T. Suithichaiyakul
Cardiomed Chula
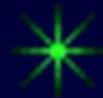
Update 2016

Hypertension Management

The cardiovascular (CV) continuum: role of risk factors

Endothelial Dysfunction

Target Organ Damage

Remodelling

Myocardial infarction & stroke

Ventricular dilation/ cognitive dysfunction

Atherosclerosis and left ventricular hypertrophy

Congestive heart failure/ secondary stroke

Micro-albuminuria

Macro-proteinuria

Endothelial dysfunction

Nephrotic proteinuria

End-stage heart disease, brain damage and dementia

Risk factors*: hypertension, diabetes, obesity, smoking, age

End-stage renal disease

Cardio/ cerebrovascular death

▸ *Intervention at any point along the chain of events may modify cardiovascular disease progression and provide cardioprotection*

*An additive effect of risk factors has been shown in the risk for a CV event

Dzau VJ, et al. Circulation 2006;114:2850–2870; Figure adapted from Dzau V, Braunwald E. Am Heart J 1991;121:1244–1263; Yusuf S, et al. Lancet 2004;364:937–952

High-Normal Blood Pressure and CVD Risk: Framingham Study

High normal 130-139/85-89 mm Hg
Normal 120-129/80-84 mm Hg } Prehypertension
Optimal <120/80 mm Hg

Men

Women

P<.001

P<.001

Cumulative Incidence (%)

Time (years)

Time (years)

Vasan et al. *N Engl J Med.* 2001;345:1291-1297.
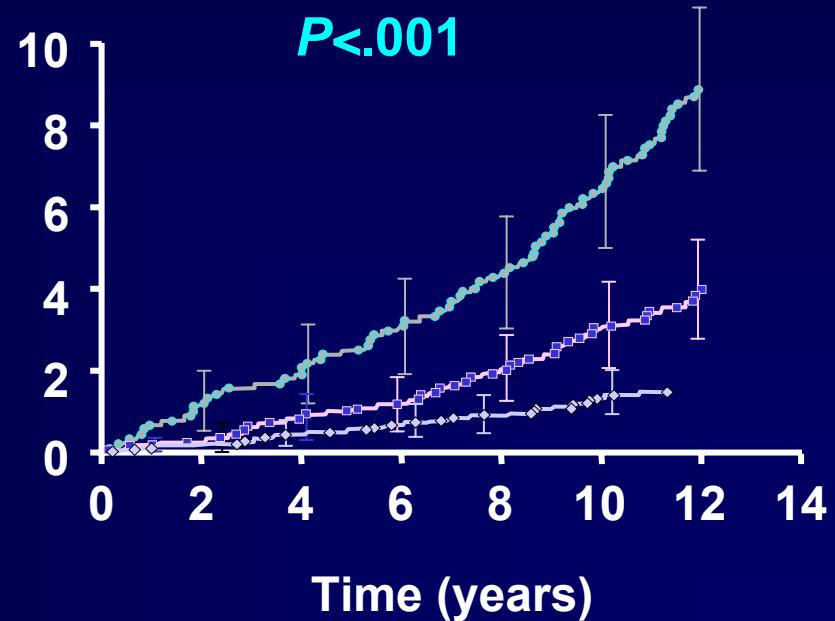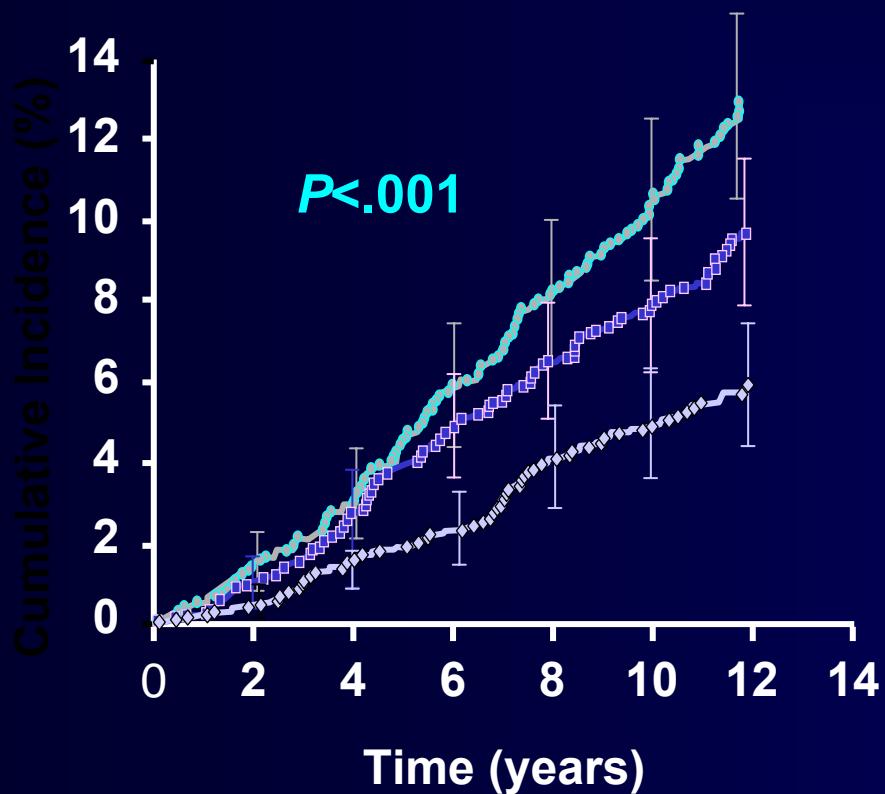
Relationship between systolic BP achieved and decline in kidney function. Summary of Studies on the progression of nephropathy.

Blood Pressure Reduction in Diabetic Kidney Disease
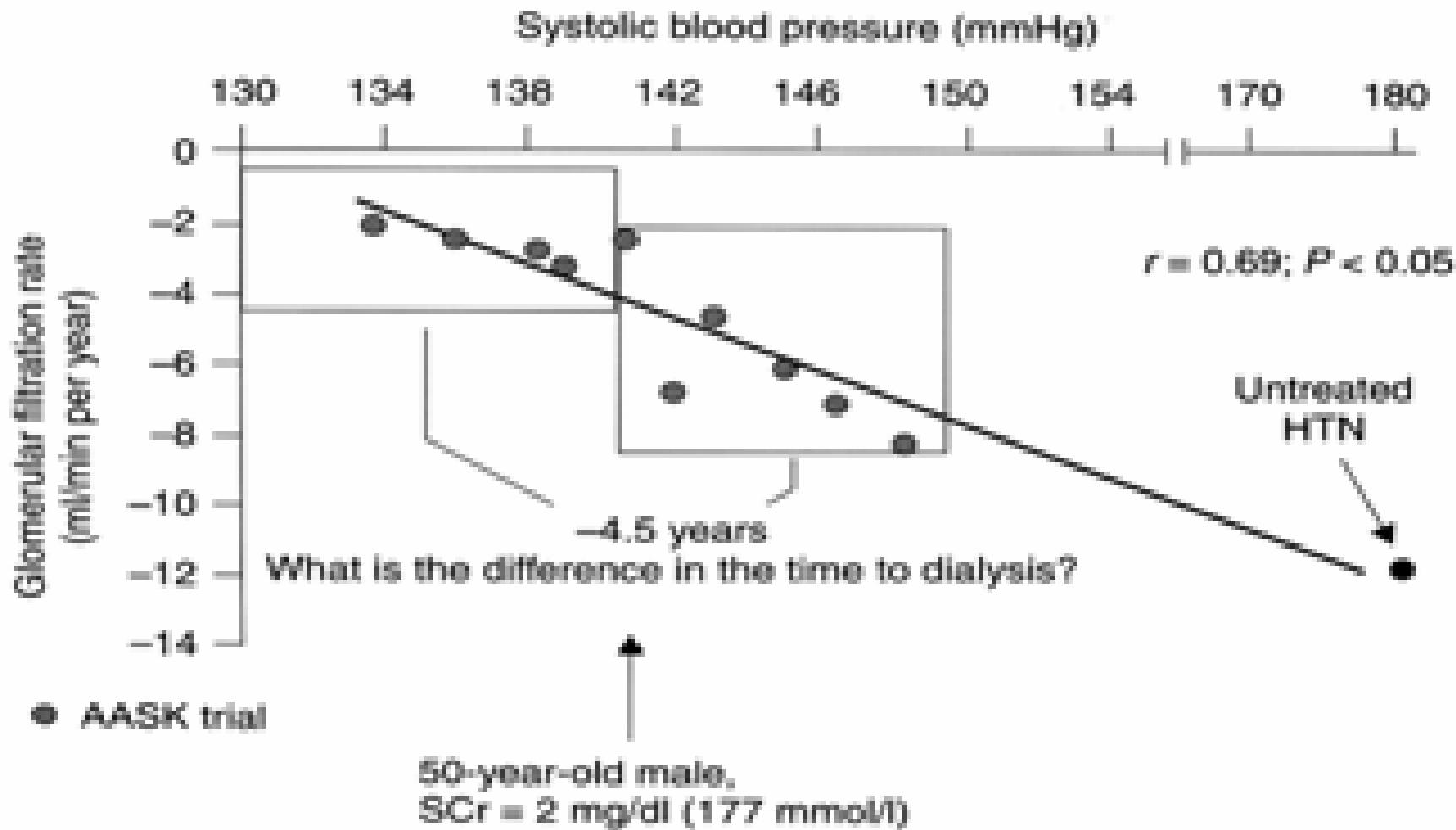
BP as a CV Risk

