

**Paciente com DM, HAS e DAC (IAM recente), HBAC 7%, IMC 42:  
A curva J teria importância no tratamento deste paciente?**

**Claudio Marcelo B. das Virgens**  
Salvador, 11 de maio de 2017

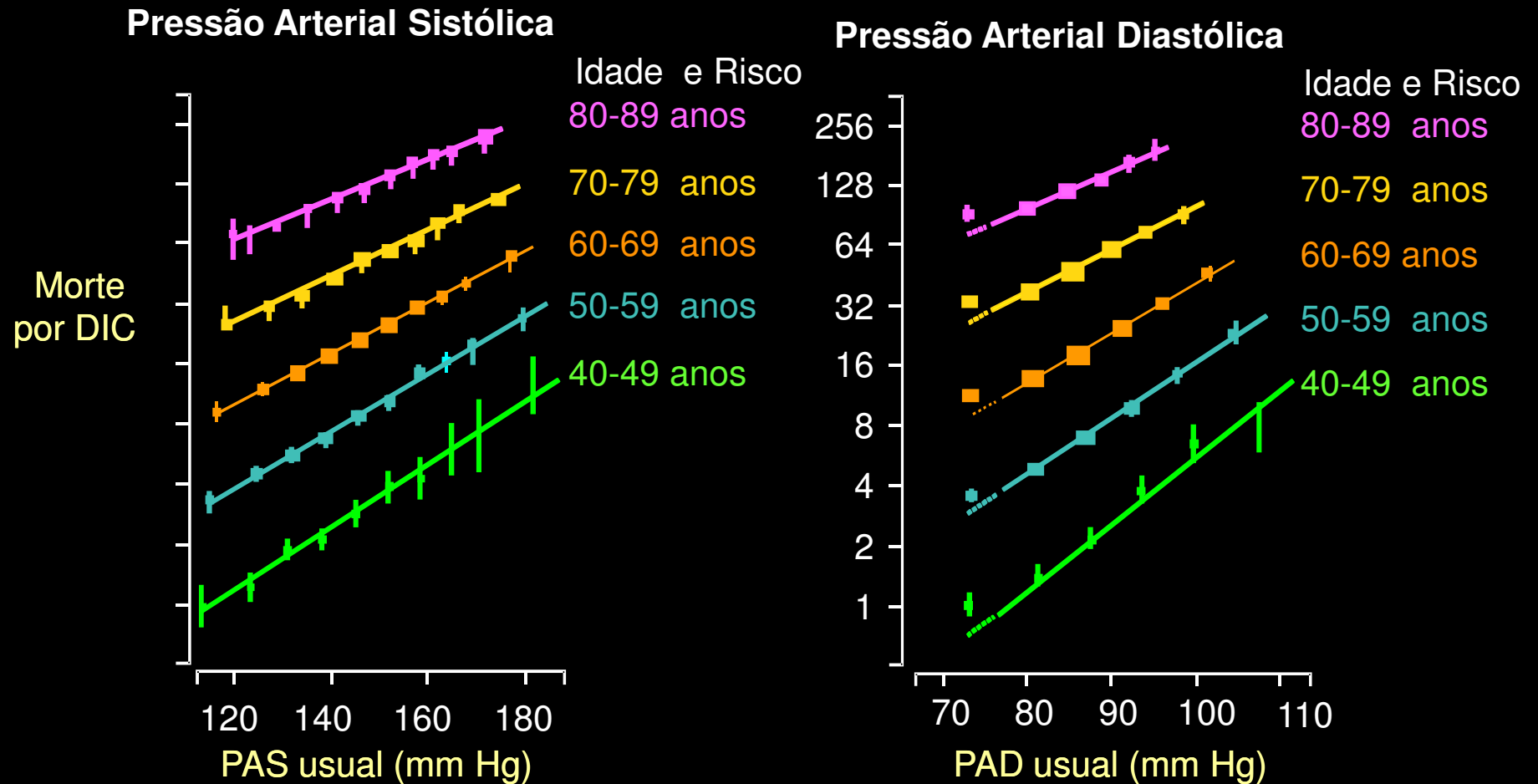
Resolução 1595/2000 do Conselho Federal de Medicina  
Declaração de potencial conflito de interesses

Ausência de conflitos de  
interesse em relação ao tema da  
conferência

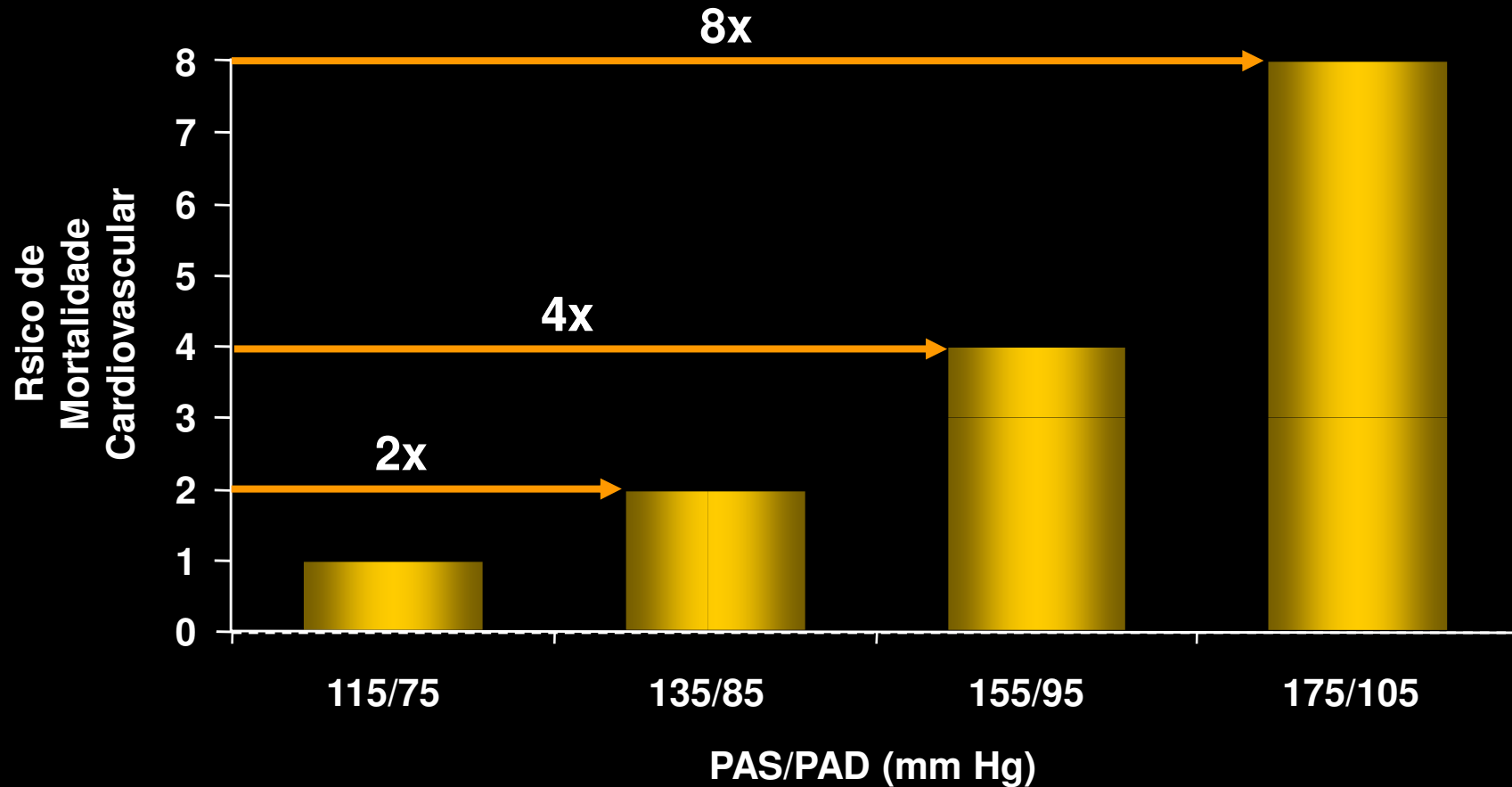
Claudio Marcelo B. das Virgens

# “Lower SBP and DBP Is Better”

## Freqüência de Doença Cardíaca Isquêmica por PAS, PAD e Idade



## O Risco de Mortalidade Cardiovascular Dobra a Cada Aumento de 20/10 mm Hg da Pressão Arterial\*



PAS = Pressão Arterial Sistólica; PAD = Pressão Arterial Diastólica.

\*idade 40-69 anos, PA de início 115/75 mm Hg

Chobanian AV et al. *JAMA*. 2003;289:2560-2572.

Lewington S et al. *Lancet*. 2002;360:1903-1913

# Dados Epidemiológicos

## Principais causas de mortalidades







# Hipertensión y riesgo vascular

[www.elsevier.es/hipertension](http://www.elsevier.es/hipertension)



## REVIEW

# Optimal blood pressure targets in 2014 – Does the guideline recommendation match the evidence base?



# Clinical Trial of BP Lowering in Diabetic Patients: Mean Achieved Systolic (SBP)

Trial	N	Mean SBP conventional	Mean SBP intensive	CVD Risk Reduction
<b>SHEP</b>	583	155	146	22-56%
<b>Syst-EUR</b>	492	162	153	62-69%
<b>HOT</b>	1,501	148	144	30-67%
<b>UKPDS</b>	1,148	154	144	32-44%
<b>ABCD</b>	470	138	132	No CVD ↓
<b>ADVANCE</b>	11,140	140	135	14% mortality ↓

SHEP - JAMA. 1991 Jun 26;265(24):3255-64.

Syst-Eur. Lancet. 1997;350:757-764.

