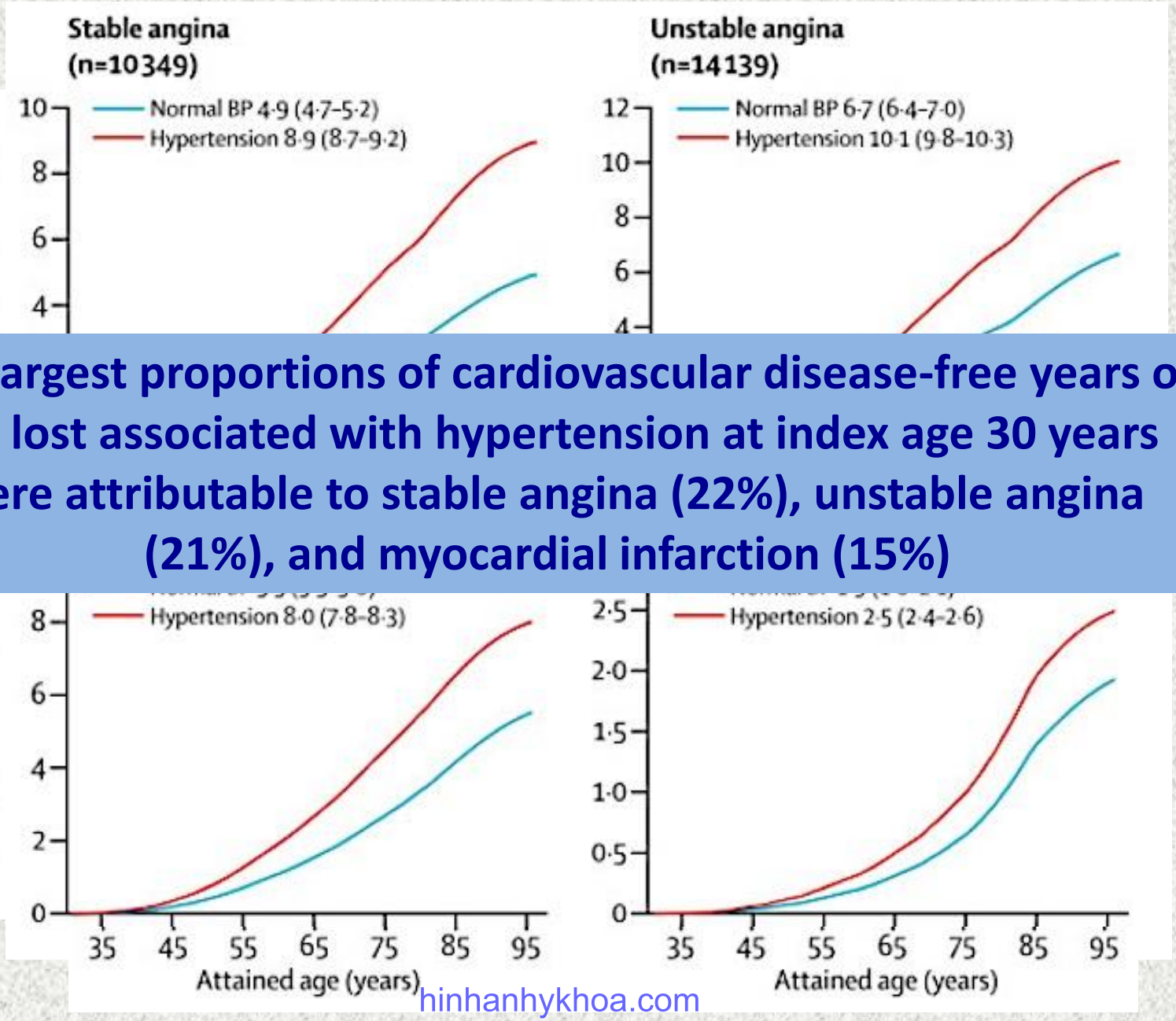
MANAGEMENT OF HTN IN PATIENTS WITH CHD

NGUYEN C. Loi, MD, FSCAI

Vice Chairman – Vietnam Society of Interventional Cardiology

Lifetime risk (95% CI) of 12 different CVD in people with HTN or normal BP from index age 30 years *(analysis on 1.25 millions people - 5·2 years median follow-up)*

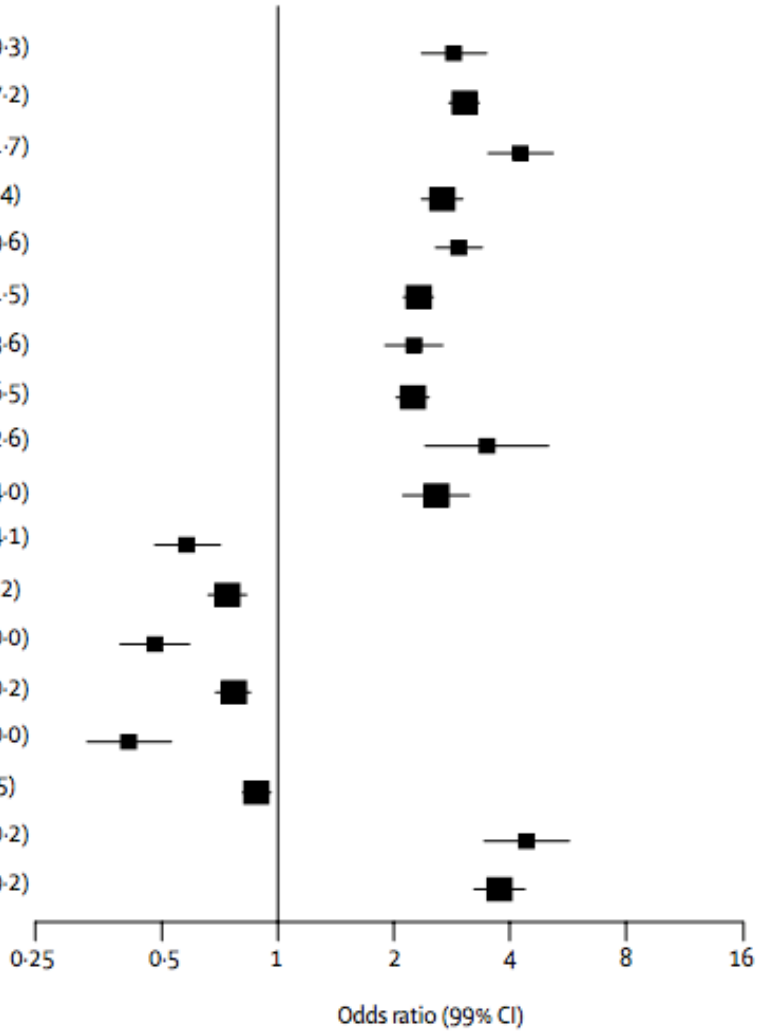


The largest proportions of cardiovascular disease-free years of life lost associated with hypertension at index age 30 years were attributable to stable angina (22%), unstable angina (21%), and myocardial infarction (15%)

Elini Rapsominiki et al. The Lancet 2014; vol 383; p 1899-1911.

Association of risk factors with acute myocardial infarction in men and women after adjustment for age, sex, and geographic region (INTERHEART STUDY)

Risk factor	Sex	Control (%)	Case (%)	Odds ratio (99% CI)	PAR (99% CI)
Current smoking	F	9·3	20·1	2·86 (2·36–3·48)	15·8% (12·9–19·3)
	M	33·0	53·1	3·05 (2·78–3·33)	44·0% (40·9–47·2)
Diabetes	F	7·9	25·5	4·26 (3·51–5·18)	19·1% (16·8–21·7)
	M	7·4	16·2	2·67 (2·36–3·02)	10·1% (8·9–11·4)
Hypertension	F	28·3	53·0	2·95 (2·57–3·39)	35·8% (32·1–39·6)
	M	19·7	34·6	2·32 (2·12–2·53)	19·5% (17·7–21·5)
Abdominal obesity	F	33·3	45·6	2·26 (1·90–2·68)	35·9% (28·9–43·6)
	M	33·3	46·5	2·24 (2·03–2·47)	32·1% (28·0–36·5)
Psychosocial index	F	–	–	3·49 (2·41–5·04)	40·0% (28·6–52·6)
	M	–	–	2·58 (2·11–3·14)	25·3% (18·2–34·0)
Fruits/veg	F	50·3	39·4	0·58 (0·48–0·71)	17·8% (12·9–24·1)
	M	39·6	34·7	0·74 (0·66–0·83)	10·3% (6·9–15·2)
Exercise	F	16·5	9·3	0·48 (0·39–0·59)	37·3% (26·1–50·0)
	M	20·3	15·8	0·77 (0·69–0·85)	22·9% (16·9–30·2)
Alcohol	F	11·2	6·3	0·41 (0·32–0·53)	46·9% (34·3–60·0)
	M	29·1	29·6	0·88 (0·81–0·96)	10·5% (6·1–17·5)
ApoB/ApoA1 ratio	F	14·1	27·0	4·42 (3·43–5·70)	52·1% (44·0–60·2)
	M	21·9	35·5	3·76 (3·23–4·38)	53·8% (48·3–59·2)
N		**15 152**	**14 820**		



Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004; 364: 937–52

Relationship of Hypertension to Coronary Atherosclerosis and Cardiac Events in Patients With Coronary CTA