CV mortality risk doubles with each 20/10 mmHg increment

Age 40–69 years

Lewington et al. Lancet 2002;360:1903–13
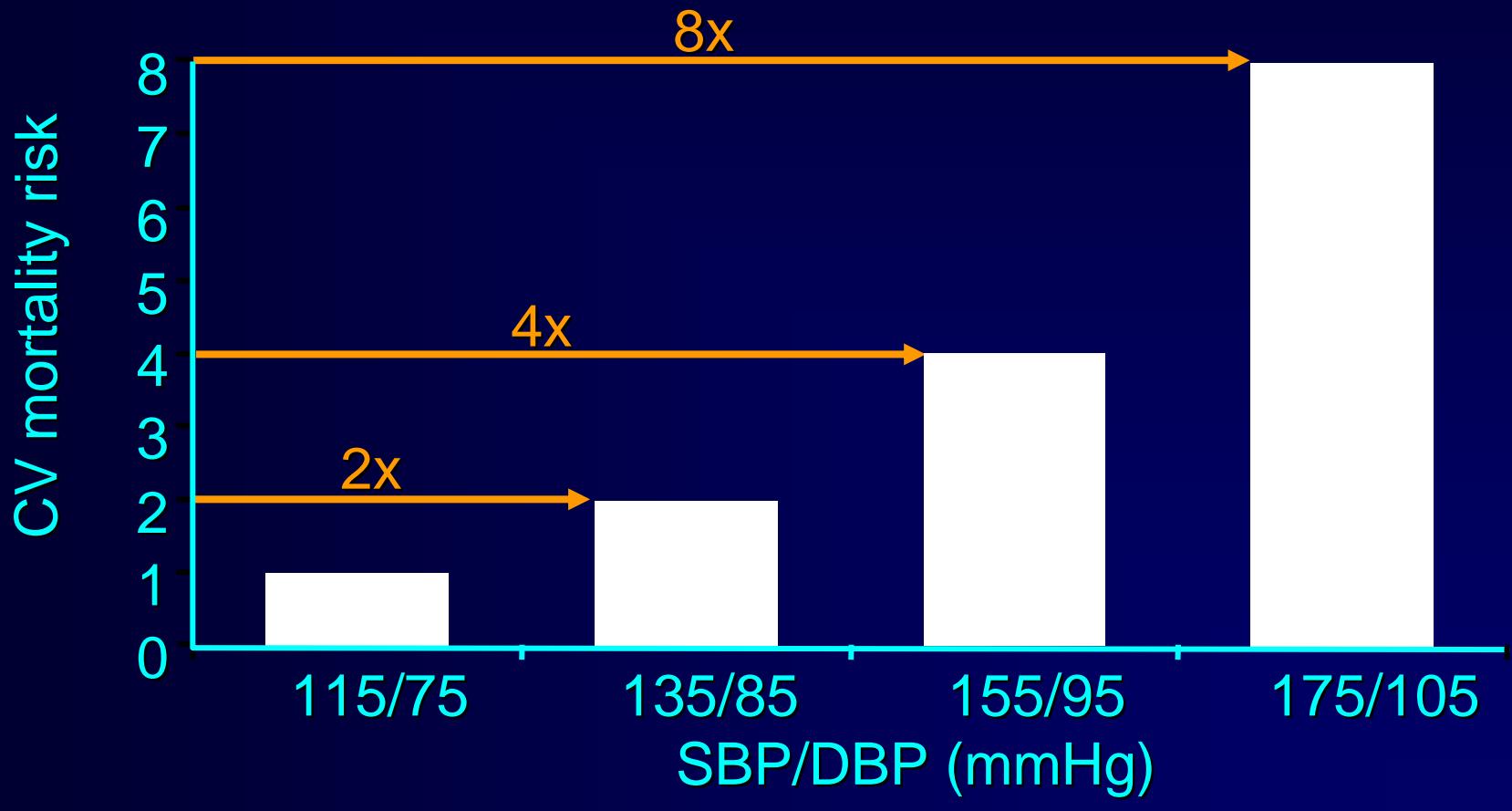
Goals of Therapy

- Reduce CVD and renal morbidity and mortality.

- Treat to BP <140/90 mmHg or BP <130/80 mmHg in patients with diabetes or chronic kidney disease.

- Achieve SBP goal especially in persons >50 years of age.
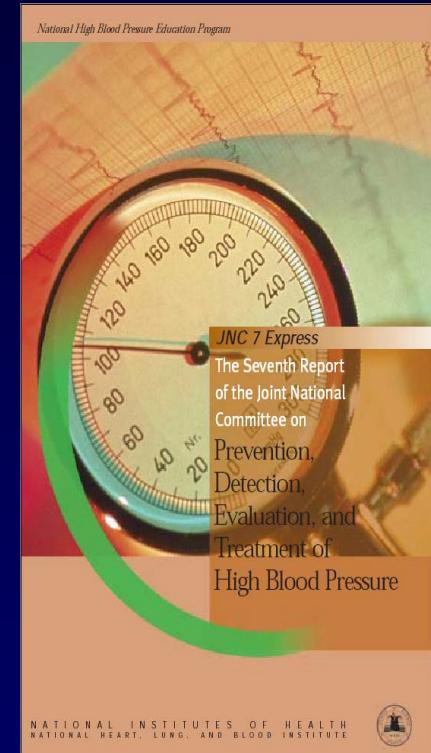
JNC-VII, 2003

Relationship Between SBP Reduction and CV Mortality
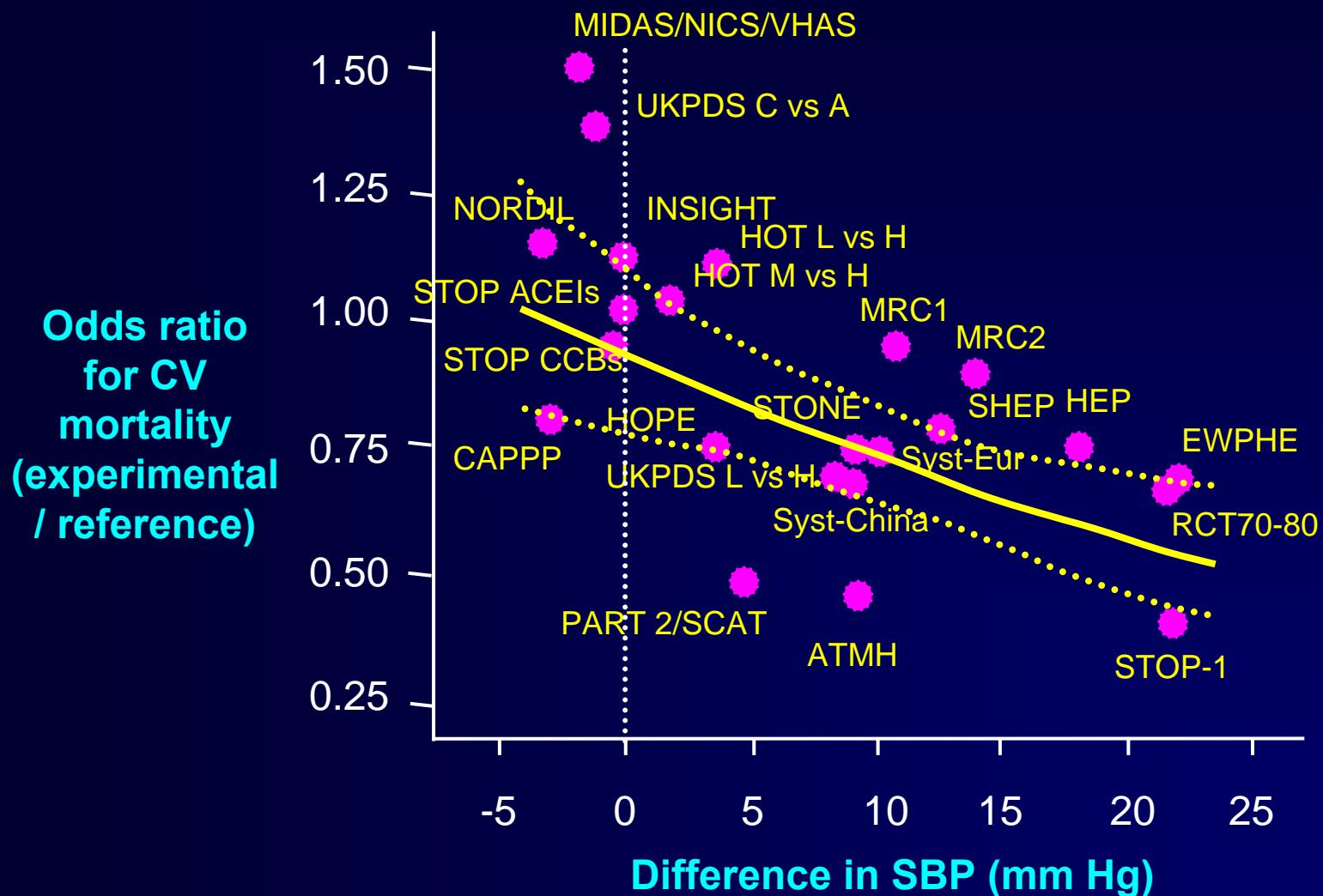

CV, cardiovascular; SBP, systolic blood pressure.
Staessen JA et al. *Lancet*. 2001;358:1305-1315.

