혈압을 어디까지 낮출 것인가?

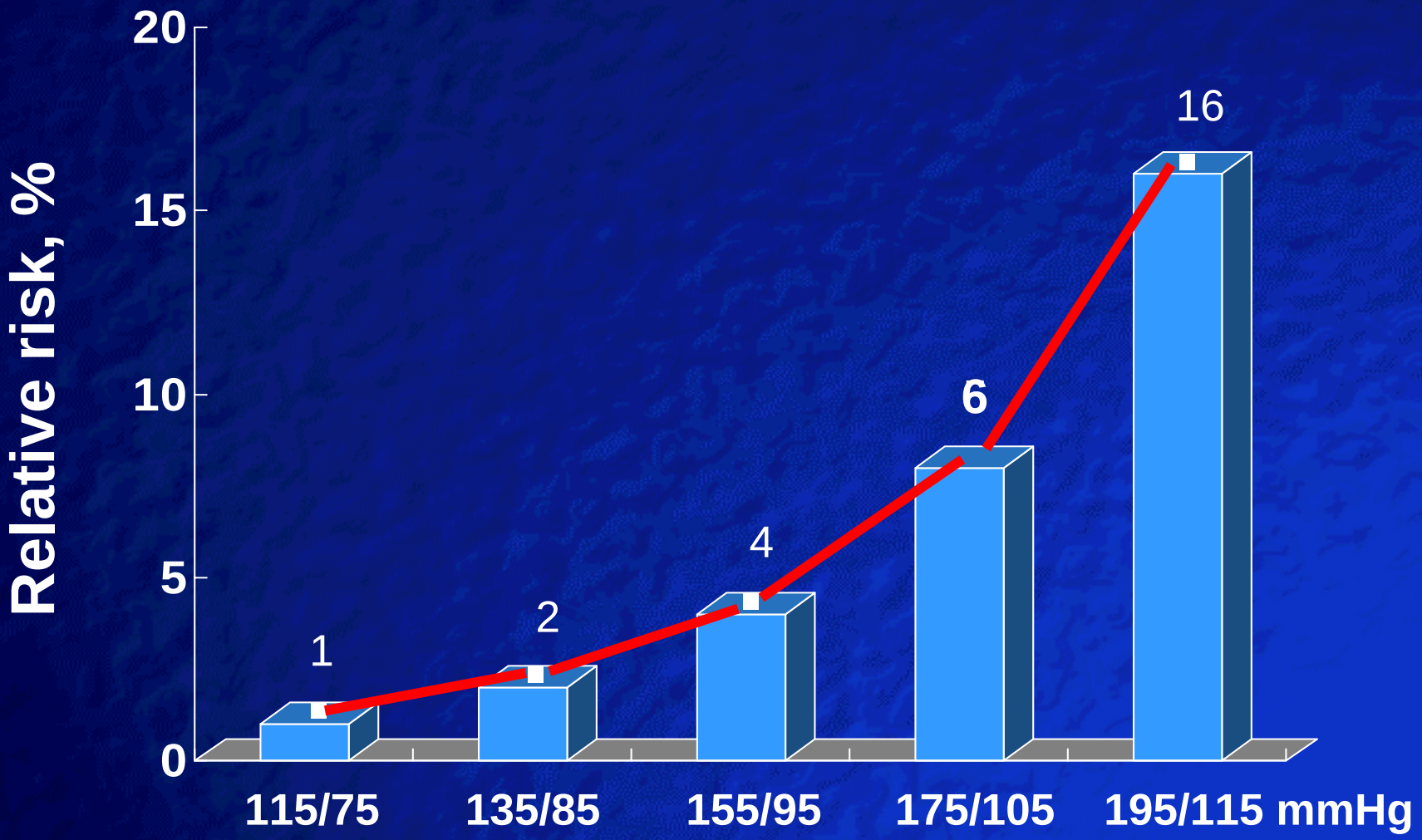
J-curve가 있다.

성균관의대 삼성제일병원 내과

박 정 배

2004 10 14-15 추계순환기 학회, 서울

Association of Blood Pressure and Risk of Cardiovascular Mortality



Lewington, et al. *Lancet* 2002

Importance of BP control

이완기 혈압이 **5-6** mmHg 줄어들면?

뇌졸중 발생

42% ↓

관상동맥질환 발생

14% ↓

이완기 혈압이 **10** mmHg 줄어들면?

뇌졸중에 의한 사망

56% ↓

관상동맥질환에 의한 사망

37% ↓

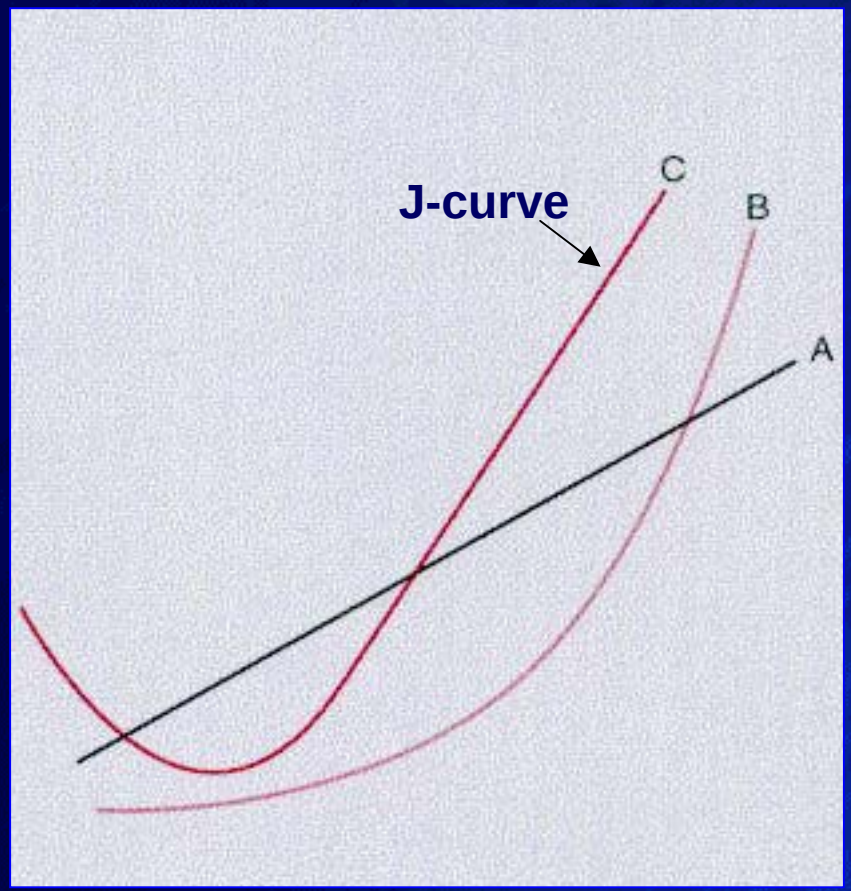
집착과 몰두는 다릅니다.

집착은 한 가지에 빠져 주변을 전혀 보지 못하는 것이고

몰두는 한 가지에 집중하되 앞뒤좌우 주변도 함께 살펴가는 것입니다.

<고도원의 아침편지에서>

J-곡선의 가설



C; Cruickshank 에 의한 J –곡선; 어느 정도 이완기 혈압이 떨어지면 심혈관계 위험은 줄지만 그 이하에서는 오히려 위험이 증가한다는 가설.

B; 규모가 큰 임상연구에서 혈압을 어느 정도 수준까지는 서서리 떨어지는 것이 좋다는 생각이다 (IPPPSH 연구에서 이완기 혈압 약95 mm Hg 정도).

A; 전통적으로 대부분의 의사들이 생각하는 것처럼 혈압을 떨어뜨리는 정도에 비례해서 심혈관계 위험이 좋아진다.
"the lower, the better."

