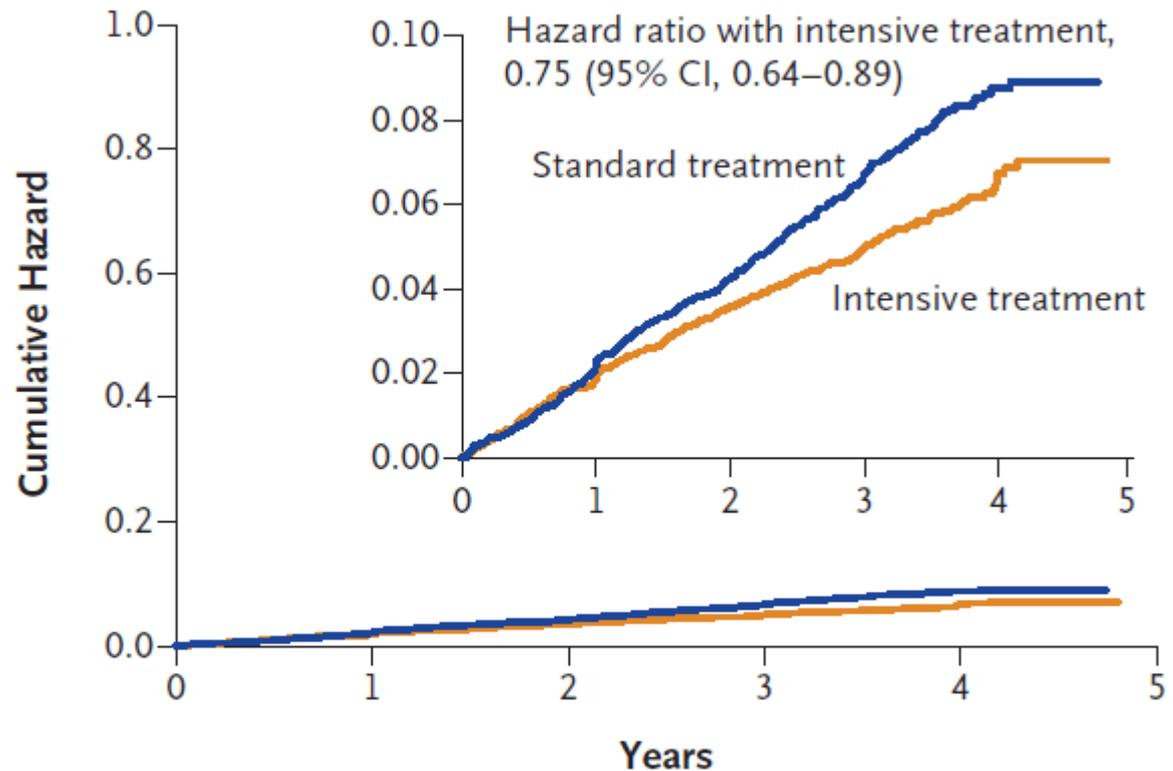


Target blood pressure for Asian population: New Answers from the Recent Study Results

Park Sungha
Yonsei University Health System
Cardiovascular Hospital
Division of Cardiology

SPRINT primary outcome

A Primary Outcome



No. at Risk

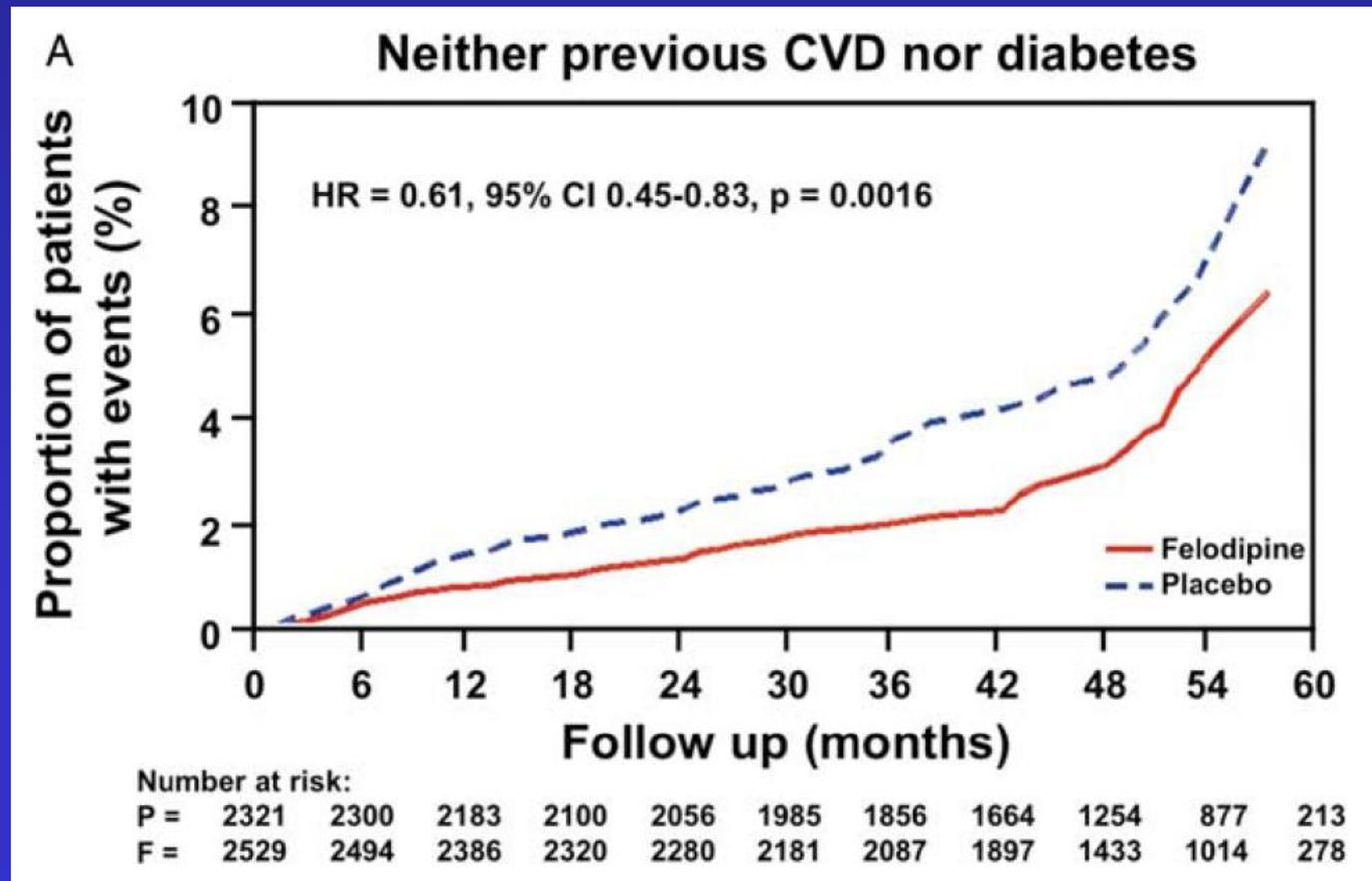
Standard treatment	4683	4437	4228	2829	721
Intensive treatment	4678	4436	4256	2900	779

**What is the treatment target
in the general hypertension
population in Asia?**

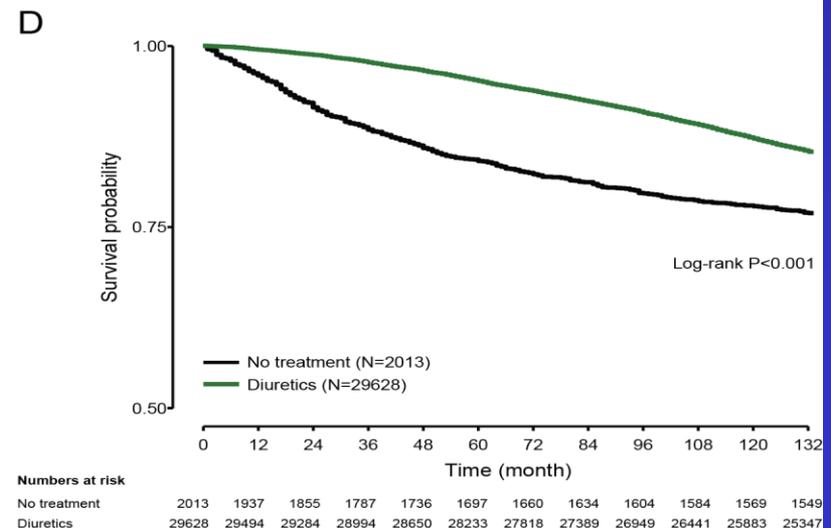
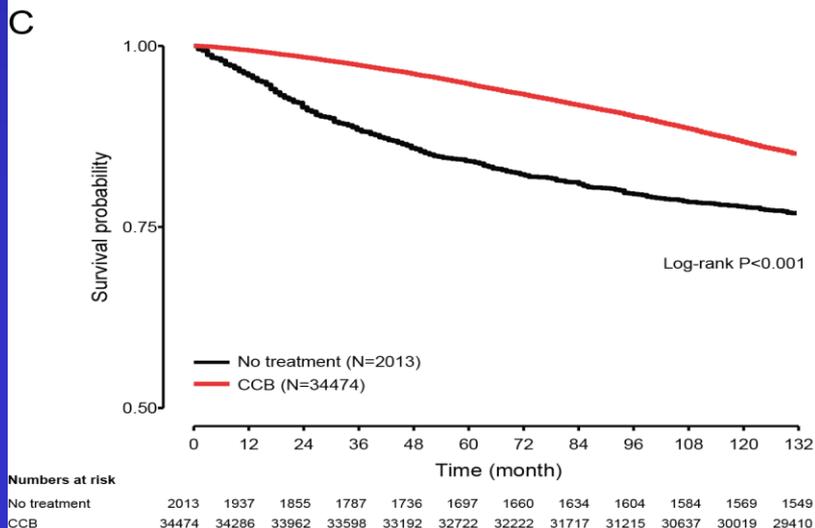
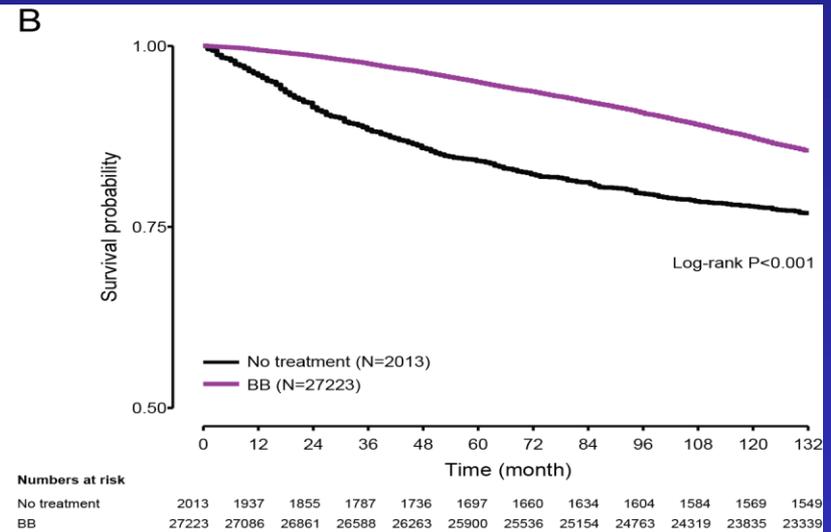
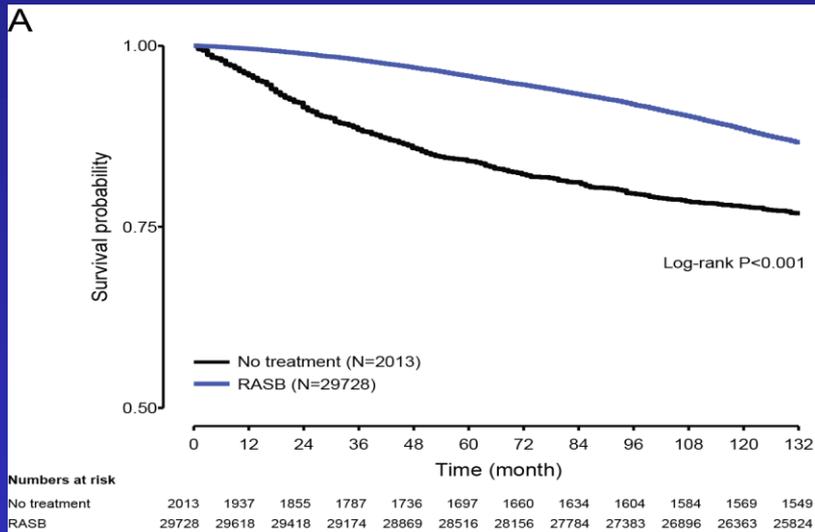
Is a systolic blood pressure target <140 mmHg indicated in all hypertensives? Subgroup analyses of findings from the randomized FEVER trial

