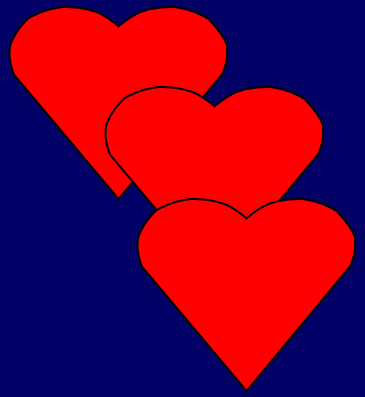
Στόχοι ΑΠ σε ειδικούς πληθυσμούς
Η σύγχυση μεταξύ των οδηγιών



Μ. Β. Παπαβασιλείου
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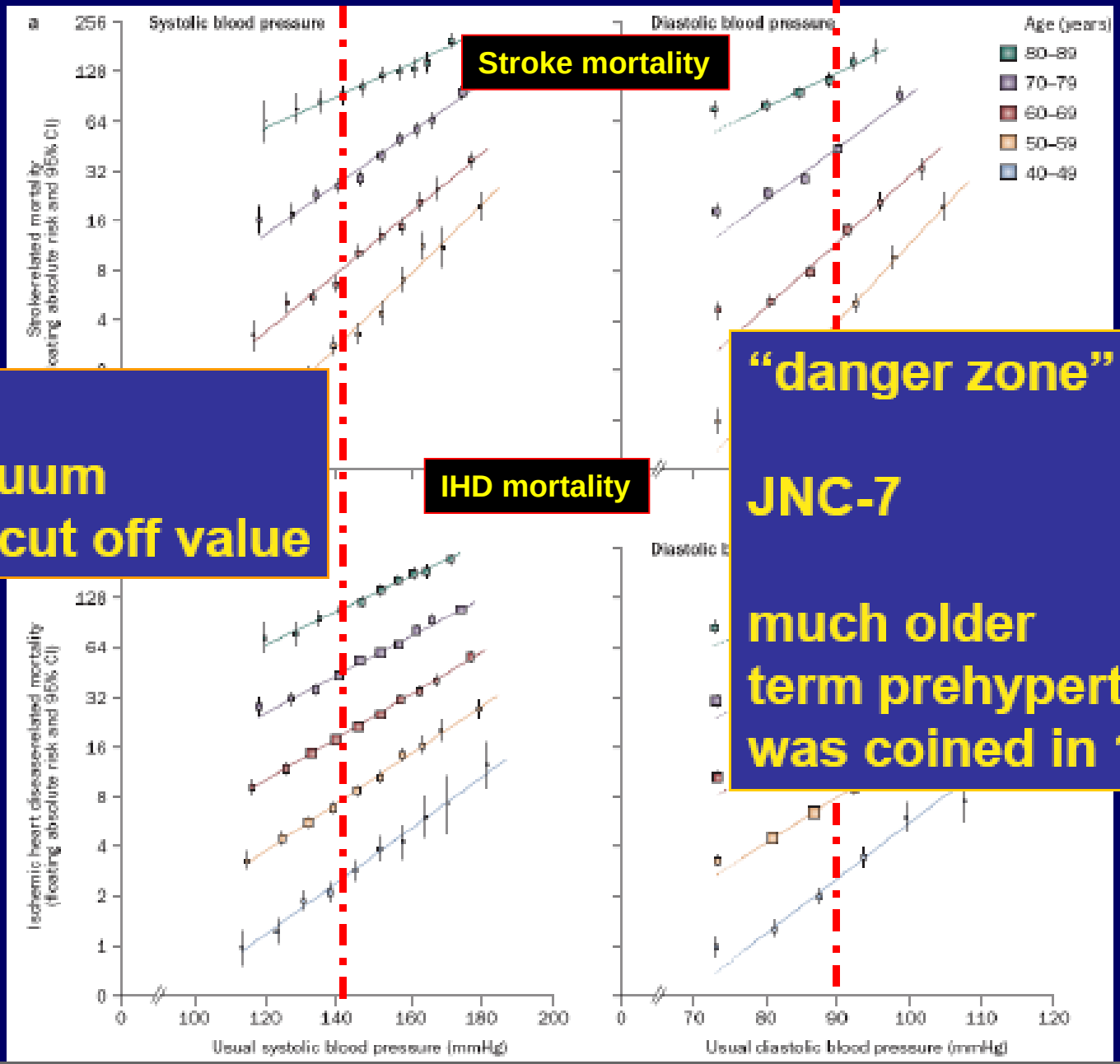
Disentangling Complexity is Challenging – Many new guidelines?

Globally Renowned Hypertension Societies

1. **JNC VII** – Joint National Committee on HT, USA
2. **WHO-ISH** – WHO - International Society on HT
3. **EHS** – European Hypertension Society
4. **BHS** – British Hypertension Society
5. **CHS** – Canadian Hypertension Society
6. **NKF** – National Kidney Foundation, USA
7. **AKA** – American Kidney Association, USA
8. **AHA** – American Heart Association, USA
9. **ACC** – American College of Cardiologist
10. JHS-Japanese society
11. ISHIB-international society in Blacks
12. **AHA/ACC/ASH Scientific Statement 2015**
13. **ESC 2016**

13 American College of Physicians 2017

Mortality from ischemic heart disease and stroke increases with increasing blood pressrue



Stroke mortality

IHD mortality

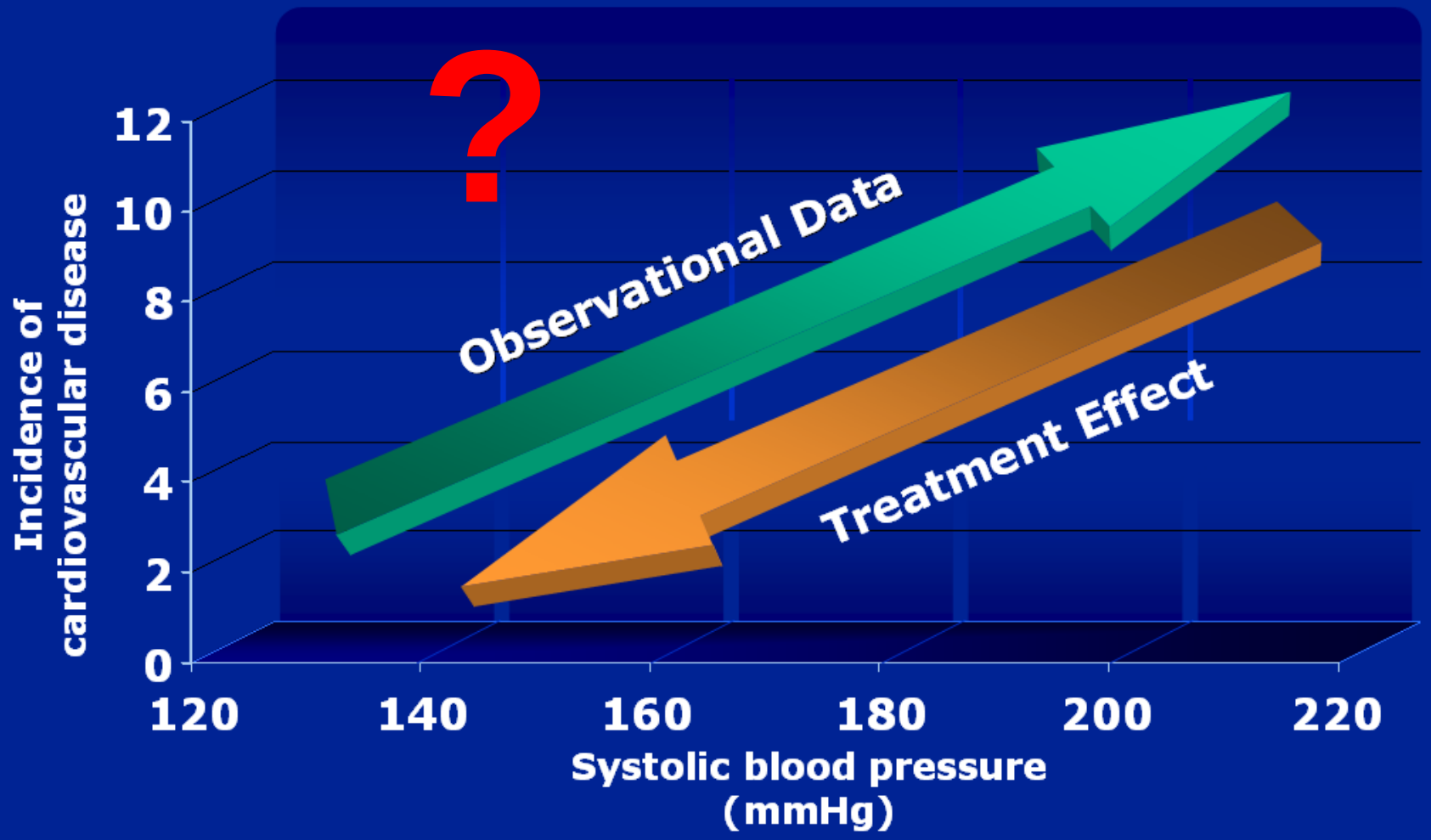
Linear
Continuum
Below cut off value

"danger zone"

JNC-7

much older
term prehypertension
was coined in 1939

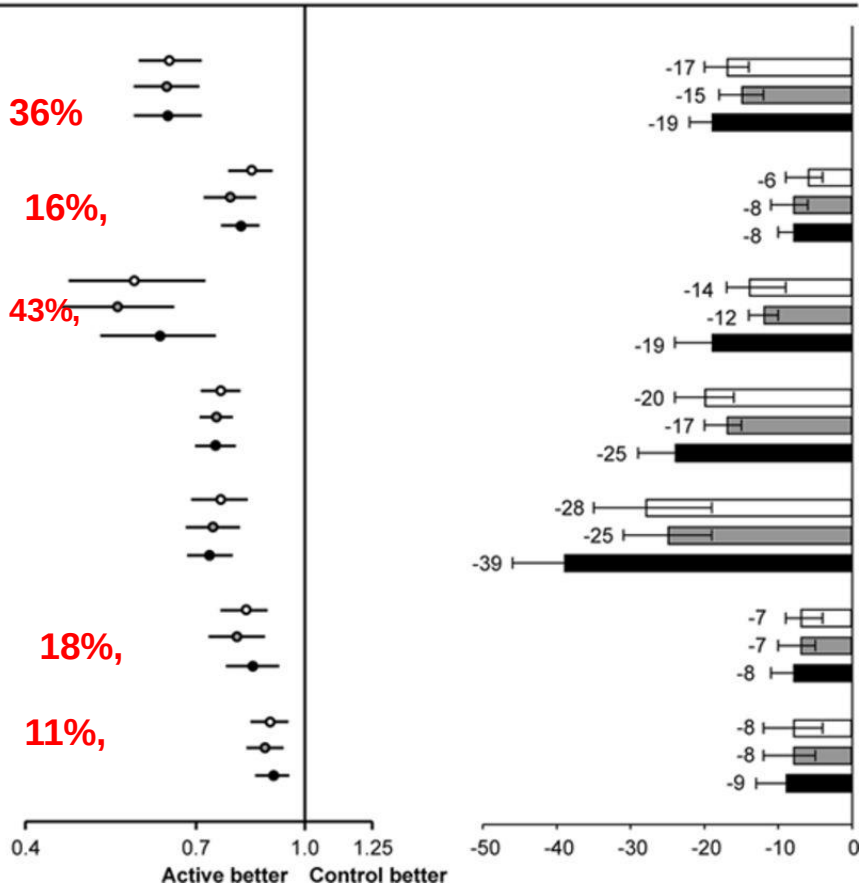
Hypertension Treatment Effect Mirrors Observational Data



Relative and absolute risk reduction of various outcomes in trials of BP lowering

standardized SBP/DBP difference between active and control groups of 10/5 mm Hg

Outcome	Trials (n)	Events (n/patients) Treated	Events (n/patients) Controls	Difference SBP/DBP (mmHg)	Standardized RR (95% CI)
Stroke					
A. Intentional	38	2200/ 71664	3059/ 76160	-8.4/-4.4	0.64 (0.58-0.71)
B. Intent. HT	31	1262/ 51179	1870/ 56326	-9.0/-4.8	0.63 (0.56-0.71)
C. Intent + Non-Intent	54	4215/115690	5298/119695	-6.6/-3.5	0.64 (0.57-0.71)
CHD					
A. Intentional	42	2358/ 72653	2697/ 76702	-8.6/-4.4	0.84 (0.79-0.90)
B. Intent. HT	35	1443/ 52168	1723/ 56868	-9.0/-4.8	0.78 (0.72-0.85)
C. Intent + Non-Intent	58	4014/116346	4498/119718	-6.7/-3.4	0.82 (0.76-0.86)
HF					
A. Intentional	24	658/ 34609	899/ 33042	-9.2/-4.3	0.57 (0.46-0.72)
B. Intent. HT	20	231/ 21517	415/ 20605	-10.6/-4.8	0.54 (0.45-0.64)
C. Intent + Non-Intent	36	2666/ 74973	3121/ 72948	-6.0/-2.9	0.62 (0.51-0.75)
Stroke + CHD					
A. Intentional	39	4485/ 71190	5598/ 75682	-8.6/-4.4	0.76 (0.71-0.81)
B. Intent. HT	32	2632/ 50705	3472/ 55848	-9.0/-4.8	0.75 (0.71-0.79)
C. Intent + Non-Intent	56	8193/115651	9668/118924	-6.7/-3.5	0.74 (0.70-0.80)
Stroke + CHD + HF					
A. Intentional	26	3479/ 44994	4138/ 43416	-10.0/-4.8	0.75 (0.69-0.83)
B. Intent. HT	22	1969/ 31902	2536/ 30979	-11.2/-5.4	0.74 (0.69-0.81)
C. Intent + Non-Intent	38	9107/ 85358	10364/ 83322	-6.9/-3.4	0.73 (0.68-0.79)
CV Death					
A. Intentional	42	2222/ 72328	2595/ 76810	-8.6/-4.4	0.82 (0.76-0.89)
B. Intent. HT	33	1473/ 51245	1778/ 56402	-9.1/-4.8	0.80 (0.73-0.88)
C. Intent + Non-Intent	58	4577/116381	4966/119641	-6.8/-3.4	0.84 (0.77-0.92)
All-cause Death					
A. Intentional	46	4371/ 74223	4844/ 78696	-8.6/-4.4	0.89 (0.84-0.95)
B. Intent. HT	37	2913/ 53140	3336/ 58288	-9.0/-4.8	0.88 (0.82-0.93)
C. Intent + Non-Intent	66	8785/120049	9246/123715	-6.7/-3.5	0.90 (0.85-0.95)



absolute risk reduction reports the number of events prevented for every 1000 patients treated for 5 years with a standardized RR

Zanchetti A, Thomopoulos C et al. Circ Res. 2015

American Heart Association

Initiation of lifestyle changes and antihypertensive drug treatment ESH 2013

Other risk factors, asymptomatic organ damage or disease	Blood Pressure (mmHg)			
	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other RF	• No BP intervention	• Lifestyle changes for several months • Then add BP drugs targeting <140/90	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
1–2 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
≥3 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
OD, CKD stage 3 or diabetes	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; HT = hypertension; OD = organ damage; RF = risk factor; SBP = systolic blood pressure.

Blood pressure goals in hypertensive patients

Recommendations	Class [a]	Level [b]
A SBP goal <140 mmHg:		
a) is recommended in patients at low–moderate CV risk;	I	B
A DBP target of <90 mmHg is always recommended, except in patients with diabetes, in whom values <85 mmHg are recommended. It should nevertheless be considered that DBP values between 80 and 85 mmHg are safe and well tolerated.	I	A

ESH 2013

BP Goal uncomplicated HTN

Comparisons to Other Guidelines

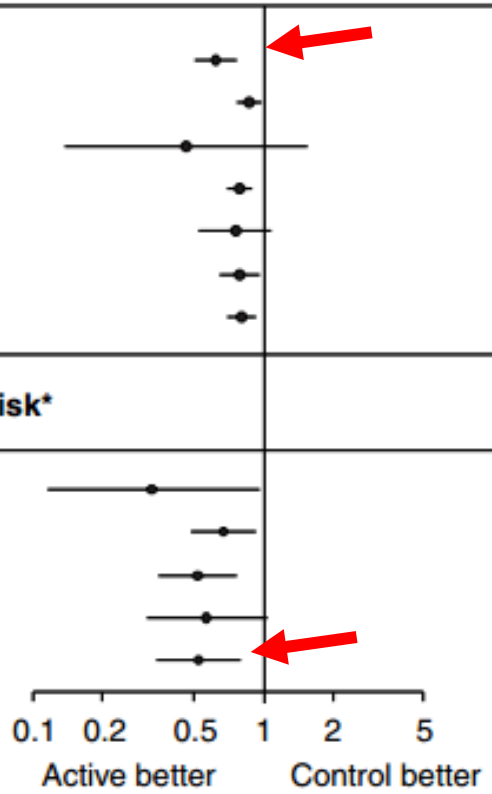
BP Goal	JNC-7	JNC-8	ASH/ISH	ESC/ESH	CHEP
Age < 60	<140/90	<140/90	<140/90	<140/90	<140/90

BP Goal	NICE	ISHIB	JHS		
Age < 60	<140/90	<135/85	<140/90 HBPm <135/85		

Adapted from Salvo M et al. *Ann Pharmacother* 2014;48:1242-8.

