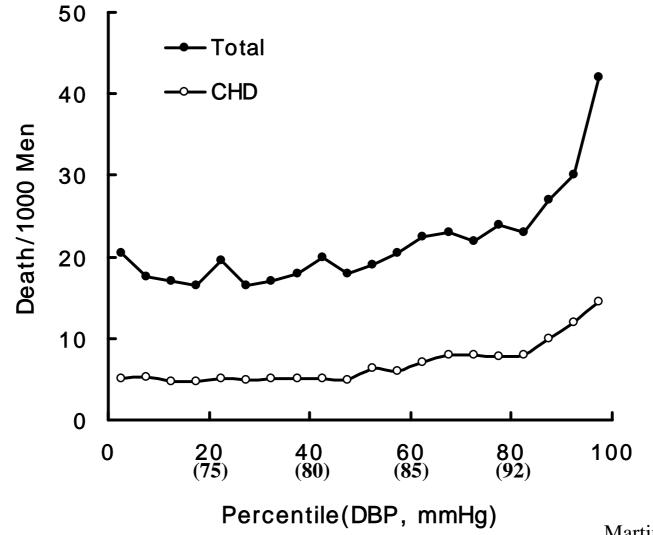
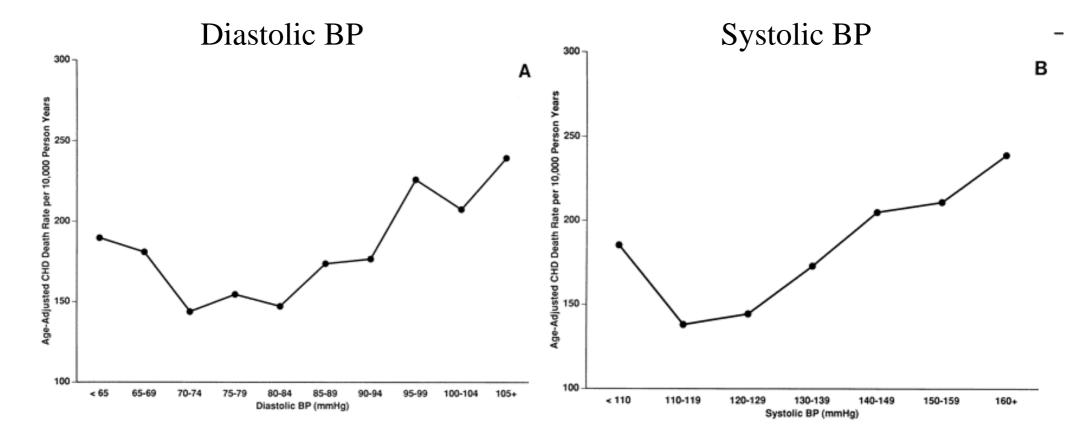
# J- Curve in Management of Hypertension Maybe Not Exist

# **Diastolic Blood Pressure and Mortality** - MRFIT -



Martin MJ, Lancet 1986:2:933

## CHD Death Rates according to Initial DBP and SBP level in MRFIT Men with MI.



Flack JM. Circulation. 1995;92:2437-2445

# **Meta-analysis of Antihypertensive Medication**

### TABLE I—POPULATION AND TRIAL DESIGN IN UNCONFOUNDED RANDOMISED TRIALS OF AT LEAST ONE YEAR OF ANTIHYPERTENSIVE DRUG TREATMENT