Zhang Y et al. *Eur Heart J* 2011;32:1500-1508

4850 out of 9711 hypertensives(SBP 138 vs 142)



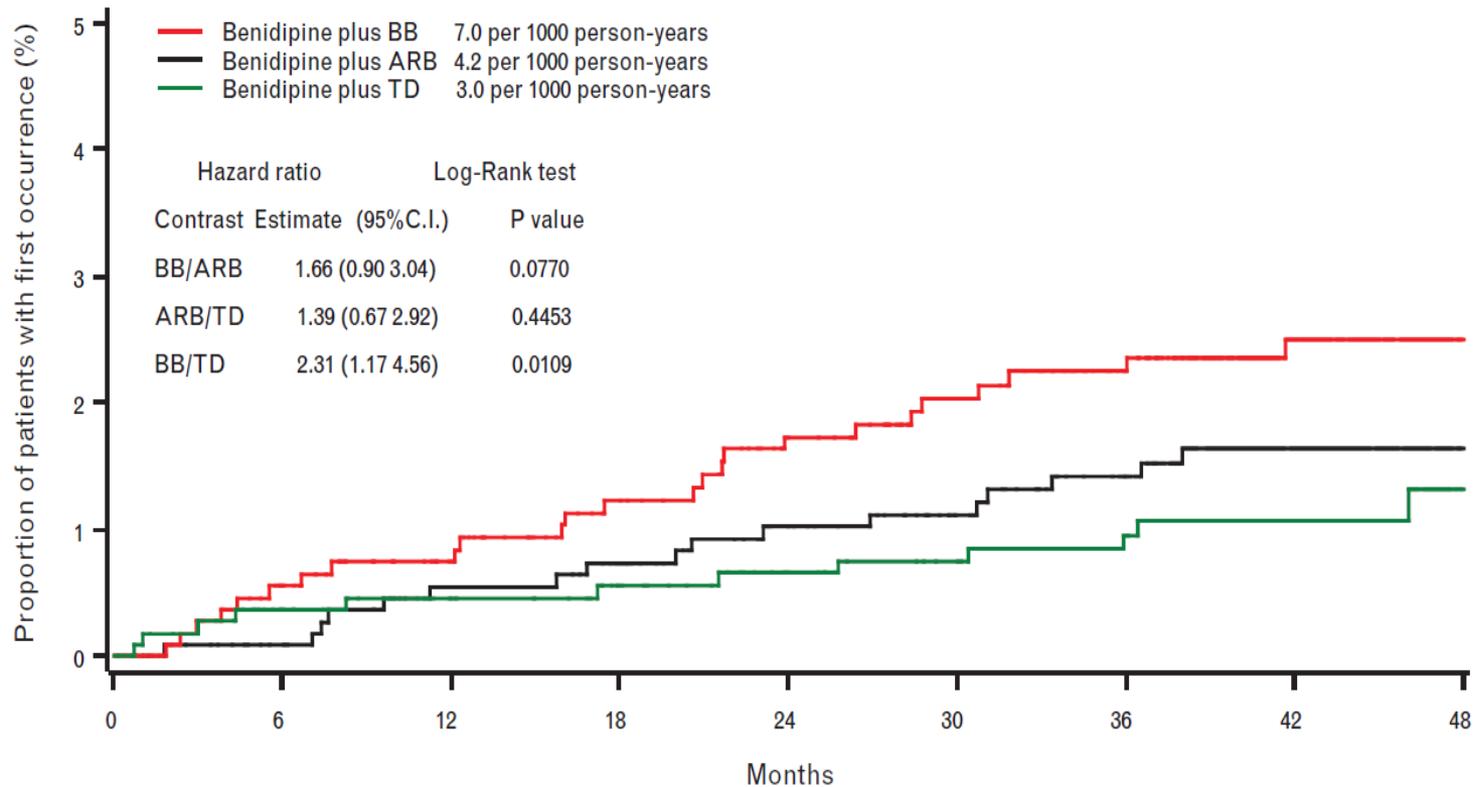
Korean National Health Insurance Cohort Registry(N=40917, no CVD, DM or CKD)



Prevention of cardiovascular events with calcium channel blocker-based combination therapies in patients with hypertension: a randomized controlled trial

Matsuzaki M et al. J Hypertens 2011;29:1649-1659

3501 hypertensives FU for 3.61 years



Number at risk

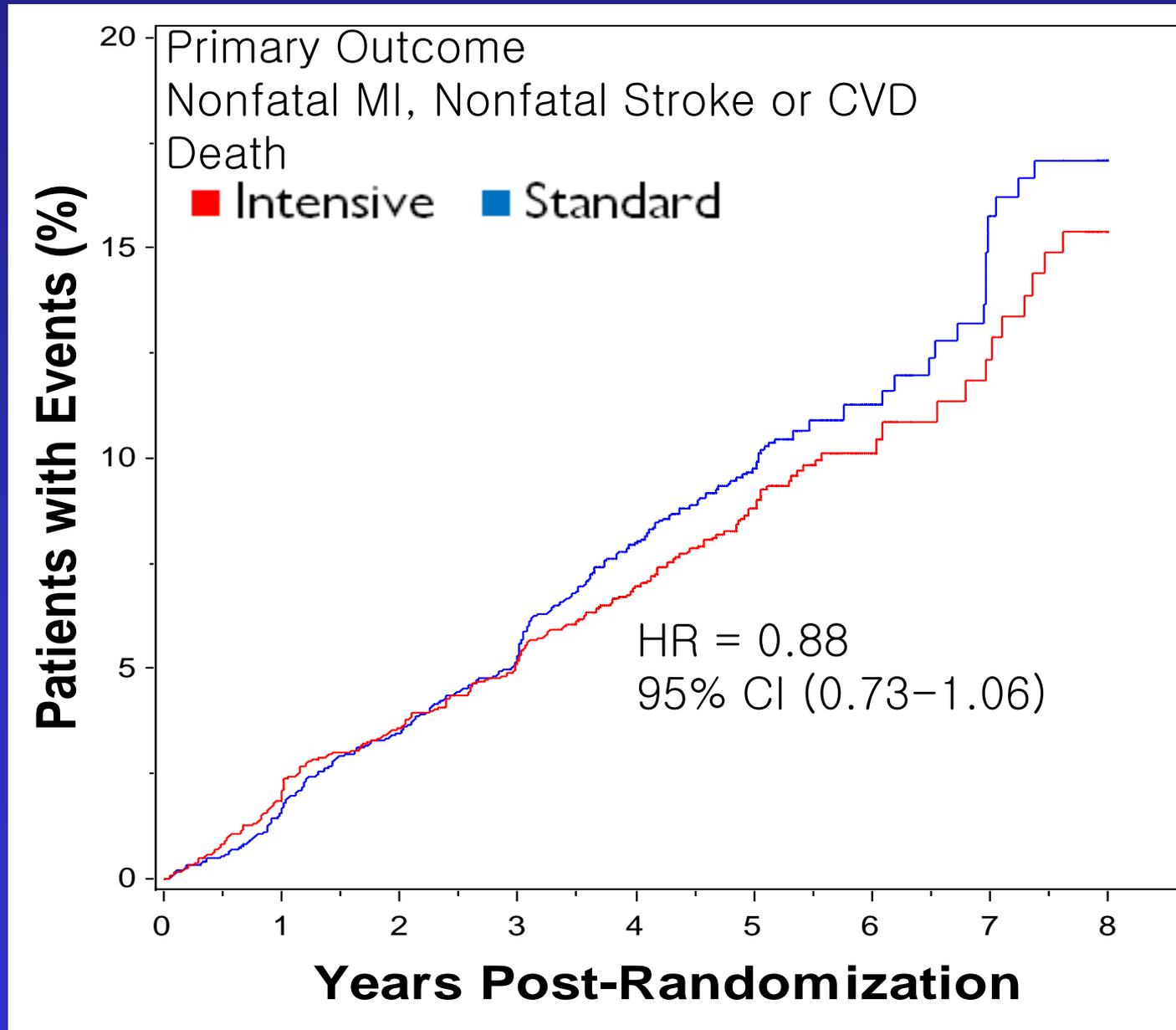
Benidipine plus BB	1089	1065	1023	998	974	947	921	612	310
Benidipine plus ARB	1110	1097	1069	1049	1030	1008	987	649	329
Benidipine plus TD	1094	1071	1044	1027	1011	998	966	630	327

HT treatment in hypertensives not at high cardiovascular risk

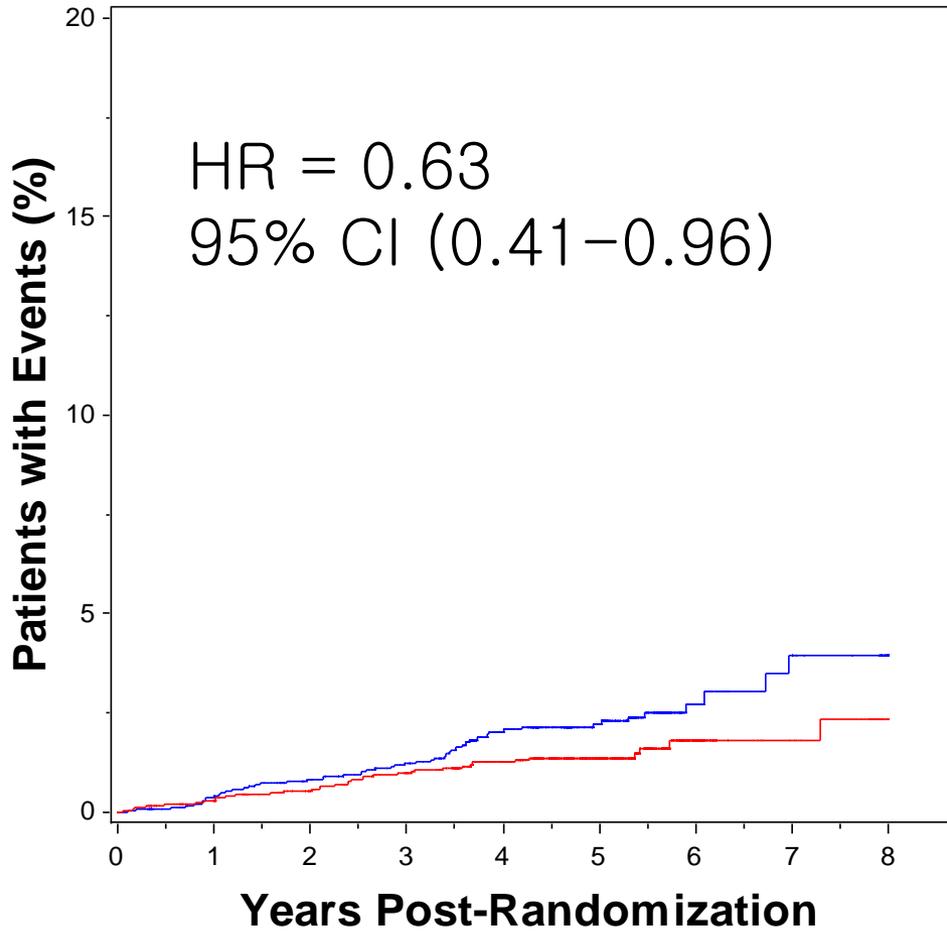
- Anti hypertensive treatment should be considered in hypertensive subjects with mild to moderate risk
- Target blood pressure should be < 140/90mmHg
- Any of the five first class agents may be used but combination of CCB + BB may be inferior in terms of stroke reduction