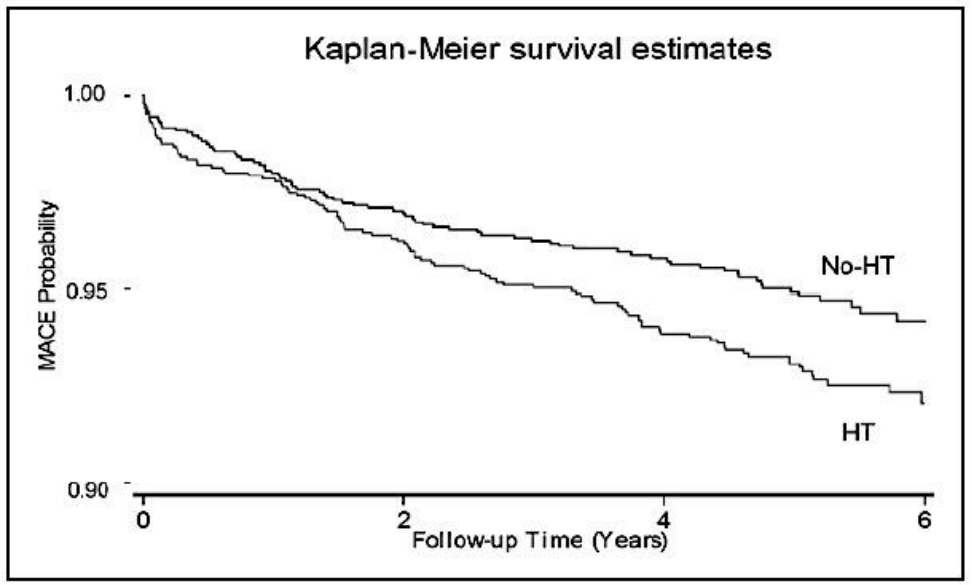
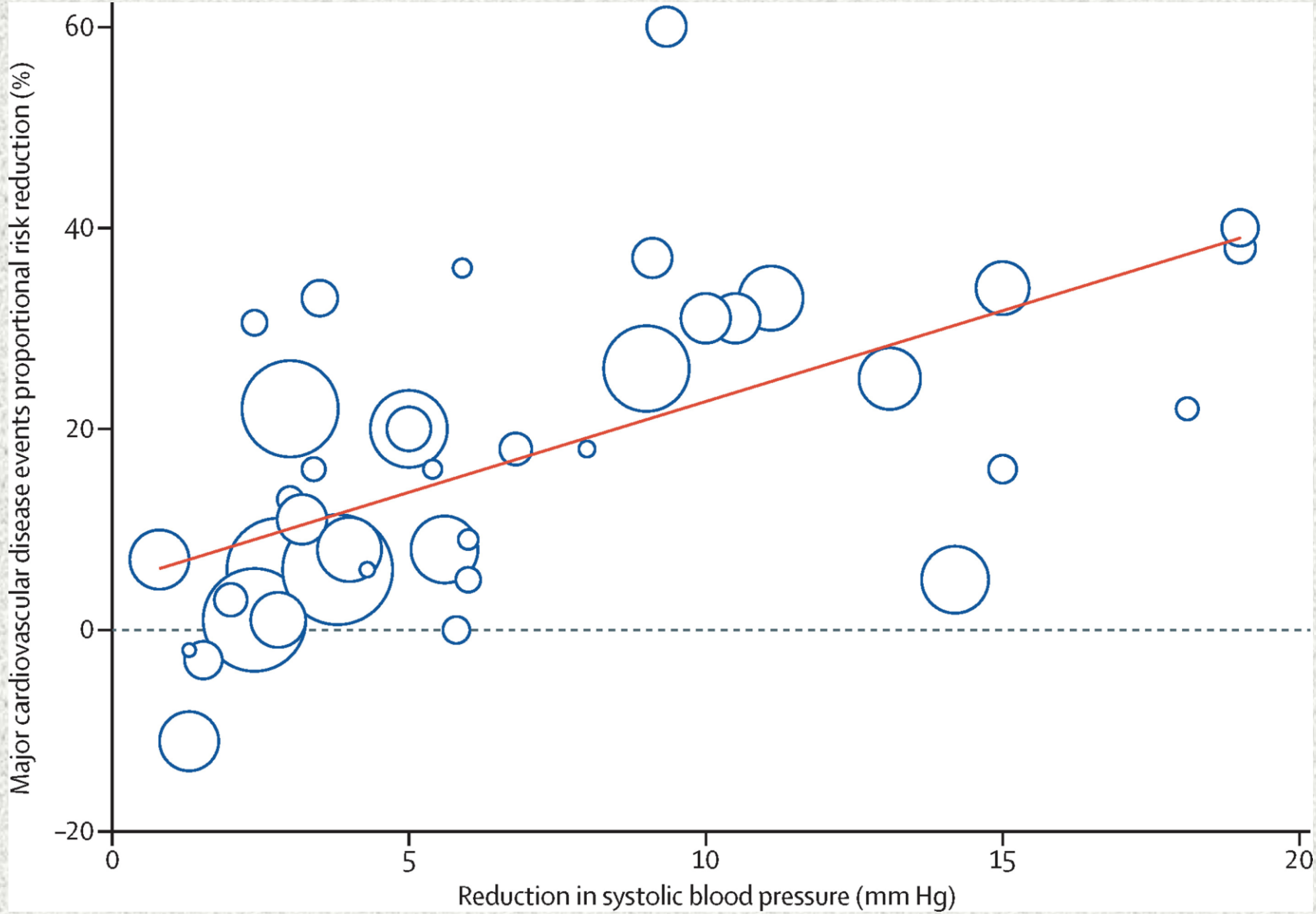


Table 3. MACE Risk

MACE Risk			
MACE	No Hypertension (n=1434)	Hypertension (n=1434)	*P* Value
MACE (%, n)	5.3 (76)	7.3 (104)	0.03
Deaths (%, n)	2.9 (42)	3.9 (56)	
Nonfatal MI (%, n)	2.4 (34)	3.4 (48)	

Rine Nakanishi et al.. Hypertension. 2017;70:293-299

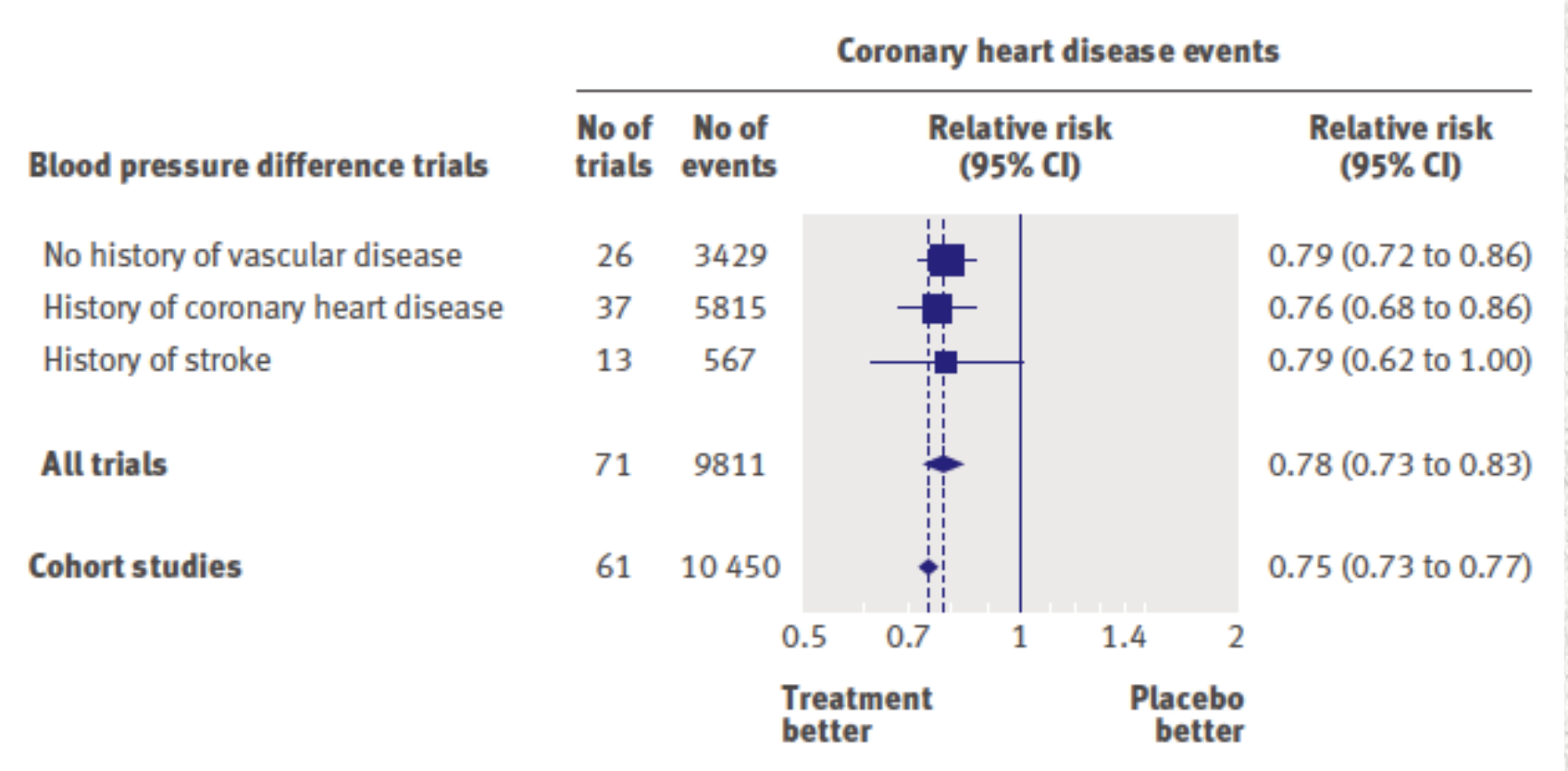
Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis (123 randomised trials)



The Lancet 2016; Vol 387; p957-967

Summary relative risk estimates for CHD events from randomised BP difference trials observed and standardised to a ***BP reduction of 10 mm Hg systolic and 5 mm Hg diastolic***

(Meta-analysis of 147 randomised trials)



M R Law. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ 2009;338:b1665

Antihypertensive Drugs for the Secondary Prevention of Cardiovascular Events in Patients With CHD

β-Blockers

β-Blocker administration remains the standard of care in patients with ***angina pectoris***, those who have had an ***MI***, and those who have ***LV dysfunction*** with or without symptoms of HF unless contraindicated.

Rosendorff C et al. Treatment of hypertension in the prevention and management of ischemic heart disease: a scientific statement from the American Heart Association Council for High Blood Pressure Research and the Councils on Clinical Cardiology and Epidemiology and Prevention. Circulation. 2007;115:2761–2788.

ACE Inhibitors

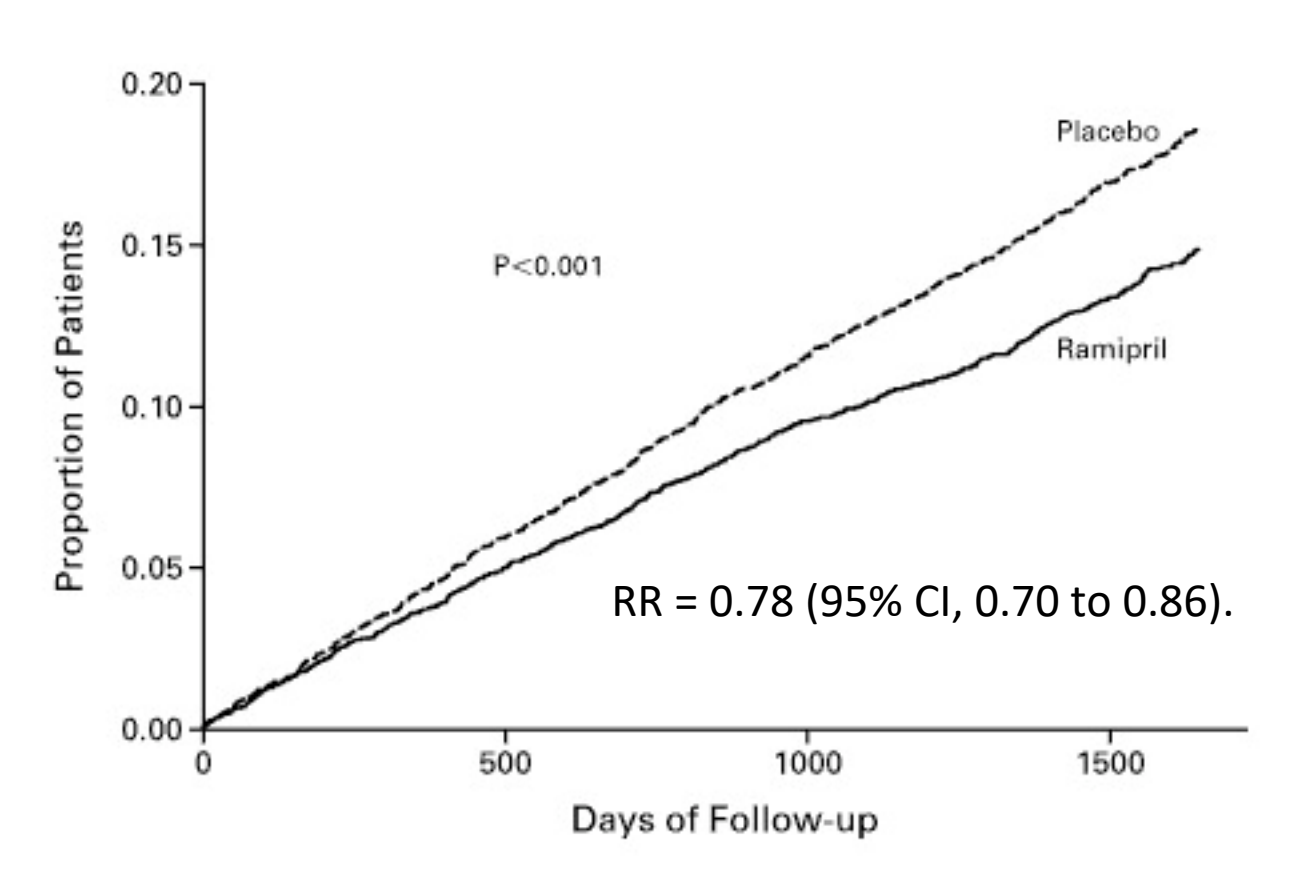
- The ACE inhibitors are effective in reducing initial IHD events and are recommended for consideration in all patients after MI.