Blood Pressure Reduction

- **Meta-analysis of 61 prospective, observational studies**

- **One million adults**

- **12.7 million person-years**

2 mmHg decrease in mean systolic blood pressure
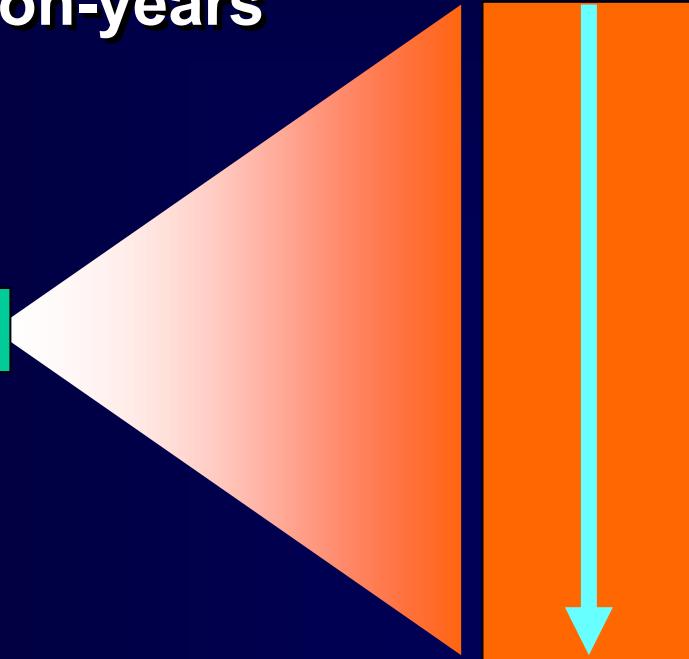
7% reduction in risk of ischemic heart disease mortality

10% reduction in risk of stroke mortality

1. Lewington S et al. Lancet. 2002;360:1903–1913.

Hypertension guidelines
Target BP

Guidelines	Target BP
BHS IV 2004[1]	≤140/85mmHg ≤130/80mmHg in patients with diabetes
ESC/ESH 2003[2] ESC/ESH 2007	≤140/90mmHg ≤130/80mmHg in patients with diabetes ≤130/80mmHg in DM, stroke, MI, Renal dysfunction, Proteinuria
JNC VII 2003[3]	≤140/90mmHg ≤130/80mmHg in patients with diabetes or renal disease
WHO/ISH 1999[4]	≤140/90mmHg ≤130/85mmHg in patients with diabetes

1. Williams B, et al. J Human Hypertens 2004;18:139–85.
2. ESC/ESH. J Hypertens 2003;21:1011–53.
3. Chobanian AV, et al. JAMA 2003;289:2560–72.
4. WHO/ISH. J Hypertens 1999;17:151–83.

Thai Hypertension Guideline

3.3 ระดับความดันโลหิตเป้าหมาย

3.3.1 BP < 140/90 มม.ปรอท ในผู้ป่วยทั่วไป (น้ำหนัก ++/คุณภาพหลักฐาน I)

3.3.2 BP < 130/80 มม.ปรอท ในผู้ป่วยอายุน้อย (น้ำหนัก +/คุณภาพหลักฐาน II)

3.3.3 BP 130-139/80-85 มม.ปรอท ในผู้ป่วยโรคเบาหวาน (น้ำหนัก +/คุณภาพหลักฐาน II)

3.3.4 BP < 130/80 มม.ปรอท ในผู้ป่วยโรคไตเรื้อรัง หาก proteinuria < 1 กรัม/วัน (น้ำหนัก ++/คุณภาพหลักฐาน I) และ < 125/75 มม.ปรอท หาก proteinuria > 1 กรัม/วัน (น้ำหนัก ±/คุณภาพหลักฐาน II)

3.3.5 BP < 130/80 มม.ปรอท ในผู้ป่วยที่มีความเสี่ยงในการเกิด CVD สูง เช่น เกิด CVD แล้ว (น้ำหนัก +/คุณภาพหลักฐาน II)

ORIGINAL ARTICLE

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

The ACCORD Study Group*

METHODS

A total of 4733 participants with type 2 diabetes were randomly assigned to intensive therapy, targeting a systolic pressure of less than 120 mm Hg, or standard therapy, targeting a systolic pressure of less than 140 mm Hg. The primary composite outcome was nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes. The mean follow-up was 4.7 years.
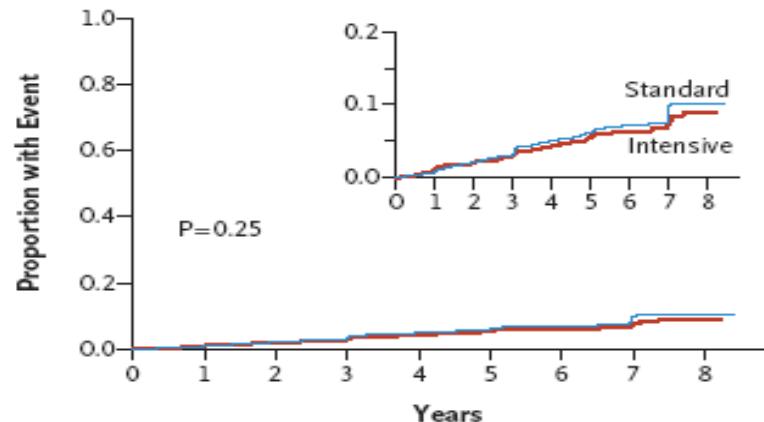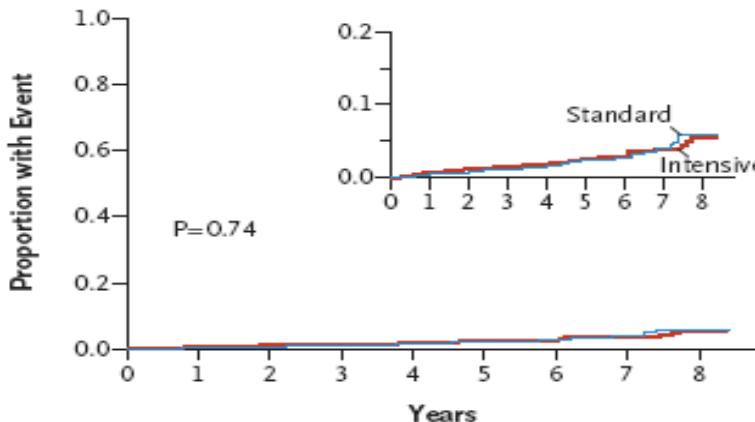
BP Achievement

139.2/76 mmHg

133.5/70.5 mmHg

119.3/64.4 mmHg

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

Results

AstraZeneca
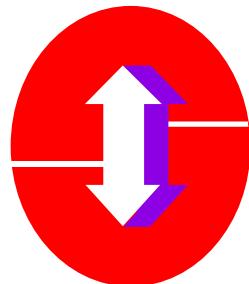
**Hypertension
Optimal
Treatment**
International Study

HOT

Study results

HOT study

HOT Study: Estimated incidence of CV events in relation to BP

82.5 mmHg — Major CV events/1000 pt yrs — 138.5 mmHg

All MI/1000 pt yrs — 142.2 mmHg

All stroke/1000 pt yrs — 142.2 mmHg

CV mortality/1000 pt yrs — 130.0 mmHg

86.5 mmHg

Mean SBP   Mean DBP

Lancet 1998;351:1755-62
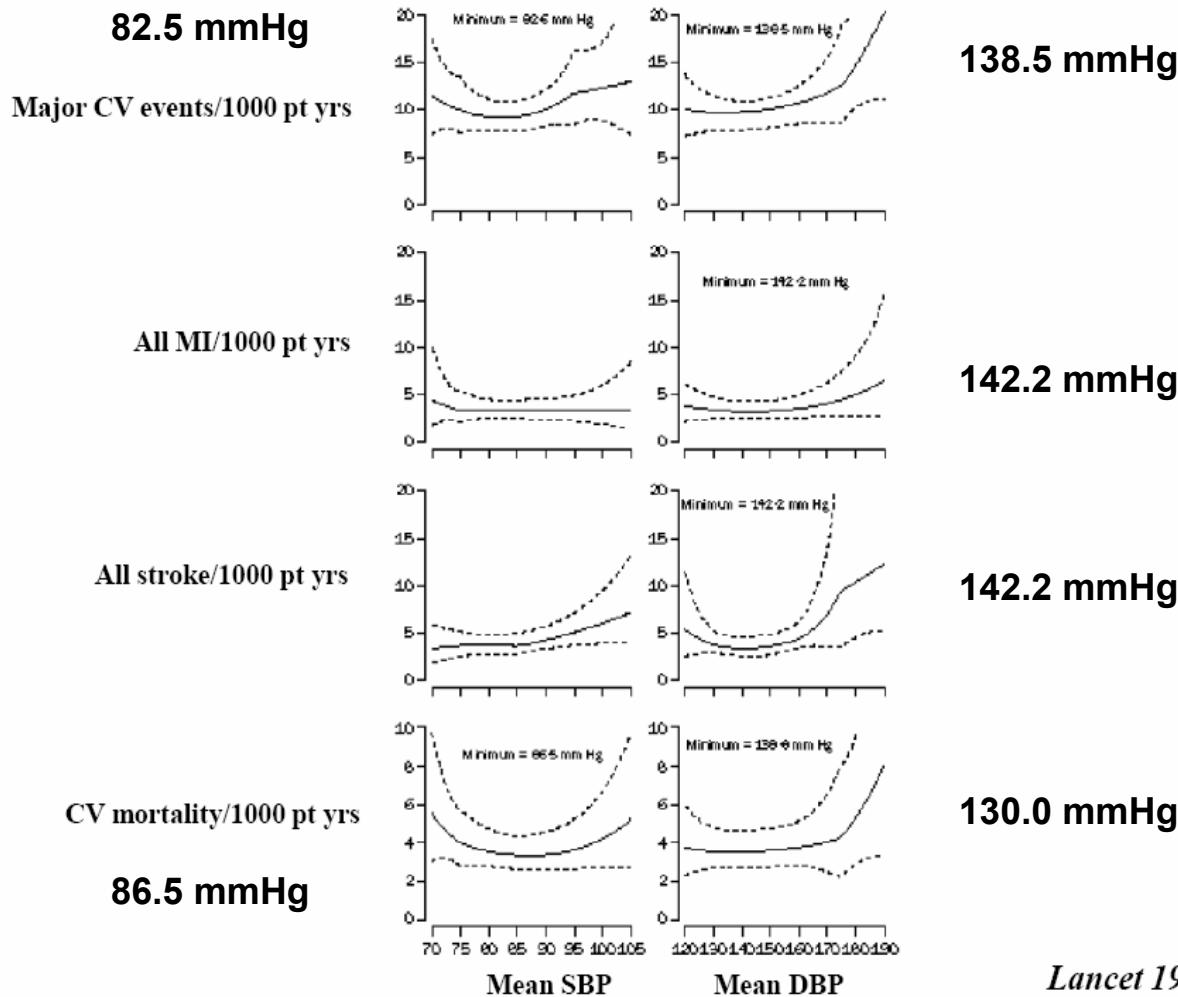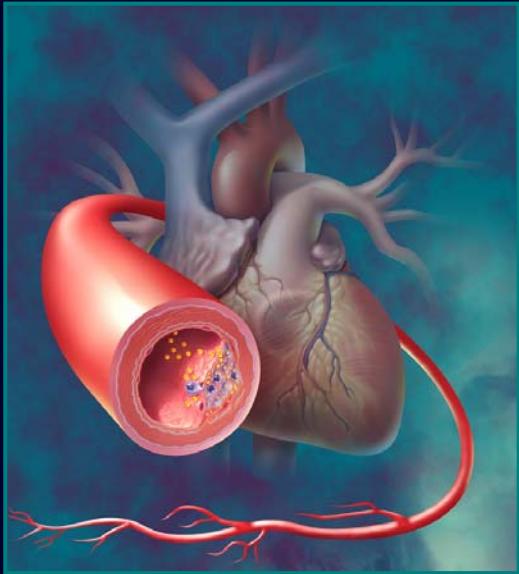
VALUE