Treatment target in diabetes and CKD

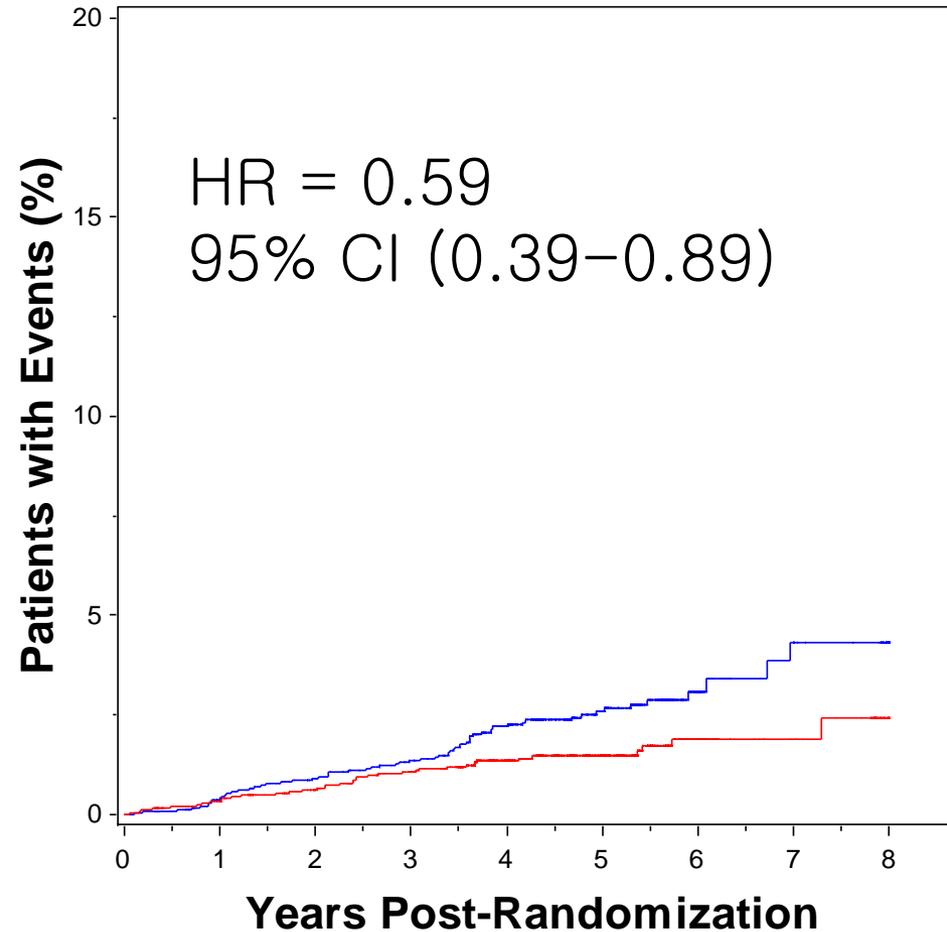
ACCORD Double 2 x 2 Factorial Design



Nonfatal Stroke

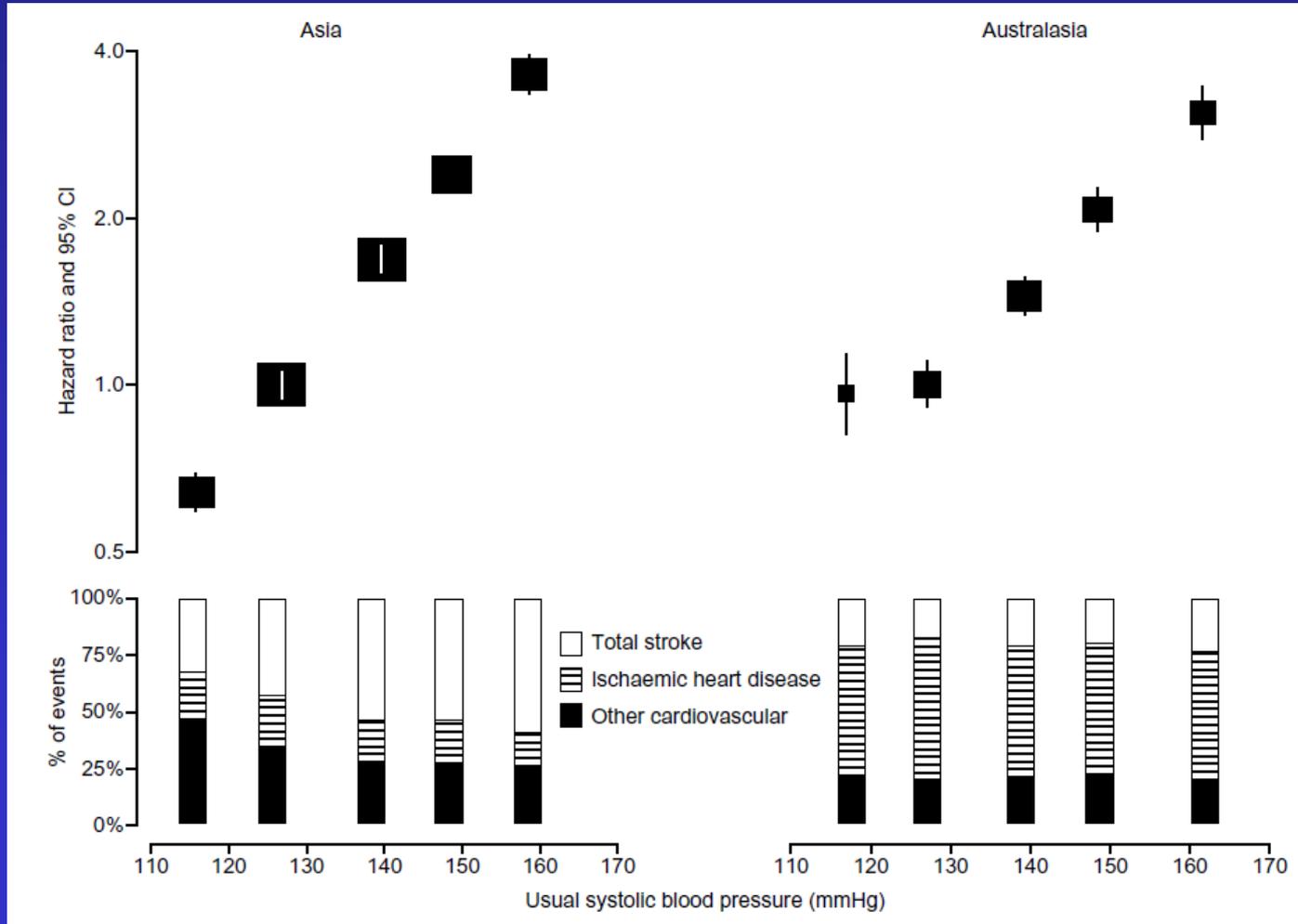


Total Stroke



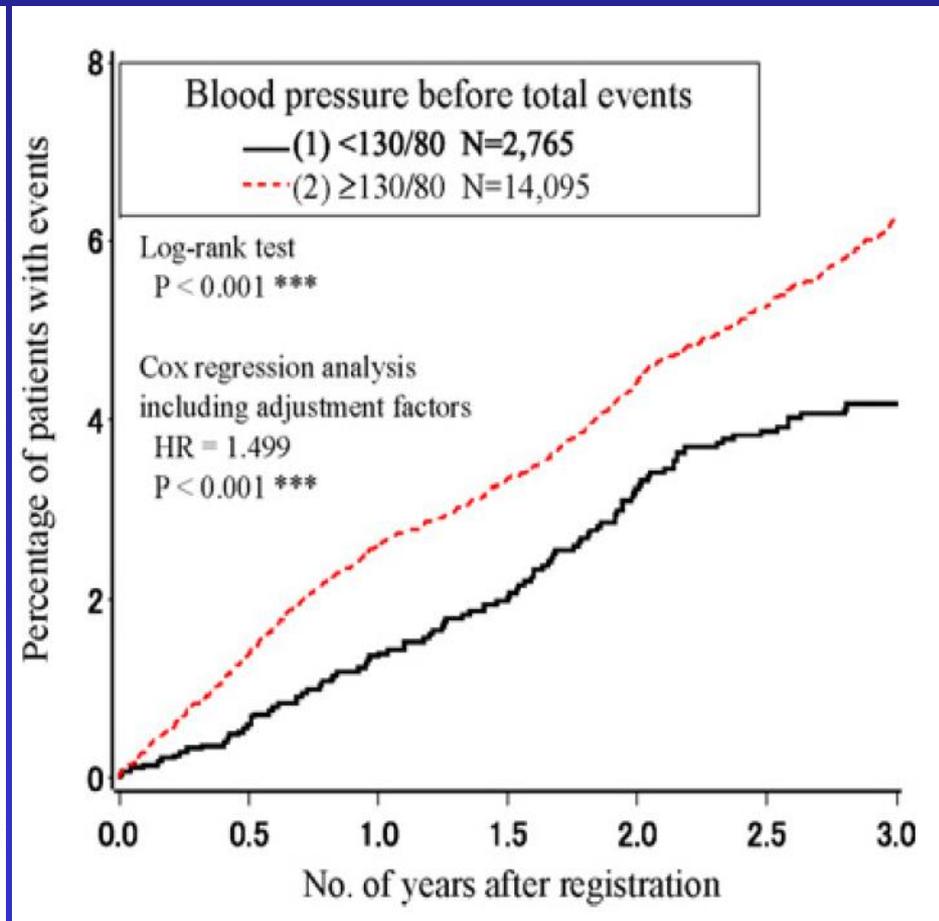
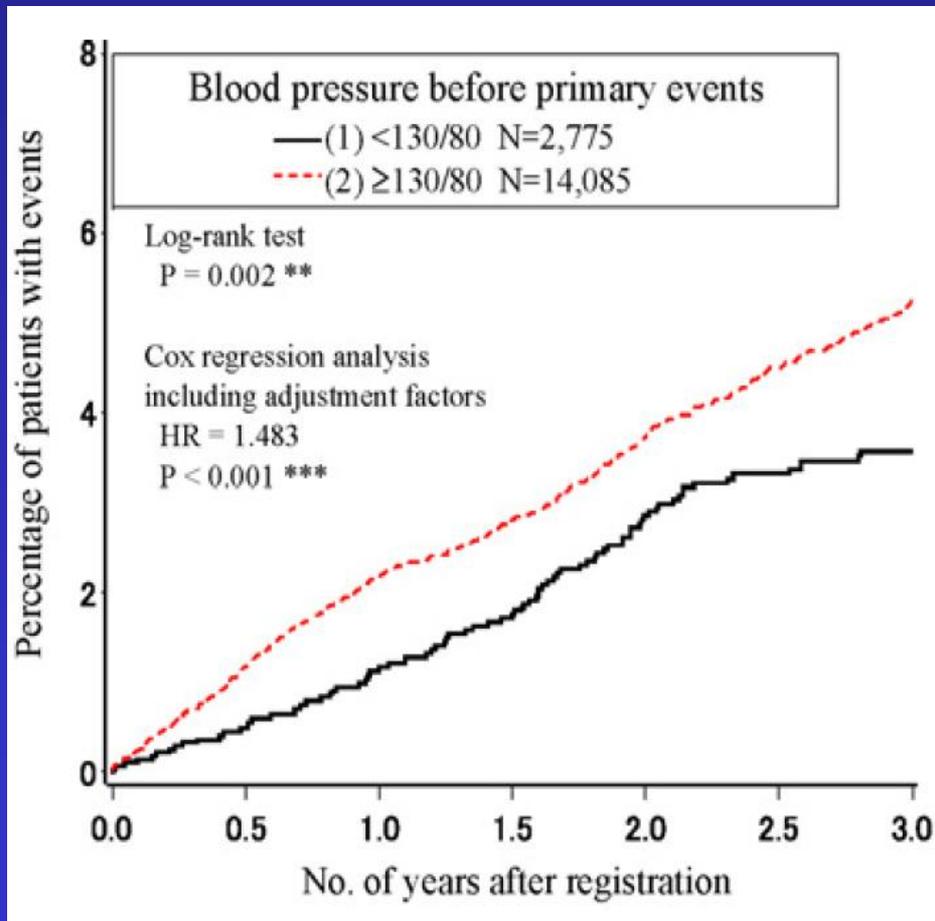
■ Intensive ■ Standard