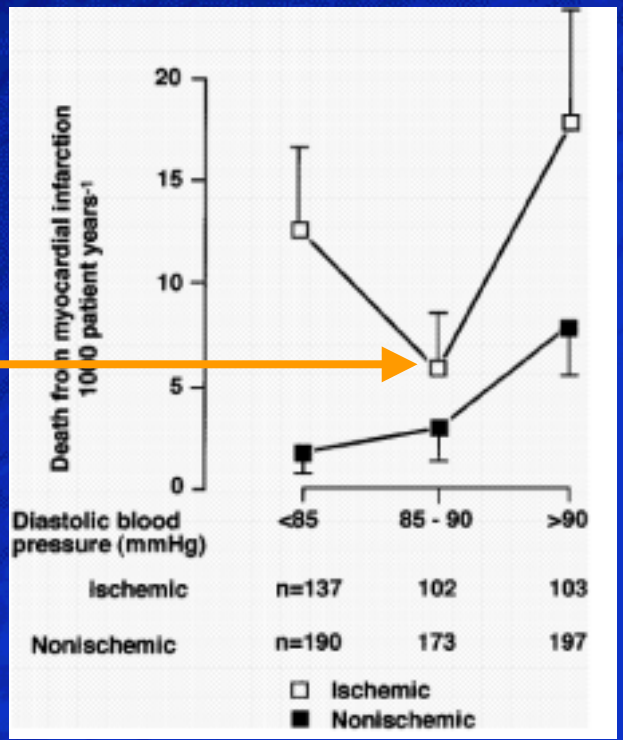
J-곡선의 가설의 배경

1979 Stewart *(Lancet)*
; excessive lowering of DBP by drug
was associated with an increase deaths from CAD.

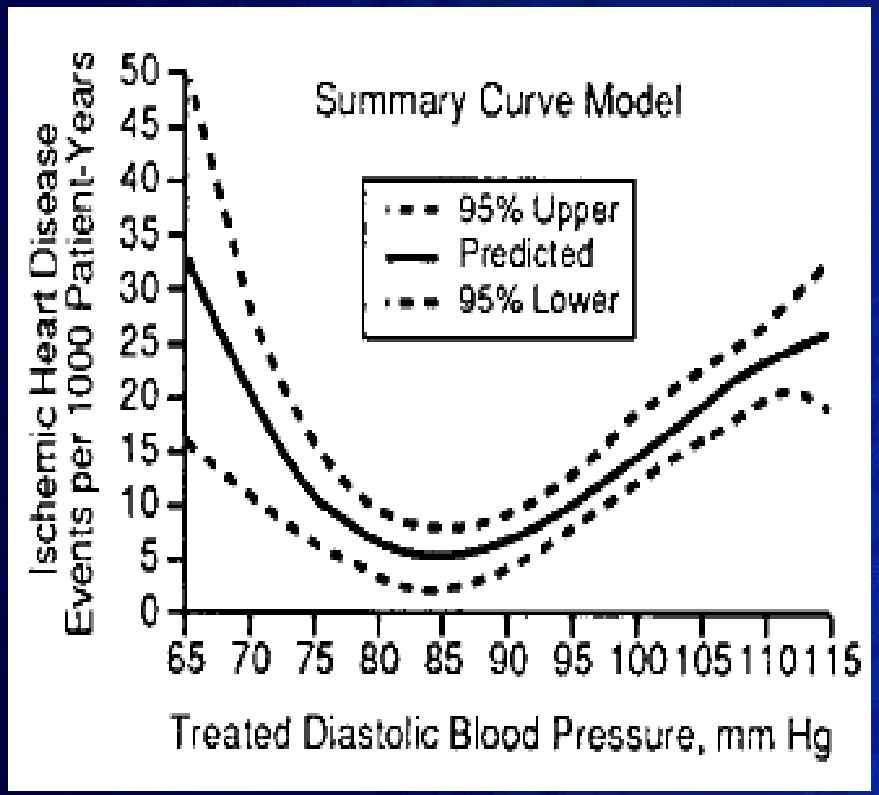
Framingham data ; 1978 *Lancet*
HAPPHY study; 1989 *Am J Hypertens*

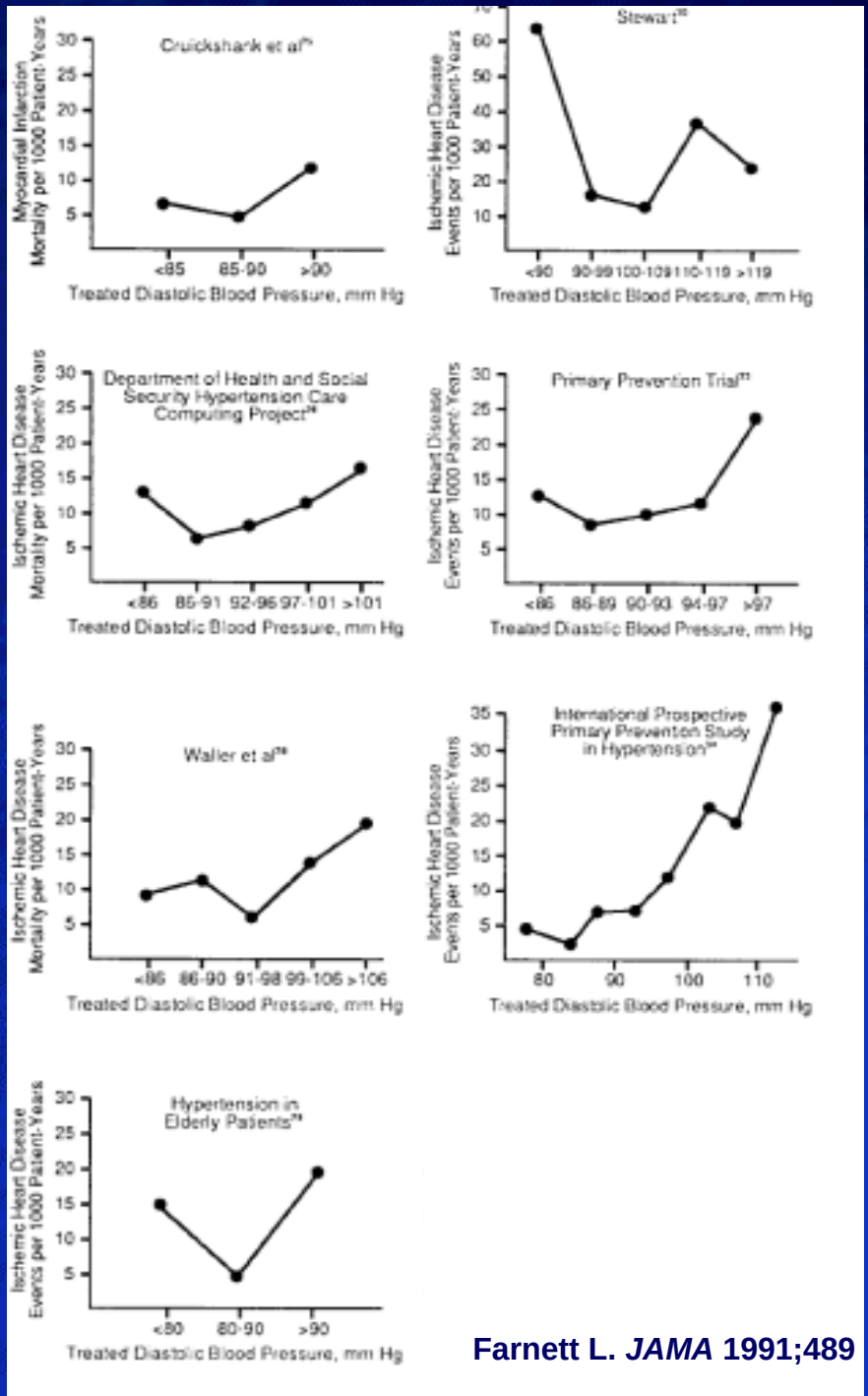
Cruickshank et al. *1987 Lancet*

MRFIT *1985 Am J Cardiol*
HDFP *1986 Drugs*



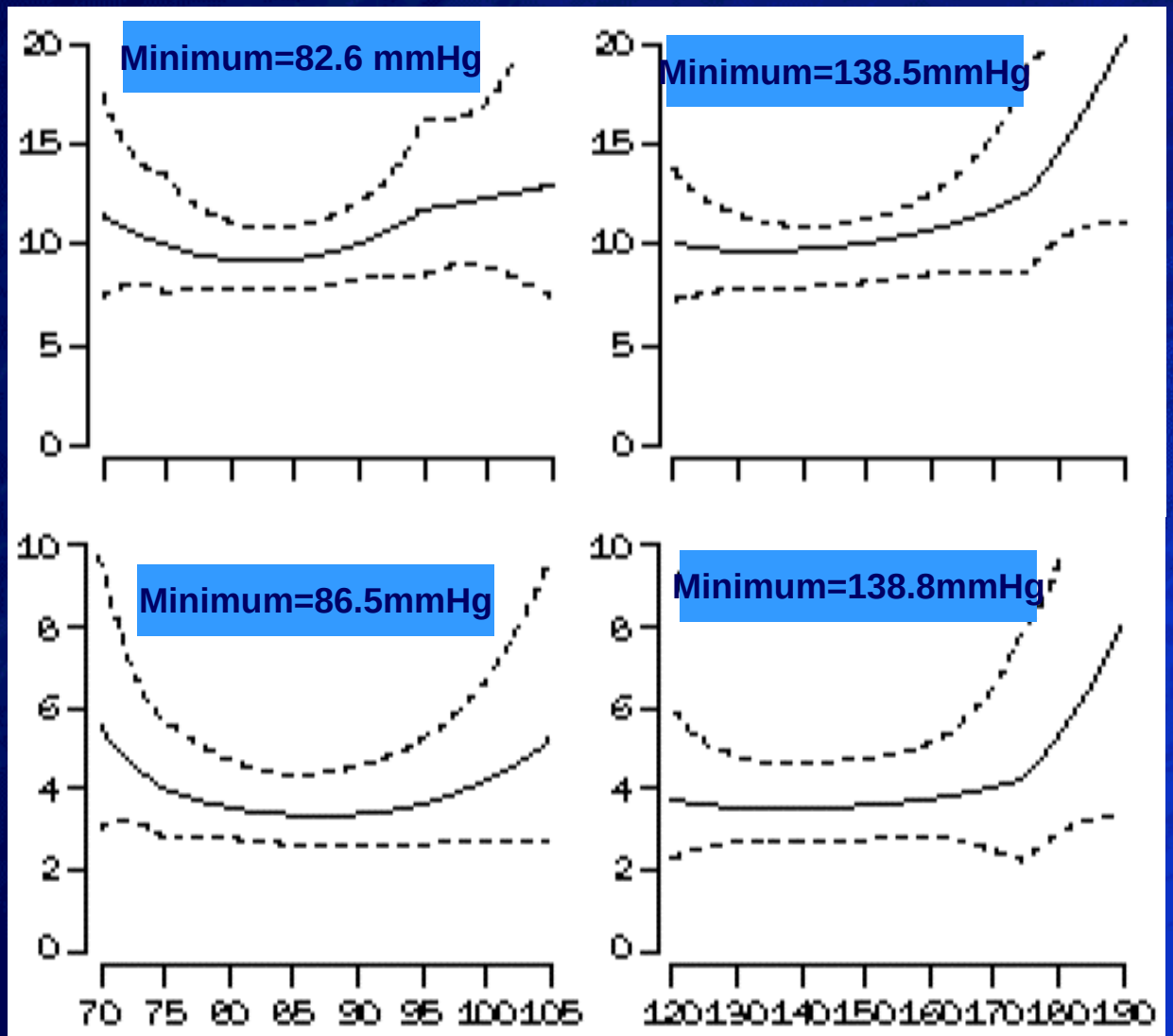
Studies that stratified cardiac events by treated DBP levels.