Valsartan Antihypertensive Long-Term Use Evaluation

Julius S et al. Lancet. June 2004;363:2022–31.

Risk of Primary Event and DBP
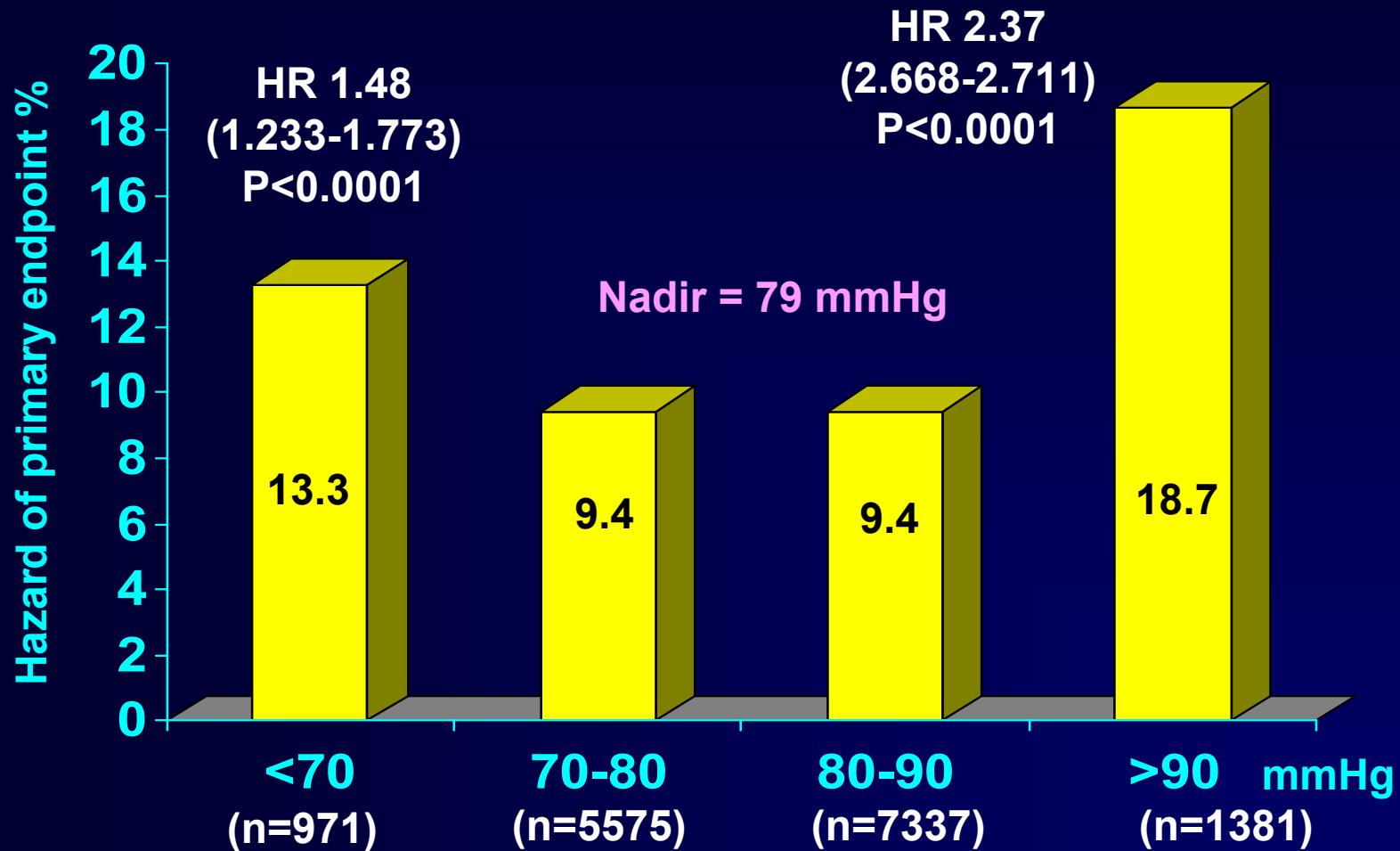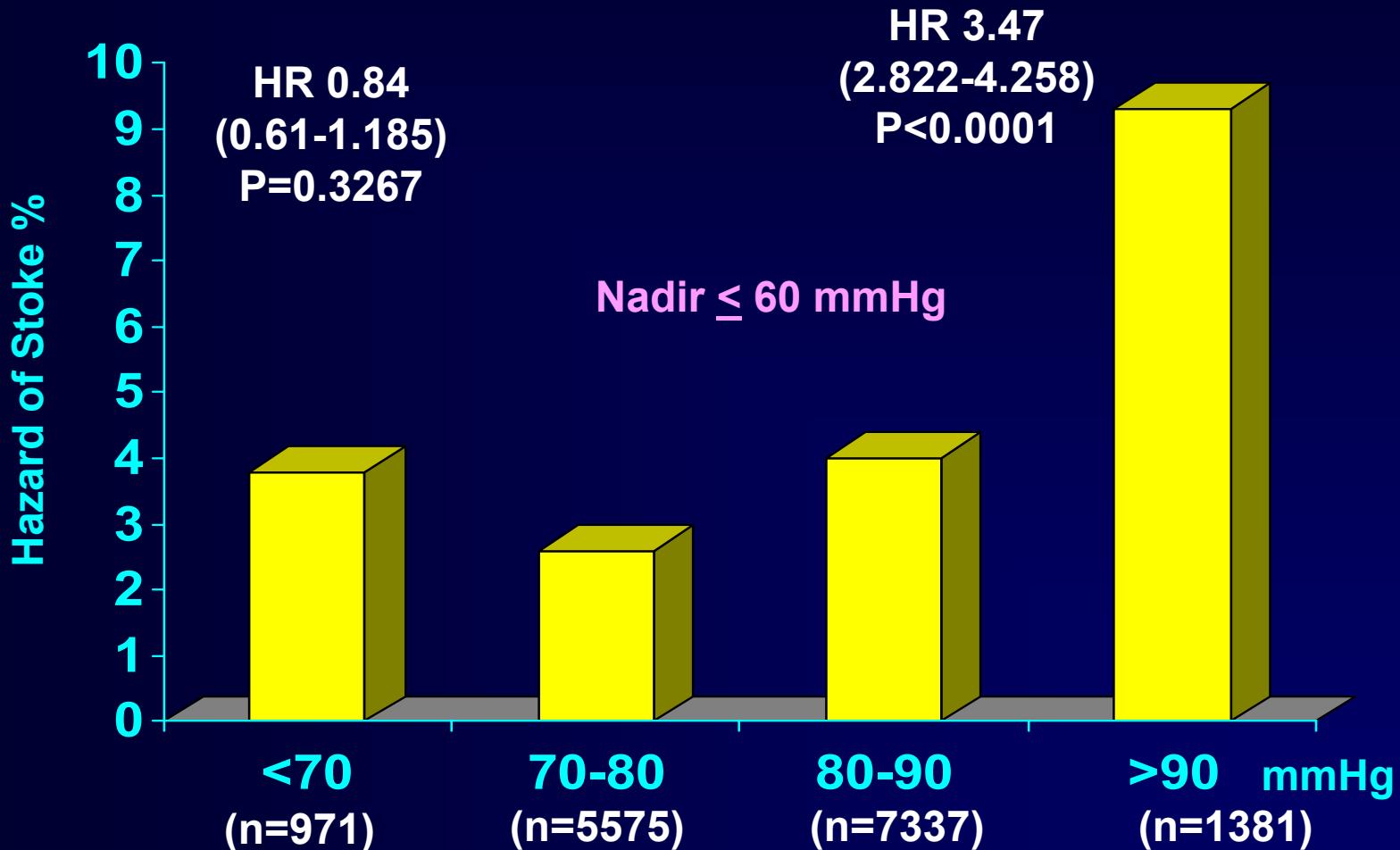
J-curve revisited: an analysis of blood pressure and cardiovascular events in the Treating to New Targets (TNT) trial[†]

Sripal Bangalore[1], Franz H. Messerli[2*], Chuan-Chuan Wun[3], Andrea L. Zuckerman[3], David DeMicco[3], John B. Kostis[4], John C. LaRosa[5], and Treating to New Targets Steering Committee and Investigators