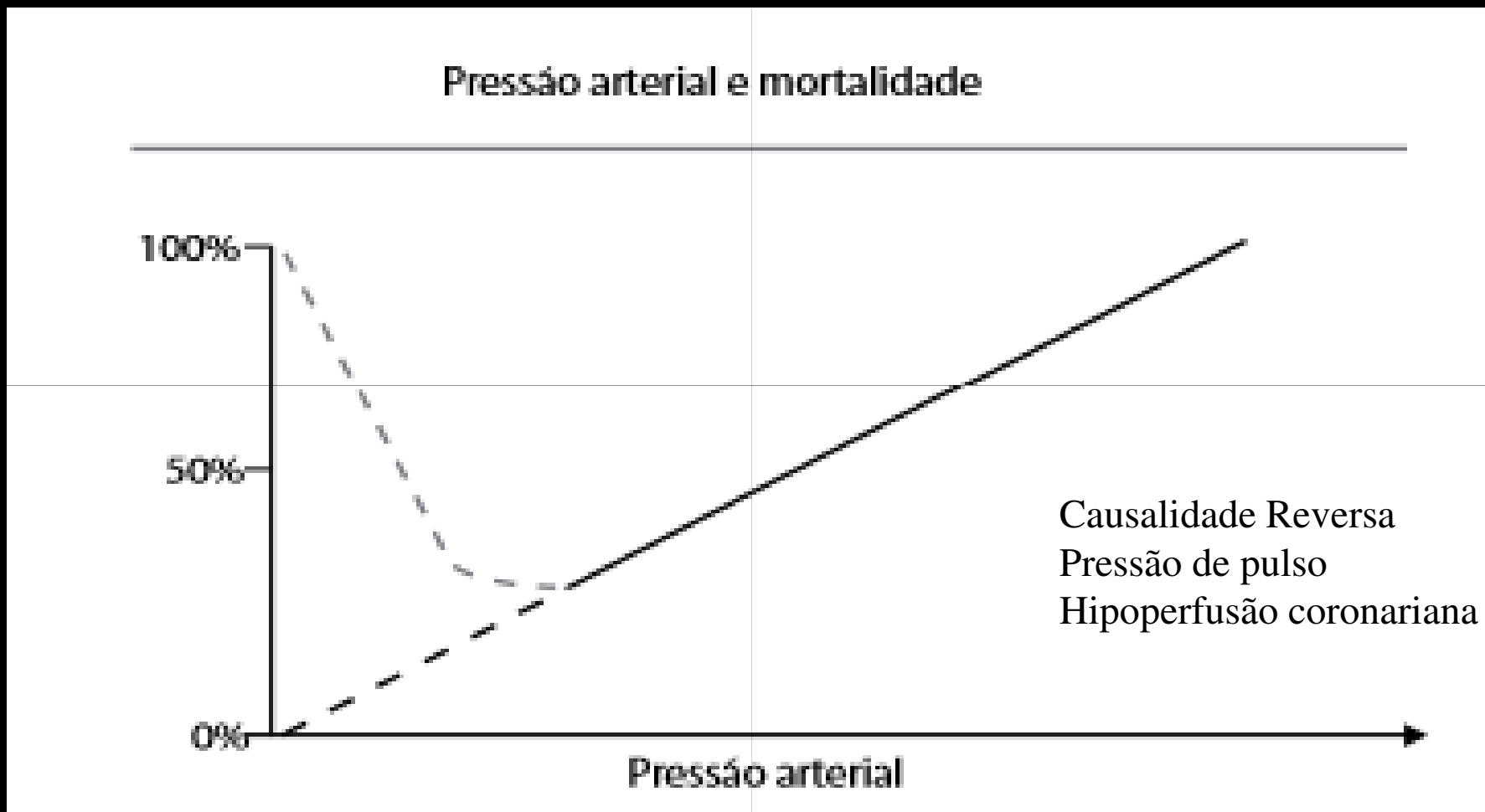
HOT randomised trial. Lancet 1998;351:1755-62.

UKPDS - THE LANCET • Vol 352 • September 12, 1998

ABCD N Engl J Med 2000; 343:1969.

ADVANCED. N Engl J Med 2008 Jun 6.

# Relation of reduction in pressure to first myocardial infarction in patients receiving treatment for severe hypertension.



Lancet 1979, 1(8121):861-865.

JACC Vol. 54, No. 20, 2009:1827-34

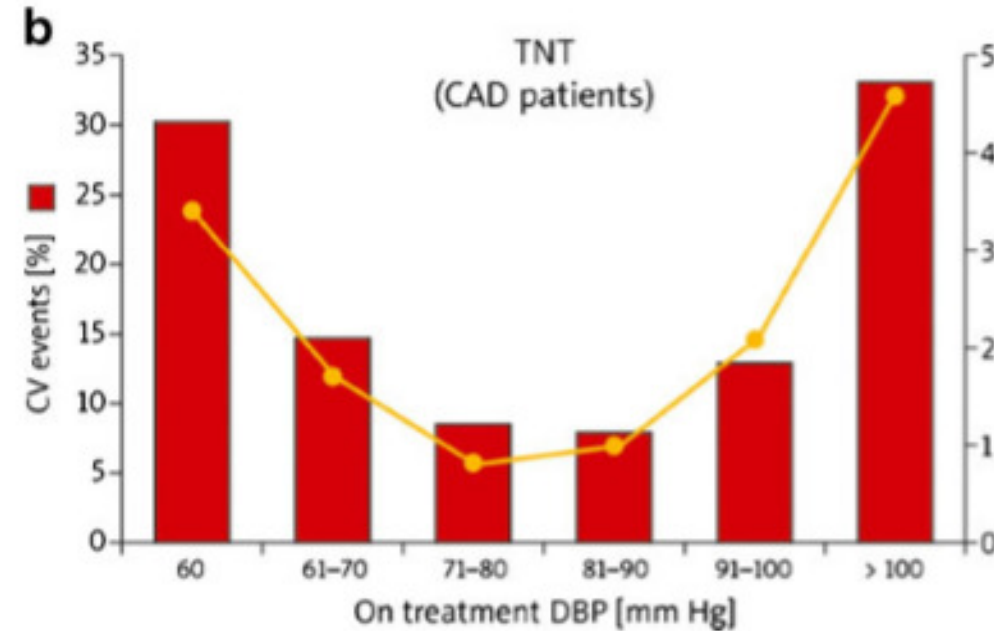
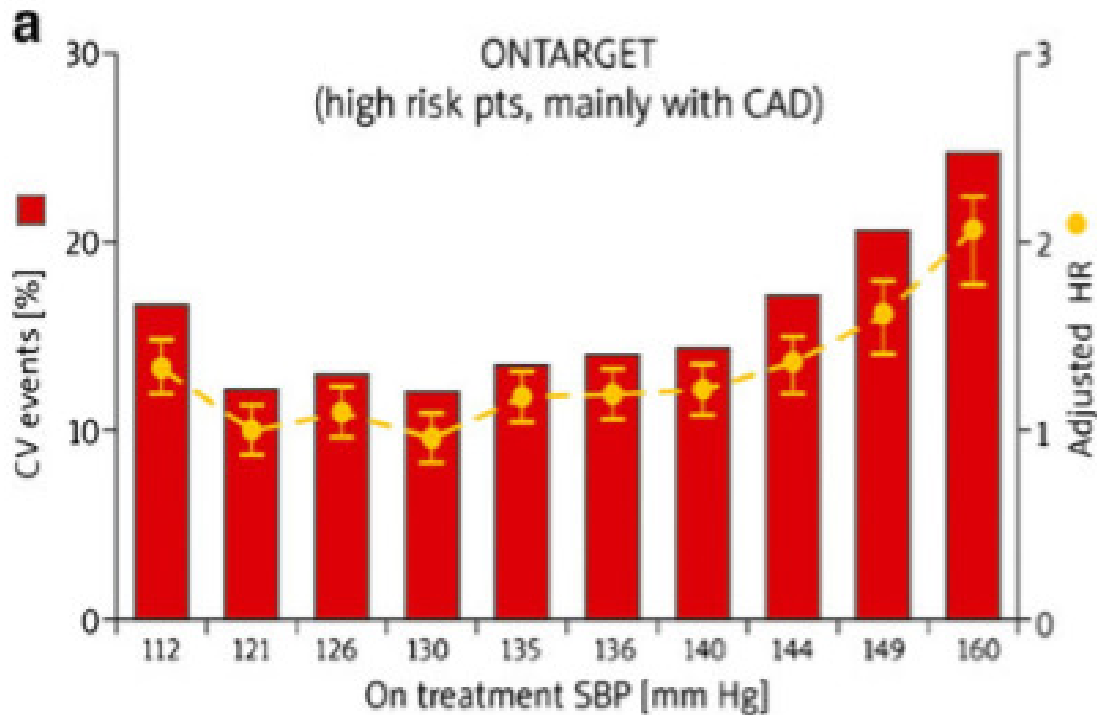
Rev Bras Hipertens vol.17(3):156-159, 2010.



# Curva J e Desfechos Cardiovasculares

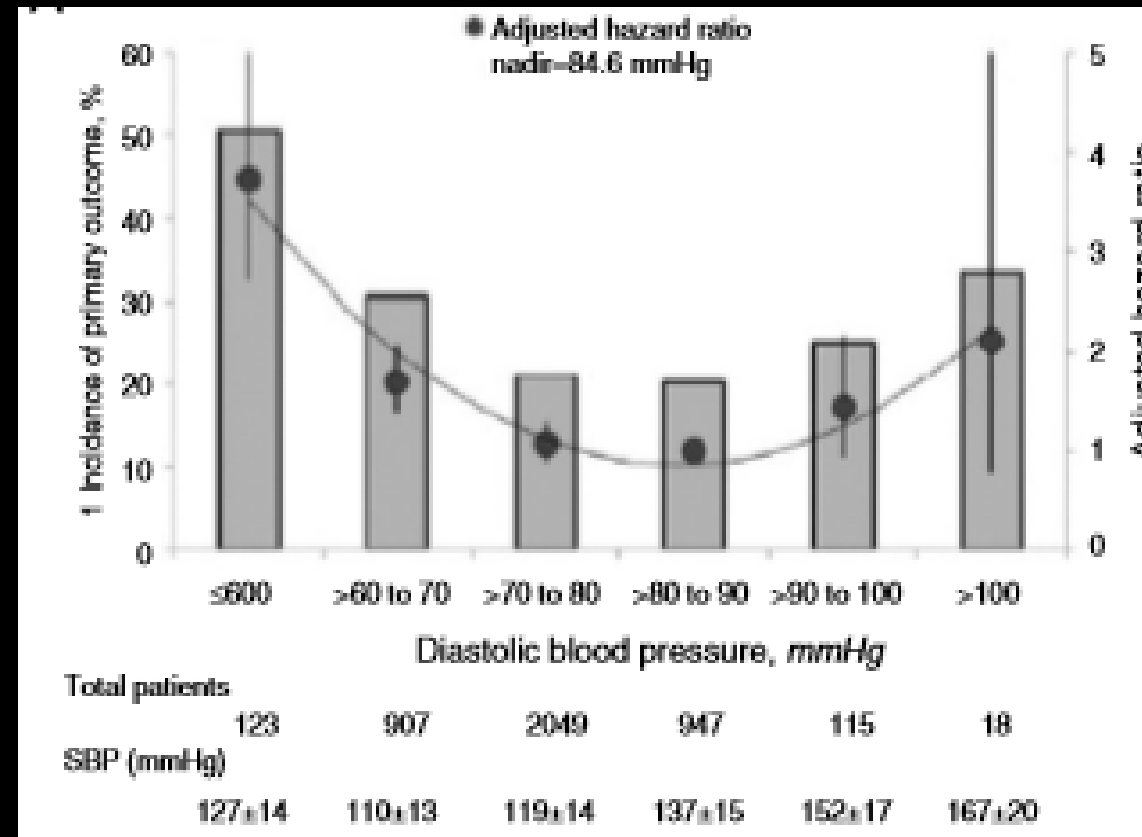
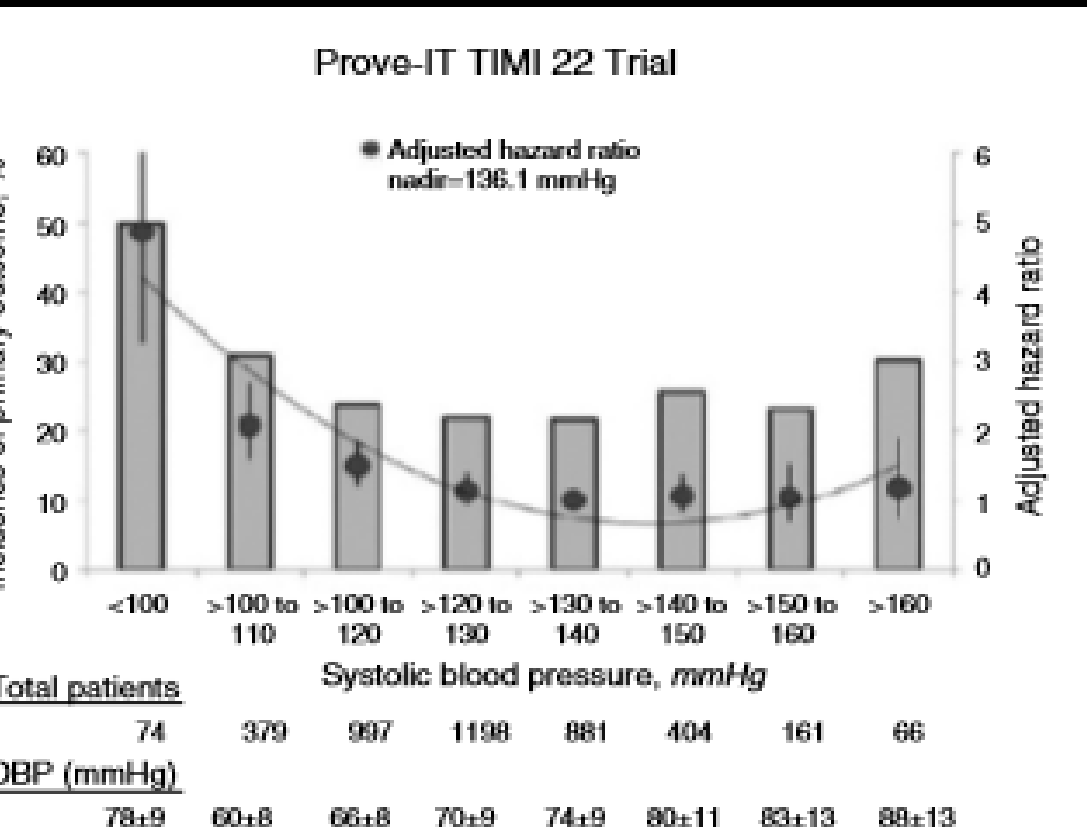
Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET)