Farnett L. *JAMA* 1991;489

HOT study *1998 Lancet*

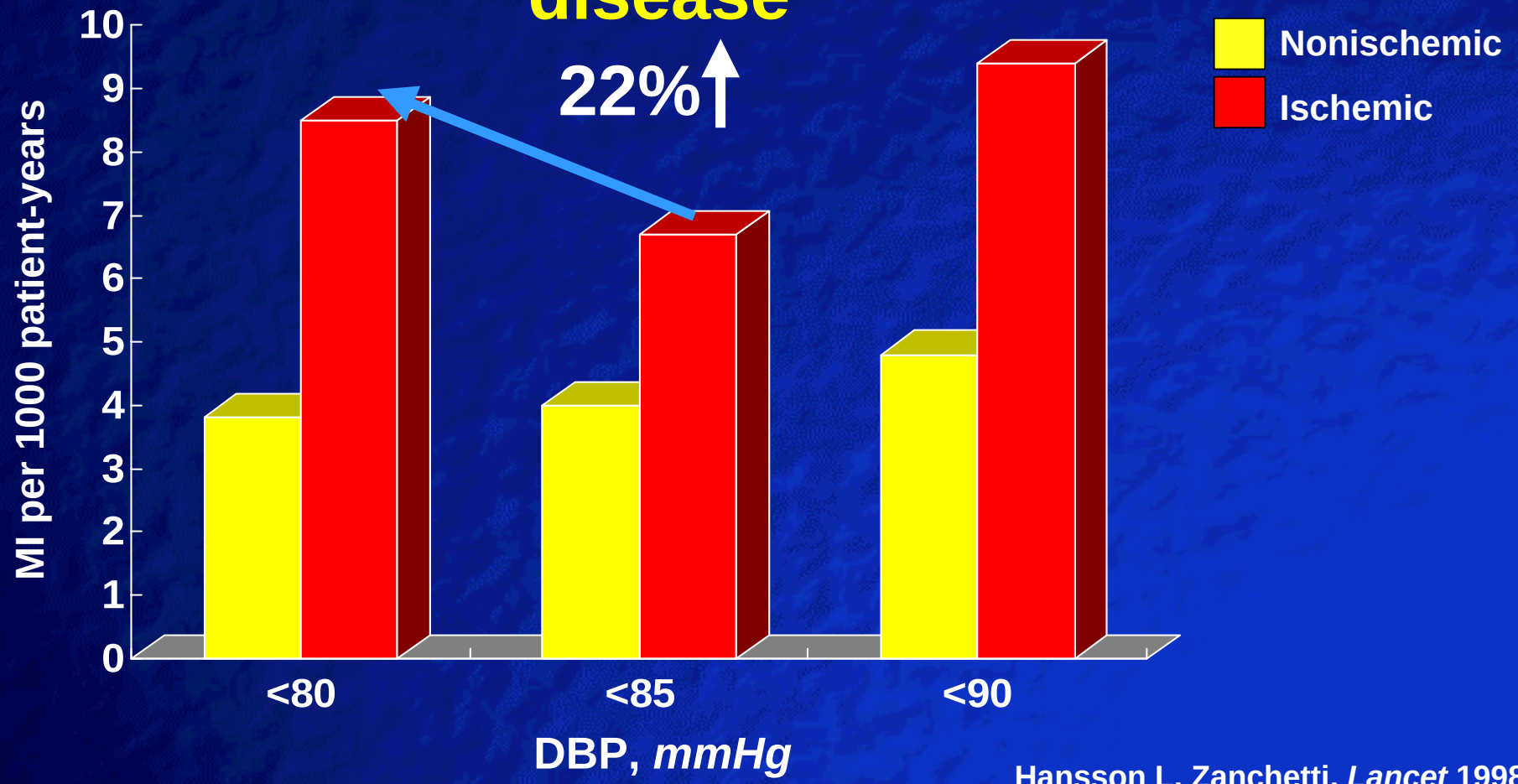


HOT study;
benefits of lowering the diastolic blood pressure down to 82·6 mm Hg.

Conclusion of the HOT study

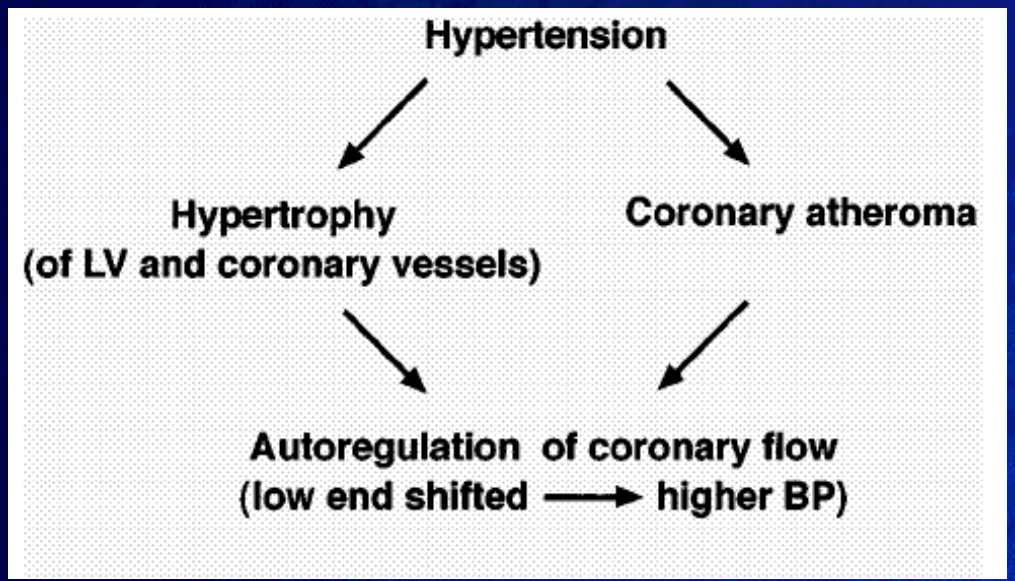
The principal results of the HOT Study demonstrate the benefits of lowering BP in patients with hypertension to 140 mm Hg systolic and 85 mm Hg diastolic, or lower. Efforts to lower BP further, down to 120 mm Hg systolic and 70 mm Hg diastolic, appear to give little further benefit, but do not cause any significant additional risk.