Trial or stratum (ref)	No of patients	Entry DBP (mm Hg)	Mean age (yr)	Male (%)	Mean follow-up (yr)	Blinding	Main drugs	Mean DBP difference (mm Hg) in attenders
Trials in which all patients ha	ad entry DBP	<110 mm Hg	2000	and the second		1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -		
VA-NHLBI (25, 26)	1012	85-105	38	81	1.5	Double	CD	7
HDFP stratum I (27-31)	7825	90-104	51†	55†	5.0	None	CD	5
Oslo (32, 33)	785	90-109‡	45	100	5.5	None	HZ	10
ANBPS (34)	3427	95-109	50	63	4.0	Single	CZ	6
MRC (35)	17 354	90-109	52	52	5.0	Single	BF or PR	6
Trials in which all patients ha	ad entry DBP	<i>≤115 mm Hg</i>	100					
VA (10, 37)	380	90-114	51	100	3.3	Double	HZ+RE+HD	19
USPHS (24)	389	90-114	44	80	7.0	Double	CZ+RU	10
HDFP stratum II (27-31)	2052	105-114	51†	55†	5.0	None	CD	7
HSCSG (36)	452	90-115	59	41	2.3	Double	MC+DS	12
Trials in which some or all pa	atients had er	ntry DBP > 115 n	nm Hg					2 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
VA (10, 37)	143	115-129	1 51	100	1.5	Double	HZ+RE+HD	27
Wolff(11)	87	100-130	49	32	1.4	Double	RE	20
Barraclough (38)	116	100-120	56	43	2.0	Single	BF or MD	13
Carter (41)	99	≥110	NR	57	4.0	None	TH	NR
HDFP stratum III (27-31)	1063	≥115	51†	55†	5.0	None	CD	6
EWPHE (39)	840	90-119	72	30	4.7	Double	HZ+TT	10
Coope (40)	884	105-120	69	31	4.4	None	AT	11
Mean or total	36 908	99	52	53	5-0	92676 <del>-</del> 3 11		6*

\*The difference in mean DRP per person year of follow-up, based on data from those who attended follow-up for blood pressure measurement, was 6:4 mm Ha. The difference

## **Meta-analysis of Antihypertensive Medication**

#### (i) STROKE IN ANTIHYPERTENSIVE TRIALS

#### (II) CHD IN ANTIHYPERTENSIVE TRIALS

TRIAL (or stratum)	NUMBERS I Treatment	OF EVENTS Control	ODDS RATIO: 4 confidence lin (TREAT : CONTR	nita TION	TRIAL (or stratum)	NUMBERS ( Treatment	DF EVENTS Control	ODDS RATIOS & confidence limita (TREAT : CONTROL)	TION 4 SD
) Trials in which all pat	lents had entry D	OP < 110 mm Hg			(a) Trials in which all path	ients had entry D	BP < 110 mm Hg		
VA-NHLBI	0/508	0/504			VA-NHLBI	B/500	5/504		
HDFP (Stratum I)	59/3903	66/3922			HDFP (Stratum I)	191/3903	236/3922		
Oslo	0/406	5/379 -			Oslo	14/406	10/379		
ANEPS	13/1721	22/1706			ANBPS	33/1721	33/1706		
MRC	60/8700	109/8654			MRC	222/8700	234/8654		
Subtoral (a):	132/15238	224/15165	+	41% SD 8	Subtotel (e):	468/15238	518/15165	+	10% SD 6
Trials in which ell pel	lienta had entry t	OBP & 115 mm Hg			(b) Triels in which ell pel	lente had entry C	38P ≤ 115 mm Hg		
VAR	5/186	20/194			VAI	11/186	13/194		
USPHS	1/193	6/196			USPHS	15/193	18/196		-
HDFP (Stratum II)	25/1048	36/1094			HDFP (Stratum II)	61/1048	63/1004		
HSCSG	43/233	52/219			HSCSO	7/233	12/219		
Sucrotar (# + b):	205/16898	336/16778	+	41% SD 7	Subtotel (a + b):	562/16898	624/16778	+	11% 50 6
] Trials in which some	or all patients ha	ed entry DBP > 115 mm	n Hg		(c) Trials in which some	or all patients ha	ed entry DBP > 115 mm	На	
VA.I	1/68	3/63 -			VAI	0/68	2/53		
Wolff	2/45	1/42			Walt	0/45	0/42		
Barradiough	0/58	0/58			Barraclough	1/58	2/58 -		
Carter	10/49	21/48			Canter	2/49	2/48		
HDFP (Stratum III)	18/534	34/529			HDFP (Stratum III)	23/534	44/529		-
EWPHE	32/416	48/424			EWPHE	48/415	59/424		
Ссоре	20/419	39/405			Coope	35/419	38/465		10
TOTAL (# + b + c):	289/18487	484/18407	+	42% SD 6	TOTAL (a + b + c):	671/10487	771/18407	+	14% SD 5
Test for heterogene	oty: X <sup>2</sup> 13 = 12.4; N	15 0,0	TREATMENT TREAT	1.5 2.0 TMENT	Test for heterogene	iñy: X <sup>2</sup> 14 = 12·1; N	is 0-0	0-5 1-0 1-6 THEATMENT TREATMENT WORSE	INT