Treating to New Targets (TNT)

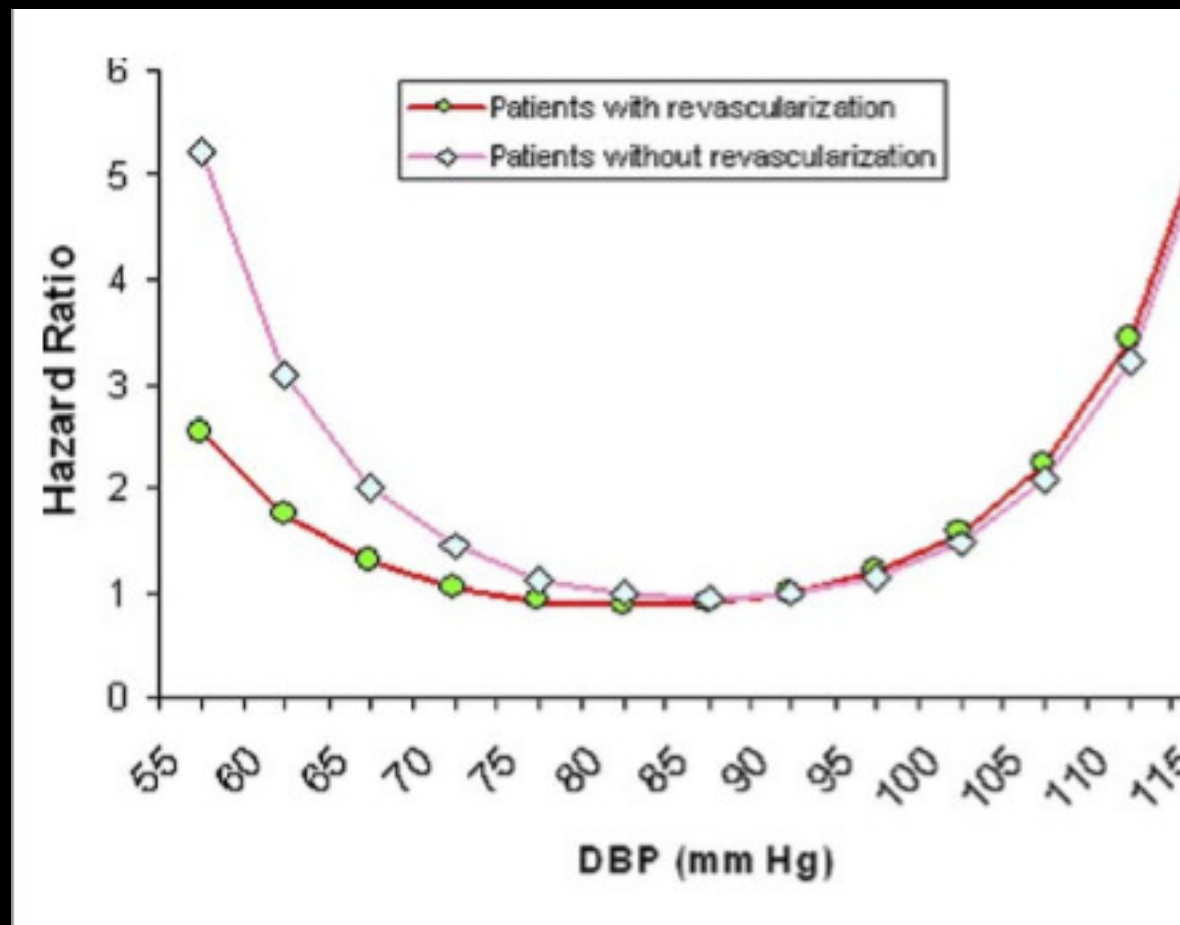
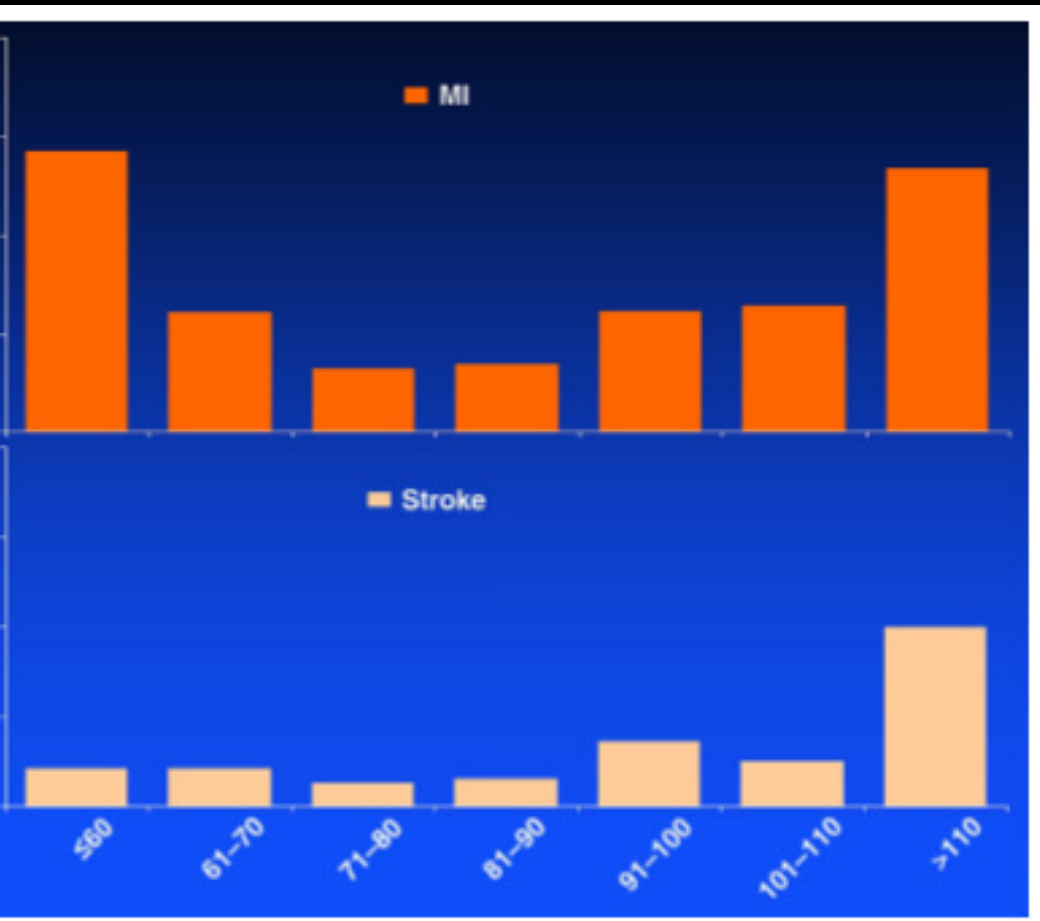


**Fig. 1** J-curve in the (a) ONTARGET ([10] modified according to [33]) and (b) TNT ([10] modified according to [37]) studies

# PRavastatin OR atorVastatin Evaluation and Infection Therapy-Thrombolysis In Myocardial Infarction (PROVEIT-TIMI) 22 trial.