Difference in the relationship between blood pressure and CV events according to race



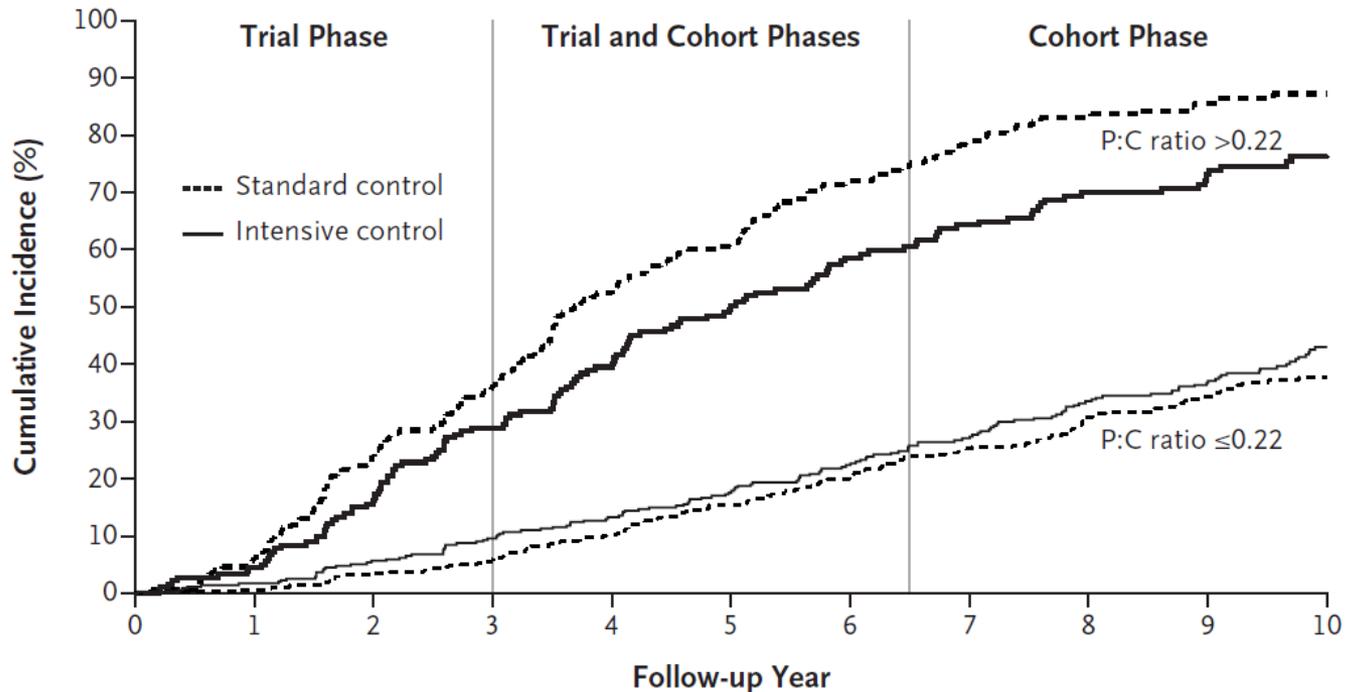
Relation between CV complications and BP level: Challenge-DM study

16,869 patients in nationwide registry: 29 months FU



Intensive Blood-Pressure Control in Hypertensive Chronic Kidney Disease

Appel LJ et al. N Engl J Med 2010;363:918-929



P:C Ratio >0.22

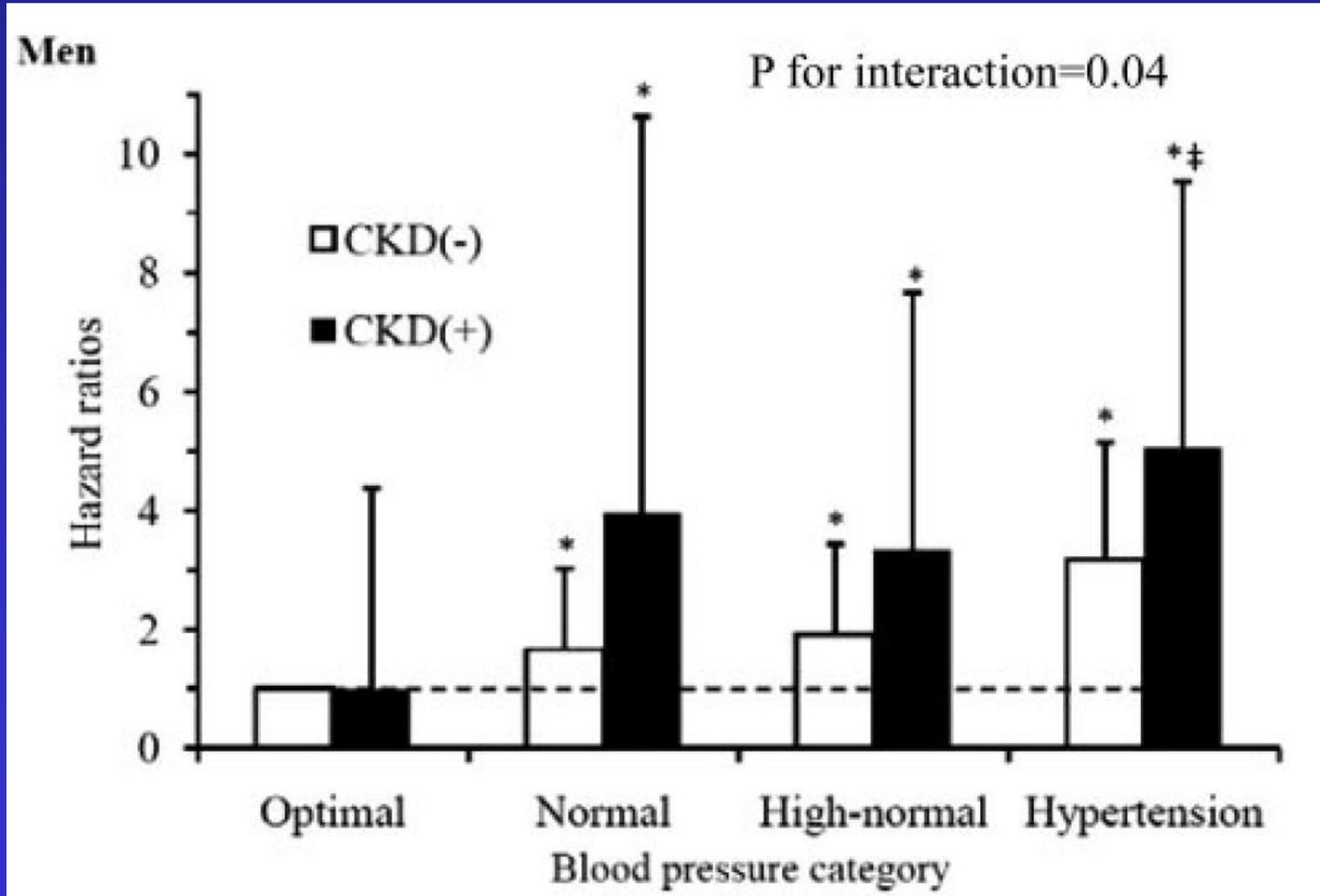
Standard control	176	165	134	113	81	66	45	32	26	22	13
Intensive control	181	172	151	128	109	87	67	56	47	40	25

P:C Ratio ≤0.22

Standard control	376	373	362	353	332	302	267	234	214	196	128
Intensive control	357	350	335	321	306	282	254	228	206	189	128

Interaction of CKD and HT for development of CVD(SUITA study)

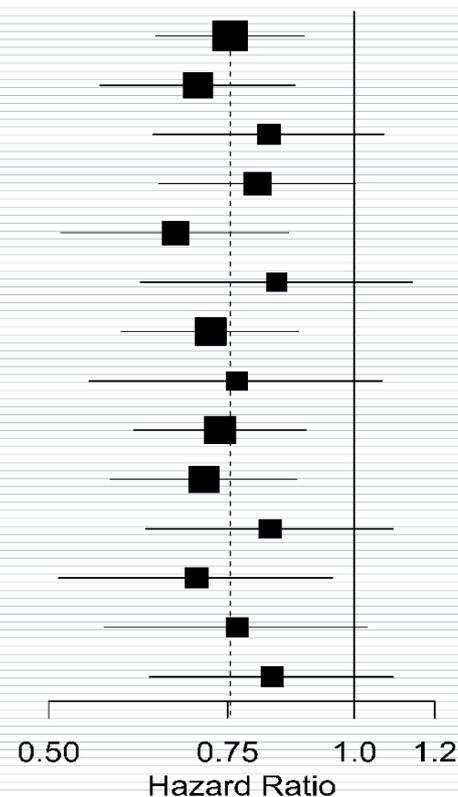
5494 individuals (ages 30 to 79, No MI or stroke)



Primary Outcome Experience in the Six Pre-specified Subgroups of Interest

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

*Treatment by subgroup interaction
*Unadjusted for multiplicity



Renal outcome in the SPRINT trial

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

Target BP in DM and CKD

- For diabetes a target SBP of 140mmHg is recommended → However, SBP below 130mmHg can be considered in high risk diabetes if tolerated
- For patients with CKD: target BP of < 130/80 should be considered

