hypertens Res 2005; 28: 385-407

Blood Pressure Reduction and Cardiovascular Prevention

FATAL AND NON-FATAL STROKE



Staessen et al Hypertens Res 2005; 28: 385-407

Review

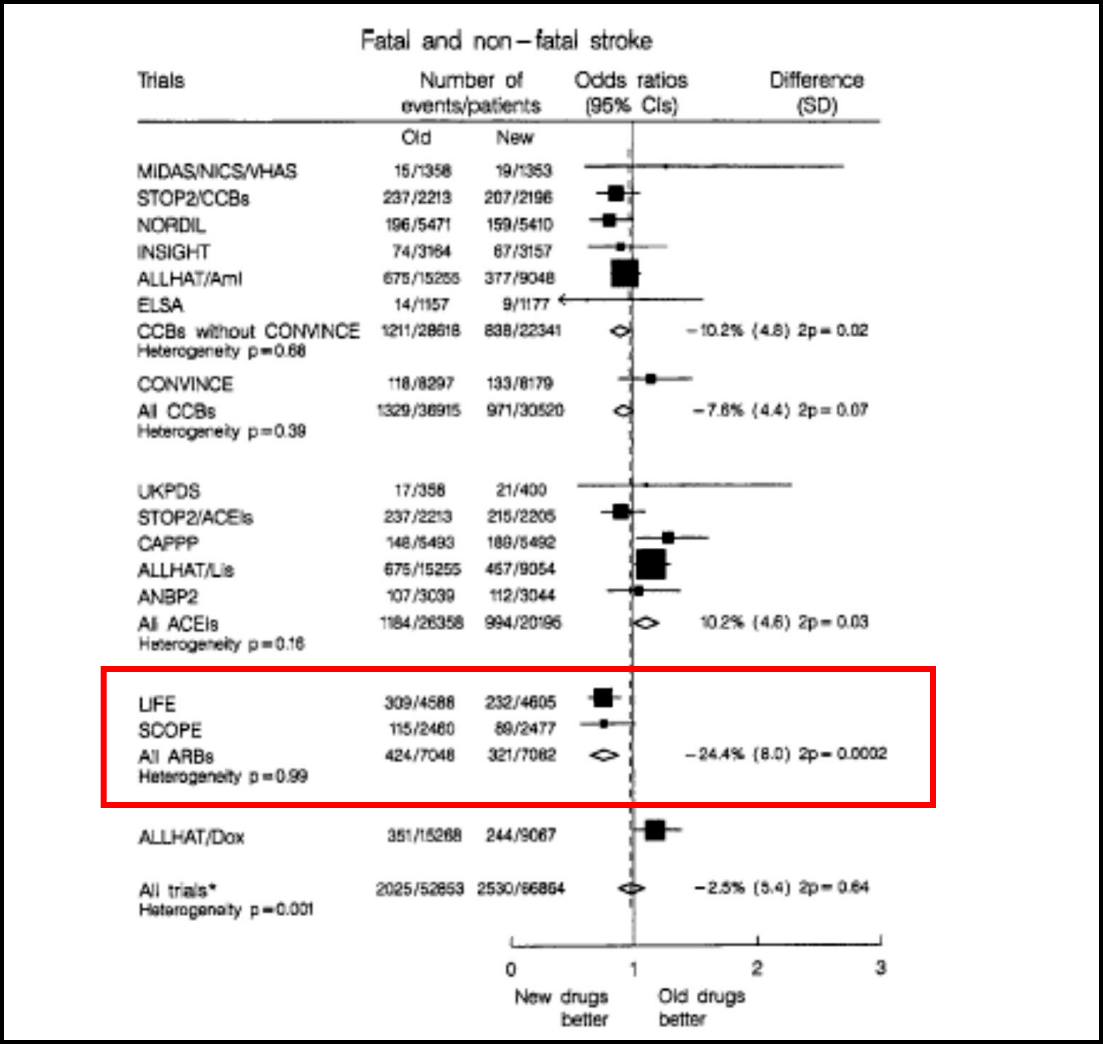
Blood Pressure Reduction and Cardiovascular Prevention: An Update Including the 2003–2004 Secondary Prevention Trials

Jan A. STAESSEN, Yan LI*, Lutgarde THIJS, and Ji-Guang WANG*

"The hypothesis that new antihypertensive drugs might influence cardiovascular prognosis over and beyond their antihypertensive effect remains unproven. Our overview emphasizes the need of tight blood pressure control, but does not allow determining to what extent blood pressure must be lowered for optimal cardiovascular protection"

Staessen et al Hypertens Res 2005; 28: 385-407

Stroke and Angiotensin II Receptor Blockade



Staessen et al Hypertens Res 2005; 28: 385-407

Does a change in angiotensin II formation caused by antihypertensive drugs affect the risk of stroke?

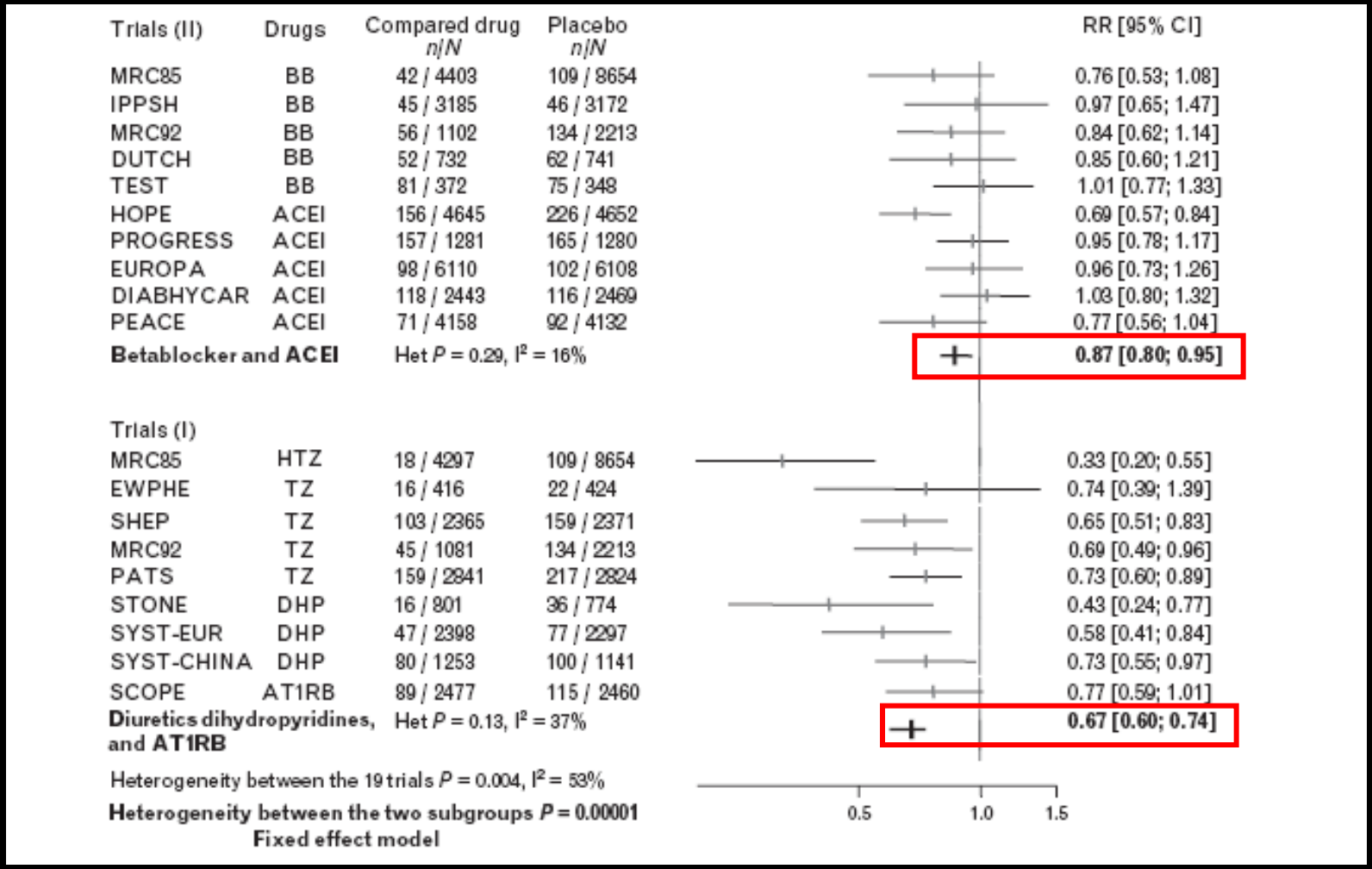
A meta-analysis of trials according to treatment with potentially different effects on angiotensin II

Florent Boutitie[a], Roxana Oprisiu[b], Jean Michel Achard[d], Hakim Mazouz[c], Jiguang Wang[f], Franz H. Messerli[g], François Gueyffier[e] and Albert Fournier[c]

Boutitie et al J Hypertens 2007; 25; 1543-1553

Effect of Drugs that Raise or Lower Angiotensin II Levels on Stroke

(26 studies 206,632 patients 7,108 strokes)



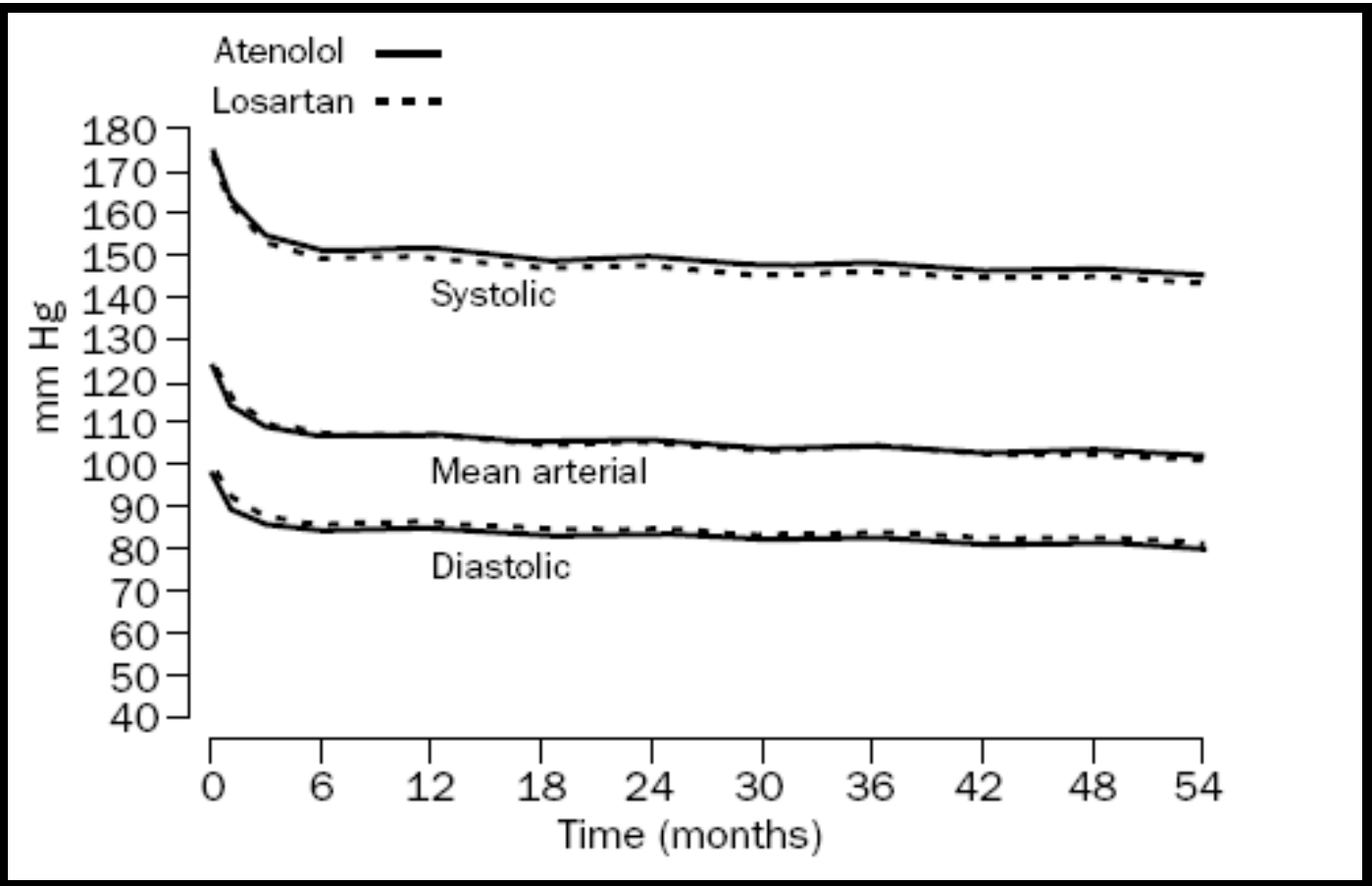
Boutitie et al J Hypertens 2007; 25; 1543-1553

Benefit beyond blood pressure reduction……?

Articles

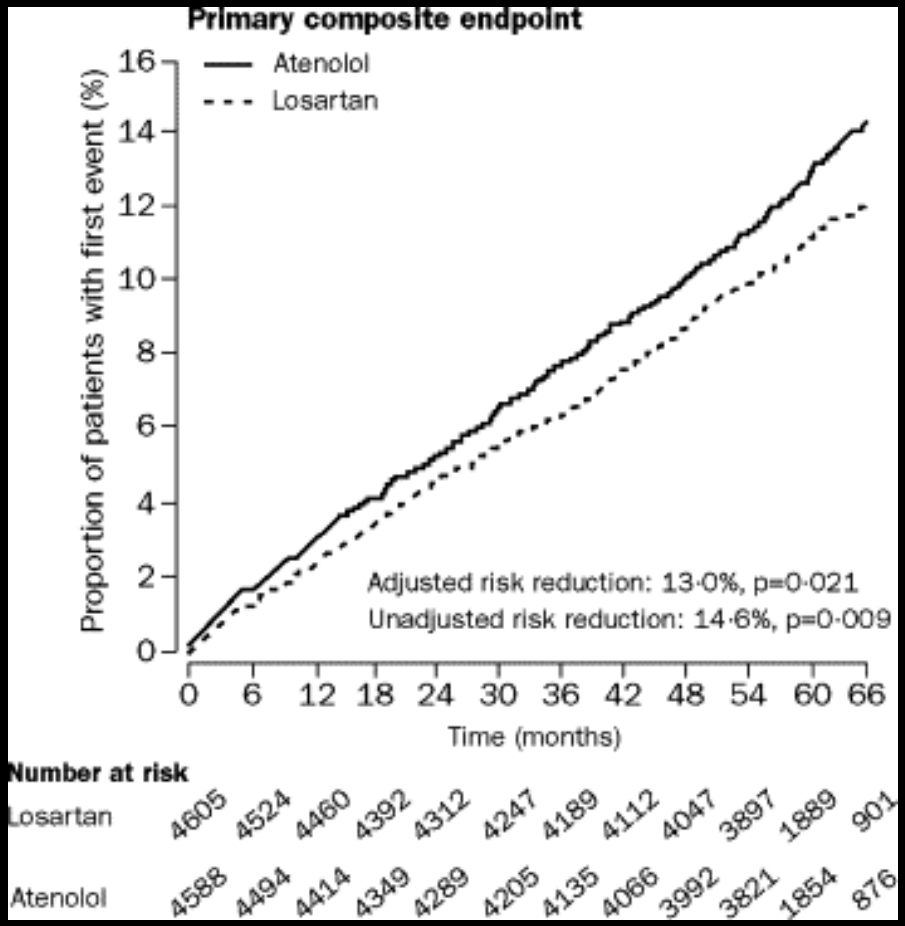
Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol

*Björn Dahlöf, Richard B Devereux, Sverre E Kjeldsen, Stevo Julius, Gareth Beevers, Ulf de Faire, Frej Fyhrquist, Hans Ibsen, Krister Kristiansson, Ole Lederballe-Pedersen, Lars H Lindholm, Markku S Nieminen, Per Omvik, Suzanne Oparil, Hans Wedel, for the LIFE study group**



Dahlof et al. *Lancet* 2002;**359**:995

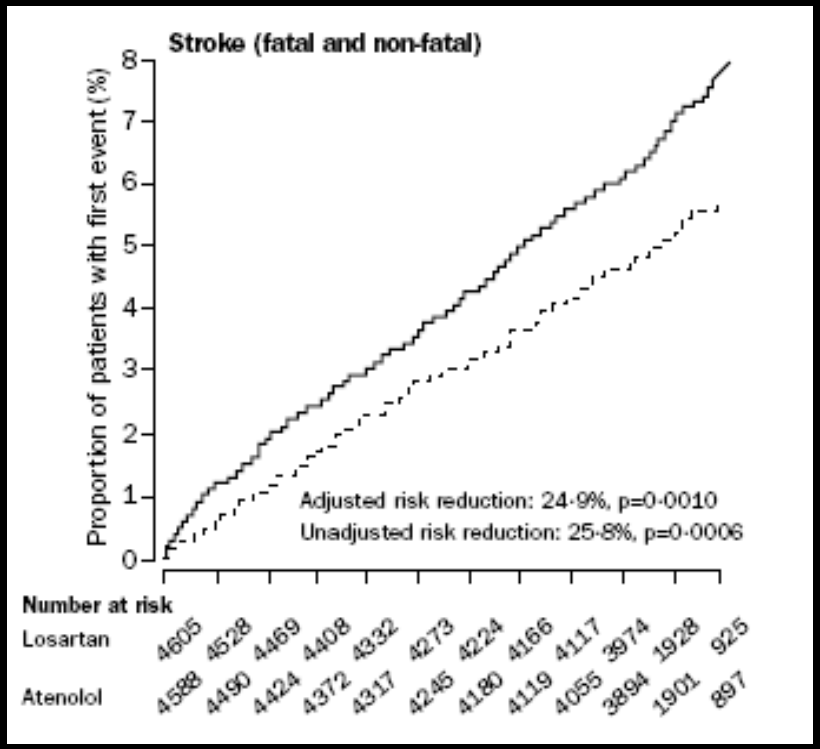
LIFE: Primary Composite Endpoint
death, MI, or stroke



Dahlof et al. *Lancet* 2002;**359**:995

LIFE: Primary Composite Endpoint

STROKE



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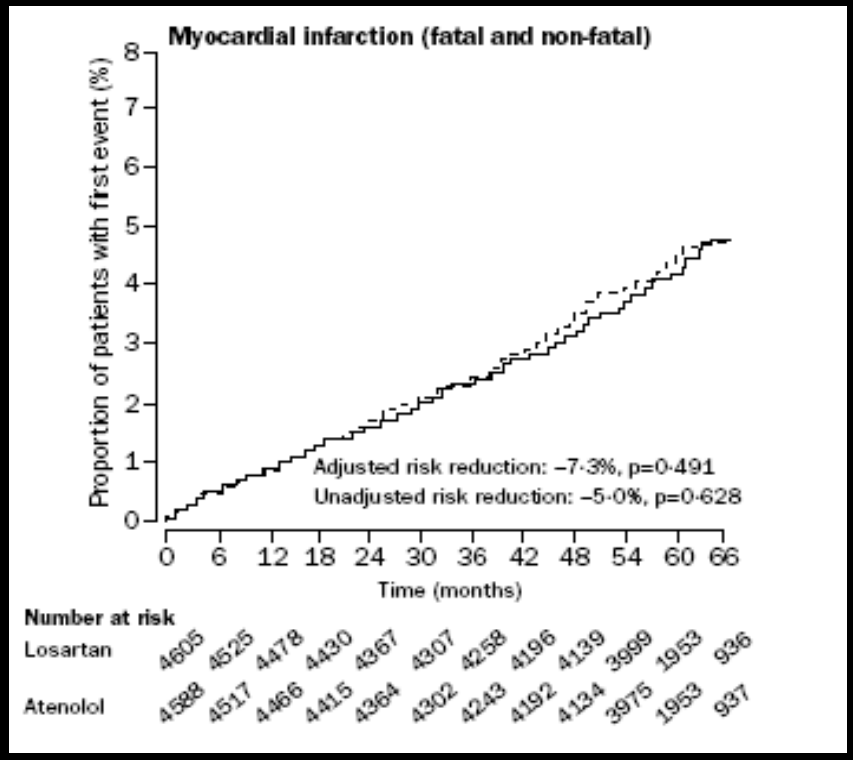
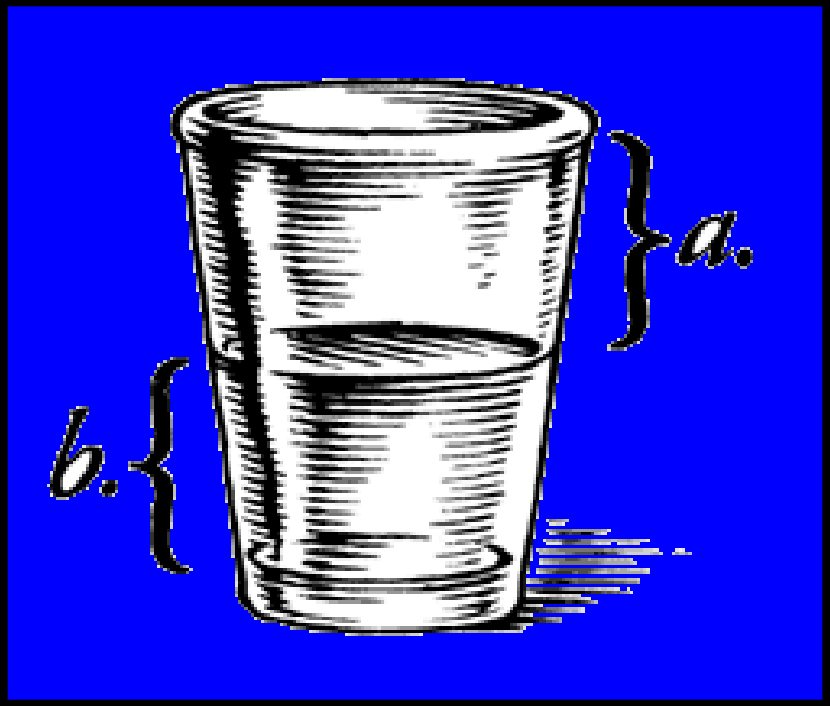


Dahlof et al. *Lancet* 2002;**359**:995

Half Full…….?