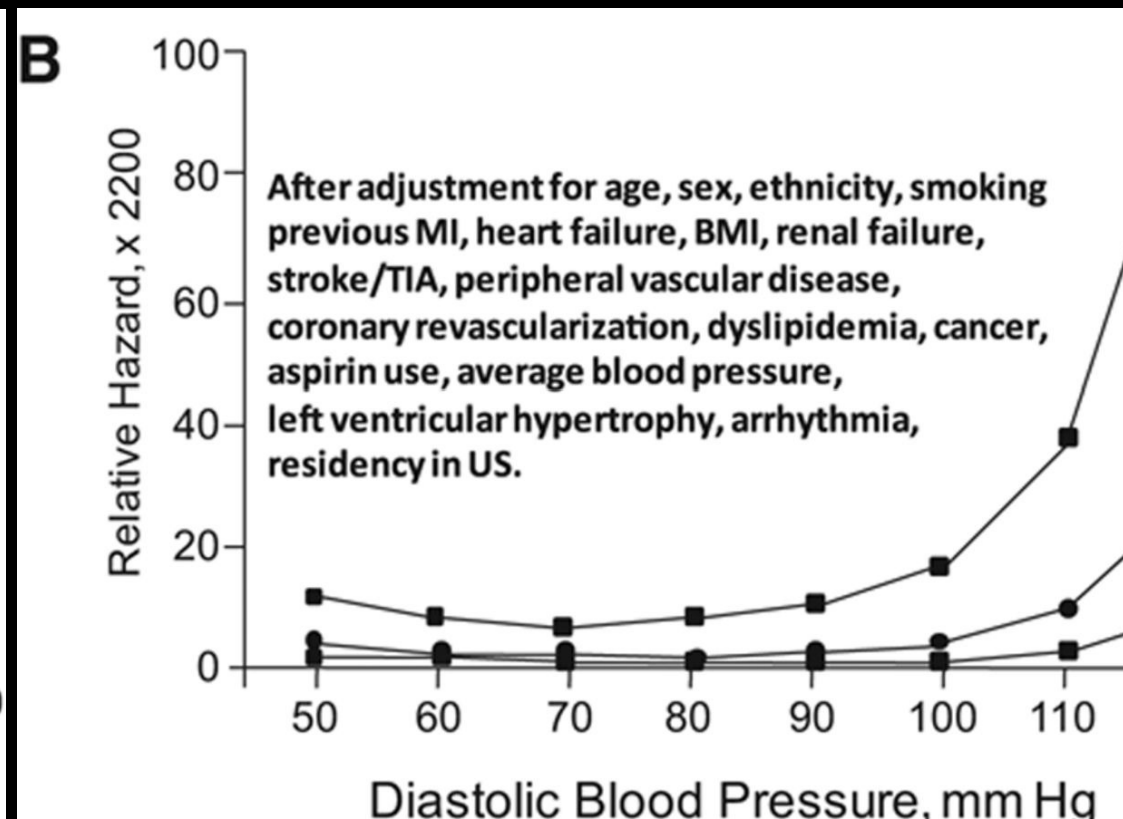
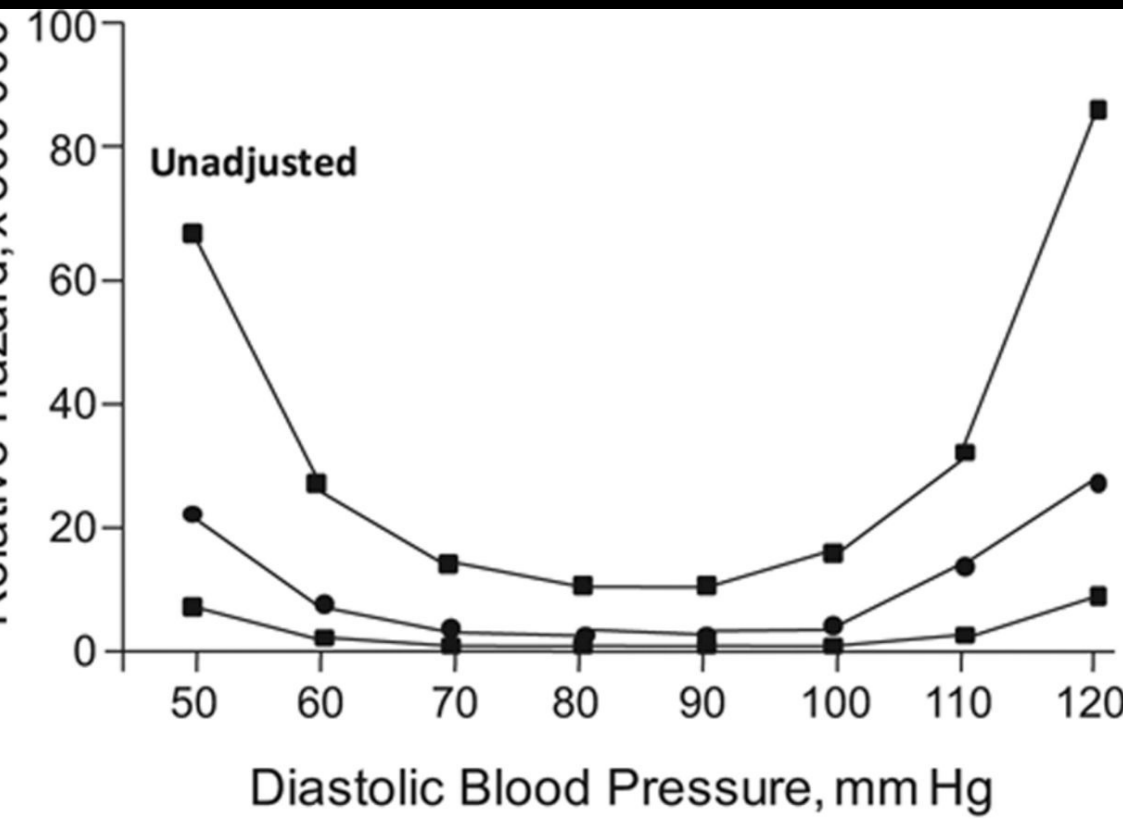
# The J-Curve Between Blood Pressure and Coronary Artery Disease or Essential Hypertension



ulation. 2010;122:2142---51.67

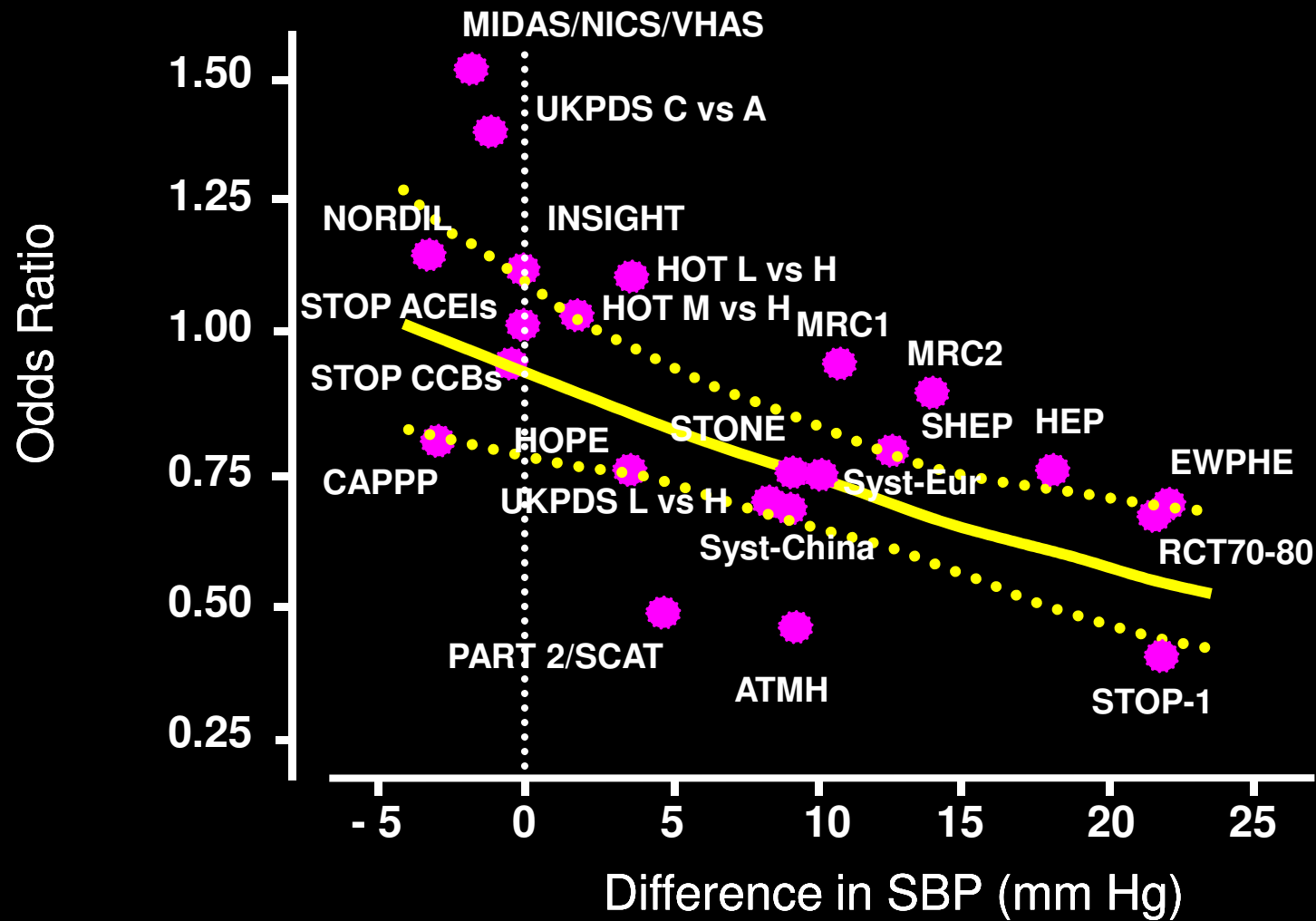
CC Vol. 54, 2009:1827-34

# Aggressive Blood Pressure Lowering Is Dangerous: The J-Curve



Unadjusted (A) and adjusted (B) relation between achieved (average in-treatment) diastolic blood pressure and risk of primary end point in hypertensive patients with coronary artery disease enrolled in the International Verapamil-Trandolapril Study.

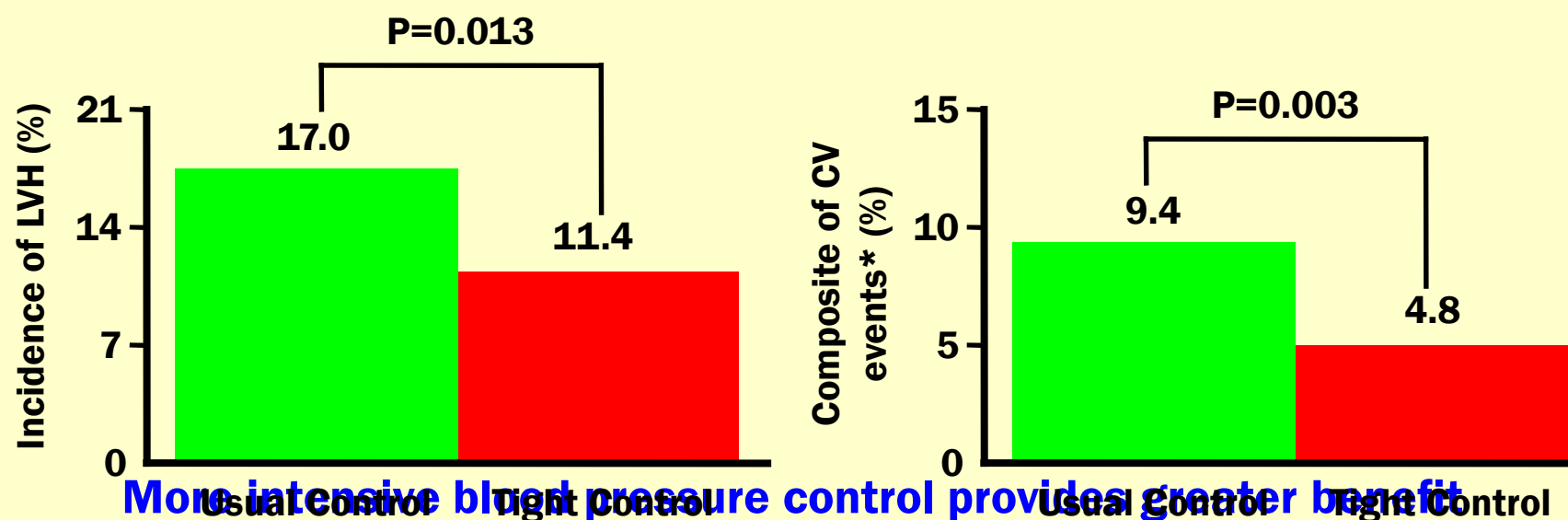
# Relação entre Redução da SBP e a Mortalidade Cardiovascular



Staessen JA, et al. *Lancet*. 2001;358:1305-15.