Effects of BP lowering in trials of grade 1 HTN

Outcome	Trials (n)	Events (n/patients) Treated	Events (n/patients) Controls	Standardized RR (95% CI)
A. Grade 1 hypertension				
Stroke	4	218/7343	312/7321	0.64 (0.51 – 0.78)
CHD	6	368/8248	403/7788	0.88 (0.77 – 0.99)
HF	2	0/ 599	3/ 575	0.46 (0.14 – 1.57)
Stroke + CHD	4	544/7343	689/7321	0.80 (0.72 – 0.88)
Stroke + CHD + HF	2	15/ 599	24/ 575	0.76 (0.53 – 1.08)
CV Death	4	218/7343	274/7321	0.78 (0.65 – 0.95)
All-cause Death	5	402/7580	487/7554	0.82 (0.72 – 0.94)
B. Grade 1 hypertension and low-moderate CV risk*				
Stroke	4	71/4061	110/4012	0.33 (0.11 – 0.98)
CHD	5	114/4729	129/4246	0.68 (0.48 – 0.95)
Stroke + CHD	4	159/4051	227/4012	0.51 (0.36 – 0.75)
CV Death	4	53/4061	74/4012	0.57 (0.32 – 1.02)
All-cause Death	4	90/4061	133/4012	0.53 (0.35 – 0.80)



Zanchetti A Expert Opinion on Pharmacotherapy 2015

To do and not to do messages from the Guidelines (3)

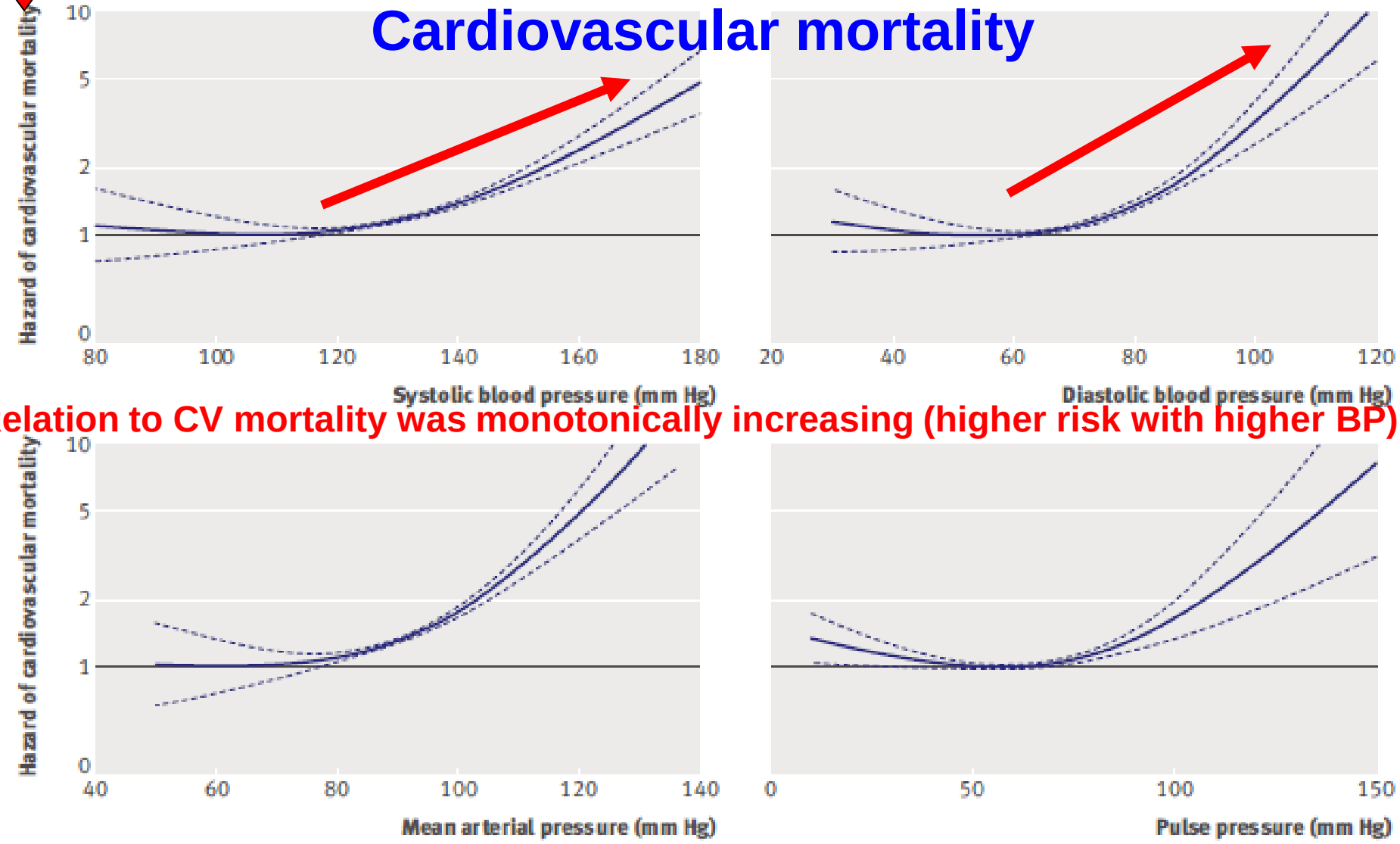
Recommendations	Class	Level
How to intervene *(cont'd)*		
In treated hypertensive patients <60 years old, SBP <140 mmHg and DBP <90 mmHg are recommended.	I	B
In patients >60 years old with SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg. In individuals >80 years and with initial SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg, provided they are in good physical and mental conditions.		
BP targets in type 2 DM are <140/85 mmHg, but a lower target of <130/80 mmHg is recommended in selected patients (e.g. younger patients at elevated risk for complications) for additional gains on stroke, retinopathy and albuminuria risk.	I	B
BP targets in patients with type 1 DM are <130/80 mmHg.	I	B
Drug treatment is recommended in patients with grade 3 hypertension irrespective of CV risk, as well as in patients with grade 1 or 2 hypertension who are at very high CV risk.	I	B
All major BP lowering drug classes (i.e. diuretics, ACE-I, calcium antagonists, ARBs, and ß-blockers) do not differ significantly in their BP-lowering efficacy and thus are recommended as BP lowering treatment.	I	A

European Heart Journal 2016 ;37:2315–2381-doi:10.1093/eurheartj/ehw106

Young adults

N=1.2 million men in Sweden Mag at entry 18.4 y follow-up 24 y

Cardiovascular mortality



Relation to CV mortality was monotonically increasing (higher risk with higher BP)

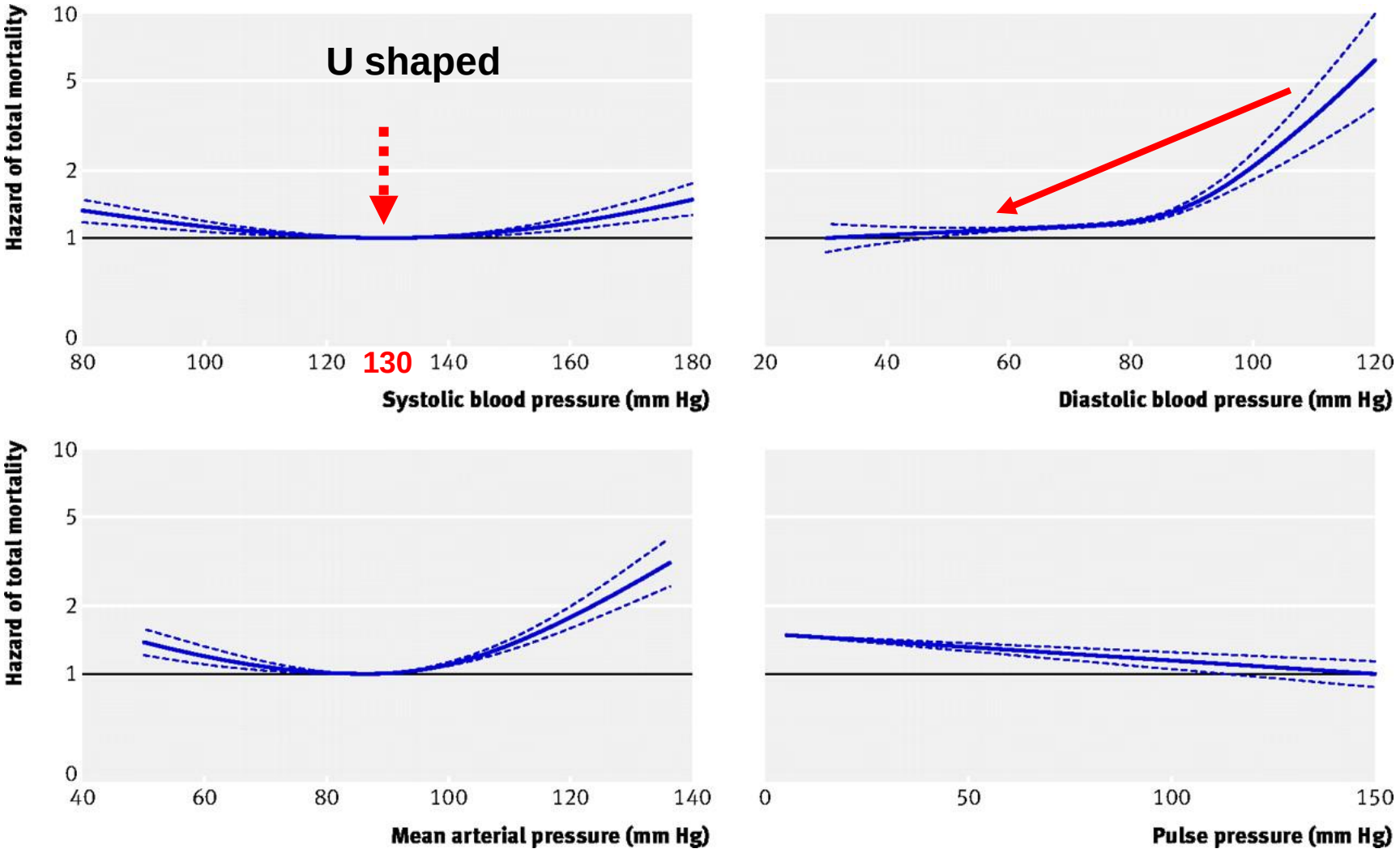
Fig 2 | Relations of systolic (top left), diastolic (top right), mean arterial (bottom left), and pulse (bottom right) pressures to cardiovascular mortality. Solid line represents hazard of cardiovascular mortality and dashed lines are 95% confidence interval limits, from multivariable regression spline Cox proportional hazards C models (adjusted for age, conscription date, conscription centre, socioeconomic position, body mass index, elbow flexion, hand grip, and knee extension strength). Y scale is logarithmic

Sundström J et al. BMJ 2011

Relations of S/DBP, mean arterial and PP to total risk of death

N=1.2 million men in Sweden Mag at entry 18.4 y follow-up 24 y

The relation of SBP to total mortality was U shaped



Sundström J et al. BMJ 2011

BMJ

Initiation of antihypertensive drug treatment

Recommendations	Class[a]	Level[b]	Ref.[c]
Prompt initiation of drug treatment is recommended in individuals with grade 2 and 3 hypertension with any level of CV risk, a few weeks after or simultaneously with initiation of lifestyle changes.	I	A	260, 265, 284
Lowering BP with drugs is also recommended when total CV risk is high because of OD, diabetes, CVD or CKD, even when hypertension is in the grade 1 range.	I	B	260, 284
Lack of evidence does also not allow recommending to initiate antihypertensive drug therapy in young individuals with isolated elevation of brachial SBP, but these individuals should be followed closely with lifestyle recommendations.	III	A	142

ESH 2013

JNC 8

Recommendation 2

In the general population <60 years, initiate pharmacologic treatment to lower BP at DBP ≥ 90mmHg and treat to a goal DBP<90 mmHg

(For ages 30-59 years, Strong Recommendation – Grade A;

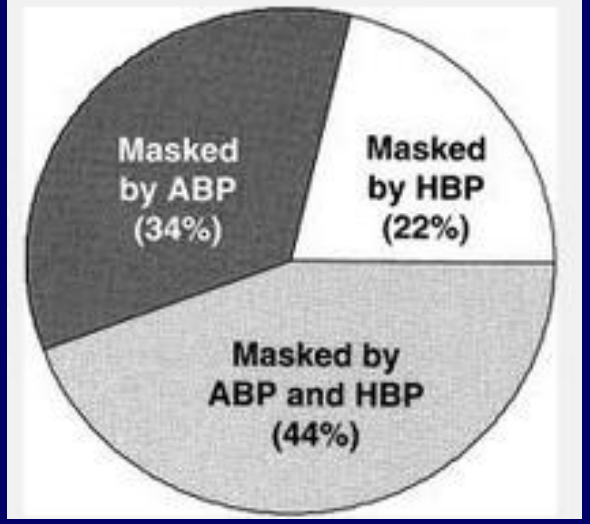
For ages 18-29 years,

Expert Opinion – Grade E)

Recommendation 3

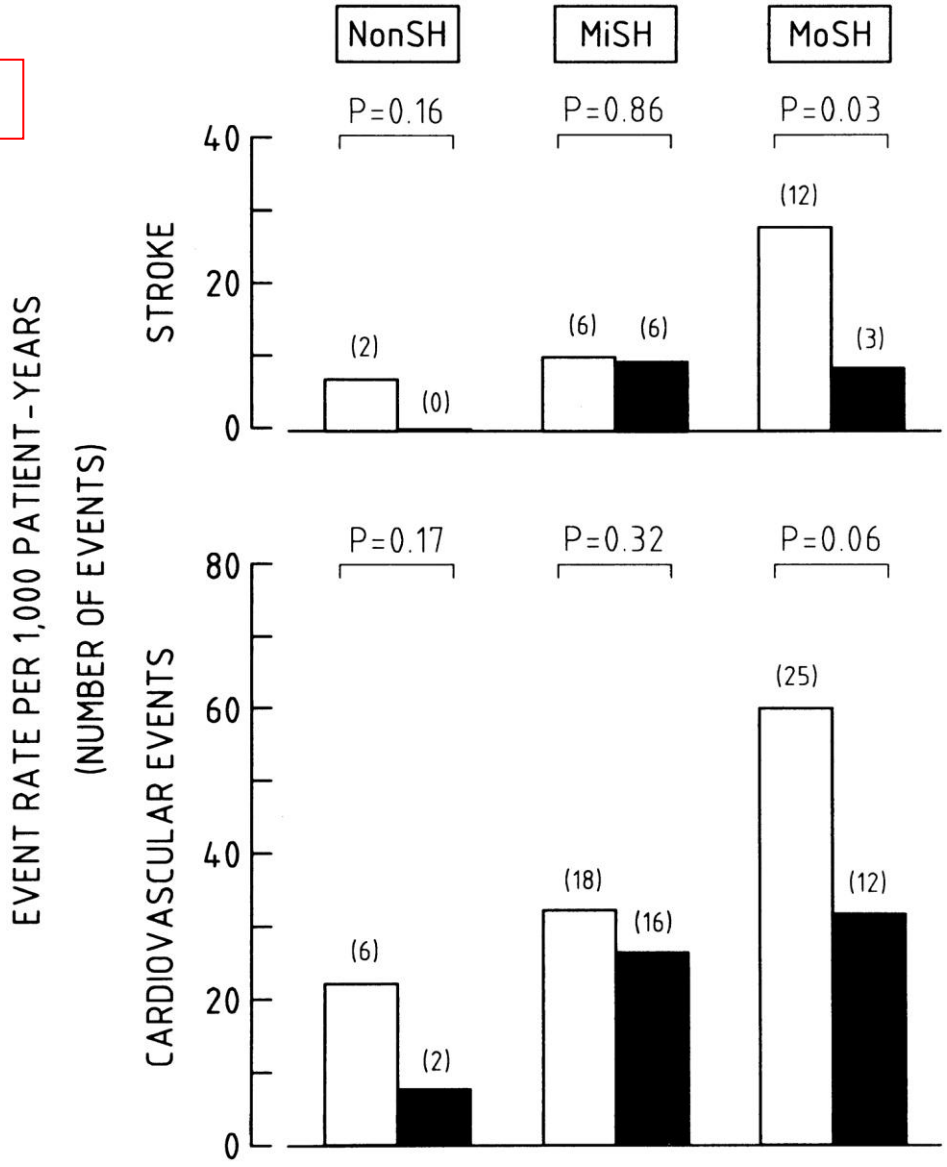
In the general population <60 years, initiate pharmacologic treatment to lower BP at SBP≥140mmHg and treat to a goal SBP <140mmHg (Expert Opinion – Grade E)

White Coat Hypertension



Number of strokes and CV events per 1000 patient-years and absolute number of events (within parentheses) during follow-up in patients with Non-SH, MiSH, and MoSH, divided according to treatment group

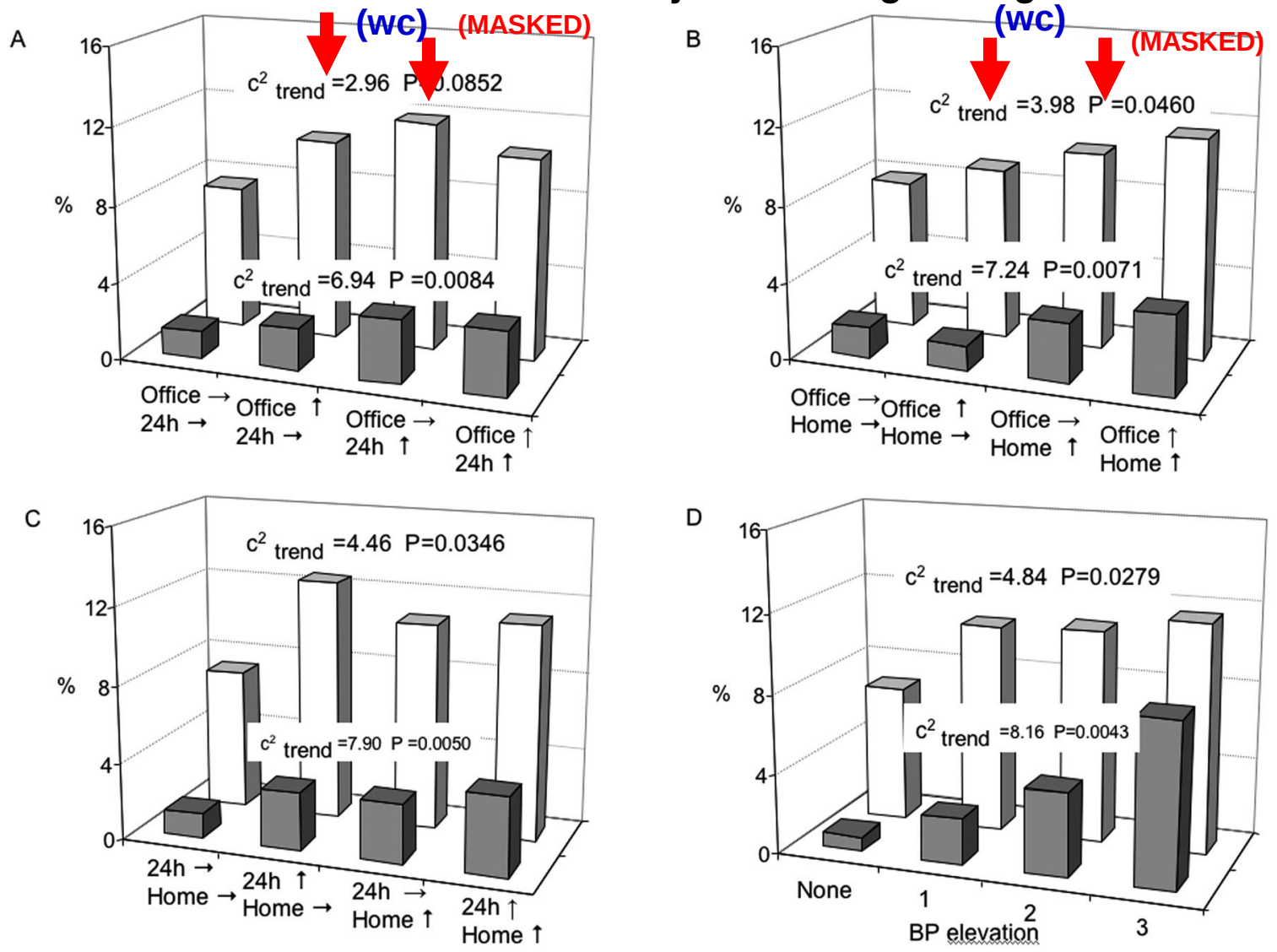
Syst-Eur Trial



American Heart Association

Robert H. Fagard et al.
Circulation. 2000;102:1139-1144

Percentage incidence of CV (▪) and all-cause death (□) over an average follow-up of 148 months in subjects with various combinations of normality or elevation in office, home, and 24-hour BP. Data are adjusted for age and gender.