…….Half Empty ?

2003 European Society of Hypertension–European Society of Cardiology guidelines for the management of arterial hypertension*

Guidelines Committee**

Journal of Hypertension 2003, 21:1011–1053

Central Blood Pressure

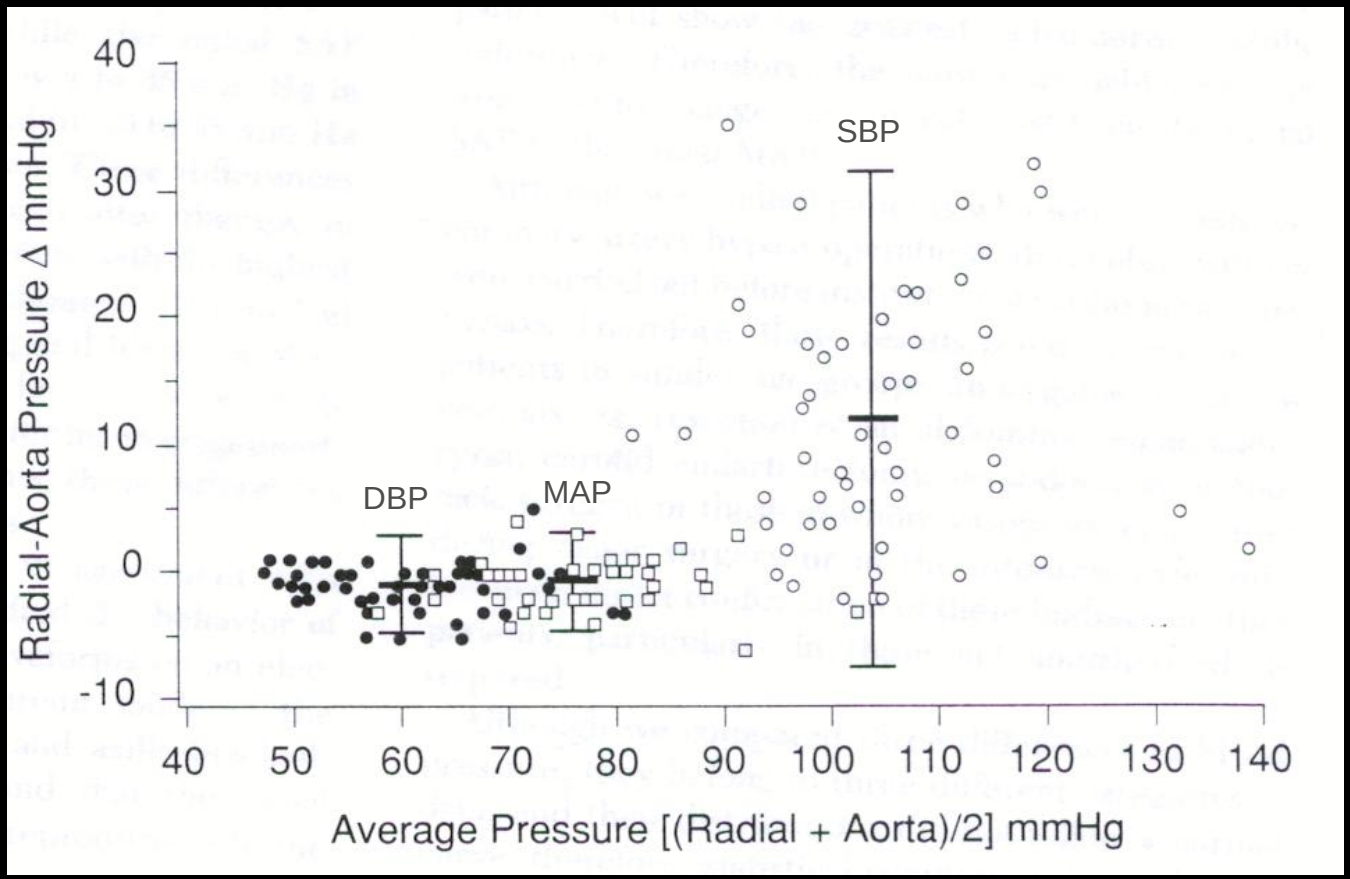
2003 European Society of Hypertension–European Society of Cardiology guidelines for the management of arterial hypertension*

Guidelines Committee**

Journal of Hypertension 2003, 21:1011–1053

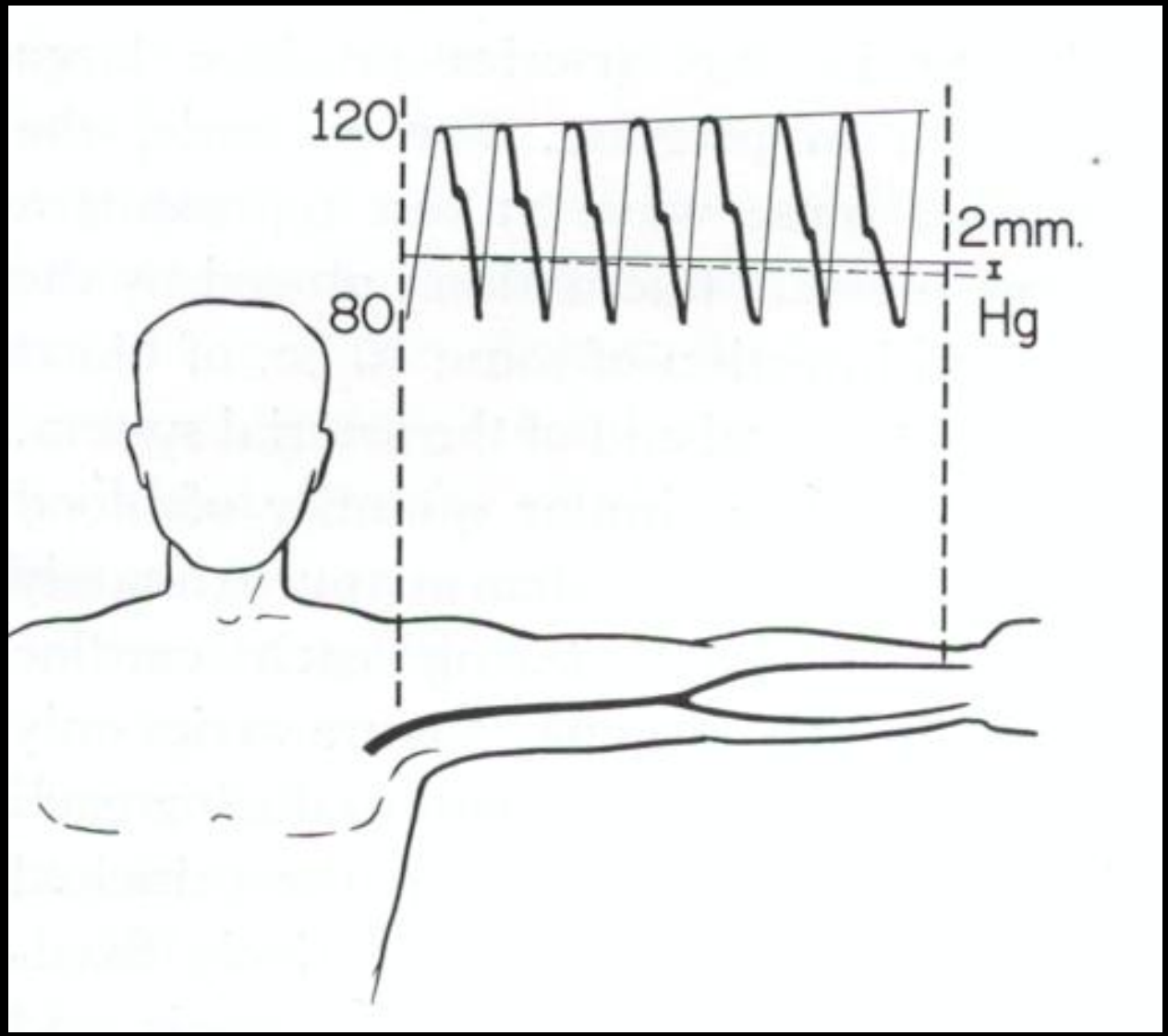
The increasing interest in systolic blood pressure and pulse pressure as predictors of cardiovascular events stimulated by trial evidence of the beneficial effects of lowering blood pressure in the elderly and in isolated systolic hypertension has stimulated the development of techniques for measuring large arterial stiffness. Two of these have been developed for possible use as diagnostic procedures namely pulse wave velocity and augmentation index as measured with the SphygmoCor device……Aortic blood pressure (the pressure exerted on the heart and brain) may be different from that measured in the arm and be a both a better predictor of outcome and may be differently affected by antihypertensive drugs

Peripheral Versus Aortic Pressure



Pauca AL et al. *Chest* 1992;**102**:1193

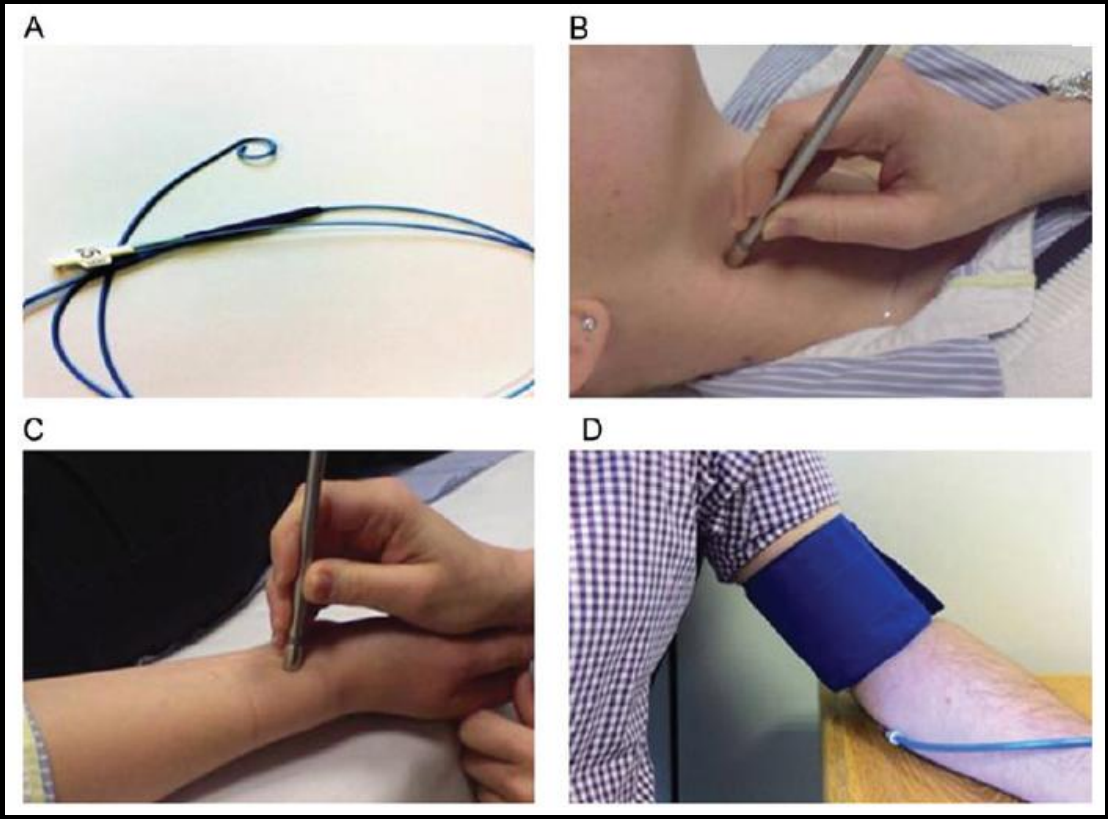
Pressure Amplification



Central blood pressure: current evidence and clinical importance

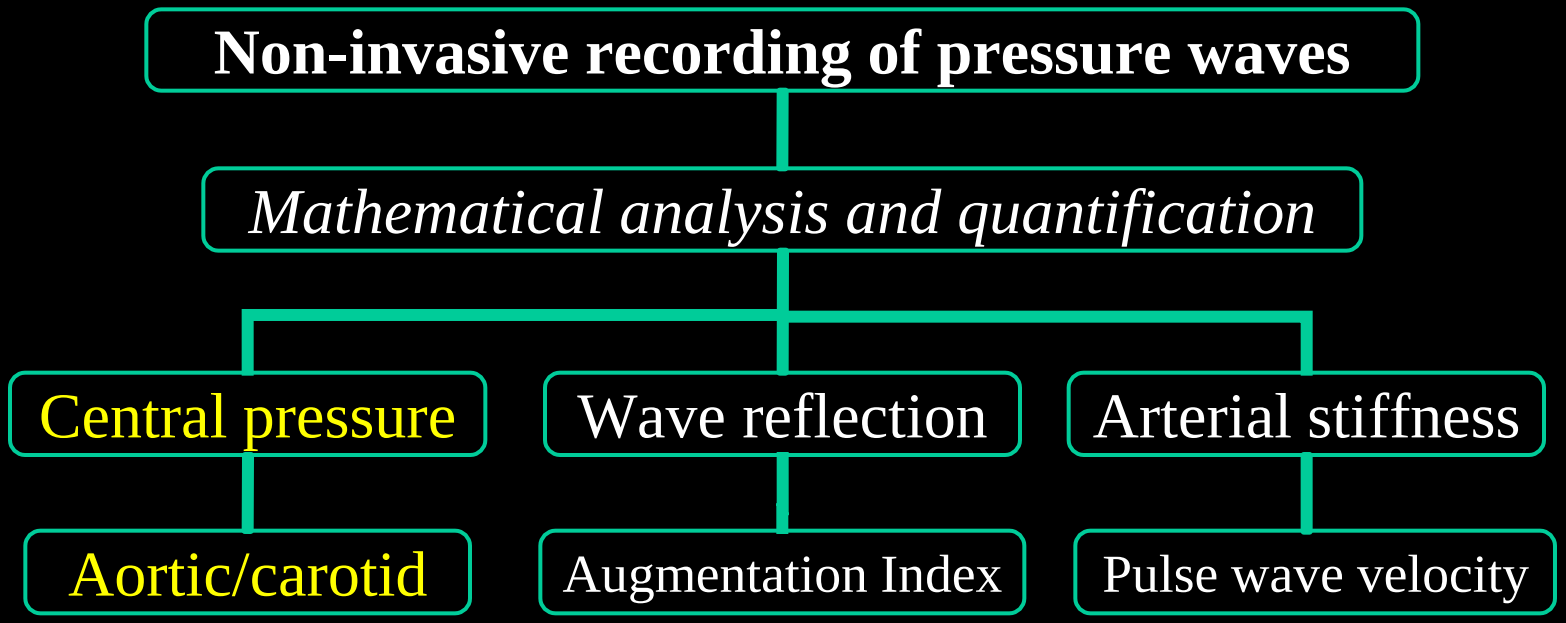
Carmel M. McEniery[1]*, John R. Cockcroft[2], Mary J. Roman[3], Stanley S. Franklin[4], and Ian B. Wilkinson[1]

[1]Clinical Pharmacology Unit, University of Cambridge, Addenbrooke's Hospital, Box 110, Cambridge CB2 2QQ, UK; [2]Department of Cardiology, Wales Heart Research Institute, Cardiff CF14 4XN, UK; [3]Division of Cardiology, Weill Cornell Medical College, New York, NY 10021, USA; and [4]University of California, UCI School of Medicine, Irvine, CA 92697-4101, USA