Collins. Lancet. 1990;335

### **Meta-analysis of Antihypertensive Medication**

#### (iii) VASCULAR DEATHS IN ANTIHYPERTENSIVE TRIALS

#### (IV) NON-VASCULAR DEATHS IN ANTIHYPERTENSIVE TRIALS

TRIAL (or stratum)	NUMBERS Treatment	OF ÉVENTS Control	ODDS RATIOS & confidence limits (TREAT : CONTROL)	REDUC- TION 4 SD	TRIAL (or etratum)	NUMBERS (	OF EVENTS Control	ODDS R & confiden (TREAT : CO	ce limits TION
e) Trials in which sil pa	lients had entry I	OBP < 110 mm Hg	1		(a) Triais in which all pat	ients had entry D	QIP < 110 mm Hg		
VA-NHLBI	2/508	0/504			VA-NHLEI	0/508	0/504		
HOFP (Stratum ()	122/3963	165/3922			HDFP (Stratum I)	109/3903	126/3922		
Osio	7/406	6/379			Oslo	3/406	3/379		
ANBPS	6/1721	18/1706			ANBPS	17/1721	17/1706		
MRC	134/8700	139/8654			MRC	114/8700	114/8654		-
Subleval (a):	273/15238	326/15165	+	17% 50 8	Suctorer (a):	243/15238	260/15165	-	7% 50 9
) Trials in which all pa	tients had entry (	OBP s 115 mm Hg			(b) Triels in which all pat	lents had entry D	98P s 115 mm Hg		
VAI	8/186	18/194			VAB	2/186	2/194		
USPHS	2/193	4/190 -			USPHS	0/193	0/196		
HDFP (Stratum II)	45/1048	41/1004			HOFP (Stratum II)	25/1048	36/1004		
HSCSG	15/233	18/219			HSCSB	11/233	5/219		
Sublomi (a + b):	343/16898	411/16778	+	18% SD 7	Subiotal (e + b):	281/16898	303/16778	-	8% SD 8
] Trials in which some	or all patients ha	d entry DBP > 115 mm	на		(c) Trials in which some	or all patients he	d entry DOP > 115	mm Hg	
VAT	0/68	4/63			VAI	0/68	C/63		
Woff	4/45	1/42			Wolff	0/45	1/42		
Barraclough	0/58	3/58			Barrackugh	1/58	0/58		
Carter	10/49	17/48			Carter	3/49	5/48		
HDFP (Stratum II)	28/534	34/529			HOFP (Stratum III)	20/534	17/529		• • •
EWPHE	67/416	93/424			EWPHE	68/416	56/424		
Coope	37/419	50/465			Сооре	23/419	19/465		
TOTAL (a + b + c):	489/18487	613/18407	+	21% SD 6	TOTAL (a + b + c):	396/18487	401/18407	+	1% SD 7
Test for heterogene	tery: X <sup>2</sup> <sub>15</sub> = 22.1: Ν	s 0.0	0.5 1.0 1.5 TREATMENT TREATMEN	2.0	Test for heterogene	wy: X <sup>9</sup> 12 = 11.2; N	s	0.0 0.5 1.0 TREATMENT 1	1.5 2.0 TREATMENT

Collins. Lancet. 1990;335

# **Goals of Therapy for Hypertension**

### • JNC VII

- Treating SBP and DBP to targets that are <140/90 mmHg is associated with a decrease in CVD complications.
- In patients with hypertension and diabetes or renal disease, the BP goal is <130/80 mmHg.</li>
- ESH & ESC
  - lowered at least below 140/90 mmHg and to definitely lower values, if tolerated, in all hypertensive patients
  - below 130/80 mmHg in diabetics.

