Rigidité artérielle, pression centrale et risque CV et rénal

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Décembre 2017

Déclaration de liens d'intérêt de Jacques Blacher :

- **Absence de participation financière dans le capital d'une entreprise liée aux médicaments.**

- **Absence de lien durable avec une entreprise liée aux médicaments (contrat de travail, rémunération régulière...).**

- **Interventions ponctuelles en rapport avec des entreprises liées aux médicaments (essais cliniques, travaux scientifiques, comités scientifiques, rapports d'expertise, conférences, colloques, actions de formation, participation à divers symposia, rédaction de brochures...) avec, le cas échéant, facturation d'honoraires ; et ceci avec la majorité des entreprises du médicaments commercialisant des produits cardiovasculaires et autres produits en rapport avec mes domaines de spécialité (Amgen, Astra-Zeneca, Bayer, Boehringer Ingelheim, Bouchara, Daiichi Sankyo, Egis, Ferring, Ipsen, Lilly, Le Quotidien du Médecin, Medtronic, Menarini, MSD, Novartis, Pharmalliance, Pierre Fabre, Pileje, Quantum genomics, Sanofi Aventis, Saint Jude, Servier, Takeda)**

- **HAS, ANSM, CNAM, MGEN**

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

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KEYWORDS
Artery;
Arterial stiffness;
Haemodynamics;
Pathophysiology;
Prognosis;
Cardiovascular events

In recent years, great emphasis has been placed on the role of arterial stiffness in the development of cardiovascular diseases. Indeed, the assessment of arterial stiffness is increasingly used in the clinical assessment of patients. Although several papers have previously addressed the methodological issues concerning the various indices of arterial stiffness currently available, and their clinical applications, clinicians and researchers still report difficulties in selecting the most appropriate methodology for their specific use. This paper summarizes the proceedings of several meetings of the European Network for Non-invasive Investigation of Large Arteries and is aimed at providing an updated and practical overview of the most relevant methodological aspects and clinical applications in this area.

Box 2: Position statement: PWV. Carotid-femoral PWV is considered as the 'gold-standard' measurement of arterial stiffness.

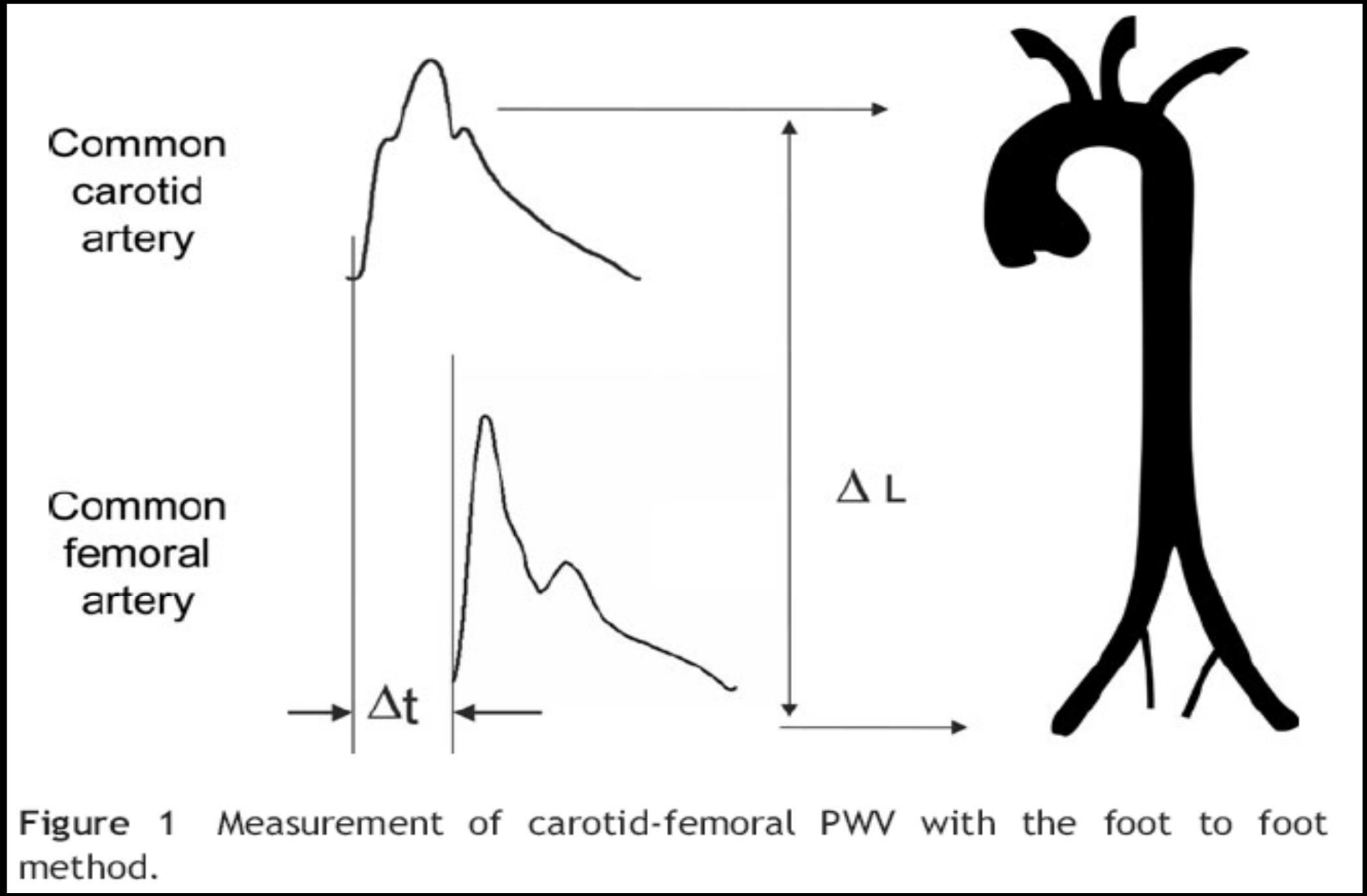


Figure 1 Measurement of carotid-femoral PWV with the foot to foot method.

Table 4 Longitudinal studies reporting the independent predictive value of arterial stiffness, according to the site of measurement

Measurement site	First author (year, country)	Events	Follow-up (years)	Type of patient (number)
Aortic PWV	Blacher (1999, Fr)	CV mortality	6.0	ESRD (241)
	Laurent (2001, Fr)	CV mortality	9.3	Hypertension (1980)
	Meaume (2001, Fr)	CV mortality	2.5	Elderly (>70) (141)
	Shoji (2001, Jp)	CV mortality	5.2	ESRD (265)
	Boutouyrie (2002, Fr)	CHD events	5.7	Hypertension (1045)
	Cruickshank (2002, GB)	All cause mortality	10.7	IGT (571)
	Laurent (2003, Fr)	Fatal strokes	7.9	Hypertension (1715)
	Sutton-Tyrrell (2005, USA)	CV mortality and events	4.6	Elderly (2488)
	Shokawa (2005, Jp)	CV mortality	10	General population (492)
	Willum-Hansen (2006, Dk)	CV mortality	9.4	General population (1678)
	Mattace-Raso (2006, Neth.)	CV mt, CHD	4.1	Elderly (2835)
Ascending aorta (invasive)	Stefanadis (2000, Gr)	Recurrent acute CHD	3	Acute CHD (54)
Carotid distensibility	Blacher (1998, Fr)	All cause mortality	2.1	ESRD (79)
	Barenbrock (2001, Ge)	CV events	7.9	ESRD (68)

IGT, impaired glucose tolerance; CHD, coronary heart disease. Countries: Dk, Denmark; Fr, France; GB, Great Britain; Ge, Germany; Gr, Greece; Jp, Japan; Ne,

Impact of Aortic Stiffness on Survival in End-Stage Renal Disease

Jacques Blacher, MD; Alain P. Guerin, MD; Bruno Pannier, MD; Sylvain J. Marchais, MD; Michel E. Safar, MD; Gérard M. London, MD

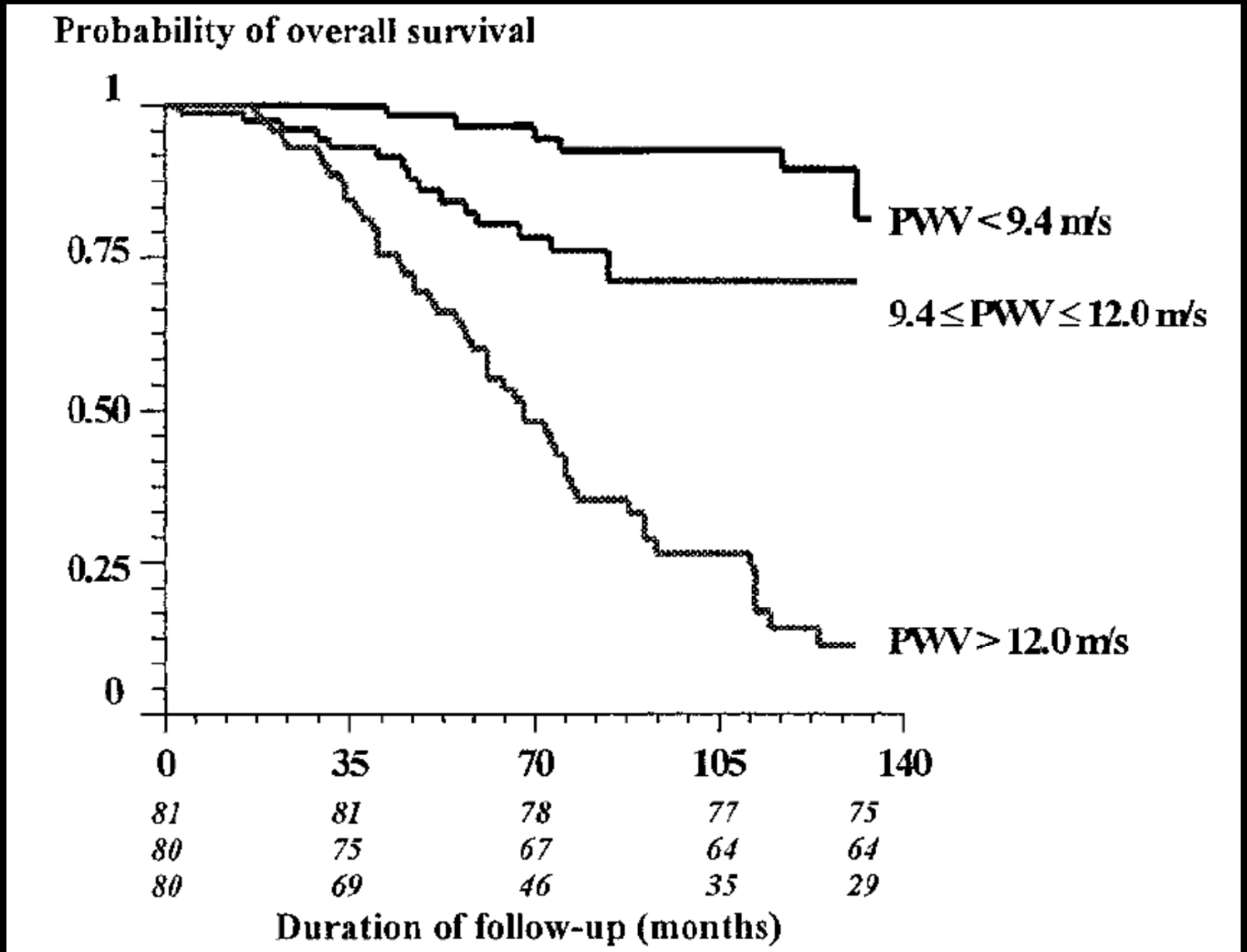
Background—Damage to large arteries is a major factor in the high cardiovascular morbidity and mortality of patients with end-stage renal disease (ESRD). Increased arterial stiffness and intima-media thickness, together with increased pulse pressure, are the principal arterial alterations. Whether increased aortic pulse-wave velocity (PWV), a classic marker of increased arterial stiffness, may predict all-cause and/or cardiovascular mortality has never been investigated.

Methods and Results—A cohort of 241 patients with ESRD undergoing hemodialysis was studied between April 1987 and April 1998. The mean duration of follow-up was 72±41 months (mean±SD). Mean age at entry was 51.5±16.3 years. Seventy-three deaths occurred, including 48 cardiovascular and 25 noncardiovascular fatal events. At entry, together with standard clinical and biochemical analyses, patients underwent echocardiography and aortic PWV measured by Doppler ultrasonography. On the basis of Cox analyses, 2 factors emerged as predictors of all-cause and cardiovascular mortality: age and aortic PWV. Hemoglobin and low diastolic pressure interfered to a smaller extent. After adjustment for all the confounding factors, an OR for PWV >12.0 versus <9.4 m/s was 5.4 (95% CI, 2.4 to 11.9) for all-cause mortality and 5.9 (95% CI, 2.3 to 15.5) for cardiovascular mortality. For each PWV increase of 1 m/s in our study population, all-cause mortality–adjusted OR was 1.39 (95% CI, 1.19 to 1.62).

Conclusions—These results provide the first direct evidence that in patients with ESRD, increased aortic stiffness determined by measurement of aortic PWV is a strong independent predictor of all-cause and mainly cardiovascular mortality. **(*Circulation*. 1999;99:2434-2439.)**

TABLE 1. Characteristics of Patients at Inclusion

Parameter	All Patients (n=241)
Tobacco lifelong dose, pack-y	9±15
Total cholesterol, mmol/L	5.2±1.2
HDL cholesterol, mmol/L	1.1±0.5
LDL cholesterol, mmol/L	3.4±1.1
Triglycerides, mmol/L	1.8±1.1
Parathyroid hormone, pg/mL	239±240
Plasma albumin, g/L	39.8±2.4
Hemoglobin, mmol/L	5.8±1.2
SBP, mm Hg	157±28
DBP, mm Hg	85±16
Heart period, ms	830±131
Aortic PWV, m/s	11.1±3.1
Previous cardiovascular events, %	24


Probability of overall survival
1
0.75
0.50
0.25
0
PWV < 9.4 m/s
9.4 ≤ PWV ≤ 12.0 m/s
PWV > 12.0 m/s
0
35
70
105
140
81 81 78 77 75
80 75 67 64 64
80 69 46 35 29
Duration of follow-up (months)

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QUARTERLY FOCUS ISSUE: PREVENTION/OUTCOMES

Prediction of Cardiovascular Events and All-Cause Mortality With Arterial Stiffness

A Systematic Review and Meta-Analysis

Charalambos Vlachopoulos, MD, Konstantinos Aznaouridis, MD, Christodoulos Stefanadis, MD
Athens, Greece