- In high-cardiovascular-risk patients (HOPE) ACEi showed cardiovascular protective effects,
  In low-cardiovascular-risk patients (EUROPA, PEACE), ACEi do not give the benefits, especially those who have received intensive treatment with revascularization and lipid-lowering agents

- The Heart Outcomes Prevention Evaluation (HOPE) Study Investigators. N Engl J Med. 2000;342:145–153.
- Fox KM et al. The EUROPA study. Lancet. 2003;362:782–788.
- PEACE Trial Investigators. Angiotensin-converting-enzyme inhibition in stable coronary artery disease. N Engl J Med. 2004;351:2058–2068.

Effects of an Angiotensin-Converting–Enzyme Inhibitor, Ramipril, on Cardiovascular Events in High-Risk Patients

The Heart Outcomes Prevention Evaluation (HOPE) Study

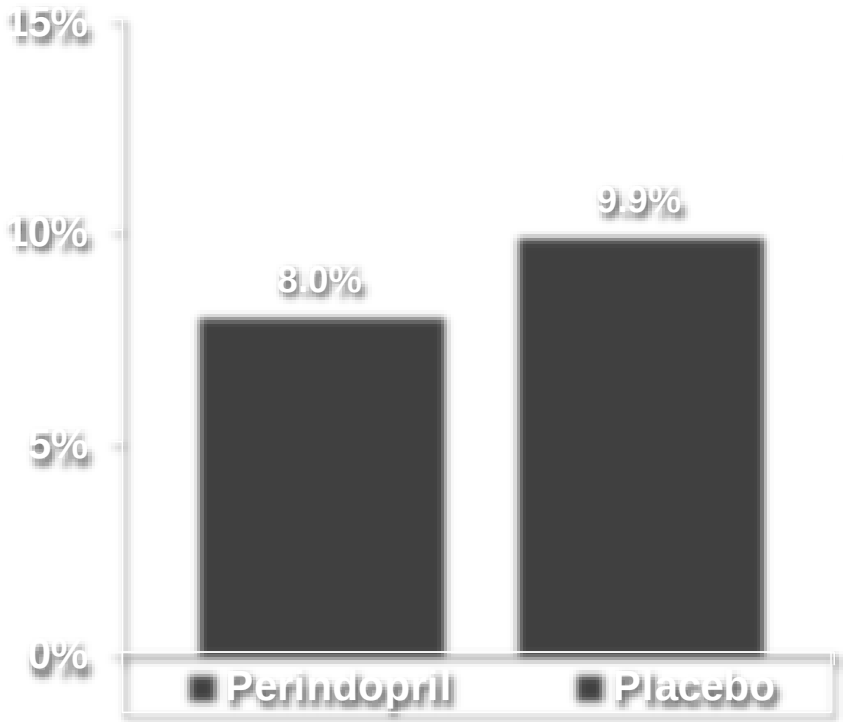


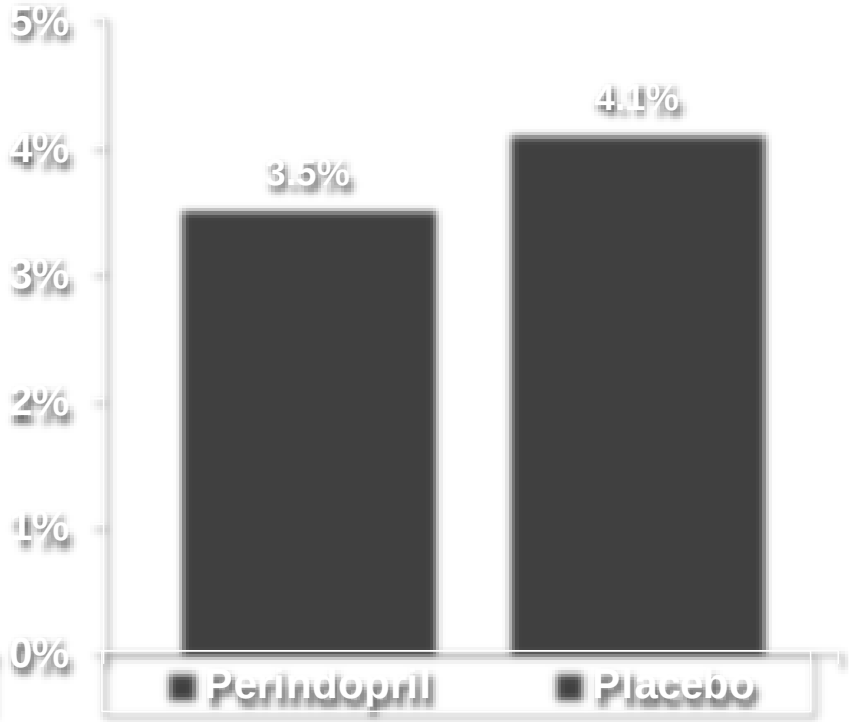
Kaplan–Meier Estimates of the composite outcome of MI, Stroke, or Death from cardiovascular causes in the Ramipril group and the placebo group.

N Engl J Med 2000; 342:145-153

12,218 low-risk patients with stable CAD, FU: 3.4 y

EUROPA Trial

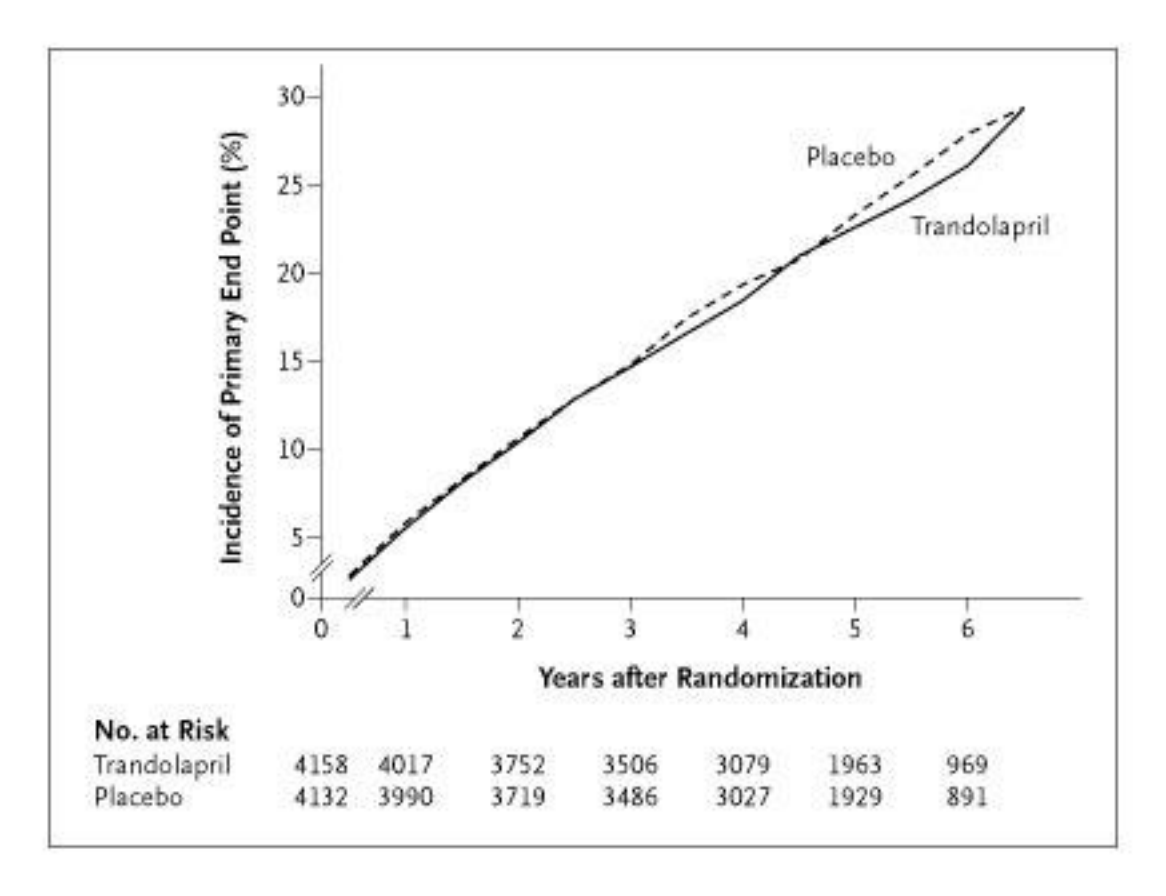




www. Clinical trial results.org

European Society of Cardiology 2003

Angiotensin-Converting–Enzyme Inhibition in Stable Coronary Artery Disease (PEACE Trial)



Cumulative Incidence of the Primary End Point, According to Treatment Group.

N Engl J Med 2004; 351:2058-2068

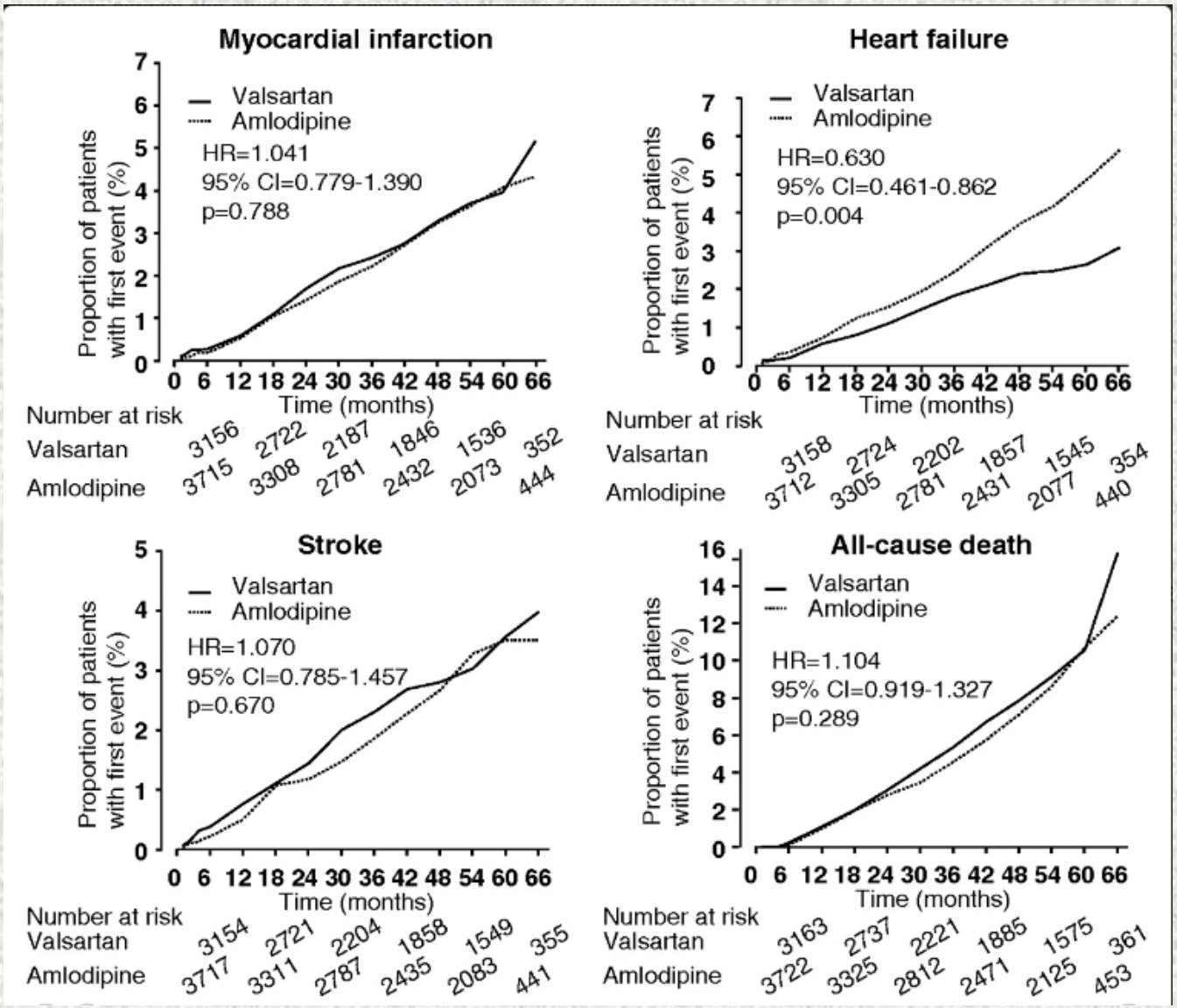
ARBs:

VALUE study *(Valsartan Antihypertensive Long-term Use Evaluation)*: protection against a composite of cardiovascular events including MI and HF *(similar to CCB amlodipine)*.