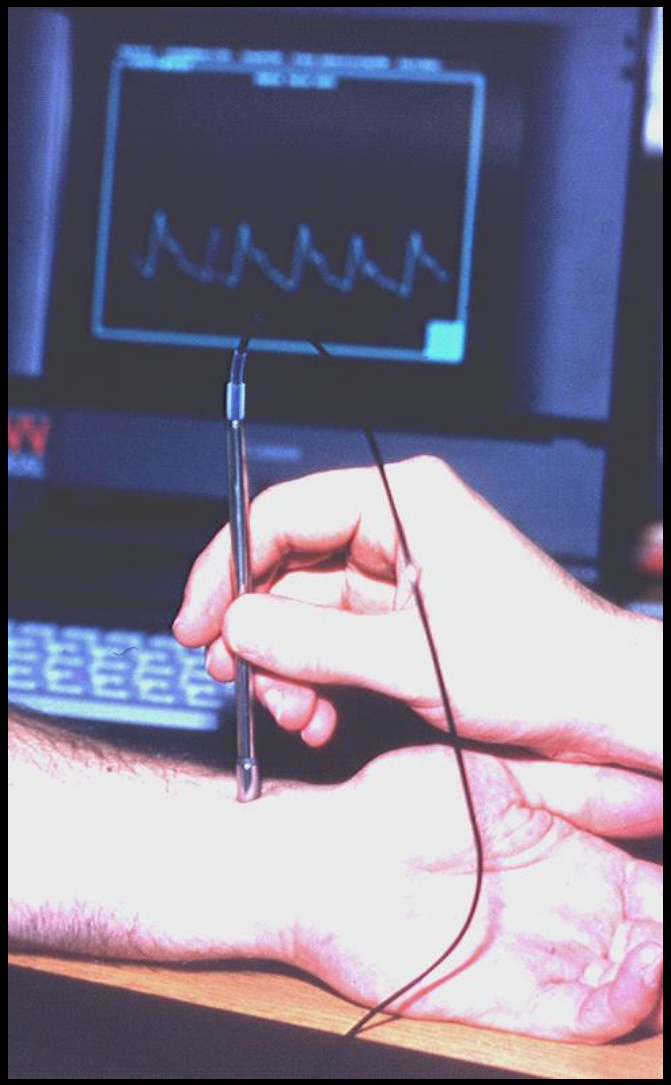


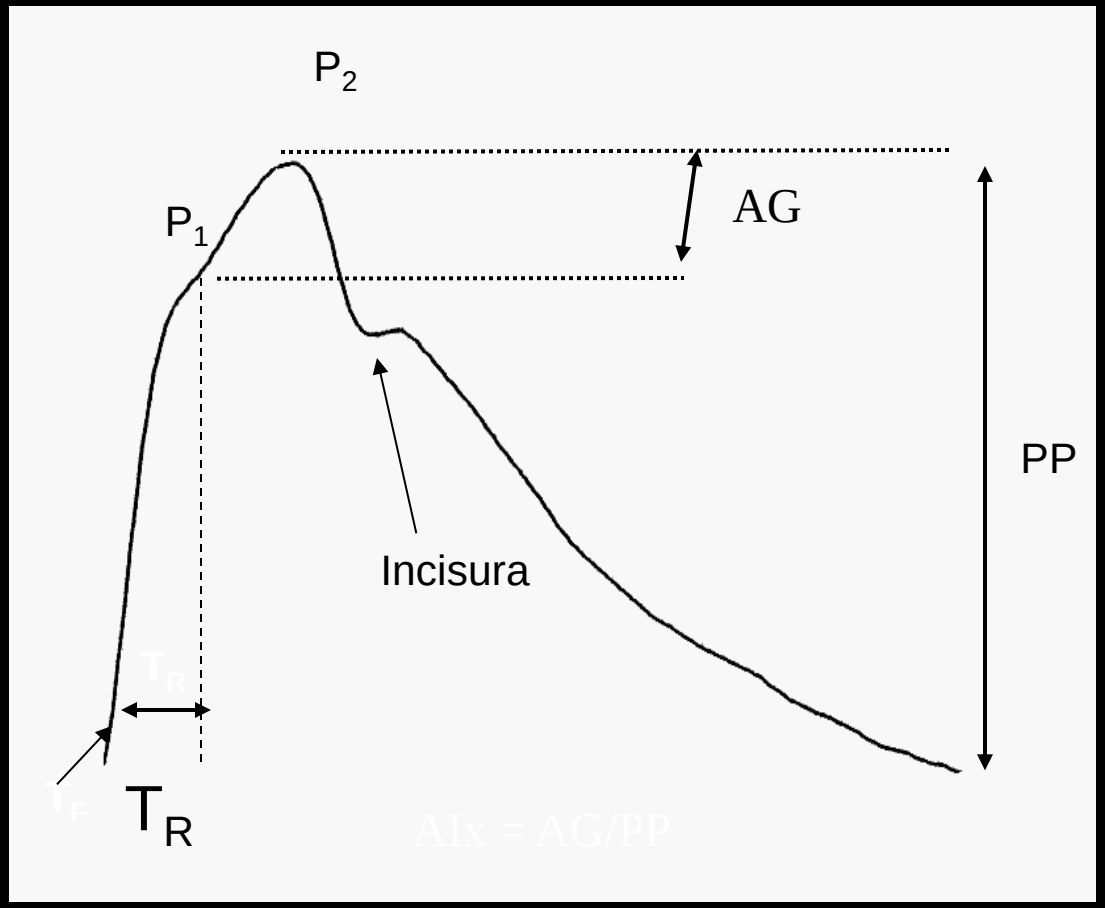
McEniery et al *Eur Heart J* 2014 (in Press)

The Basic Technique



Pulse Wave Analysis





European Heart Journal (2006) 27, 2588–2605
doi:10.1093/eurheartj/ehl254

EUROPEAN SOCIETY OF CARDIOLOGY®

Special article

Expert consensus document on arterial stiffness: methodological issues and clinical applications

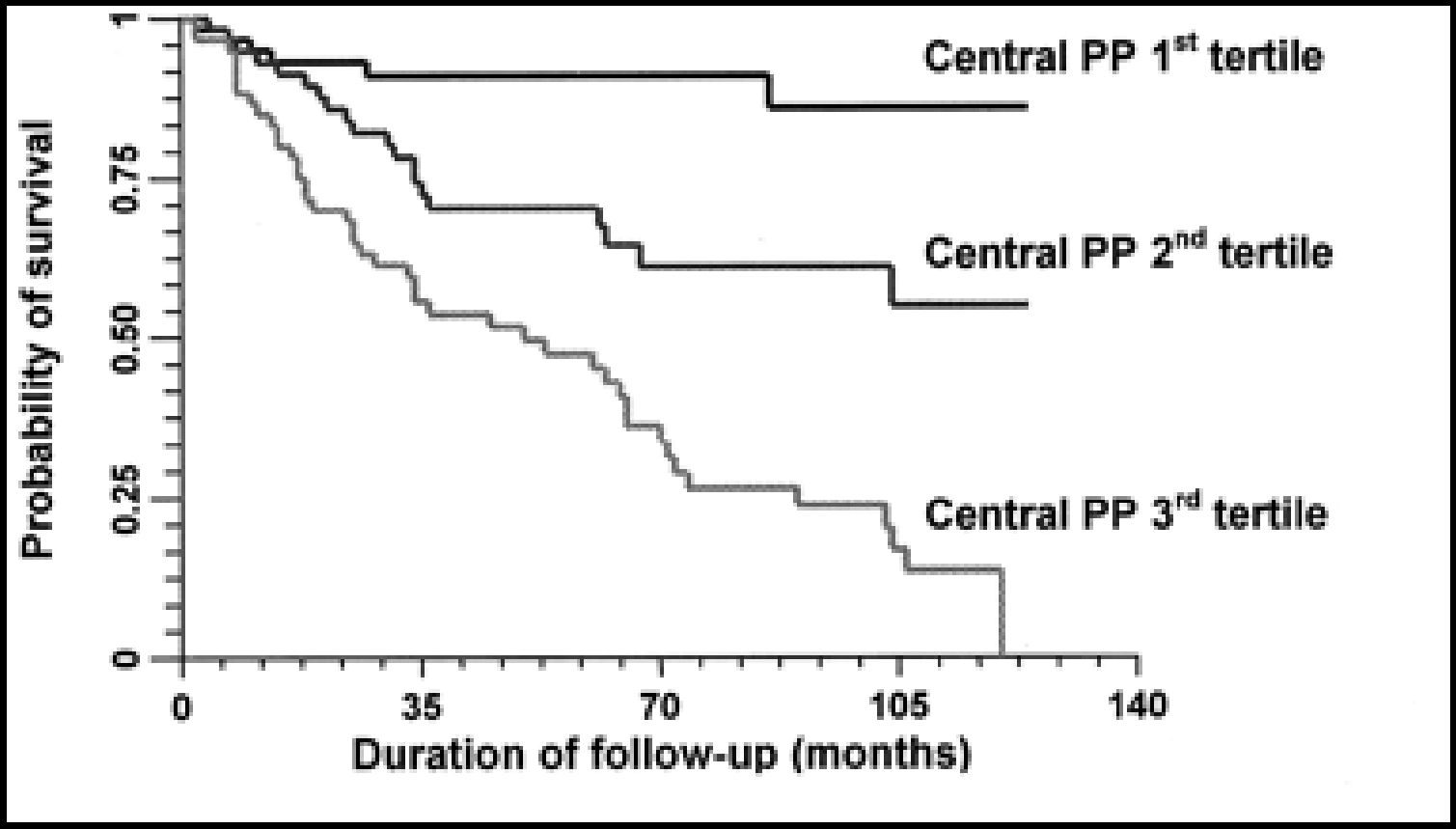
Stephane Laurent[1*], John Cockcroft[2], Luc Van Bortel[3], Pierre Boutouyrie[1], Cristina Giannattasio[4], Daniel Hayoz[5], Bruno Pannier[6], Charalambos Vlachopoulos[7], Ian Wilkinson[8], and Harry Struijker-Boudier[9] on behalf of the European Network for Non-invasive Investigation of Large Arteries

Box 1: Position statement: Brachial and central PP. Because of pulse pressure amplification between central and peripheral arteries, it is inaccurate to use brachial pulse pressure as a surrogate for aortic or carotid pulse pressure, particularly in young subjects.

Laurent *et al.*, Eur Heart J 2006; 27: 2588-2605

Central Pulse Pressure Predicts Mortality in ESRF

n=180; mean age 25; 4 year follow up



Safar et al, *Hypertension* 2002;**39**:735

Central Pressure More Strongly Relates to Vascular Disease and Outcome Than Does Brachial Pressure

The Strong Heart Study

Mary J. Roman, Richard B. Devereux, Jorge R. Kizer, Elisa T. Lee, James M. Galloway, Tauqeer Ali, Jason G. Umans, Barbara V. Howard

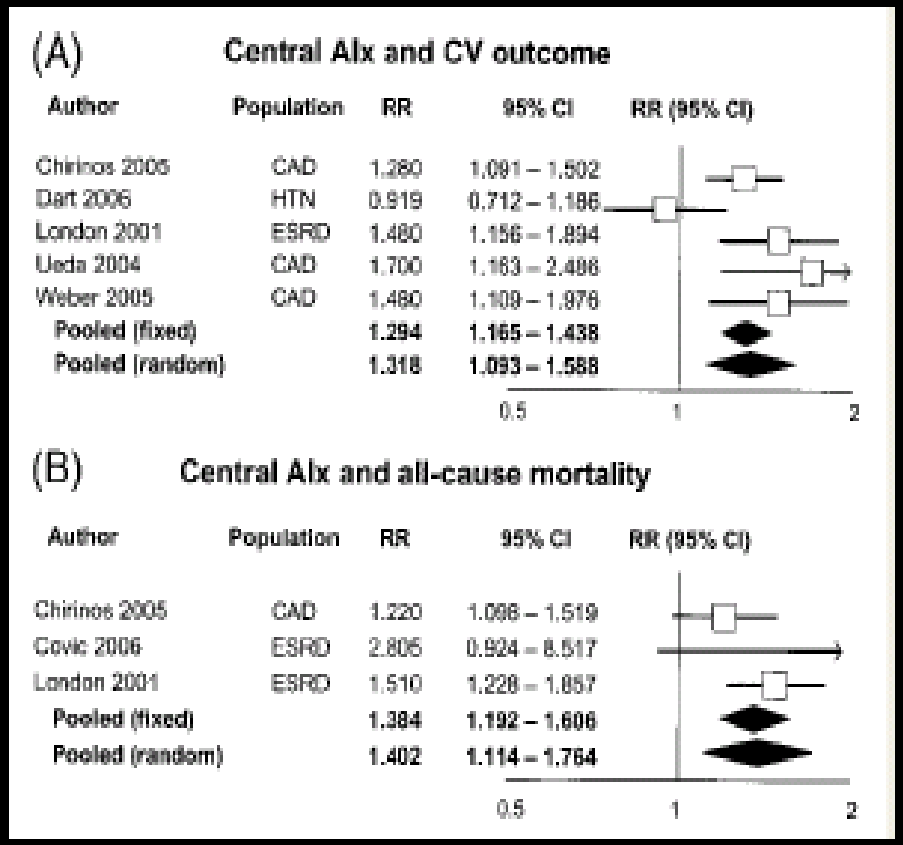
TABLE 4. Multivariable Cox Models of Relation of Traditional Risk Factors and Central and Brachial Blood Pressures to Cardiovascular Outcome

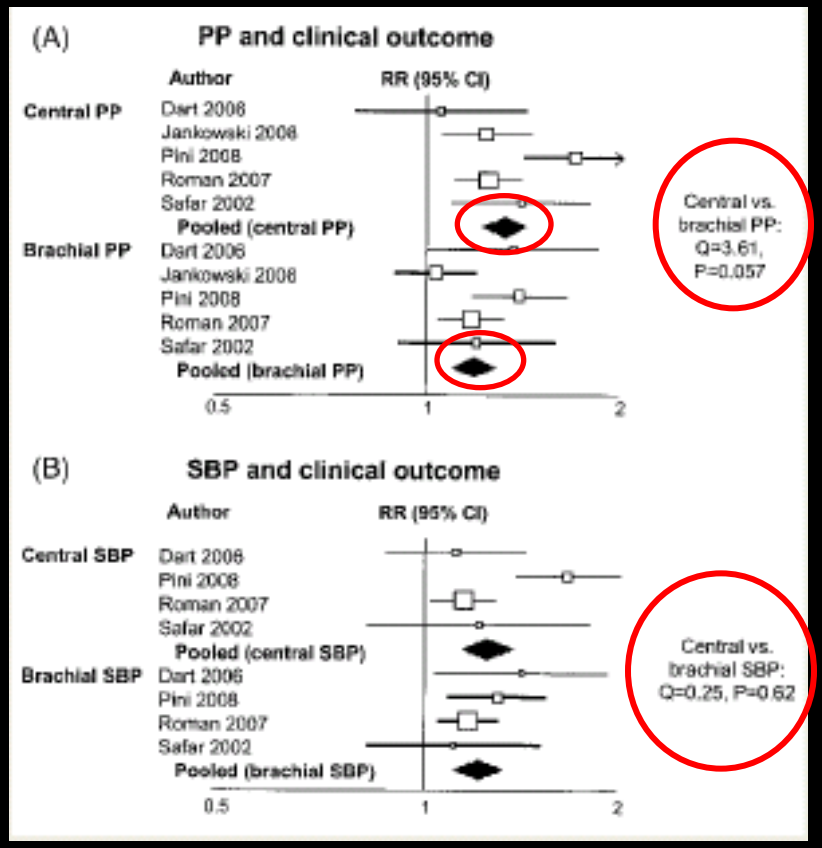
Variable	HR (95% CIs)	HR (95% CIs)	HR (95% CIs)	HR (95% CIs)	HR (95% CIs)
Age, year	1.06 (1.04–1.07)*	1.05 (1.04–1.07)*	1.06 (1.04–1.07)*	1.05 (1.03–1.07)*	1.05 (1.04–1.07)*
Male gender	1.13 (0.87–1.45)	1.17 (0.91–1.52)	1.13 (0.88–1.46)	1.22 (0.94–1.58)	1.10 (0.83–1.45)
BMI, kg/m^2	0.99 (0.97–1.01)	0.99 (0.97–1.01)	0.99 (0.97–1.01)	0.99 (0.97–1.01)	0.99 (0.97–1.01)
Smoking	1.45 (1.10–1.91)†	1.44 (1.09–1.89)†	1.42 (1.08–1.87)‡	1.39 (1.06–1.83)‡	1.37 (1.01–1.85)‡
Cholesterol:HDL	1.05 (0.98–1.13)	1.06 (0.99–1.13)	1.05 (0.98–1.13)	1.05 (0.98–1.13)	1.09 (1.01–1.18)‡
Creatinine, mg/dL	1.20 (1.12–1.28)*	1.18 (1.11–1.27)*	1.20 (1.12–1.28)*	1.18 (1.10–1.26)*	1.13 (1.03–1.23)‡
Fibrinogen, mg/dL	1.001 (1.000–1.002)†	1.001 (1.000–1.002)†	1.001 (1.000–1.002)†	1.001 (1.000–1.002)§	1.001 (1.000–1.002)‡
Diabetes mellitus	2.48 (1.91–3.22)*	2.44 (1.88–3.17)*	2.47 (1.91–3.21)*	2.41 (1.86–3.13)*	2.42 (1.838–3.22)*
Heart rate, bpm	1.012 (1.001–1.022)‡	1.013 (1.002–1.023)‡	1.013 (1.008–1.143)‡	1.012 (1.001–1.022)‡	1.013 (1.001–1.025)‡
Brachial SBP	1.08 (1.02–1.14)‡				
Brachial PP		1.10 (1.03–1.18)†			
Central SBP			1.07 (1.01–1.14)‡		
Central PP				1.15 (1.07–1.24)*	
Arterial stiffness					1.06 (1.01–1.11)‡

Roman et al *Hypertension* 2007; 50: 197-203

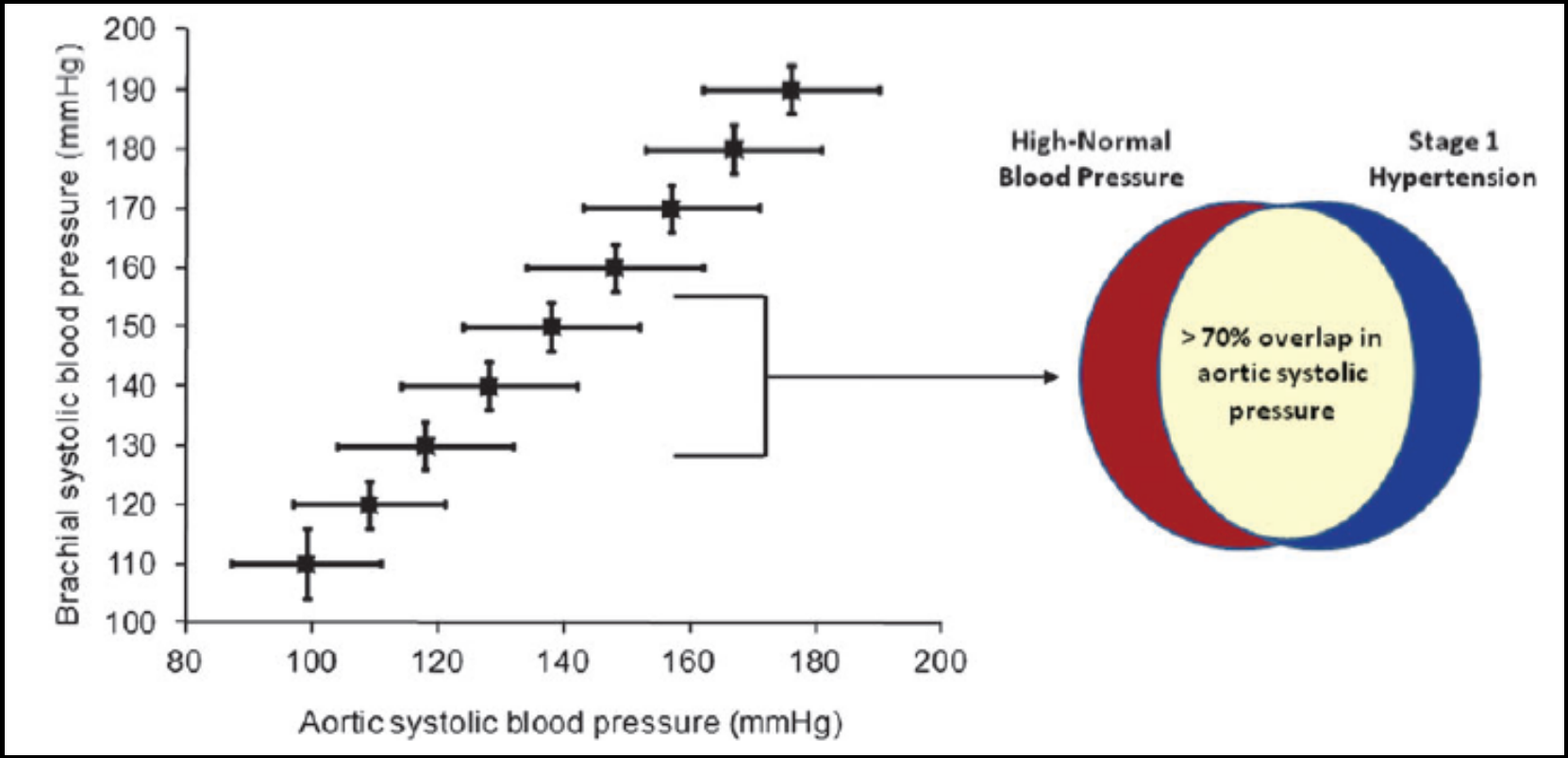
Prediction of cardiovascular events and all-cause mortality with central haemodynamics: a systematic review and meta-analysis

Charalambos Vlachopoulos[1*†], Konstantinos Aznaouridis[1†], Michael F. O'Rourke[2], Michel E. Safar[3], Katerina Baou[1], and Christodoulos Stefanadis[1]





Overlap in Aortic Systolic Pressure Despite no Overlap in Brachial Systolic Pressure (n=5648)



McEniery et al *Eur Heart J* 2014 (in Press)

2003 European Society of Hypertension–European Society of Cardiology guidelines for the management of arterial hypertension*