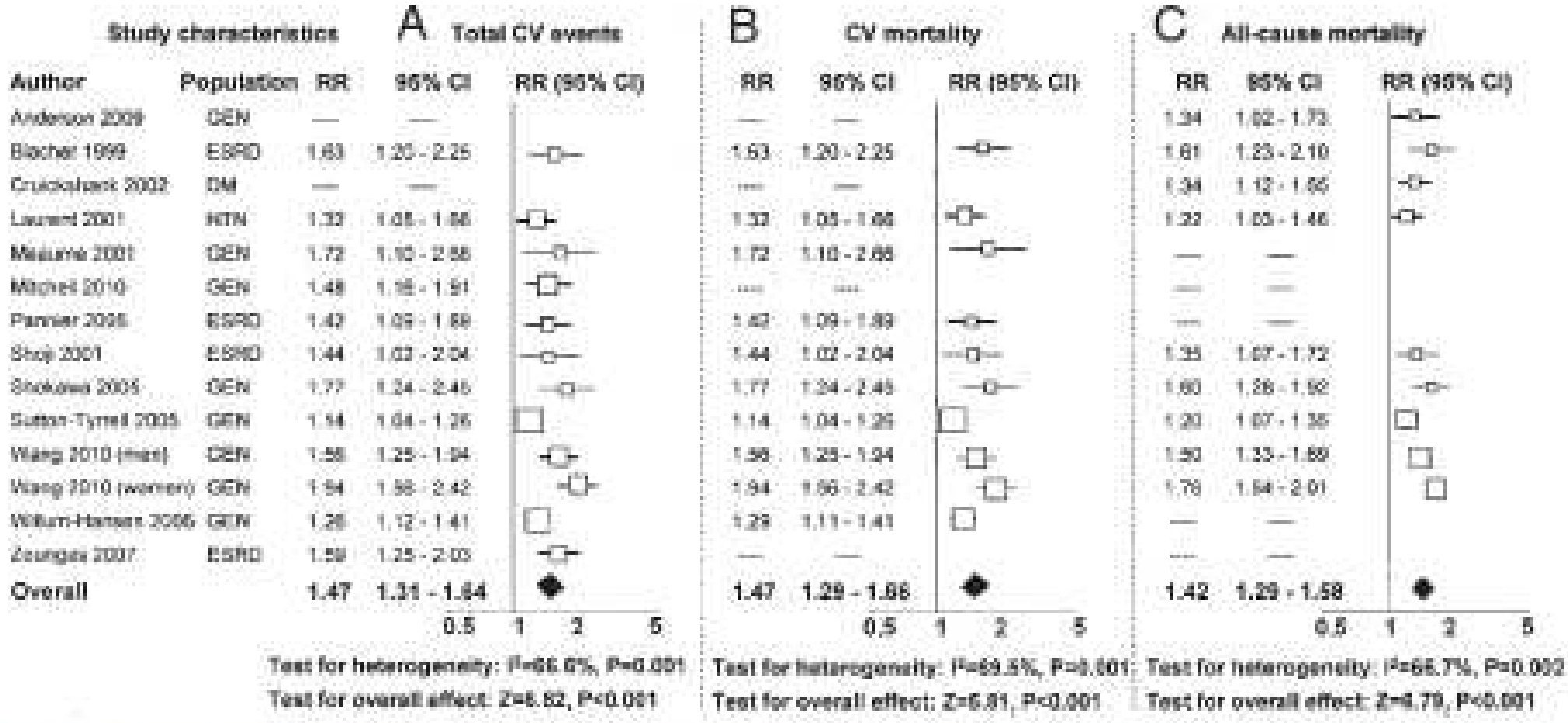


Figure 4 RR and 95% CI for a 1-SD Increase in Aortic PWV and Clinical Events

RR and 95% CI for a 1-SD increase in aortic PWV and total CV events (**A**), CV mortality (**B**), and all-cause mortality (**C**). Studies are listed alphabetically. Symbols and abbreviations as in Figure 2.

Arterial Stiffness and Cardiovascular Events
The Framingham Heart Study

Gary F. Mitchell, MD; Shih-Jen Hwang, PhD; Ramachandran S. Vasan, MD; Martin G. Larson, ScD; Michael J. Pencina, PhD; Naomi M. Hamburg, MD; Joseph A. Vita, MD; Daniel Levy, MD*; Emelia J. Benjamin, MD, ScM*

Background—Various measures of arterial stiffness and wave reflection have been proposed as cardiovascular risk markers. Prior studies have not assessed relations of a comprehensive panel of stiffness measures to prognosis in the community.

Methods and Results—We used proportional hazards models to analyze first-onset major cardiovascular disease events (myocardial infarction, unstable angina, heart failure, or stroke) in relation to arterial stiffness (pulse wave velocity [PWV]), wave reflection (augmentation index, carotid-brachial pressure amplification), and central pulse pressure in 2232 participants (mean age, 63 years; 58% women) in the Framingham Heart Study. During median follow-up of 7.8 (range, 0.2 to 8.9) years, 151 of 2232 participants (6.8%) experienced an event. In multivariable models adjusted for age, sex, systolic blood pressure, use of antihypertensive therapy, total and high-density lipoprotein cholesterol concentrations, smoking, and presence of diabetes mellitus, higher aortic PWV was associated with a 48% increase in cardiovascular disease risk (95% confidence interval, 1.16 to 1.91 per SD; $P=0.002$). After PWV was added to a standard risk factor model, integrated discrimination improvement was 0.7% (95% confidence interval, 0.05% to 1.3%; $P<0.05$). In contrast, augmentation index, central pulse pressure, and pulse pressure amplification were not related to cardiovascular disease outcomes in multivariable models.

Conclusions—Higher aortic stiffness assessed by PWV is associated with increased risk for a first cardiovascular event. Aortic PWV improves risk prediction when added to standard risk factors and may represent a valuable biomarker of cardiovascular disease risk in the community. (***Circulation***. **2010;121:505-511.**)

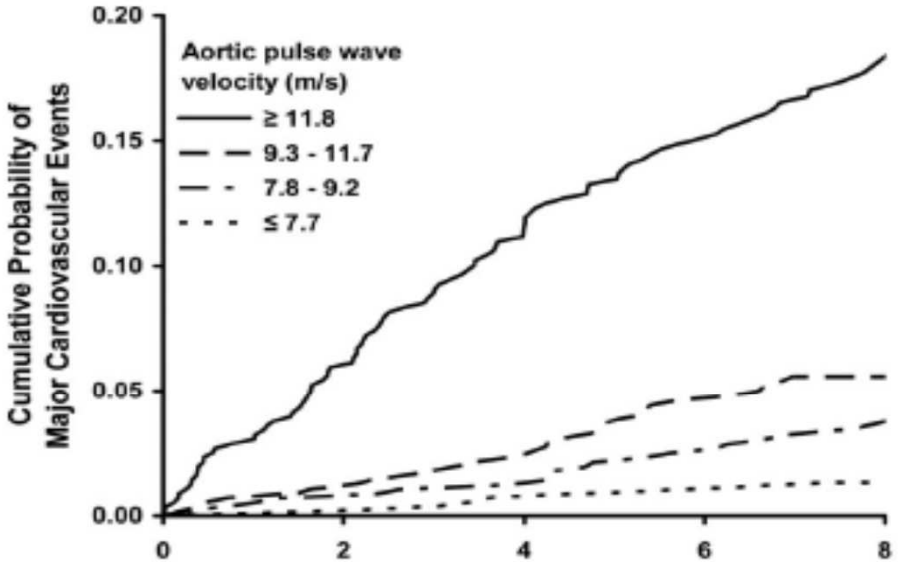


Table 3. Measures of Model Fit, Discrimination, and Calibration for Various Cardiovascular Event Models With and Without Carotid-Femoral (Aortic) PWV

	Model Fit			Discrimination	Calibration	
Model	−2 Log Likelihood	Akaike Information Criterion	Schwartz's Bayesian Information Criterion	C Statistic (95% CI)	χ^2	*P*
Age, sex	2155	2159	2165	0.762 (0.723–0.801)	8.7	0.46
Add PWV	2136	2142	2151	0.782 (0.746–0.818)*	2.9	0.97
Age, sex, total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, smoking, diabetes mellitus, and hypertension treatment	2126	2142	2166	0.796 (0.764–0.828)	4.3	0.89
Add PWV	2116	2134	2162	0.800 (0.768–0.832)†	2.6	0.98

For a description of the tests displayed in the table, please refer to Methods, Statistical Analysis.
*Comparison of C statistics in rows 1 and 2, $P=0.006$.
†Comparison of C statistics in rows 3 and 4, $P=0.3$.

- **Le concept de rigidité artérielle va-t-il « translater » des chercheurs vers les cliniciens ?**

Risk assessment strategies

- **Central versus peripheral ?**

- **Comparison of different biomarkers - problem of intercorrelations**

Brachial BP overestimates systolic and pulse central BP

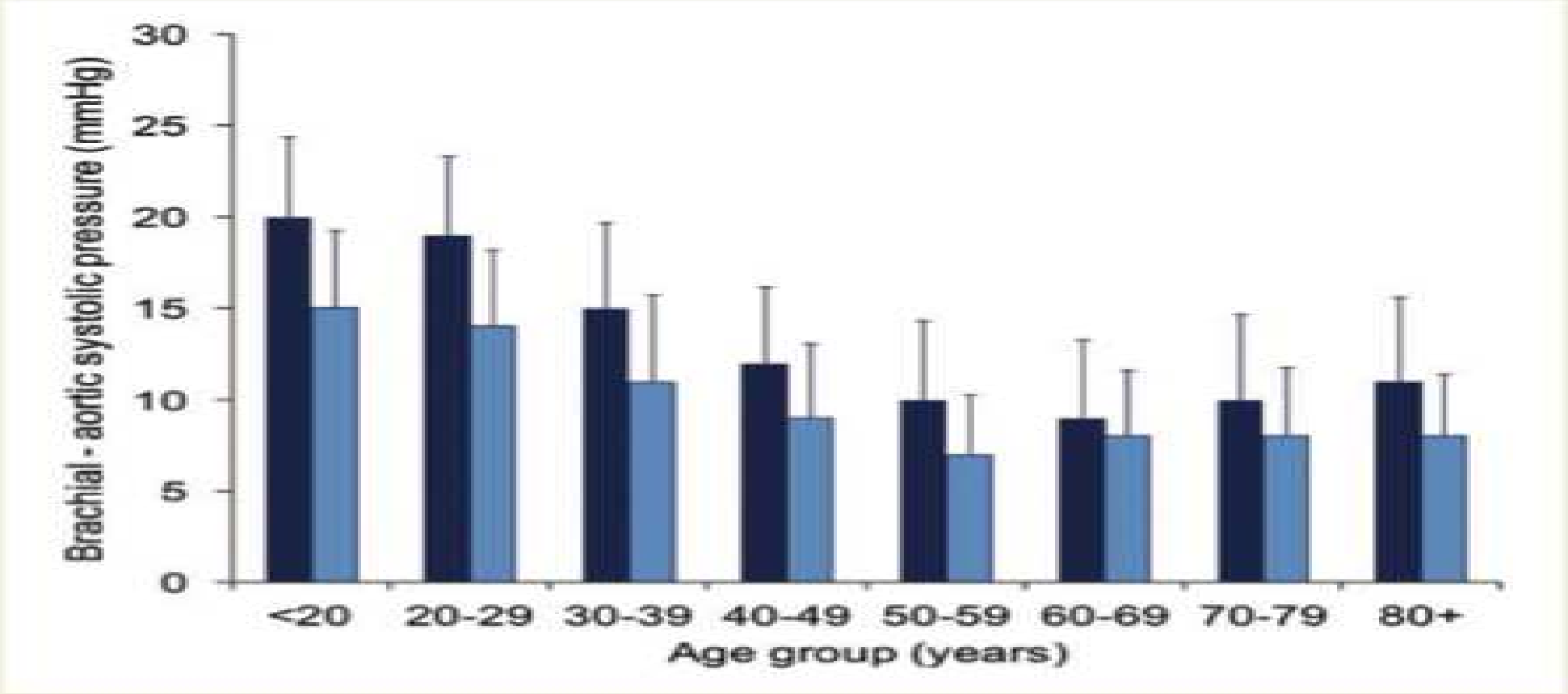
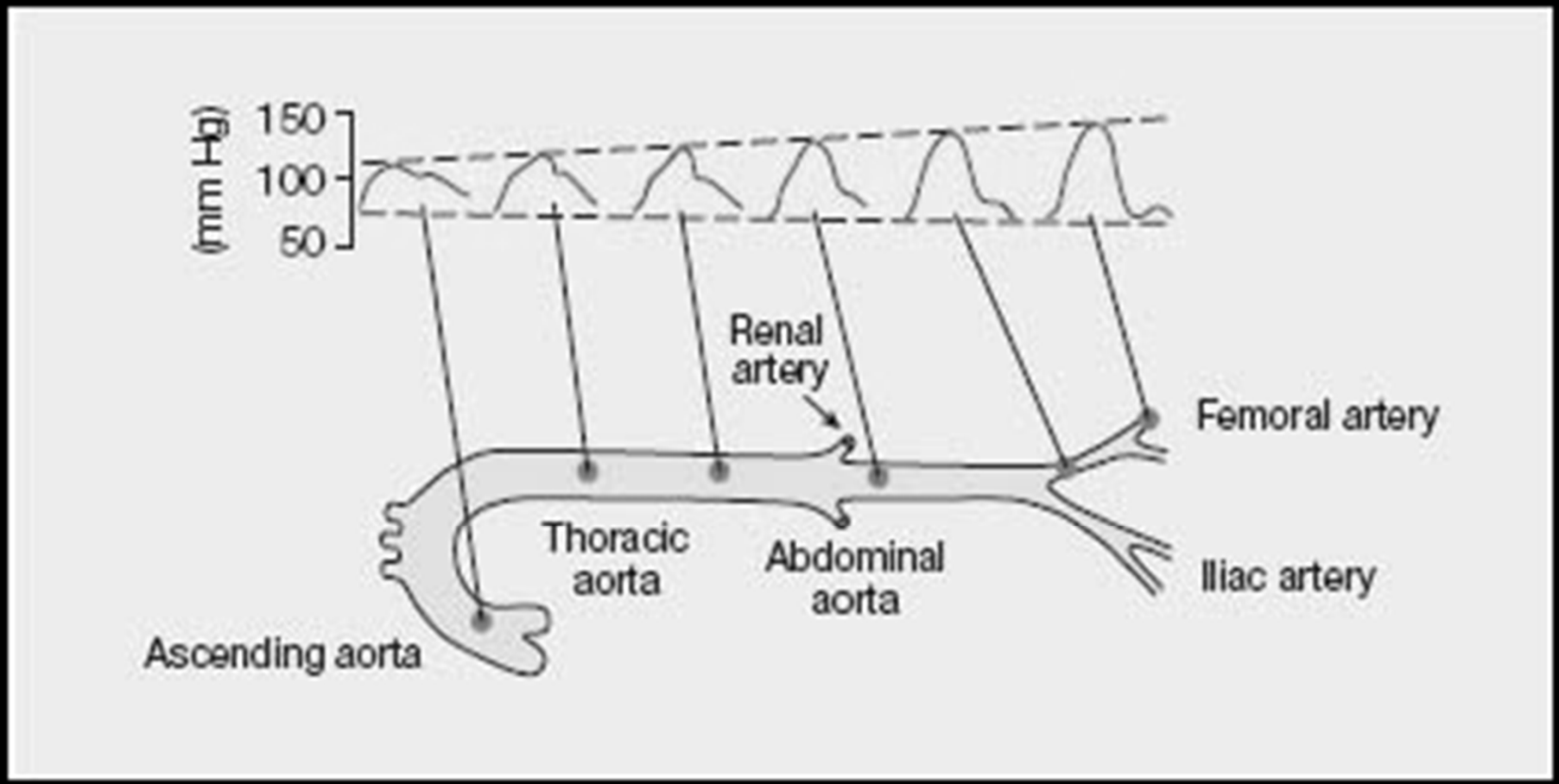