BP target in the elderly

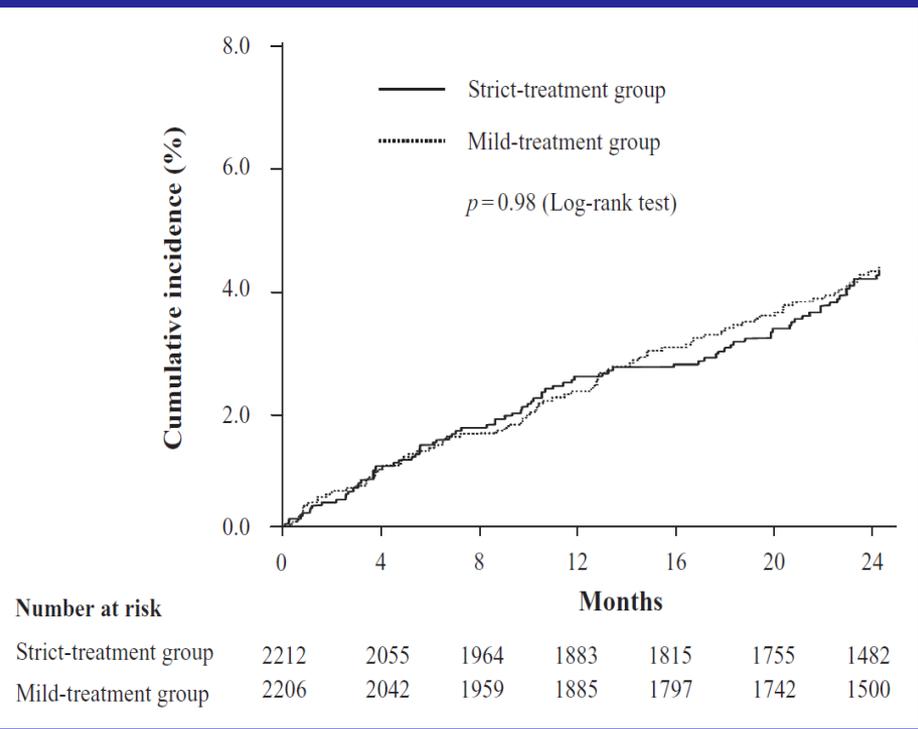
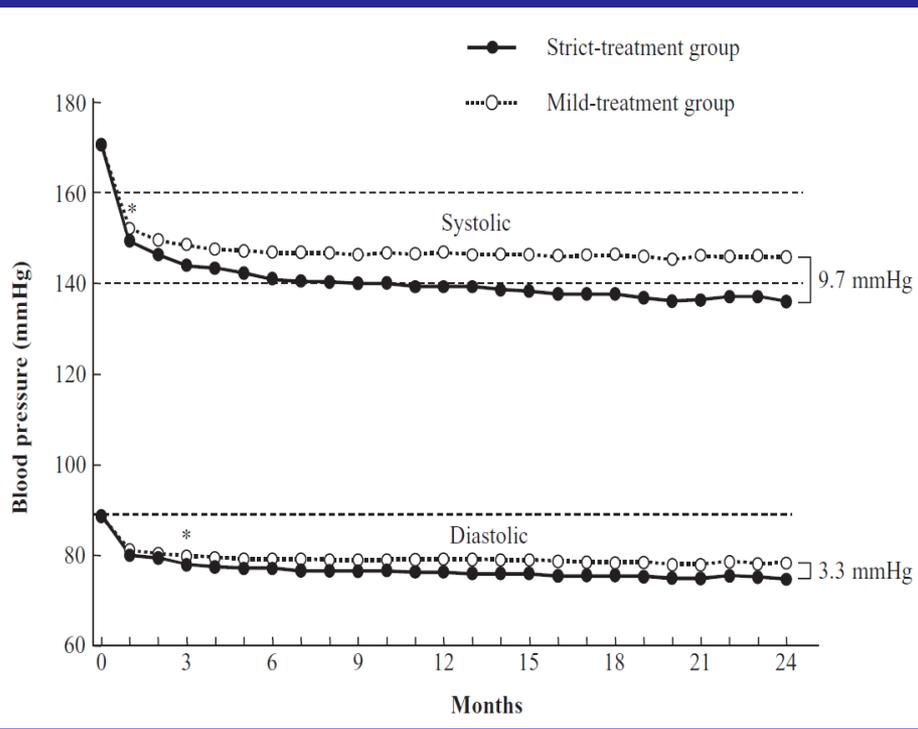
Japanese Trial to Assess Optimal Systolic Blood pressure in Elderly Hypertensive Patients(JATOS)

- Patients with essential hypertension(65-85 years of age with SBP > 160mmHg)
- 2212 patients with strict treatment of SBP < 140mmHg and usual treatment(140-159mmHg)
- Primary endpoint of cardiovascular disease and renal failure

Hypertens Res 2008;31(12):2115-2127

Hypertens Res 2008;31:2115-2127

Japanese Trial to Assess Optimal Systolic Blood pressure in Elderly Hypertensive Patients(JATOS)

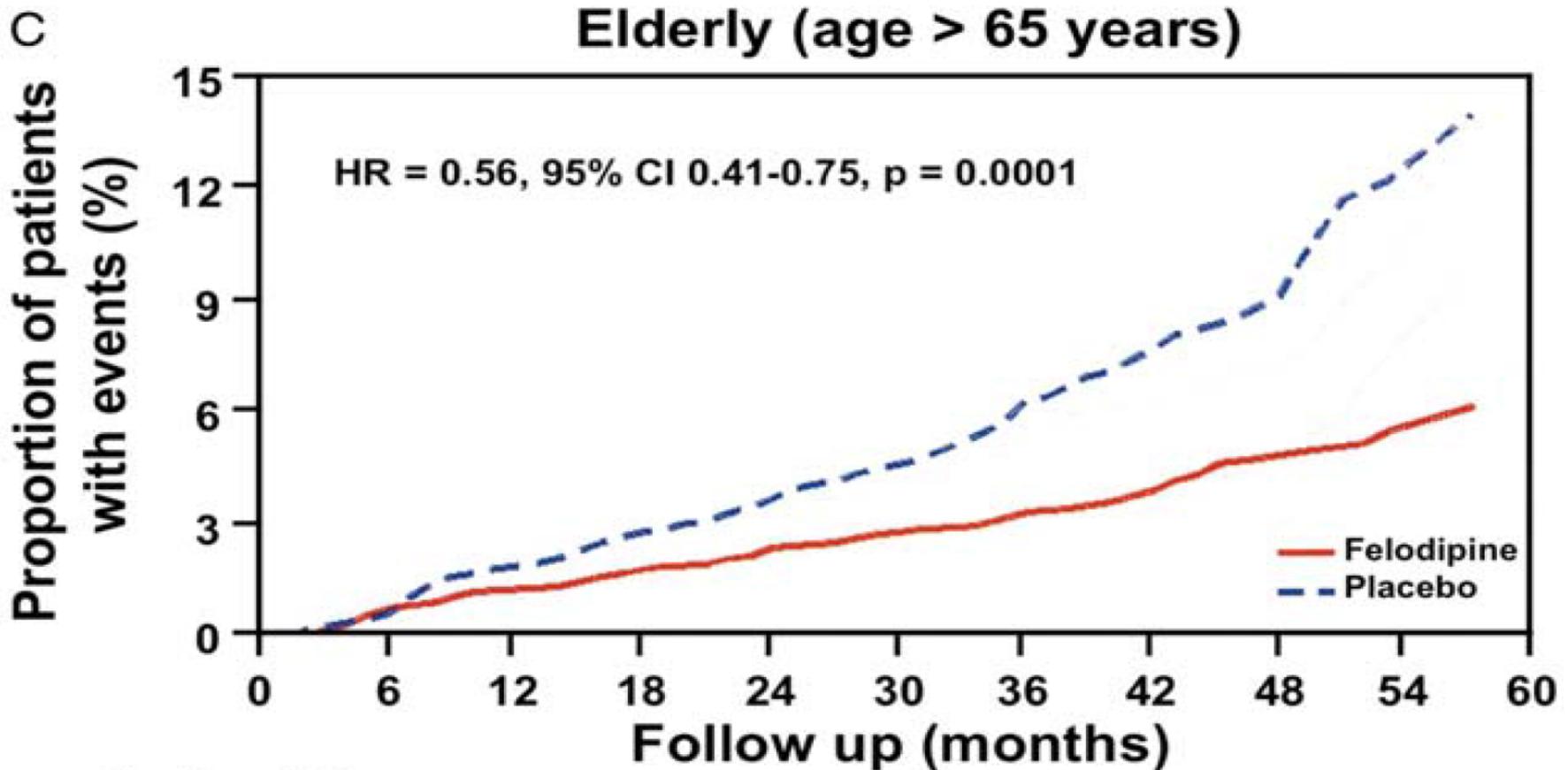


Hypertens Res 2008;31(12):2115-2127

Hypertens Res 2008;31:2115-2127

Subgroup analyses of the elderly in the FEVER trial

6532 out of 9711 hypertensives(SBP 138 vs 142)



Number at risk:

P =	1548	1532	1449	1390	1350	1304	1223	1097	875	857	212
F =	1631	1602	1524	1477	1438	1394	1280	1123	903	793	198

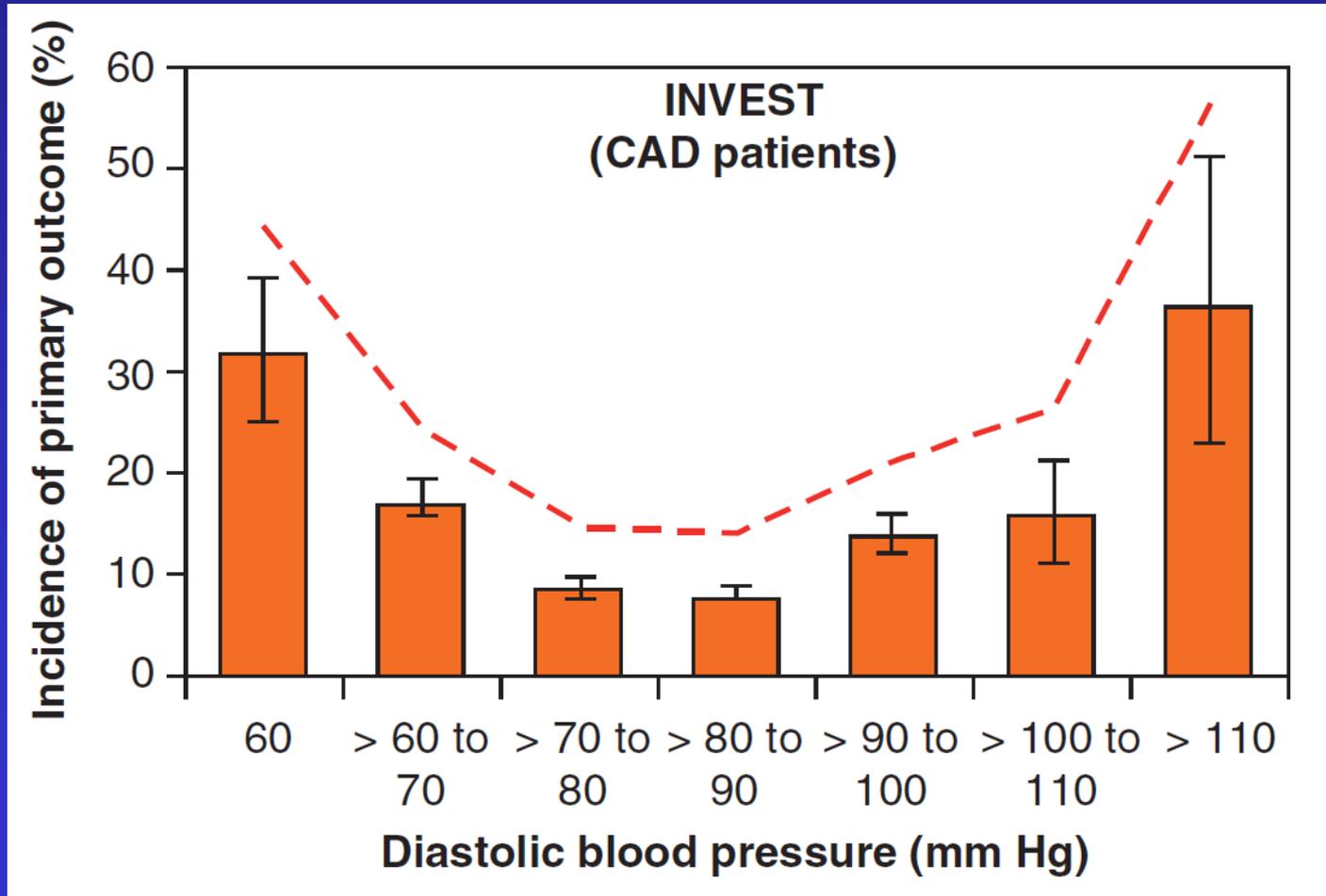
Target BP in the elderly

- All hypertension in non-frail elderly should be treated with anti hypertensive medications
- There should be an initial target SBP of < 150mmHg
- Patients who tolerate additional lowering may have their SBP lowered to below 130-140mmHg