# Cardio-SIS Trial

1,111 patients  $\geq 55$  years with SBP  $\geq 150$  mm Hg randomized to treatment to achieve usual BP control (SBP  $< 140$  mm Hg) or intensive BP control (SBP  $< 130$  mm Hg)



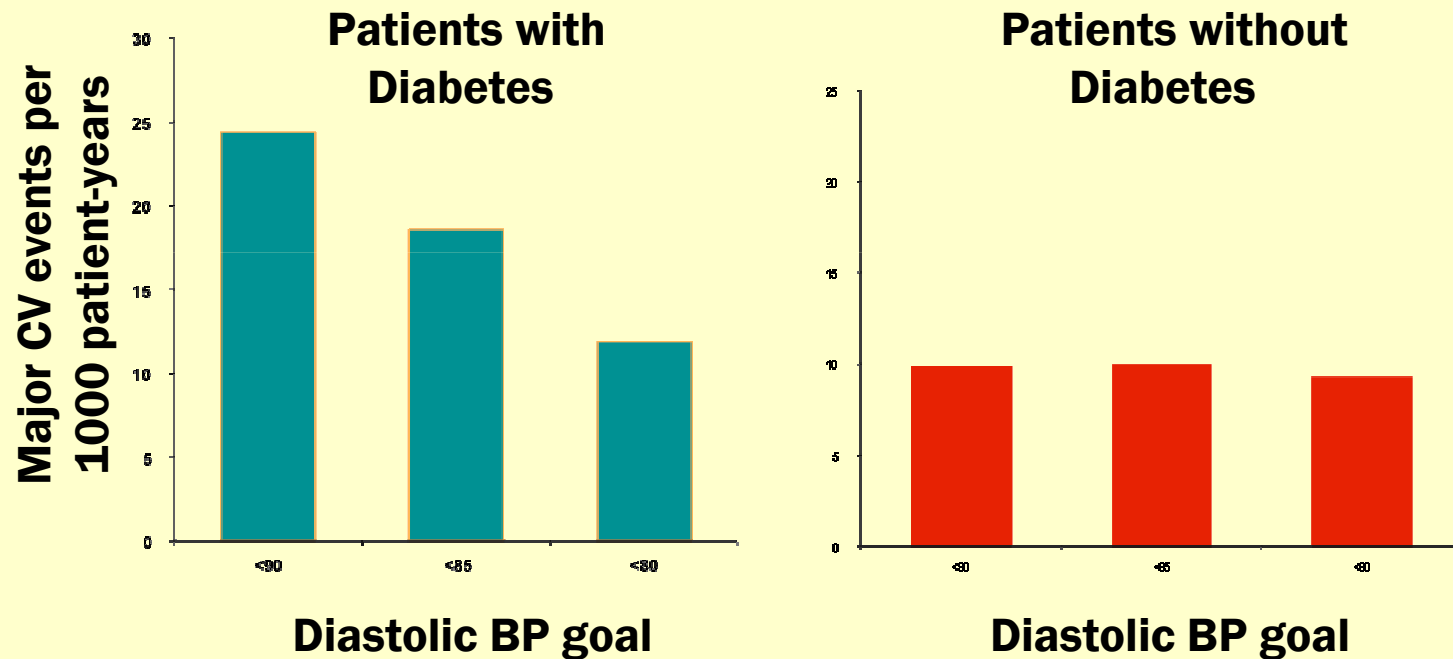
\*Composite of death, MI, CVA, TIA, CHF, angina, new AF, revascularization, aortic dissection, PAD, and ESRD

AF=Atrial fibrillation, ESRD=End stage renal disease, CHF=Congestive heart failure, CVA=Cerebrovascular accident, LVH=Left ventricular hypertrophy, MI=Myocardial infarction, PAD=Peripheral artery disease, SBP=Systolic blood pressure, TIA=Transient ischemic attack



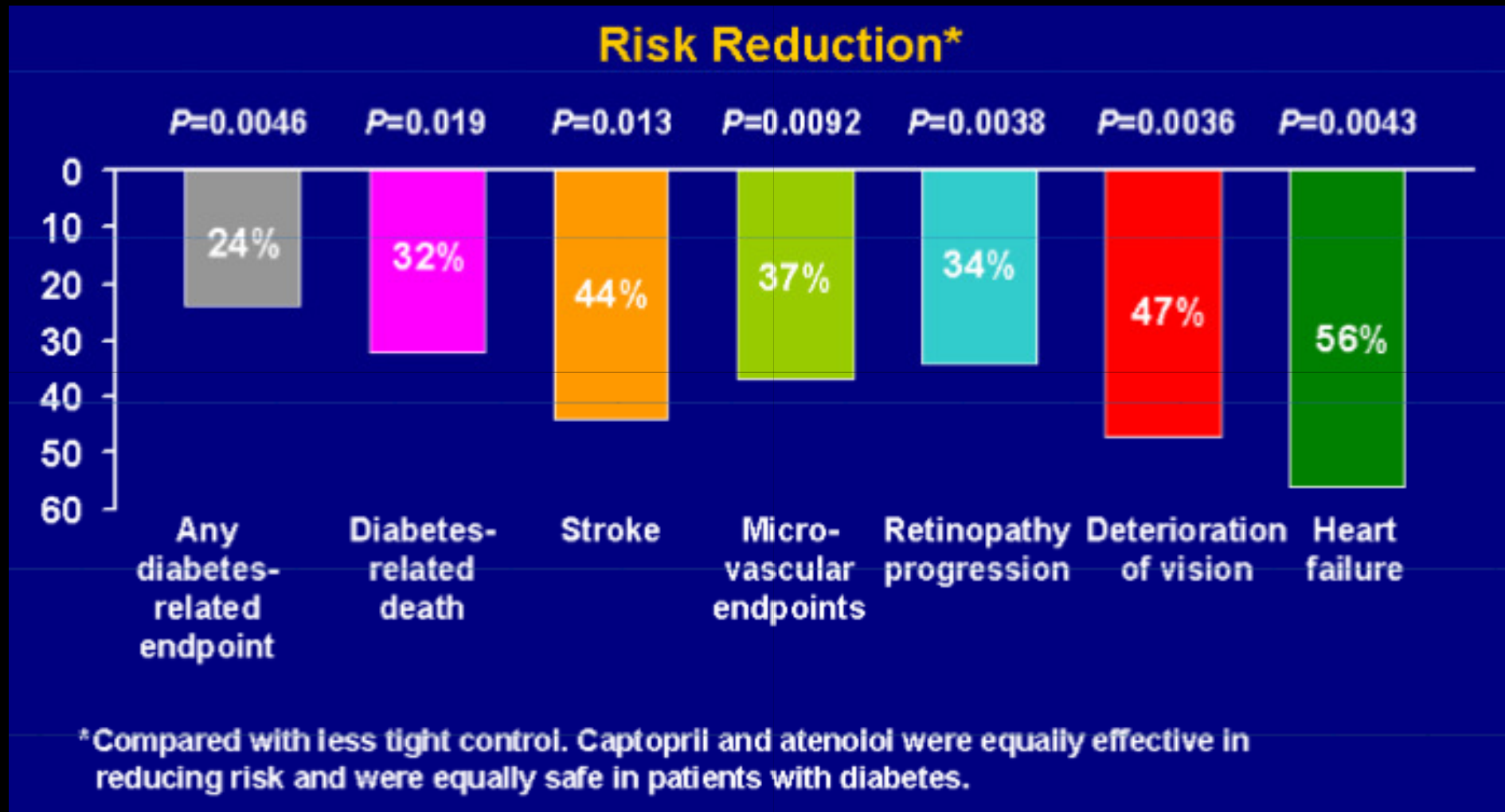
# Hypertension Optimal Treatment (HOT) Study

18,790 patients with a baseline diastolic BP of 100-115 mm Hg randomized to a target diastolic BP of  $\leq 90$  mm Hg,  $\leq 85$  mm Hg, or  $\leq 80$  mm Hg