### Three-Year Morbidity in Dalby, Sweden (40-59 year Men)

	Treated Patients (n=66)	Normotensives (n=75)	p value
CVD	21%	1%	< 0.001
CHD	20%	1%	<0.001
DM	8%	5%	ns
BP (mmHg)			
Untreated	183/114		
Treated	149/91	133/80	< 0.001

# **J- Curve in Management of Hypertension**

**Stewart IM**. Relation of reduction in pressure to first myocardial infarction in patients receiving treatment for severe hypertension. Lancet. **1979** Apr 21;1(8121):861-5. The findings suggest that the blood-pressure in severe middle-aged hypertensives should seldom be reduced by more than 22% or to diastolic levels less than **104-110 mm Hg**.

Cruickshank JM, Thorp JM, Zacharias FJ. Benefits and potential harm of lowering high blood pressure. Lancet. **1987** Mar 14;1(8533):581-4.

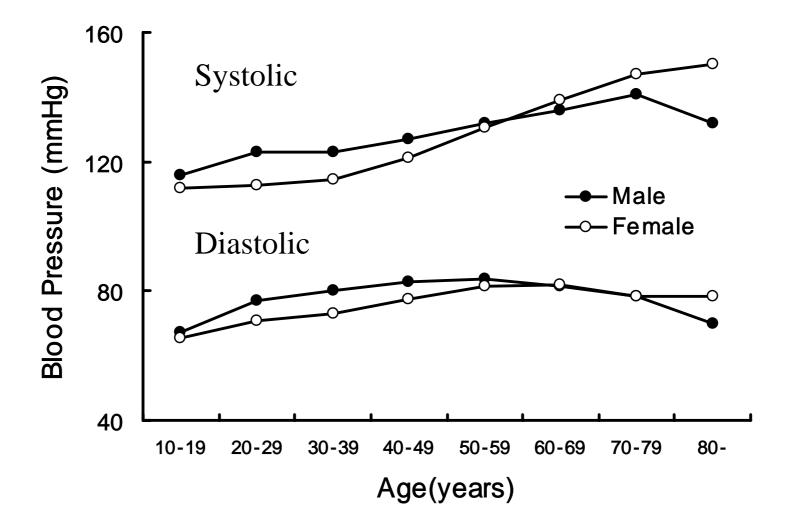
There was a J-shaped relation, in those with evidence of **ischaemic heart disease**, the frequency of death from myocardial infarction was lowest at treated DBP of **85-90 mm Hg**.

**Berglund G**. Goals of antihypertensive therapy. Is there a point beyond which pressure reduction is dangerous? Am J Hypertens. **1989** Jul;2(7):586-93. Review. (Gothenburg) Caution should be to avoid decreasing diastolic BP below **85 mm Hg**.

**Farnett L**, Mulrow CD, Linn WD, Lucey CR, Tuley MR. The J-curve phenomenon and the treatment of hypertension. Is there a point beyond which pressure reduction is dangerous? JAMA. **1991** Jan 23-30;265(4):489-95. Meta-Analysis

Low treated diastolic blood pressure levels, ie, below **85 mm Hg**, are associated with increased risk of cardiac events.