VALIANT trial *(Valsartan in Acute Myocardial Infarction Trial):* Valsartan had effects similar to those of the ACE inhibitor (Captopril) in reducing cardiovascular event end points.

TRANSCEND study *(Telmisartan Randomised Assessment Study in ACE Intolerant Subjects With Cardiovascular Disease)*: Telmisartan had modest benefits on the composite outcome end point of cardiovascular death, MI, and stroke and was well tolerated.

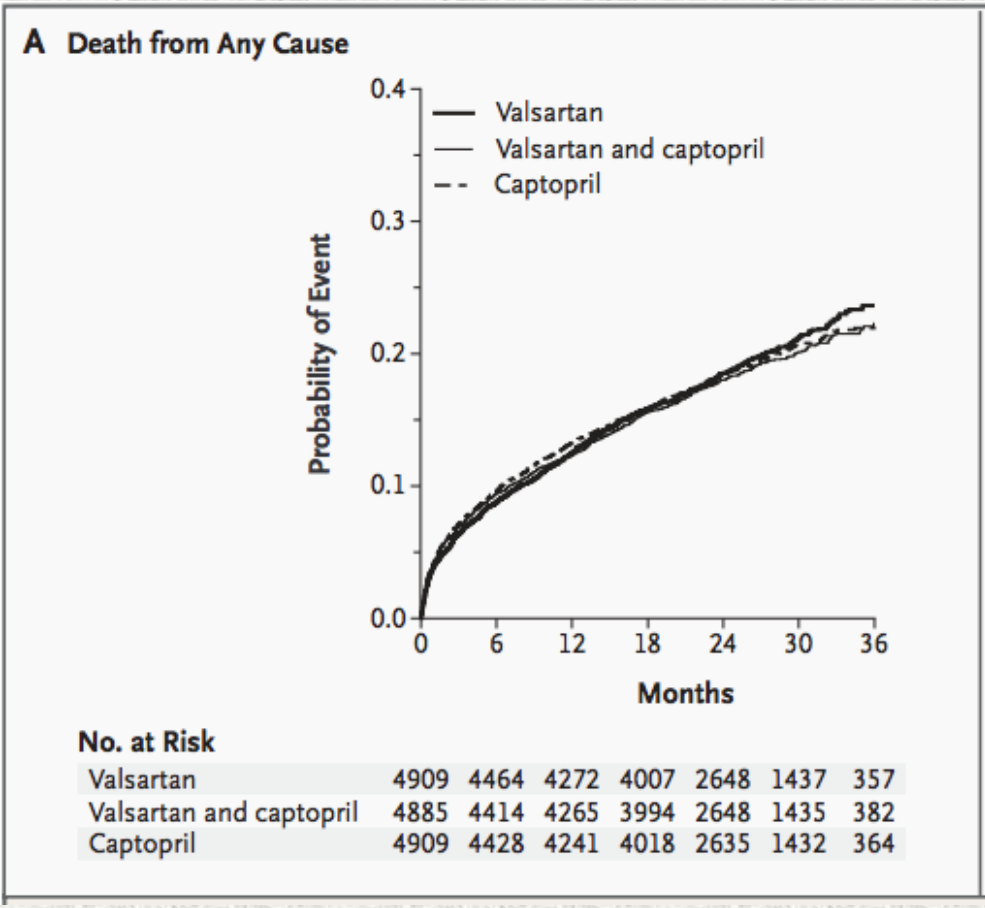
Valsartan Antihypertensive Long-term Use Evaluation
(VALUE Study)



Hypertension. 2006;48:385-391

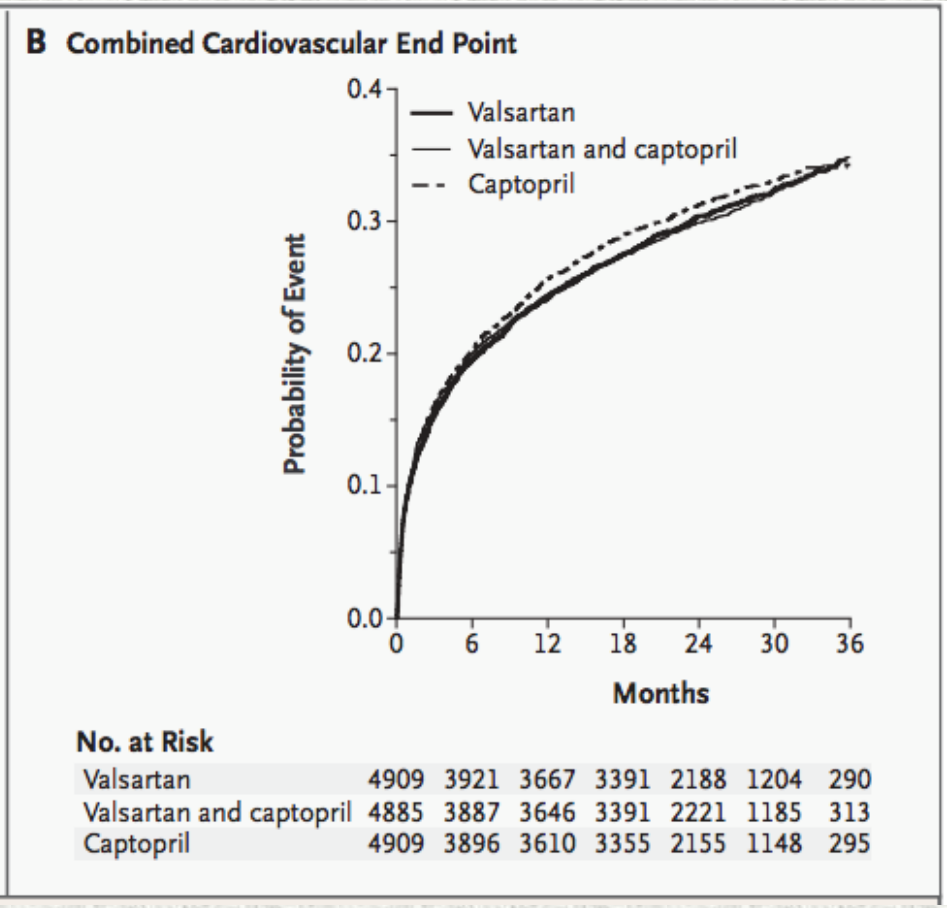
Valsartan, Captopril, or Both in Myocardial Infarction Complicated by Heart Failure, Left Ventricular Dysfunction, or Both

(VALIANT Trial)



No. at Risk

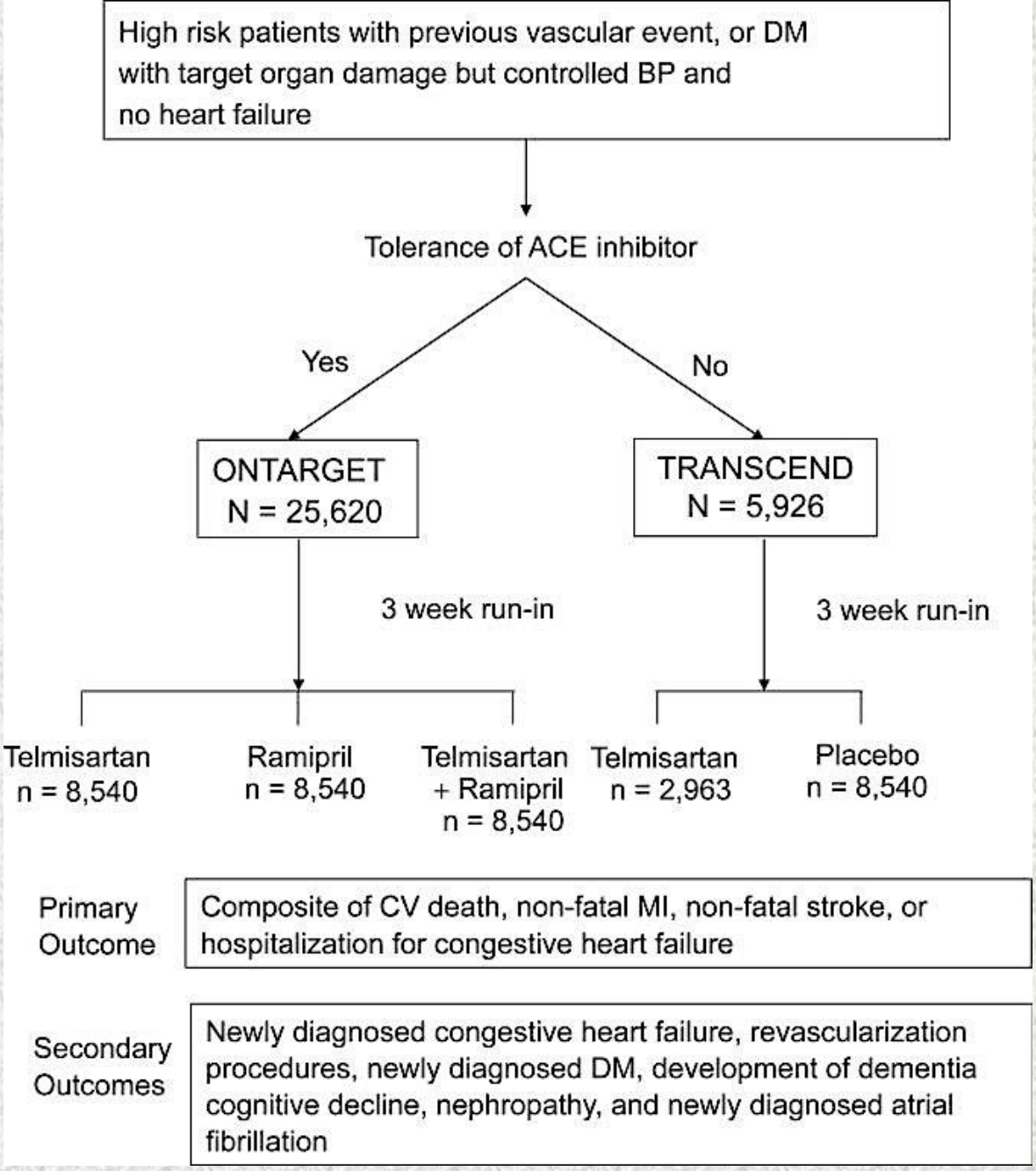
Valsartan	4909	4464	4272	4007	2648	1437	357
Valsartan and captopril	4885	4414	4265	3994	2648	1435	382
Captopril	4909	4428	4241	4018	2635	1432	364



No. at Risk

Valsartan	4909	3921	3667	3391	2188	1204	290
Valsartan and captopril	4885	3887	3646	3391	2221	1185	313
Captopril	4909	3896	3610	3355	2155	1148	295

N Engl J Med 2003;349;20: 1893-1906



N Engl J Med 2008; 358:1547-1559

Results of the ONTARGET and TRANSCEND studies

Table 3. Incidence of the Primary Outcome, Its Components, and Death from Any Cause.