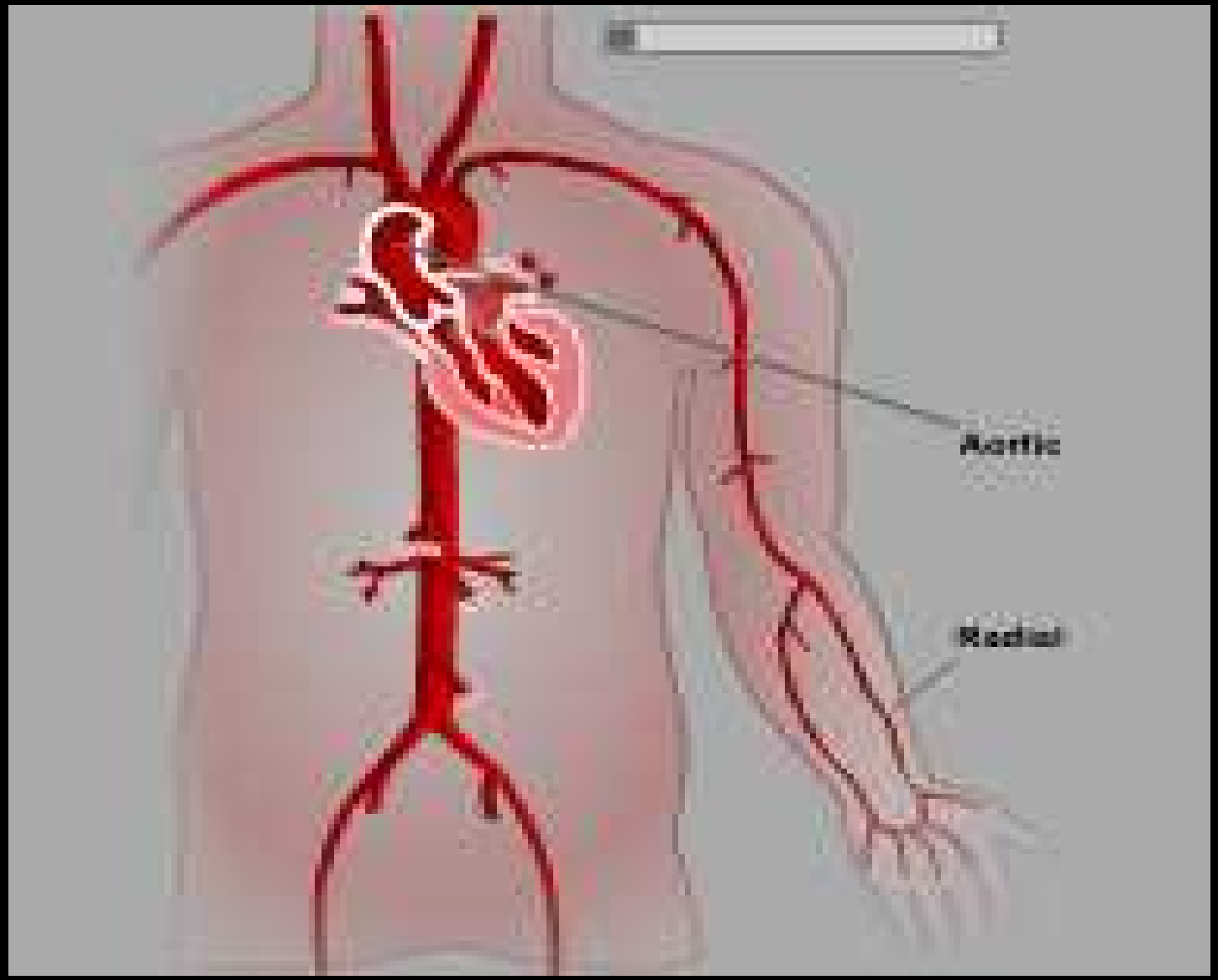
Figure 2 Difference between brachial and aortic systolic blood pressure (SphygmoCor) in healthy men (dark blue bars; $n = 2779$) and women (light blue bars; $n = 2869$). The data represent means $\pm$ SD.

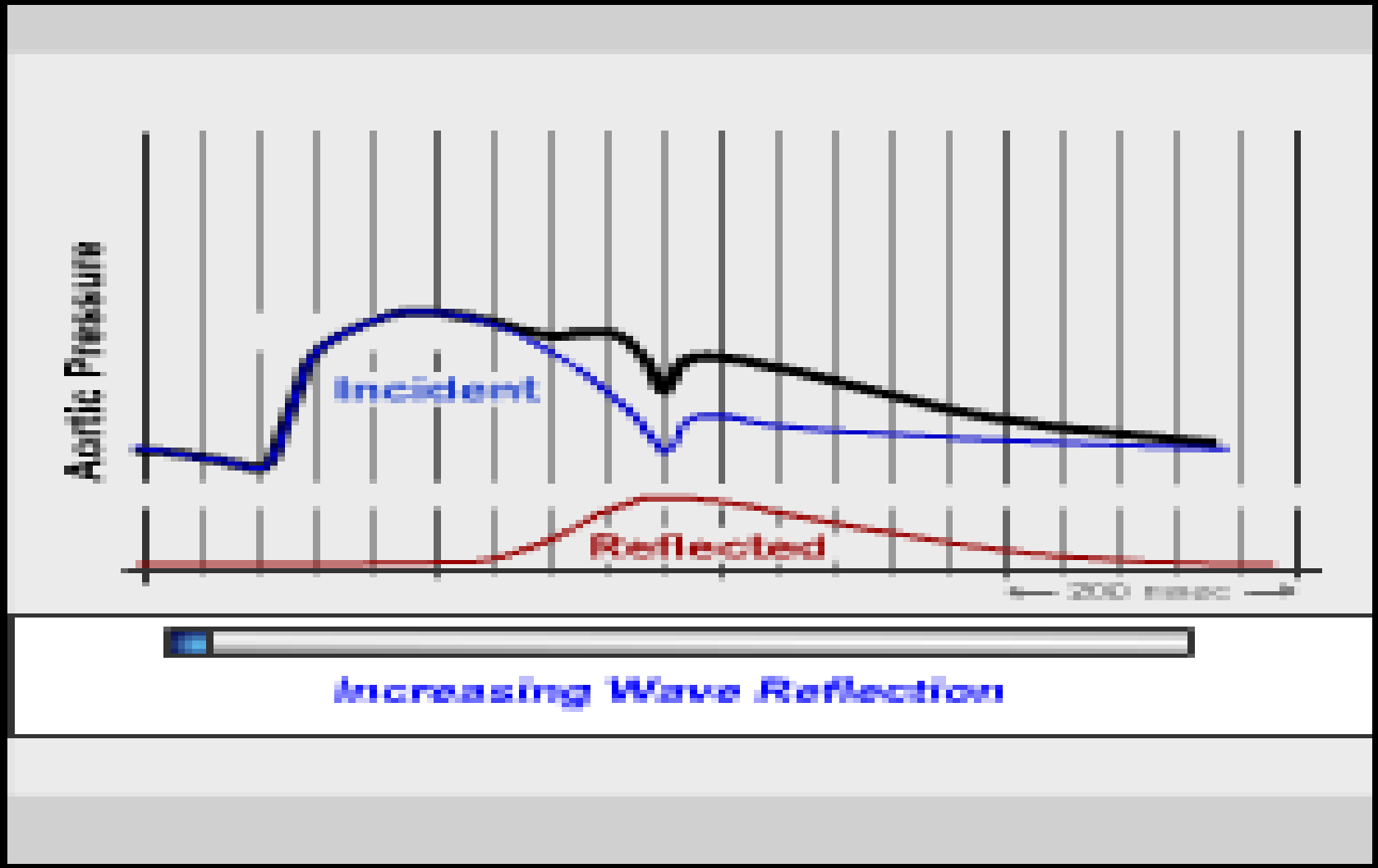
McEniery C, et al. Eur Heart J 2014

Wave amplification of systolic blood pressure and pulse pressure along the aorta in young individual.



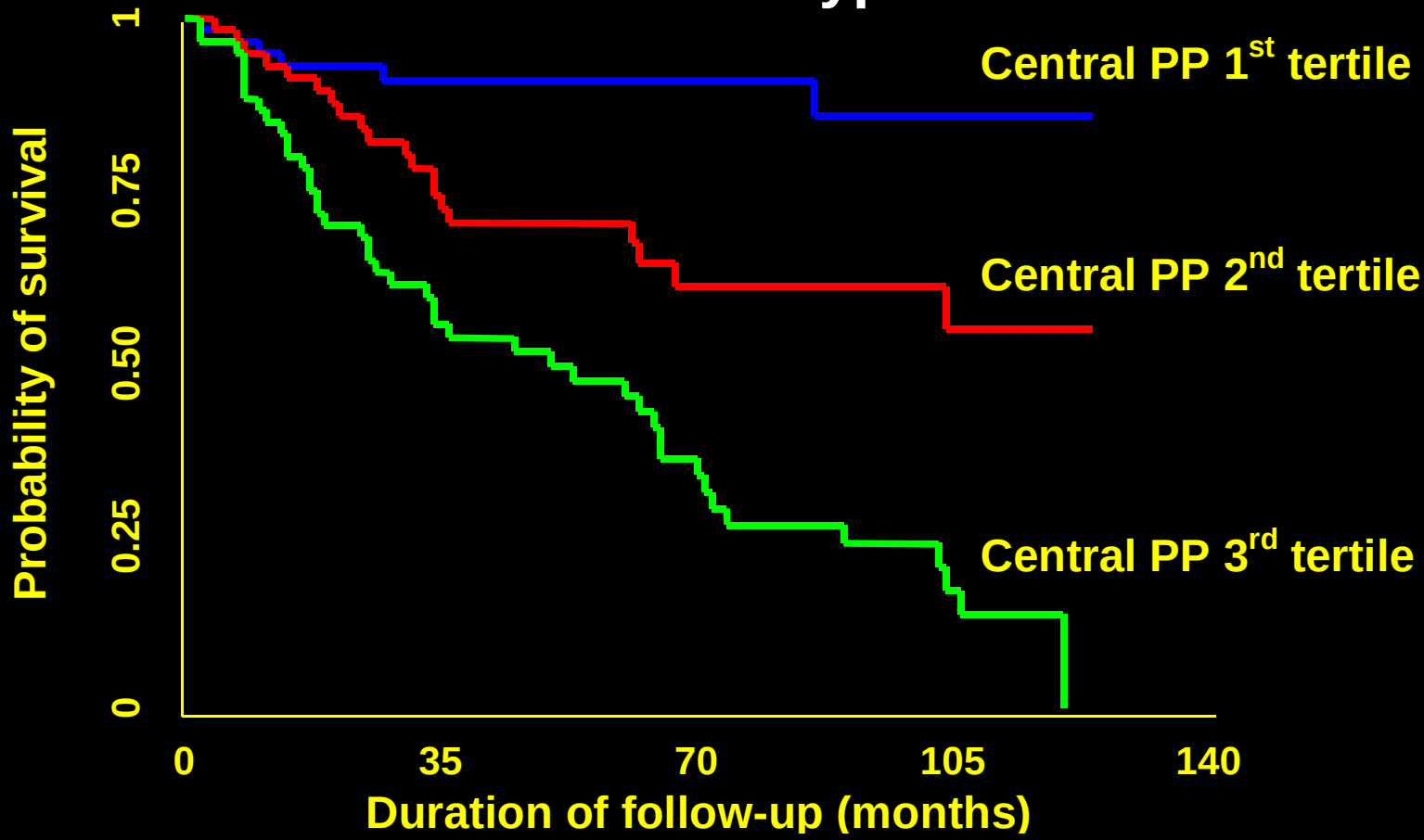
Nichols WW, O'Rourke MF. McDonald's Blood Flow in Arteries. Theoretical, Experimental and Clinical Principles. 4th ed. London, UK: Edward Arnold; 2006.


Aortic
Radial

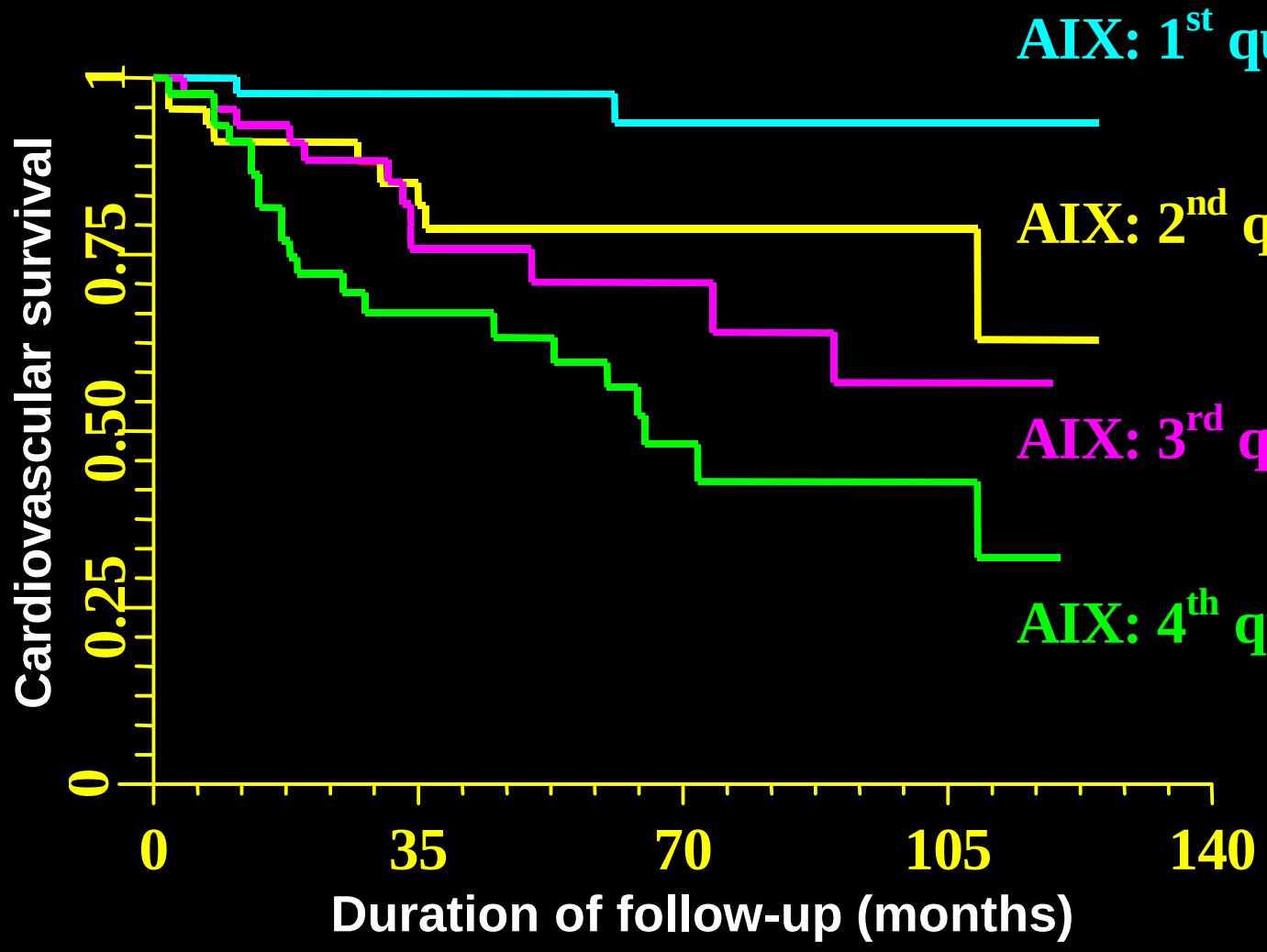

Aortic Pressure
Incident
Reflected
200 msec
Increasing Wave Reflection

Probabilities of survival in the study population according to the level of central PP divided into tertiles. Comparison between survival curves was highly significant (p<0.001)