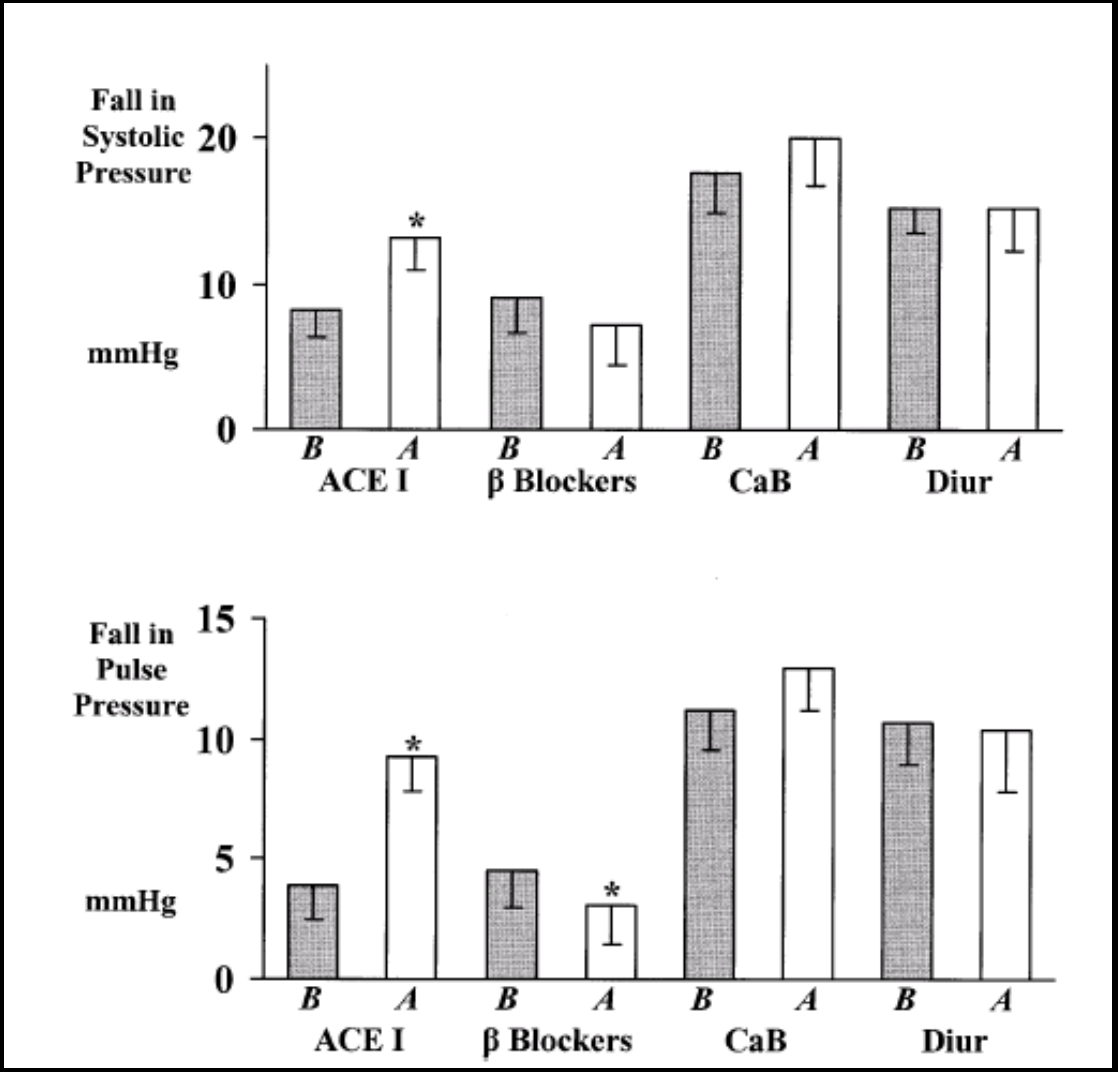
Guidelines Committee**

Journal of Hypertension 2003, 21:1011–1053

Central Blood Pressure

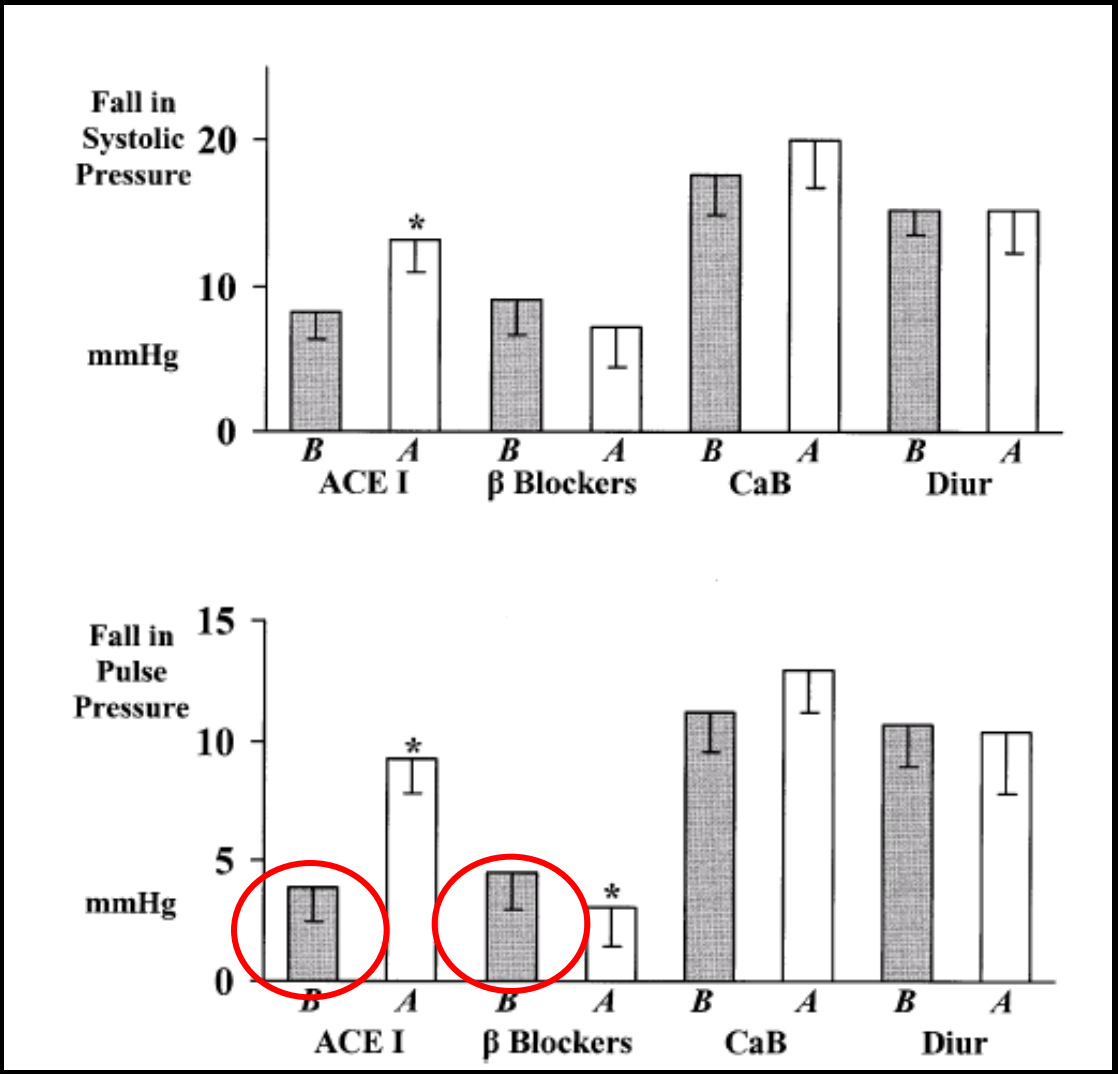
Is it differentially affected by drugs….?

Fall in SBP and PP at Brachial Artery and Aortic Root with Different Classes of Antihypertensive Agent



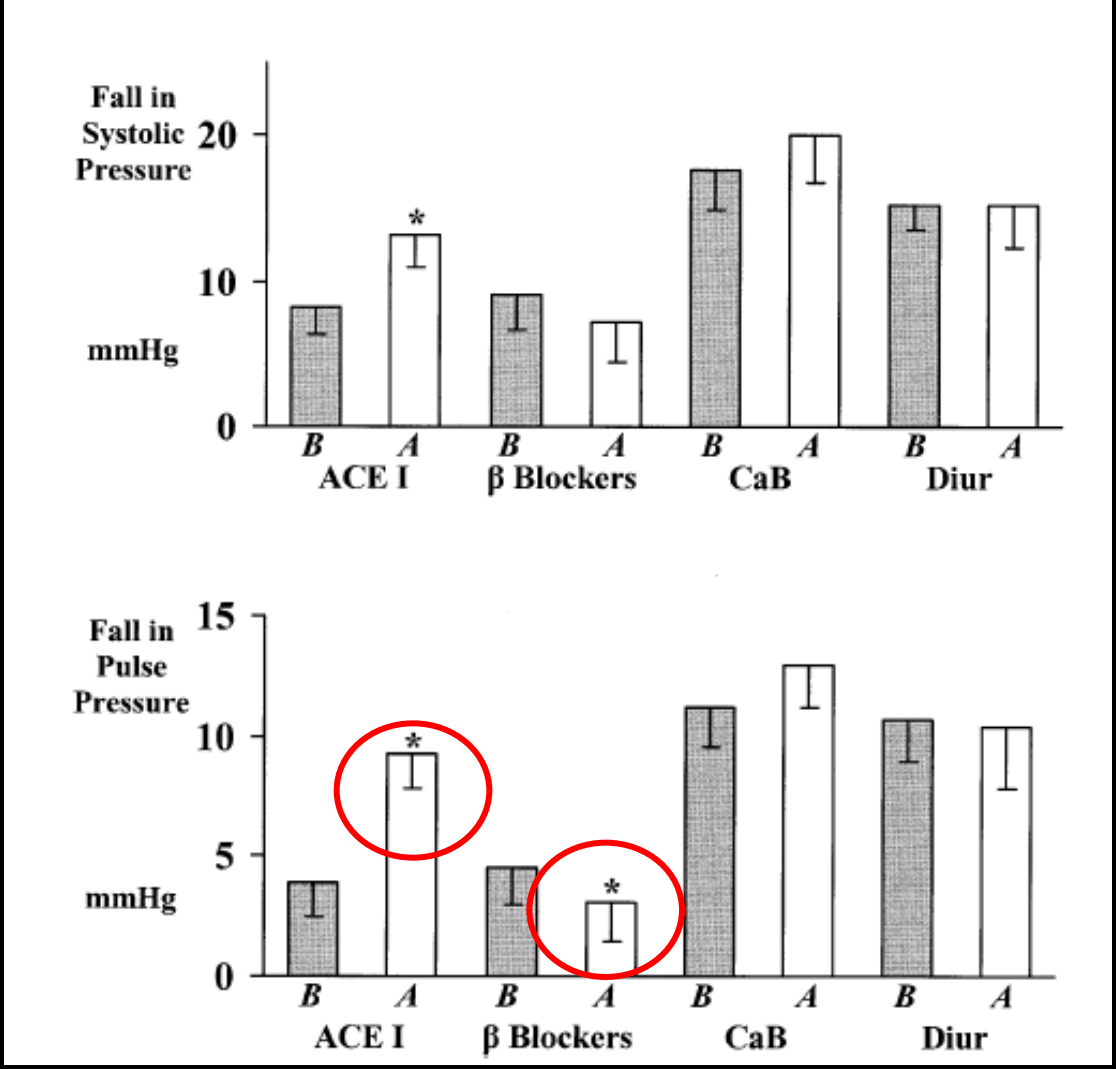
Morgan *et al.*, Am J Hypertens 2004; 17: 118-23

Fall in SBP and PP at Brachial Artery and Aortic Root with Different Classes of Antihypertensive Agent



Morgan *et al.*, Am J Hypertens 2004; 17: 118-23

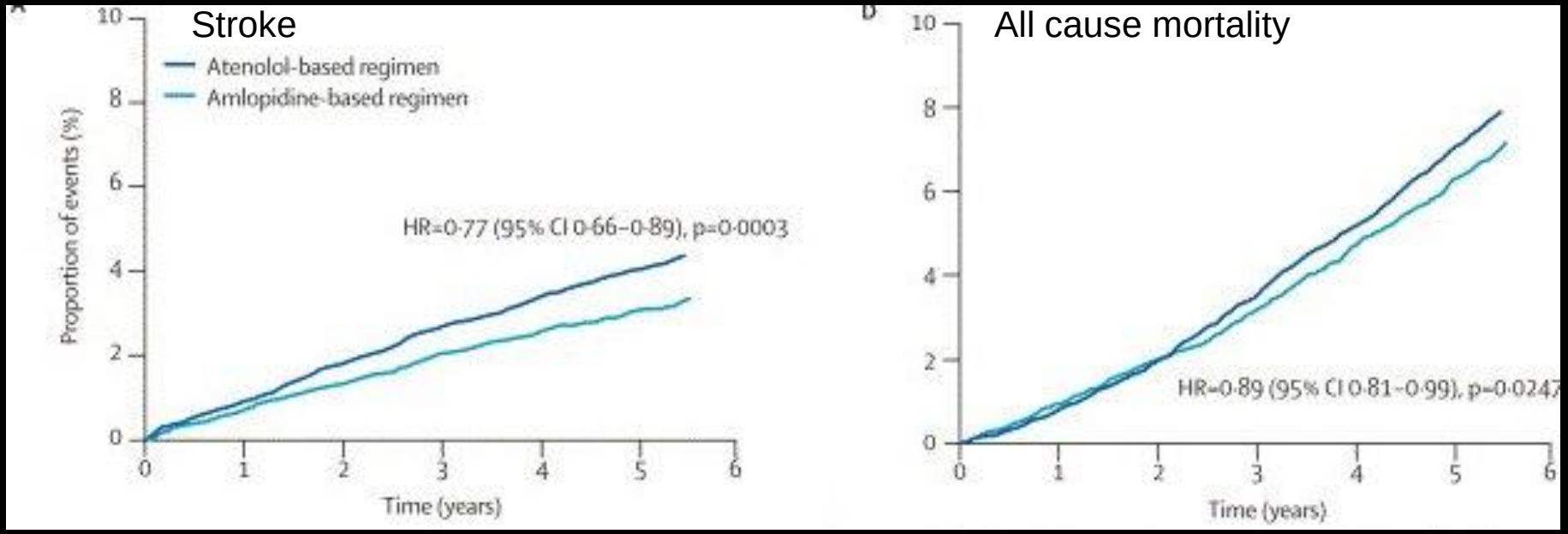
Fall in SBP and PP at Brachial Artery and Aortic Root with Different Classes of Antihypertensive Agent



Morgan *et al.*, Am J Hypertens 2004; 17: 118-23

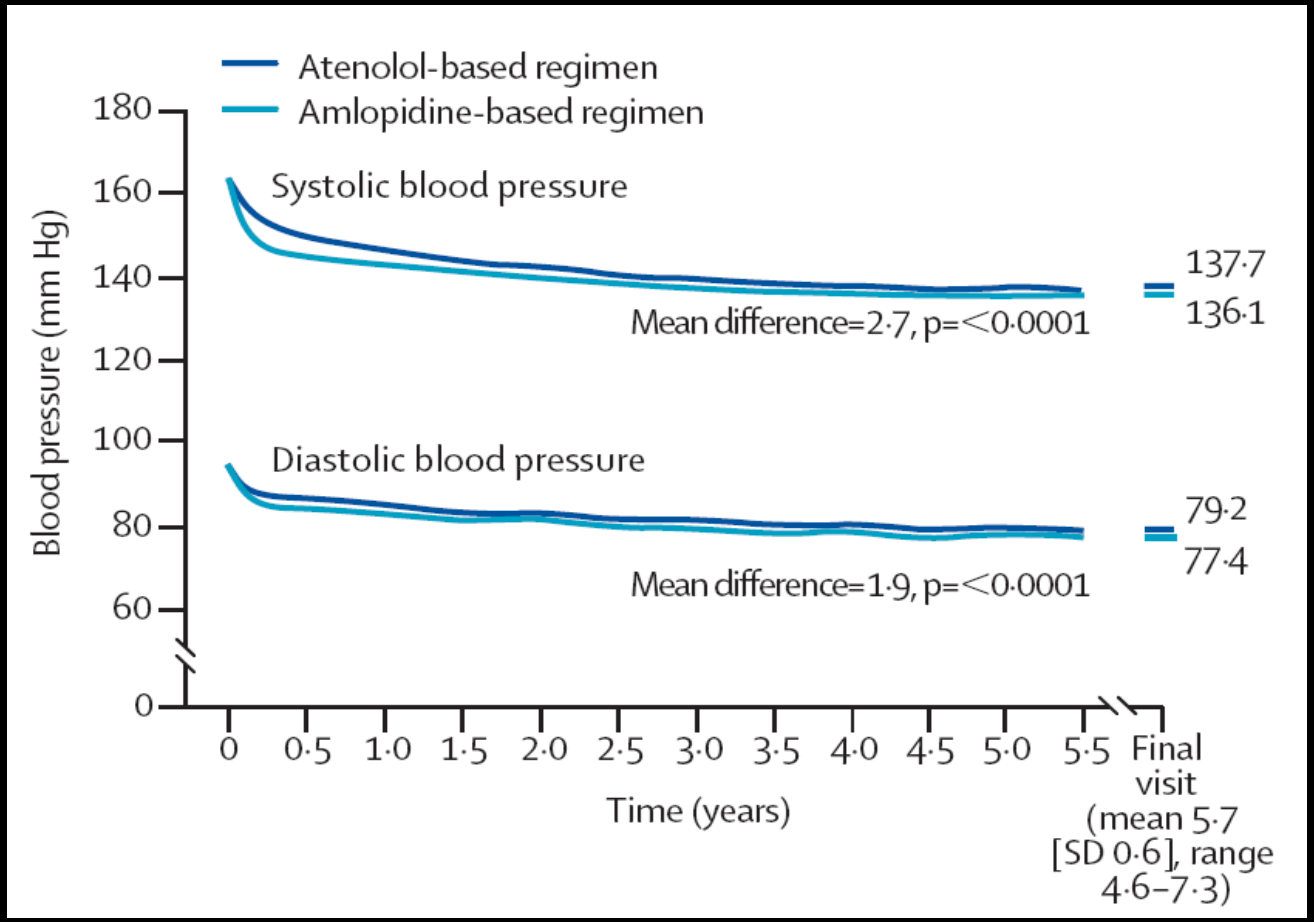
ASCOT Study

n=19,257, mean age 63



B Dahlof et al. Lancet 2005;366:895

Blood Pressure in ACSOT



B Dahlof et al. Lancet 2005;**366**:895

Benefit beyond blood pressure reduction……?