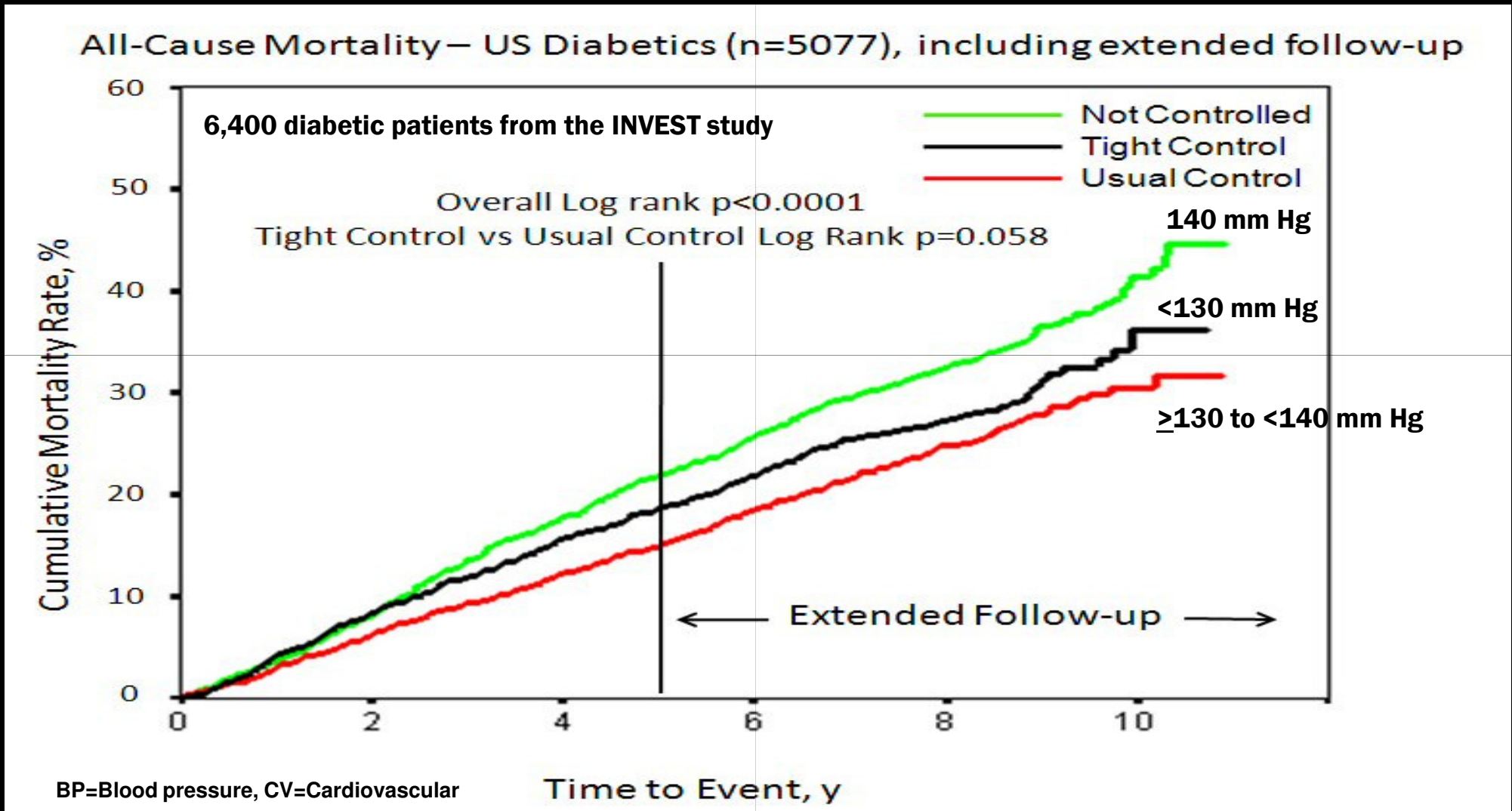


**More intensive blood pressure control provides greater benefit in diabetics**

# UKPDS Results: Tight BP Control

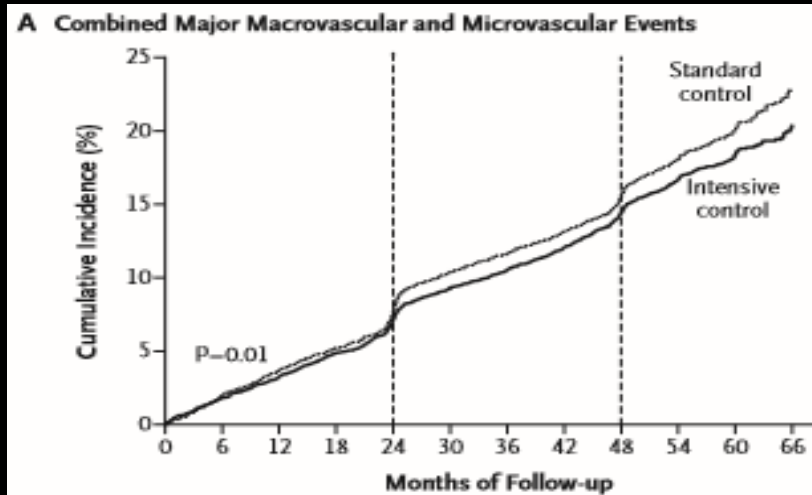


# International Verapamil-Trandolapril Study (INVEST)—DM Substudy



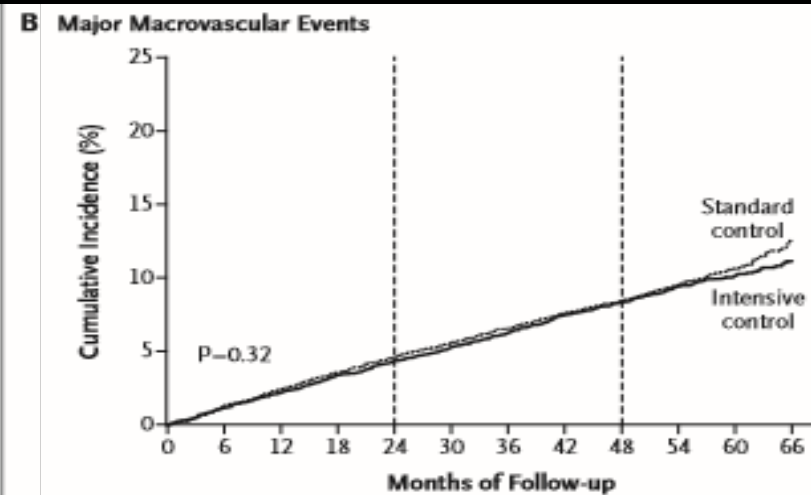
# Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes

## The ADVANCE Collaborative Group



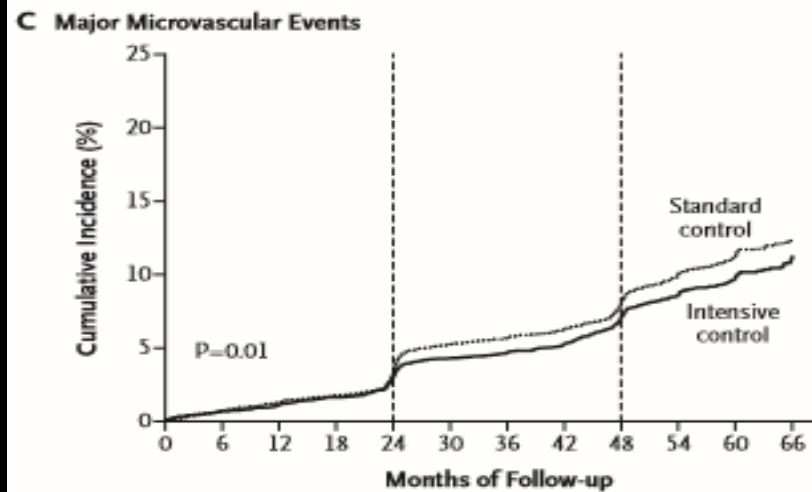
No. at Risk

Intensive	5570	5457	5369	5256	5100	4957	4867	4756	4599	4044	1883	447
Standard	5569	5448	5342	5240	5065	4903	4808	4703	4545	3992	1921	470



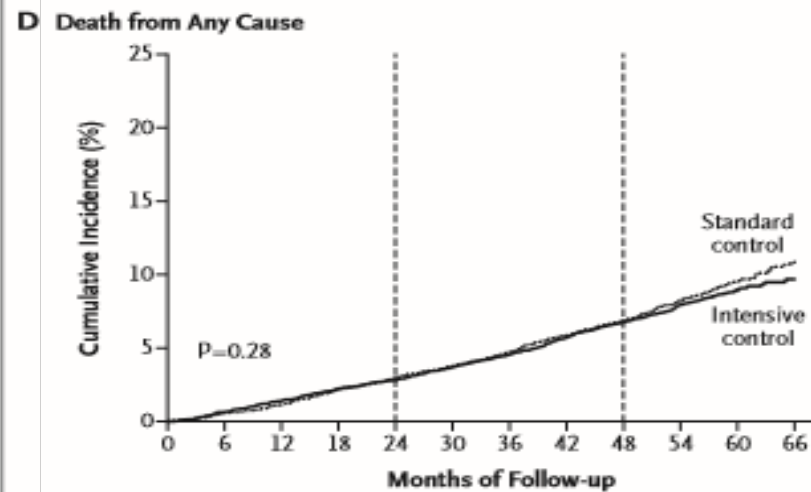
No. at Risk

Intensive	5570	5494	5428	5338	5256	5176	5097	5005	4927	4396	2071	486
Standard	5569	5486	5413	5330	5237	5163	5084	4995	4922	4385	2108	509



No. at Risk

Intensive	5571	5495	5430	5358	5233	5120	5055	4968	4824	4258	1992	473
Standard	5569	5498	5431	5353	5207	5069	4995	4911	4764	4204	2024	494



No. at Risk

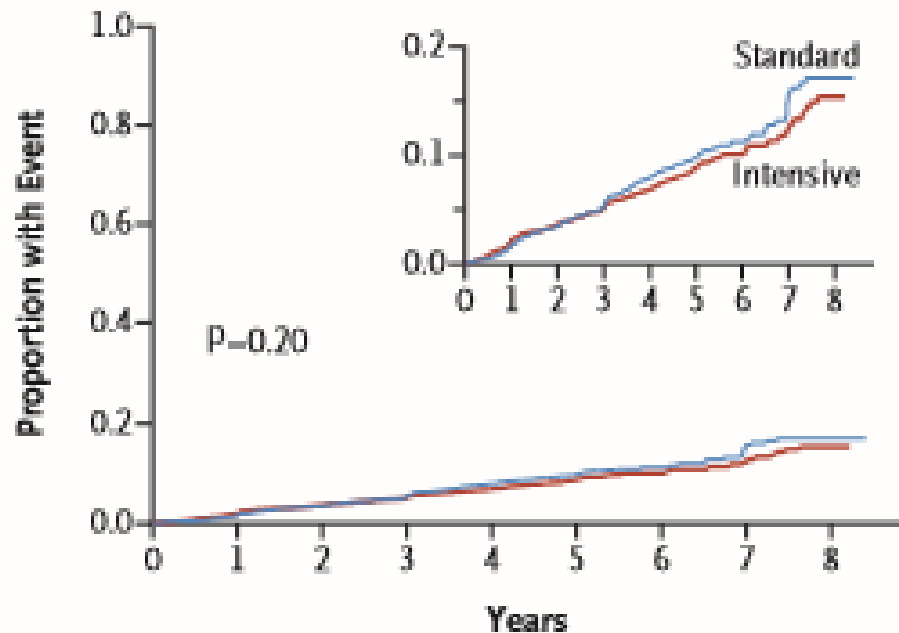
Intensive	5571	5533	5490	5444	5411	5361	5312	5246	5189	4653	2211	523
Standard	5569	5537	5503	5445	5399	5354	5301	5237	5178	4643	2240	544

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

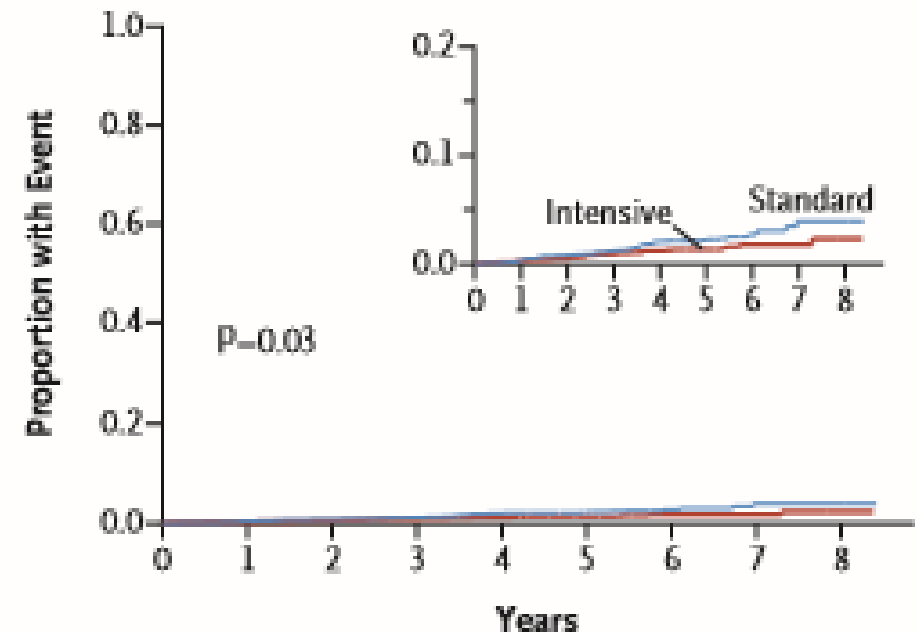
## The ACCORD Study Group

1407

**A Primary Outcome**



**B Nonfatal Stroke**



**No. at Risk**

Intensive	2362	2273	2182	2117	1770	1080	298	175	80
Standard	2371	2274	2196	2120	1793	1127	358	195	108