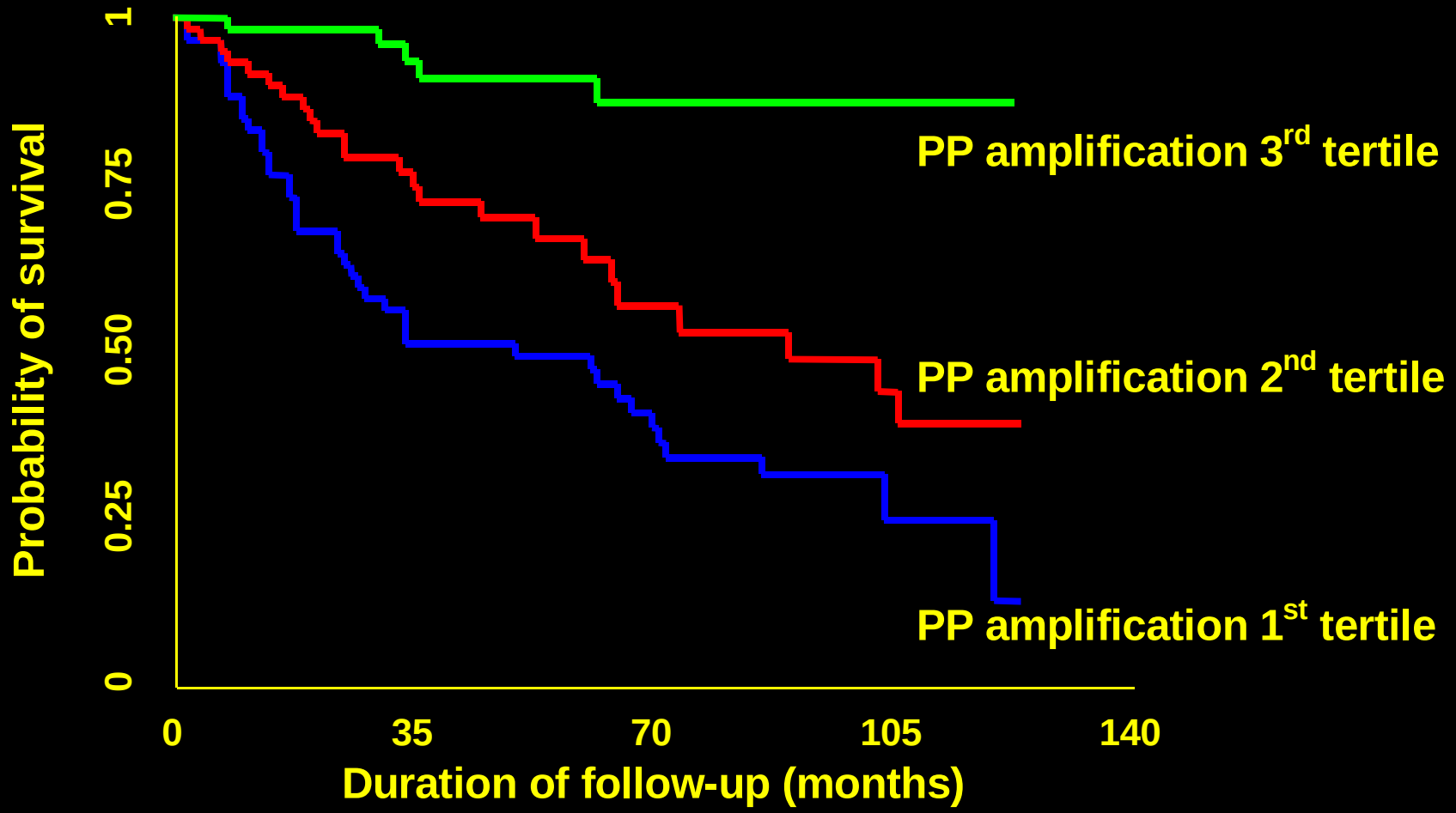
Safar et al. Hypertension 2002



Augmentation Index (AIX) and CV survival



London and al. Hypertension 2001


Probability of survival
0
0.25
0.50
0.75
1
0
35
70
105
140
Duration of follow-up (months)
PP amplification 3rd tertile
PP amplification 2nd tertile
PP amplification 1st tertile

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

Abstract—Brachial blood pressure is predictive of cardiovascular outcome; however central pressure may better represent the load imposed on the coronary and cerebral arteries and thereby bear a stronger relationship to vascular damage and prognosis. Relations of brachial and central pressures to carotid artery hypertrophy (intimal-medial thickness and vascular mass), extent of atherosclerosis (plaque score), and incident cardiovascular events were examined in the Strong Heart Study. Central pressures were calculated using radial applanation tonometry. Among 3520 participants, central and brachial pulse pressures were more strongly related to vascular hypertrophy and extent of atherosclerosis than were systolic pressures. Central pulse pressure was more strongly related to all 3 arterial measures than was brachial pulse pressure (r=0.364 versus 0.309 for plaque score; $P<0.001$ for comparison of Spearman correlation coefficient; r=0.293 versus 0.249 for intimal-medial thickness; $P<0.002$; r=0.320 versus 0.289 for vascular mass; $P<0.05$). Among the 2403 participants free of clinical cardiovascular disease at baseline, 319 suffered fatal or nonfatal cardiovascular events during mean follow-up of 4.8±1.3 years. After adjustment for age, gender, current smoking, body mass index, cholesterol:HDL ratio, creatinine, fibrinogen, diabetes, and heart rate, central pulse pressure predicted cardiovascular events more strongly than brachial pulse pressure (hazards ratio=1.15 per 10 mm Hg, χ^2=13.4, $P<0.001$ versus hazards ratio=1.10, χ^2=6.9, P=0.008). In conclusion, noninvasively-determined central pulse pressure is more strongly related to vascular hypertrophy, extent of atherosclerosis, and cardiovascular events than is brachial blood pressure. These findings support prospective examination of use of central blood pressure as a treatment target in future trials. (***Hypertension*. 2007;50:197-203.**)

TABLE 3. Comparison of Demographic Variables and Cardiovascular Disease Risk Factors in Participants Free of Prevalent Cardiovascular Disease at Baseline Subdivided According to Incident Cardiovascular Events During Follow-Up

Variable	No Events (n=2084)	Events (n=319)	*P* Value
Age, years	62.5±7.5	65.6±7.4	<0.001
Male gender, %	34.8	36.1	0.672
Body mass index, kg/m²	31.4±6.6	30.8±6.4	0.128
Hypertension, %	50.3	63.0	<0.001
Diabetes mellitus, %	44.1	67.5	<0.001
Current smoking, %	27.5	28.3	0.777
Brachial SBP, mm Hg	131±19	135±23	<0.001
Brachial PP, mm Hg	56±16	62±20	<0.001
Central SBP, mm Hg	121±17	127±22	<0.001
Central PP, mm Hg	41±15	48±18	<0.001
Heart rate, bpm	69±11	71±12	<0.001
Total cholesterol/HDL cholesterol	4.7±1.5	5.0±1.7	<0.003
Creatinine, mg/dL	0.93±0.91	1.33±1.65	<0.001
Fibrinogen, mg/dL	380±119	413±143	<0.001

Roman et al, Hypertension. 2007;50:197-203.

TABLE 2. Relations of Central and Brachial Blood Pressures and Arterial Stiffness to Carotid Hypertrophy and Extent of Atherosclerosis*

Variable	Intimal-Medial Thickness	Vascular Mass	Plaque Score
Brachial SBP	0.196	0.264	0.221
Central SBP	0.257	0.317	0.288
Brachial PP	0.249	0.289	0.309
Central PP	0.293	0.320	0.364
Arterial stiffness index	0.252	0.329	0.353
P value, brachial PP vs brachial SBP†	<0.001	<0.02	<0.001
P value, central PP vs central SBP†	<0.001	ns	<0.001
P value, central vs brachial SBP†	<0.001	<0.001	<0.001
P value, central vs brachial PP†	<0.002	<0.05	<0.001
P value, arterial stiffness vs brachial SBP†	<0.005	<0.001	<0.001
P value, arterial stiffness vs brachial PP†	ns	ns	<0.02

SBP indicates systolic blood pressure; PP, pulse pressure; ns, not significant.
*All correlations $P<0.001$.
†Correlations compared by Z statistics.

Roman et al, Hypertension. 2007;50:197-203.

Pulsatile but Not Steady Component of Blood Pressure Predicts Cardiovascular Events in Coronary Patients

Piotr Jankowski, Kalina Kawecka-Jaszcz, Danuta Czarnecka, Małgorzata Brzozowska-Kiszka, Katarzyna Styczkiewicz, Magdalena Loster, Małgorzata Kloch-Badełek, Jerzy Wiliński, Adam M. Curyło, Dariusz Dudek; on behalf of the Aortic Blood Pressure and Survival Study Group

Abstract—Although the differences between central and peripheral blood pressure (BP) values have been known for decades, the consequences of decision making based on peripheral rather than central BP have only recently been recognized. There are only a few studies assessing the relationship between intraaortic BP and cardiovascular risk. In addition, the relationship between central BP and the risk of cardiovascular events in a large group of coronary patients has not yet been evaluated. Therefore, the aim of the study was to determine the prognostic significance of central BP-derived indices in patients undergoing coronary angiography. Invasive central BPs were taken at baseline, and study end points were ascertained during over a 4.5-year follow-up in 1109 consecutive patients. The primary end point (cardiovascular death or myocardial infarction or stroke or cardiac arrest or heart transplantation or myocardial revascularization) occurred in 246 (22.2%) patients. Central pulsatility was the most powerful predictor of the primary end point (hazard ratio [HR] 1.30, 95% confidence interval [CI] 1.14 to 1.48). Central pulse pressure was also independently related to the primary end point (HR 1.25, 95% CI 1.09 to 1.43). Central mean BP as well as peripheral BP parameters were not independently related to the primary end point risk. Central pulsatility was also related to risk of cardiovascular death or myocardial infarction or stroke. The pulsatile component of BP is the most important factor related to the cardiovascular risk in coronary patients. It is more closely associated with cardiovascular risk than steady component of BP. (***Hypertension*****. 2008;51:848-855.)**

Key Words: blood pressure ■ central pulse pressure ■ pulsatility ■ cardiovascular risk ■ atherosclerosis ■ coronary artery disease

Table 3. Independent and BP-Related Predictors of the Primary End Point

Variable	Hazard Ratio (95% Confidence Interval)	Wald Statistics	*P*
Independent non-BP related predictors			
Ejection fraction, per SD	0.80 (0.70 to 0.92)	9.57	0.0020
Mean coronary artery stenosis, per SD	1.25 (1.08 to 1.44)	9.14	0.0055
Previous myocardial infarction (yes-1, no-0)	1.38 (1.03 to 1.86)	4.68	0.0305
Sex (male-1, female-0)	1.44 (1.03 to 2.02)	4.49	0.0341
Glomerular filtration rate, per SD	0.85 (0.73 to 0.99)	4.15	0.0416
Diabetes (yes-1, no-0)	1.39 (1.00 to 1.95)	3.85	0.0496
Invasive ascending aortic blood pressure*			
Mean blood pressure, per SD	1.01 (0.89 to 1.16)	0.04	0.8362
Pulse pressure, per SD	1.25 (1.09 to 1.43)	10.07	0.0015
Pulsatility, per SD	1.30 (1.14 to 1.48)	14.64	0.0001
Sphygmomanometer brachial blood pressure*			
Mean blood pressure, per SD	1.04 (0.92 to 1.18)	0.42	0.5194
Pulse pressure, per SD	1.03 (0.86 to 1.22)	0.08	0.7759
Pulsatility, per SD	1.07 (0.94 to 1.21)	0.91	0.3388

SD indicates standard deviation.

*BP-derived indices were added separately to the model consisting of independent non-BP related predictors of the primary end point.

Table 4. Hazard Ratios of the Primary End Point According to BP-Derived Indices

	Hazard Ratio (95% Confidence Interval)	
Index	Model 1	Model 2
Invasive ascending aortic blood pressure		
Mean blood pressure per SD	0.98 (0.87 to 1.12)	1.02 (0.88 to 1.17)
Pulse pressure per SD	1.15 (1.00 to 1.32)	1.24 (1.06 to 1.45)
Pulsatility per SD	1.22 (1.05 to 1.40)	1.28 (1.10 to 1.49)
Sphygmomanometer brachial blood pressure		
Mean blood pressure per SD	1.00 (0.88 to 1.13)	1.03 (0.90 to 1.18)
Pulse pressure per SD	0.99 (0.83 to 1.17)	1.04 (0.90 to 1.20)
Pulsatility per SD	1.02 (0.90 to 1.16)	1.04 (0.90 to 1.18)

SD indicates standard deviation.

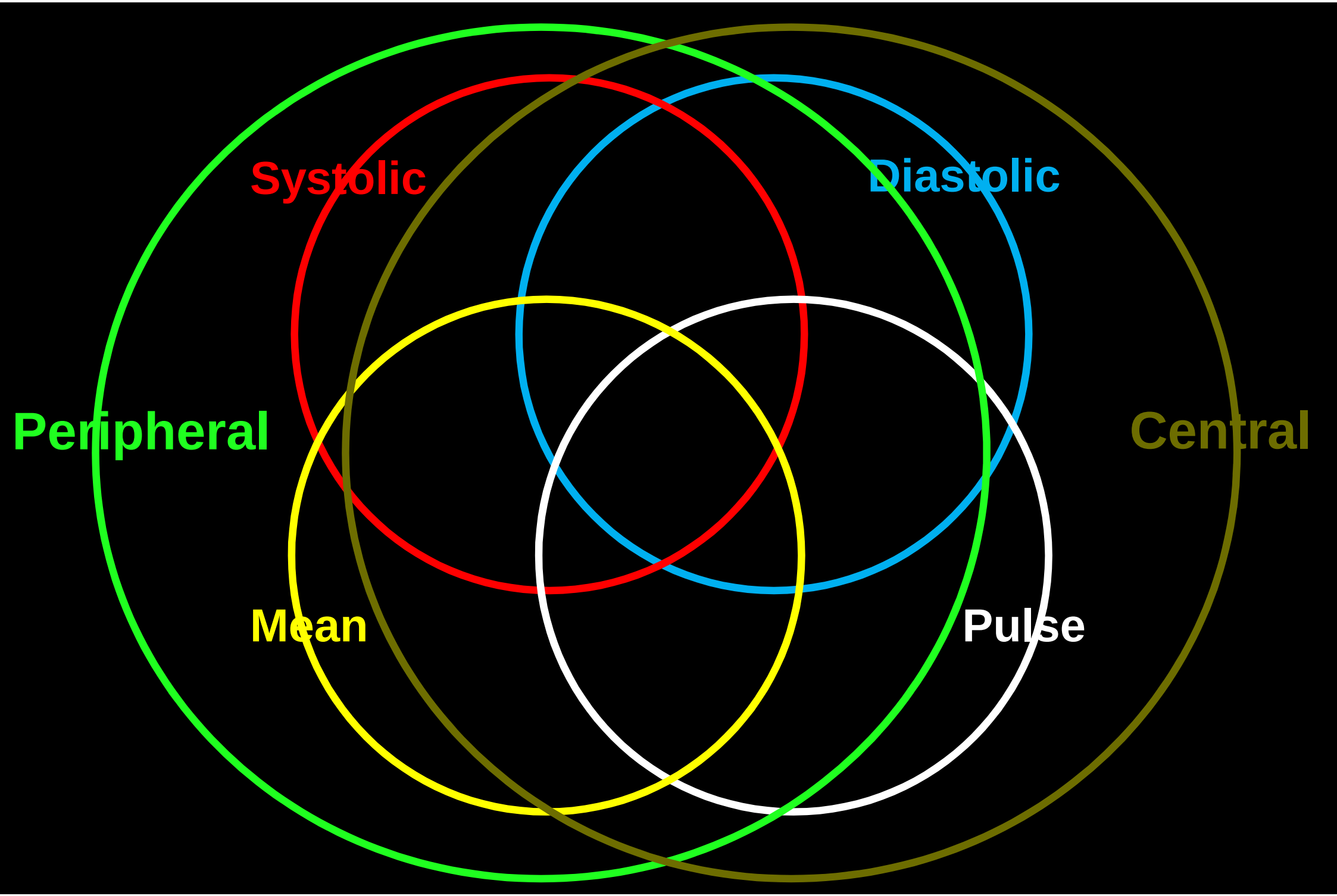
Model 1, adjusted for age and gender; Model 2, adjusted for age, gender, ejection fraction, mean coronary artery stenosis, heart failure, heart rate, risk factors, cardiovascular history, GFR, and prescribed drugs.

Jankowski P, et al. Hypertension 2008 ; 51 : 848-55.

Risk assessment strategies

- Central versus peripheral ?