## **Blood Pressures and Age** First National Health and Nutrition Survey, 1998

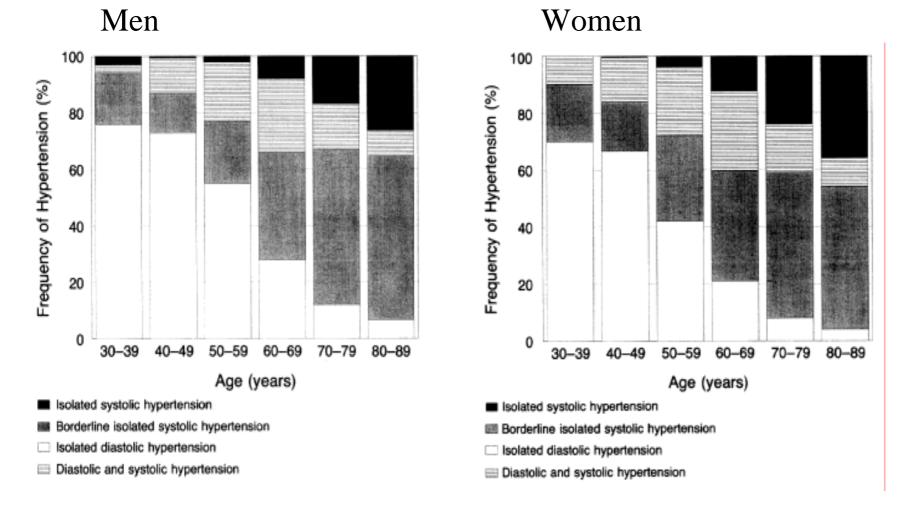


### Incidence of CHD and SBP, DBP, and PP by Age Groups Framingham Study

	ß2	SE2	Wald	HR (95% CI)
Age <50 y				
SBP	0.13	0.04	10.8	1.14 (1.06-1.24)**
DBP	0.29	0.06	21.8	1.34 (1.18-1.51)***
PP	0.02	0.07	0.1	1.02 (0.89-1.17)
Age 50-59 y				
SBP	0.08	0.03	6.3	1.08 (1.02-1.15)*
DBP	0.10	0.06	2.9	1.11 (0.99-1.24)
PP	0.11	0.05	5.4	1.11 (1.02-1.22)*
Age ≥60 y				
SBP	0.16	0.03	30.0	1.17 (1.11-1.24)***
DBP	0.11	0.06	3.2	1.12 (0.99-1.27)
PP	0.21	0.04	36.9	1.24 (1.16-1.33)***

Proportional-Hazard Regression Coefficients. \*;p<0.05, \*\*;p<0.01, \*\*\*;p<0.001 HR was associated with a 10 mm Hg increase in BP.

### Relative Frequencies of Hypertension Status According to Age. Framingham Study



Sagie et al. NEJM 329:1912

Prospective RCT for the Effect of Intensified Anti-hypertensive Tx

- Diastolic Hypertension with/without Systolic Hypertension
  - The BBB Study in Sweden
  - Hypertension Optimal Treatment (HOT)
- Isolated Hypertension
  - No Study
  - SHEP, STOP-Hypertension, MRC tiral

# The BBB Study

- Study Design
  - 2127 treated HT patients with DBP 90-100 mmHg (45-67 years)
  - Further reduction of DBP to 80 mmHg vs unchanged
  - 4 year follow-up
- Results
  - 6-7 mmHg difference of DBP
  - No increase of the number or severity of side effects of drugs
  - No difference in the hard endpoints, stroke and MI