Non Fatal MI and Fatal CAD
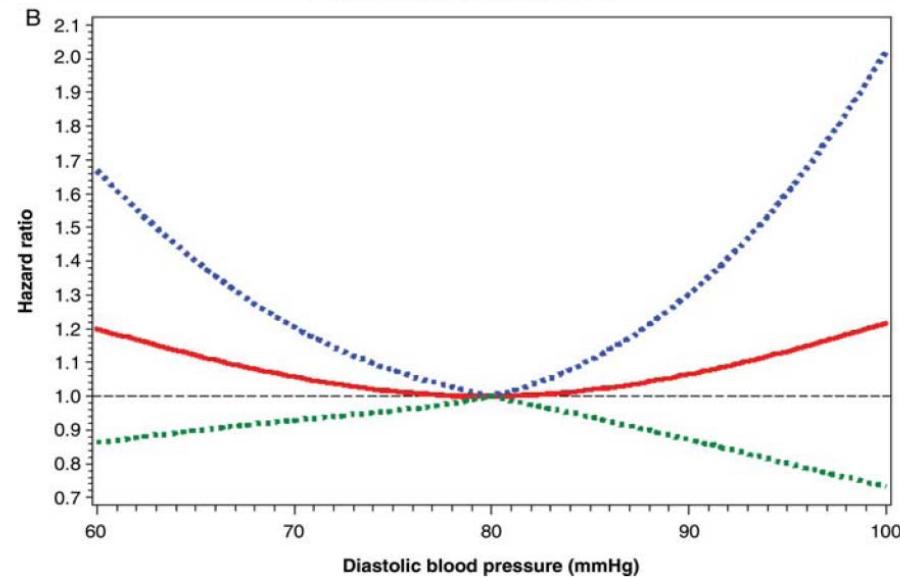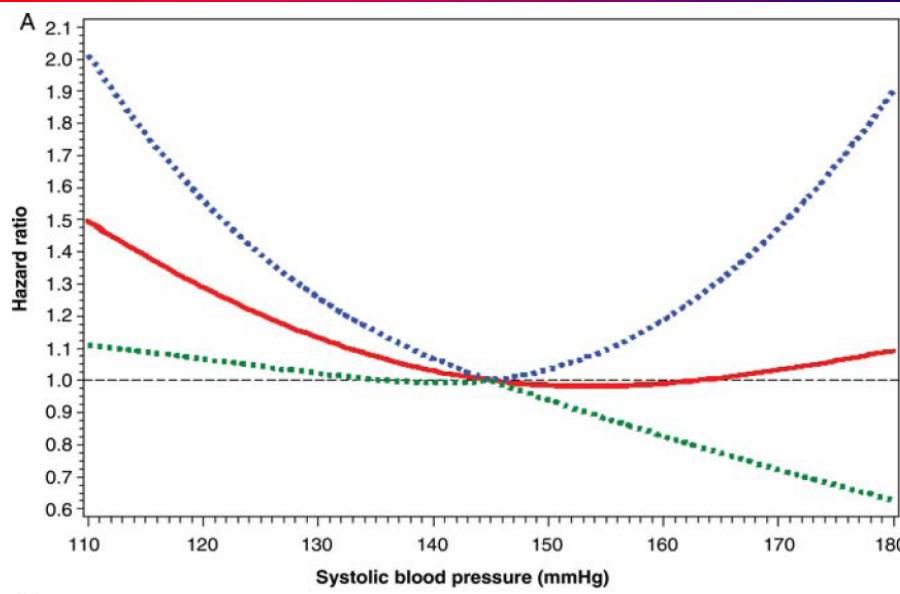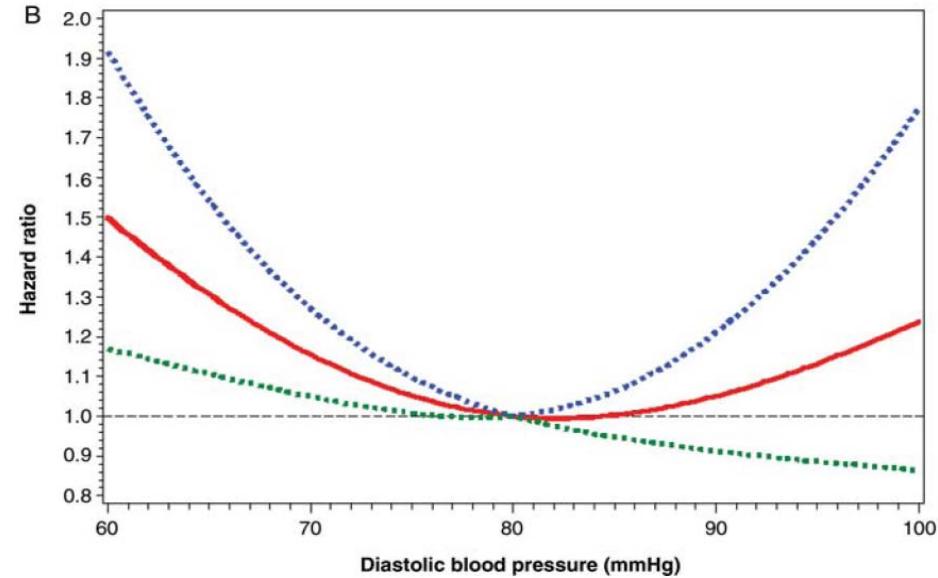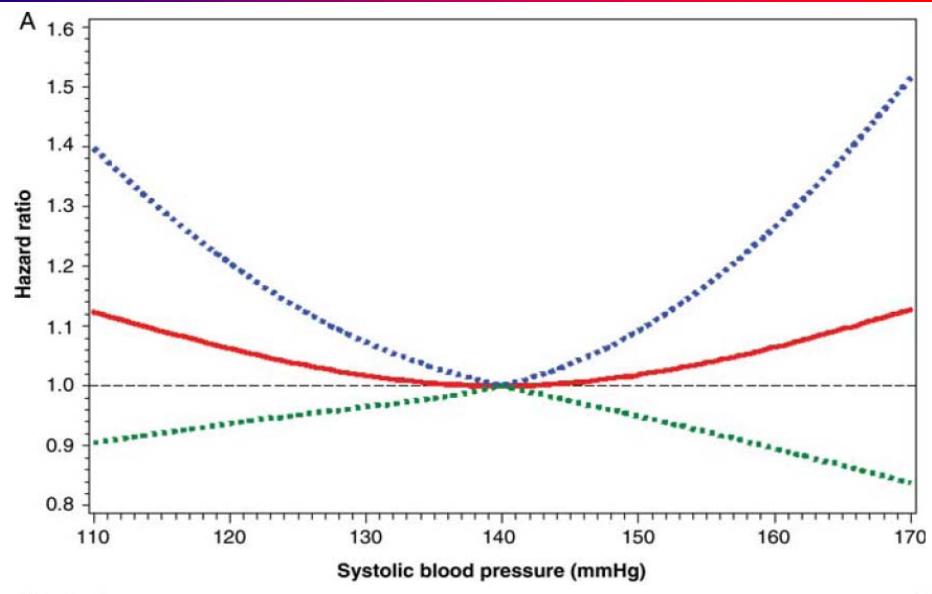
ONTARGET

Adjusted risk of outcome events by deciles of achieved systolic blood pressure
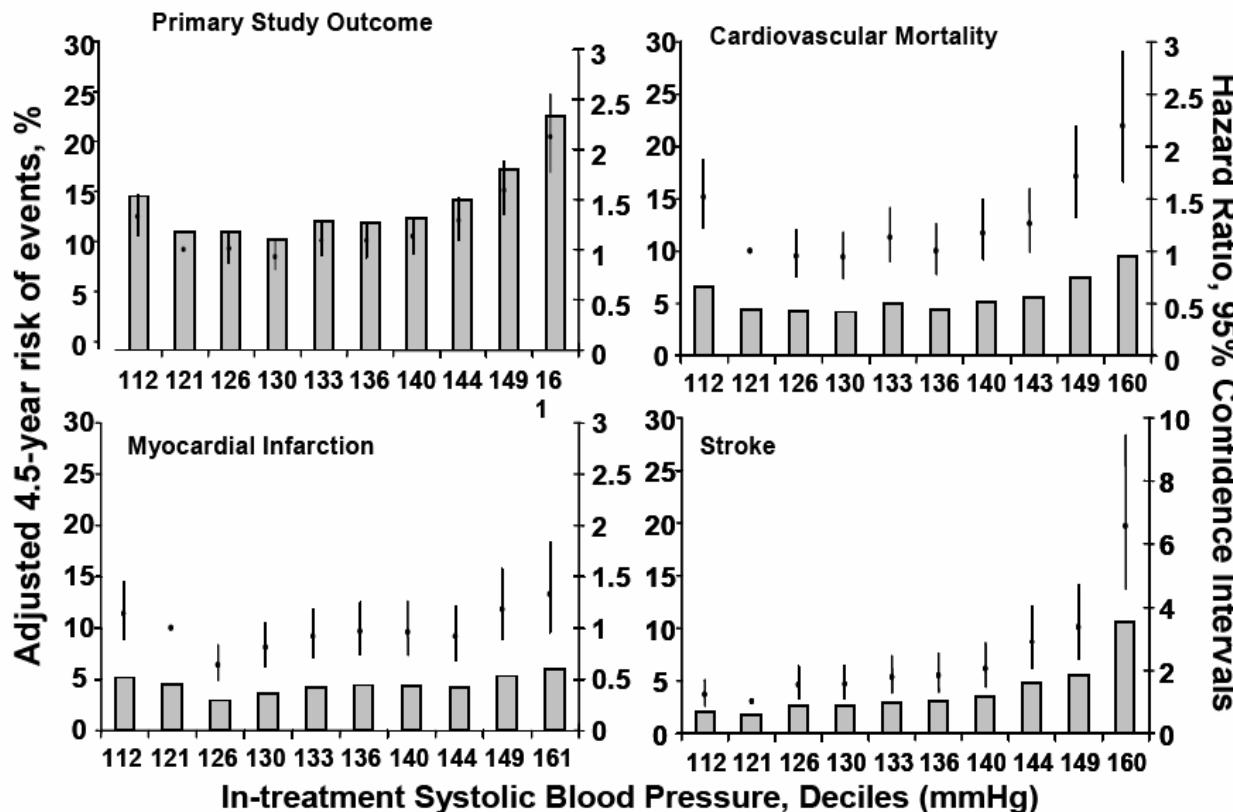
2013 ESH/ESC Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