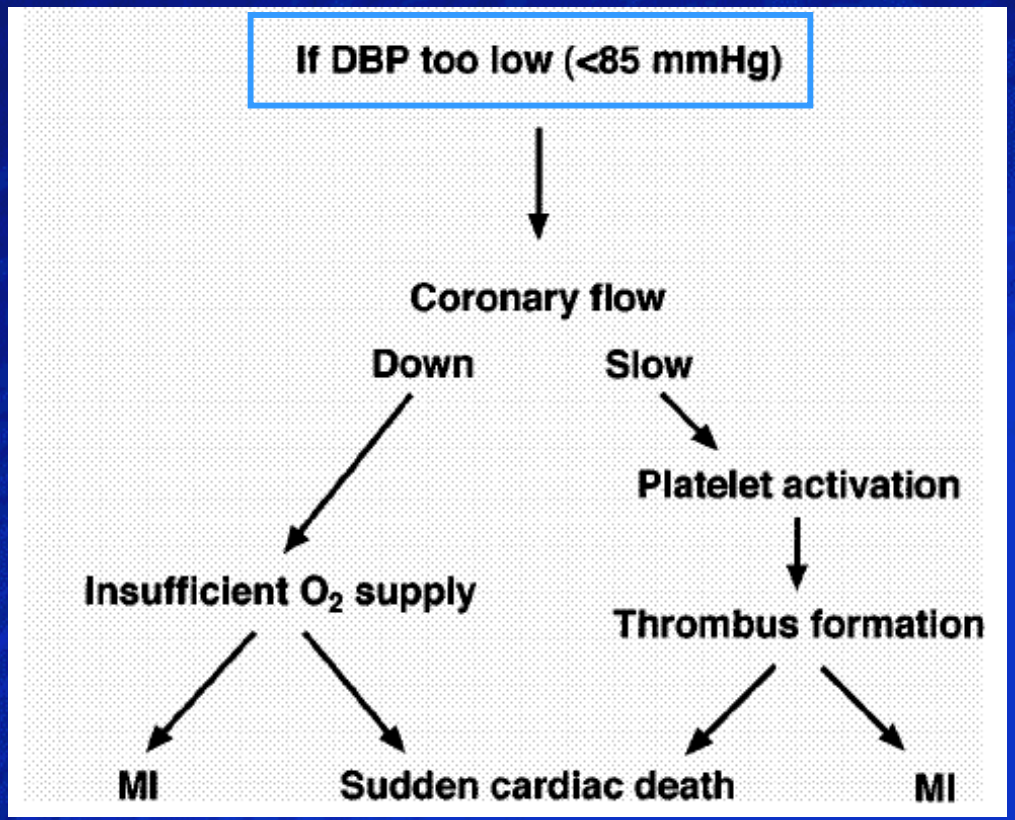
The Re-analysis of HOT study; J-Curve between treated DBP and MI in hypertensive patients with ischemic heart disease



Hansson L, Zanchetti, *Lancet* 1998

J-곡선 가설의 설명


Hypertension
Hypertrophy
(of LV and coronary vessels)
Coronary atheroma
Autoregulation of coronary flow
(low end shifted → higher BP)


If DBP too low (<85 mmHg)
Coronary flow
Down
Slow
Platelet activation
Insufficient O_2 supply
Thrombus formation
MI
Sudden cardiac death
MI

How to far lower blood pressure ?

For and against a J-Curve relationship for various cardiovascular end points.

Study†	Stroke Incidence	Stroke Mortality	Myocardial Infarction		Total Mortality	Diastolic Blood Pressure J-Point, mm Hg
			Incidence	Mortality		
Cruickshank et al[25]	. . .	PRO¶	. . .	PRO	CON	85-90
DHCCP[26]	. . .	CON	. . .	PRO	CON	86-91
HDFP[27]	. . .	. . .	. . .	. . .	PRO	26#
Waller et al[28]	. . .	CON	. . .	PRO	CON	91-98
HEP[29]	. . .	. . .	PRO‡	PRO	. . .	80-89
Stewart[30]	. . .	. . .	PRO‡	PRO‡	. . .	100-109
NYEC[31]	CON	CON	PRO	PRO	. . .	Δ≥17
EWPHE[32]	. . .	PRO§	. . .	PRO§	PRO	. . .**
PPT[33]	PRO‡§	PRO‡§	PRO‡	PRO‡	. . .	86-89
IPPPSH[34]	. . .	. . .	PRO‡‖	PRO‡‖	. . .	92
ANBP[35]	PRO‡§‖	PRO‡§‖	PRO‡§‖	PRO‡§‖	. . .	85-89
MRC[36]	. . .	. . .	CON	. . .	. . .	Not shown

Post-hoc analysis of International Verapamil SR-Trandolapril (INVEST) study at the 2004 American College of Cardiology.

INVEST study

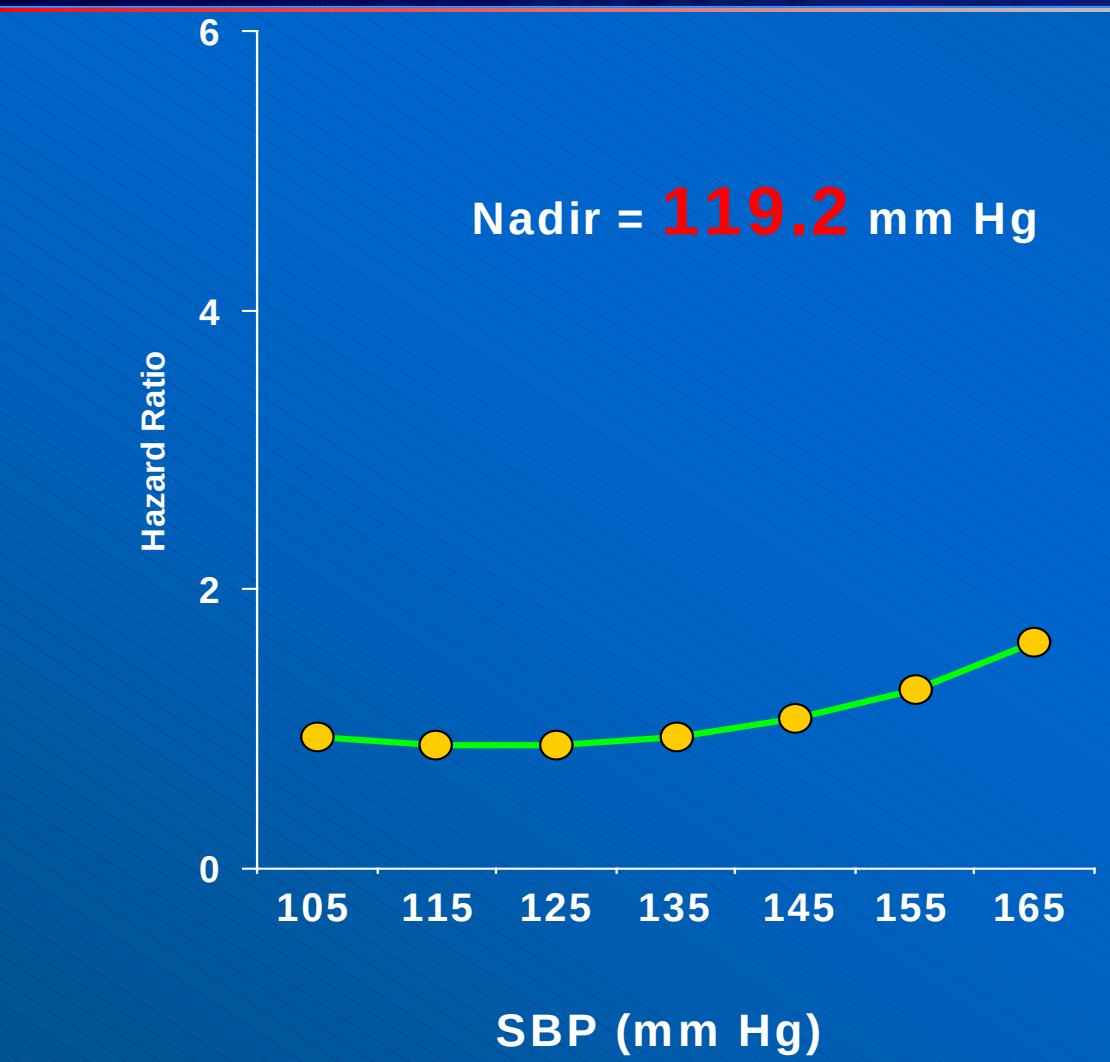
A calcium antagonist vs a non-calcium antagonist hypertension treatment strategy for patients with coronary artery disease. The International Verapamil-Trandolapril Study (INVEST): a randomized controlled trial. JAMA. 2003 Dec 3;290(21):2805-16

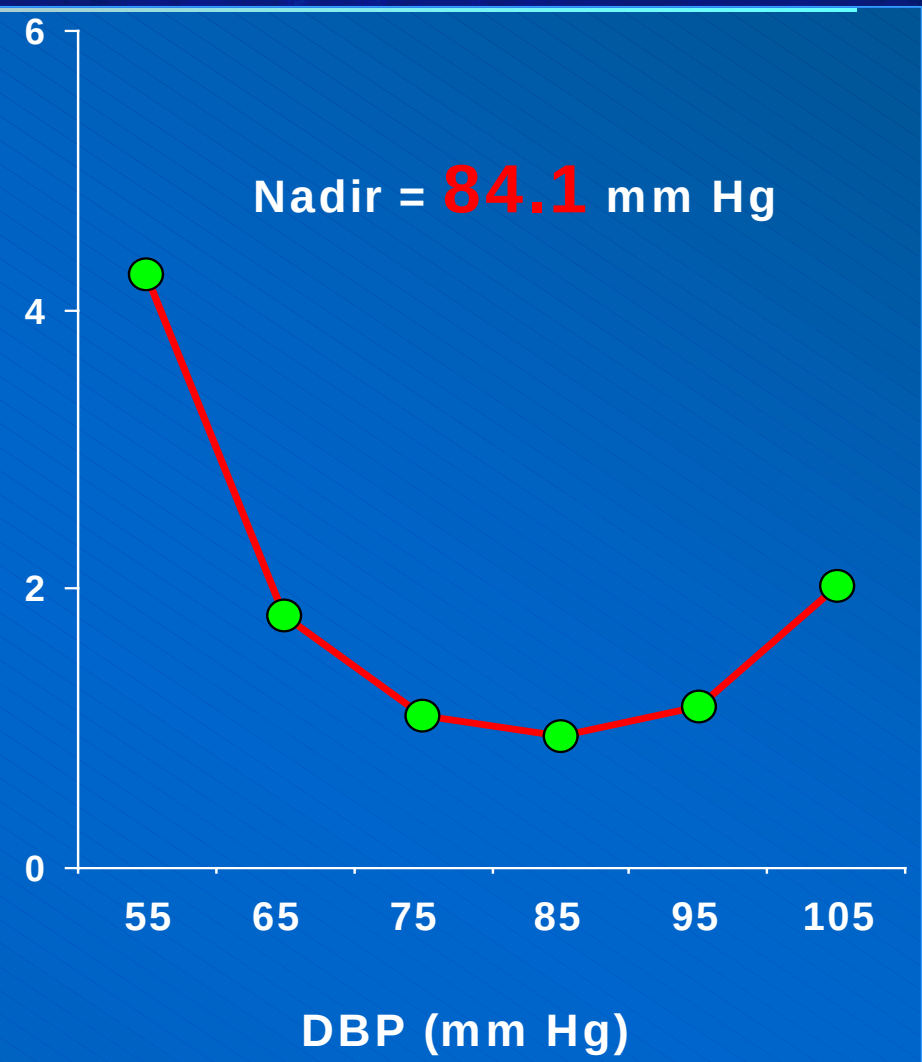
Pepine CJ, et al.