Hypertension

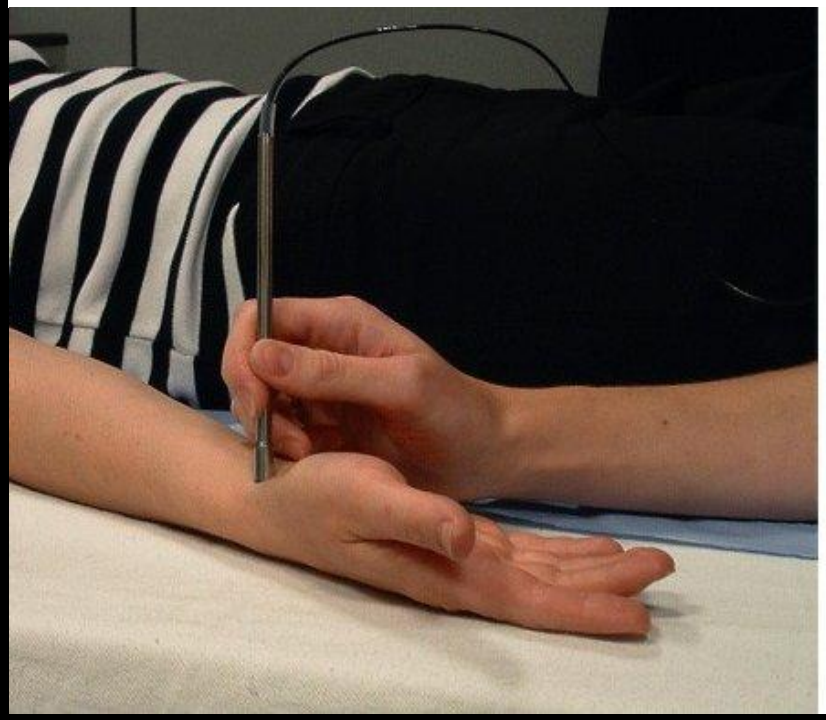
Differential Impact of Blood Pressure–Lowering Drugs on Central Aortic Pressure and Clinical Outcomes

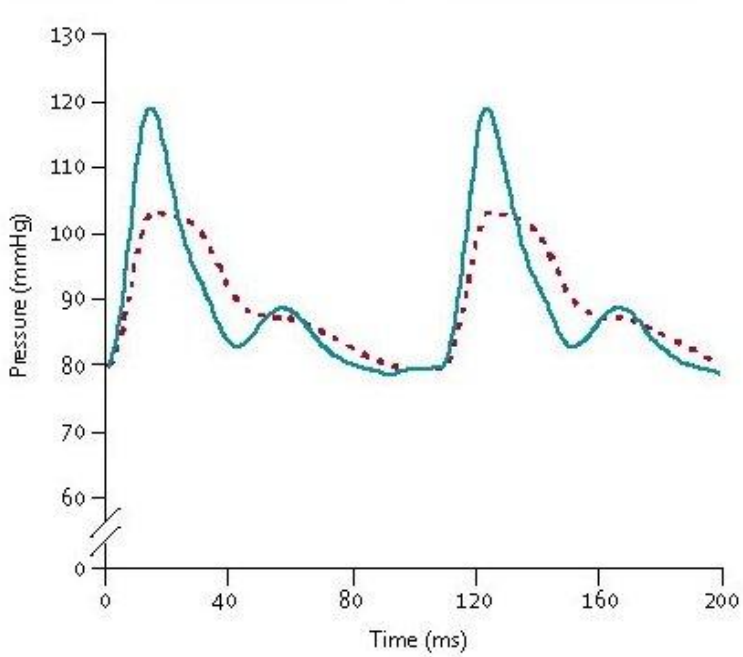
Principal Results of the Conduit Artery Function Evaluation (CAFE) Study

The CAFE Investigators, for the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) Investigators

CAFE Steering Committee and Writing Committee: Bryan Williams, MD, FRCP; Peter S. Lacy, PhD; Simon M. Thom, MD, FRCP; Kennedy Cruickshank, MD; Alice Stanton, MB, PhD, FRCPI; David Collier, MBBS, PhD; Alun D. Hughes, MBBS, PhD; H. Thurston, MD, FRCP

Study Advisor: Michael O'Rourke, MD, FRACP



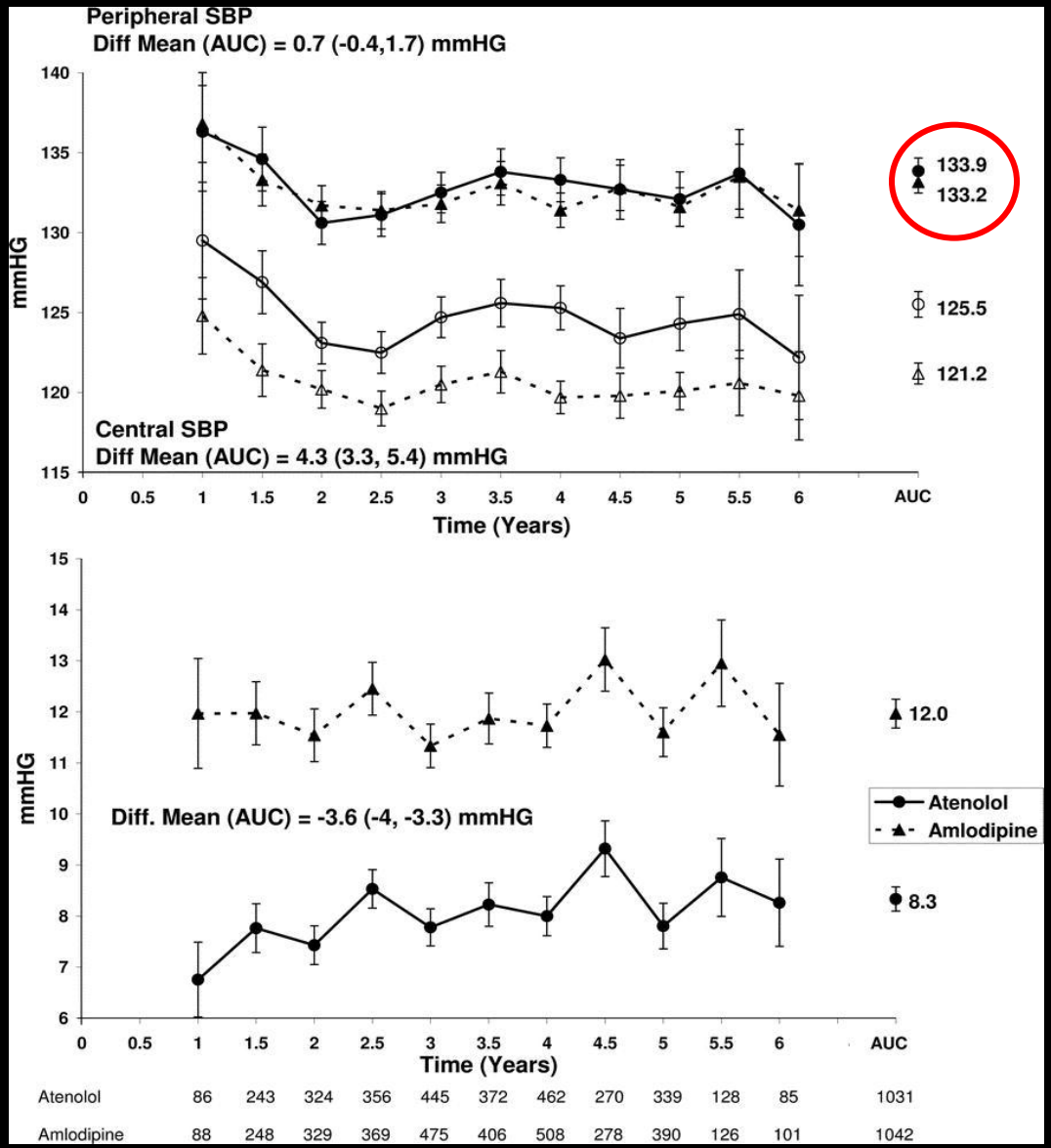


Wilkinson et al. *Lancet* 2006; 367:267-9

Effects of Atenolol / Thiazide and Amlodipine / Perindopril on Systolic Blood Pressure in the CAFÉ Study

Systolic BP

Systolic Pressure Difference (Brachial minus Central Aortic)



CAFE Investigators, Circulation 2006; 113: e-pub

Effects of Atenolol / Thiazide and Amlodipine / Perindopril on Systolic Blood Pressure in the CAFÉ Study

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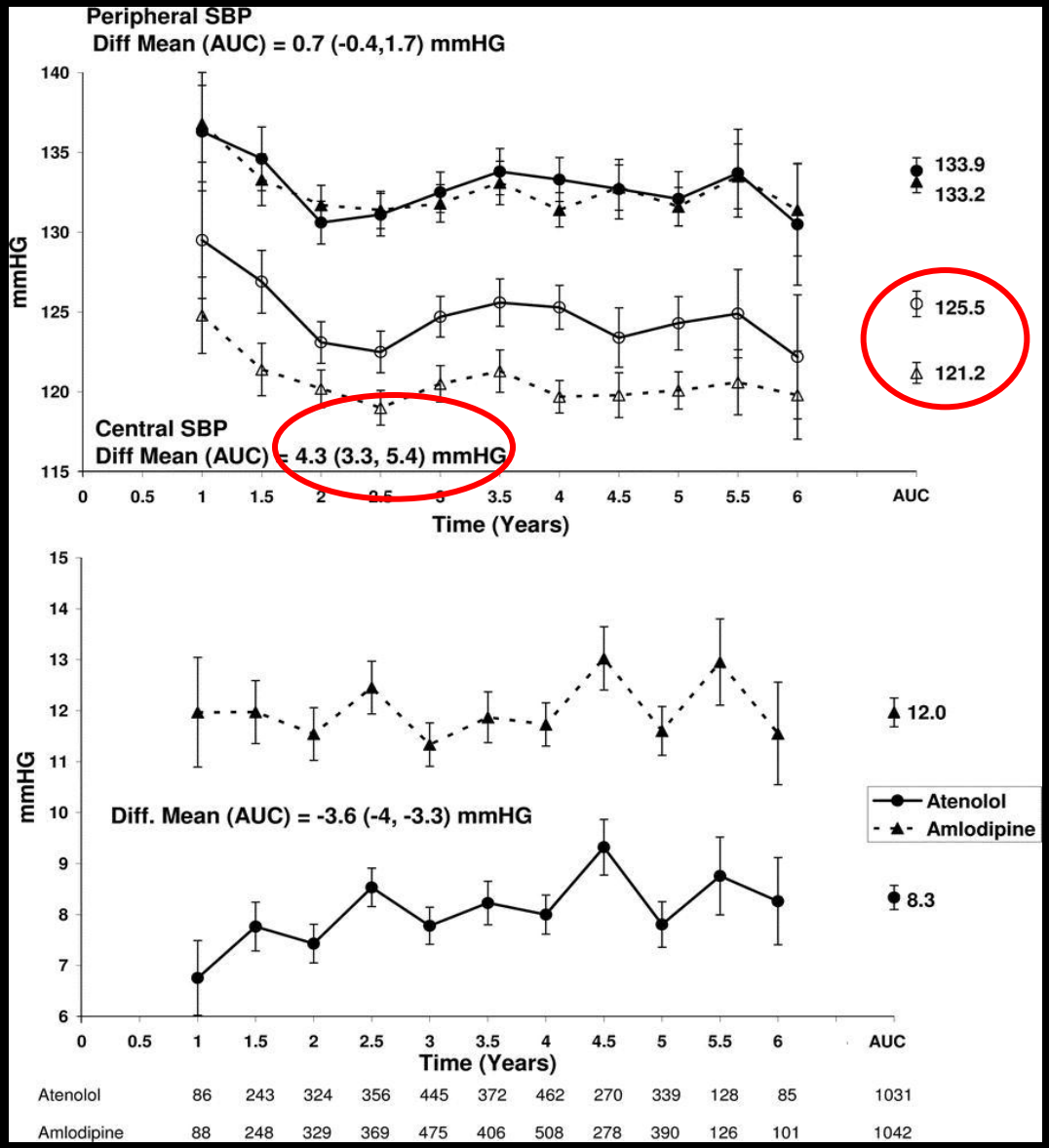
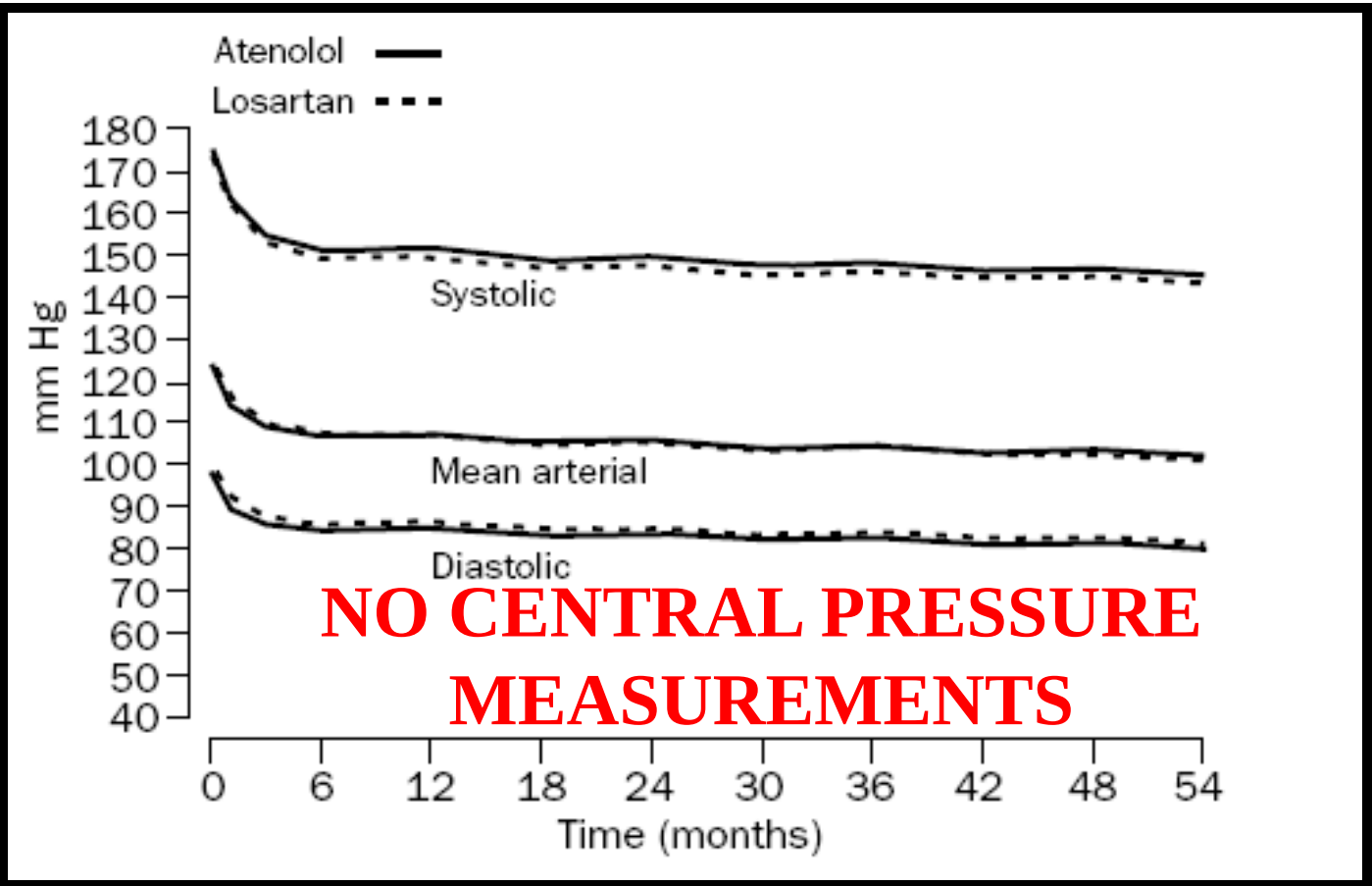


CAFE Investigators, Circulation 2006; 113: e-pub

Articles

Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol

*Björn Dahlöf, Richard B Devereux, Sverre E Kjeldsen, Stevo Julius, Gareth Beevers, Ulf de Faire, Frej Fyhrquist, Hans Ibsen, Krister Kristiansson, Ole Lederballe-Pedersen, Lars H Lindholm, Markku S Nieminen, Per Omvik, Suzanne Oparil, Hans Wedel, for the LIFE study group**



NO CENTRAL PRESSURE MEASUREMENTS

Dahlof et al. *Lancet* 2002;**359**:995

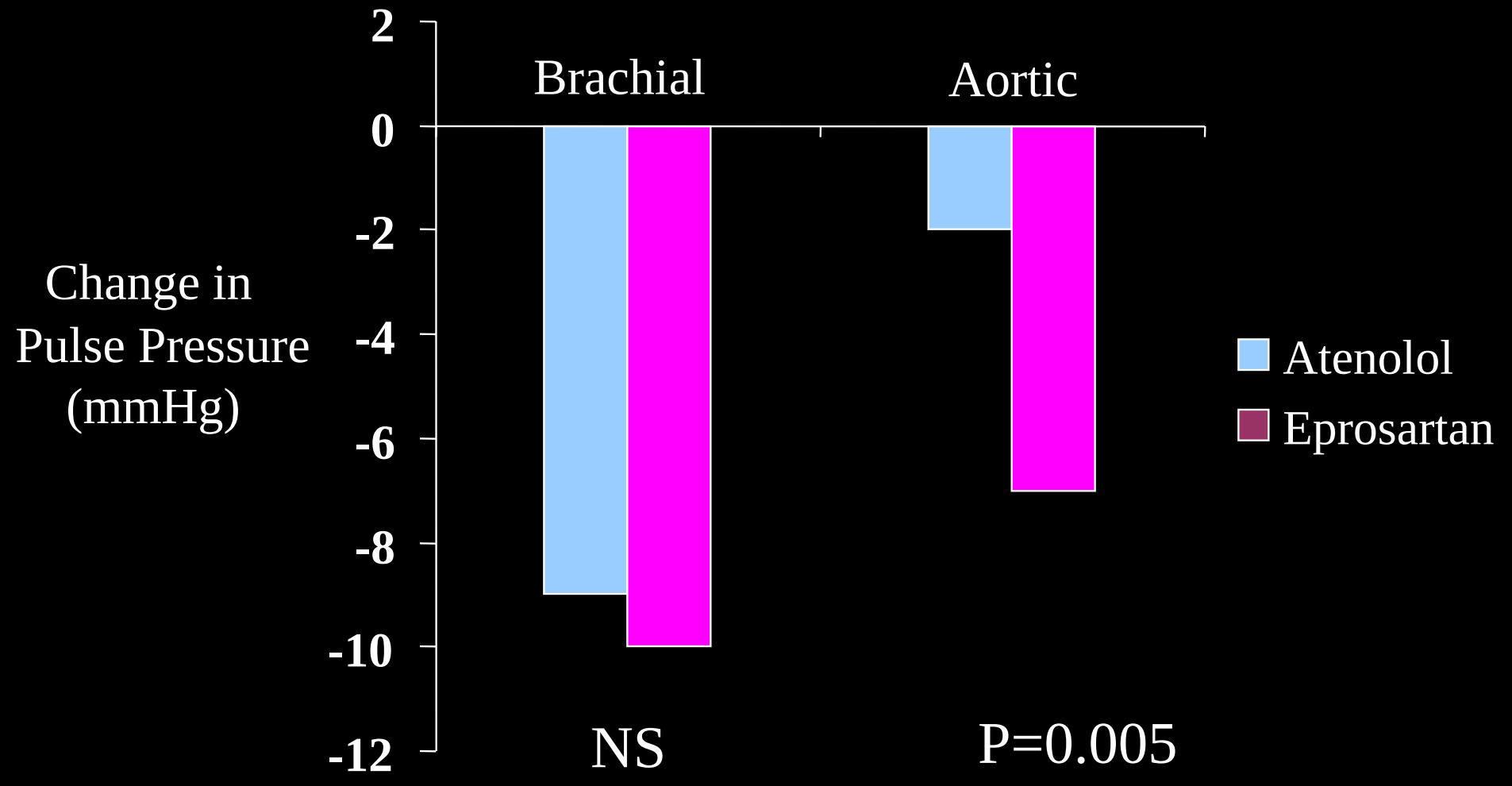
Atenolol and Eprosartan: Differential Effects on Central Blood Pressure and Aortic Pulse Wave Velocity

Zahid Dhakam, Carmel M. McEniery, Yasmin,
John R. Cockcroft, Morris J. Brown, and Ian B. Wilkinson