# Hypertension Optimal Treatment (HOT)

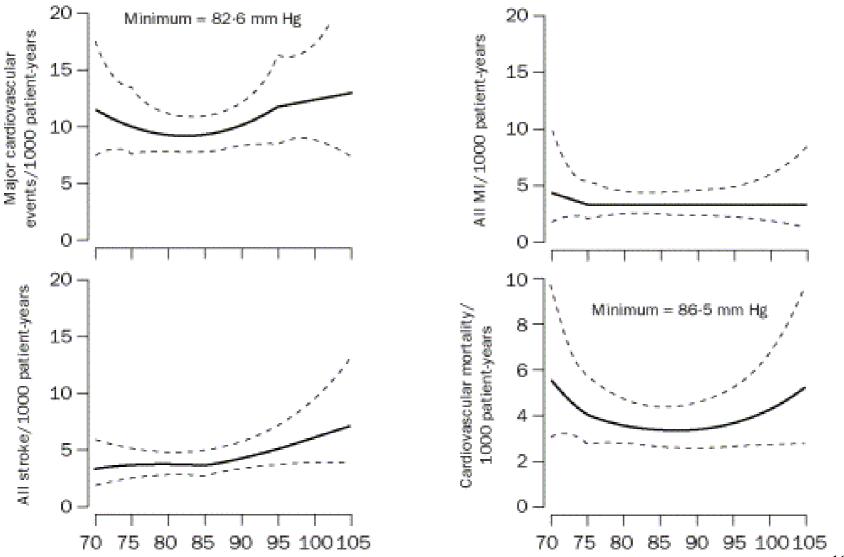
- 18790 patients from 26 countries, aged 50-80 years (mean 61.5 years) with DBP between 100 mmHg and 115 mmHg
- 3 groups with target DBP ≤ 90 mmHg, 85 mmHg, and 80 mmHg
- Felodipine as baseline therapy with the addition of other agents, Aspirin
- Follow-up 3.8 years (3.3-4.9 years)

### **Events in Relation to Target Diastolic BP** -HOT-

Target BP*	Number of events	Events rate**	p for trend		Target BP*	Number of events	Events rate**	p for trend
Major car	diovascula	r events			Cardiovas	cular mort	alitv	
90 mm Hg	232	9.9			90 mm Hg		3.7	
85 mm Hg	234	10.0			85 mm Hg		3.8	
80 mm Hg	<u>,</u> 217	9.3	0.50		U			0.40
All myoca	rdial infar	ction			80 mm Hg		4.1	0.49
90 mm Hg	84	3.6			Total mor	tality		
85 mm Hg		2.7			90 mm Hg	188	7.9	
80 mm Hg	61	2.6	0.05		85 mm Hg	194	8.2	
All stroke					80 mm Hg	207	8.8	0.32
90 mm Hg	94	4.0		=				
85 mm Hg	<u>;</u> 111	4.7		:	*: actual BP; 8	85.2. 83.2. 8	1.1 mmHg	respectively
80 mm Hg	89	3.8	0.74		**; per 1000 p			

Lancet 1998;351:1755

### **CV Events in Relation to Achieved DBP** -HOT-



Lancet 1998;351:1755

### **Events in Patients with Diabetes Mellitus HOT**

Target BP*	Number of events	Events rate**	p for trend	Target BP*	Number of events	Events rate**	p for trend
Major ca	rdiovascula	r events		Cardiovas	cular mort	ality	
90 mm Hg	g 45	24.4		90 mm Hg		11.1	
85 mm Hg	g 34	18.6		85 mm Hg		11.2	
80 mm Hg	g 22	11.9	0.005	80 mm Hg		3.7	0.016
All myoca	ardial infar	ction		e	-	5.7	0.010
90 mm Hg	g 14	7.5		Total mor	tality		
85 mm Hg	g 8	4.3		90 mm Hg	30	15.9	
80 mm Hg	g 7	3.7	0.11	85 mm Hg	29	15.5	
All stroke	6			80 mm Hg	17	9.0	0.068
90 mm Hg	g 17	9.1					
85 mm Hg	g 13	7.0		*: actual BP;	84.9, 82.9,	81.0 mmHg	g respectiv
80 mm Hg	g 12	6.4	0.34	**; per 1000	patient-year		

Lancet 1998;351:1755

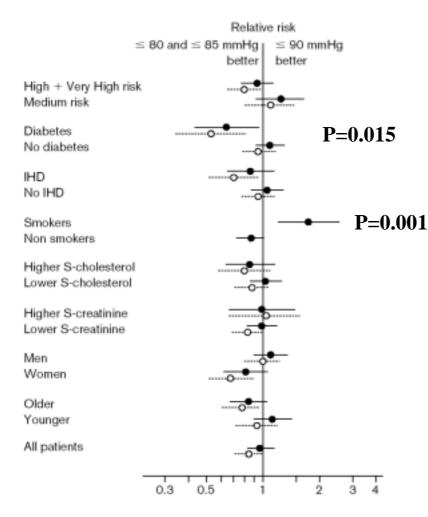
### Events in 3080 Patients with IHD -HOT-