Randomized, open label, blinded end point study of 22 576 hypertensive CAD patients aged 50 years or older

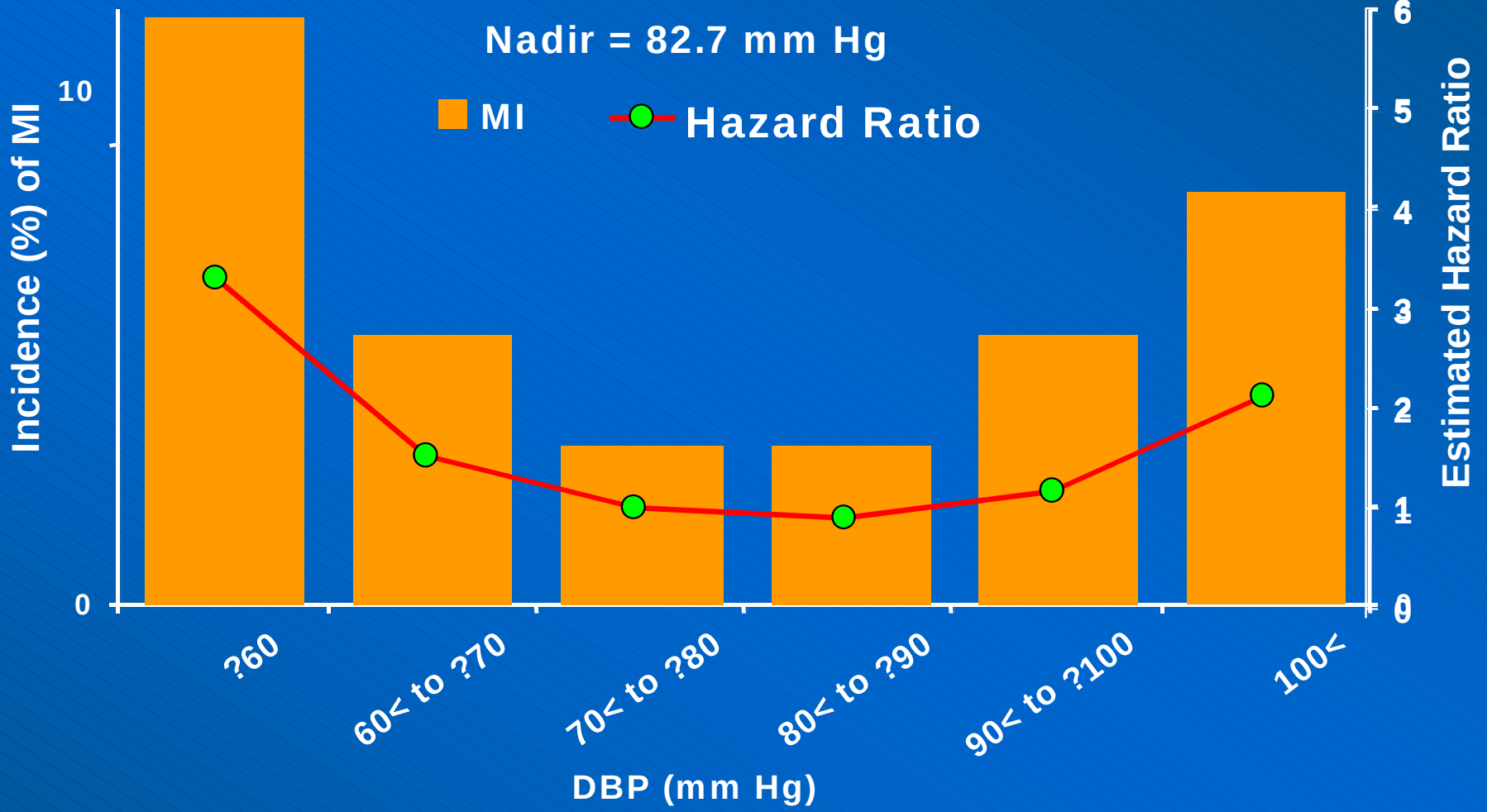
The verapamil-trandolapril-based strategy was as clinically effective as the atenolol-hydrochlorothiazide-based strategy in hypertensive CAD patients

Primary


Nadir = 119.2 mm Hg
Hazard Ratio
6
4
2
0
105
115
125
135
145
155
165
SBP (mm Hg)

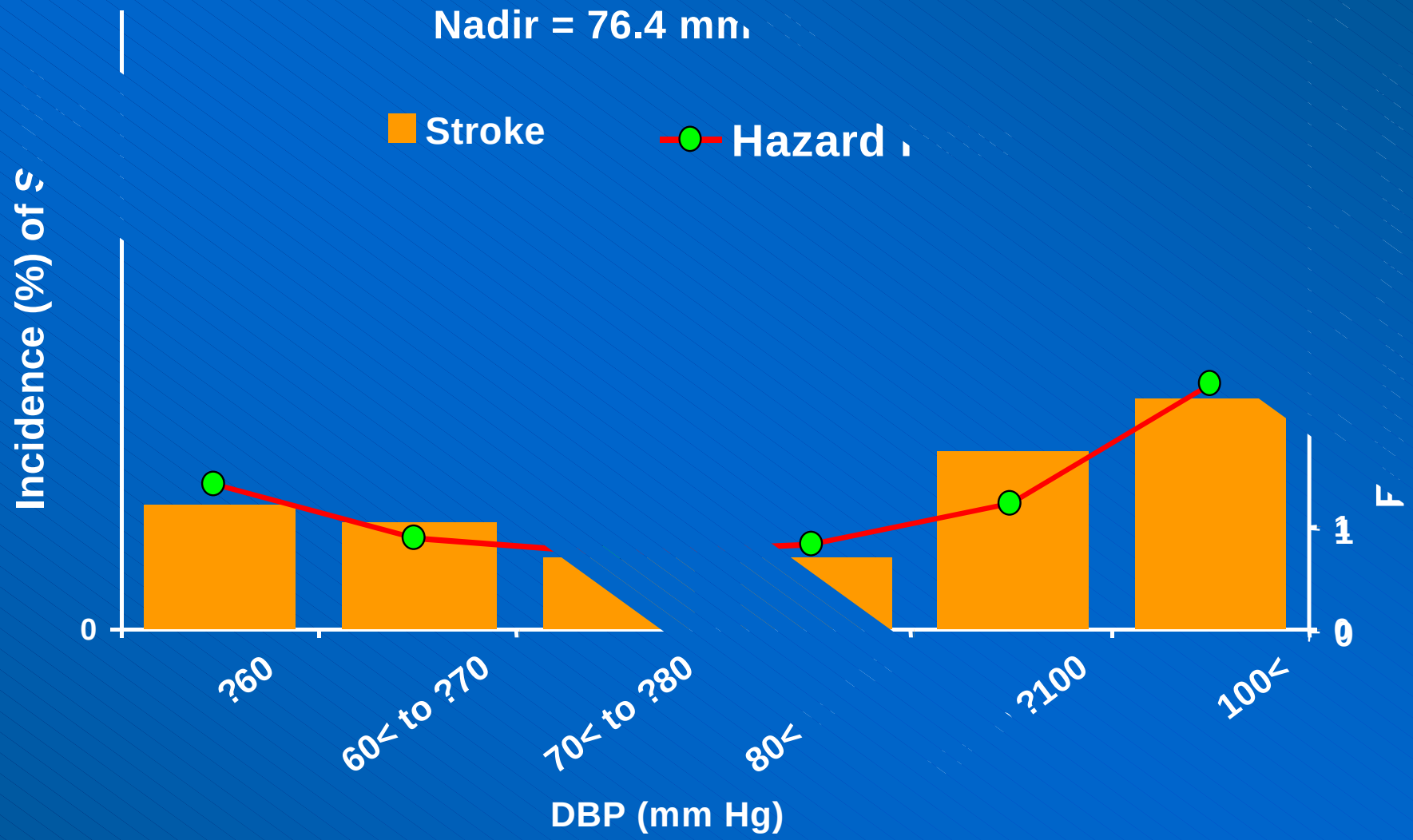

Nadir = 84.1 mm Hg
6
4
2
0
55
65
75
85
95
105
DBP (mm Hg)

'and N



Total patients	177	2239	11324	7378	1214	244

DBP: Risk for Fatal and Nonfatal Stroke



Total patients	175	2253	11320	7366	12

Kannel WB et al. A likely explanation for the J-curve of blood pressure cardiovascular risk. *Am J Cardiol* 2004; 94(3):380-4.