Authors/Task Force Members: Giuseppe Mancia (Chairperson) (Italy)*, Robert Fagard (Chairperson) (Belgium)*, Krzysztof Narkiewicz (Section co-ordinator) (Poland),

Blood pressure goals in hypertensive patients*

Recommendations	Class	Level
A systolic BP goal of <140 mmHg:		
a) is recommended in patients at low-moderate CV risk,	I	B
b) is recommended in patients with diabetes,	I	A
c) should be considered in patients with previous stroke or TIA,	IIa	B
d) should be considered in patients with coronary heart disease,	IIa	B
e) should be considered in patients with diabetic or non-diabetic chronic kidney disease.	IIa	B
A diastolic BP 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

*See dedicated section for recommendations in special conditions and populations

ESH European Society of Hypertension

EUROPEAN SOCIETY OF CARDIOLOGY®

Elderly

Recommendations	Class	Level
In elderly hypertensives with SBP ≥160 mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A
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
In frail elderly patients, it is recommended to leave decisions on anti-hypertensive therapy to the treating physician, and based on monitoring of the clinical effects of treatment.	I	C
Continuation of well-tolerated antihypertensive treatment should be considered when a treated individual becomes octogenarian.	IIa	C
All hypertensive agents are recommended and can be used in the elderly, although diuretics and calcium antagonists may be preferred in isolated systolic hypertension.	I	A

ESH European Society of Hypertension

EUROPEAN SOCIETY OF CARDIOLOGY®

The HYpertension in the Very Elderly Trial

N. Beckett, R. Peters, A. Fletcher, C. Bulpitt on behalf of the HYVET committees and investigators

HYVET

- Results
  - Mean BP at the end of the trial
    - **Indapamide +/- perindopril - 143/78 mm Hg**
    - **Placebo – 158/84 mm Hg**
  - 48.0% of indapamide patients achieved goal BP vs. 19.9% of placebo patients (p<0.001)
  - Outcomes with indapamide +/- perindopril
    - **30% reduction in stroke (p=0.06)**
    - **64% reduction in heart failure (p<0.001)**
    - **21% reduction in all-cause mortality (p=0.02)**

Beckett NS et al. *N Engl J Med* 2008;358:1887-98.

Per-Protocol

	HR	95% CI	P
All stroke	**- 34%**	**0.46 - 0.95**	**0.025**
Total mortality	**- 28%**	**0.59 - 0.88**	**0.001**
Fatal stroke	**- 45%**	**0.33 - 0.93**	**0.021**
Cardiovascular mortality	**-27%**	**0.55-0.97**	**0.029**
Heart failure	**-72%**	**0.17-0.48**	**<0.001**
Cardiovascular events	**- 37%**	**0.51-0.71**	**<0.001**

Target BP

Blood pressure goals in hypertensive patients

Recommendations	Class[a]	Level[b]	Ref.[c]
A SBP goal <140 mmHg:			
a) is recommended in patients at low–moderate CV risk;	I	B	266, 269, 270
b) is recommended in patients with diabetes;	I	A	270, 275, 276
c) should be considered in patients with previous stroke or TIA;	IIa	B	296, 297
d) should be considered in patients with CHD;	IIa	B	141, 265
e) should be considered in patients with diabetic or non-diabetic CKD.	IIa	B	312, 313
In elderly hypertensives less than 80 years old with SBP ≥160 mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A	265
In fit elderly patients less than 80 years old SBP values <140 mmHg may be considered, whereas in the fragile elderly population SBP goals should be adapted to individual tolerability.	IIb	C	-
In individuals older than 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	287
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	269, 290, 293

CHD = coronary heart disease; CKD = chronic kidney disease; CV = cardiovascular; DBP = diastolic blood pressure; SBP = systolic blood pressure; TIA = transient ischaemic attack.

[a]Class of recommendation.

[b]Level of evidence.

[c]Reference(s) supporting levels of evidence.

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

Recommendations (1/3)

	BP thresholds	Goals
✓ **_Recommendation_ 1** *(Strong recommendation)* General population **≥60 years**	SBP **≥150 mm Hg** or DBP **≥90 mm Hg**	SBP **<150 mm Hg** and DBP **<90 mm Hg**
✓ **_Recommendation_ 2** *(Strong recommendation)* General population **<60 years**	DBP **≥90 mm Hg**	DBP **<90 mm Hg**
Recommendation 3 *(Expert opinion)* General population **<60 years**	SBP **≥140 mm Hg**	SBP **<140 mm Hg**

2015 Thai Guideline
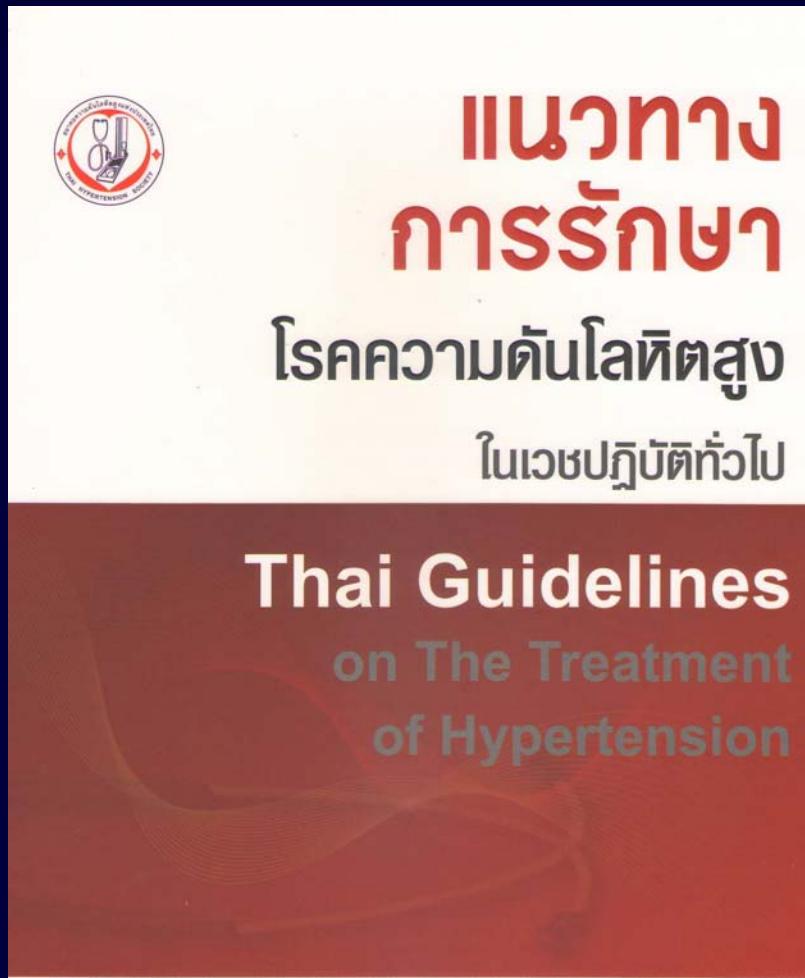
Target BP

3.3 ระดับความดันโลหิตเป้าหมาย

3.3.1 ความดันโลหิต < 140/90 มม.ปรอท ในผู้ป่วยทั่วไป (น้ำหนัก ++/คุณภาพหลักฐาน I)

3.3.2 ความดันโลหิต < 140-150/90 มม.ปรอท ในผู้ป่วยที่อายุมากกว่า 60 ปี แต่น้อยกว่า 80 ปี (น้ำหนัก ++/คุณภาพหลักฐาน I)

3.3.3 ความดันโลหิต < 150/90 มม.ปรอท ในผู้ป่วยที่อายุ ≥ 80 ปี (น้ำหนัก ++/คุณภาพหลักฐาน I)

3.3.4 ความดันโลหิต < 130/80 มม.ปรอท ในผู้ป่วยอายุ < 50 ปี (น้ำหนัก +/คุณภาพหลักฐาน IV)

3.3.5 ความดันโลหิต < 140/90 มม.ปรอท ในผู้ป่วยโรคเบาหวาน (น้ำหนัก ++/คุณภาพหลักฐาน I)

3.3.6 ความดันโลหิต < 140/90 มม.ปรอท ในผู้ป่วย CKD ที่ไม่มี albuminuria และโรคไตเรื้อรังที่มี albuminuria น้อยกว่า 30 มก.ต่อวัน (น้ำหนัก ++/คุณภาพหลักฐาน II)

3.3.7 ความดันโลหิต < 130/80 มม.ปรอท ในผู้ป่วย CKD ที่มี albuminuria ตั้งแต่ 30 มก.ต่อวันขึ้นไป (น้ำหนัก +/คุณภาพหลักฐาน III)

3.3.8 ความดันโลหิต < 140/90 มม.ปรอท ในผู้ป่วยที่เคยเป็น CVD แล้ว (น้ำหนัก +/คุณภาพหลักฐาน II)

SPRINT Research Question

> **Examine effect of more intensive high blood pressure treatment than is currently recommended**

↓

**Randomized Controlled Trial
Target Systolic BP**
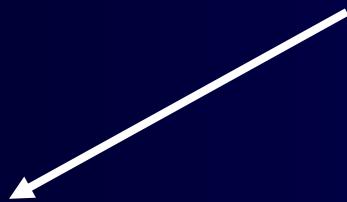
**Intensive Treatment
Goal SBP < 120 mm Hg**
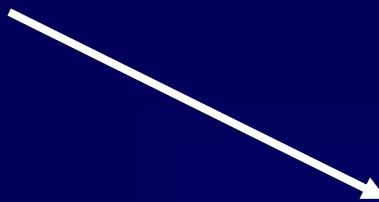
**Standard Treatment
Goal SBP < 140 mm Hg**