Double Blind Randomised Cross Over Study

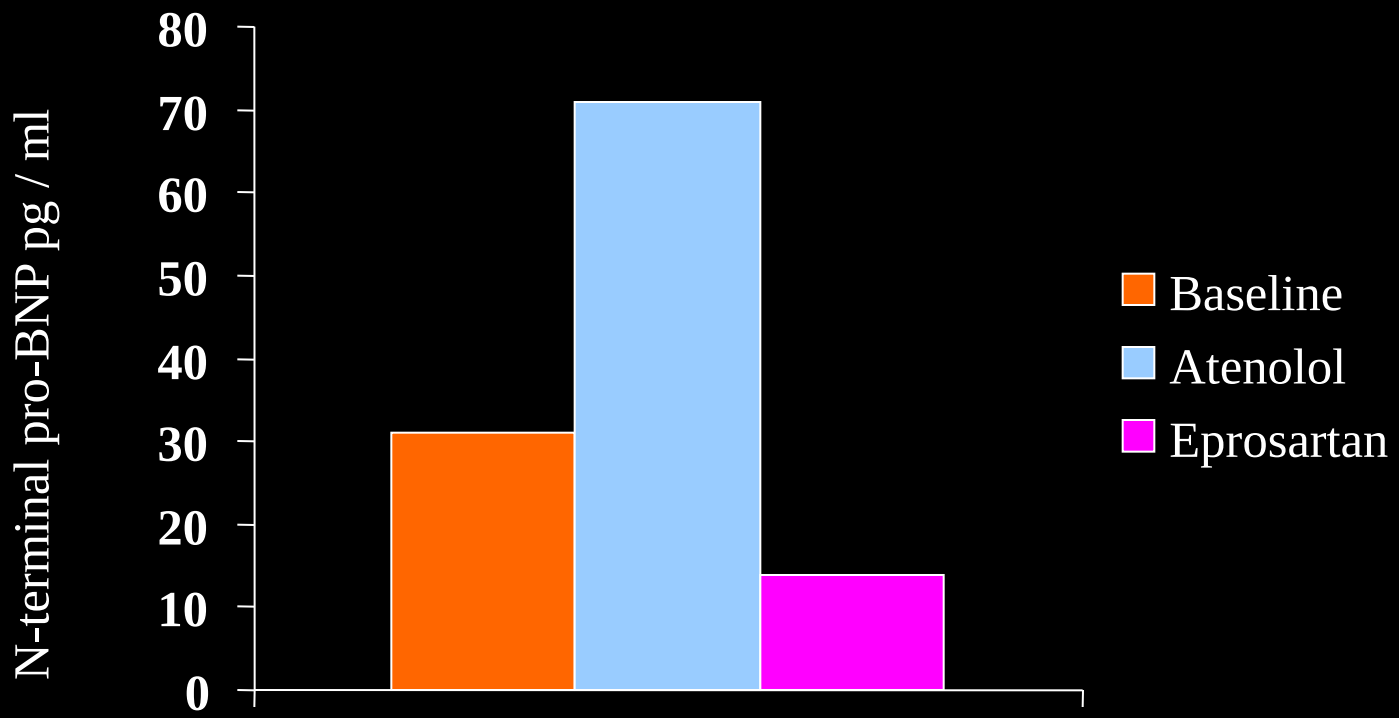
Dhakam et al *Am J Hypertens* 2006; 19: 214-219

Differential Effects of Eprosartan and Atenolol on Brachial and Aortic Pulse Pressures



Dhakam et al *Am J Hypertens* 2006; 19: 214-219

Effect of Eprosartan or Atenolol on N-terminal pro-BNP



Dhakam et al *Am J Hypertens* 2006; 19: 214-219

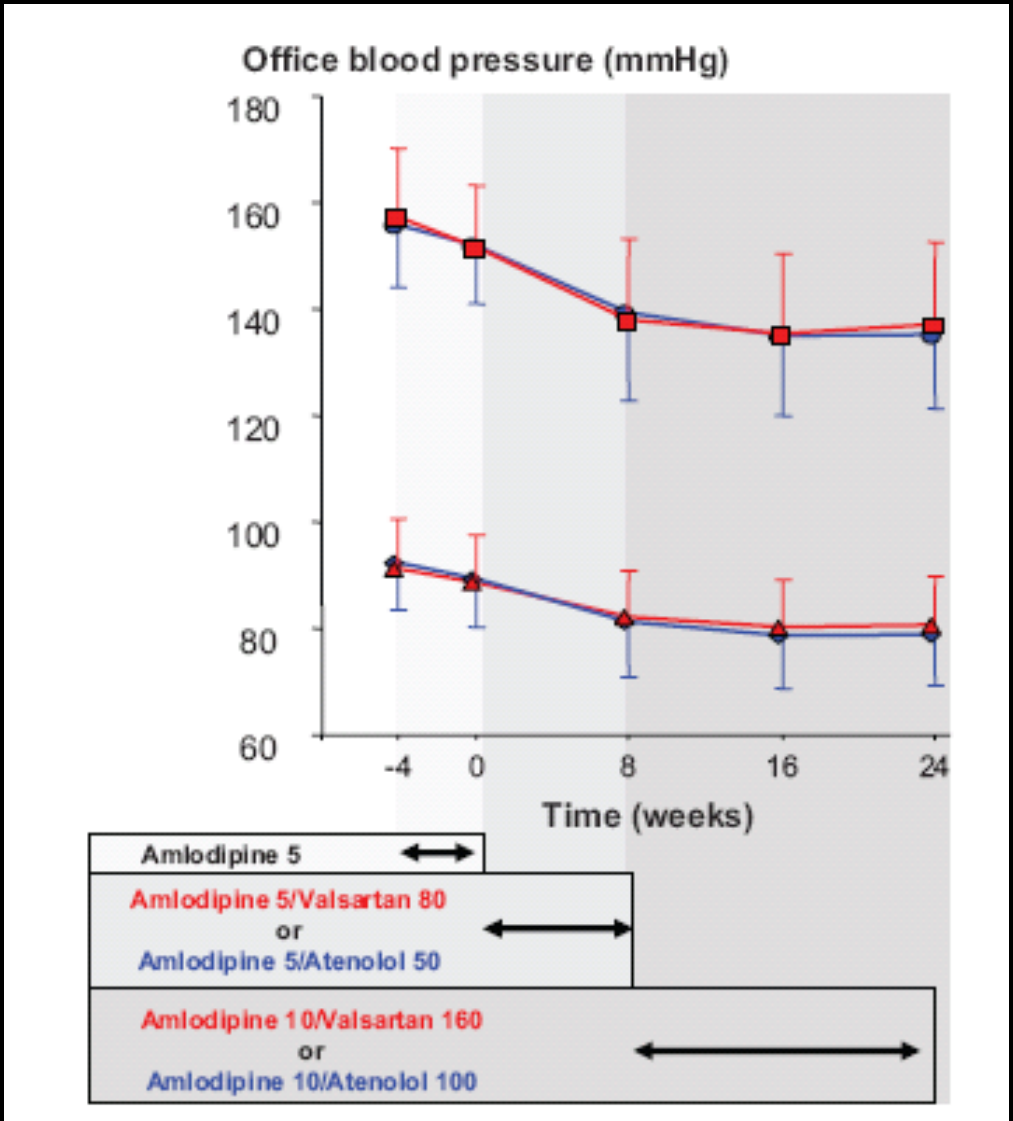
Amlodipine-Valsartan Combination Decreases Central Systolic Blood Pressure More Effectively Than the Amlodipine-Atenolol Combination

The EXPLOR Study

Pierre Boutouyrie, Assya Achouba, Patrick Trunet, Stéphane Laurent, for the EXPLOR Trialist Group

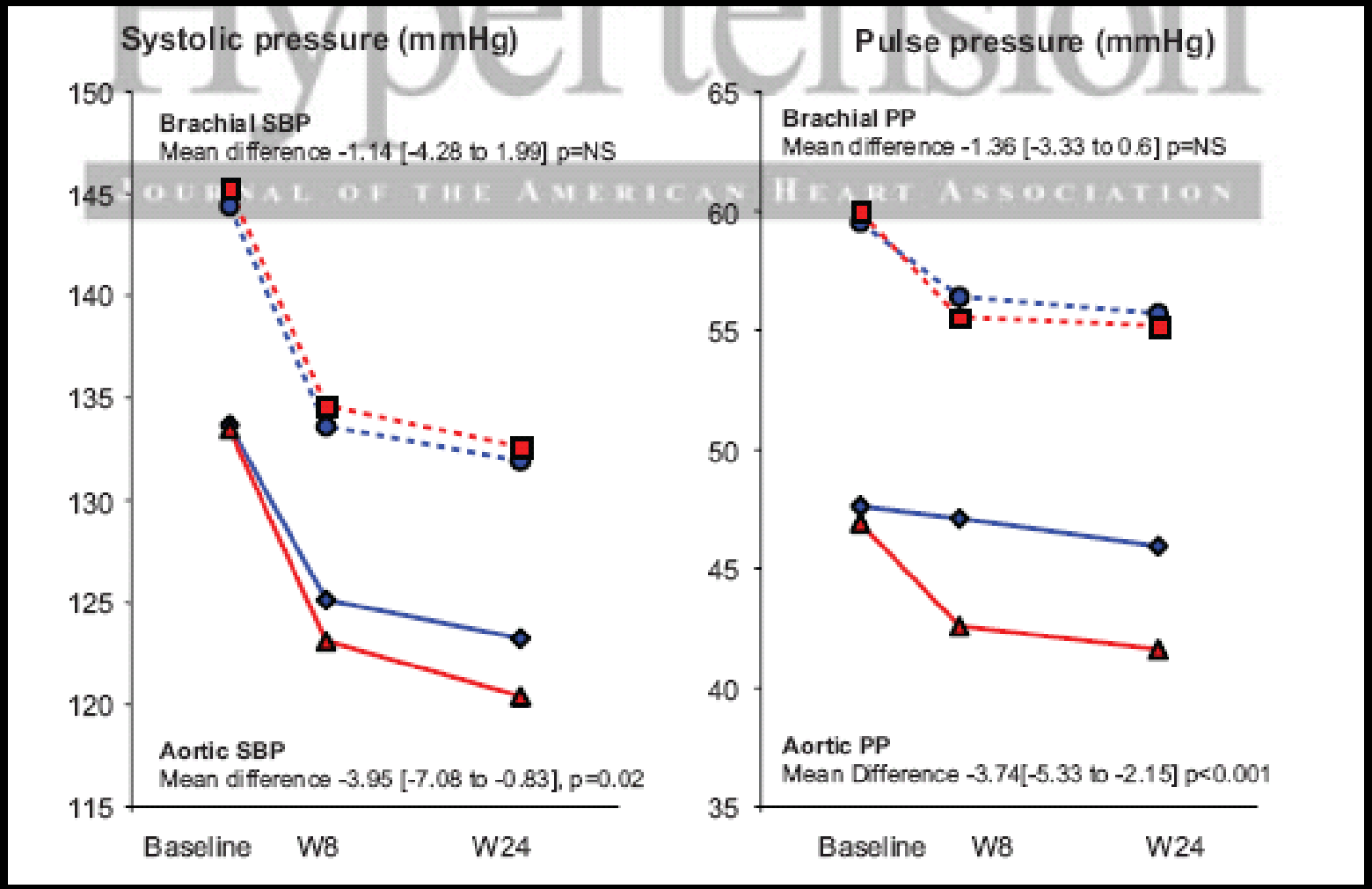
Boutouyrie et al *Hypertension* 2010 (e-Pub ahead of print)

Effect of Amlodipine/Valsartan or Amlodipine/Atenolol on Peripheral Blood Pressure



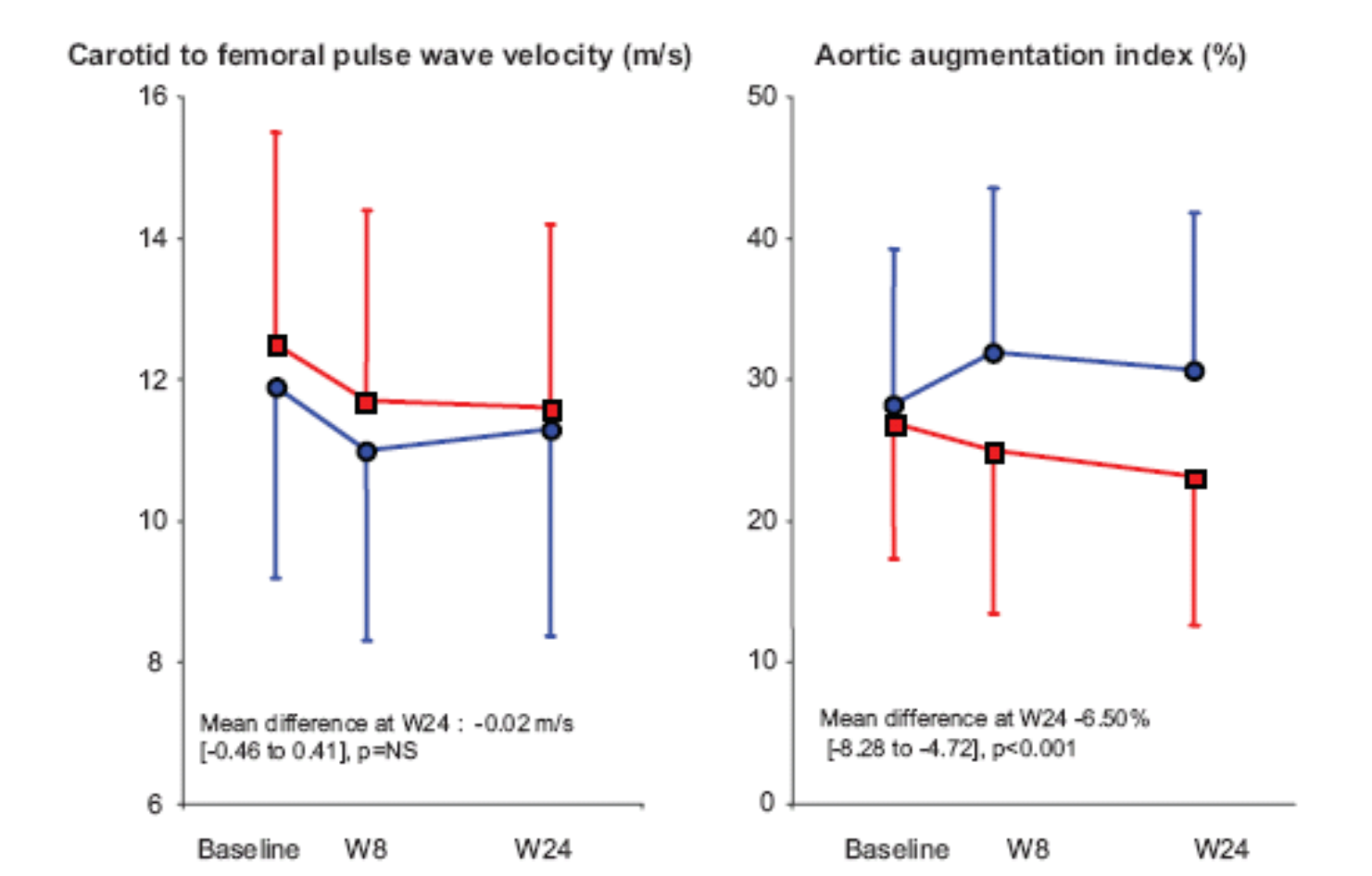
Boutouyrie et al *Hypertension* 2010 (e-Pub ahead of print)

Effect of Amlodipine/Valsartan orAmlodipine/Atenolol on Central Blood Pressure



Boutouyrie et al *Hypertension* 2010 (e-Pub ahead of print)

Effect of Amlodipine/Valsartan orAmlodipine/Atenolol on aPWV and AIx



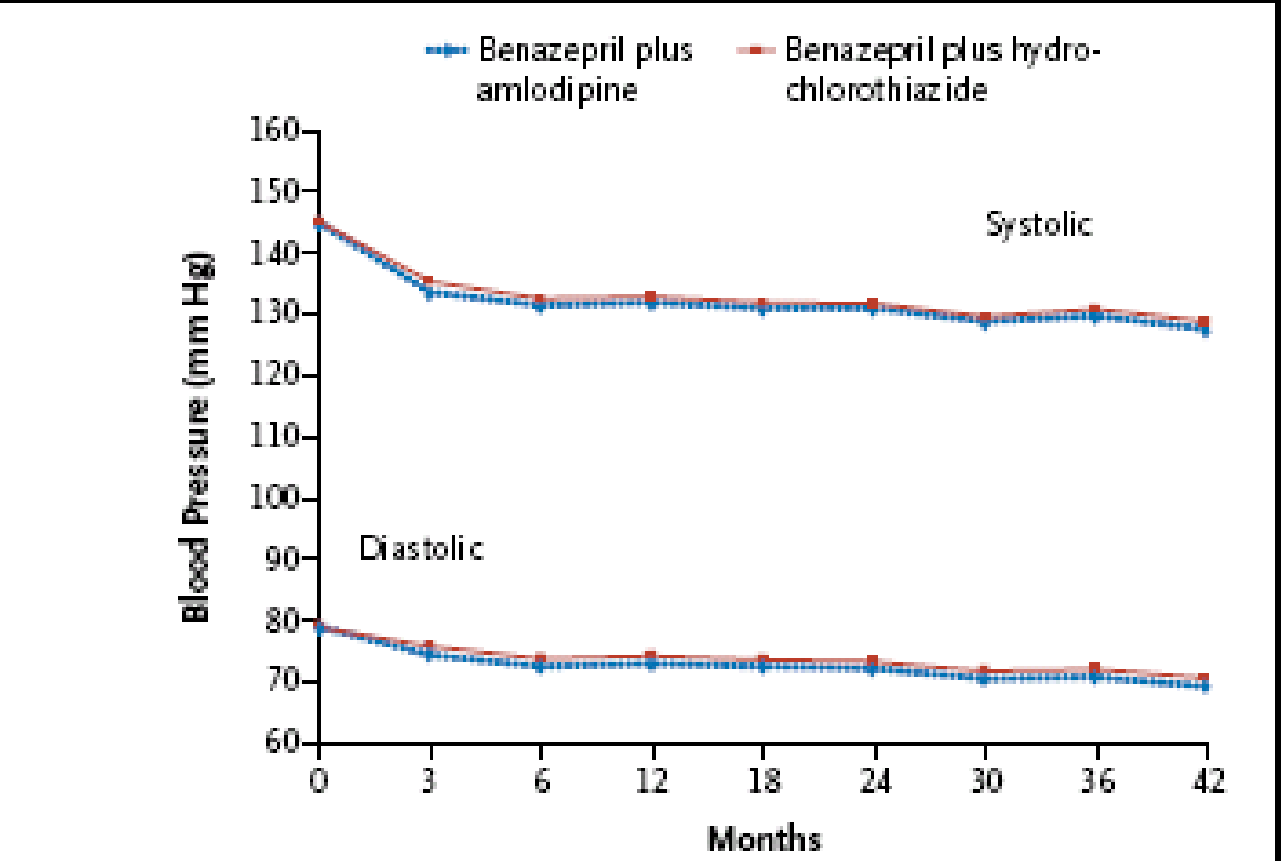
Boutouyrie et al *Hypertension* 2010 (e-Pub ahead of print)

Benazepril plus Amlodipine or Hydrochlorothiazide for Hypertension in High-Risk Patients

Kenneth Jamerson, M.D., Michael A. Weber, M.D., George L. Bakris, M.D., Björn Dahlöf, M.D., Bertram Pitt, M.D., Victor Shi, M.D., Allen Hester, Ph.D., Jitendra Gupte, M.S., Marjorie Gatlin, M.D., and Eric J. Velazquez, M.D., for the ACCOMPLISH trial investigators*