- Comparison of different biomarkers - problem of intercorrelations


Systolic
Diastolic
Peripheral
Central
Mean
Pulse

Area under ROC curves, crude and adjusted HRs per 1 SD increment

Variable	Mean±SD	AUC	Crude HR	Adjusted HR
Brachial SBP	156±28	0.64±0.10	1.3 (1.0-1.7)	1.1 (0.8-1.3)
Carotid SBP	152±29	0.71±0.11	1.6 (1.2-2.1)	1.2 (0.8-1.4)
DBP	83±15	0.65±0.10	0.5 (0.4-0.7)	0.8 (0.6-1.0)
MBP	108±17	0.50±0.09	0.8 (0.7-1.1)	0.7 (0.9-1.2)
Brachial PP	73±23	0.78±0.11	1.8 (1.5-2.3)	1.2 (0.9-1.5)
Carotid PP	68±25	0.84±0.11	2.2 (1.7-2.7)	1.4 (1.1-1.8)
Bra./carot. PP	110±16	0.85±0.11	0.2 (0.1-0.4)	0.5 (0.3-0.8)
Aortic PWV	11.7±3.1	0.83±0.11	2.1 (1.7-2.6)	1.3 (1.0-1.7)
LV mass index	172±46	0.68±0.11	1.5 (1.2-1.8)	1.2 (0.9-1.6)

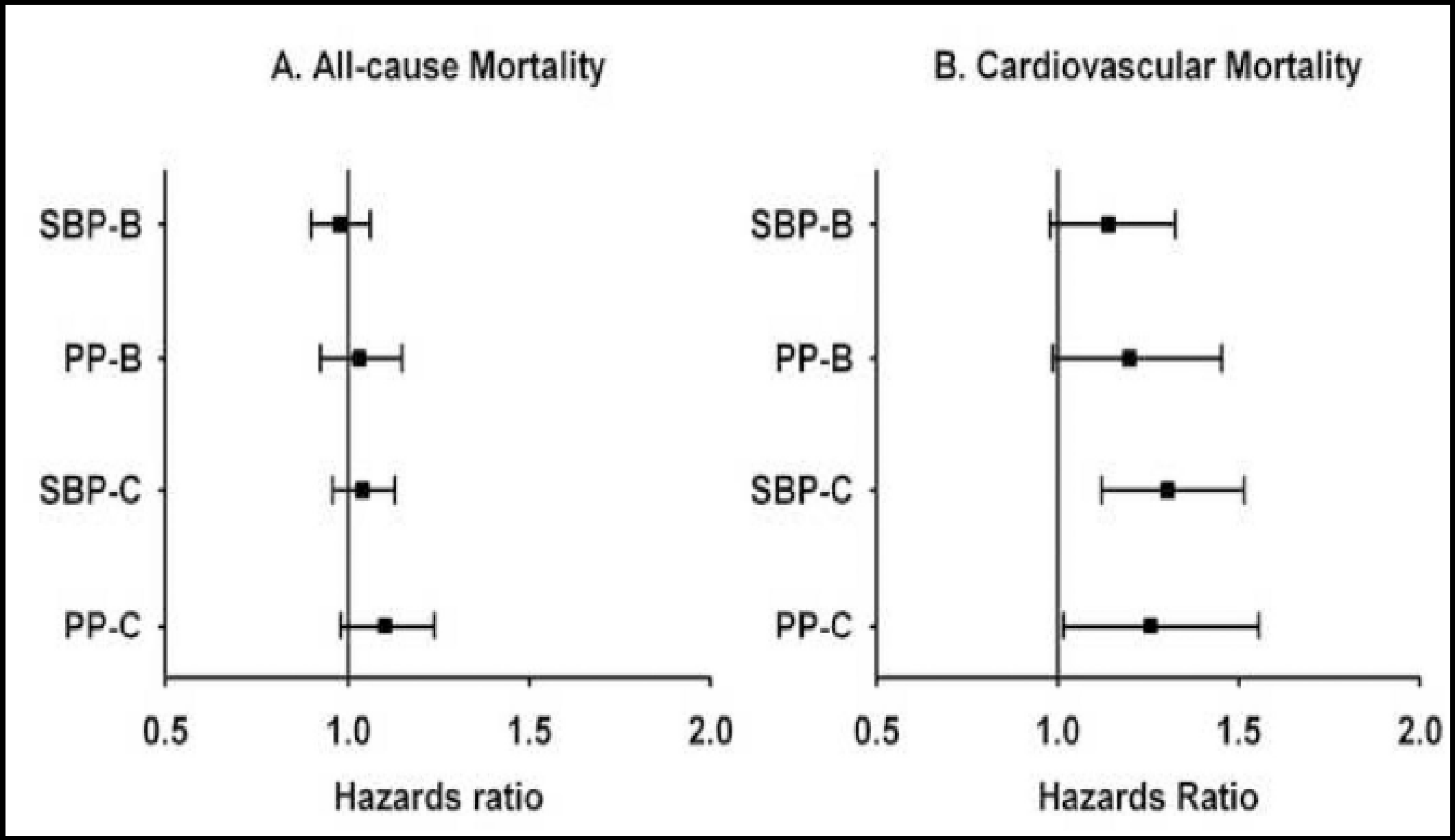
Prospective validation

Hazards ratios and 95% confidence intervals for all-cause and cardiovascular mortality by univariate analysis

Variables	All-cause mortality		Cardiovascular mortality	
	Women	Men	Women	Men
Age, years	**1.111 (1.082–1.142)**	**1.098 (1.074–1.123)**	**1.114 (1.060–1.170)**	**1.100 (1.054–1.148)**
Current smoking	**4.172 (1.505–11.563)**	1.297 (0.828–2.030)	0.048 (0.000– >10)	1.535 (0.647–3.642)
Body mass index, kg/m^2	1.014 (0.949–1.083)	**0.919 (0.854–0.989)**	0.995 (0.879–1.127)	1.036 (0.908–1.182)
Fasting Plasma Glucose, mmol/l	**1.140 (1.051–1.236)**	0.752 (0.549–1.030)	**1.183 (1.058–1.322)**	0.607 (0.324–1.138)
Cholesterol/HDL ratio	**1.262 (1.042–1.529)**	1.070 (0.917–1.247)	1.380 (0.994–1.916)	**1.289 (1.068–1.557)**
PWV, m/s	**1.243 (1.167–1.324)**	**1.182 (1.103–1.268)**	**1.306 (1.176–1.451)**	**1.223 (1.084–1.381)**
AI, %	1.010 (0.990–1.030)	**1.033 (1.017–1.050)**	1.014 (0.979–1.051)	**1.061 (1.029–1.094)**
LVM, g	**1.008 (1.003–1.014)**	**1.006 (1.002–1.011)**	**1.013 (1.004–1.022)**	**1.011 (1.003–1.018)**
LVMI, g/m^2	**1.018 (1.009–1.027)**	**1.018 (1.010–1.026)**	**1.028 (1.013–1.043)**	**1.023 (1.010–1.037)**
IMT, mm	**5.996 (2.432–14.781)**	**3.276 (1.690–6.349)**	**10.717 (2.510–45.761)**	**4.044 (1.224–13.360)**
eGFR, ml/min/1.73 m^2	**0.971 (0.961–0.980)**	**0.973 (0.962–0.983)**	**0.961 (0.945–0.977)**	**0.971 (0.951–0.991)**
SBP-B, 10 mmHg	**1.151 (1.040–1.273)**	**1.108 (1.006–1.221)**	**1.295 (1.083–1.547)**	**1.332 (1.111–1.597)**
PP-B, 10 mmHg	**1.250 (1.095–1.426)**	**1.357 (1.204–1.530)**	**1.408 (1.124–1.765)**	**1.540 (1.244–1.906)**
SBP-C, 10 mmHg	**1.234 (1.122–1.356)**	**1.114 (1.012–1.226)**	**1.510 (1.271–1.795)**	**1.353 (1.149–1.594)**
PP-C, 10 mmHg	**1.500 (1.318–1.708)**	**1.359 (1.206–1.531)**	**1.767 (1.413–2.210)**	**1.432 (1.153–1.778)**

Wang, J Hypertens. 2009 ; 27(3): 461–467.

Added predictive value (multivariate analysis)



Wang KL, et al. Central or peripheral systolic or pulse pressure: which best relates to target organs and future mortality? J Hypertens 2009; 27: 461-7.

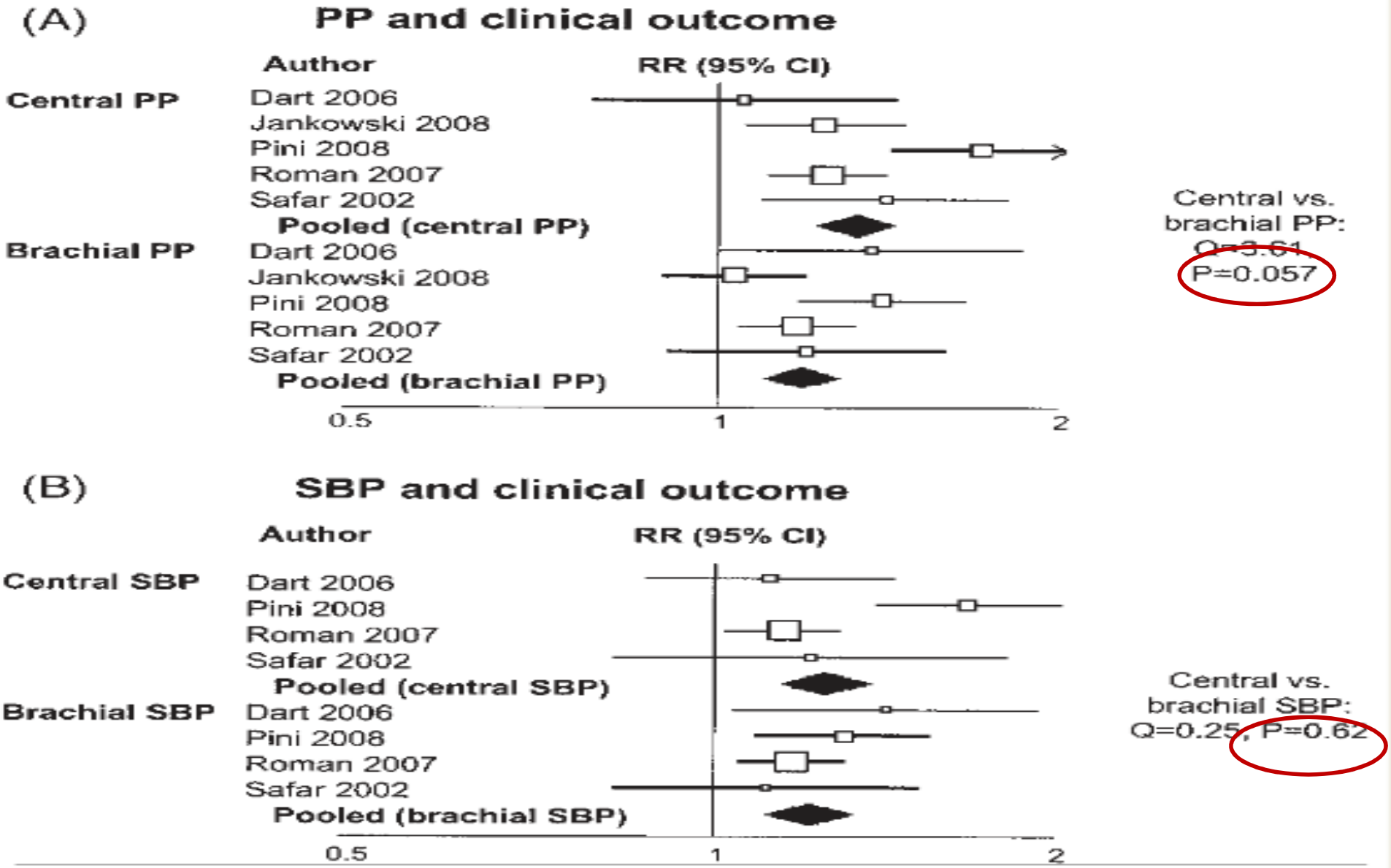
Added predictive value

Table 1 Central aortic pressures and major clinical outcomes in recent clinical studies

Patient group	Follow-up (months)	Outcome	Number of events	Dominant BP variable in multivariate analysis	Hazard ratio per 10 mmHg[a] or SD (95% CI)	Reference
End-stage renal disease	52	All cause mortality	70	Central pulse pressure (C)	1.4 (1.1–1.8)	Safar *et al.* [5]
Male coronary heart disease patients	39	All cause mortality	64	Central pulse pressure (D)	1.18[a] (1.05–1.33)	Chirinos *et al.* [6]
Treated hypertensive patients	36	Composite of CV and renal events	305	Central pulse pressure (R)	1.11[a] (1.0–1.21)	Williams *et al.* [3]
Unselected cohort of American Indians	58	Fatal and nonfatal CV events	319	Central pulse pressure (R)	1.15[a] (1.07–1.24)	Roman *et al.* [7]
Unselected elderly population	96	CV mortality	45	Central systolic pressure (C)	1.33[a] (1.03–1.72)	Pini *et al.* [8]
Coronary heart disease patients	54	Fatal and nonfatal CV events	246	Central pulse pressure (D)	1.25 (1.09–1.43)	Jankowski *et al.* [9]
Unselected Chinese community	120	CV mortality	130	Central systolic pressure (C)	1.30[a] (1.12–1.52)	Wang *et al.* [10]

Recent published studies reporting analyses relating brachial and central aortic pressure indices to major clinical outcomes. The dominant pressure variable is shown after adjustment for other variables in multivariate regression analyses. CV, cardiovascular; R, central pressure derived from radial pulse wave analysis; C, carotid pulse wave analysis; D, direct invasive measurement. [a]Identifies data expressed per 10 mmHg change in pressure.

Added predictive value ?