Demographic and Baseline Characteristics

	Total N=9361	Intensive N=4678	Standard N=4683
Mean (SD) age, years	67.9 (9.4)	67.9 (9.4)	67.9 (9.5)
% ≥75 years	28.2%	28.2%	28.2%
Female, %	35.6%	36.0%	35.2%
White, %	57.7%	57.7%	57.7%
African-American, %	29.9%	29.5%	30.4%
Hispanic, %	10.5%	10.8%	10.3%
Prior CVD, %	20.1%	20.1%	20.0%
Mean 10-year Framingham CVD risk, %	20.1%	20.1%	20.1%
Taking antihypertensive meds, %	90.6%	90.8%	90.4%
Mean (SD) number of antihypertensive meds	1.8 (1.0)	1.8 (1.0)	1.8 (1.0)
Mean (SD) Baseline BP, mm Hg			
Systolic	139.7	139.7	139.7 (15.4)
Diastolic	78.1 (11.9)	78.2 (11.9)	78.0 (12.0)

Selected Baseline Laboratory Characteristics

	Total N=9361	Intensive N=4678	Standard N=4683
Mean (SD) eGFR, mL/min/1.73 m^2	71.7 (20.6)	71.8 (20.7)	71.7 (20.5)
% with eGFR<60 mL/min/1.73m^2	28.3	28.4	28.1
Mean (SD) Urine albumin/creatinine, mg/g	42.6 (166.3)	44.1 (178.7)	41.1 (152.9)
Mean (SD) Total cholesterol, mg/dL	190.1 (41.2)	190.2 (41.4)	190.0 (40.9)
Mean (SD) Fasting plasma glucose, mg/dL	98.8 (13.5)	98.8 (13.7)	98.8 (13.4)

Primary Outcome and Primary Hypothesis

- ## Primary outcome
  - CVD composite: first occurrence of
    - MI
    - ACS (non-MI ACS)
    - Stroke
    - Acute decompensated HF
    - CVD

- ## Primary hypothesis*
    - CVD composite event rate lower in intensive compared to standard treatment

Expected 4-6 yrs of follow-up (actual 3.76 yrs.)

Systolic BP During Follow-up

Year 1

Mean SBP
136.2 mm Hg

Standard

Mean SBP
121.4 mm Hg

Intensive

1.9	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9	Std Classes
2.3	2.7	2.8	2.8	2.8	2.8	2.8	2.8	2.8	3.0	Int Classes

| 0 | | 1 | | 2 | Years | 3 | | 4 | | 5 |

| 4683 | 4345 | 4222 | 4092 | 3997 | 3904 | 3115 | 1974 | 1000 | 274 | Standard N |
| 4678 | 4375 | 4231 | 4091 | 4029 | 3920 | 3204 | 2035 | 1048 | 286 | Intensive N |
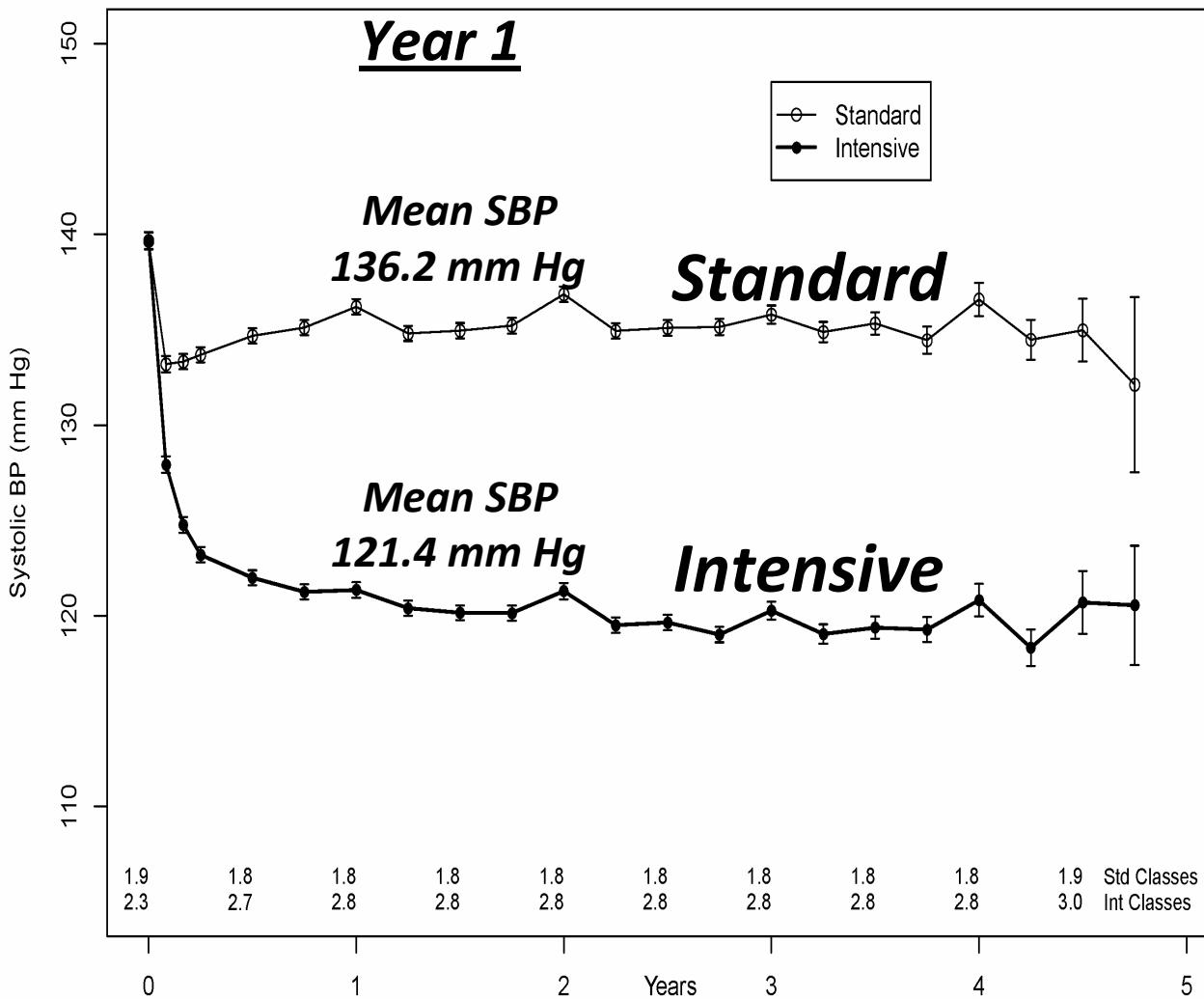
Average SBP
(During Follow-up)

Standard: 134.6 mm Hg

Intensive: 121.5 mm Hg

Average number of antihypertensive medications

Number of participants

SPRINT Primary Outcome Cumulative Hazard

Hazard Ratio = 0.75 (95% CI: 0.64 to 0.89)

Standard
(319 events)

Intensive
(243 events)

During Trial (median follow-up = 3.26 yrs)
Number Needed to Treat (NNT)
to prevent a primary outcome = 61

	0	1	2	3	4	5
Std	4683	4437	4228	2829	721	
Int	4678	4436	4256	2900	779	
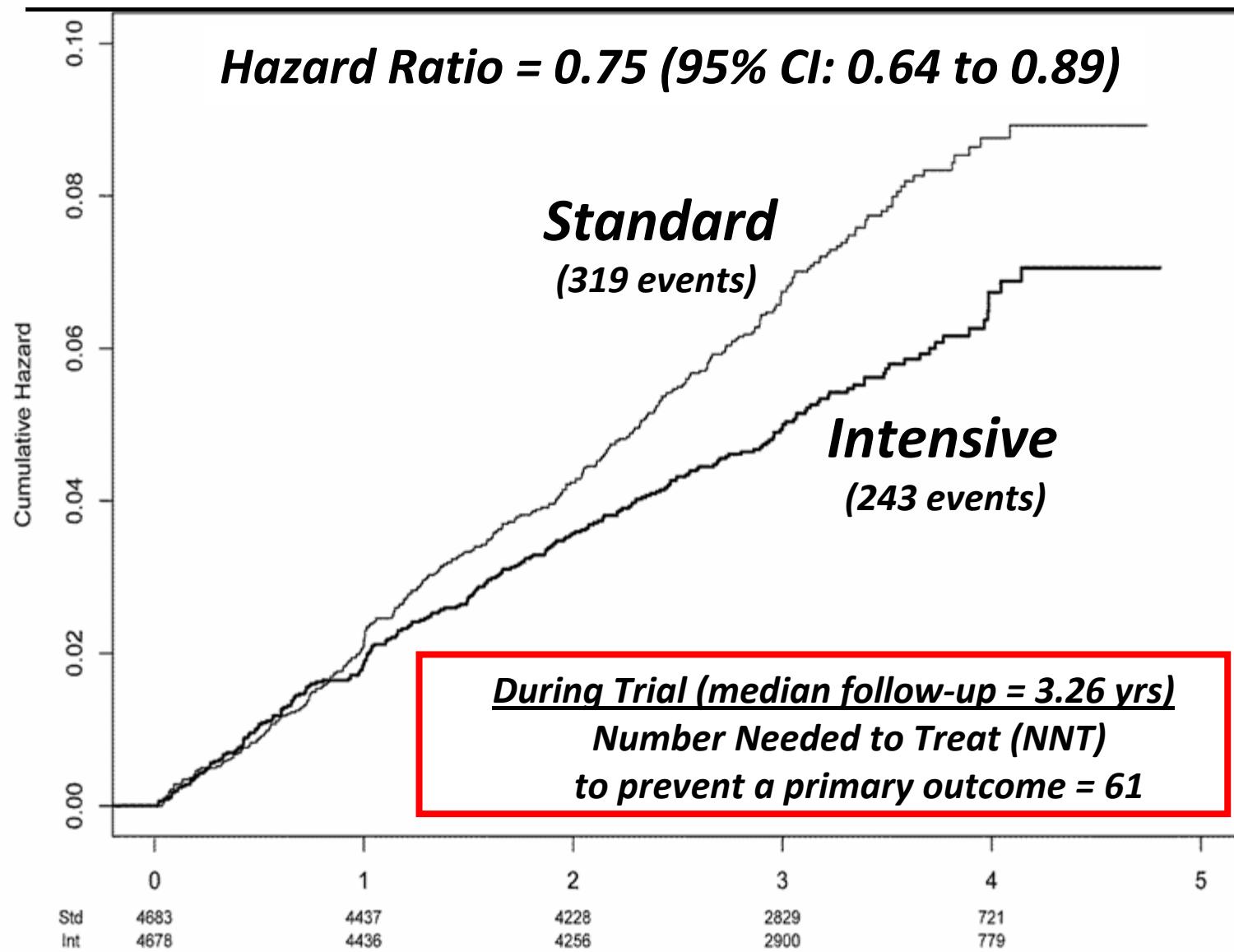
SPRINT Primary Outcome and its Components Event Rates and Hazard Ratios