**No. at Risk**

Intensive	2362	2291	2223	2174	1841	1128	313	186	88
Standard	2371	2287	2235	2186	1879	1196	382	215	114

**No. at Risk**

Intensive	2174	2071	1973	1792	1150	445	156	156
Standard	2208	2136	2077	1860	1241	504	203	201

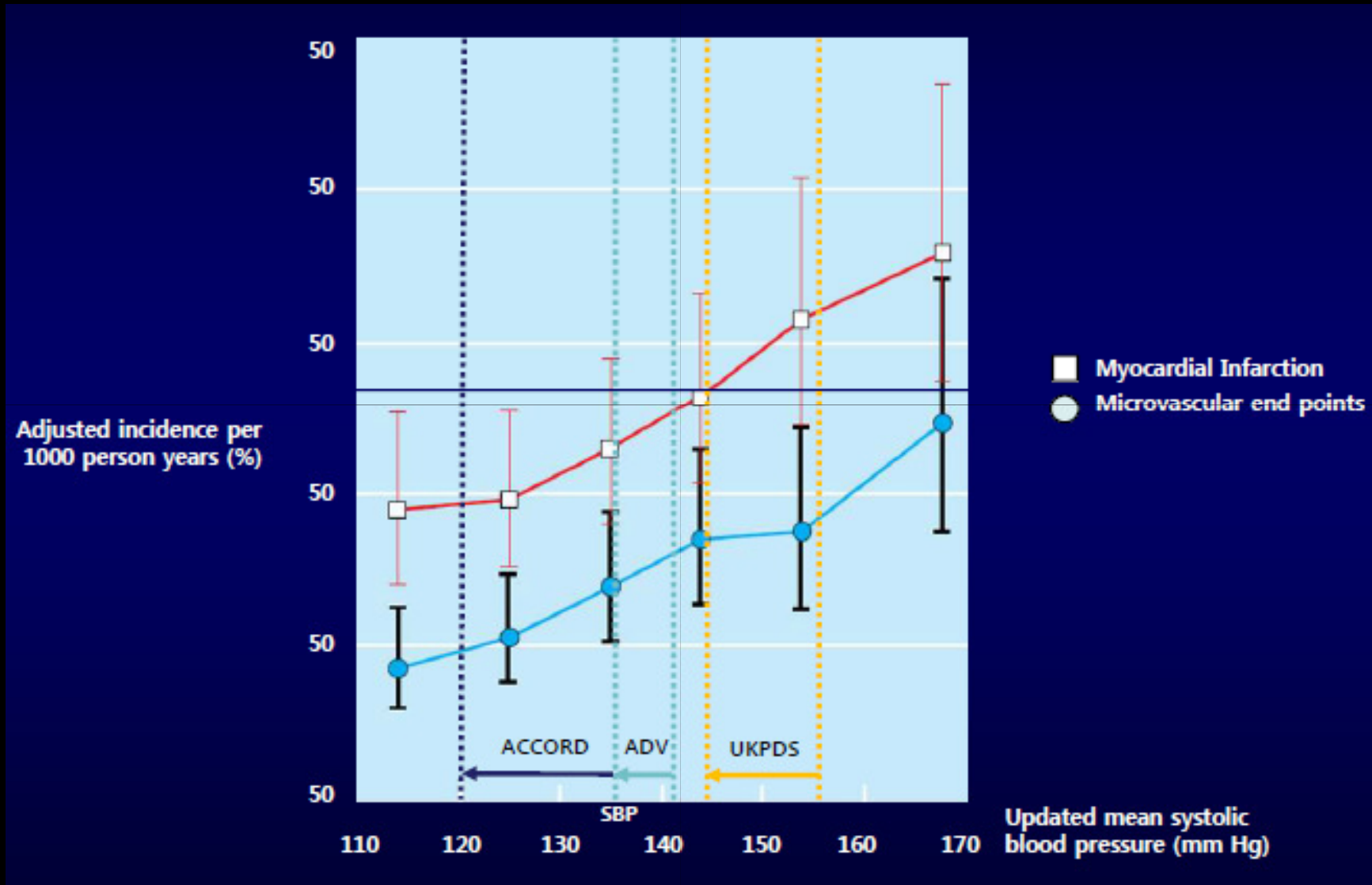
# ACCORD Results are Mixed

Outcome	Intensive Events (%/yr)	Standard Events (%/yr)	HR (95% CI)	P
CVD (Primary)	208 (1.87)	237 (2.09)	0.88 (0.73-1.06)	0.20
Cardiovascular Deaths	60 (0.52)	58 (0.49)	1.06 (0.74-1.52)	0.74
<b>Total Stroke</b>	<b>36 (0.32)</b>	<b>62 (0.53)</b>	<b>0.59 (0.39-0.89)</b>	<b>0.01</b>

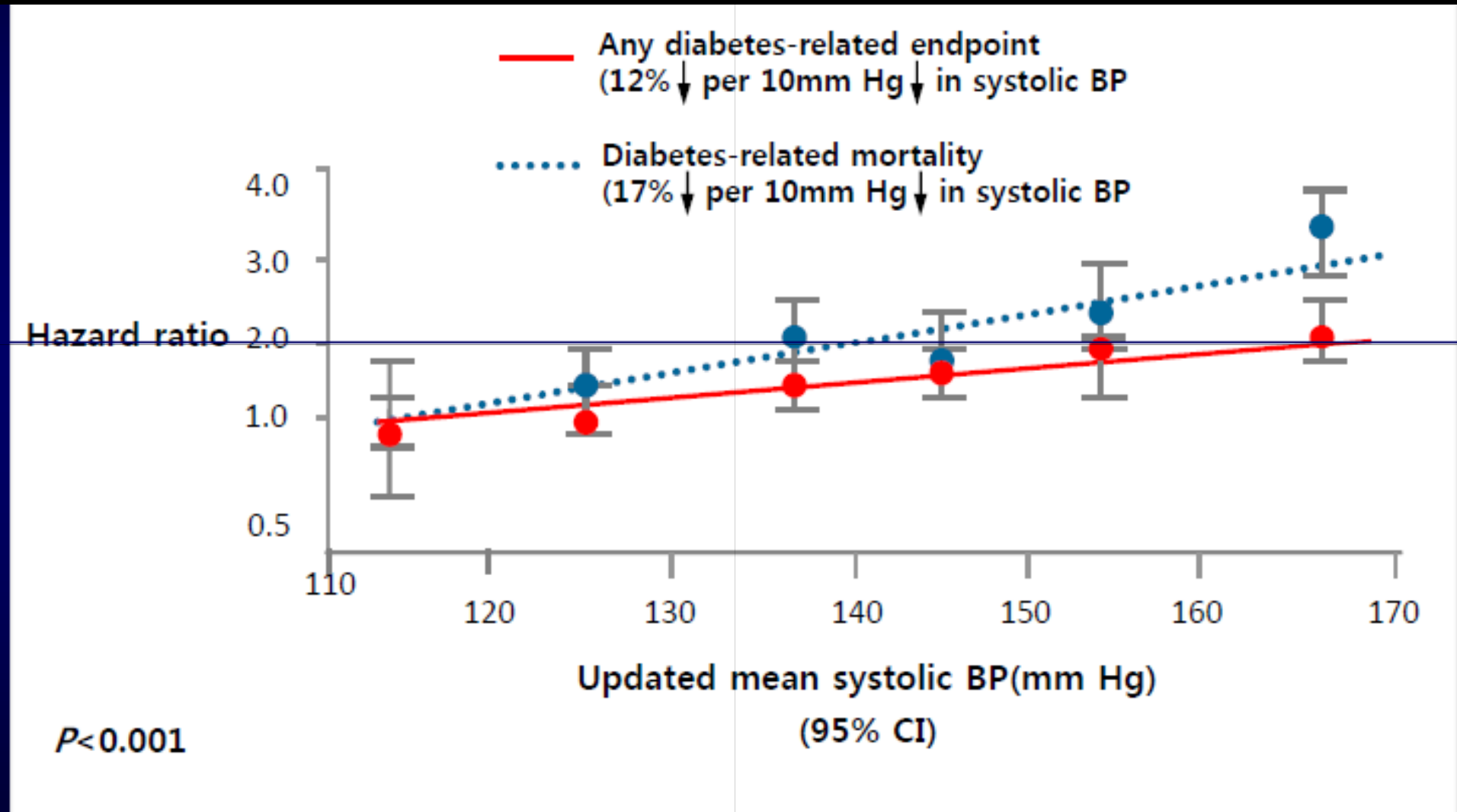
ACCORD study group. *NEJM* 2010;362:1575-1585



# UKPDS, ADVANDE AND ACCORD Trial



# No J-Curve in UKPDS



# What Make This Difference?

	<i>ACCORD</i>	<i>INVEST</i>	<i>ONTARGET</i>	<i>UKPDS</i>
<b>Age</b>	62	66	66.4	<b>53</b>
<b>DM duration (years)</b>	10	May be long?	% of DM Pts = 37.5	<b>0</b>
<b>Prior CV event (%)</b>	34%	100%	MI 49%, stable angina 34.8%	<b>0</b>