Mancia G et al. Hypertension 2006

American Heart Association
Learn and Live

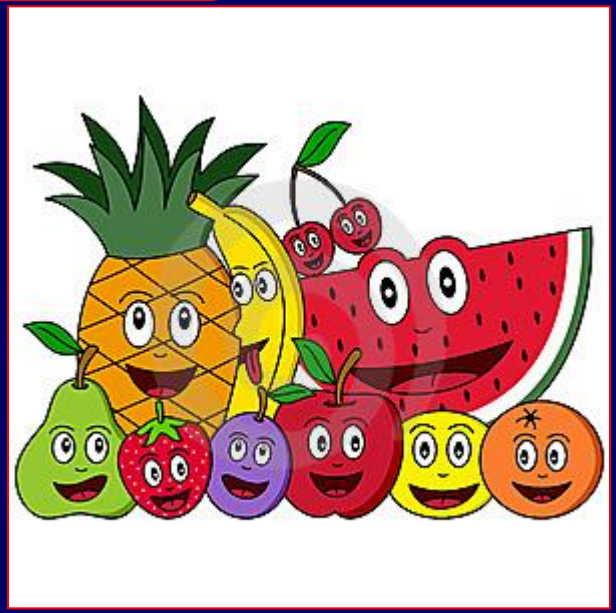
Treatment strategies in white-coat and masked hypertension

Recommendations	Class[a]	Level[b]
In white-coat hypertensives without additional risk factors, therapeutic intervention should be considered to be limited to lifestyle changes only, but this decision should be accompanied by a close follow-up.	IIa	C
In white-coat hypertensives with a higher CV risk because of metabolic derangements or asymptomatic OD, drug treatment may be considered in addition to lifestyle changes.	IIb	C
In masked hypertension, both lifestyle measures and antihypertensive drug treatment should be considered, because this type of hypertension has been consistently found to have a CV risk very close to that of in- and out-of-office hypertension.	IIa	C

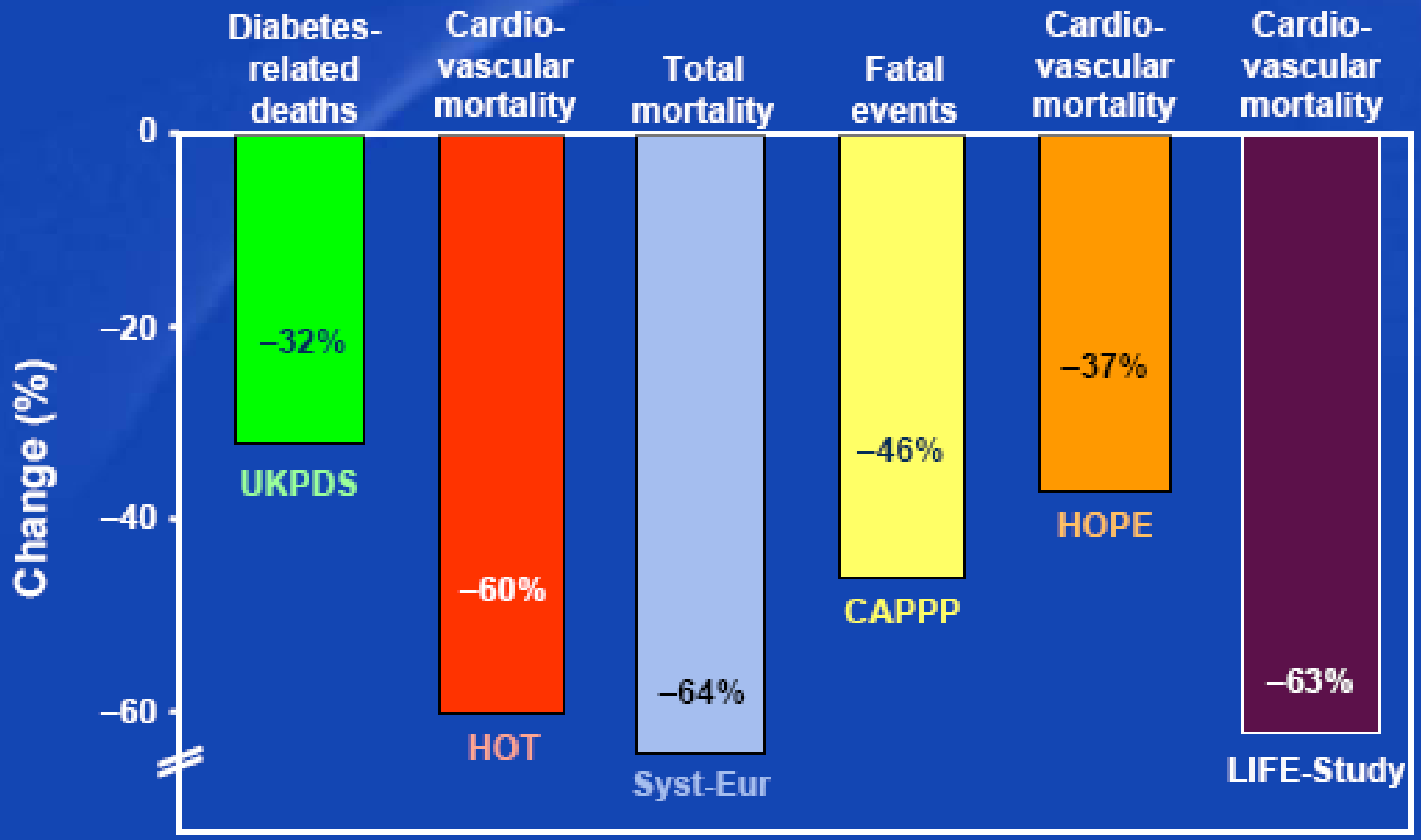
CV, cardiovascular; OD, organ damage.
a Class of recommendation.
b Level of evidence.

ESH 2013

DIABETES

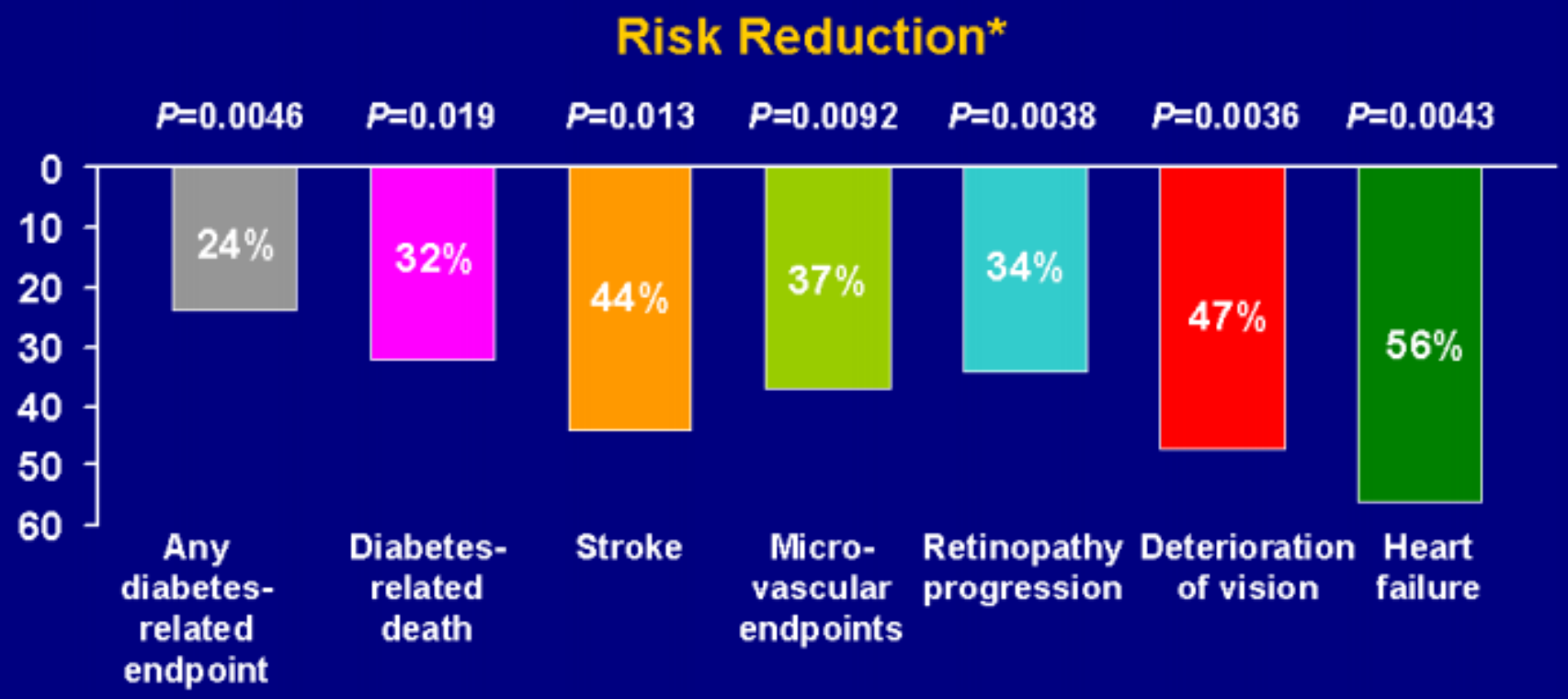


Effect of lowering blood pressure in diabetes



BP-lowering (mmHg)						
Intervention group	–16/–12	–30/–24	–22.1/–6.9	–13/–10	–2/–3	–31/–17
Control group	–6/–7	–26/–20	–13.5/–2.9	–13/–10	1/–2	–29/–17
Δ (Difference)	–10/–5	–4/–4	8.6/–4.0	0/0	3/1	2/0

UKPDS Results: Tight BP Control

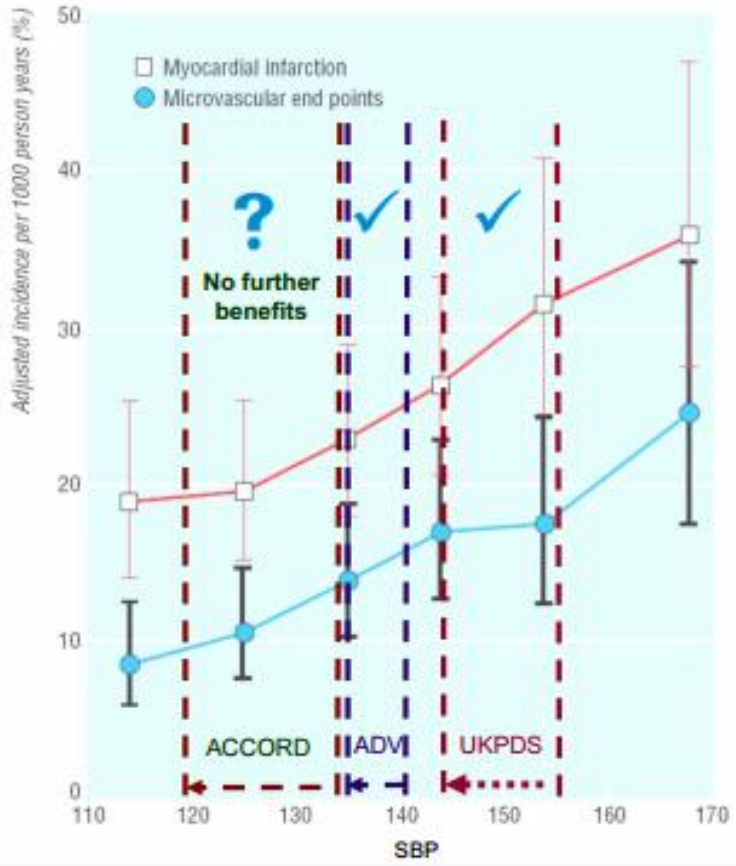


*Compared with less tight control. Captopril and atenolol were equally effective in reducing risk and were equally safe in patients with diabetes.

	baseline	mean over 9 years
Less tight control	160 / 94	154 / 87
Tight control	161 / 94	144 / 82

UKPDS Group. *BMJ.* 1998;317:703-713.

BP reduction in type 2 diabetes
UKPDS – ADVANCE - ACCORD



BMJ 2000

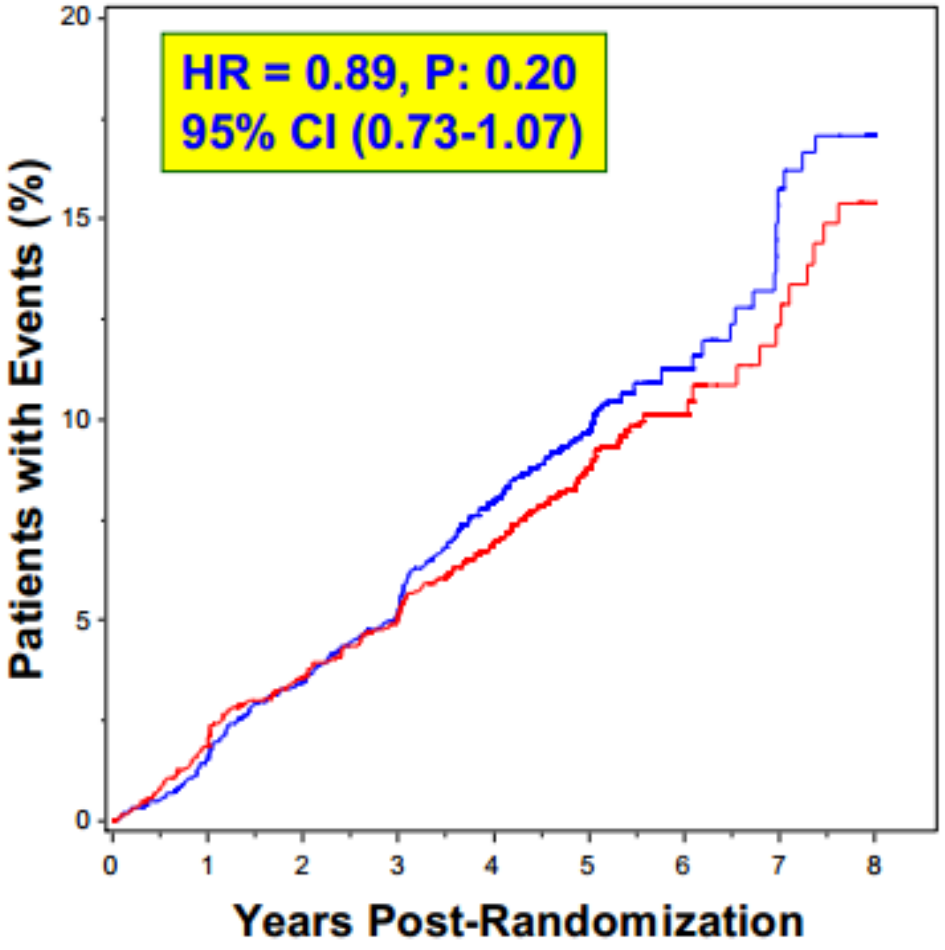
BP question: does a therapeutic strategy targeting SBP <120 mmHg reduce CVD events compared to a strategy targeting SBP <140 mmHg in patients with type 2 diabetes at high risk for CVD events?

ACCORD BP trial

Primary Outcome
Nonfatal MI, Nonfatal Stroke or CVD Death

HR = 0.89, P: 0.20
95% CI (0.73-1.07)

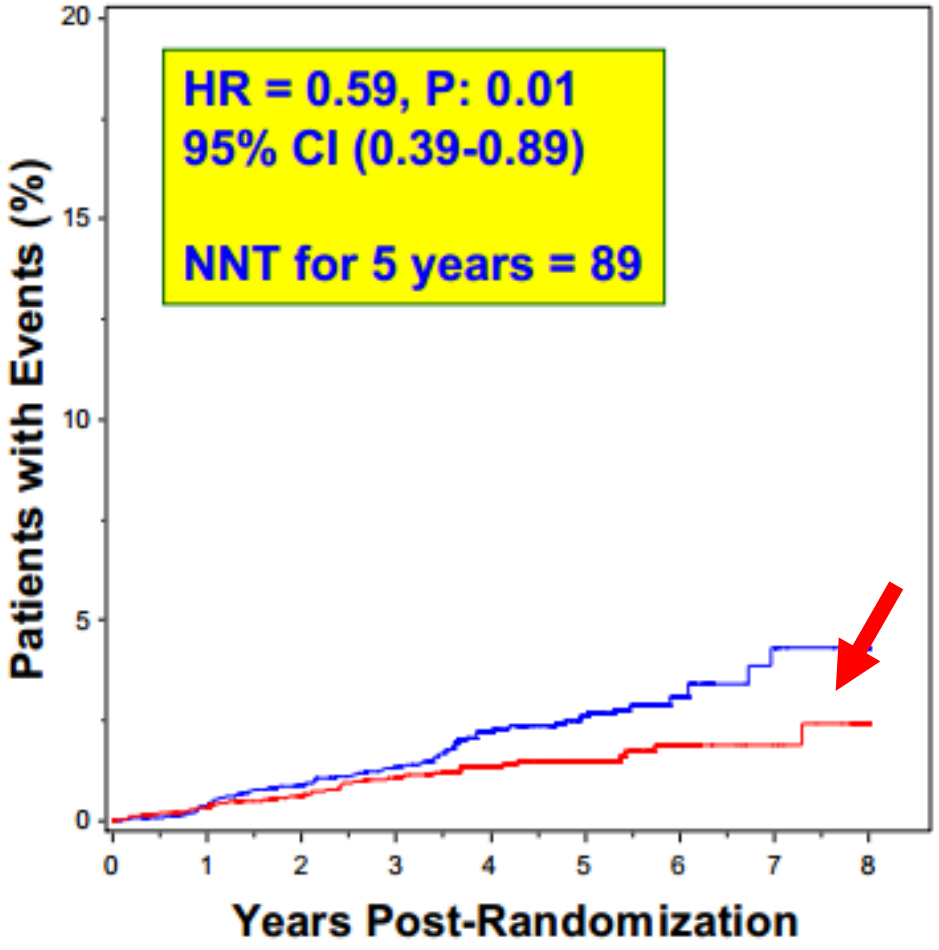
Average : 133.5 Standard vs. 119.3 Intensive,