**BP target in HT with
CAD and HT at high
risk of CAD**

J curve in HT patients with CAD

22,576 patients with HT and CAD

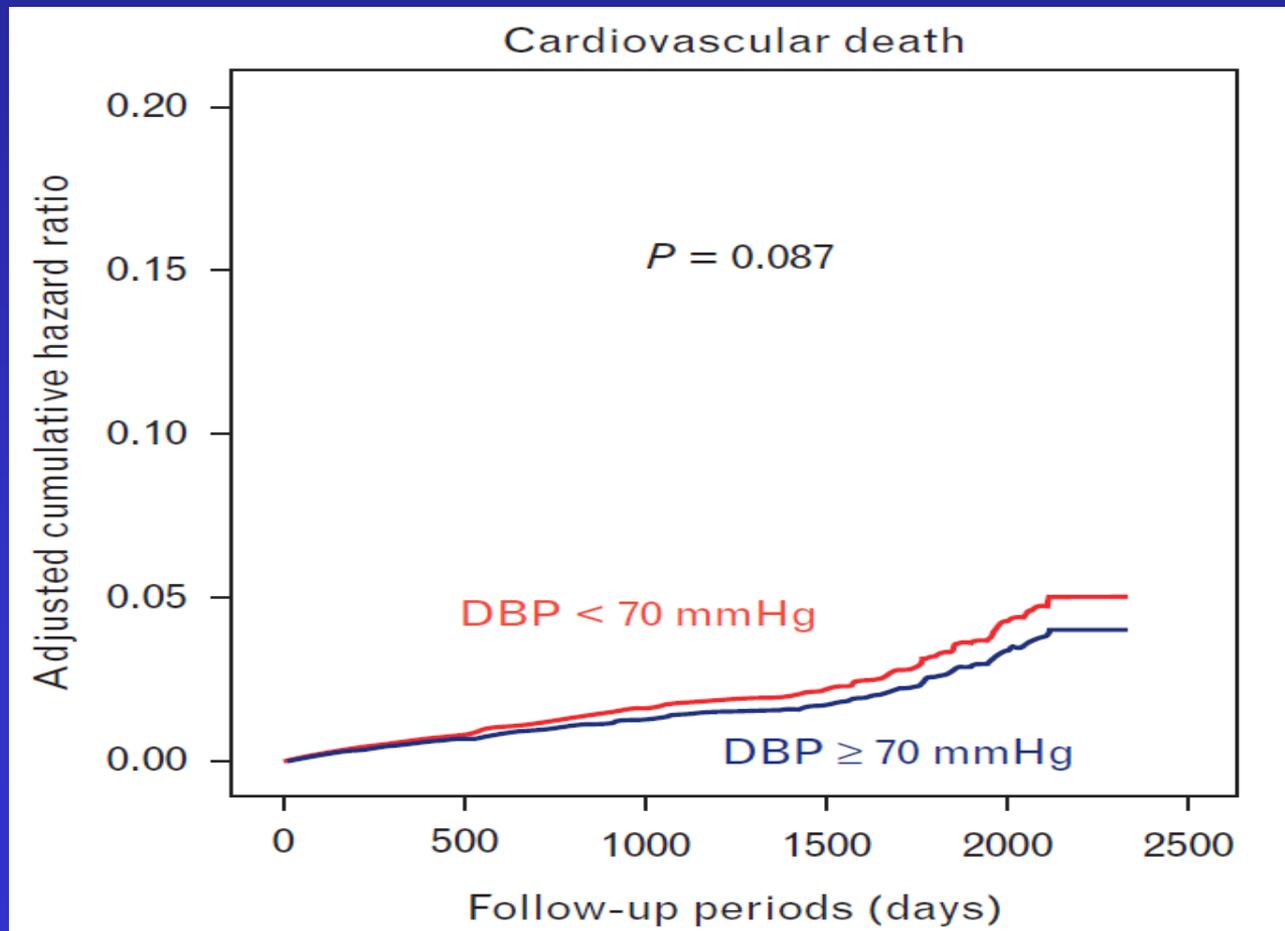


Low DBP may not be an independent risk for cardiovascular death in revascularized coronary artery disease patients

Hisashi Kai^a, Takafumi Ueno^b, Takeshi Kimura^c, Hisashi Adachi^d,
Yutaka Furukawa^e, Toru Kita^e, Tsutomu Imaizumi^a, on behalf
of CREDO-Kyoto Investigators

Kai H et al. J Hypertens 2011;29:1889-1896

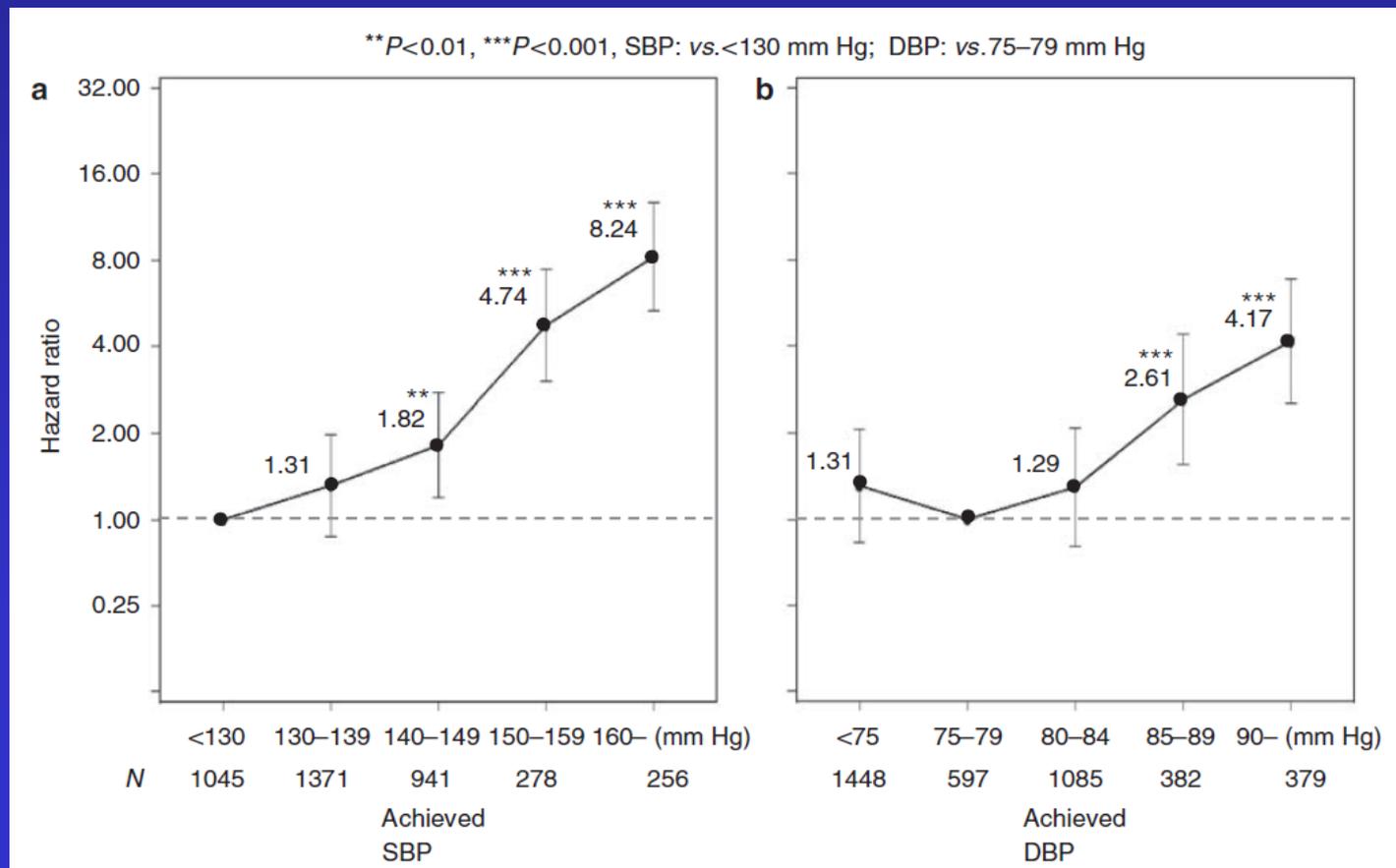
7180 stable CAD (Median FU: 3.6 years) Adjusted for age, sex, eGFR, heart failure,
prior CVD, PP, LV systolic dysfunction, prior MI



Relationship between the achieved blood pressure and the incidence of cardiovascular events in Japanese hypertensive patients with complications: a sub-analysis of the CASE-J trial

Ogihara T et al. *Hypertens Res* 2009;32:248-254

Patients with DM, CKD or LVH(85% of 4553 subjects)



Target BP in previous CVD and/or patients at high risk of CVD

- Consideration for target BP < 130/80mmHg should be given
- All first line agents may be used unless there are compelling indication to use certain class of medications

Blood-pressure targets in patients with recent lacunar stroke: the SPS3 randomised trial

The SPS3 Study Group*

Lancet 2013;382:507-515

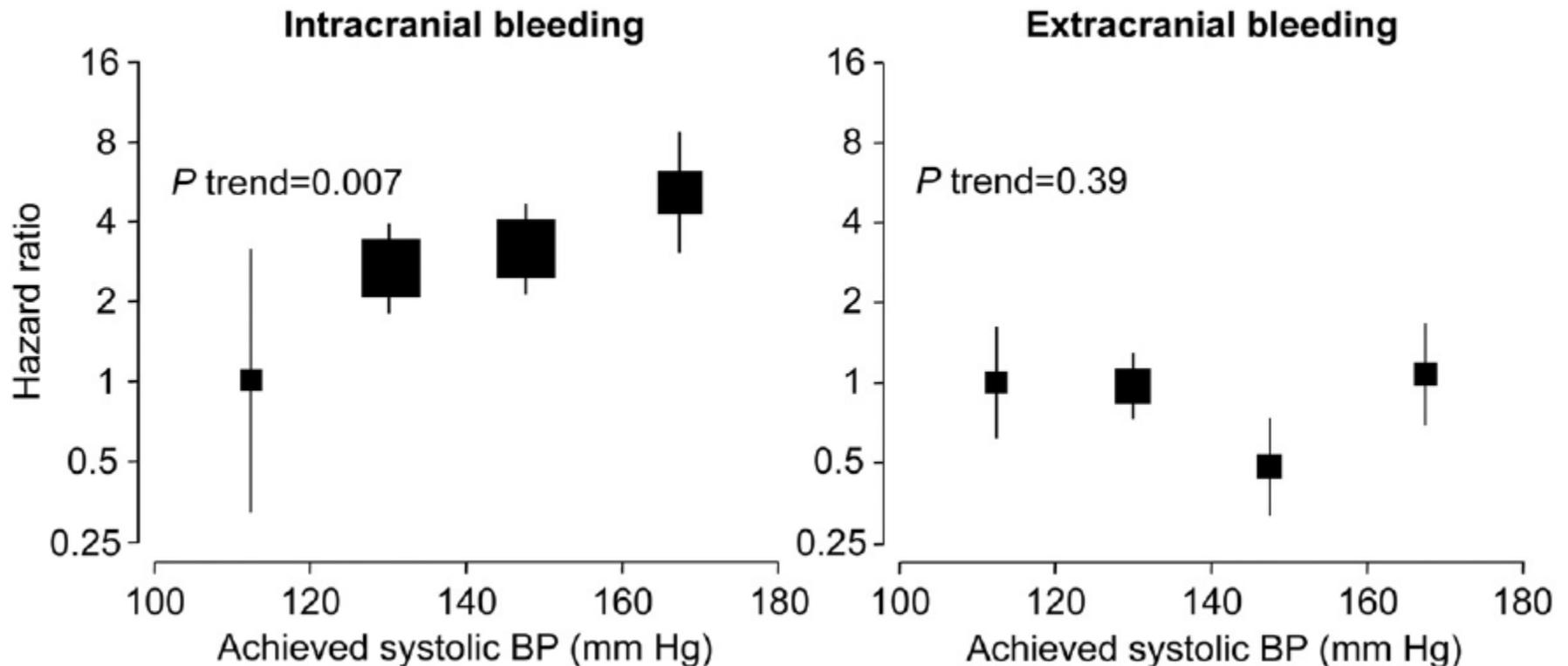
- 3020 subjects with recent lacunar infarct
- Open label: SBP < 130(127mmHg) vs SBP; 130-149(138mmHg)
- Non significant reduction in stroke(HR: 0.81, 95 % CI: 0.64-1.03, P = 0.08)
- Composite outcome of stroke, MI or vascular death(HR: 0.84, 0.68-1.04, P = 0.32)
- Significant reduction of ICH(HR: 0.37, 0.15-0.95, P = 0.03)