	Intensive		Standard			
	No. of Events	Rate, %/year	No. of Events	Rate, %/year	HR (95% CI)	P value
Primary Outcome	243	1.65	319	2.19	0.75 (0.64, 0.89)	<0.001
All MI	97	0.65	116	0.78	0.83 (0.64, 1.09)	0.19
Non-MI ACS	40	0.27	40	0.27	1.00 (0.64, 1.55)	0.99
All Stroke	62	0.41	70	0.47	0.89 (0.63, 1.25)	0.50
All HF	62	0.41	100	0.67	0.62 (0.45, 0.84)	0.002
CVD Death	37	0.25	65	0.43	0.57 (0.38, 0.85)	0.005

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

Hazard Ratio: 0.50 0.75 1.0 1.2
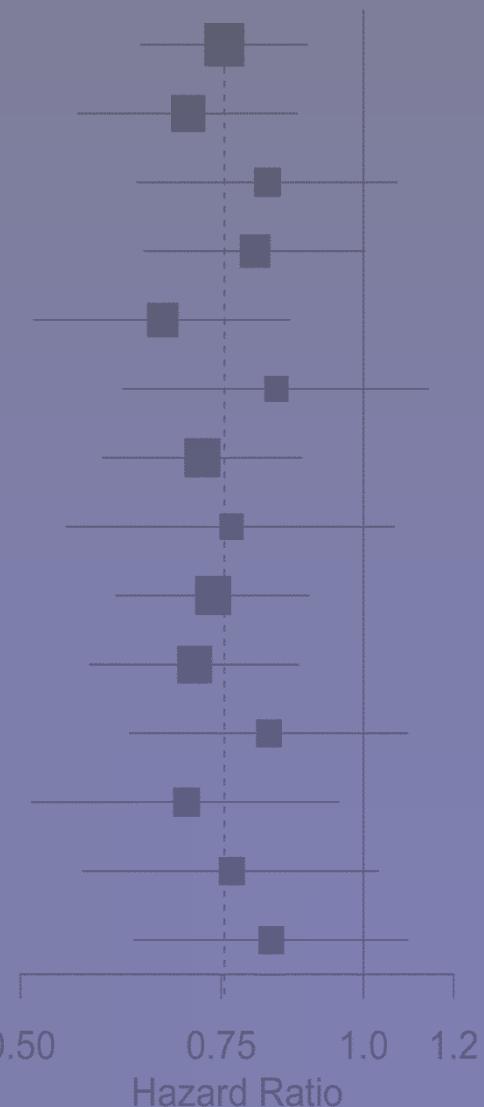
All-cause Mortality *Cumulative Hazard*

Hazard Ratio = 0.73 (95% CI: 0.60 to 0.90)

Legend:
— Standard
— Intensive

Standard *(210 deaths)*

Intensive *(155 deaths)*

During Trial (median follow-up = 3.26 yrs)
Number Needed to Treat (NNT)
to Prevent a death = 90

Cumulative Hazard (y-axis): 0.00, 0.02, 0.04, 0.06, 0.08, 0.10

	0	1	2	3	4	5
Std	4683	4528	4383	2998	789	
Int	4678	4516	4390	3016	807	

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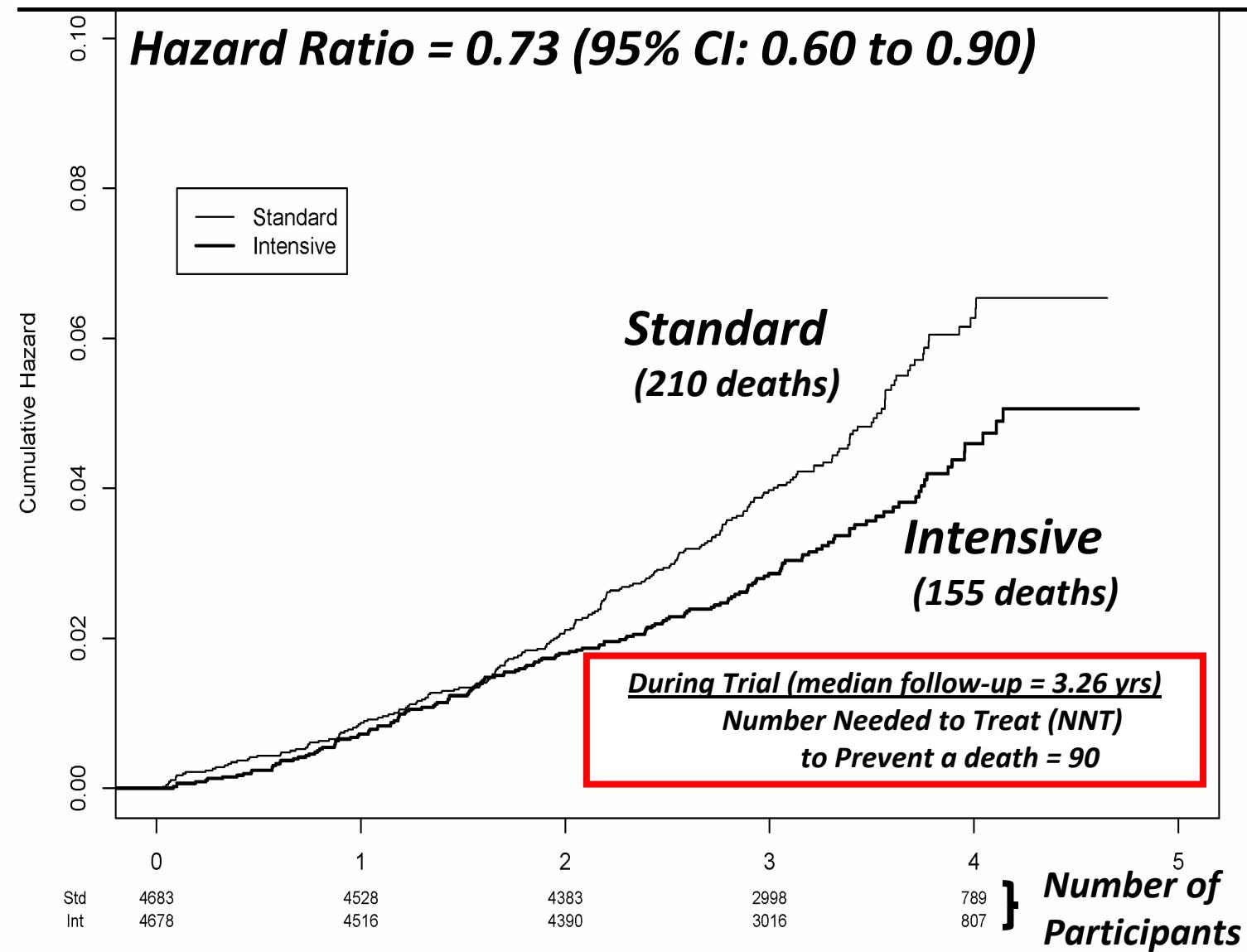
All-cause Mortality Experience in the Six Pre-specified Subgroups of Interest

Subgroup	Intensive	Standard	HR	Int P
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)	

*
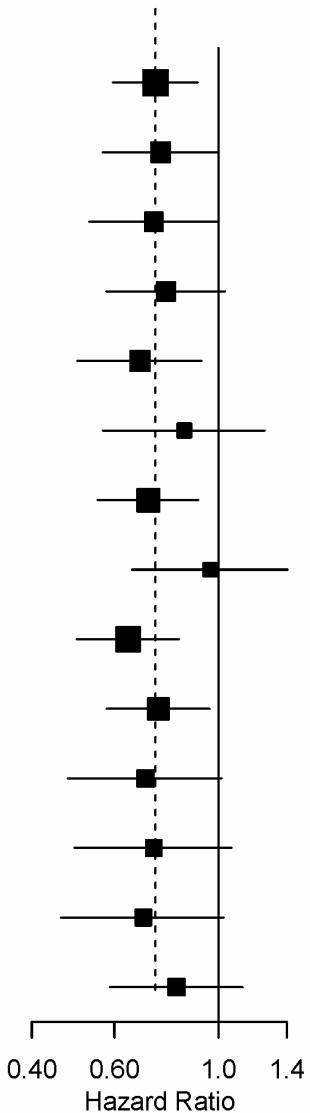
p=0.34, after Hommel adjustment for multiple comparisons

Hazard Ratio

0.40   0.60   1.0   1.4