Outcome	Ramipril (N=8576)	Telmisartan (N=8542)	Combination Therapy (N=8502)	Telmisartan vs. Ramipril	Combination Therapy vs. Ramipril
	number (percent)			*risk ratio (95% CI)*	
Death from cardiovascular causes, myocardial infarction, stroke, or hospitalization for heart failure*	1412 (16.5)	1423 (16.7)	1386 (16.3)	1.01 (0.94–1.09)	0.99 (0.92–1.07)
Death from cardiovascular causes, myocardial infarction, or stroke†	1210 (14.1)	1190 (13.9)	1200 (14.1)	0.99 (0.91–1.07)	1.00 (0.93–1.09)
Myocardial infarction‡	413 (4.8)	440 (5.2)	438 (5.2)	1.07 (0.94–1.22)	1.08 (0.94–1.23)
Stroke‡	405 (4.7)	369 (4.3)	373 (4.4)	0.91 (0.79–1.05)	0.93 (0.81–1.07)
Hospitalization for heart failure‡	354 (4.1)	394 (4.6)	332 (3.9)	1.12 (0.97–1.29)	0.95 (0.82–1.10)
Death from cardiovascular causes	603 (7.0)	598 (7.0)	620 (7.3)	1.00 (0.89–1.12)	1.04 (0.93–1.17)
Death from noncardiovascular causes	411 (4.8)	391 (4.6)	445 (5.2)	0.96 (0.83–1.10)	1.10 (0.96–1.26)
Death from any cause	1014 (11.8)	989 (11.6)	1065 (12.5)	0.98 (0.90–1.07)	1.07 (0.98–1.16)

“ADVERSE EVENT”

Tháng 7/2018 CQLD – BYT đã có công văn thu hồi trên 80 thuốc có chứa thành phần Valsartan được SX từ nguyên liệu Valsartan do công ty Zhejiang Huahai Pharmaceutical – Trung Quốc, nguyên liệu chứa tạp chất NDMA có nguy cơ gây ung thư.

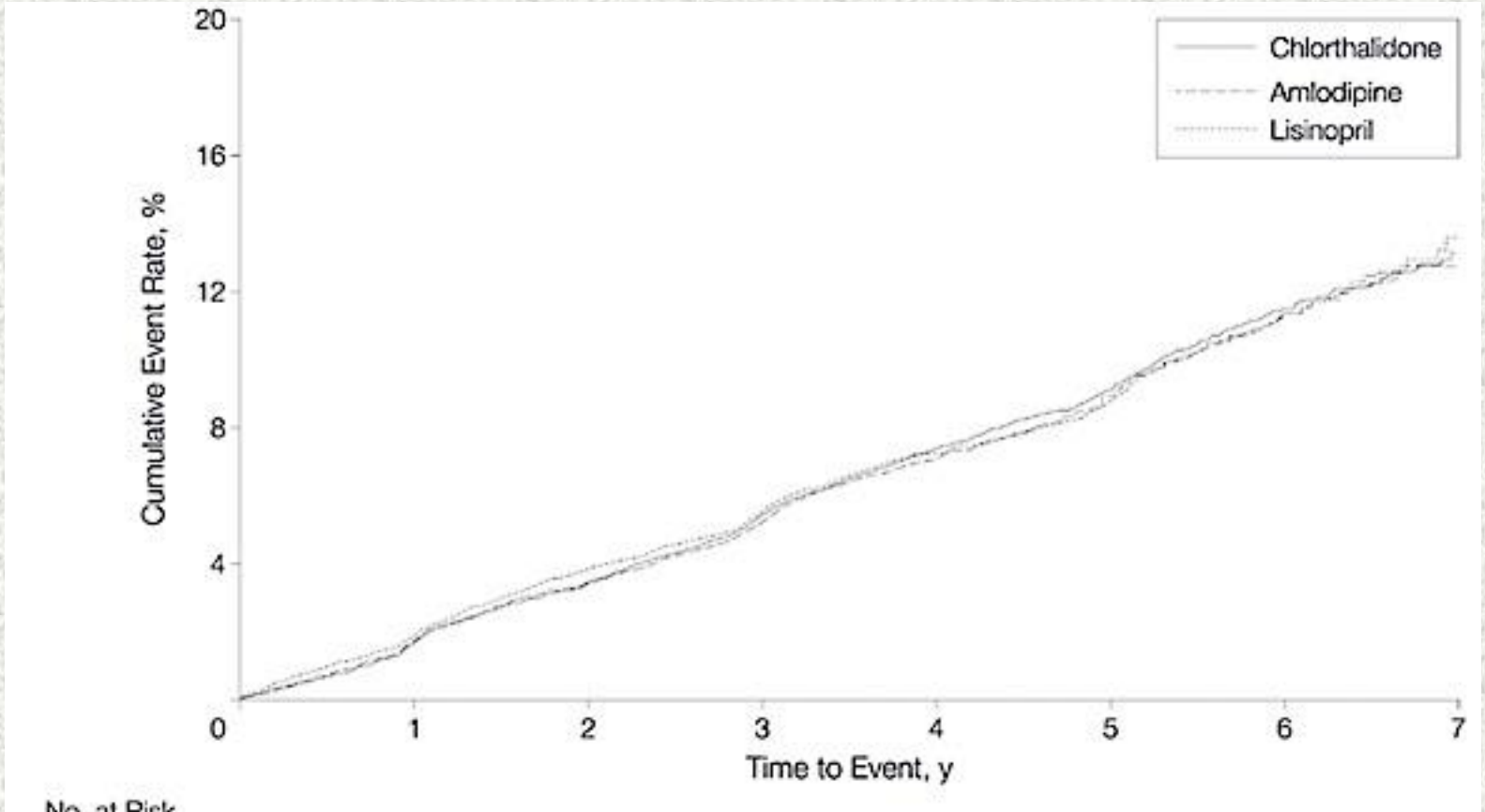
Tuy nhiên, một số thuốc chứa Valsartan với nguồn nguyên liệu an toàn vẫn được CQLD – BYT cho phép tiếp tục được SX, nhập khẩu, lưu hành và sử dụng trên thị trường như:

> *Diovan (Valsartan)* – **Novartis**

> *Hyvalor (Valsartan)* – **United Pharma**

Major Outcomes in High-Risk Hypertensive Patients Randomized to ACE Inhibitor or Calcium Channel Blocker vs Diuretic

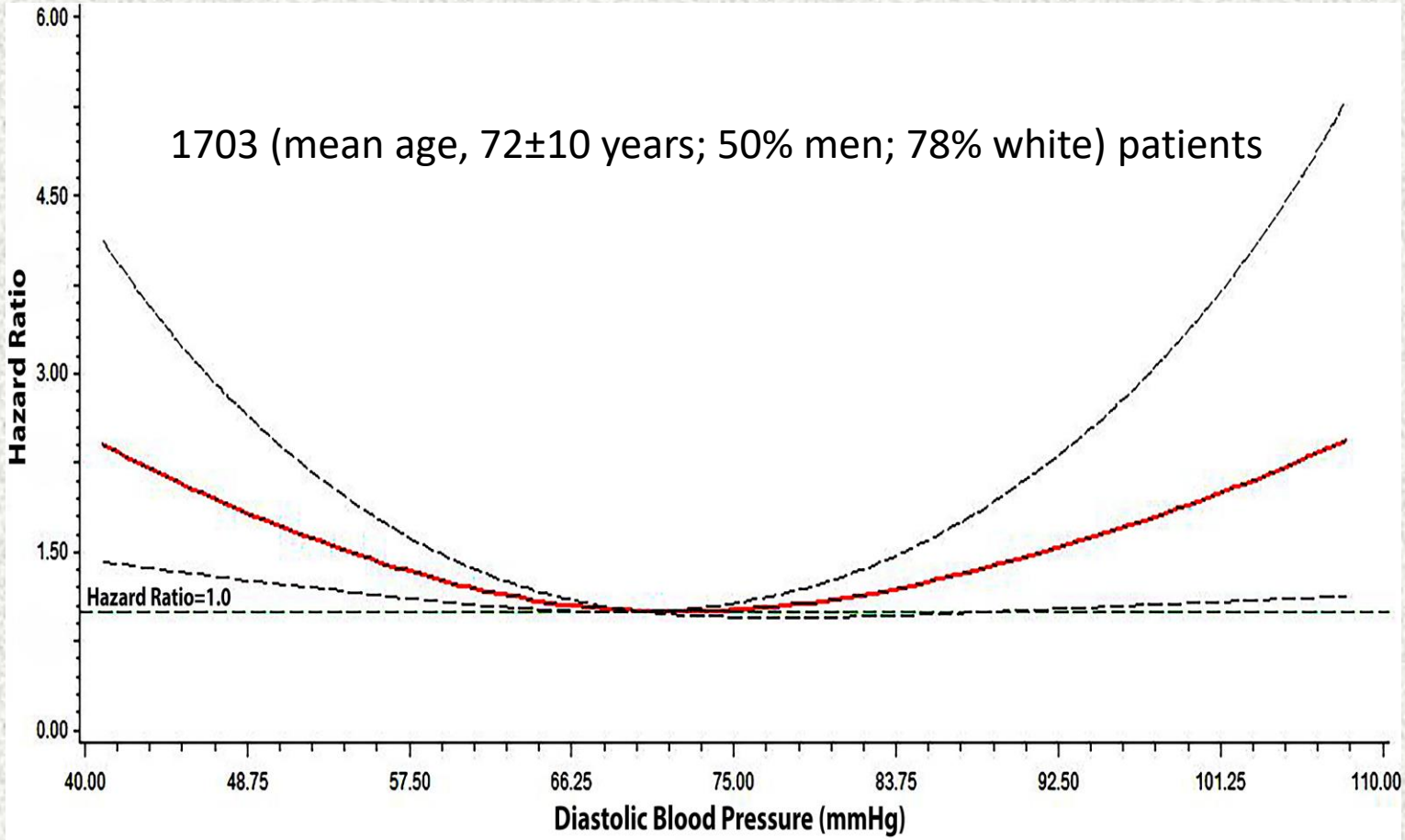
The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)



No. at Risk								
Chlorthalidone	15255	14477	13820	13102	11362	6340	2956	209
Amlodipine	9048	8576	8218	7843	6824	3870	1878	215
Lisinopril	9054	8535	8123	7711	6662	3832	1770	195