Vlachopoulos, European Heart Journal (2010) 31, 1865–1871

From risk assessment to risk reduction strategies

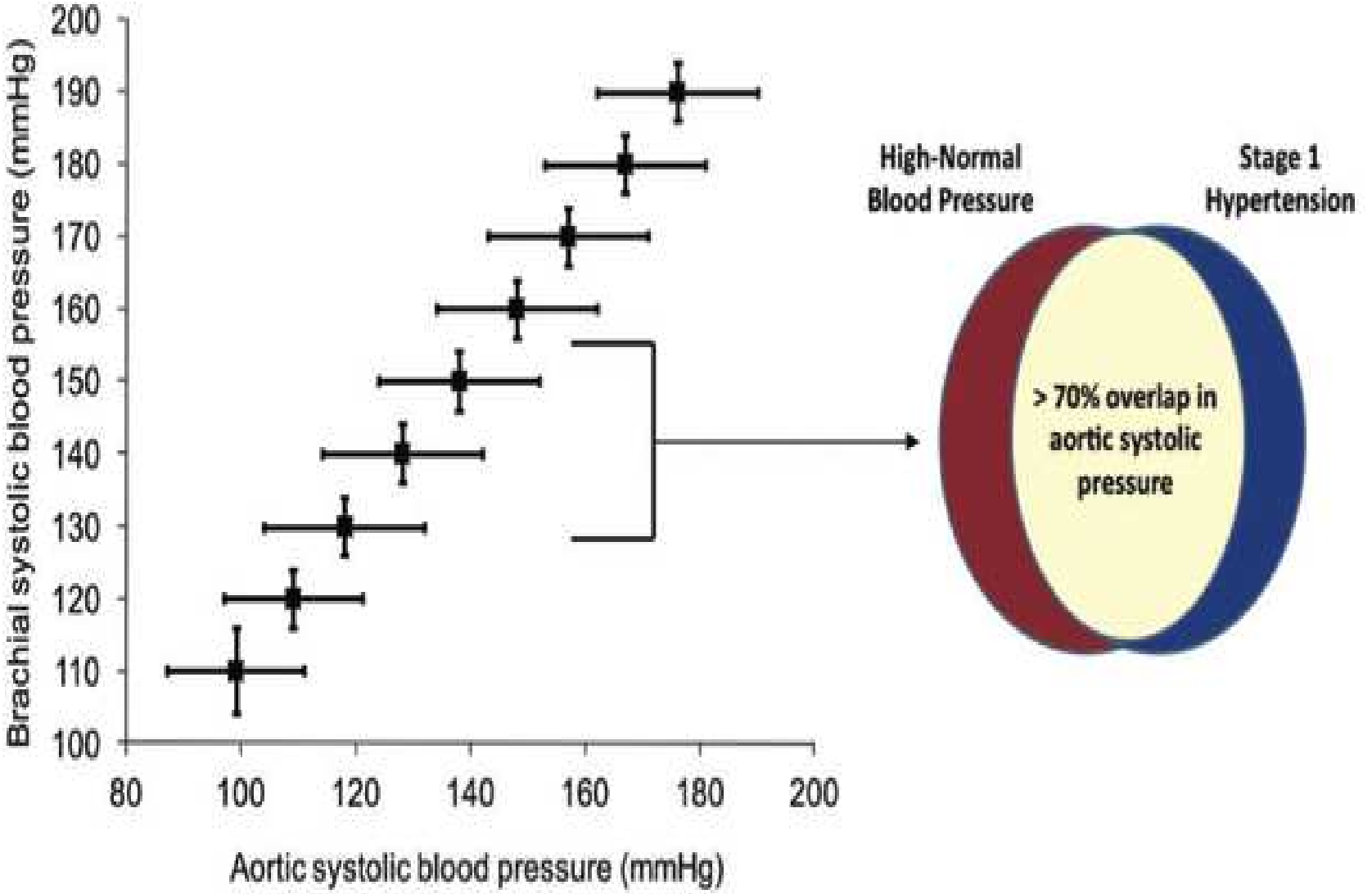


Figure 3 Overlap in aortic systolic blood pressure despite no overlap in brachial systolic pressure, in healthy men and women ($n = 5648$). Over 70% of individuals with high-normal blood pressure had aortic systolic pressures in common with individuals with stage 1 hypertension.[28]

McEniery C, et al. Eur Heart J 2014

From risk assessment to risk reduction strategies

- **Residual risk**
- **Systolic versus diastolic ?**
- **BP versus PWV ?**
- **Peripheral BP versus central BP ?**
- **Young versus old versus oldest old**
- **Prevention of CAD versus prevention of stroke ?**
- **Prêt-à-porter versus haute couture**

Journal of Human Hypertension (2009), 1–8

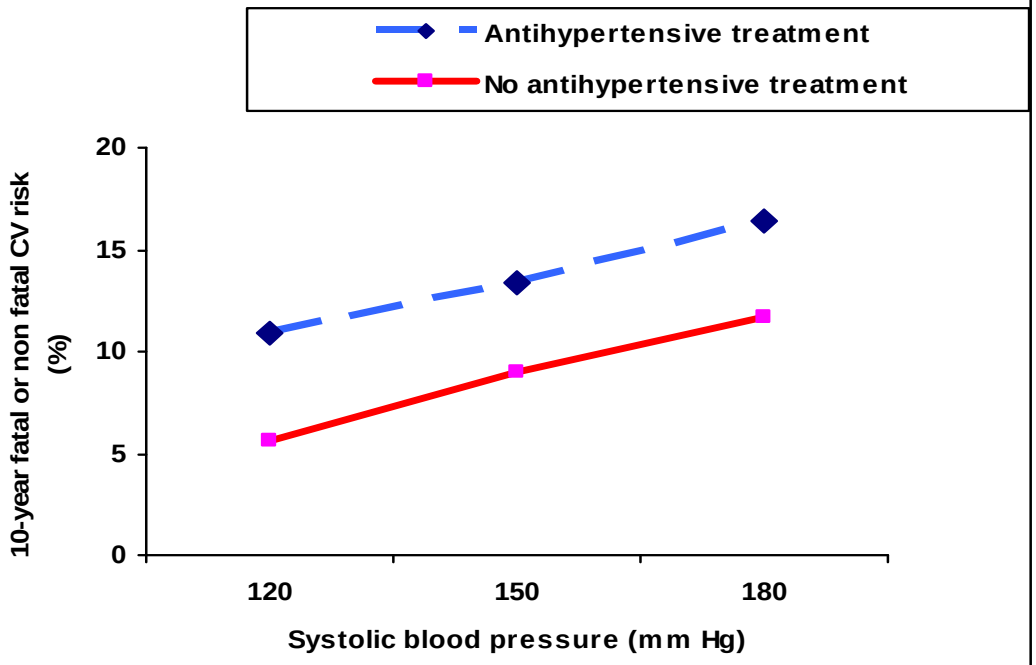
www.nature.com/jhh

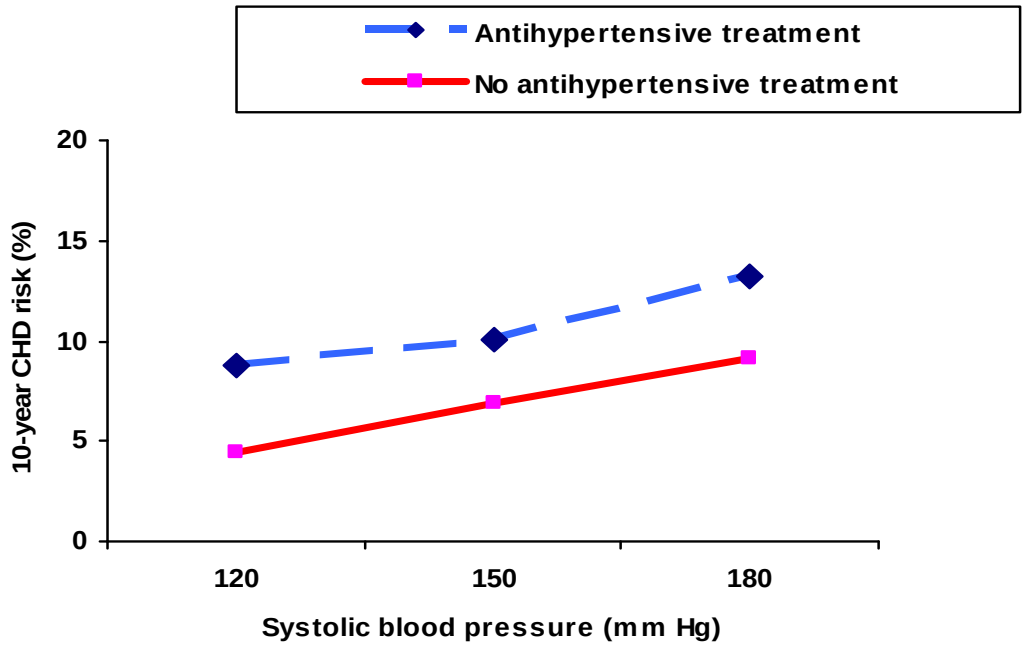
ORIGINAL ARTICLE

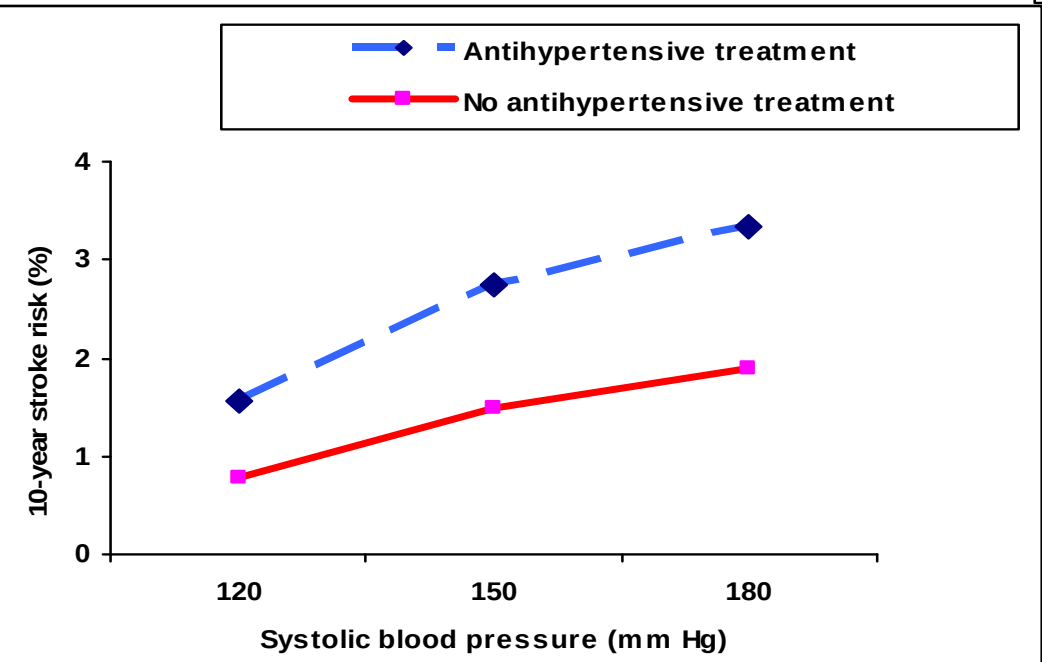
Residual cardiovascular risk in treated hypertension and hyperlipidaemia: the PRIME Study

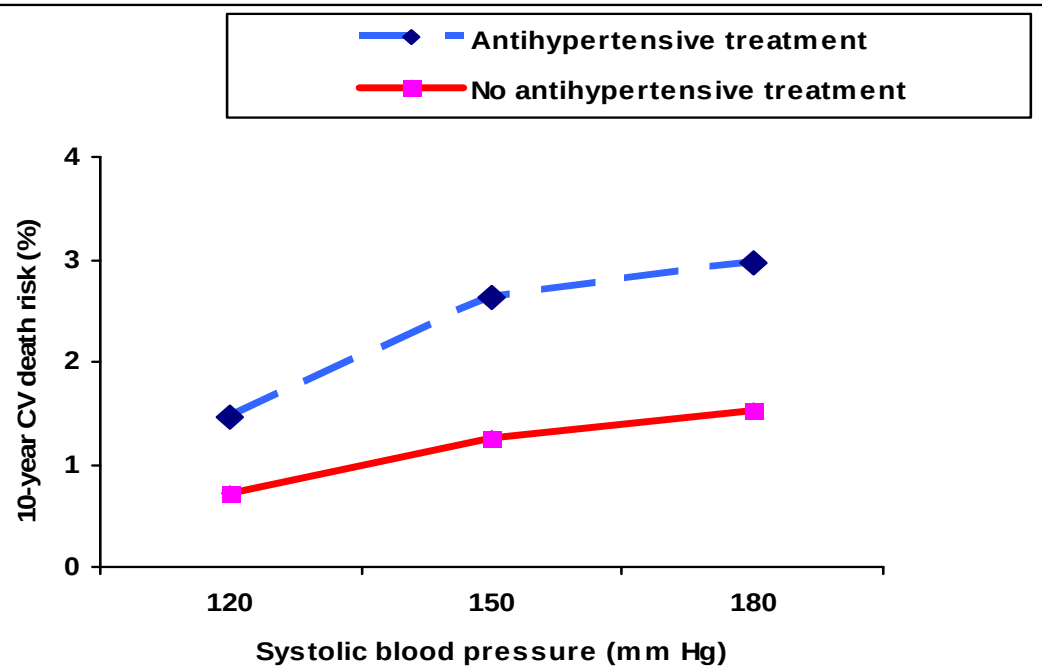
J Blacher[1,2], A Evans[3], D Arveiler[4], P Amouyel[5], J Ferrières[6], A Bingham[1], J Yarnell[3], B Haas[4], M Montaye[5], J-B Ruidavets[6] and P Ducimetière[1], on behalf of the PRIME Study Group

[1]INSERM, Hôpital Paul Brousse, Villejuif, France; [2]Hôtel-Dieu, APHP, Université Paris Descartes, Paris, France; [3]Belfast-MONICA, Department of Epidemiology and Public Health, Queen's University Belfast, Belfast, UK; [4]MONICA-Strasbourg, Laboratoire d'Epidémiologie et de Santé Publique, Faculté de Médecine, Université Louis Pasteur, Strasbourg, France; [5]INSERM, U 744, Institut Pasteur, MONICA-Lille, Lille, France and [6]MONICA-Toulouse, INSERM, Faculté de Médecine Purpan, Toulouse, France


Antihypertensive treatment
No antihypertensive treatment
10-year fatal or non fatal CV risk (%)
0
5
10
15
20
120
150
180
Systolic blood pressure (mm Hg)


Antihypertensive treatment
No antihypertensive treatment
10-year CHD risk (%)
0
5
10
15
20
120
150
180
Systolic blood pressure (mm Hg)


Antihypertensive treatment
No antihypertensive treatment
10-year stroke risk (%)
0
1
2
3
4
120
150
180
Systolic blood pressure (mm Hg)


Antihypertensive treatment
No antihypertensive treatment
10-year CV death risk (%)
0
1
2
3
4
120
150
180
Systolic blood pressure (mm Hg)

From risk assessment to risk reduction strategies

- Residual risk
- Systolic versus diastolic ?
- BP versus PWV ?
- Peripheral BP versus central BP ?
- Young versus old versus oldest old
- Prevention of CAD versus prevention of stroke ?
- Prêt-à-porter versus haute couture

Special Communication

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults

Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

Paul A. James, MD; Suzanne Oparil, MD; Barry L. Carter, PharmD; William C. Cushman, MD; Cheryl Dennison-Himmelfarb, RN, ANP, PhD; Joel Handler, MD; Daniel T. Lackland, DrPH; Michael L. LeFevre, MD, MSPH; Thomas D. MacKenzie, MD, MSPH; Olugbenga Ogedegbe, MD, MPH, MS; Sidney C. Smith Jr, MD; Laura P. Svetkey, MD, MHS; Sandra J. Taler, MD; Raymond R. Townsend, MD; Jackson T. Wright Jr, MD, PhD; Andrew S. Narva, MD; Eduardo Ortiz, MD, MPH

JAMA. doi:10.1001/jama.2013.284427
Published online December 18, 2013.

Second, in the DBP trials that demonstrated the benefit of treating DBP to lower than 90 mm Hg, many of the study participants who achieved DBP of lower than 90 mm Hg were also likely to have achieved SBPs of lower than 140 mm Hg with treatment. It is not possible to determine whether the outcome benefits in these trials were due to lowering DBP, SBP, or both.

In many studies focused on DBP, participants also had elevated SBP so it was not possible to determine whether the benefit observed in those trials arose from lowering DBP, SBP, or both.

In addition, UKPDS was a mixed systolic and diastolic BP goal study (combined SBP and DBP goals), so it cannot be determined if the benefits were due to lowering SBP, DBP, or both.