Effects of Blood Pressure Lowering on Intracranial and Extracranial Bleeding in Patients on Antithrombotic Therapy

The PROGRESS Trial

Arima H et al. Stroke 2012;43:1675-1677

N= 6105, FU; 3.9 years



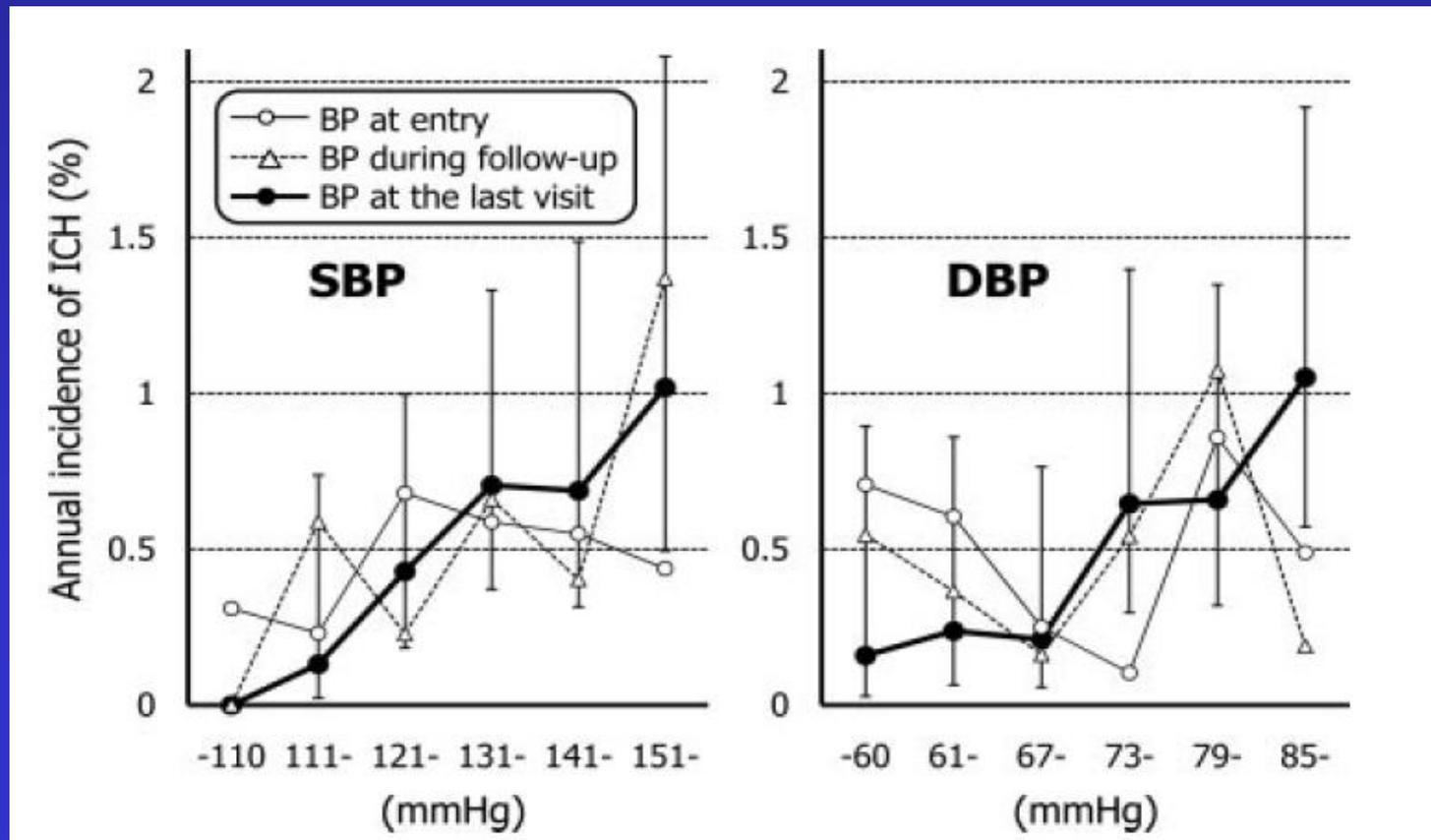
Blood Pressure Levels and Bleeding Events During Antithrombotic Therapy

The Bleeding With Antithrombotic Therapy (BAT) Study

Toyoda K et al. Stroke 2010;41:1440-1444

N=4001, Median FU: 19 months

Optimal cutoff level for increased risk of ICH \geq 130/81mmHg



**How much should recent
clinical trials, including
SPRINT, impact the target
BP in Asia?**

No changes in target BP for

- Previous stroke
- Hypertensive subjects under the age of 50
- Low risk hypertensives without history of CHD or CKD with framingham risk score less than 15
- What about diabetes?, CKD with proteinuria?

SBP target can be lowered to below 130mmHg if tolerated for

- Patients over the age of 50 with previous CHD
- High risk hypertensives over the age of 50 without previous history of CHD or MI
- Non frail elderly hypertensives
- Chronic kidney disease
- Patients undergoing antplatelet, antithrombotic therapy
- High risk diabetics in the asian population?

***Thank you very much
for your attention***



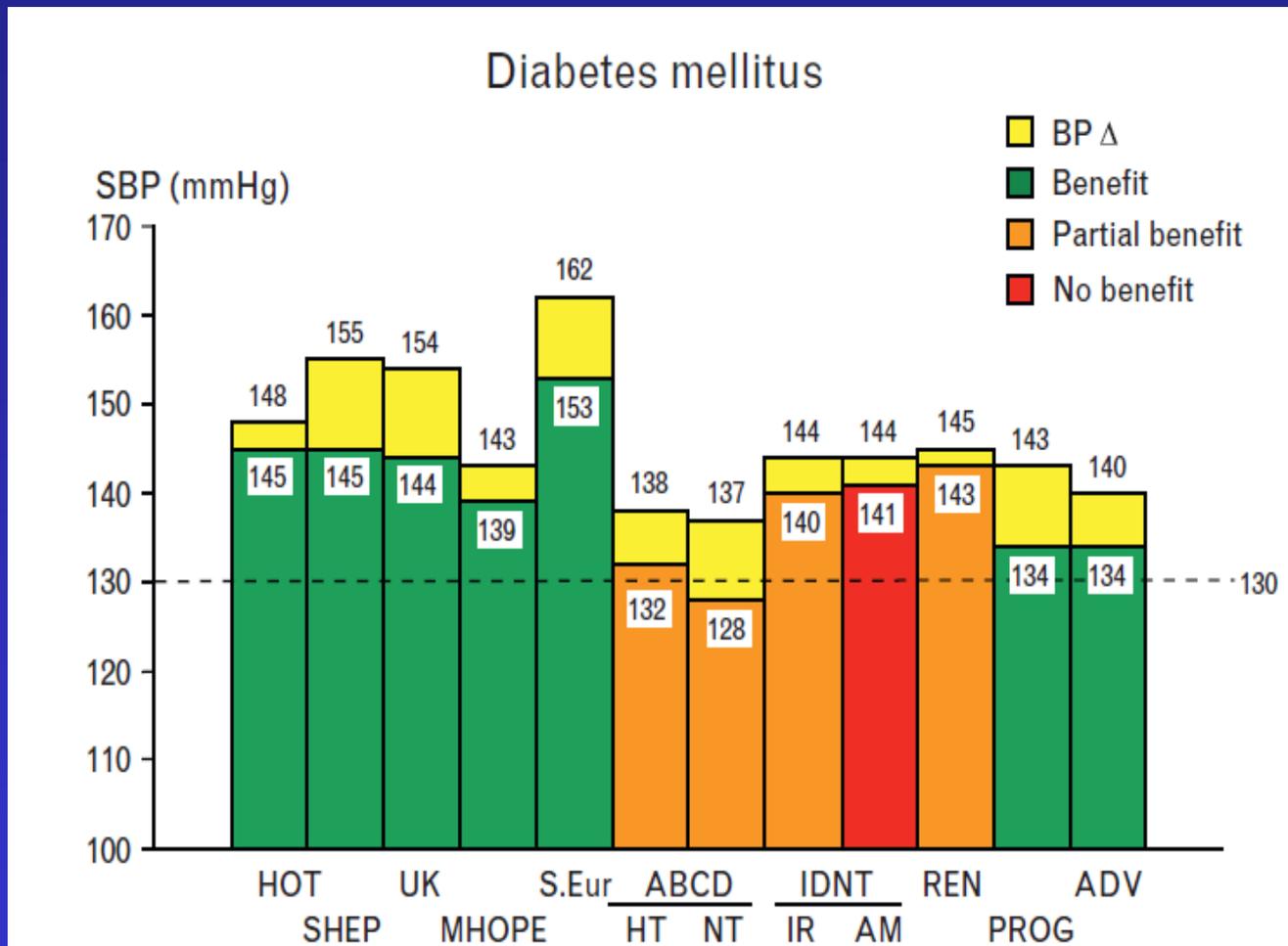
Effects of Thiazide-Type and Thiazide-Like Diuretics on Cardiovascular Events and Mortality

Systematic Review and Meta-Analysis

Olde Engberink RHG et al. Hypertension 2015;65:1033-1040

- Meta regression analysis of 21 studies with > 480,000 patient years
- Thiazide like diuretics associated with 12% additional reduction of CV events($P=0.049$) and 21% additional reduction of heart failure($P=0.023$)
- Thiazide type diuretics did not reduce coronary events or all cause mortality

2009 ESH guidelines



*Abbreviations of trials : M.HOPE; MICROHOPE; ABCD (HT, hypertensives; NT, normotensives); IDNT, IDNT (IR, irbesartan; AM, amlodipine); REN, RENAAL; PROG, PROGRESS; ADV, ADVANCE; ACC, ACCESS; PROF, PROFESS; PREV, PREVENT; EU, EUROPA; ACT, ACTION; CAM, CAMELOT