Total Stroke

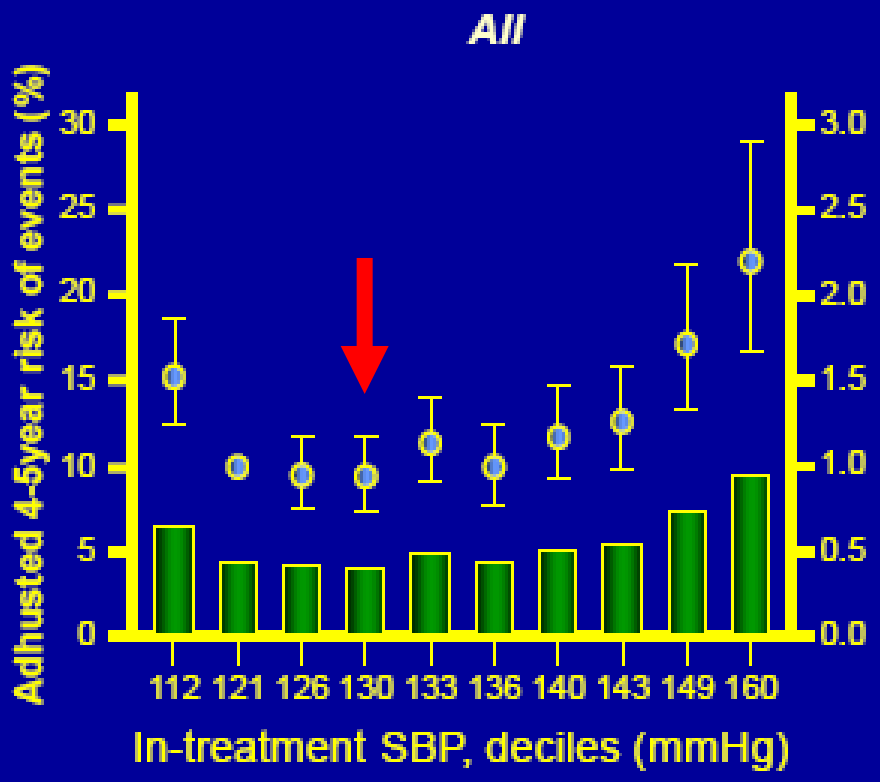
HR = 0.59, P: 0.01
95% CI (0.39-0.89)

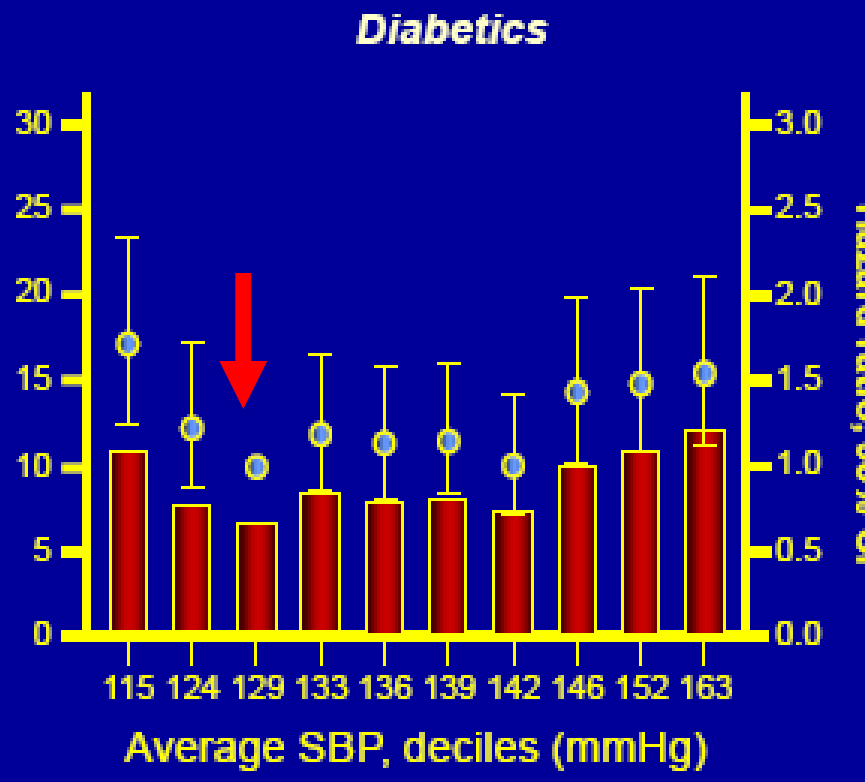
NNT for 5 years = 89



Intensive Standard

ONTARGET: Reducing SBP to <130 mmHg increases the risk of cardiovascular mortality*



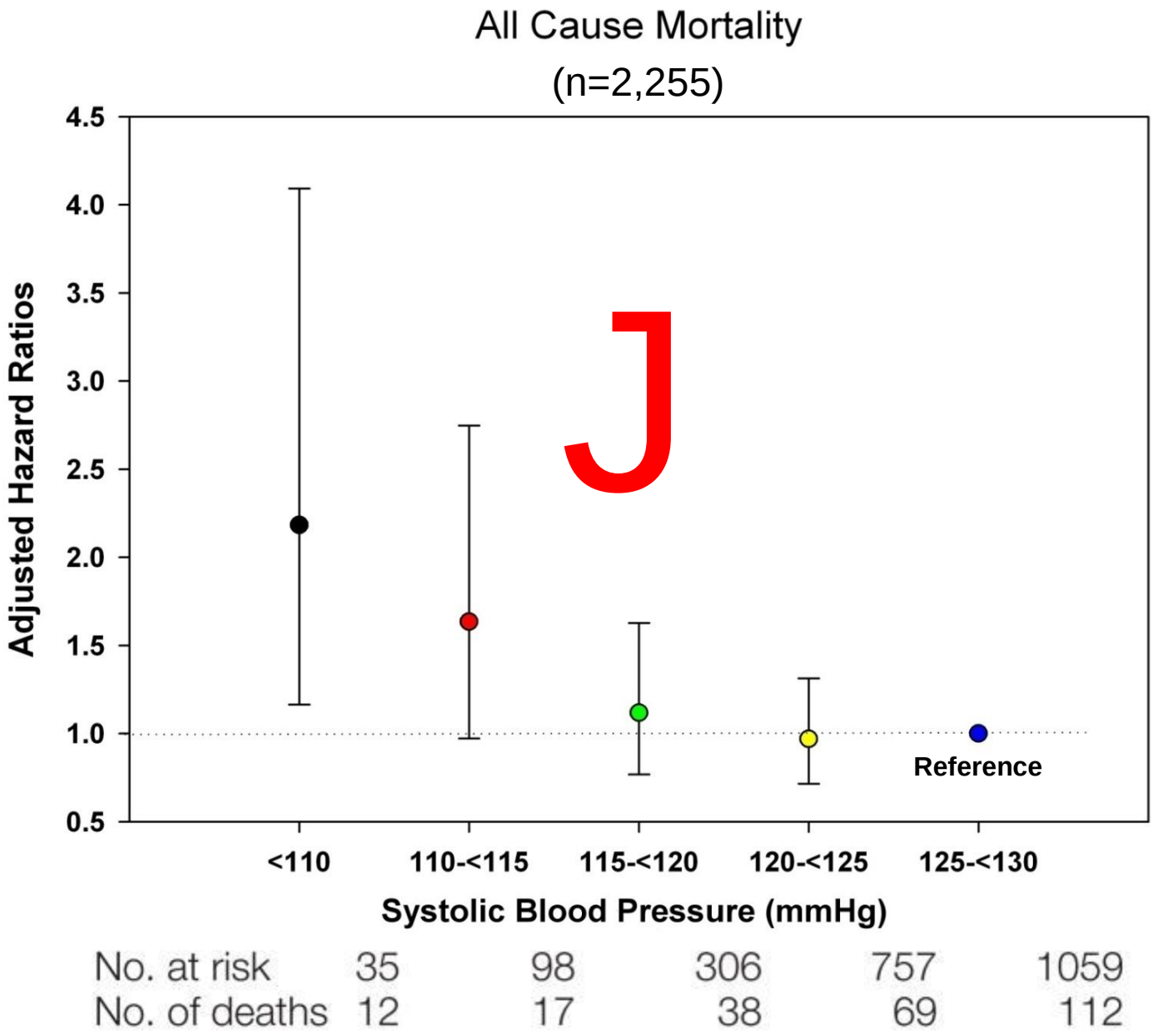


Sleight et al, J Hypertens 27 (2009): 1360-1369

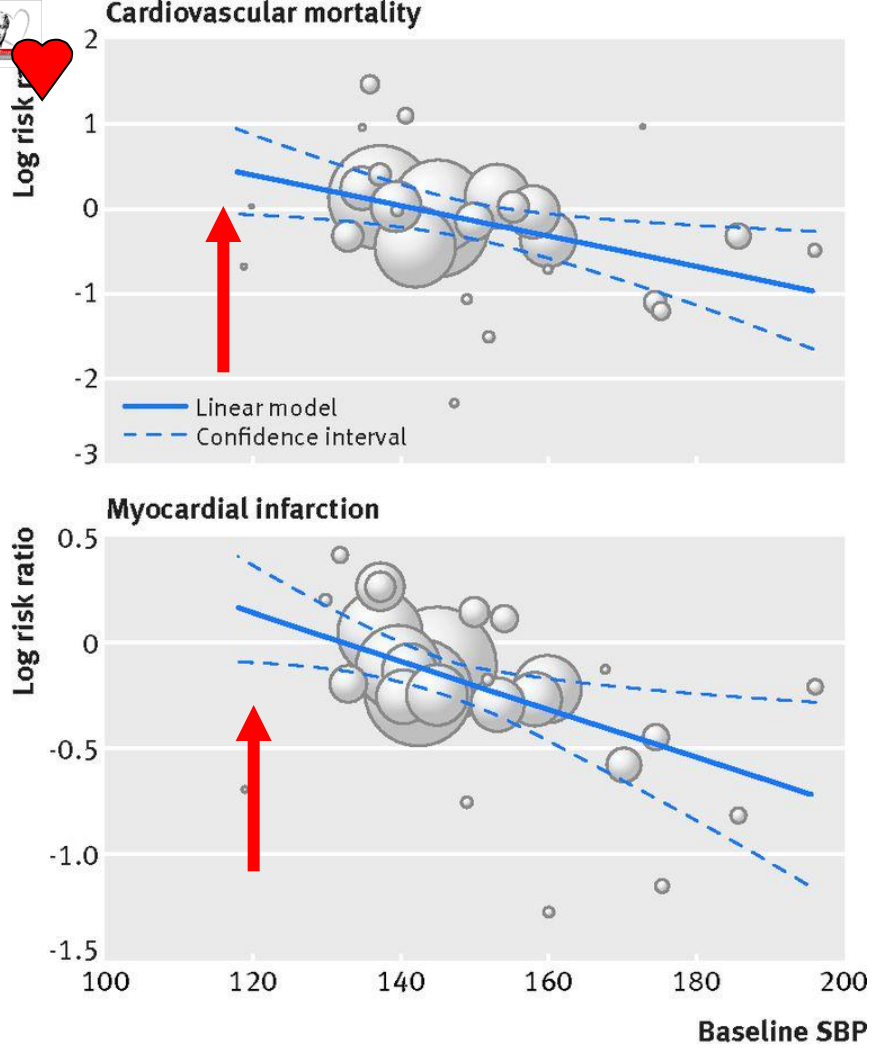
Redon et al JACC 2011, in press

Adjusted Risk of All-Cause Mortality

INVEST Diabetics N=6400



Cooper-DeHoff RM et al JAMA 2010



Outcome	Relative risk (95% CI)	P value
Mortality	1.04 (0.98 to 1.10)	0.151
Cardiovascular mortality	1.15 (1.03 to 1.29)	0.015
Myocardial infarction	1.12 (1.03 to 1.22)	0.011
Stroke	1.07 (0.98 to 1.18)	0.137
Heart failure	1.05 (0.93 to 1.20)	0.401
End stage renal disease	1.05 (0.90 to 1.22)	0.496

Effect of antihypertensive treatment at different BP levels in patients with DM: systematic review and meta-analyses

Results from metaregression analyses of treatment effect in relation to baseline SBP
RR is expressed as change in treatment effect for each 10 mm Hg lower baseline SBP

Mattias Brunström,et al BMJ 2016

What is the Goal BP and Initial Therapy in Kidney Disease or Diabetes to Reduce CV Risk?

Group	Goal BP (mmHg)	Initial Therapy
ADA (2012)	<130/80	ACE Inhibitor/ARB*
KDOQI (NKF) (2007)	<130/80	ACE Inhibitor/ARB
ESH (2007+ 2009)	<130/80	ACE Inhibitor/ARB*
KDOQI (NKF) (2004)	<130/80	ACE Inhibitor/ARB*
JNC 7 (2003)	<130/80	ACE Inhibitor/ARB*
Am. Diabetes Assoc (2003)	<130/80	ACE Inhibitor/ARB*
Canadian HTN Soc. (2002)	<130/80	ACE Inhibitor/ARB*
Am. Diabetes Assoc (2002)	<130/80	ACE Inhibitor/ARB*
Natl. Kidney Foundation (2000)	<130/80	ACE Inhibitor*
British HTN Soc. (1999)	<140/80	ACE Inhibitor
WHO/ISH (1999)	<130/85	ACE Inhibitor
JNC VI (1997)	<130/85	ACE Inhibitor

Treatment strategies in patients with diabetes

Recommendations	Class[a]	Level[b]	Ref.[c]
While initiation of antihypertensive drug treatment in diabetic patients whose SBP is ≥160 mmHg is mandatory, it is strongly recommended to start drug treatment also when SBP is ≥140 mmHg. **(stage ≥1)**	I	A	275, 276 290–293
A SBP goal <140 mmHg is recommended in patients with diabetes.	I	A	270,275, 276,295
The DBP target in patients with diabetes is recommended to be <85 mmHg.	I	A	290, 293

a Class of recommendation.
b Level of evidence.
c Reference(s) supporting levels of evidence.

ESH 2013

Comparisons to Other Guidelines

BP Goal	JNC-7	JNC-8	ASH/ISH	ESC/ESH	CHEP
Diabetes	<130/80	<140/90	<140/90	<140/85	<130/80

BP Goal	ADA	JHS			
Diabetes	< 140/80 or lower	<140/90 or <130/80			

Adapted from Salvo M et al. *Ann Pharmacother* 2014;48:1242-8.

To do and not to do messages from the Guidelines (3)

Recommendations	Class	Level
How to intervene *(cont'd)*		
In treated hypertensive patients <60 years old, SBP <140 mmHg and DBP <90 mmHg are recommended. In patients >60 years old with SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg. In individuals >80 years and with initial SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg, provided they are in good physical and mental conditions.	I	B
BP targets in type 2 DM are <140/85 mmHg, but a lower target of <130/80 mmHg is recommended in selected patients (e.g. younger patients at elevated risk for complications) for additional gains on stroke, retinopathy and albuminuria risk.	I	B
BP targets in patients with type 1 DM are <130/80 mmHg.	I	B
Drug treatment is recommended in patients with grade 3 hypertension irrespective of CV risk, as well as in patients with grade 1 or 2 hypertension who are at very high CV risk.	I	B
All major BP lowering drug classes (i.e. diuretics, ACE-I, calcium antagonists, ARBs, and ß-blockers) do not differ significantly in their BP-lowering efficacy and thus are recommended as BP lowering treatment.	I	A

European Heart Journal 2016 ;37:2315–2381-doi:10.1093/eurheartj/ehw106

EUROPEAN SOCIETY OF CARDIOLOGY®

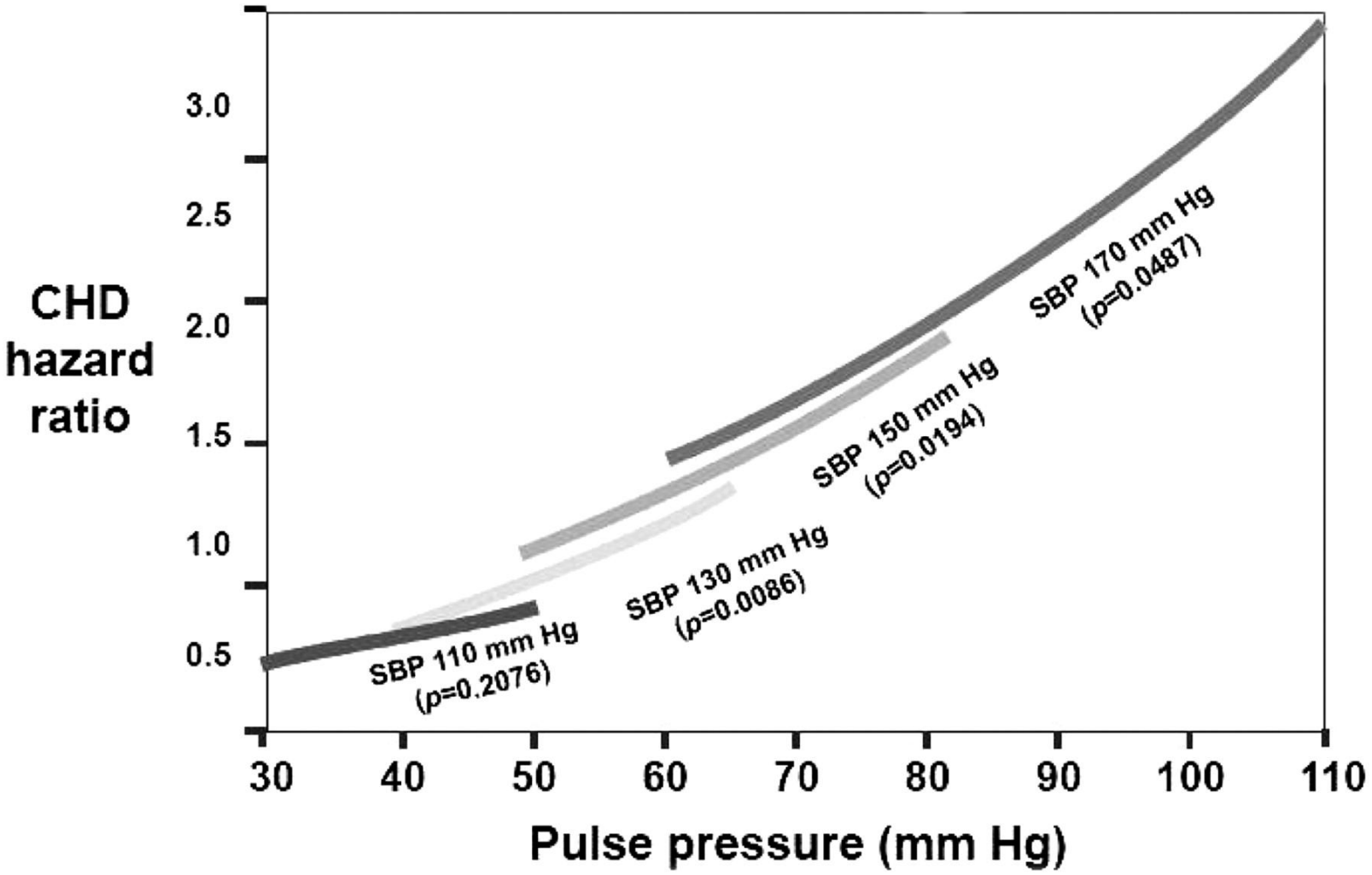
ELDERLY

Applied age definitions within investigated guidelines

Age term	ESH-ESC 2007 [5] (years)	ESH-ESC 2009 [6] (years)	JNC7 2003 [8] (years)	CHEP 2010 [7] (years)	DHL 2008 [10] (years)	SHG 2009 [11] (years)	NICE 2011 [9] (years)	ACCF/AHA 2011 [3] (years)	JNC8
Adults	–	<65	<65	<60	<60	–	<55 ?	<65	<60
Old (elderly)	–	65–79	65–x	60–x	60–79	–	65–79	65–74 (young old) 75–84 (older old) ≥85 (old old)	>60
Very old (very elderly)	≥80	≥80	–	≥80	≥80	–	≥80		