JAMA. 2002;288(23):2981-2997

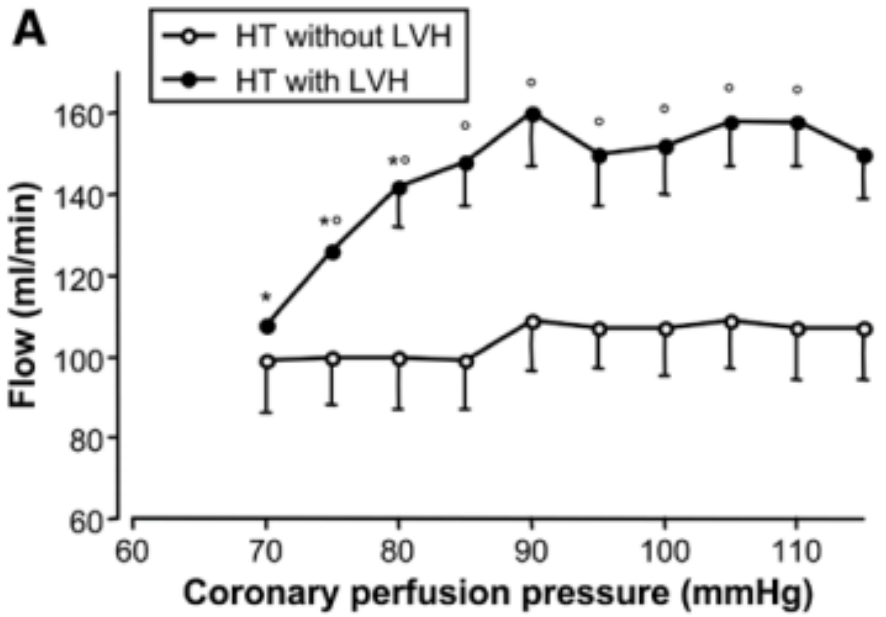
Diastolic Blood Pressure and Adverse Outcomes in the TOPCAT (Treatment of Preserved Cardiac Function Heart Failure With an Aldosterone Antagonist) Trial

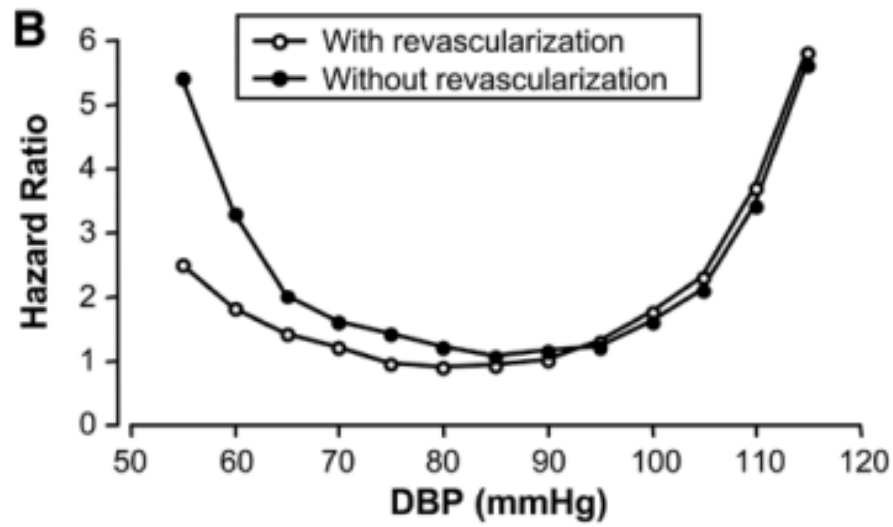


Risk of death across diastolic blood pressure. Each hazard ratio was computed with the median DPB value of 70 mm Hg as the reference and was adjusted for age, sex, race, smoking, SBP, serum creatinine, diabetes mellitus, body mass index, aspirin, statin, randomization group, NYHA class, CAD, and stroke. Dotted lines represent the 95% confidence interval.

J Am Heart Assoc. 2018;7:e007475.

Aggressive Blood Pressure Lowering Is Dangerous: The J-Curve





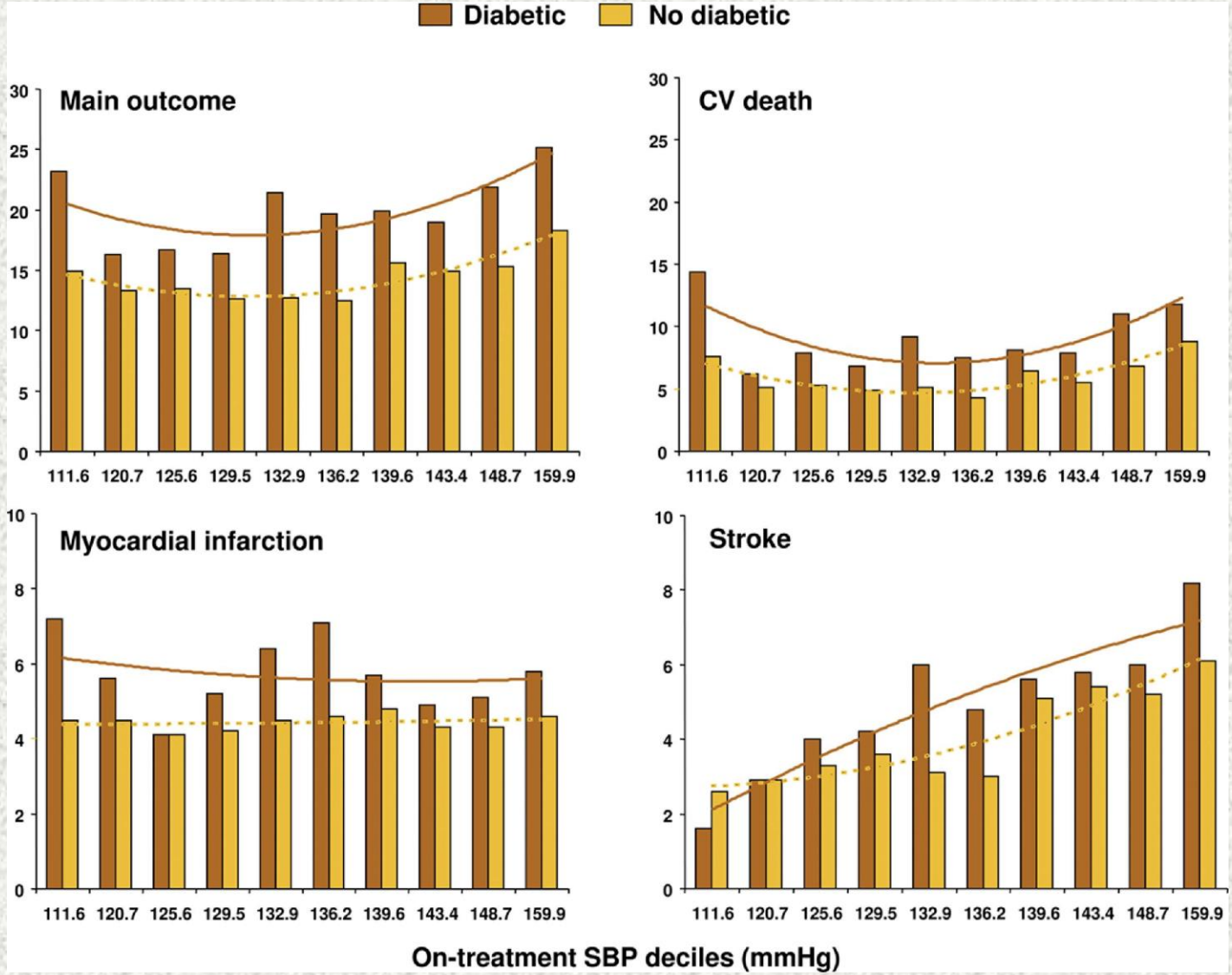
A, *The effects of reducing coronary perfusion pressure by intravenous infusion of nitroprusside on coronary blood flow (measured in the great cardiac vein) in hypertensive patients with and without left ventricular hypertrophy (LVH).*

B, *The cardiovascular event incidence at different achieved diastolic blood pressure (DBP) levels in patients with coronary artery disease (CAD) who did not undergo coronary revascularization compared with those who had the procedure.*

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

Proportion of outcome events by achieved SBP, divided into deciles

ONTARGET Trial (*25,584 patients older than 55 years*)



Journal of the American College of Cardiology
Volume 59, Issue 1, 3 January 2012, Pages 74-83

The quadratic relationship between in-treatment systolic blood pressure (SBP) and events is shown separately for diabetic patients and nondiabetic patients

BMJ

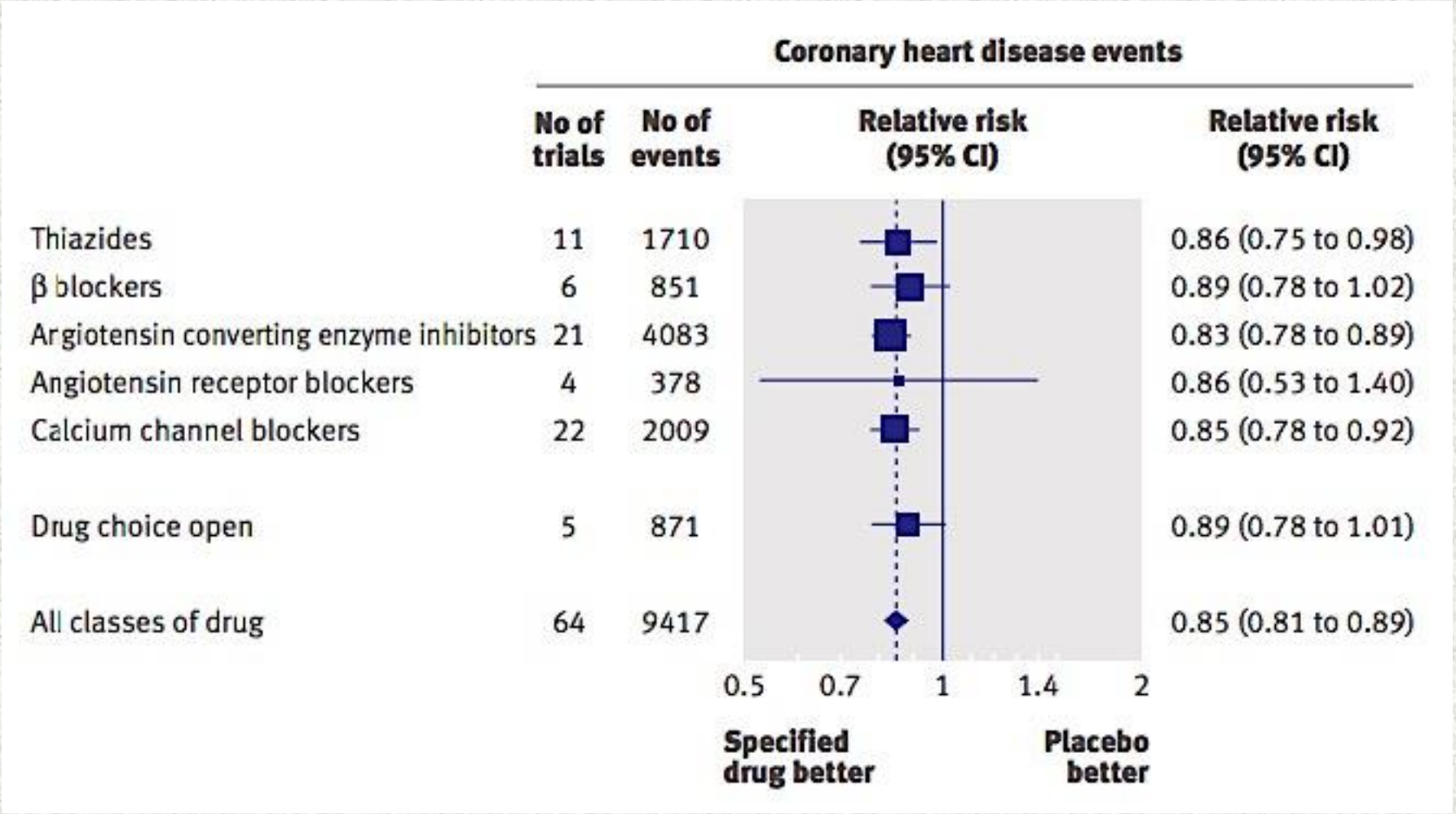
RESEARCH

Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies

M R Law, professor of epidemiology J K Morris, professor of medical statistics N J Wald, professor of environmental and preventive medicine