Jamerson et al *N Engl J Med* 2008; 359: 2417-2428

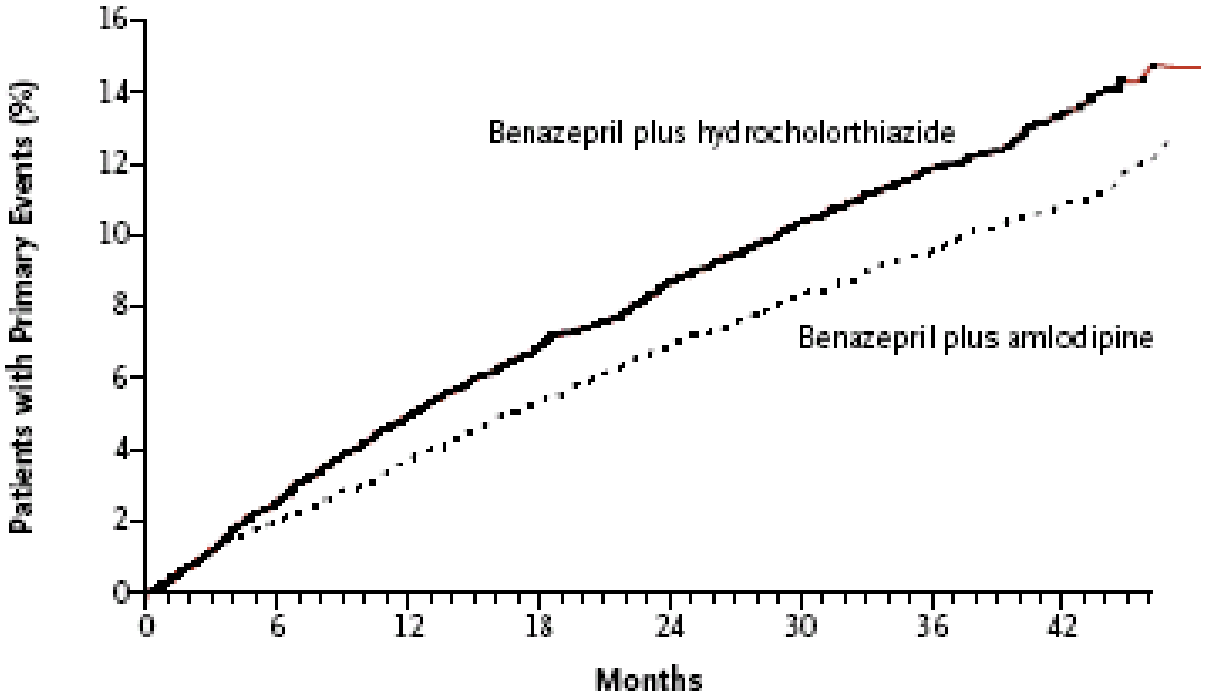
Effects of Treatment on Systolic and Diastolic Blood Pressure



No. at Risk									
Benazepril plus amlodipine	5740	5517	5404	5178	5010	4866	4298	2804	1074
Benazepril plus hydrochlorothiazide	5757	5537	5408	5222	5033	4825	4299	2529	1042

Jamerson et al *N Engl J Med* 2008; 359: 2417-2428

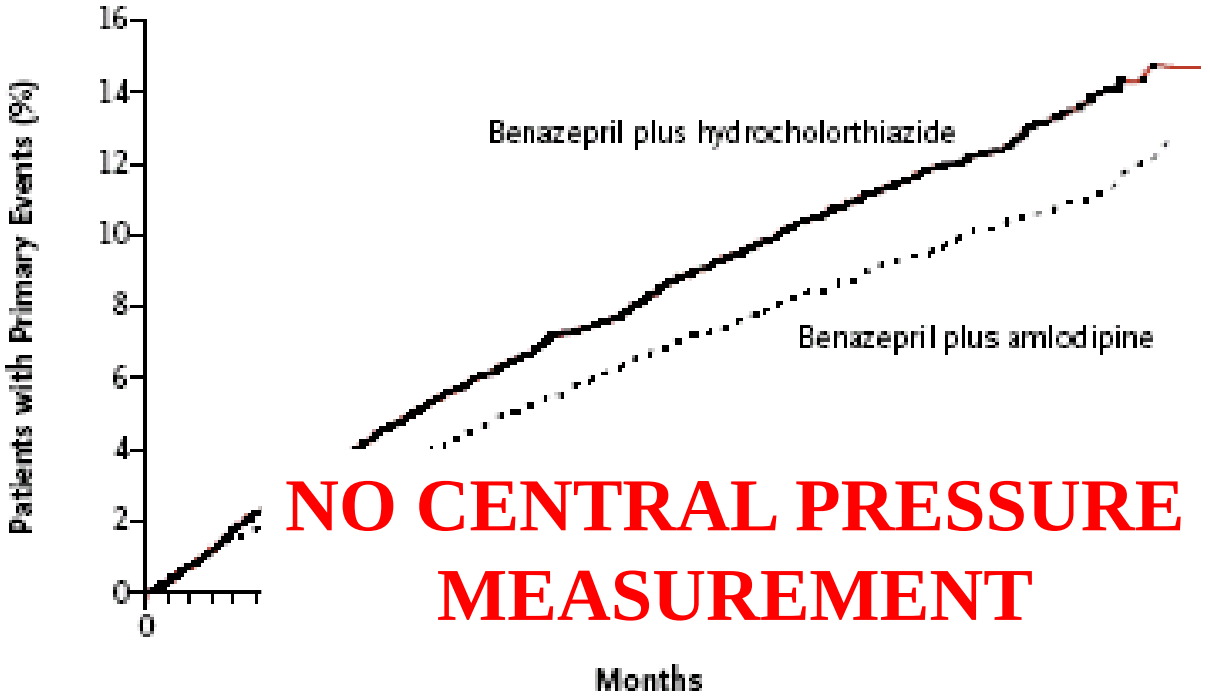
Effects of Treatment on Primary Composite End Point



No. at Risk							
Benazepril plus amlodipine	5512	5317	5141	4959	4739	2826	1447
Benazepril plus hydrochlorothiazide	5483	5274	5082	4892	4655	2749	1390

Jamerson et al *N Engl J Med* 2008; 359: 2417-2428

Effects of Treatment on Primary Composite End Point



No. at Risk							
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Benazepril plus hydrochlorothiazide	5483	5274	5082	4892	4655	2749	1390

Jamerson et al *N Engl J Med* 2008; 359: 2417-2428

Differential Effects Between a Calcium Channel Blocker and a Diuretic When Used in Combination With Angiotensin II Receptor Blocker on Central Aortic Pressure in Hypertensive Patients

Yoshio Matsui, Kazuo Eguchi, Michael F. O'Rourke, Joji Ishikawa, Hiroshi Miyashita, Kazuyuki Shimada, Kazuomi Kario

Matsui et al *Hypertension* 2009; 54: 716-723

Changes in Aortic Parameters in the Olmesartan/Azelnidipine And Olmesartan/Hydrochlorthiazide Groups

Variable	Olmesartan/Azelnidipine (n=103)	Olmesartan/HCTZ (n=104)	Between-Group Difference*	P*
Aortic PWV, m/s				
Baseline	10.2±2.0	10.3±2.2		
End of study	8.9±1.9	9.8±2.2		
End of study*	8.9 (8.7 to 9.2)	9.7 (9.5 to 10.0)	0.8 (0.5 to 1.1)	<0.001
Aortic AIx, %				
Baseline	34.7±6.3	34.6±8.1		
End of study	31.2±8.5	32.0±9.6		
End of study*	30.7 (29.3 to 32.2)	31.8 (30.4 to 33.2)	1.1 (−1.0 to 3.0)	0.30
Aortic AIx@75, %				
Baseline	31.7±6.3	31.4±6.8		
End of study	26.0±7.5	28.4±7.9		
End of study*	25.4 (24.3 to 26.5)	28.2 (27.2 to 29.3)	2.8 (1.3 to 4.4)	<0.001

Matsui et al *Hypertension* 2009; 54: 716-723

Changes in Brachial Blood Pressure in the Olmesartan/Azelnidipine and Olmesartan/Hydrochlorthiazide Groups

Variable	Olmesartan/Azelnidipine (n=103)	Olmesartan/HCTZ (n=104)	Between-Group Difference*	P*
Brachial SBP, mm Hg				
Baseline	153.9±18.3	155.0±19.4		
End of study	131.8±18.8	134.4±21.2		
End of study*	131.7 (128.2 to 135.2)	134.4 (130.9 to 137.8)	2.6 (−2.2 to 7.5)	0.29
Brachial DBP, mm Hg				
Baseline	83.3±10.0	82.9±10.5		
End of study	71.2±9.1	74.4±10.5		
End of study*	71.2 (69.6 to 72.7)	74.3 (72.8 to 75.9)	3.2 (1.0 to 5.4)	0.005
Brachial PP, mm Hg				
Baseline	70.5±16.4	72.1±17.3		
End of study	60.6±15.9	60.0±18.0		
End of study*	60.6 (58.1 to 63.2)	59.9 (57.4 to 62.4)	−0.8 (−4.3 to 2.8)	0.68
MAP, mm Hg				
Baseline	109.0±11.6	109.0±12.0		
End of study	91.2±11.6	95.8±13.2		
End of study*	91.2 (89.0 to 93.3)	95.7 (93.5 to 97.8)	4.5 (1.5 to 7.6)	0.004

Matsui et al *Hypertension* 2009; 54: 716-723

Changes in Central Blood Pressure in the Olmesartan/Azelnidipine and Olmesartan/Hydrochlorthiazide Groups

Central SBP, mm Hg				
Baseline	143.8±17.5	145.1±19.5		
End of study	120.1±18.4	125.3±21.4		
End of study*	119.9 (116.4 to 123.5)	125.1 (121.6 to 128.6)	5.2 (0.3 to 10.2)	0.039
Central DBP, mm Hg				
Baseline	84.6±10.2	84.0±10.6		
End of study	72.1±9.3	75.3±10.7		
End of study*	72.1 (70.5 to 73.6)	75.3 (73.8 to 76.9)	3.3 (1.1 to 5.5)	0.004
Central PP, mm Hg				
Baseline	59.2±15.6	61.0±17.3		
End of study	48.0±15.1	50.0±18.0		
End of study*	47.9 (45.3 to 50.5)	49.7 (47.1 to 52.3)	1.8 (−1.9 to 5.4)	0.33
HR, bpm				
Baseline	68.8±11.7	68.2±11.7		
End of study	64.9±10.3	67.4±11.8		
End of study*	64.9 (63.5 to 66.2)	67.7 (66.4 to 69.1)	2.9 (0.9 to 4.8)	0.004

Matsui et al *Hypertension* 2009; 54: 716-723

Comparison of the Effects of Antihypertensive Agents on Central Blood Pressure and Arterial Stiffness in Isolated Systolic Hypertension

Isla S. Mackenzie, Carmel M. McEniery, Zahid Dhakam, Morris J. Brown, John R. Cockcroft, Ian B. Wilkinson

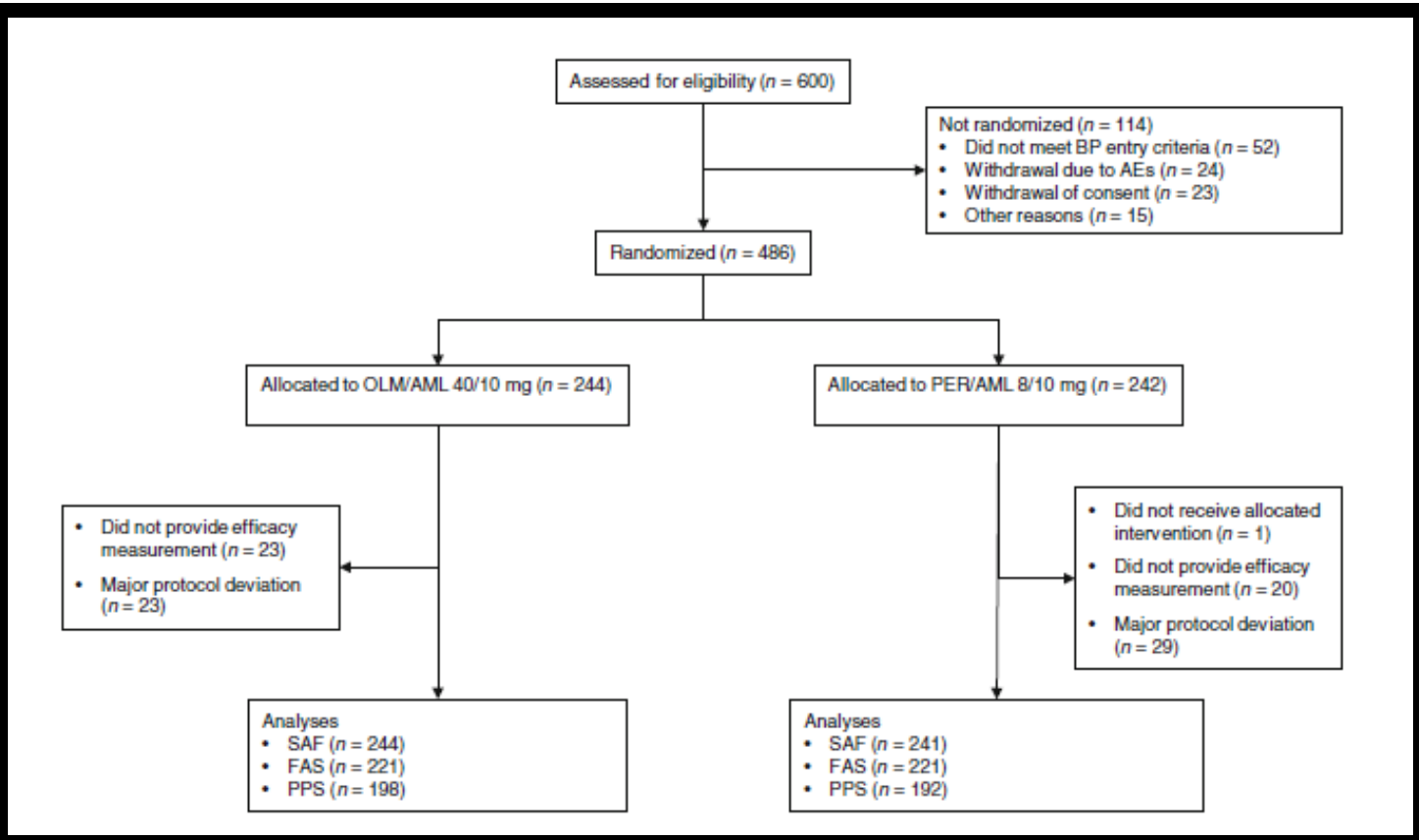
Table 2. Hemodynamic Indices Before and After the 10-Week Active Therapy Period

	Perindopril		Atenolol		Lercanidipine		Bendrofluazide		2-Way ANOVA, Time, Drug
Parameter	Placebo	10 wk	Placebo	10 wk	Placebo	10 wk	Placebo	10 wk	
Peripheral SBP, mm Hg	153±3	136±4*	156±2	138±4*	146±2	133±3*	154±3	140±3*	<0.001, 0.1
Peripheral DBP, mm Hg	80±2	75±2*	84±2	76±2*	80±2	79±3	85±2	82±3	<0.001, 0.3
Peripheral PP, mm Hg	72±4	61±4*	72±3	62±3*	66±3	54±4*	69±4	58±4*	<0.001, 0.3
Central SBP, mm Hg	140±4	123±4*	144±3	130±4*	132±2	118±3*	139±2	126±2*	<0.001, 0.02‡
Central PP, mm Hg	58±4	46±3*	59±2	53±3	51±3	38±4*	53±4	42±3*	<0.001, 0.02‡§
P1 height, mm Hg	42±3	36±3*	42±2	35±2*	37±2	30±2*	39±2	32±2*	<0.001, 0.1
PP amplification	1.33±0.08	1.35±0.06	1.24±0.03	1.17±0.02*	1.31±0.04	1.42±0.06	1.33±0.04	1.38±0.04	0.2, 0.03‡
MAP, mm Hg	104±2	96±2*	108±2	97±3*	102±2	97±2	109±2	102±2*	<0.001, 0.1
HR, bpm	71±3	73±3	67±2	57±3*	73±2	75±3	75±3	77±3	0.4, 0.001†‡§
AP, mm Hg	15±2	10±2*	17±2	19±2	14±2	8±2*	13±2	11±2	0.002, 0.02‡
AIx, %	25±3	20±4	29±2	34±2*	26±2	19±3*	25±3	24±3	0.2, 0.03†‡§
Aortic PWV, m/s	9.01±0.59	9.34±0.47	9.64±0.50	8.82±0.46	9.54±0.60	9.79±0.89	10.25±0.28	10.55±0.57	0.9, 0.4

Mackenzie et al *Hypertension* 2009; 54: 409-413

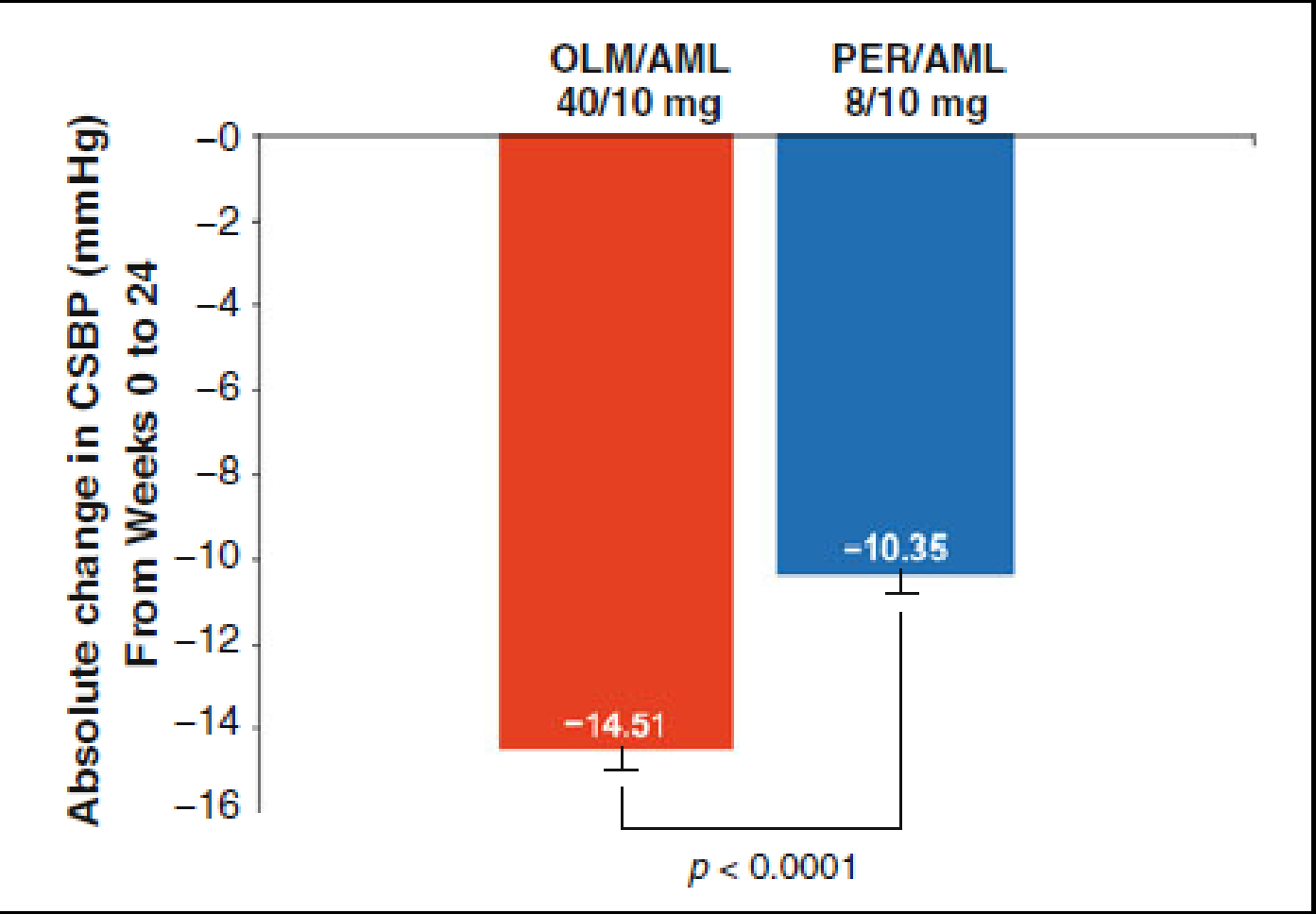
The Fixed-Dose Combination of Olmesartan/Amlodipine Was Superior in Central Aortic Blood Pressure Reduction Compared with Perindopril/Amlodipine: A Randomized, Double-Blind Trial in Patients with Hypertension