Data; the combined original and offspring cohorts of the Framingham Heart Study

Hypothesis; increased CV events at lower DBP would be largely confined to those subjects who had high SBP and therefore higher pulse pressure.

Endpoint; the 10-year risk of 951 nonfatal CVD events and 204 CVD deaths

Cardiovascular risk (crude rate) by diastolic BP in subjects with systolic BP >140 mm Hg (Framingham cohorts)

Diastolic BP (mm Hg)	Men (%)	Women (%)	Combined (%)
<80	45.5	24.6	31.1
80-89	24.9	15.5	19.4
>90	24.1	18.6	21.6

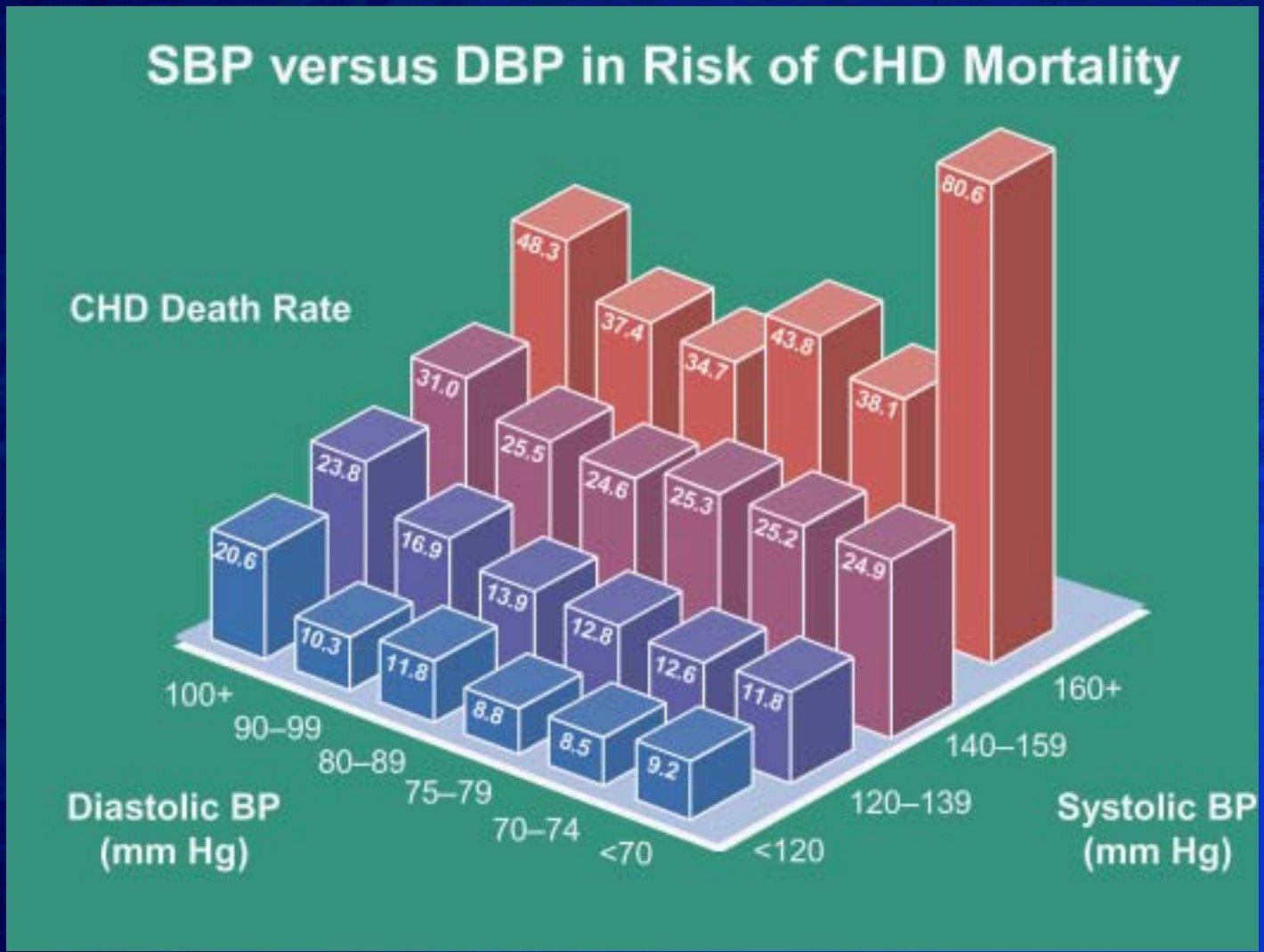
Kannel WB et al. *Am J Cardiol* 2004; 94:380-384.

Risk of nonfatal CVD events by pulse pressure (Framingham cohorts)

Quartile of pulse pressure (mm Hg)	Multivariable- risk-factor- adjusted risk ratio	95% CI	p
13.5-38.5	1.0	--	--
39-45.5	1.05	0.83-1.33	NS
46-55	1.22	0.97-1.52	<0.1
55.5-136	1.66	1.32-2.07	<0.001

Kannel WB et al. *Am J Cardiol* 2004; 94:380-384.

SBP-Associated Risks : MRFIT



Neaton JD et al. Arch Intern Med 1992;152:56

J-curve in CVD risk with lowest diastolic pressures limited to those with high systolic pressure: Framingham Cohort Study

Fig 3.—An increase in mortality is shown in patients with low blood pressure levels (baseline-annuals) enrolled in the Hypertension and Detection Follow-up Program (adapted from Cooper et al[27]).