Target BP*	Number of events	Events rate**	p for trend	-	Target BP*	Number of events	Events rate**	p for trend
Major car	diovascula	r events			MI mortal	itv		
90 mm Hg	77	20.5			90 mm Hg	v	1.0	
85 mm Hg	68	17.9			e		0.8	
80 mm Hg	62	16.4	ns		85 mm Hg			
All myoca	rdial infar	ction			80 mm Hg		0.5	ns
90 mm Hg	35	9.3			Stroke mo	rtality		
85 mm Hg	26	6.8			90 mm Hg	5	1.3	
80 mm Hg	31	8.3	ns		85 mm Hg	6	1.5	
All stroke					80 mm Hg	5	1.3	ns
90 mm Hg	35	9.3						
85 mm Hg	30	7.9			*: actual BP; 8	85.2, 83.2, 8	1.1 mmHg	respective
80 mm Hg	20	5.3	0.046		**; per 1000 p		0	Y I

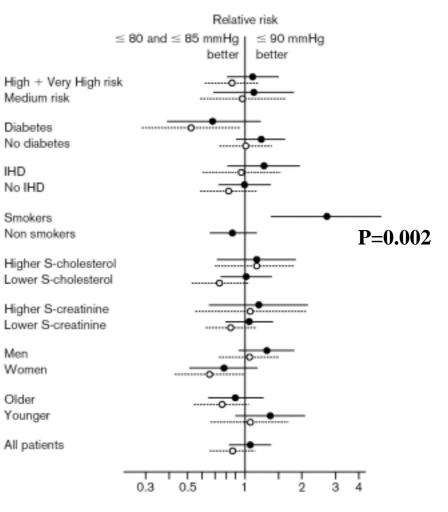
Lancet 1998;351:1755, Cruickshank Cardiovasc Drugs Ther. 2000;1