Schäfer HH et al Swiss Med Wkly 2012
JAMA 2013

Joint influences of SBP and PP on CHD

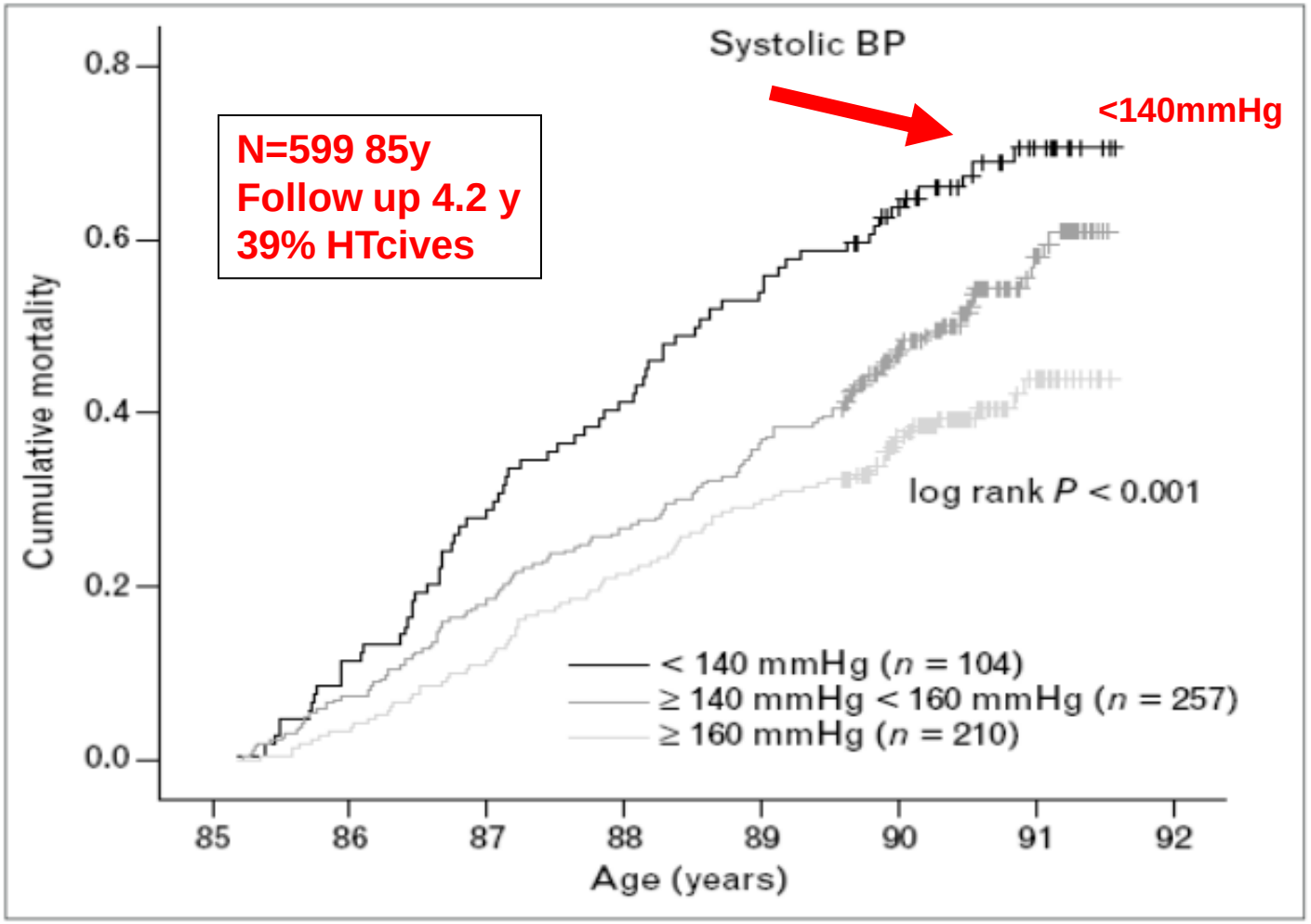


American Heart Association

Aronow W S et al. Circulation. 2011;123:2434-2506

Imperial College London

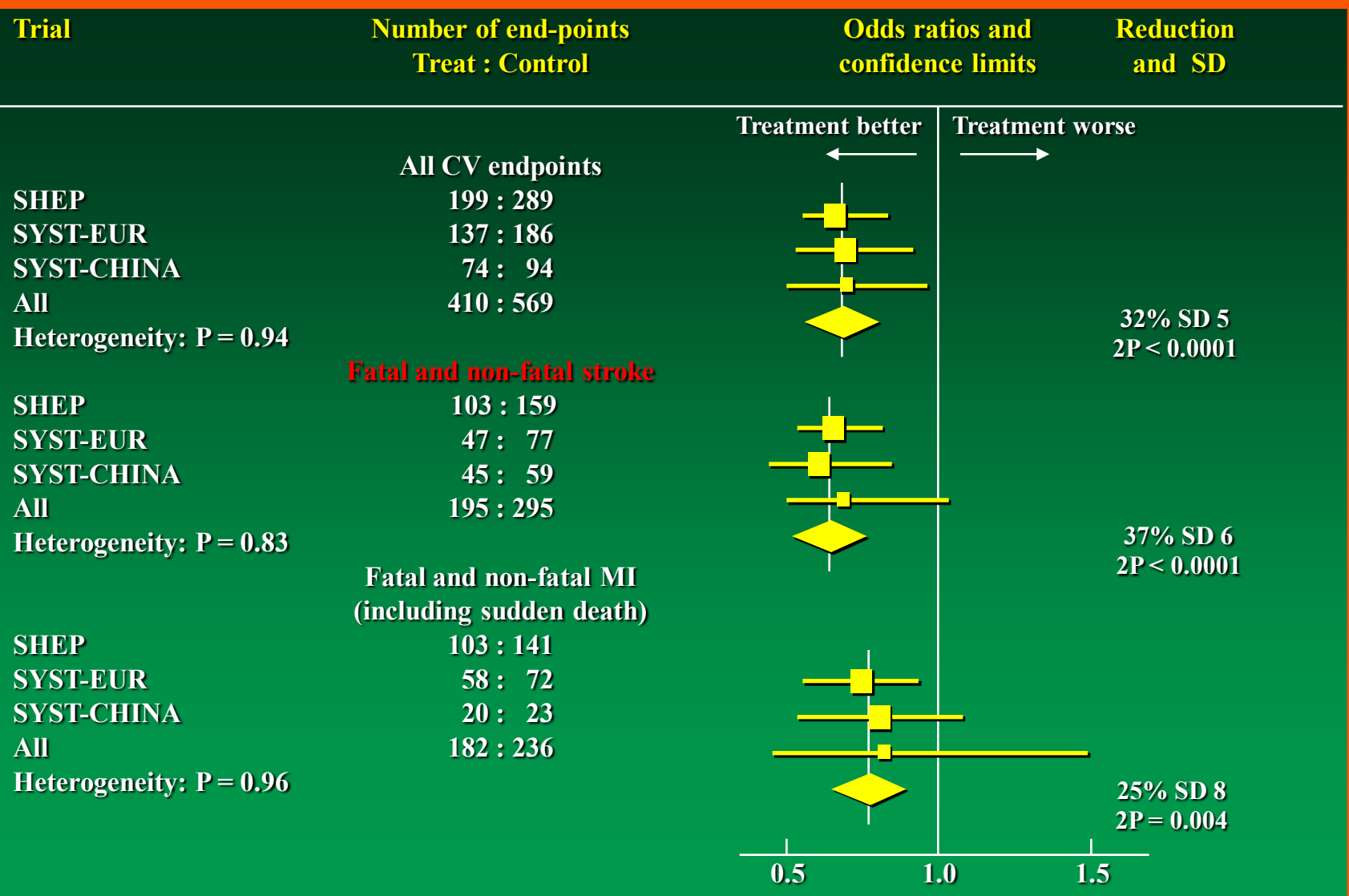
Epidemiologic population studies suggest better survival with higher levels of blood pressure



BP values below 140/70 mmHg are associated with excess mortality

(van Bremmel et al J Hypertens 2006 24: 287-292)

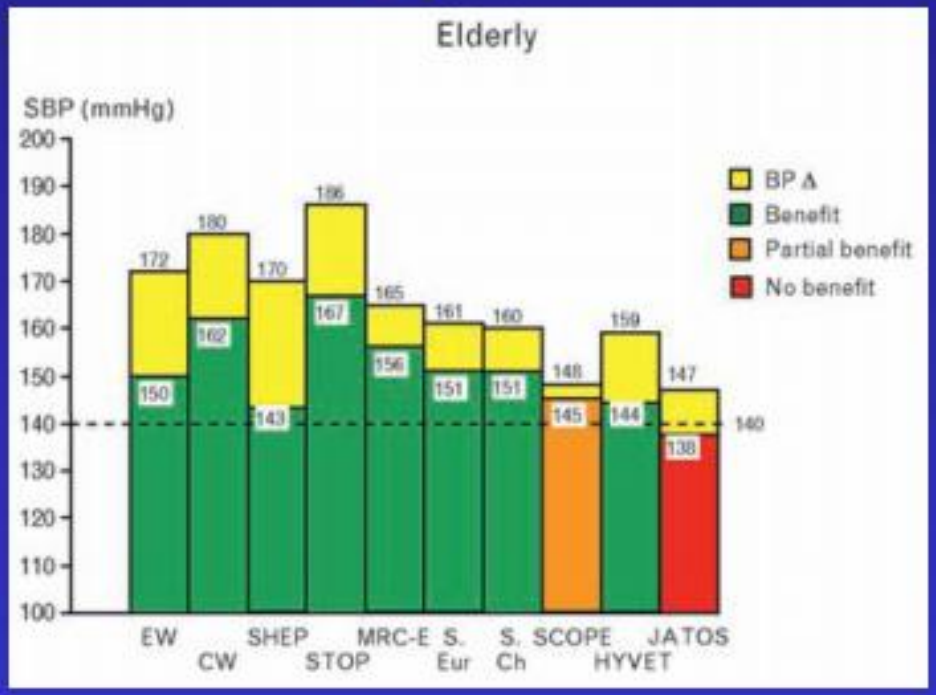
Benefit of Antihypertensive Drug Treatment in Older Patients with Isolated Systolic Hypertension



Staessen JA Eur Heart J 1999; (Suppl P): 3-8

Important differences compared with previous guidelines: Elderly

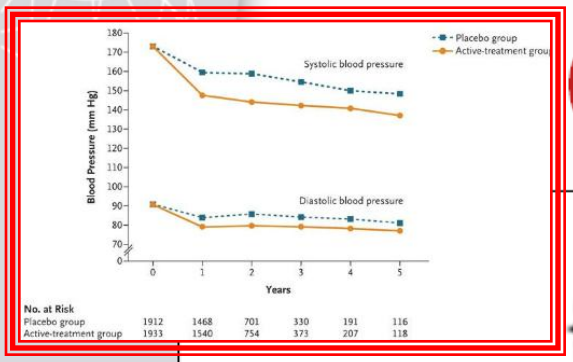
When should antihypertensive drug treatment be initiated and to what levels should SBP be lowered? A critical reappraisal

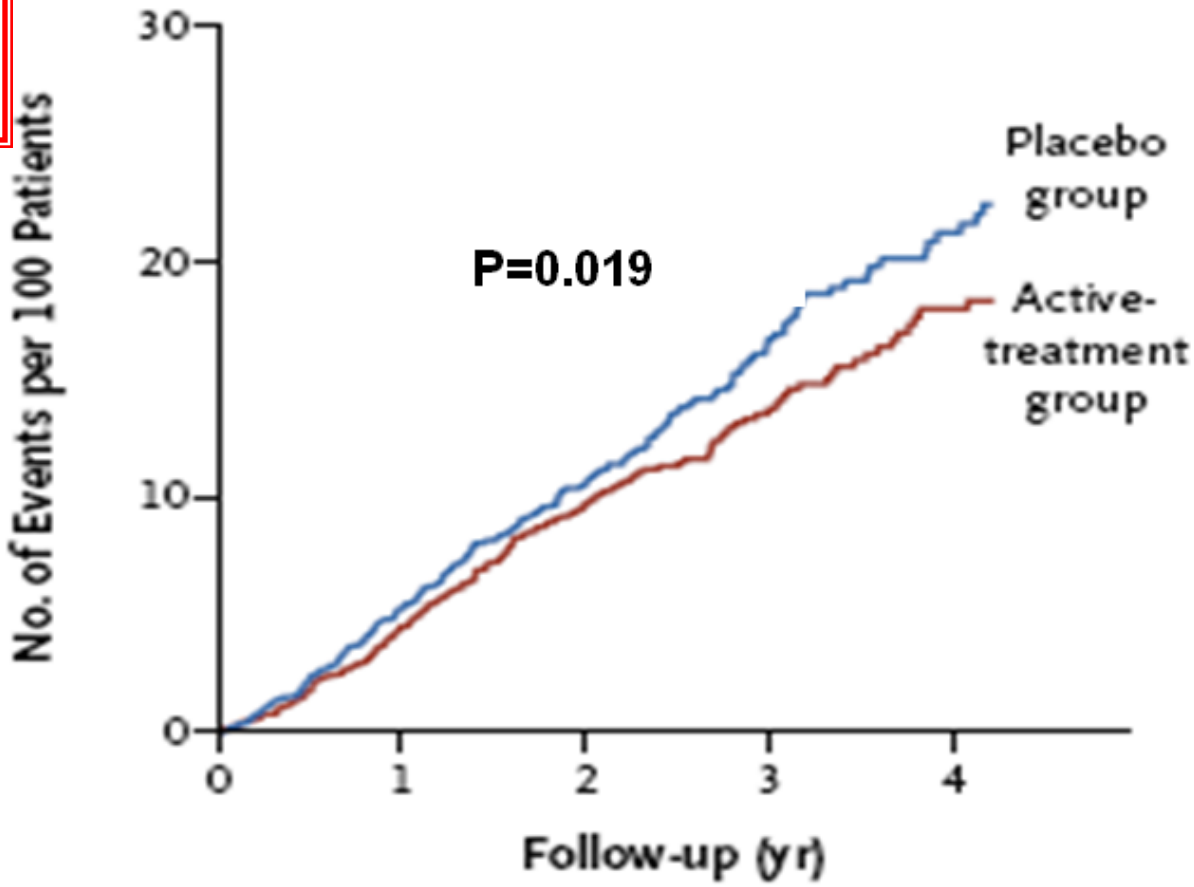


- In the large number of RCTs showing reduction in CV events through BP lowering, the average SBP never attained values <140mmHg including HYVET
- 2 recent Japanese trials unable to observe benefits by lowering SBP to 136 and 137mmHg rather than 145 and 142mmHg
- **Subgroup analysis in the FEVER showed reduction of CV events by lowering SBP just below 140mmHg (139.7mmHg compared with 145mmHg)**

Zanchetti A et al J Hypertens. 2009 May;27(5):923-34 1,

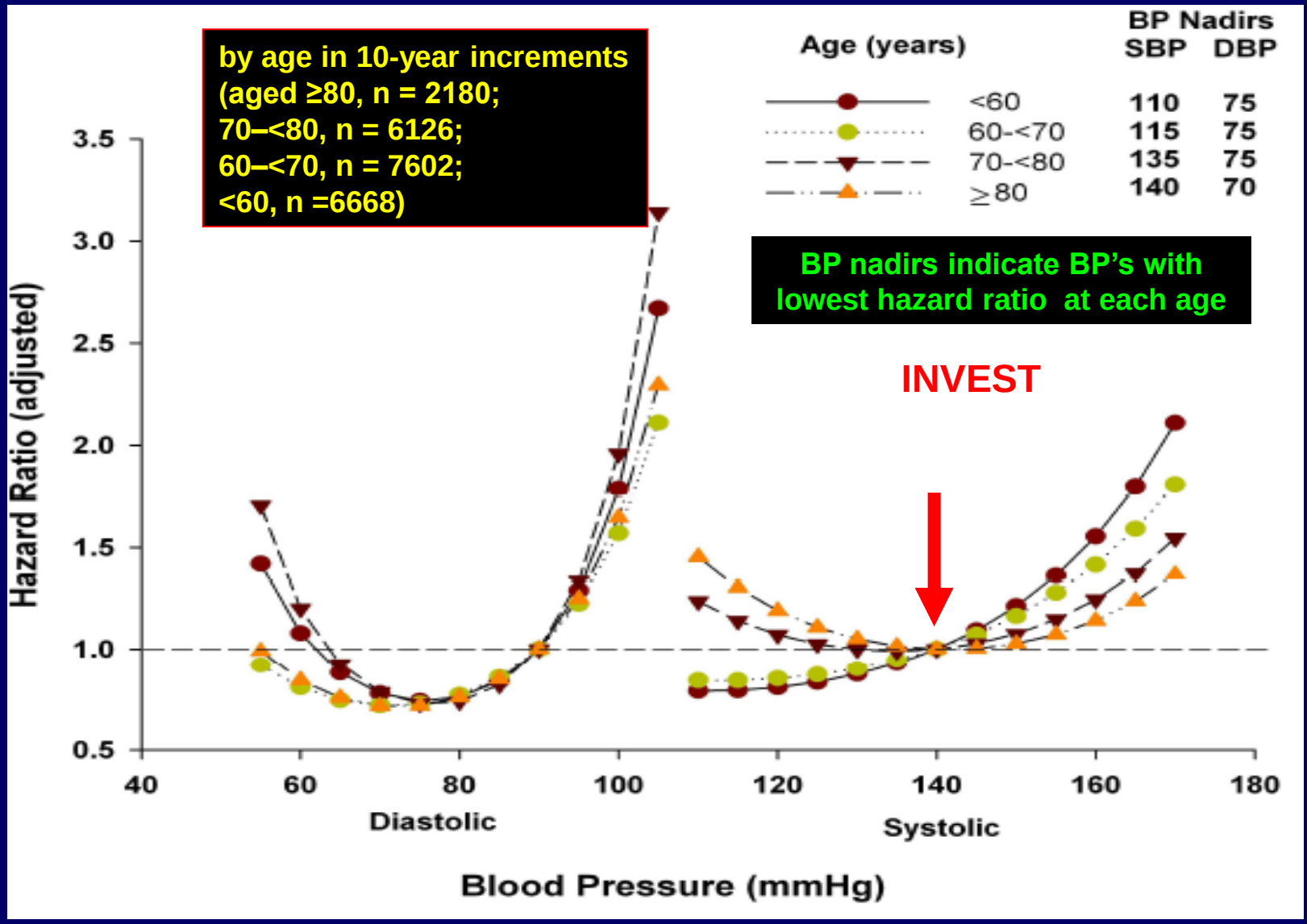
Total Mortality (21% reduction)





No. at Risk					
Placebo group	1912	1492	814	379	202
Active-treatment group	1933	1565	877	420	231

Risk of Adverse Outcomes Among Elderly CAD Patients by Age and BP



Denardo et al. *Am J Med* 123:719-726, 2010

Antihypertensive treatment strategies in the elderly

Recommendations	Class[a]	Level[b]	Ref.[c]
In elderly hypertensives with SBP ≥160 mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A	141, 265
In fit elderly patients <80 years old antihypertensive treatment may be considered at SBP values ≥140 mmHg with a target SBP <140 mmHg if treatment is well tolerated.	IIb	C	-
In individuals older than 80 years with an initial SBP ≥160 mmHg it is recommended to reduce SBP to between 150 and 140 mmHg, provided they are in good physical and mental conditions.	I	B	287

a Class of recommendation.
b Level of evidence.
c Reference(s) supporting levels of evidence.