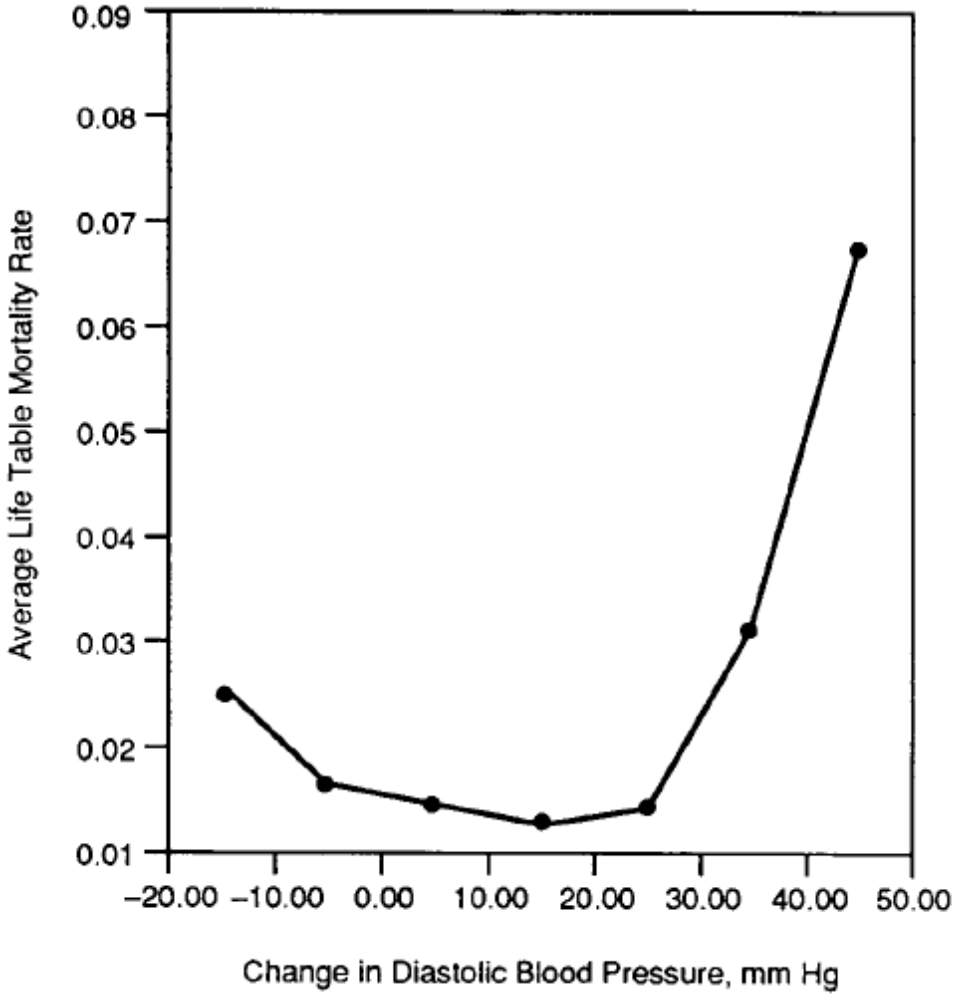
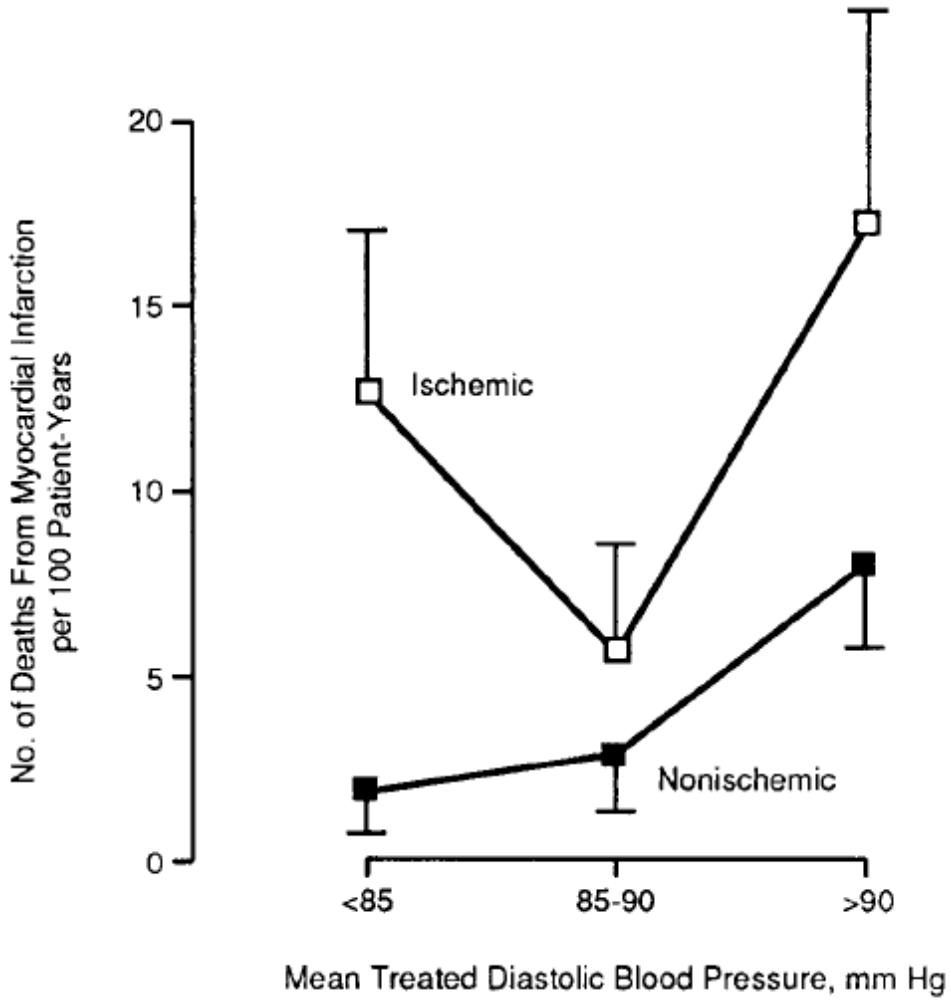


Fig 4.—A J-curve relationship between mean treated blood pressure and death from myocardial infarction is shown only for patients with preexisting heart disease (adapted from Cruickshank et al[25]).



Summary;
J-curve relationship between DBP and MI

1st group; treatment-induced and hypertensives with ischemic HD.

- DBP<80 increases the risk of a MI but not stroke

Other 3 groups; reversed causality

= underlying disease causes the low BP and the increased risk of MI

2nd; low BP d/t ischemic LV dysfunction

- J curve btw MI and both DBP and SBP

3rd; low BP d/t malnutrition or cancer

- J curve btw CVD & non-CVD and both DBP & SBP

4th; subjects w/ stiff arteries (mainly elderly)

CVD correlates with high SBP and low DBP

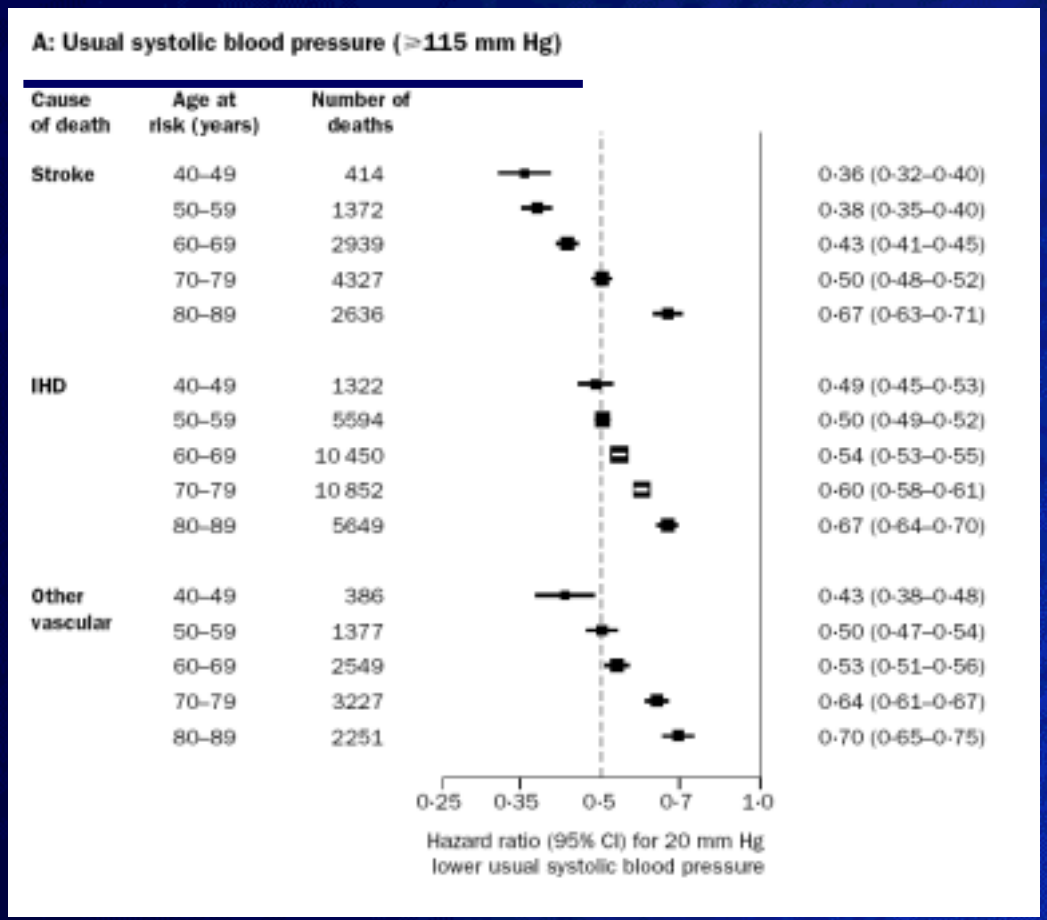
- J curve btw DBP and CVD exacerbated by treatment.