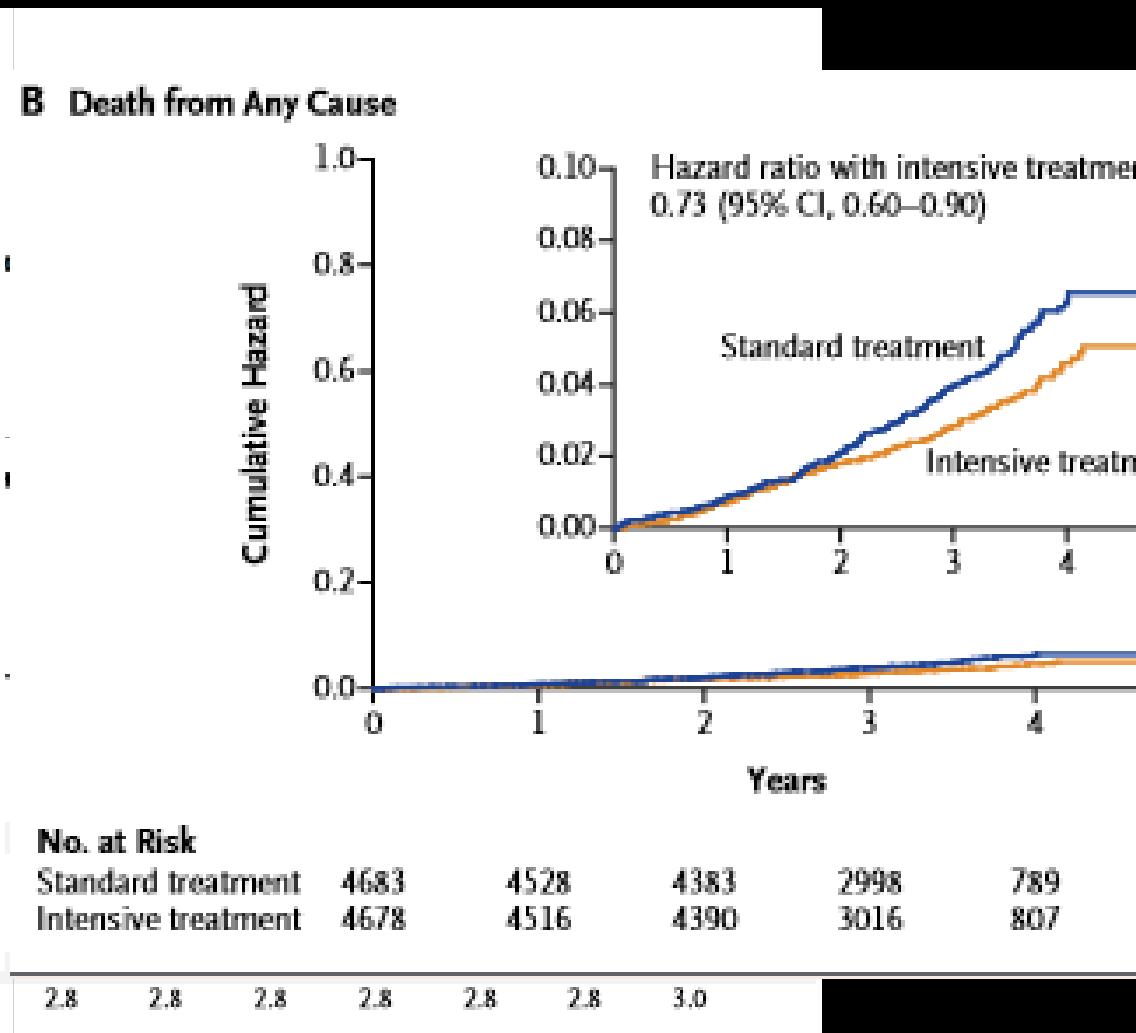
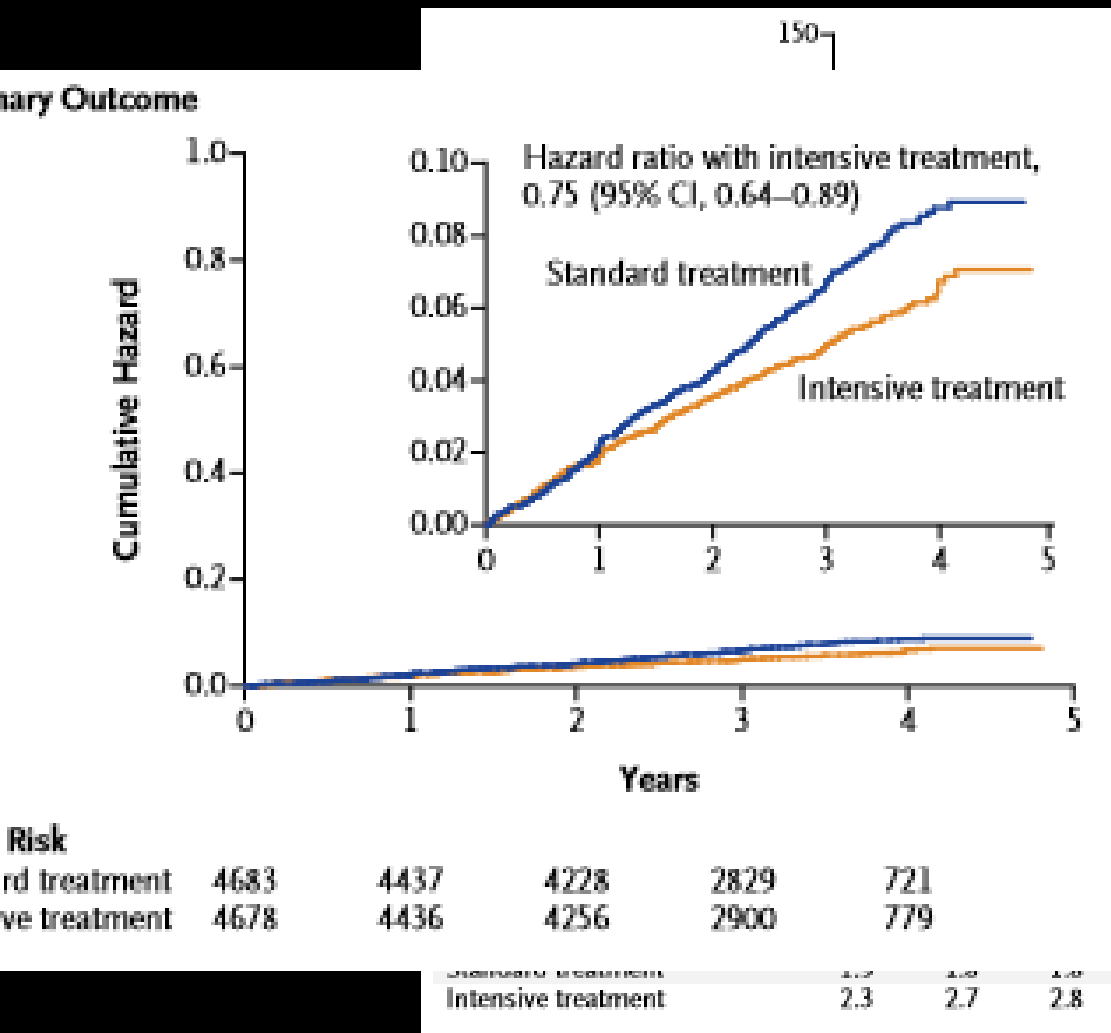
## A Lesson from Unsuccessful Trial - ABC Management in ACCORD

	Intensive	Standard
A1c (average)	6.4%	7.5%
Blood pressure - systolic (average)	119.3 mmHg	133.5 mmHg
Cholesterol (at the end)		
LDL cholesterol	81.1 mg/dl	80 mg/dl
Triglyceride	122 mg/dl	144 mg/dl
HDL cholesterol	41.2 mg/dl	40.5 mg/dl

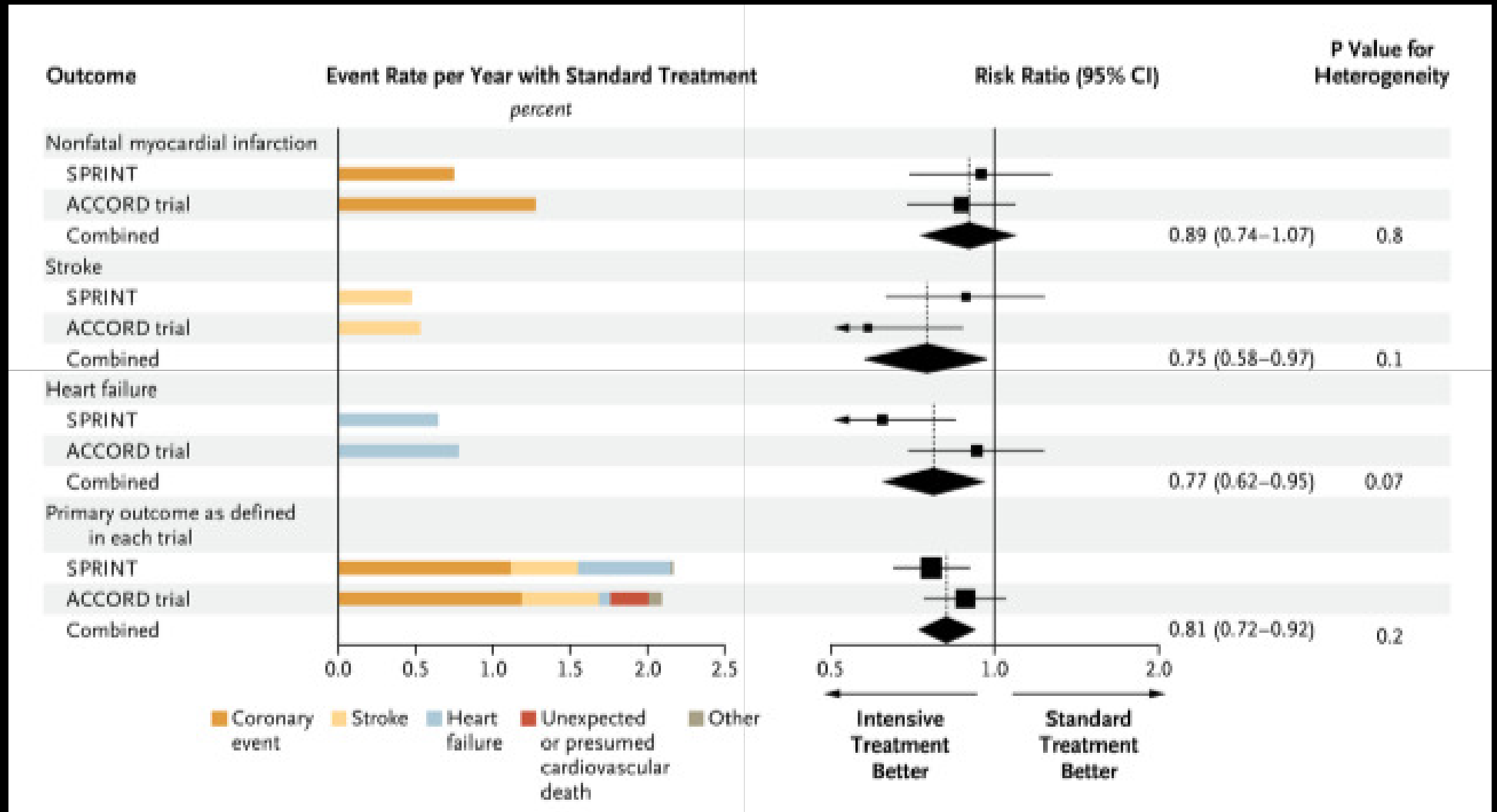
***Event rate in the standard therapy group was  
50% lower than the expected rate  
- Multifactorial intervention is important!***

# A Randomized Trial of Intensive versus Standard Blood-Pressure Control

## The SPRINT Research Group



# Hypertension Treatment ACCORDing to SPRINT





## A curva J teria importância no tratamento em DM?

1. Recomenda-se manter níveis pressóricos sistólicos < 130 mmHg em portadores de DM e em pacientes de muito alto risco cardiovascular (eventos CV prévio).
2. O fenômeno da Curva – J pode ocorrer em portadores de doença aterosclerótica arterial, na vigência de controle pressórico excessivo.