From risk assessment to risk reduction strategies

- Residual risk
- Systolic versus diastolic ?
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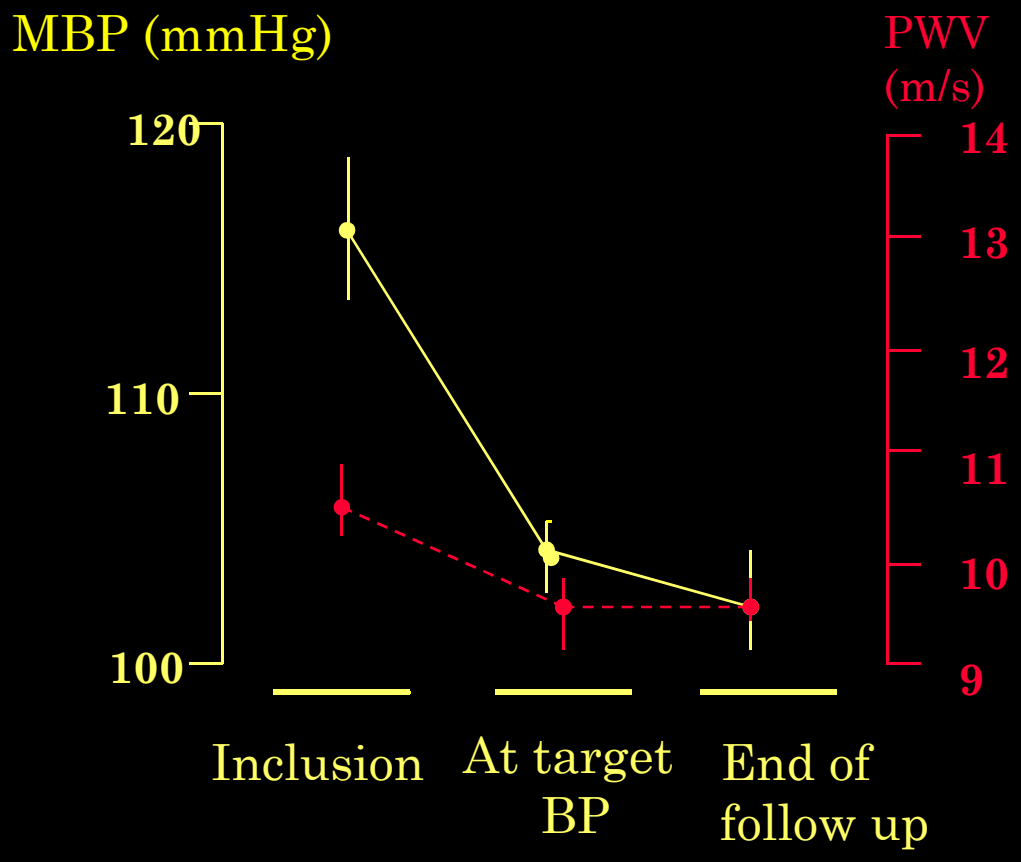
IMPACT OF AORTIC STIFFNESS ATTENUATION ON SURVIVAL OF PATIENTS IN END-STAGE RENAL FAILURE

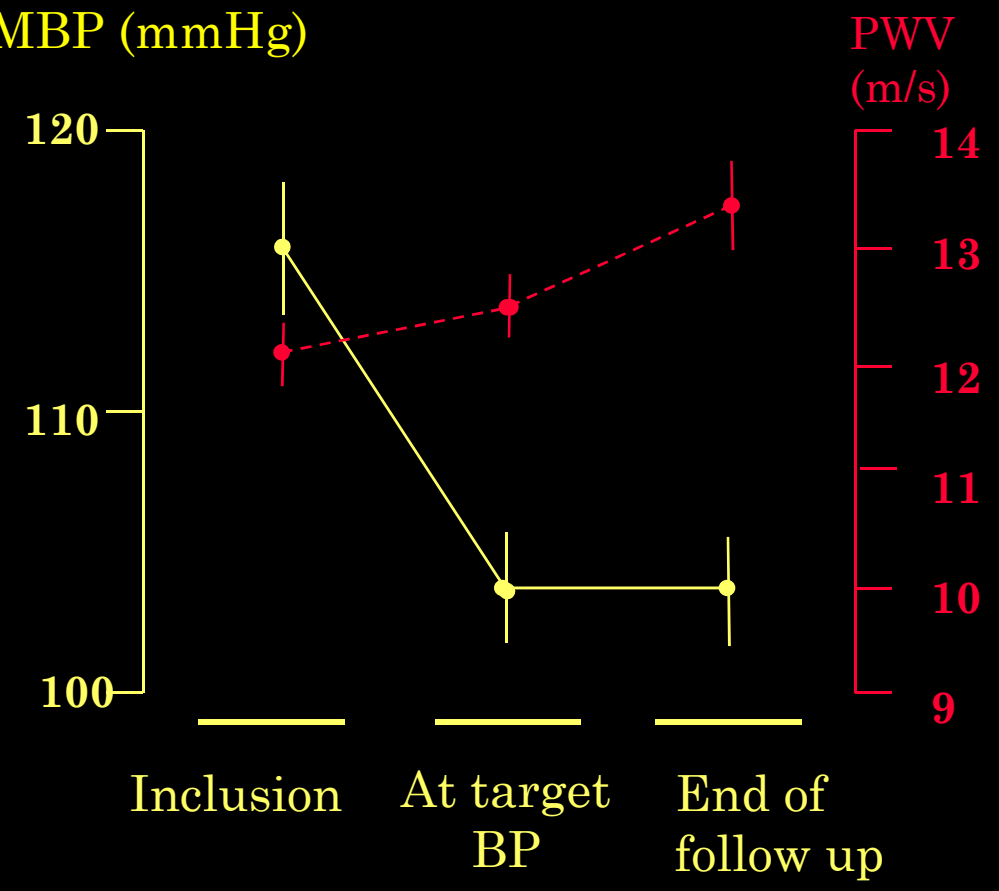
- 1st step: dry weight
- 2nd step: ACE inhibitor or calcium antagonist
- 3rd step: calcium antagonist or ACE inhibitor (if not well tolerated)
- 4th step: ACE inhibitor or calcium antagonist + beta-blocker
- 5th step: ACE inhibitor + calcium antagonist + beta-blocker

Guérin et al. Circulation 2001;103:987-992

Changes of Mean Blood Pressure and aortic PWV



Survivors



Non Survivors

Guerin and al. Impact of aortic stiffness attenuation on survival of patient in end stage renal failure. Circulation. 2001; 103:987-992

From risk assessment to risk reduction strategies

- Residual risk
- Systolic versus diastolic ?
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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

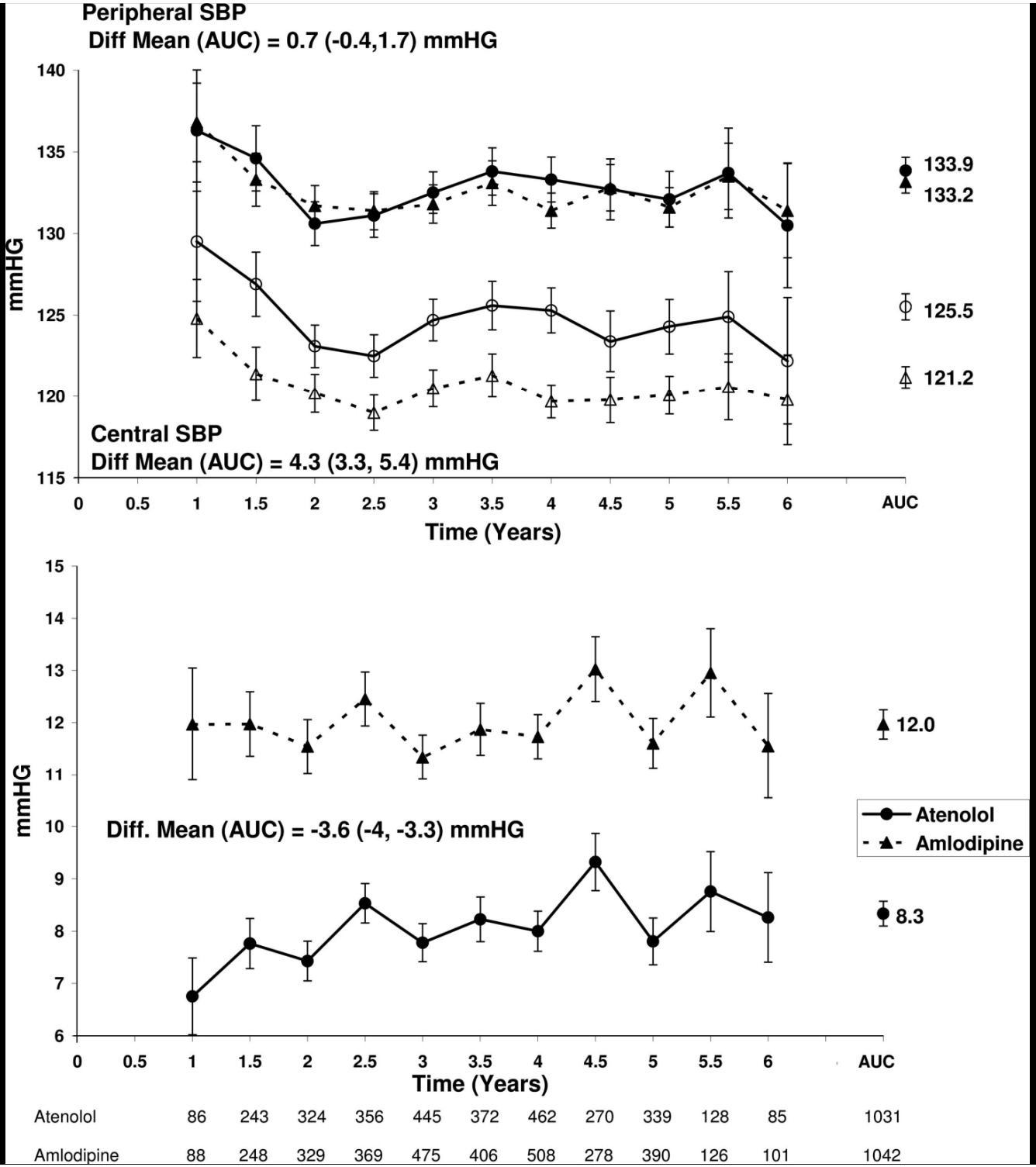
CAFE Steering Committee and Writing Committee: Bryan Williams, MD, FRCP; Peter S. Lacy, PhD; Simon M. Thom, MD, FRCP; Kennedy Cruickshank, MD; Alice Stanton, MB, PhD, FRCPI; David Collier, MBBS, PhD; Alun D. Hughes, MBBS, PhD; H. Thurston, MD, FRCP

Study Advisor: Michael O'Rourke, MD, FRACP

Background—Different blood pressure (BP)–lowering drugs could have different effects on central aortic pressures and thus cardiovascular outcome despite similar effects on brachial BP. The Conduit Artery Function Evaluation (CAFE) study, a substudy of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), examined the impact of 2 different BP lowering-regimens (atenolol±thiazide-based versus amlodipine±perindopril-based therapy) on derived central aortic pressures and hemodynamics.

Methods and Results—The CAFE study recruited 2199 patients in 5 ASCOT centers. Radial artery applanation tonometry and pulse wave analysis were used to derive central aortic pressures and hemodynamic indexes on repeated visits for up to 4 years. Most patients received combination therapy throughout the study. Despite similar brachial systolic BPs between treatment groups (Δ0.7 mm Hg; 95% CI, −0.4 to 1.7; $P=0.2$), there were substantial reductions in central aortic pressures with the amlodipine regimen (central aortic systolic BP, Δ4.3 mm Hg; 95% CI, 3.3 to 5.4; $P<0.0001$; central aortic pulse pressure, Δ3.0 mm Hg; 95% CI, 2.1 to 3.9; $P<0.0001$). Cox proportional-hazards modeling showed that central pulse pressure was significantly associated with a post hoc–defined composite outcome of total cardiovascular events/procedures and development of renal impairment in the CAFE cohort (unadjusted, $P<0.0001$; adjusted for baseline variables, $P<0.05$).

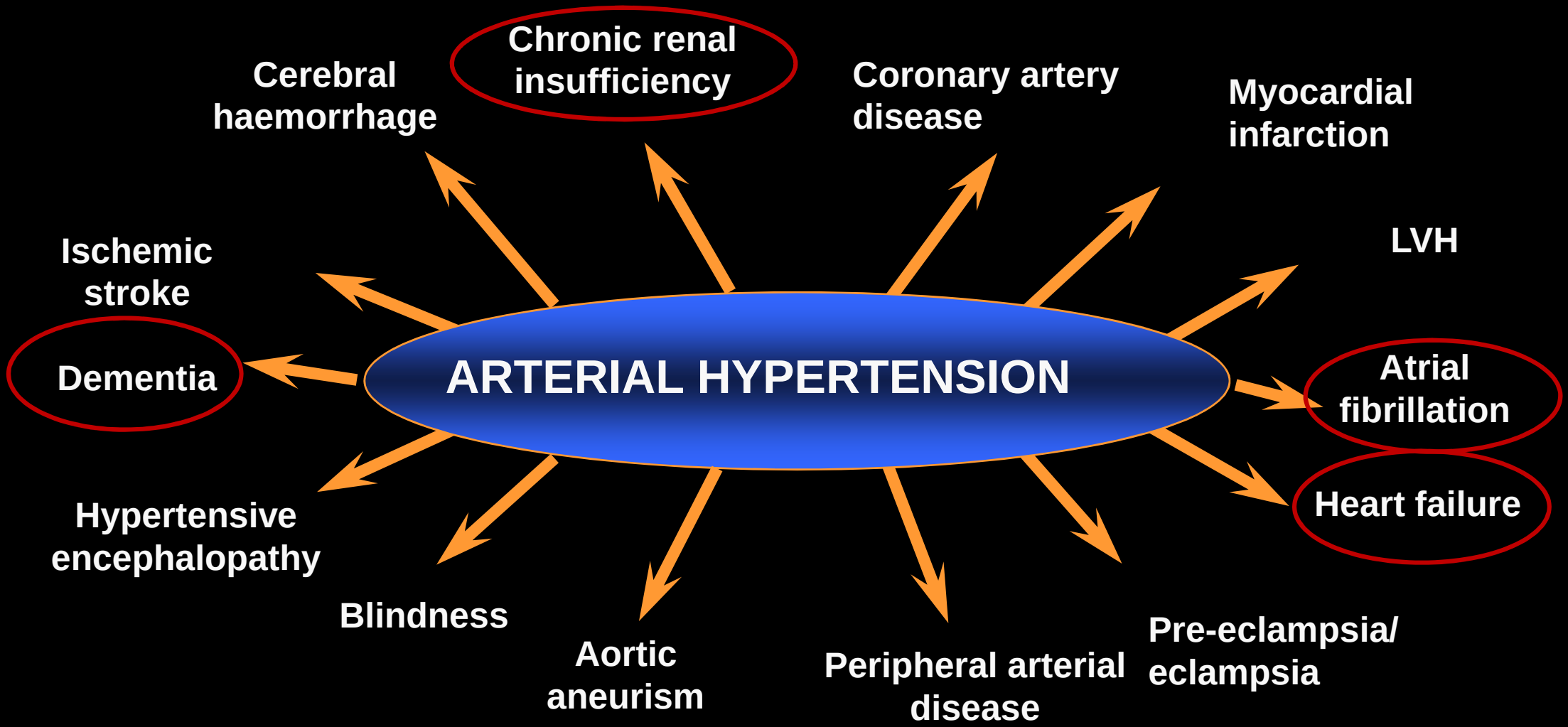
Conclusions—BP-lowering drugs can have substantially different effects on central aortic pressures and hemodynamics despite a similar impact on brachial BP. Moreover, central aortic pulse pressure may be a determinant of clinical outcomes, and differences in central aortic pressures may be a potential mechanism to explain the different clinical outcomes between the 2 BP treatment arms in ASCOT. (***Circulation.* 2006;113:1213-1225.**)


Peripheral SBP
Diff Mean (AUC) = 0.7 (-0.4,1.7) mmHG
mmHG
140
135
130
125
120
115
133.9
133.2
125.5
121.2
Central SBP
Diff Mean (AUC) = 4.3 (3.3, 5.4) mmHG
0 0.5 1 1.5 2 2.5 3 3.5 4 4.5 5 5.5 6 AUC
Time (Years)
15
14
13
12
11
10
9
8
7
6
12.0
Atenolol
Amlodipine
Diff. Mean (AUC) = -3.6 (-4, -3.3) mmHG
8.3
0 0.5 1 1.5 2 2.5 3 3.5 4 4.5 5 5.5 6 AUC
Time (Years)
Atenolol 86 243 324 356 445 372 462 270 339 128 85 1031
Amlodipine 88 248 329 369 475 406 508 278 390 126 101 1042

From risk assessment to risk reduction strategies

- Residual risk
- Systolic versus diastolic ?
- BP versus PWV ?
- Peripheral BP versus central BP ?
- Young versus old versus oldest old
- Prevention of CAD versus prevention of stroke ?
- Prêt-à-porter versus haute couture

Hypertension : complications



From risk assessment to risk reduction strategies

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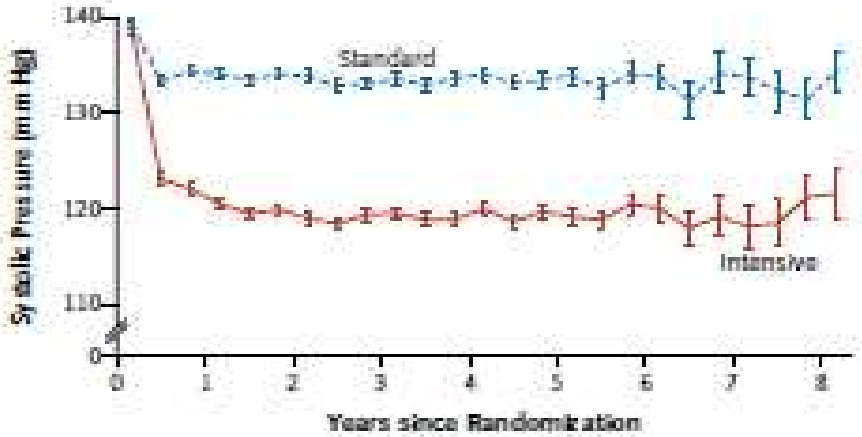
ORIGINAL ARTICLE

Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus

The ACCORD Study Group*



Mean No. of Medications Prescribed								
Intensive	3.2	3.4	3.4	3.5	3.5	3.5	3.4	3.4
Standard	1.9	2.1	2.1	2.2	2.2	2.3	2.3	2.3
No. of Patients								
Intensive	2174	2071	1973	1792	1150	445	156	156
Standard	2208	2136	2077	1860	1241	504	203	201

Figure 1. Mean Systolic Blood-Pressure Levels at Each Study Visit.
I bars indicate 95% confidence intervals.