Luis Ruilope · Angie Schaefer



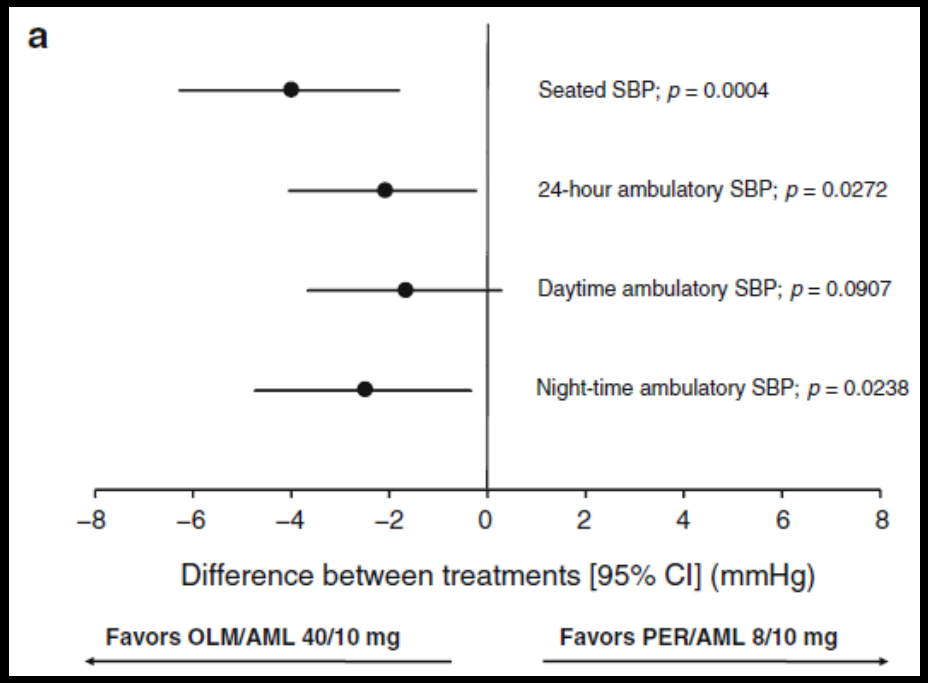
Ruilope & Schaefer *Adv Ther* 2013; 30: 1086-1099

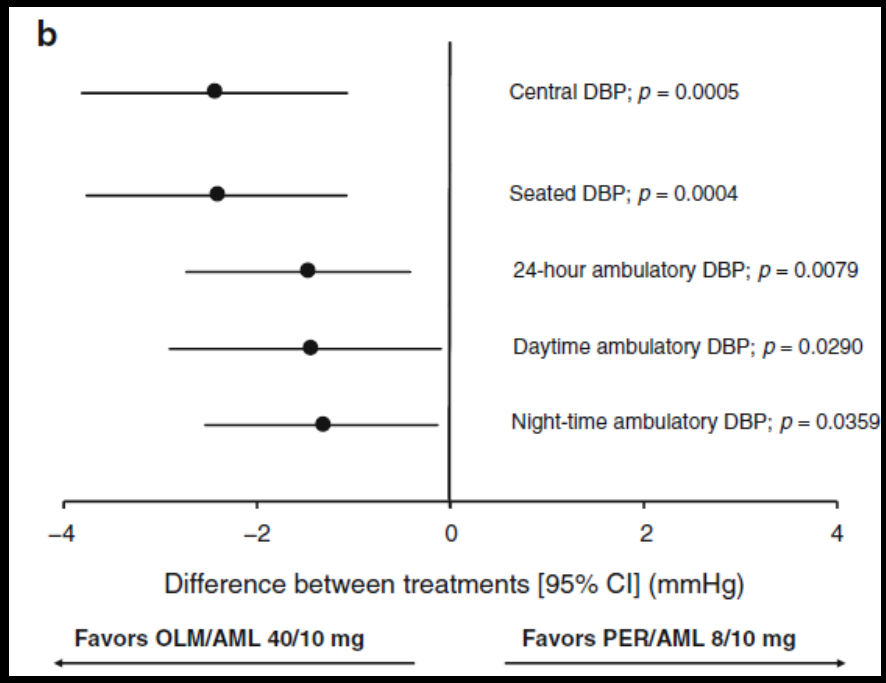
Absolute Change in Central Systolic Blood Pressure



Ruilope & Schaefer *Adv Ther* 2013; 30: 1086-1099

Forest Plot of the Differences Between Patients Treated with OLM/AML 40/10mg and PER/AML 8/10 mg





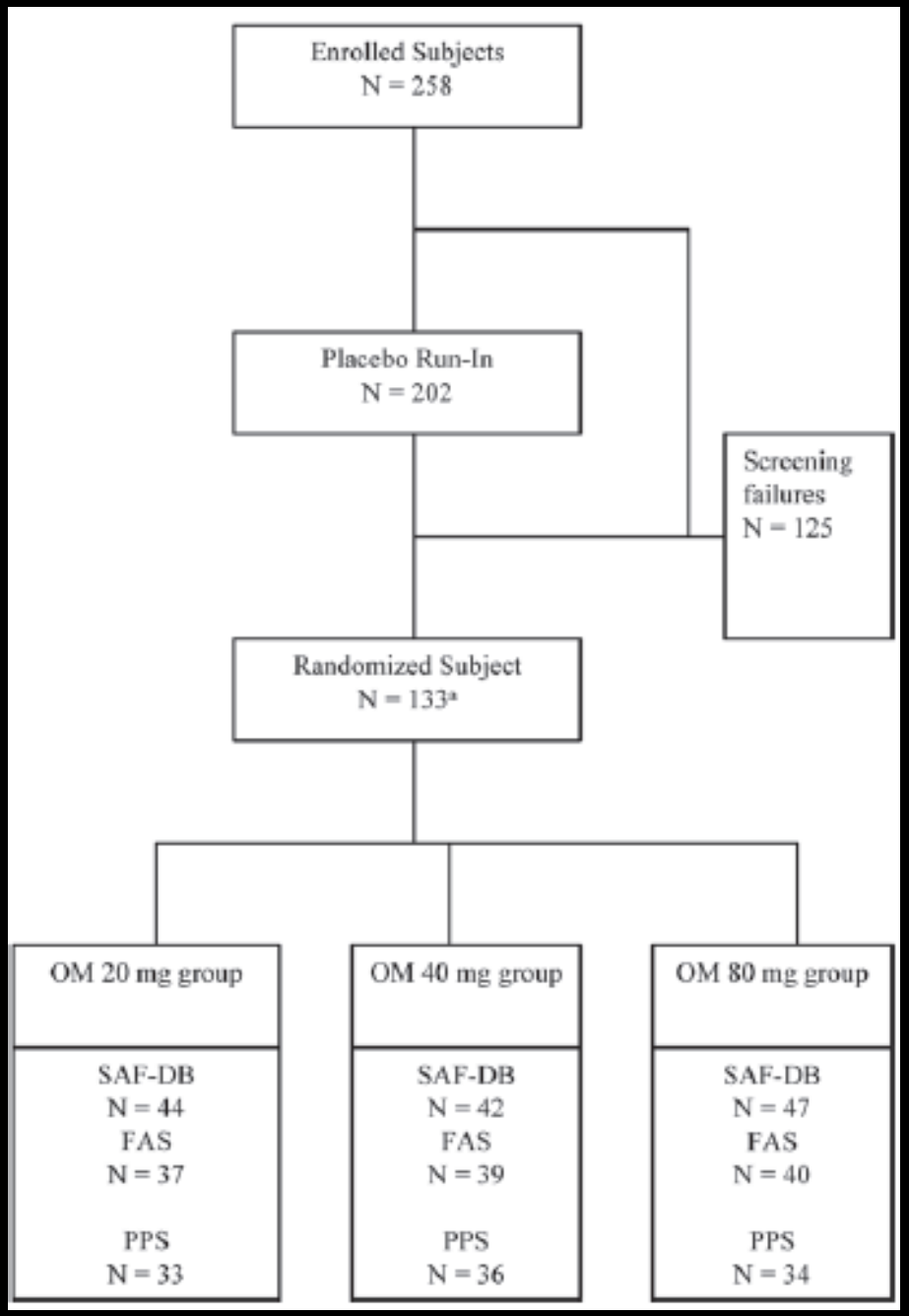
Ruilope & Schaefer *Adv Ther* 2013; 30: 1086-1099

Original Article

Dose-Dependent Arterial Destiffening and Inward Remodeling After Olmesartan in Hypertensives With Metabolic Syndrome

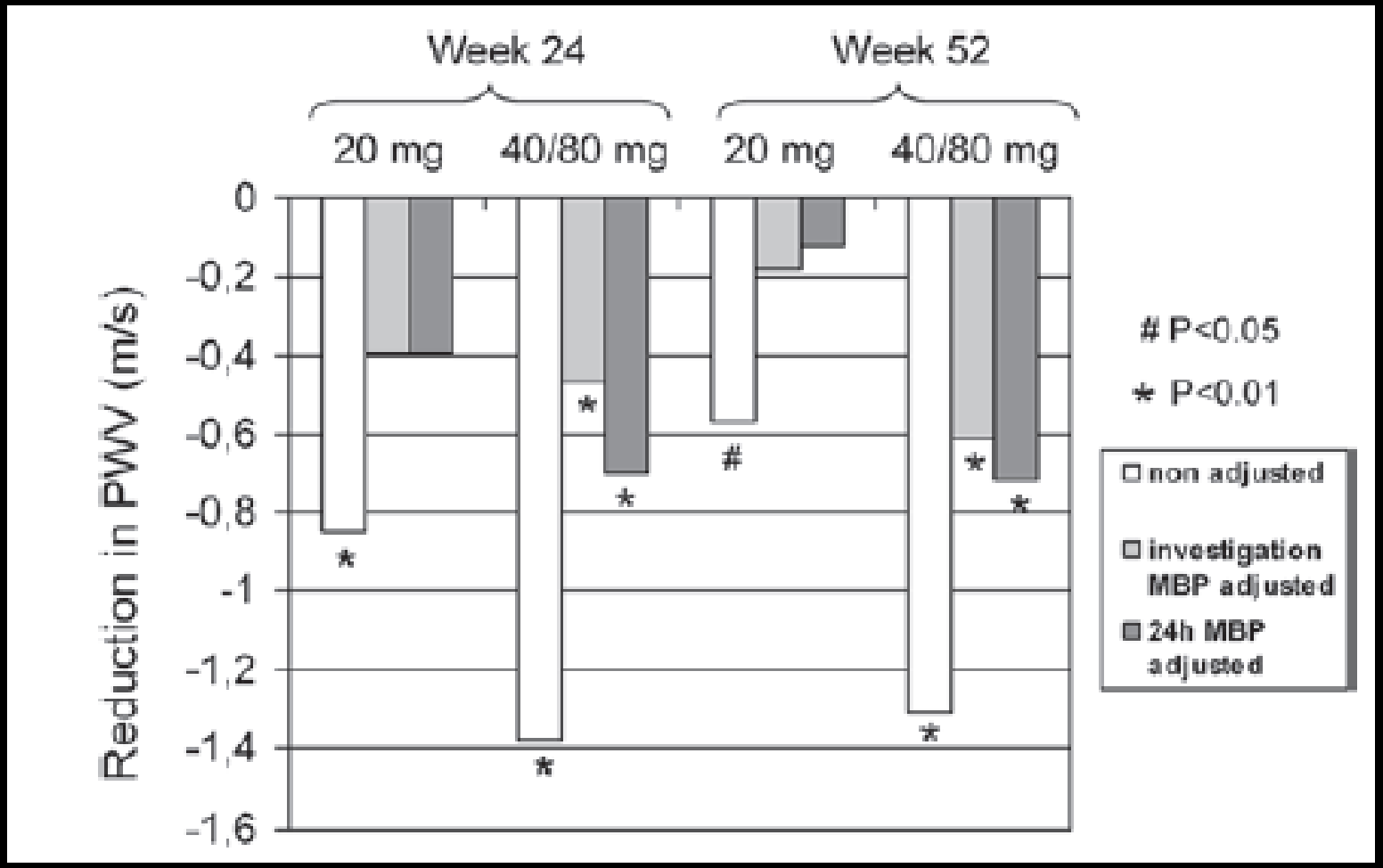
Stephane Laurent, Pierre Boutouyrie, on behalf of the Vascular Mechanism Collaboration

Laurent & Boutouyrie *Hypertension* 2014; (In Press)



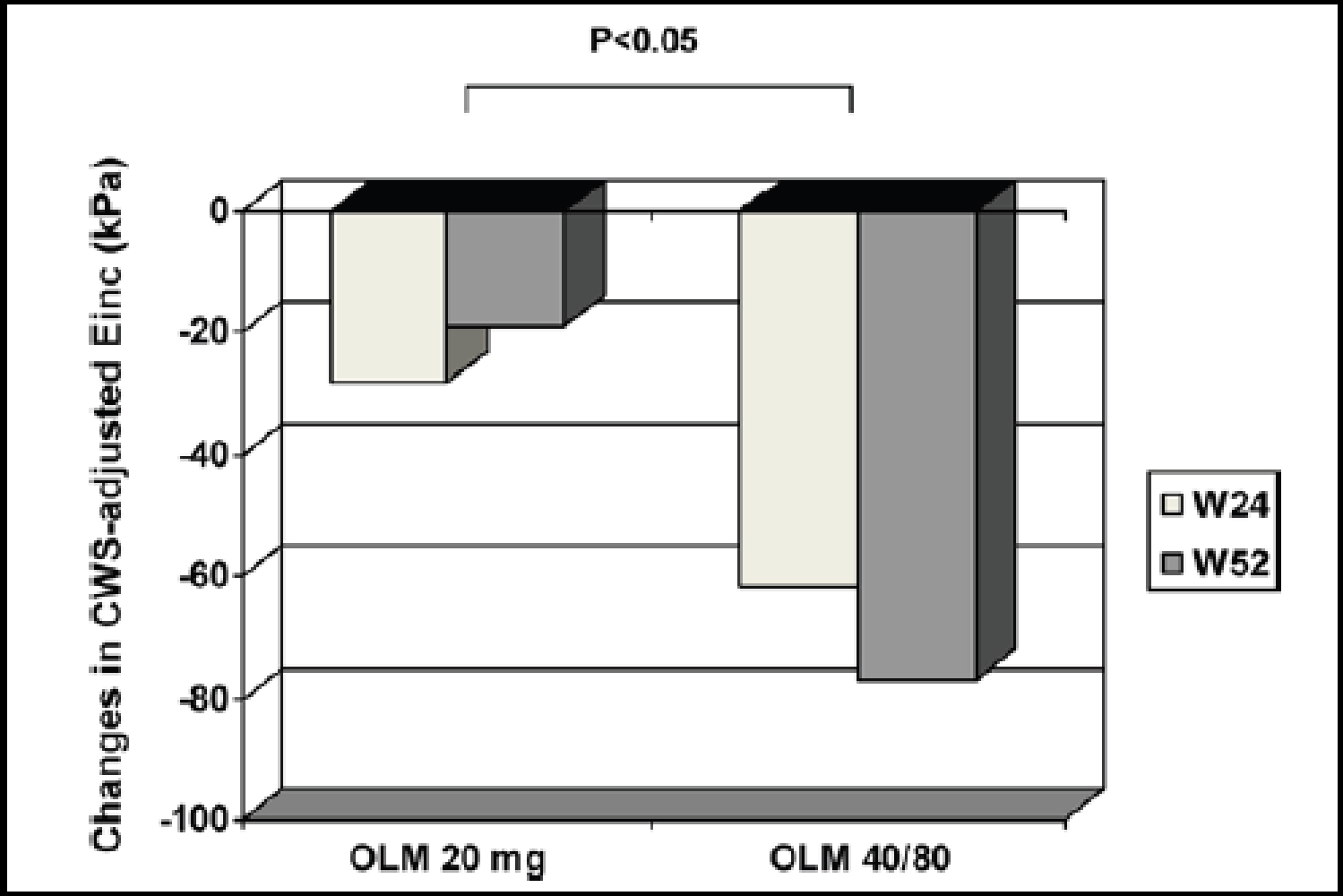
Laurent & Boutouyrie *Hypertension* 2014; (In Press)

Reduction in aPWV from Baseline at Weeks 24 and 52 Nonadjusted and Adjusted to MAP Reduction



Laurent & Boutouyrie *Hypertension* 2014; (In Press)

Reduction in Carotid Stiffness as Assessed by Elastic Modulus After adjustment for Circumferential Wall Stress

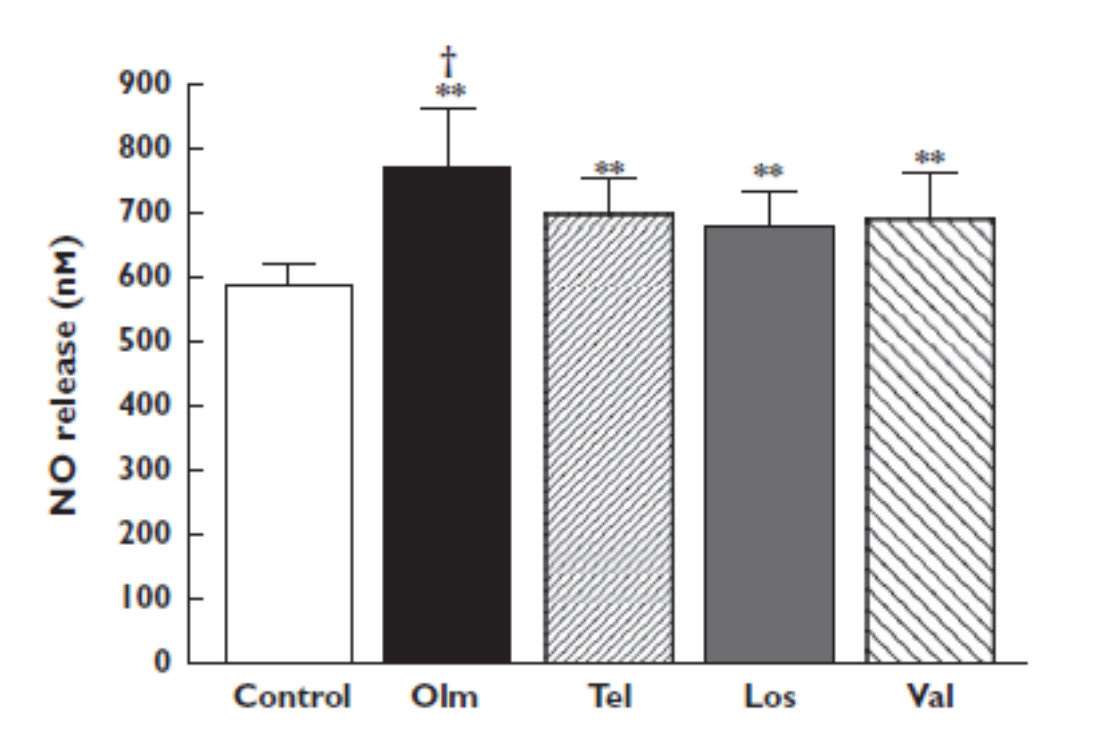


Laurent & Boutouyrie *Hypertension* 2014; (In Press)

Effects of angiotensin receptor blockers on endothelial nitric oxide release: the role of eNOS variants

R. Preston Mason,[1,2] Robert F. Jacob,[2] Ruslan Kubant,[3] Adam Jacoby,[3] Febee Louka,[3] J. Jose Corbalan[3] & Tadeusz Malinski[3]

[1]Cardiovascular Division, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, [2]Elucida Research, Beverly, Massachusetts and [3]Department of Chemistry and Biochemistry, Ohio University, Athens, Ohio, USA



Mason et al *Br J Clin Pharm* 2012; 74: 141-146

AJH 2005; 18:1S–2S

Introduction

Pulse Contour Analysis and Augmentation Index: It's Time to Move Beyond Cuff Blood Pressure Measurement

Joseph L. Izzo, Jr.

Central systolic BP different from peripheral systolic BP

Central systolic BP better predictor of outcome than peripheral BP

Central and peripheral BP differentially affected by antihypertensive agents