ESH 2013

BP Goal

Comparisons to Other Guidelines

BP Goal	JNC-7	JNC-8	ASH/ISH	ESC/ESH	CHEP
Age 60-79	<140/90	<150/90	<140/90	<140/90	<140/90
Age 80+	<140/90	<150/90	<150/90	<150/90	<150/NA

BP Goal	NICE		JHS		
Age 60-79	<140/90 (<80y)	(DABPm/ HBPm: 135/85)			
Age 80+	<150/90 ABPm/HBP <145/85	(DABPm/ HBPm: 145/85)	<150/90 (≥ 75y) HBPm<145/85 <140/90 if tolerated HBPm<135/85		

Adapted from Salvo M et al. *Ann Pharmacother* 2014;48:1242-8.

Management of hypertension (2)

Recommendations	Class	Level
In patients >60 years old with SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg.	I	B
In fit patients <80 years old, a target SBP <140 mmHg may be considered if treatment is well tolerated. In some of these patients a target SBP <120 mmHg may be considered if at (very) high-risk and tolerate multiple BP lowering drugs.	IIb	B
In individuals >80 years and with initial SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg, provided they are in good physical and mental conditions.	I	B
In frail elderly patients, a careful treatment intensity (e.g. number of BP lowering drugs) and BP targets should be considered, and clinical effects of treatment should be carefully monitored.	IIa	B

ESC 2016

Guidelines on hypertension in patients 60 years or older by the American College of Physicians and the American Academy of Family Physicians[5,6]

- Clinicians should initiate treatment in patients aged 60 yr or older who have persistent systolic blood pressure at or above 150 mm Hg to achieve a target of less than 150 mm Hg to reduce risk for stroke, cardiac events, and death.
- If patients 60 yr or older have a history of stroke or transient ischemic attack or have high cardiovascular risk, physicians should consider starting or increasing drug therapy to achieve systolic blood pressure of less than 140 mm Hg to reduce risk for stroke and cardiac events.
- Consider initiating or intensifying pharmacologic treatment in some adults aged 60 yr or older at high cardiovascular risk based on individualized assessment, to achieve a target systolic blood pressure of less than 140 mm Hg to reduce the risk of stroke or cardiac events. Factors include comorbidity, medication burden, risk of adverse events, and cost. Generally, increased cardiovascular risk includes known cardiovascular disease, diabetes, or chronic kidney disease with a glomerular filtration rate (GFR) of less than 45 mL/min/1.73 m^2.

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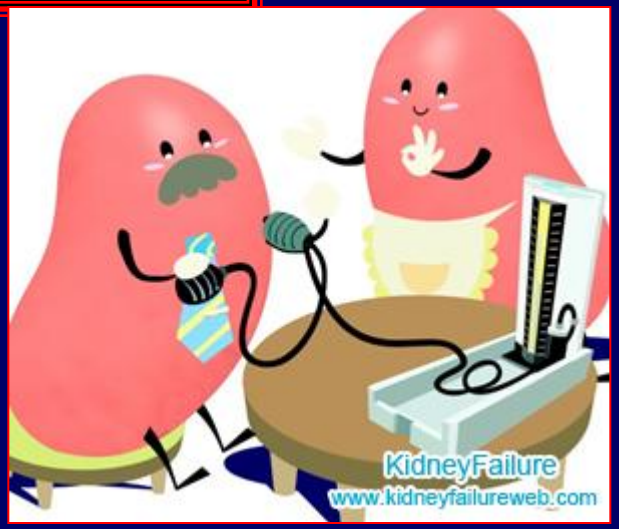
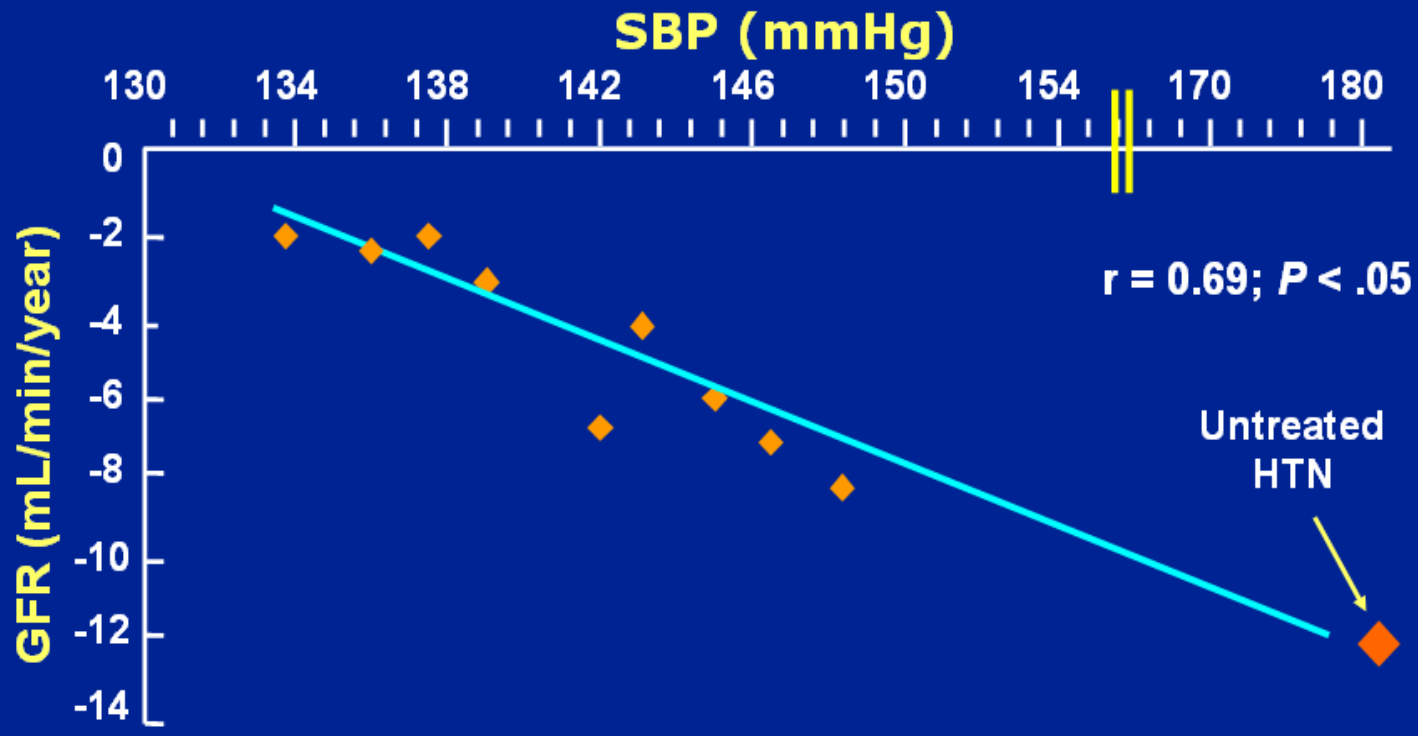
CKD



Meta Analysis: Lower Systolic BP Results in Slower Rates of Decline in GFR in Diabetics and Non-Diabetics

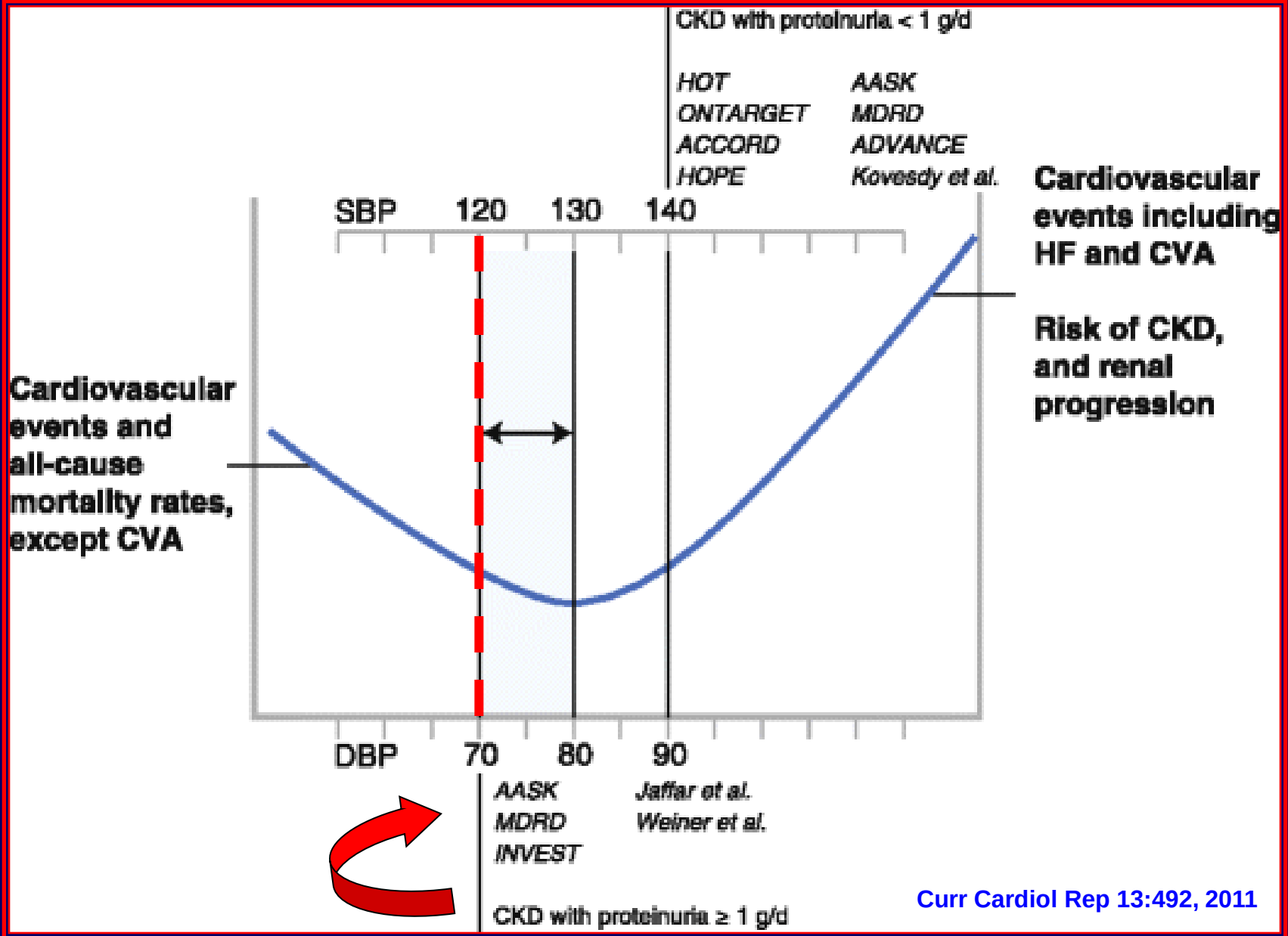


Parving HH, et al. Br Med J. 1989.
Viberti GC, et al. JAMA. 1993.
Klahr S, et al. N Eng J Med. 1994.
Hebert L, et al. Kidney Int. 1994.
Lebovitz H, et al. Kidney Int. 1994.
Moschio G, et al. N Engl J Med. 1996.
Bakris GL, et al. Kidney Int. 1996.
Bakris GL. Hypertension. 1997.
The GISEN Group. Lancet. 1997.

Bakris GL, et al. Am J Kidney Dis. 2000;36(3):646-661.

Slide Source
Hypertension Online
www.hypertensiononline.org

Synthesis of cardiorenal outcomes according to achieved BP from clinical trials demonstrating a U-shaped relationship



Curr Cardiol Rep 13:492, 2011

SPRINT
Systolic Blood Pressure Intervention Trial

Renal outcome

Outcome	Intensive treatment		Standard treatment		HR(95% CI)	P Value
	Patients(%)	% per year	Patients(%)	% per year		
CKD	**(N = 1330)**		**(N=1316)**			
Composite renal outcome	**14(1.1)**	0.33	**15(1.1)**	0.36	0.89(0.42-1.87)	0.76
≥ 50% reduction of eGFR	**10(0.8)**	0.23	**11(0.8)**	0.26	0.87(0.36-2.07)	0.75
Dialysis	**6(0.5)**	0.14	**10(0.8)**	0.24	0.57(0.19-1.54)	0.27
KT	0		0			
Incident albuminuria	49/526(9.3)	3.02	59/500(11.8)	3.90	0.72(0.48-1.07)	0.11
W/O CKD	**(N=3332)**		**(N=3345)**			
≥ 30% reduction in eGFR to < 60ml/min	**127(3.8)**	**1.21**	**37(1.1)**	**0.35**	**3.49(2.44-5.10)**	**< 0.001**
Incident albuminuria	110/1769(6.2)	2.00	135/1831(7.4)	2.41	0.81(0.63-1.04)	0.10

- *CKD at baseline: incidence of decline in eGFR ≥50% or ESRD*
- *no CKD at baseline: incidence of decline in eGFR ≥30% & to <60 mL/min/1.73m²*
- *Incidence of albuminuria; Doubling of urinary albumin/creatinine (<10 to >10 mg/g)*

Therapeutic strategies in hypertensive patients with nephropathy

Recommendations	Class[a]	Level[b]	Ref.[C]
Lowering SBP to <140 mmHg should be considered.	IIa	B	303, 313
When overt proteinuria is present, SBP values <130 mmHg may be considered, provided that changes in eGFR are monitored.	IIb	B	307, 308, 313

a Class of recommendation
b Level of evidence

ESH 2013

Comparisons to Other Guidelines

BP Goal	JNC-7	JNC-8	ASH/ISH	ESC/ESH	CHEP
CKD	<130/80	<140/90	<140/90	<140/90 <130/90	<140/90

KDIGO

24 Hour Urinary Protein Excretion

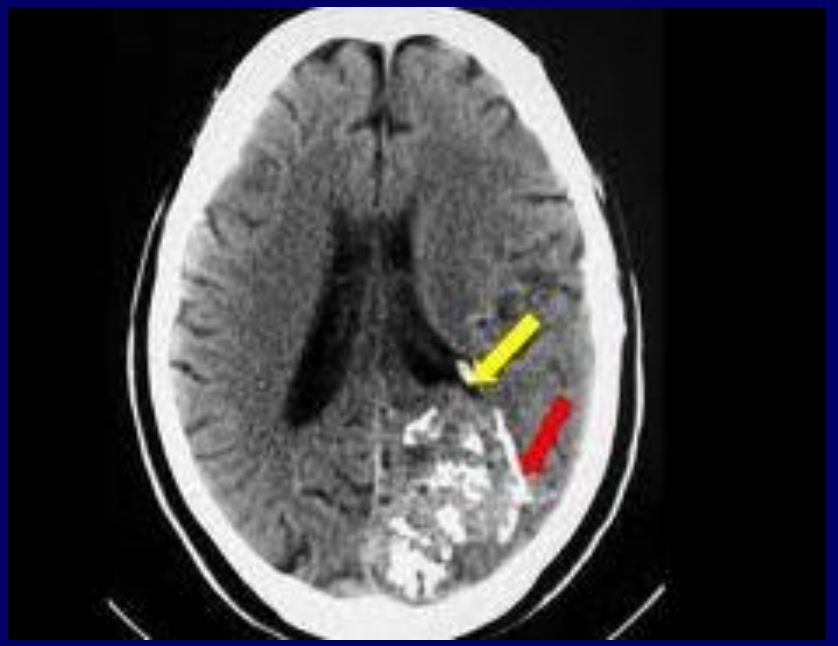
	0-30mg	30mg-300mg	>300mg
Non-diabetic Adults	≤ 140/90 1B	130/80 2D	130/80 2C
Diabetic Adults (Non dialysis dependent)	≤ 140/90 1B	130/80 2D	130/80 2D
Post-transplant Adults	≤ 130/80 2D	130/80 2D	130/80 2D
Elderly	≤ 140/90 (but set targets after consideration of co-morbidities)		

ISHIB

Diabetes/nondiabetic renal disease with proteinuria >1 g/24 h*
Goal BP: <130/80 mm Hg

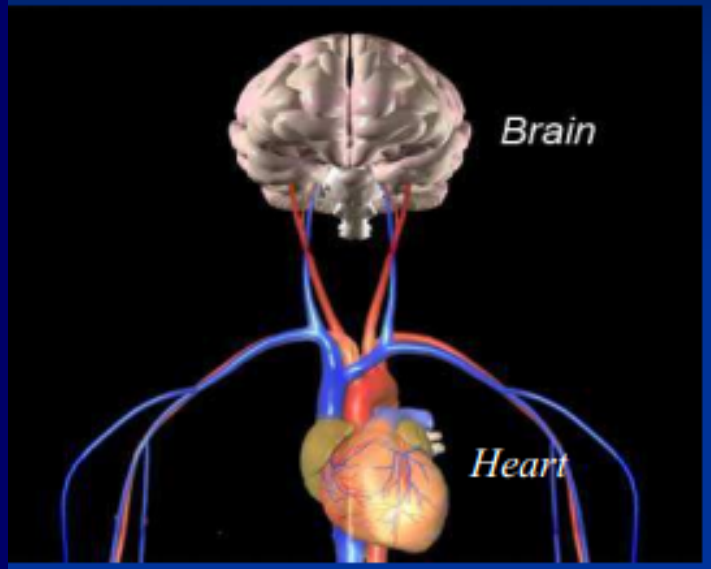
Adapted from Salvo M et al. *Ann Pharmacother* 2014;48:1242-8.