Table 3. Primary and Secondary Outcomes.

Outcome	Intensive Therapy (N=2363)		Standard Therapy (N=2371)		Hazard Ratio (95% CI)	P Value
	no. of events	%/yr	*no. of events*	%/yr		
Primary outcome*	208	1.87	237	2.09	0.88 (0.73–1.06)	0.20
Prespecified secondary outcomes						
Nonfatal myocardial infarction	126	1.13	146	1.28	0.87 (0.68–1.10)	0.25
Stroke						
Any	36	0.32	62	0.53	0.59 (0.39–0.89)	0.01
Nonfatal	34	0.30	55	0.47	0.63 (0.41–0.96)	0.03
Death						
From any cause	150	1.28	144	1.19	1.07 (0.85–1.35)	0.55
From cardiovascular cause	60	0.52	58	0.49	1.06 (0.74–1.52)	0.74
Primary outcome plus revascularization or nonfatal heart failure	521	5.10	551	5.31	0.95 (0.84–1.07)	0.40
Major coronary disease event†	253	2.31	270	2.41	0.94 (0.79–1.12)	0.50
Fatal or nonfatal heart failure	83	0.73	90	0.78	0.94 (0.70–1.26)	0.67

* The primary outcome was a composite of nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes.
† Major coronary disease events, as defined in the protocol, included fatal coronary events, nonfatal myocardial infarction, and unstable angina.

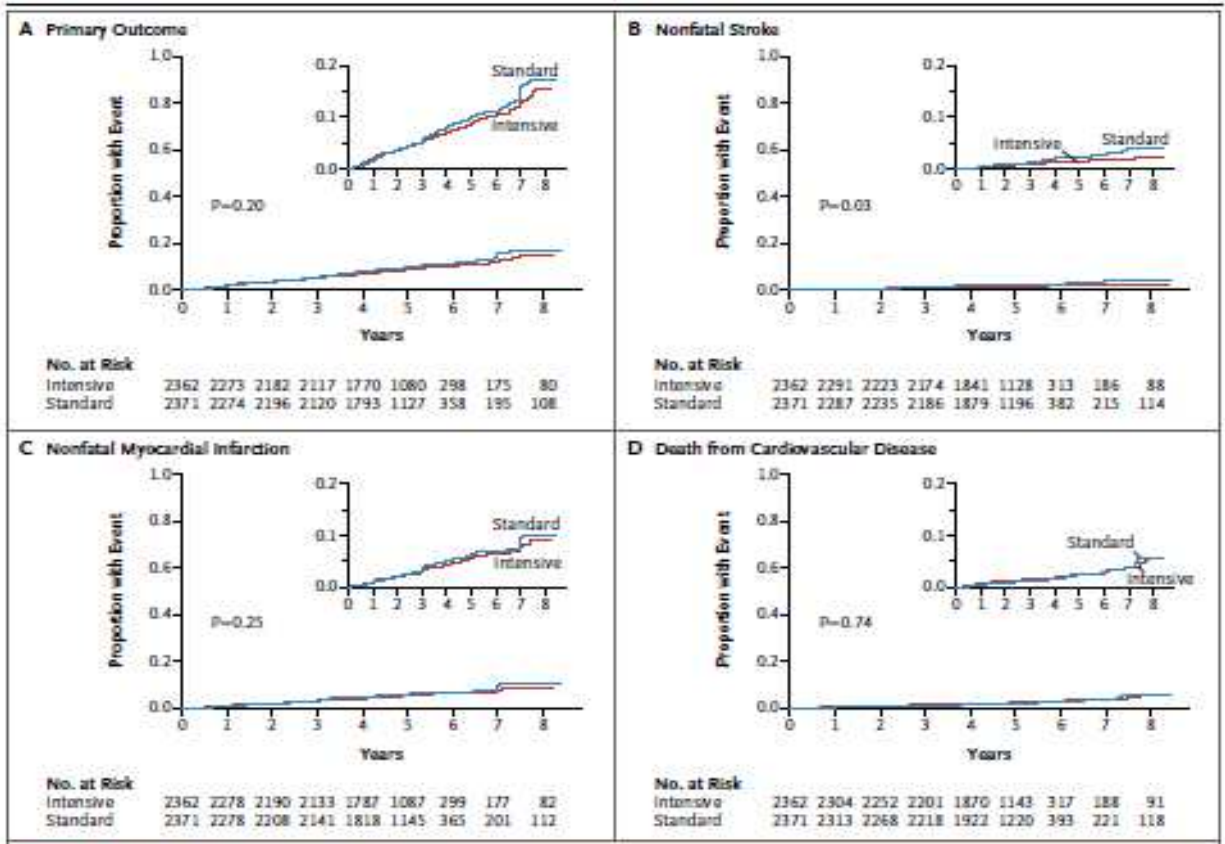


Figure 2. Kaplan–Meier Analyses of Selected Outcomes.
Shown are the proportions of patients with events for the primary composite outcome (Panel A) and for the individual components of the primary outcome (Panels B, C, and D). The insets show close-up versions of the graphs in each panel.

From risk assessment to risk reduction strategies

- Residual risk
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Therapeutic target ?

«Improvement in quality of care could be achieved using central BP to manage patients with uncomplicated essential hypertension.»

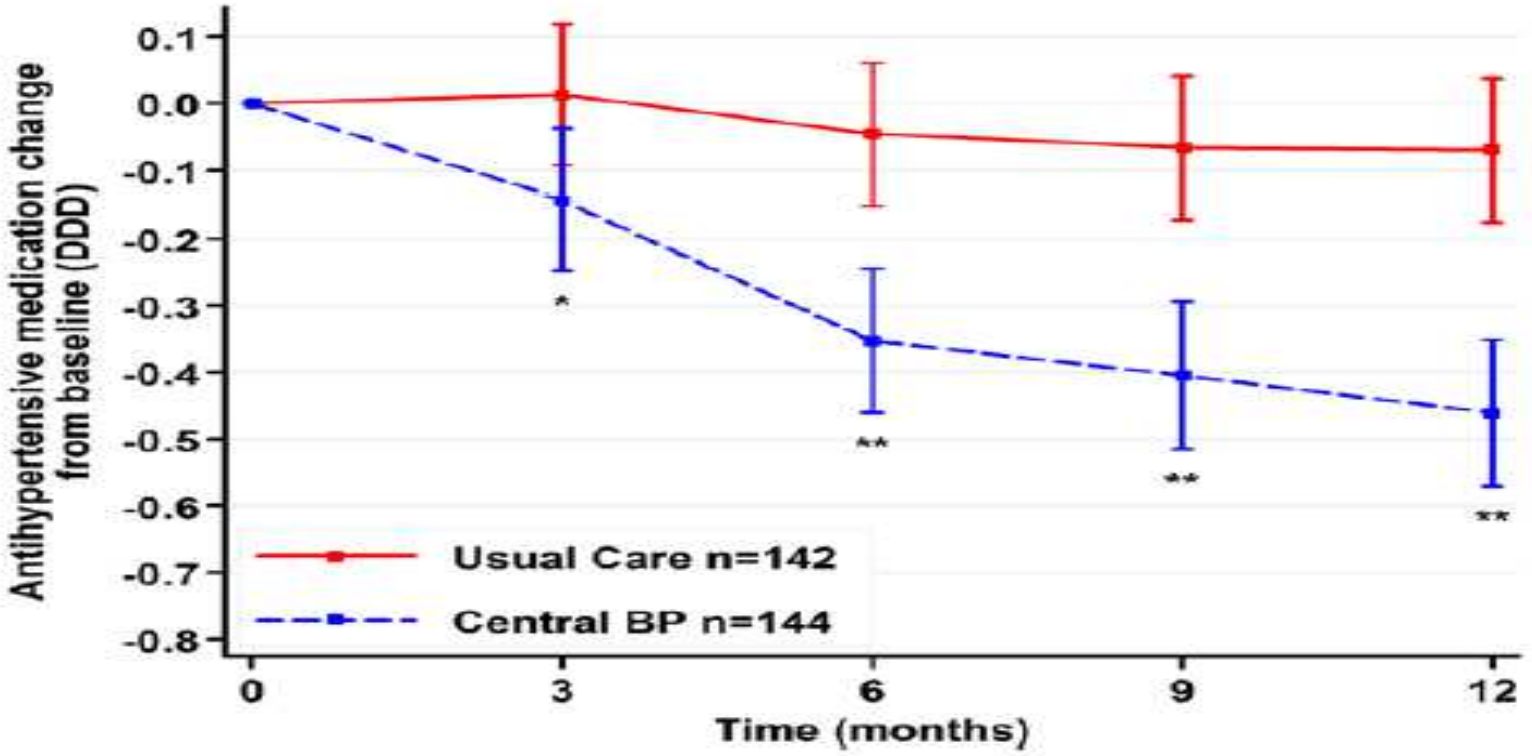
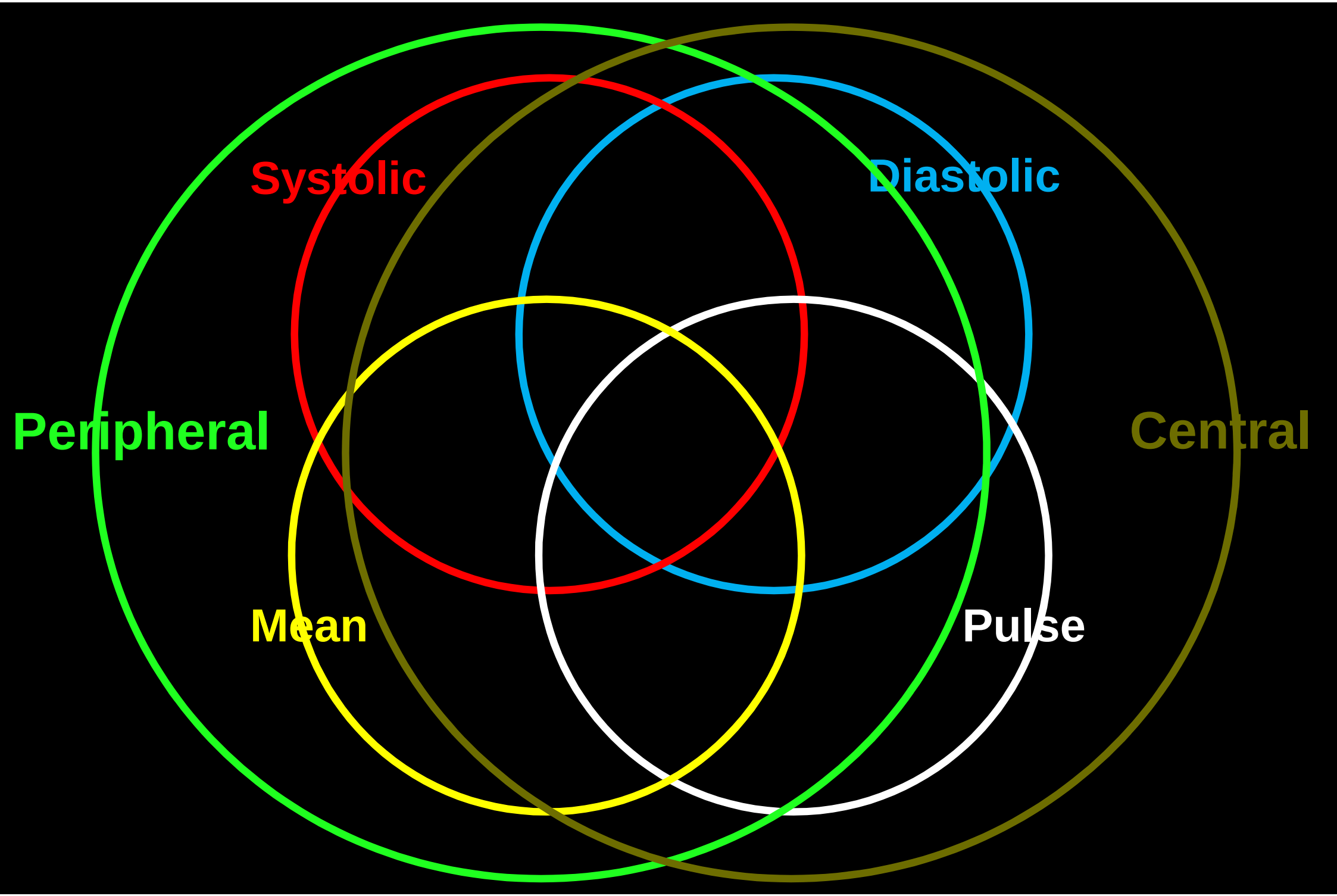


Figure 3. Between-group change in daily defined dose (DDD) of antihypertensive medications. Change is from baseline to each follow-up, adjusting for age, sex, and body mass index. Error bars indicate 95% confidence interval and **P*=0.008, ***P*<0.001. BP indicates blood pressure.

Sharman et al. ***Hypertension. 2013;62:1138-1145***

From risk assessment to risk reduction strategies
CONCLUSION

- **Reliable BP measurements**
- **Better understanding of the patho-physiology**
- **Meta-analysis of observational studies and therapeutic trials (structural models):**
  - **Association of different BP parameters to CV risk**
  - **Association of different BP parameters to CV risk reduction**
- **Dedicated therapeutic trials**
  - **Focussing on one parameter versus another**
  - **Difficult to interpret because of collinearity**


Systolic
Diastolic
Peripheral
Central
Mean
Pulse

QCM post-test

- **Il fait plein soleil et 25° à Paris ; pourquoi quitter Tours ?**

- **A: A cause de J.M. Halimi**
- **B: A cause de J.M. Halimi**
- **C: A cause de J.M. Halimi**
- **D: A cause de J.M. Halimi**
- **E: A cause de J.M. Halimi**