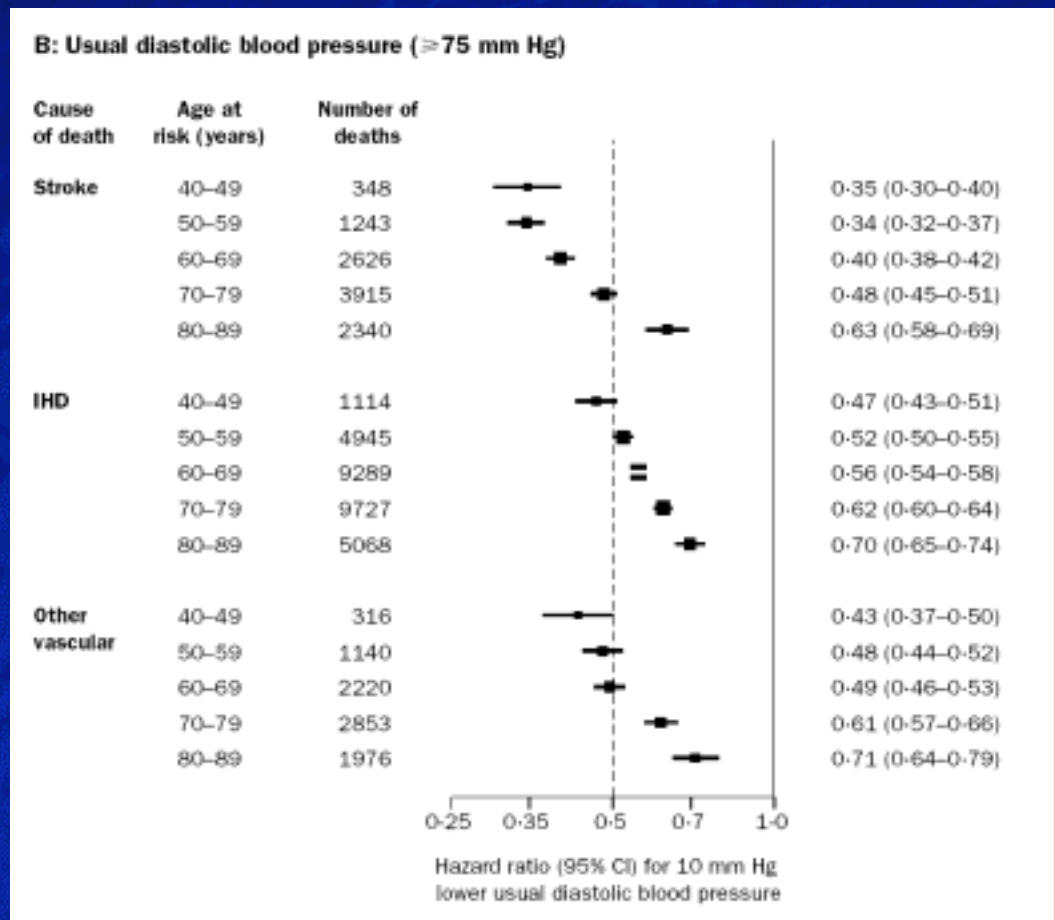
Conclusions

Where the risk of MI is very high, such as hypertensive patients with CAD history, it seems appropriate not to be over zealous in lowering BP, aiming for a DBP in the low 80s mmHg. However, for other types of patients, particularly where the dominant risk is stroke, it is appropriate to be more aggressive in lowering BP.

Rebutal

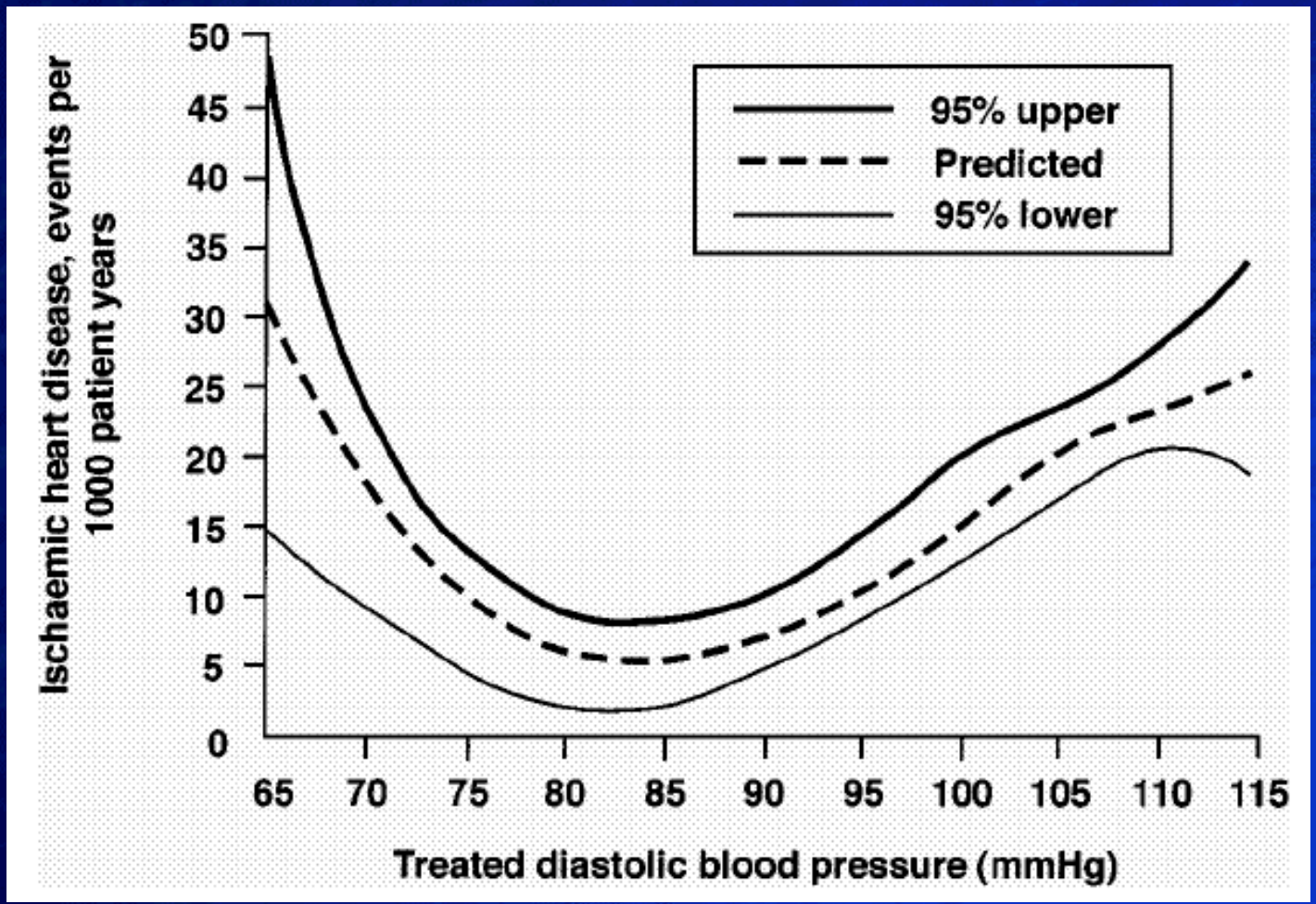
Linear relationships between both DBP and SBP, and stroke and CHD mortality





Prospective Studies Collaboration Lancet* 2002;360:1903

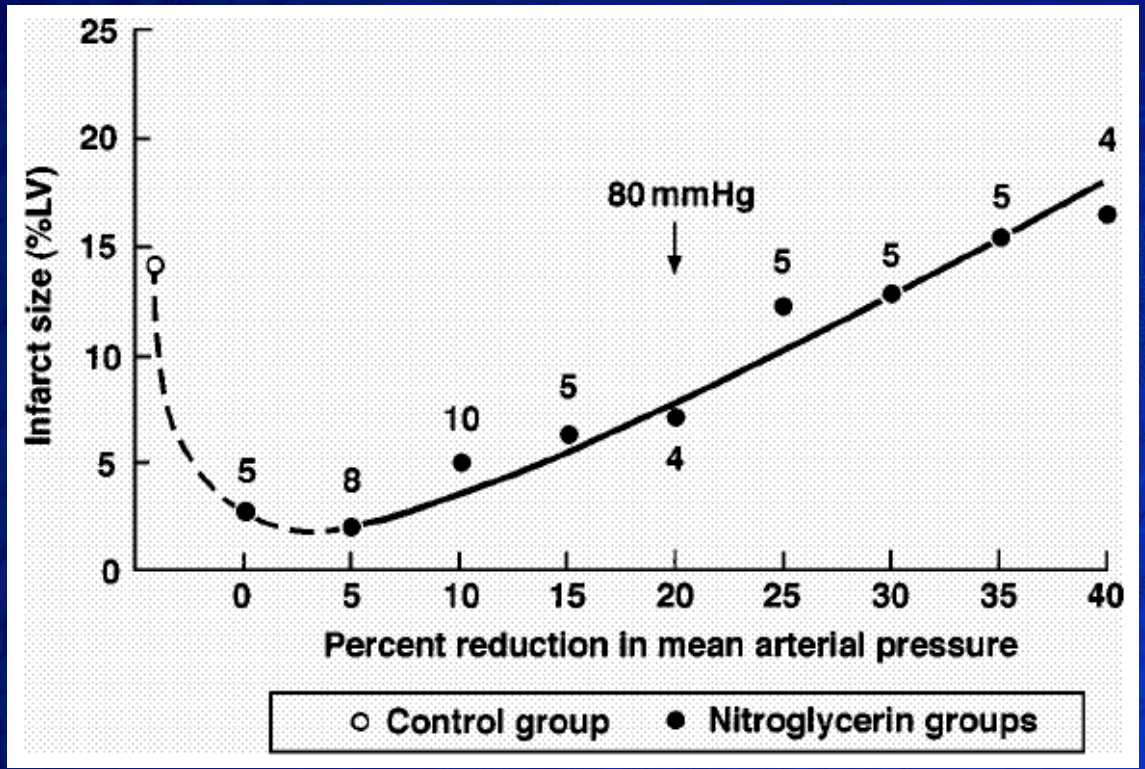
Arguments against J-Curve I;
Logically there must be a J-curve, but it could appear when DBP approaches close to zero



Farnett L.. *JAMA* 1991;489

Arguments against J-Curve II;

Patients in the acute post-Mi gain benefit from β-blocker in spite of therapeutically induced low BP.



A; Benefit from β-blocker mostly resulted from bradycardia, which would compensatae for any potential harm associated with a fall in BP. Drugs like nitrates, which lower BP but increase heart rate, increase infarct size when BP is lowered 10-40%.

The curve is "certain"

JNC VI guidelines (1997)

“the positive relationship between decreasing SBP & DBP and cardiovascular risk is strong and continuous for those with and without CHD.”

JNC 7 guidelines (2003)

"patients with occlusive coronary artery disease are put at risk of coronary events if diastolic pressure is low."

생각을 바꾸면 세상이 더 즐거워 집니다.