464,000 participants divided into 3 groups: no history of vascular disease, with history of CHD and with history of stroke

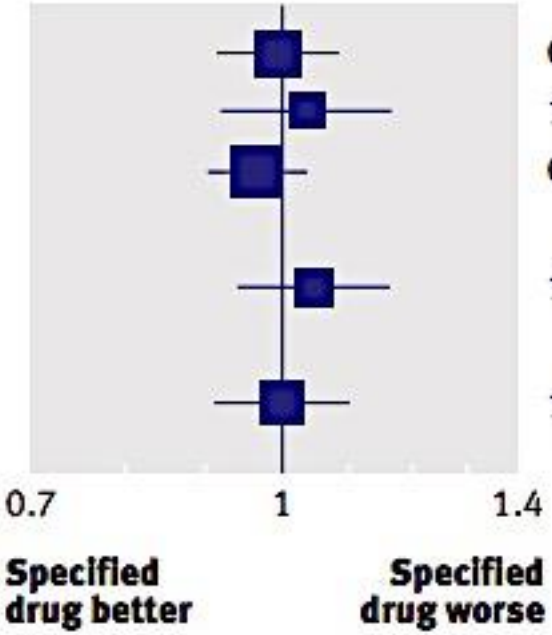
Relative risk estimates of CHD events in single drug blood pressure difference trials according to class of drug (excluding CHD events in trials of β blockers in people with history of CHD)



M R Law. BMJ 2009;338:b1665

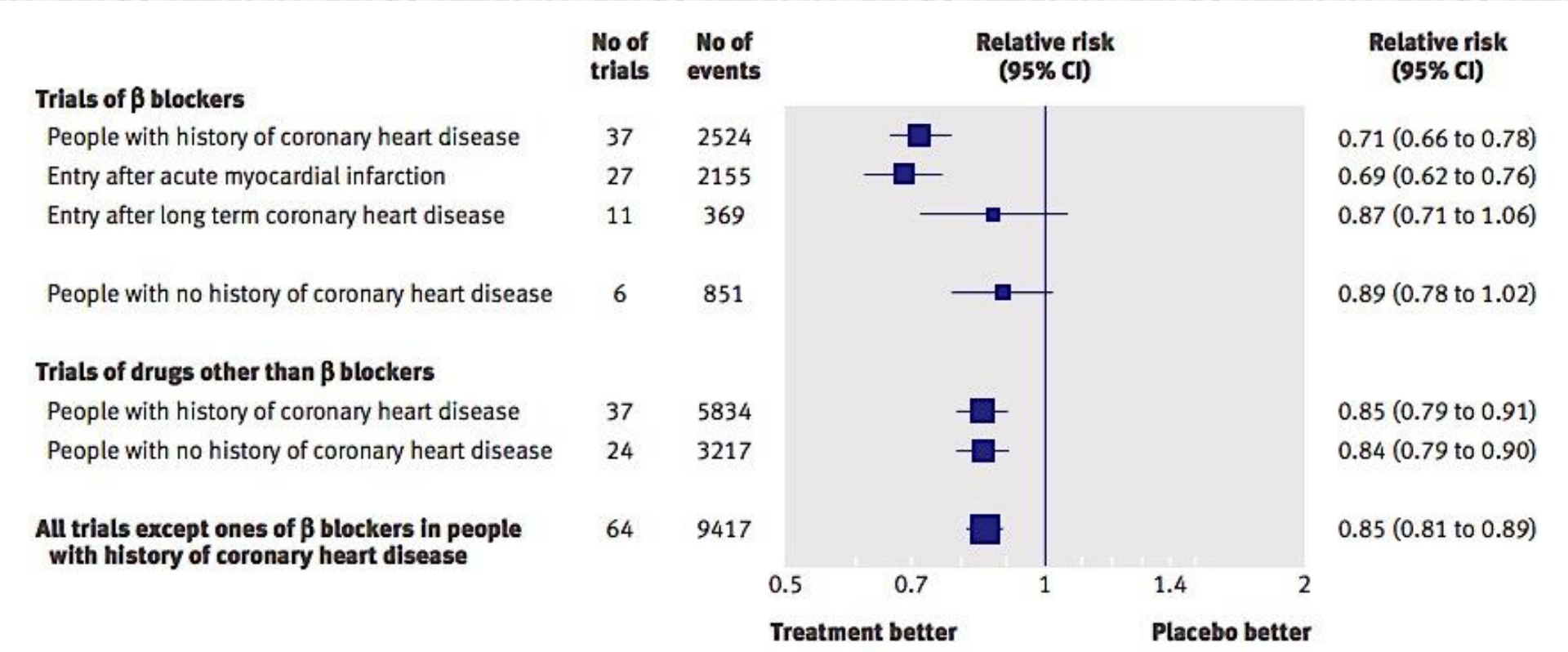
Relative risk estimates of CHD events in 46 drug comparison trials comparing each of the five classes of BP lowering drug with any other class of drug (excluding CHD events in trials of β blockers in people with a history of CHD)

	Blood pressure difference (mm Hg)		Coronary heart disease events			
	Systolic	Diastolic	No of trials	No of events	Relative risk (95% CI)	Relative risk (95% CI)
Thiazides *v* any other	-1.4	0.2	15	4229		0.99 (0.91 to 1.08)
β blockers *v* any other	1.4	0.6	10	2182		1.04 (0.92 to 1.17)
Angiotensin converting enzyme inhibitors *v* any other	0.9	0.4	21	6026		0.97 (0.90 to 1.03)
Angiotensin receptor blockers *v* any other	-0.4	0.1	10	2744		1.04 (0.94 to 1.16)
Calcium channel blockers *v* any other	-0.4	-0.9	21	6288		1.00 (0.91 to 1.10)



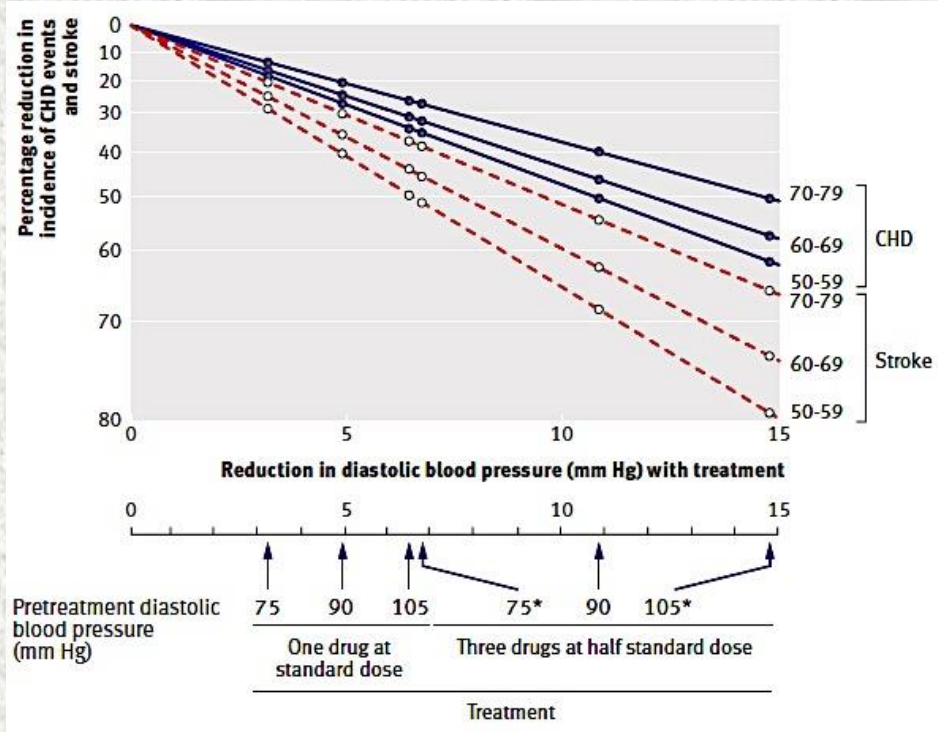
M R Law. BMJ 2009;338:b1665

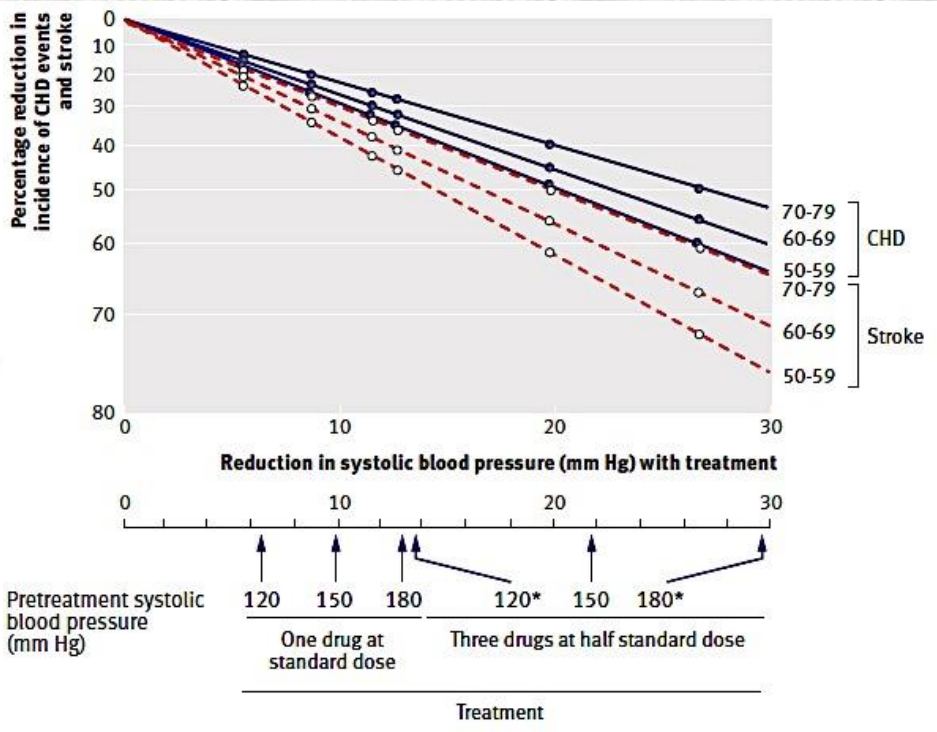
Relative risk estimates of CHD events in single drug blood pressure difference trials according to drug (β blockers or other), presence of CHD, and for β blockers according to acute MI on entry