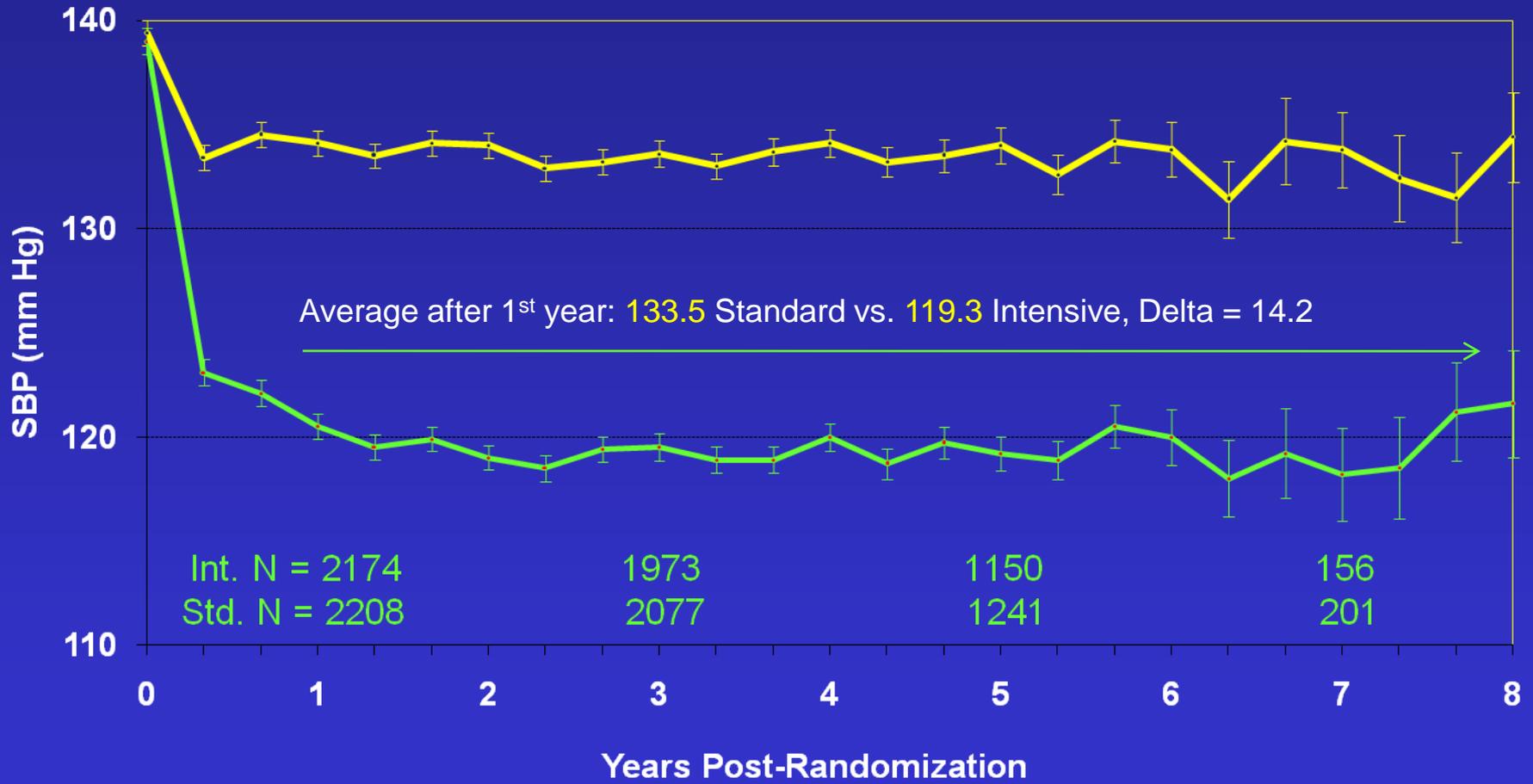
Important differences compared with previous guidelines: DM

- Lowering BP < 130/80mmHg in high-risk patients (diabetes or a history of CV or renal disease) is **not supported by RCT evidence.**
- In diabetes, HOT, UKPDS trials showing benefits from DBP reductions to between 80–85mmHg
 - No trial where SBP was reduced < 130mmHg
 - ‘normotensive’ ABCD study is very small and showed benefit only in secondary endpoint
- **Target BP in diabetes: 140/85(ESC, KSH)**
- **What about JNC VIII?: 140/90**

Systolic Pressures (mean \pm 95% CI)

Mean # Meds

Intensive:	3.2	3.4	3.5	3.4
Standard:	1.9	2.1	2.2	2.3



— Intensive — Standard

ACCORD study group. N Engl J Med 2010

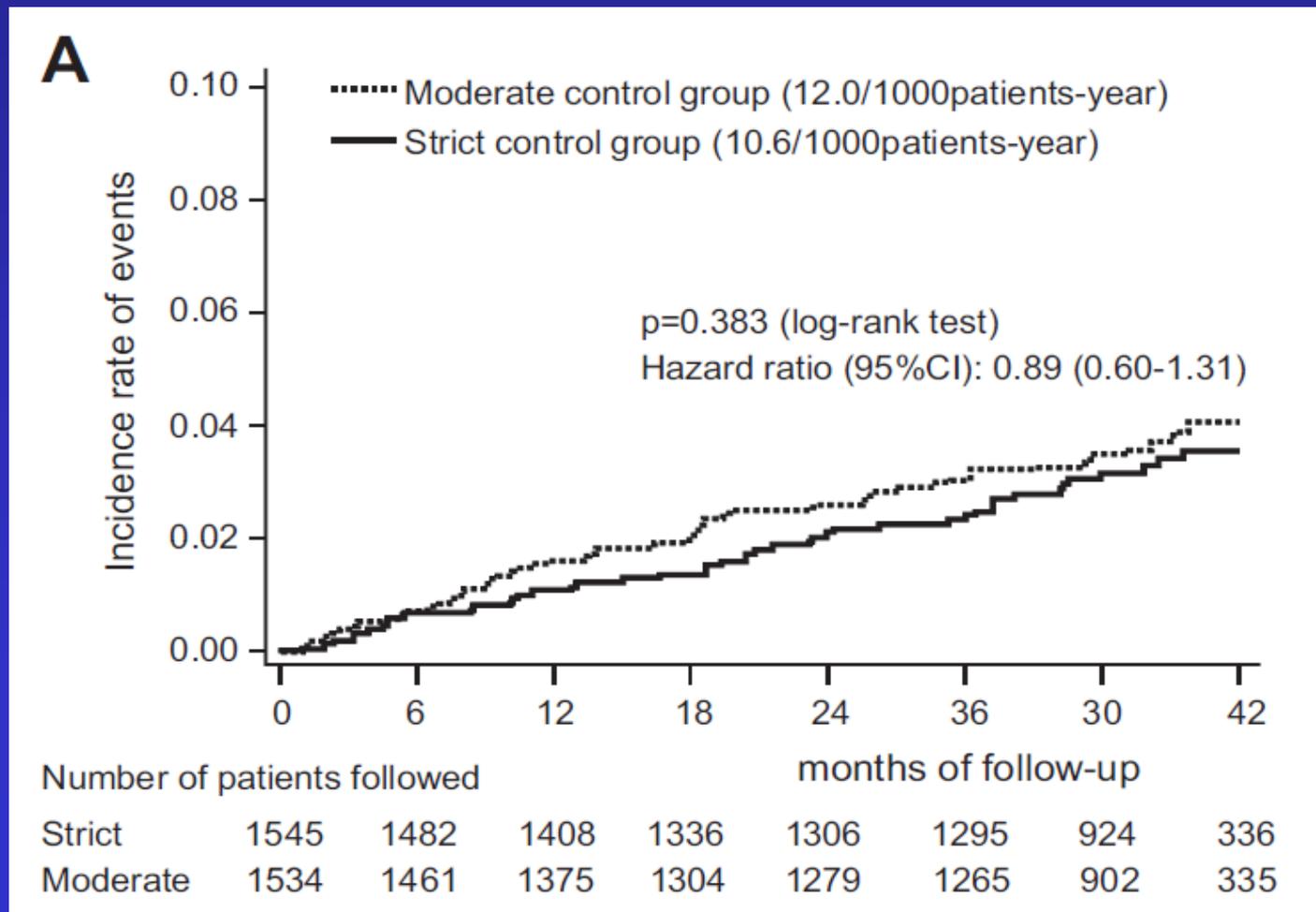
Kidney Disease: Improving Global Outcomes(KDIGO) 2012 guideline for HT management in CKD

Albuminuria	BP target	Preferred agent
< 30 mg/day	$\leq 140/90$ mmHg	None
30-300 mg/day	$\leq 130/80$ mmHg	ACEI or ARB
> 300mg/day	$\leq 130/80$ mmHg	ACEI or ARB

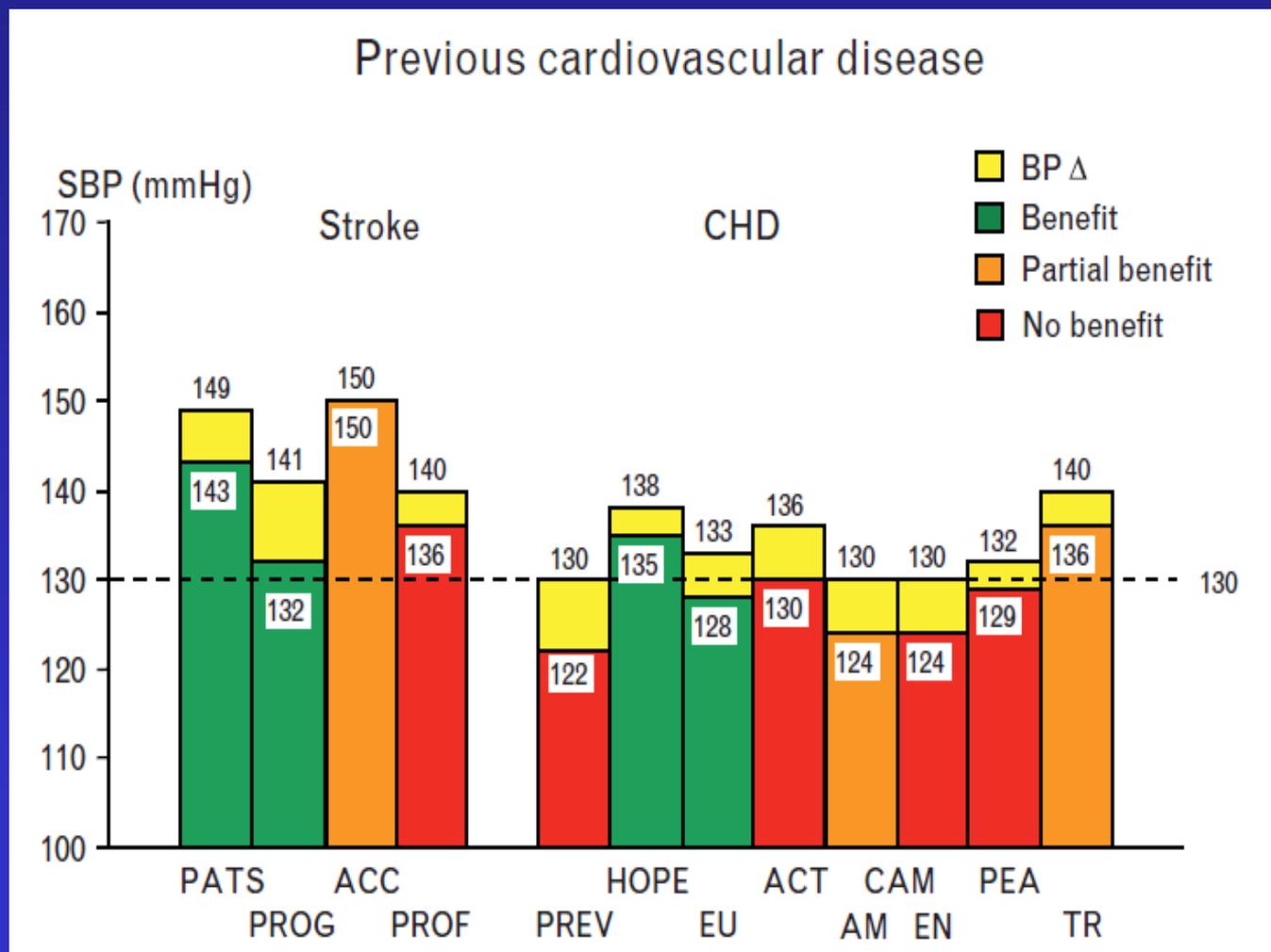
Target Blood Pressure for Treatment of Isolated Systolic Hypertension in the Elderly

Valsartan in Elderly Isolated Systolic Hypertension Study

Ogihara T et al. *Hypertension* 2010;56:196-202



Blood pressure target in subjects with previous CVD



ACCORD Double 2 x 2 Factorial Design

	Lipid		BP		
	Placebo	Fibrate	Intensive	Standard	
Intensive Glycemic Control	1383	1374	1178	1193	5128
Standard Glycemic Control	1370	1391	1184	1178	5123
	2753	2765	2362	2371	10,251
	5518		4733*		

* 94% power for 20% reduction in event rate, assuming standard group rate of 4% / yr and 5.6 yrs follow-up

ACCORD study group. *N Engl J Med* 2010

Reduction in Microalbuminuria as an Integrated Indicator for Renal and Cardiovascular Risk Reduction in Patients With Type 2 Diabetes

Shin-ichi Araki,¹ Masakazu Haneda,² Daisuke Koya,³ Hideki Hidaka,⁴ Toshiro Sugimoto,¹ Motohide Isono,¹ Keiji Isshiki,¹ Masami Chin-Kanasaki,¹ Takashi Uzu,¹ and Atsunori Kashiwagi¹

Diabetes 2007;56:1727-1730