Previous stroke



J-curve conception

Questions



Systolic BP ?

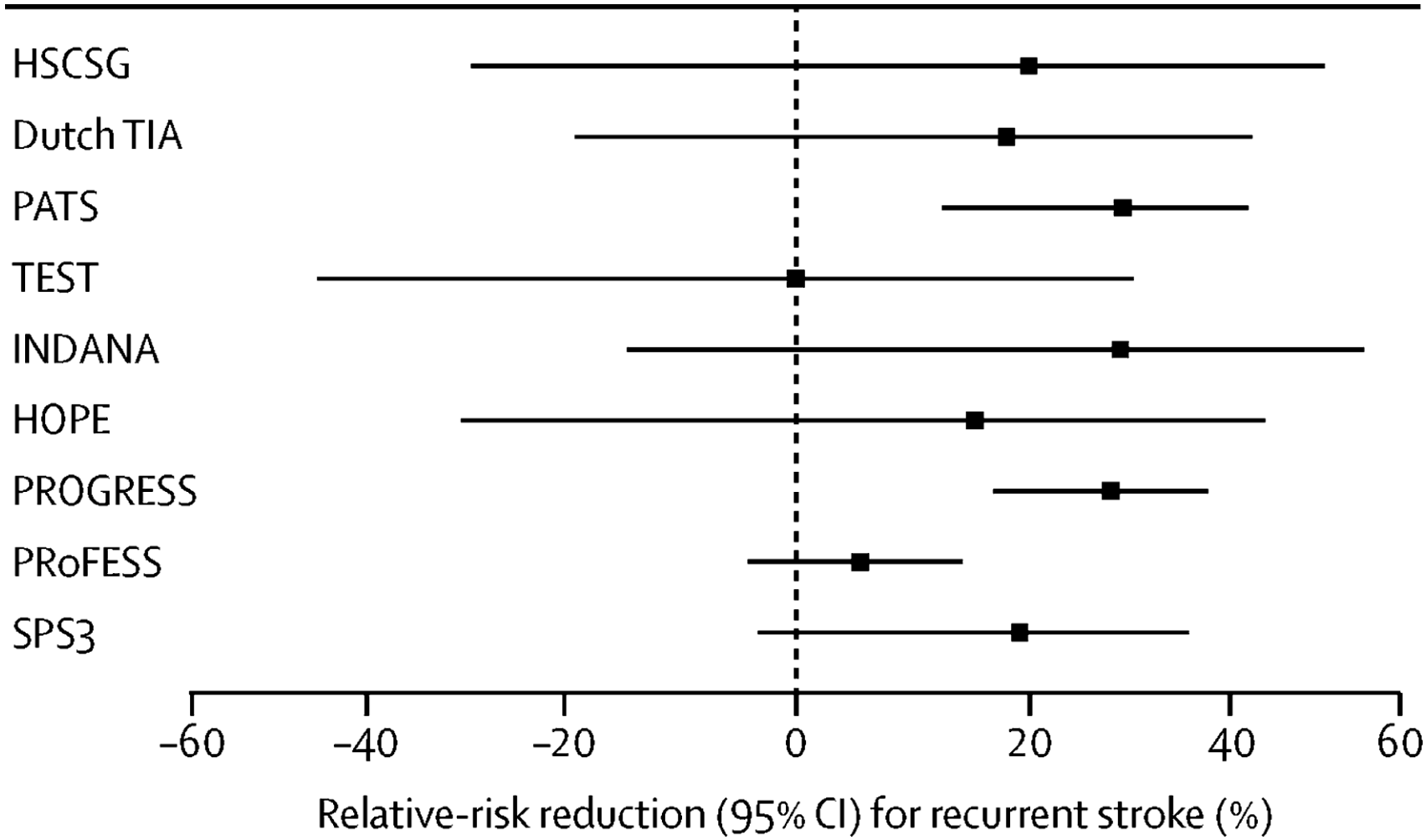
Diastolic BP ?

BP - 0 = 100% mortality J – curve

In physiological range of BP

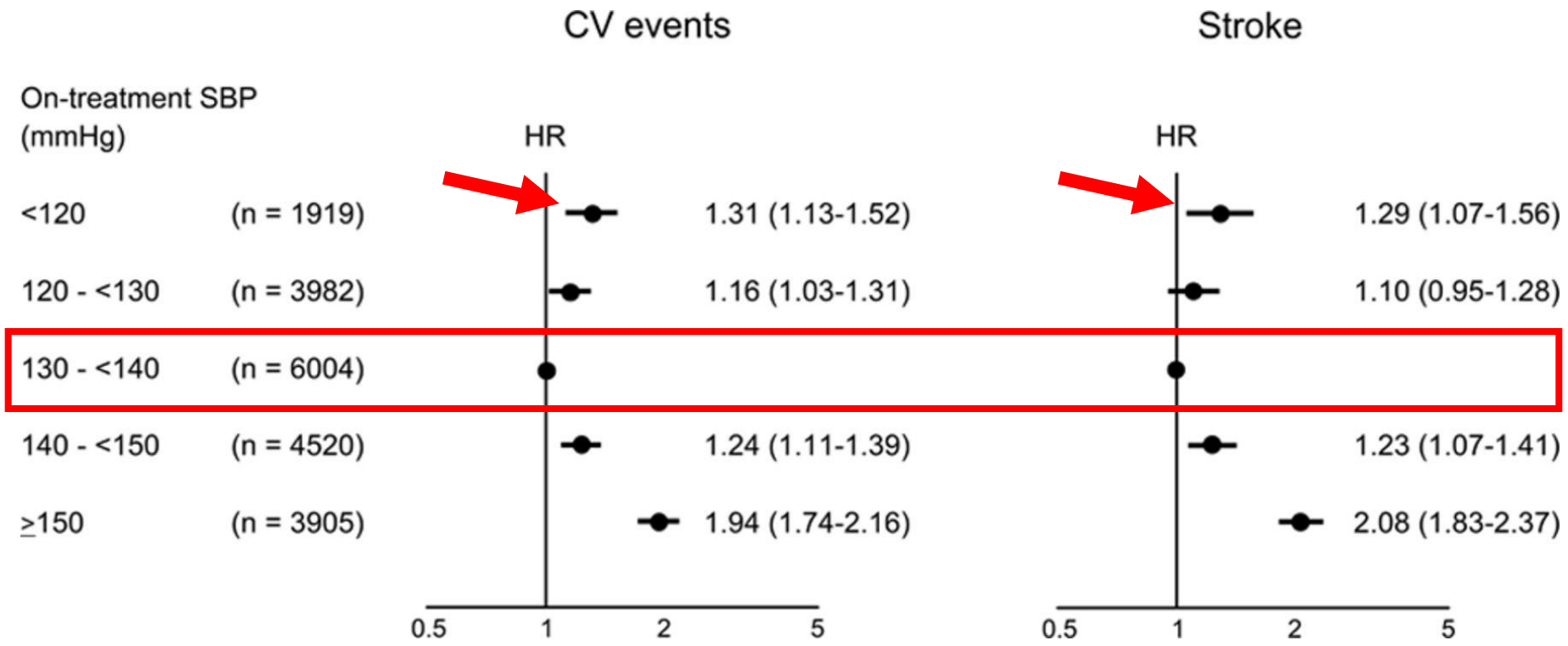
J – curve

Randomised trials of long-term blood-pressure lowering for secondary stroke prevention



Lancet. 2013

Risk of CV events and stroke recurrence according to different on-treatment SBP values in patients with a history of stroke



Giuseppe Mancia, and Guido Grassi Hypertension. 2014;63:29-36

American Heart Association.

Recommendations	Class[a]	Level[b]	Ref.[c]
It is not recommended to intervene with BP-lowering therapy during the first week after acute stroke irrespective of BP level, although clinical judgement should be used in the face of very high SBP values.	III	B	544, 545
Antihypertensive treatment is recommended in hypertensive patients with a history of stroke or TIA, even when initial SBP is in the 140–159 mmHg range.**(≥Stage 1)**	I	B	280, 296
In hypertensive patients with a history of stroke or TIA, a SBP goal of <140 mmHg should be considered.	IIa	B	280, 296, 297
In elderly hypertensives with previous stroke or TIA, SBP values for intervention and goal may be considered to be somewhat higher.	IIb	B	141, 265

Therapeutic strategies in hypertensive patients with cerebrovascular disease

ESH 2013

a Class of recommendation
b Level of evidence

BP Goals

AHA/ACC/ASH Scientific Statement

BP Goal, mm Hg	Condition	Class/Level of Evidence
<150/90	Age >80 y	IIa/B
<140/90	CAD	I/A
	ACS	IIa/C
	HF	IIa/B
<130/80	CAD	IIb/C
	Post–myocardial infarction, stroke or TIA, carotid artery disease, PAD, AAA	IIb/C

AAA indicates abdominal aortic aneurysm; ACS, acute coronary syndrome; BP, blood pressure; CAD, coronary artery disease; HF, heart failure; PAD, peripheral arterial disease; and TIA, transient ischemic attack.

Hypertension 2015

Guidelines on hypertension in patients 60 years or older by the American College of Physicians and the American Academy of Family Physicians[5,6]

- Clinicians should initiate treatment in patients aged 60 yr or older who have persistent systolic blood pressure at or above 150 mm Hg to achieve a target of less than 150 mm Hg to reduce risk for stroke, cardiac events, and death.
- If patients 60 yr or older have a history of stroke or transient ischemic attack or have high cardiovascular risk, physicians should consider starting or increasing drug therapy to achieve systolic blood pressure of less than 140 mm Hg to reduce risk for stroke and cardiac events.
- Consider initiating or intensifying pharmacologic treatment in some adults aged 60 yr or older at high cardiovascular risk based on individualized assessment, to achieve a target systolic blood pressure of less than 140 mm Hg to reduce the risk of stroke or cardiac events. Factors include comorbidity, medication burden, risk of adverse events, and cost. Generally, increased cardiovascular risk includes known cardiovascular disease, diabetes, or chronic kidney disease with a glomerular filtration rate (GFR) of less than 45 mL/min/1.73 m^2.

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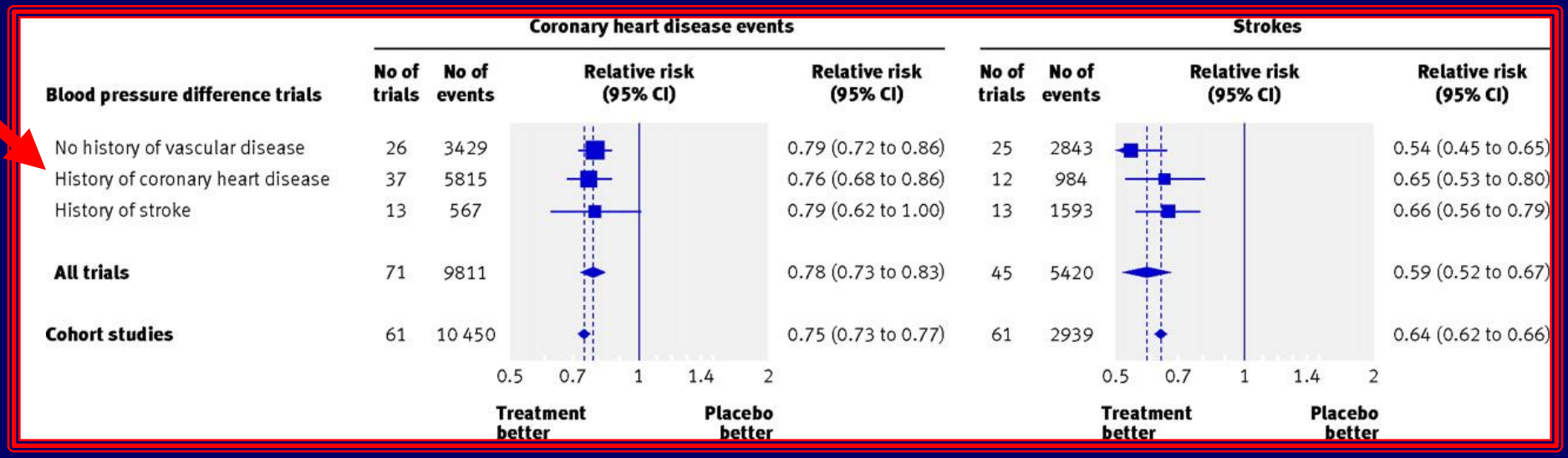
HEART DIASEASE

RR estimates of CHD events and stroke for a BP reduction of S/DBP : 10/ 5 mm Hg , in the BP difference trials and in epidemiological cohort studies

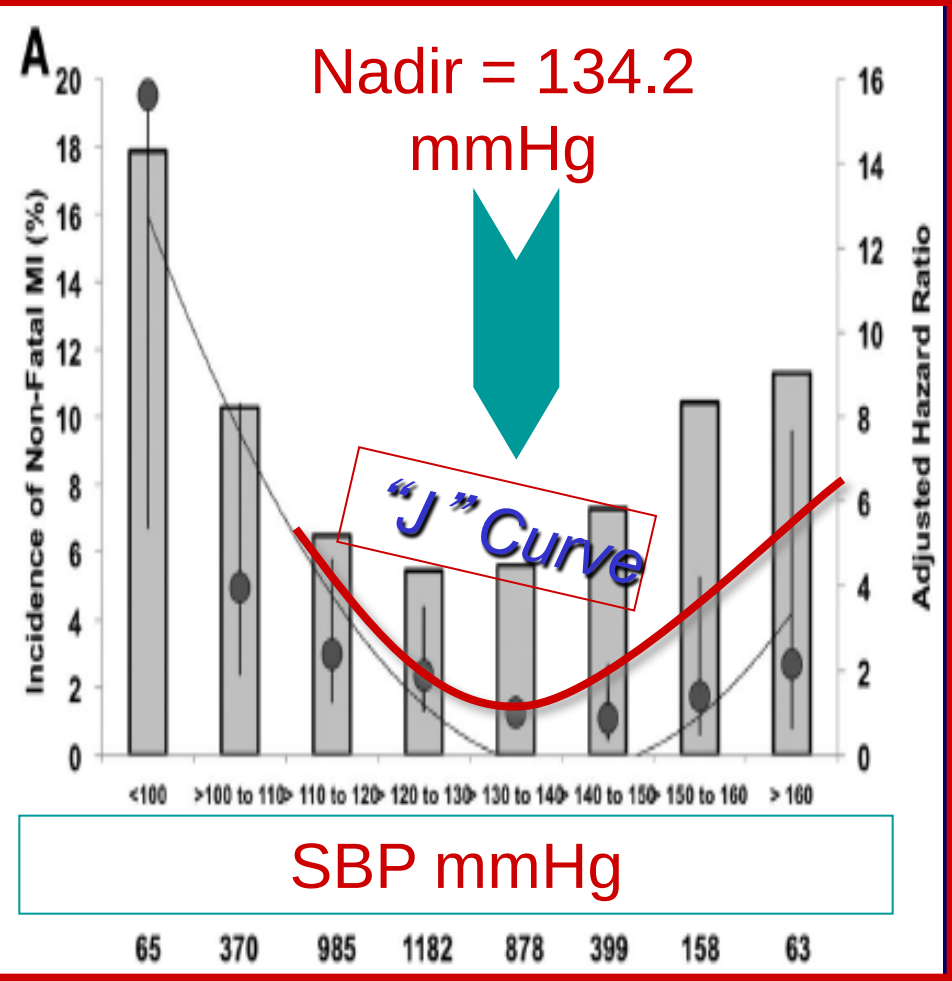


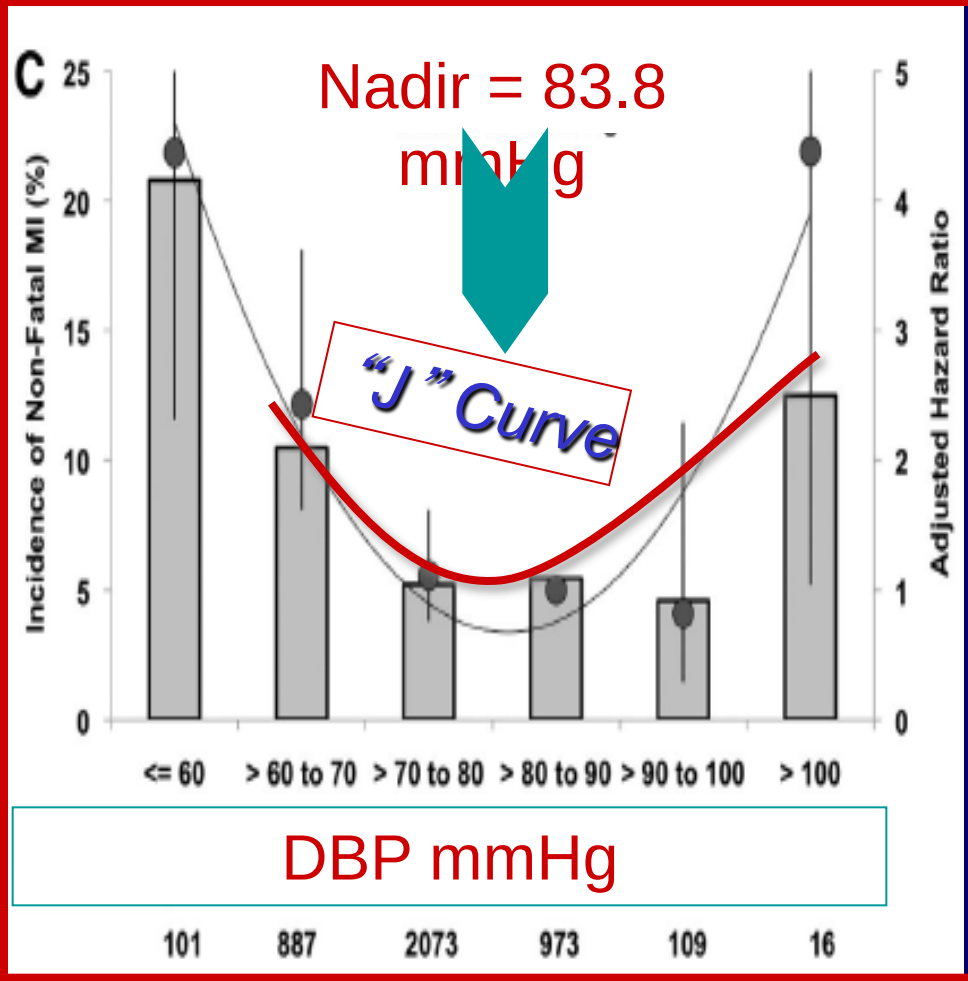
Law M R et al. BMJ 2009;338:bmj.b1665

thebmj

What is the optimal BP after Acute Coronary Syndomes? PROVE IT TIMI 22

Non-fatal Myocardial Infarction





Bangalore S et al Circulation 2010; 122: 2142-2151

Therapeutic strategies in hypertensive patients with heart disease

Recommendations	Class[a]	Level[b]	Ref.[c]
In hypertensive patients with CHD, a SBP goal <140 mmHg should be considered.	IIa	B	141, 265

a Class of recommendation b Level of evidence

ESH 2013

Treatment of Hypertension in Patients With CAD Scientific Statement From the AHA/ ACC/ASH

BP Goal, mm Hg	Condition	Class/Level of Evidence
<140/90	CAD	IIa/B
	ACS	IIa/C
	HF	IIa/B
<130/80	CAD	IIb/B
	Post–myocardial infarction, stroke or TIA, carotid artery disease, PAD, AAA	IIb/B

AAA indicates abdominal aortic aneurysm; ACS, acute coronary syndrome; BP, blood pressure; CAD, coronary artery disease; HF, heart failure; PAD, peripheral arterial disease; and TIA, transient ischemic attack.