M R Law. BMJ 2009;338:b1665

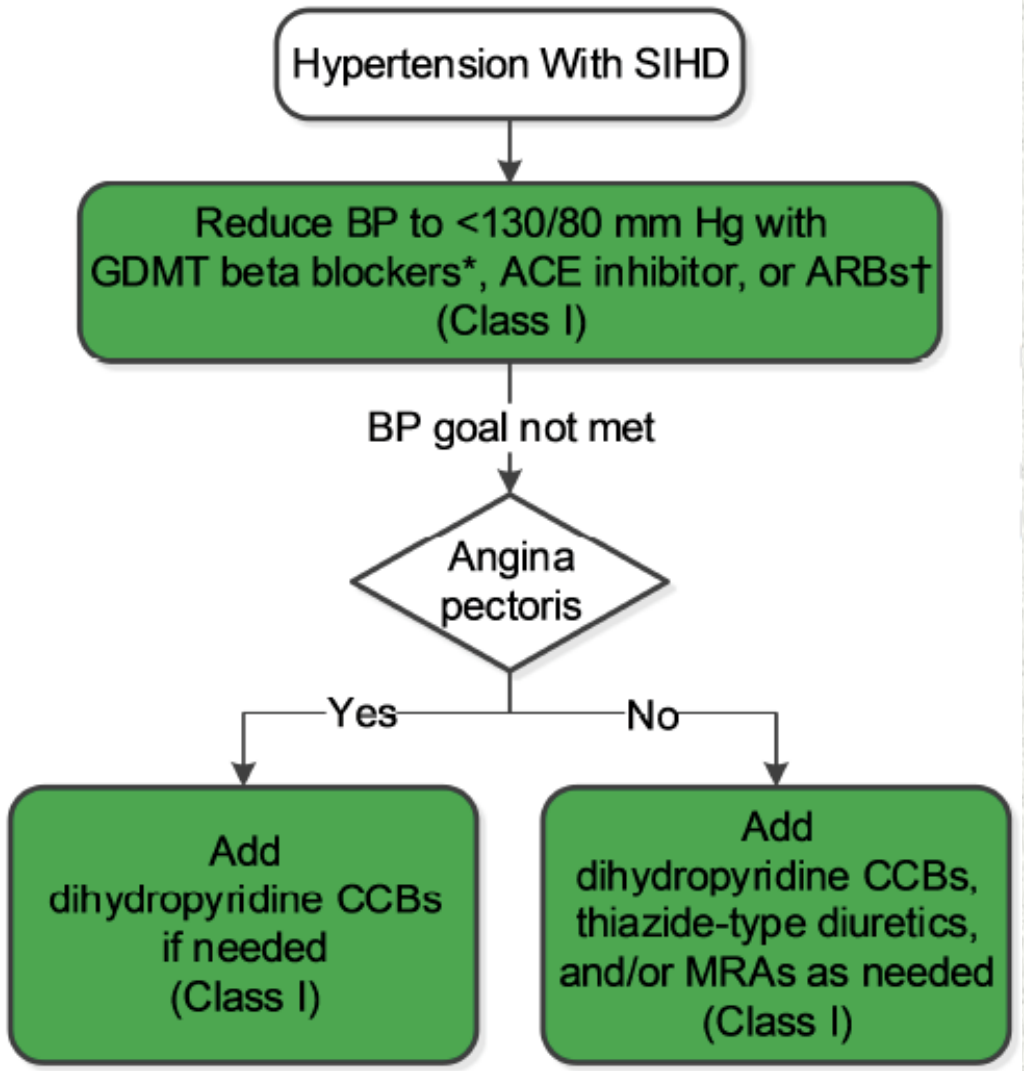
Reduction in incidence of CHD events and stroke in relation to reduction in BP according to dose and combination of drugs, pretreatment BP, and age.





M R Law. BMJ 2009;338:b1665

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults



IIa	B-NR	4. In adults who have had a MI or acute coronary syndrome, it is reasonable to continue GDMT (6) beta blockers beyond 3 years as long-term therapy for hypertension (13, 14).
IIb	C-EO	5. Beta blockers and/or CCBs might be considered to control hypertension in patients with CAD (without HF*r*EF) who had an MI more than 3 years ago and have angina.

Management of Hypertension in patients with ACS

AHA/ACC/ASH Scientific Statement

Treatment of Hypertension in Patients With Coronary Artery Disease

A Scientific Statement From the American Heart Association, American College of Cardiology, and American Society of Hypertension

Circulation May 12, 2015

- ACS / HTN: short-acting β1-selective BB without ISA (***metoprolol tartrate or bisoprolol***).
- BB therapy should be initiated orally within 24 hours of presentation

I	A

- Hemodynamically unstable patients or decompensated HF: the initiation of BB should be delayed until stabilization

I	A

- Severe HTN or ongoing ischemia, intravenous BB (***esmolol***) can be considered.

IIa	B

AHA/ACC/ASH Scientific Statement 2015 - Treatment of Hypertension in Patients With Coronary Artery Disease

- ACS and HTN, nitrates considered to lower BP or to relieve ongoing ischemia or pulmonary congestion.

I	C

- Contraindication or intolerable to the use of a BB
- Ongoing ischemia
- No LV dysfunction or HF ,

→ nondihydropyridine CCB: ***verapamil or diltiazem***

IIa	B

- Angina or HTN is not controlled on a BB alone, a longer-acting dihydropyridine CCB may be added after optimal use of an ACE inhibitor.

AHA/ACC/ASH Scientific Statement 2015 - Treatment of Hypertension in Patients With Coronary Artery Disease

- Patient has an anterior MI, or
- hypertension persists, or
- Patient has evidence of LV dysfunction or HF, or
- Patient has diabetes mellitus.

→ ACE inhibitor
or ARB should be added

I	A
I	B

- Persistent HTN not controlled with a β-blocker:

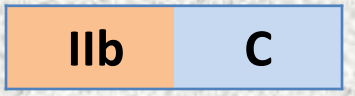
→ - ACE inhibitor, and
- Aldosterone antagonist, a thiazide or thiazide-type diuretic may be added in selected patients for BP control.

I	B

Lower risk ACS patients with preserved EF and no diabetes mellitus, ACEi can be considered a first-line agent for BP control.

Target BP is <140/90 mm Hg in hemodynamically stable ACS.

Target BP of <130/80 mm Hg at the time of hospital discharge.



AHA/ACC/ASH Scientific Statement 2015 - Treatment of Hypertension in Patients With Coronary Artery Disease

ESC
European Society of Cardiology
European Heart Journal (2018) **39**, 3021–3104
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ESC/ESH GUIDELINES

2018 ESC/ESH Guidelines for the management of arterial hypertension

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

Therapeutic strategies in hypertensive patients with CAD

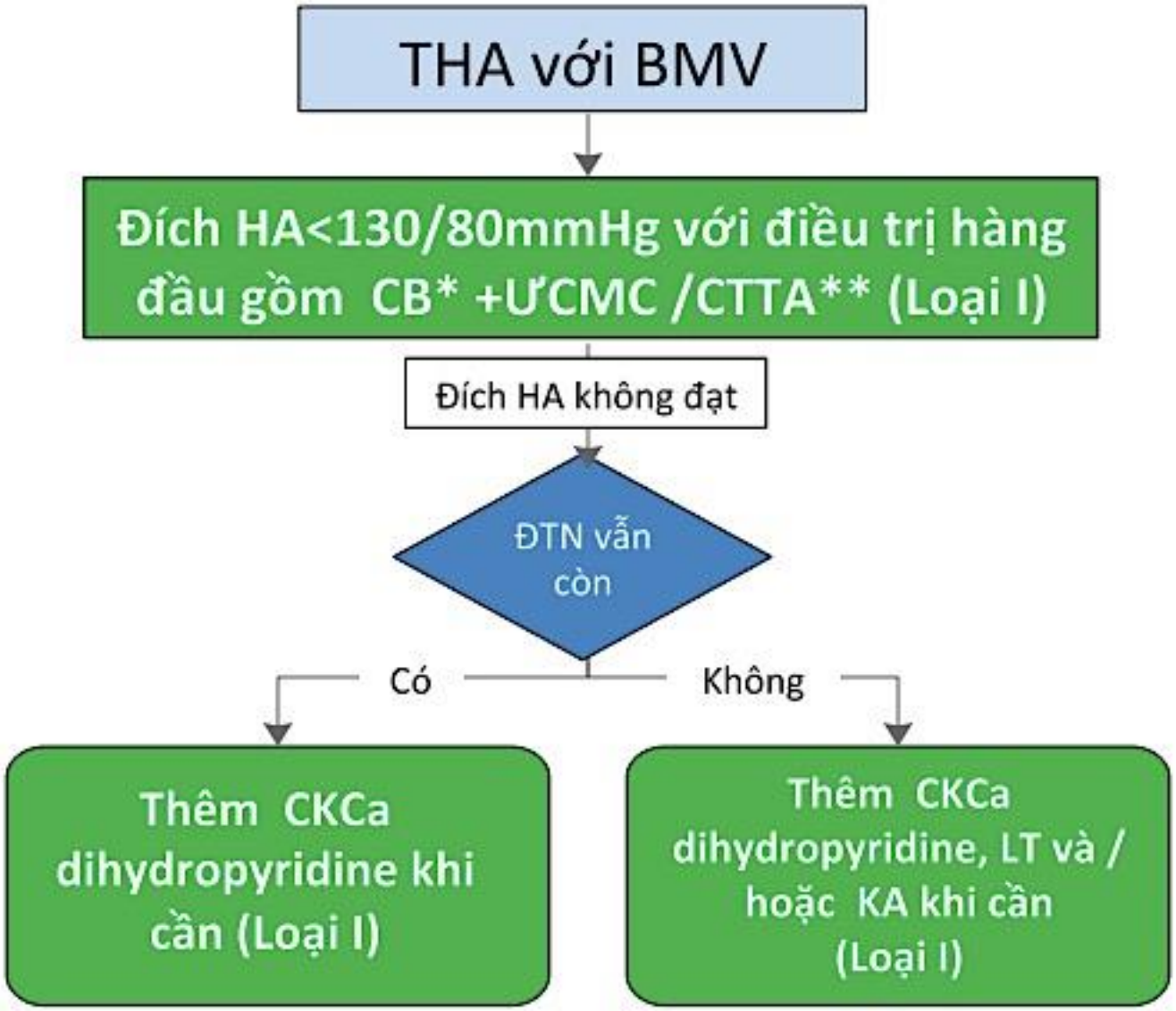
Recommendations	Class[a]	Level[b]
In patients with CAD receiving BP-lowering drugs, it is recommended:		
• To target SBP to ≤ 130 mmHg if tolerated, but not <120 mmHg.[2,496]	I	A
• In older patients (aged ≥65 years), to target to an SBP range of 130–140 mmHg.[2,496]	I	A
• To target DBP to <80 mmHg, but not <70 mmHg.	I	C
In hypertensive patients with a history of myocardial infarction, beta-blockers and RAS blockers are recommended as part of treatment.[503]	I	A
In patients with symptomatic angina, beta-blockers and/or CCBs are recommended.[503]	I	A

Challenge !!

KHUYẾN CÁO VỀ CHẨN ĐOÁN VÀ ĐIỀU TRỊ TĂNG HUYẾT ÁP

2018

Hình 13: Điều Trị THA Với Bệnh Mạch Vành



Bảng 38: Khuyến cáo điều trị THA ở bệnh nhân có bệnh mạch vành

Khuyến Cáo	Loại	Mức Chứng Cứ
Ngưỡng HA cần điều trị thuốc là > 140/90 mmHg (>130/85mmHg ở HABT cao có nguy cơ rất cao có bệnh tim mạch đặc biệt BMV)	I	B
Đích điều trị hạ HATT có BMV trong khoảng ranh giới 120-<130mmHg , nếu >65 tuổi đích HATT 130-<140mmHg	I	A
Đích HATTr trong khoảng ranh giới 70-<80mmHg	I	C
Thuốc ƯCMC/ CTTA+ CB là chỉ định hàng đầu, thêm thuốc khác (CKCa, LT và hoặc Kháng aldosterone) khi cần để kiểm soát HA	I	B
THA có NMCT hoặc hội chứng mạch vành cấp cần điều trị BB tiếp tục trong 3 năm	IIa	B
CB và /hoặc CKCa có thể xem xét điều trị THA có BMV (không có Suy Tim EF giảm) mà có NMCT cách 3 năm và có cơn đau thắt ngực	IIb	C

CONCLUSIONS

- Blood pressure lowering drugs reduce the risk of CHD events, especially in people with a history of vascular disease.

- The effect of blood pressure lowering drugs in reducing the risk of disease is entirely or largely due to blood pressure reduction.
  Caution should be paid at DBP < 70mmHg or SBP < 20mmHg.
  The different classes of blood pressure lowering drugs lower blood pressure to a similar extent

- β blockers had a special effect over and above that due to blood pressure reduction in preventing recurrent CHD events in people with a history of CHD compared with other drugs.
  The extra effect was limited to a few years after MI, compared with no recent infarct