Hypertension 2015

Guidelines on hypertension in patients 60 years or older by the American College of Physicians and the American Academy of Family Physicians[5,6]

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- Consider initiating or intensifying pharmacologic treatment in some adults aged 60 yr or older at high cardiovascular risk based on individualized assessment, to achieve a target systolic blood pressure of less than 140 mm Hg to reduce the risk of stroke or cardiac events. Factors include comorbidity, medication burden, risk of adverse events, and cost. Generally, increased cardiovascular risk includes known cardiovascular disease, diabetes, or chronic kidney disease with a glomerular filtration rate (GFR) of less than 45 mL/min/1.73 m^2.

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Meta-Analysis: Treating to BP Goals Lower Than 140/90 mmHg Does Not Reduce Mortality or Morbidity

OUTCOMES	RELATIVE RISK	95 % CI
Total mortality	0.92	0.86-1.15
MI	0.90	0.74-1.09
Stroke	0.99	0.79-1.25
CHF	0.88	0.59-1.32
Major CV events	0.94	0.83-1.07
End-Stage renal disease (ESRD)	1.01	0.81-1.27

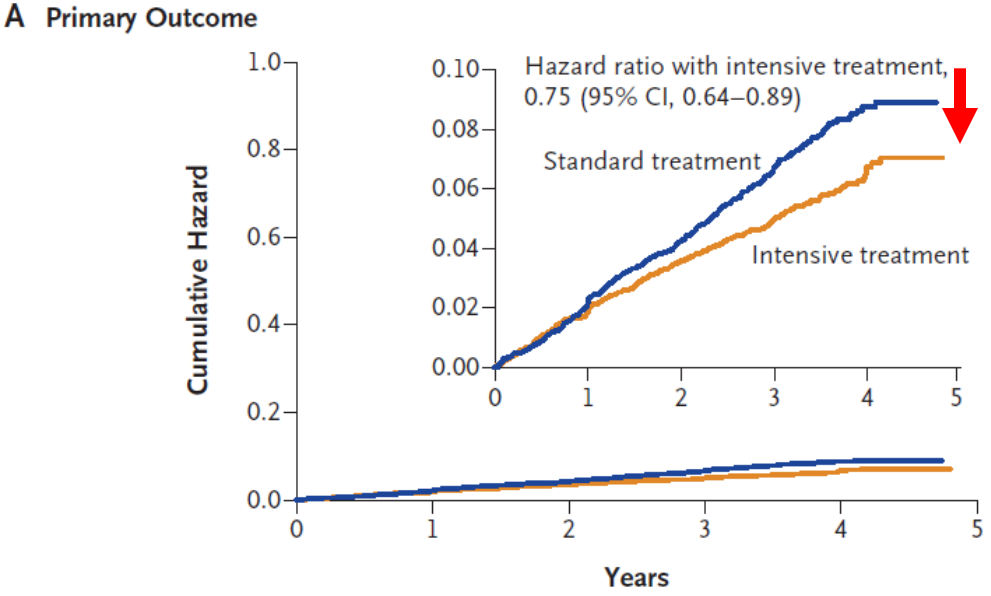
n= 22,089

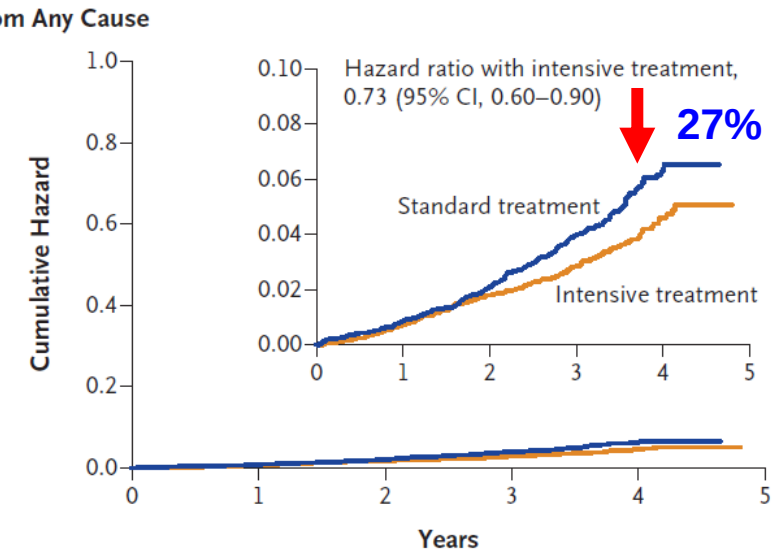
Arguedas JA, et al. Cochrane Database Syst. Rev. 2009:CD004349.

Primary outcomes

- CVD composite: first occurrence ofMI; non-MI ACS; Stroke; Acute decompensated HF; CVDdeath(NO ESRD)

SPRINT
Systolic Blood Pressure Intervention Trial





No. at Risk

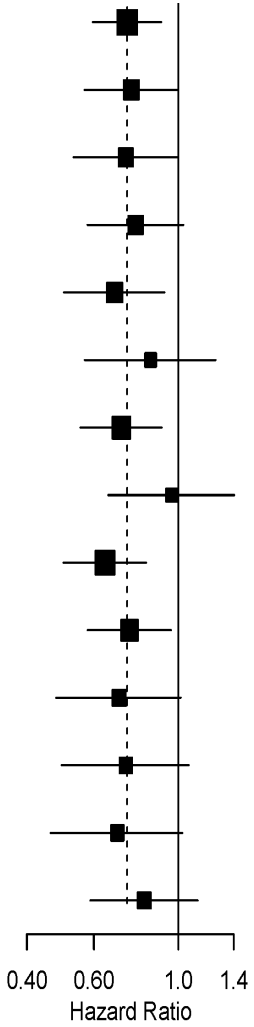
Standard treatment	4683	4437	4228	2829	721
Intensive treatment	4678	4436	4256	2900	779

No. at Risk

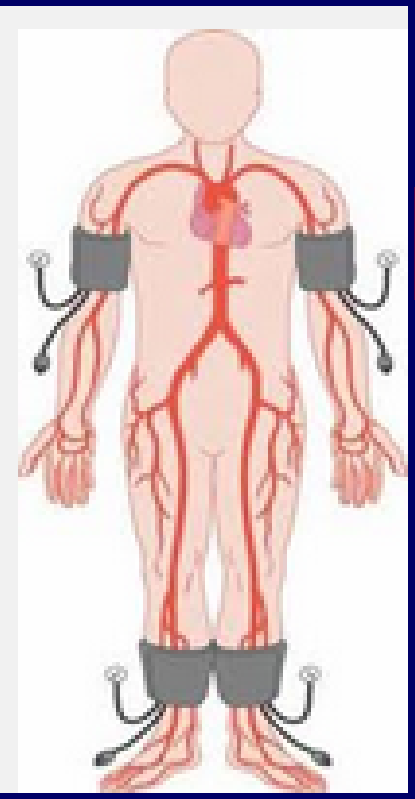
Standard treatment	4683	4528	4383	2998	789
Intensive treatment	4678	4516	4390	3016	807

All-cause Mortality Experience in the Six Pre-specified Subgroups of Interest

Overall	155/4678 (3.31)	210/4683 (4.48)	0.73 (0.60,0.90)	
No Prior CKD	85/3348 (2.54)	115/3367 (3.42)	0.75 (0.57,1.00)	0.76
Prior CKD	70/1330 (5.26)	95/1316 (7.22)	0.73 (0.53,1.00)	
Age < 75	82/3361 (2.44)	104/3364 (3.09)	0.77 (0.58,1.03)	0.58
Age ≥ 75	73/1317 (5.54)	106/1319 (8.04)	0.68 (0.50,0.92)	
Female	46/1684 (2.73)	54/1648 (3.28)	0.85 (0.57,1.26)	0.49
Male	109/2994 (3.64)	156/3035 (5.14)	0.71 (0.55,0.91)	
African−American	53/1454 (3.65)	55/1493 (3.68)	0.96 (0.65,1.40)	*0.06
Non African−American	102/3224 (3.16)	155/3190 (4.86)	0.64 (0.50,0.82)	
No Prior CVD	106/3738 (2.84)	140/3746 (3.74)	0.75 (0.58,0.96)	0.78
Prior CVD	49/940 (5.21)	70/937 (7.47)	0.70 (0.48,1.02)	
SBP ≤ 132	46/1583 (2.91)	64/1553 (4.12)	0.73 (0.49,1.07)	0.70
132 < SBP < 145	41/1489 (2.75)	63/1549 (4.07)	0.69 (0.46,1.03)	
SBP ≥ 145	68/1606 (4.23)	83/1581 (5.25)	0.81 (0.59,1.13)	



*p=0.34, after Hommel adjustment for multiple comparisons



PERIPHERAL ARTERY DISEASE

Therapeutic strategies in hypertensive patients with atherosclerosis, arteriosclerosis and PAD

Recommendations	Class[a]	Level[b]	Ref.[c]
In the presence of carotid atherosclerosis, prescription of calcium antagonists and ACE inhibitors should be considered as these agents have shown a greater efficacy in delaying atherosclerosis progression than diuretics and beta-blockers.	IIa	B	186, 581
In hypertensive patients with a PWV above 10 m/s all antihypertensive drugs should be considered provided that a BP reduction to <140/90 mmHg is consistently achieved.	IIa	B	138, 582, 586
Antihypertensive therapy is recommended in hypertensive patients with PAD to achieve a goal of <140/90 mmHg, because of their high risk of myocardial infarction, stroke, heart failure, and CV death.	I	A	284

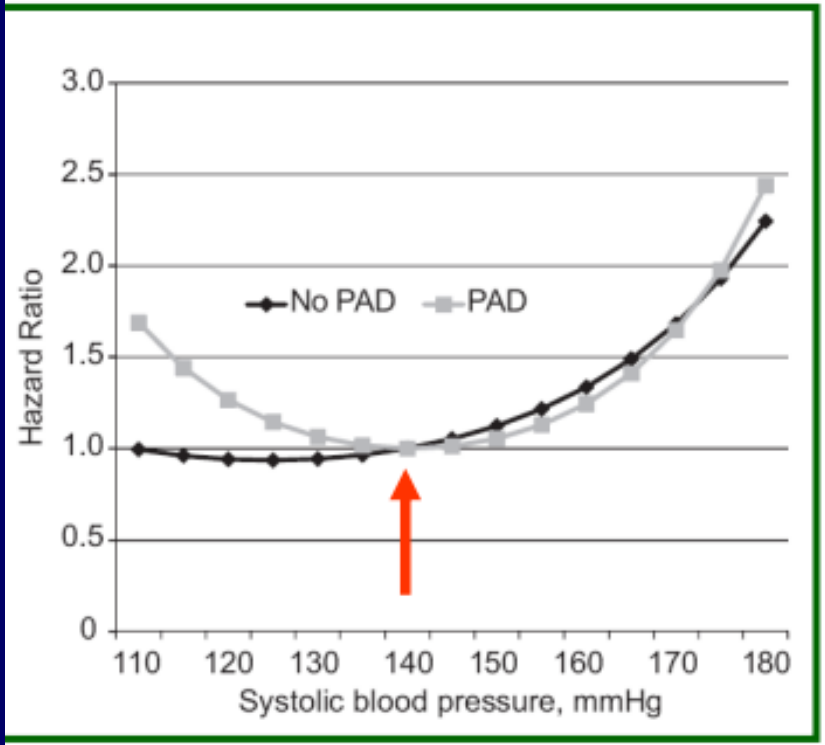
ESH 2013

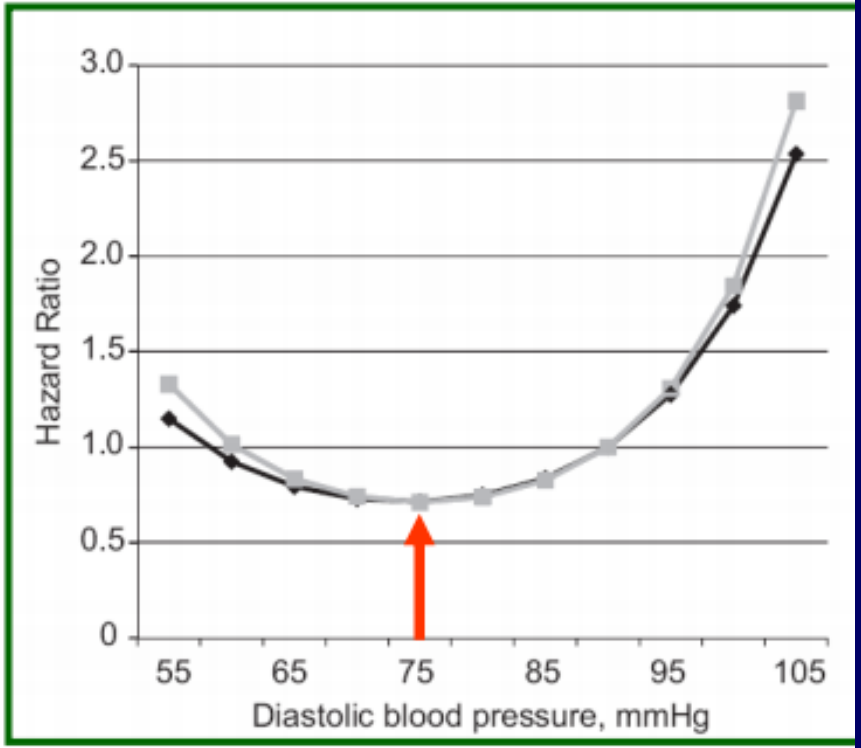
a Class of recommendation
b Level of evidence

Outcomes Among Hypertensive Patients With Concomitant Peripheral and Coronary Artery Disease

HRs for the primary outcome plotted against average systolic BP (LT) and average diastolic BP (RT)

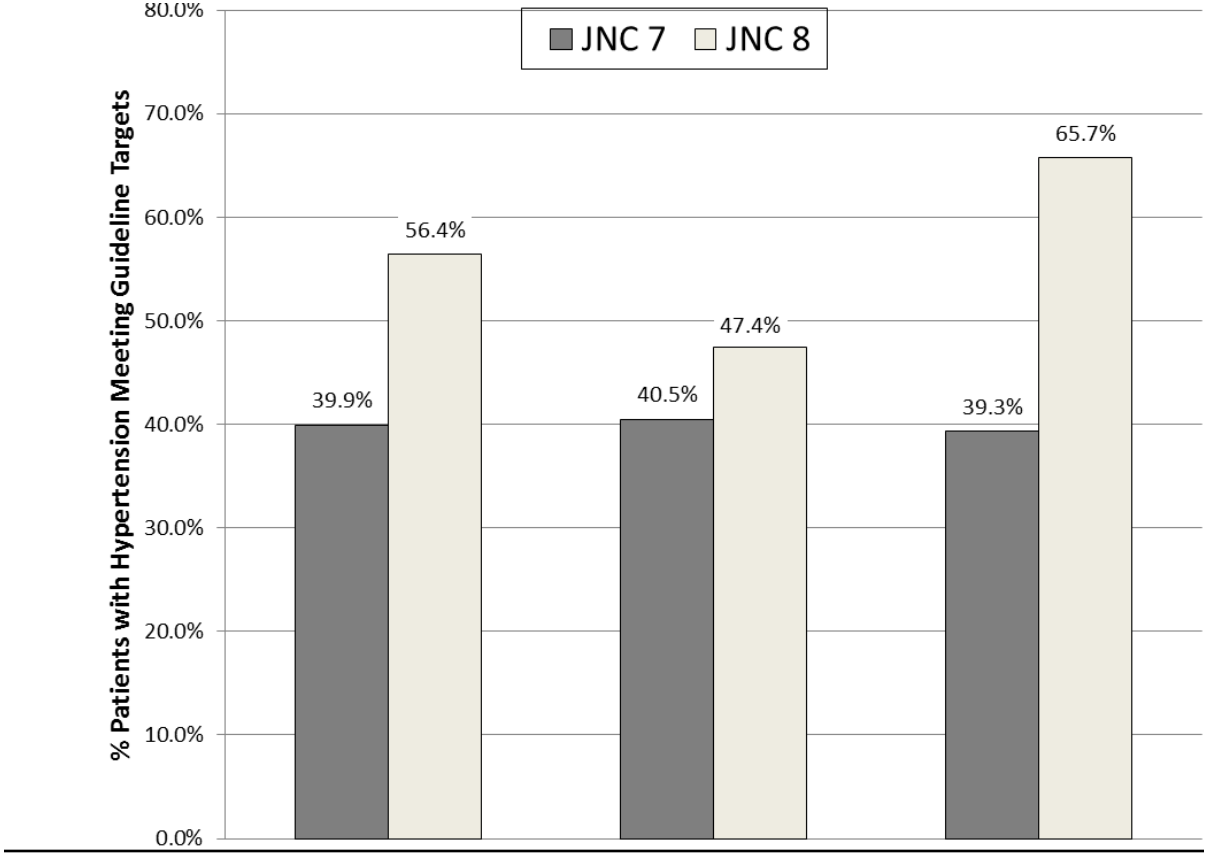
INVEST





Bavry A et al Hypertension 2010

JNC-8 Implications for the USA



	ALL US Adults	Ages 18-59	Ages 60+
JNC 7: HTN	66.6 M	32.8 M	33.8 M
Controlled	26 (39.9%)	13.3 (40.5%)	13.3 (39.3%)
JNC 8: HTN	60.8 M	30.8 M	30.0 M
Controlled	34.3 (56.4%)	14.6 (47.4%)	19.7 (65.7%)