# Subgroup Analysis of HOT

#### **CV Event**



#### **CV Mortality**



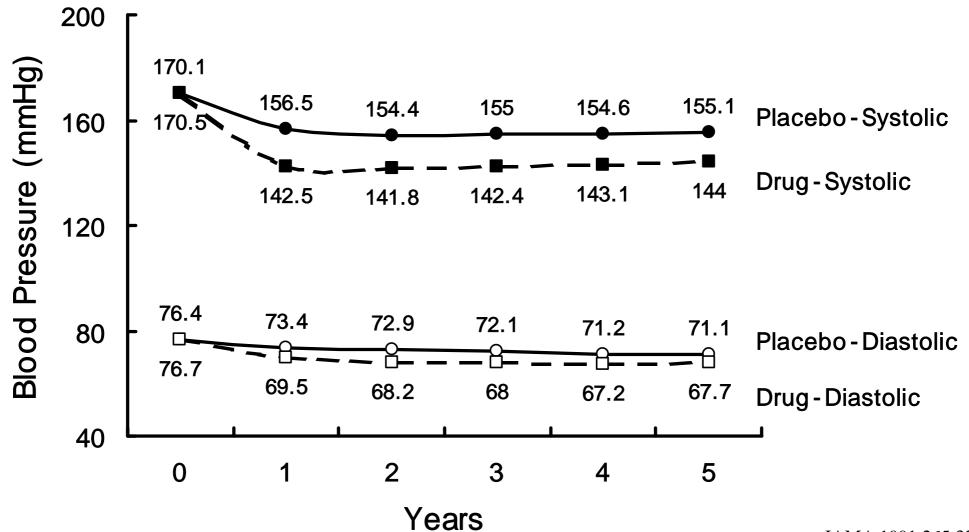
#### Zanchetti A. J Hypertens. 2003;2

### Systolic Hypertension in the Elderly Program (SHEP)

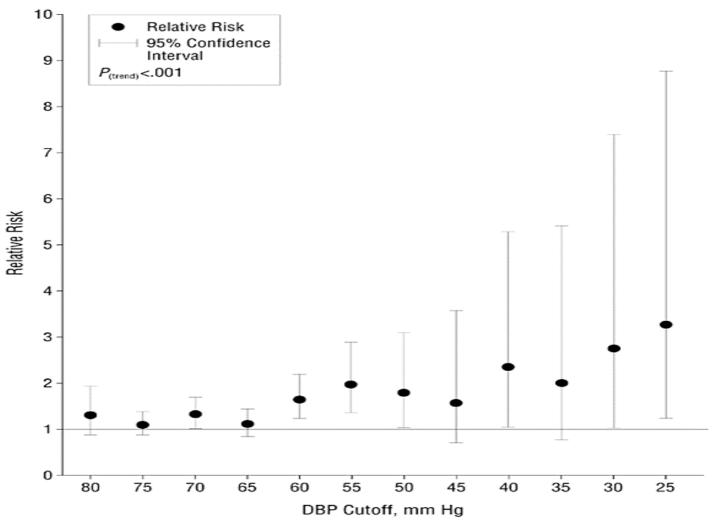
Old age ( $\geq 60$  y), systolic pressure  $\geq 160$  mmHg and diastolic pressure  $\leq 90$  mmHg Placebo vs.chlorthalidone with atenolol Average 4.5 years follow-up

		Placebo (n=2371)	Active (n=2365)	Relative Risk (95% CI)
Death	Total	242	213	0.87(0.73-1.05)
	Cardiovascular	112	90	0.80(0.60-1.05)
	Other	103	109	1.05(0.80-1.38)
Event	Stroke	149	96	0.63(0.49-0.82)
	MI	74	50	0.67(0.47-0.96)
	LVH	102	48	0.46(0.33-0.65)
Combined	Nonfatal MI+CHD death	141	104	0.73(0.57-0.94)
	CHD	184	140	0.75(0.60-0.94)
	CVD	414	289	0.68(0.58-0.79)

# Systolic and Diastolic Pressure during Follow-up in SHEP

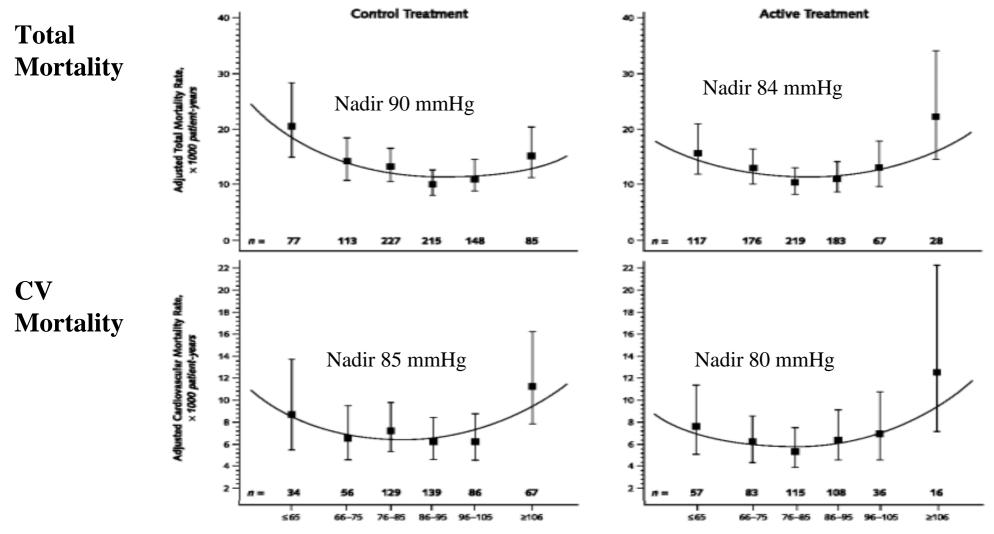


### RR for CVD by DBP in Treatment Group -SHEP-



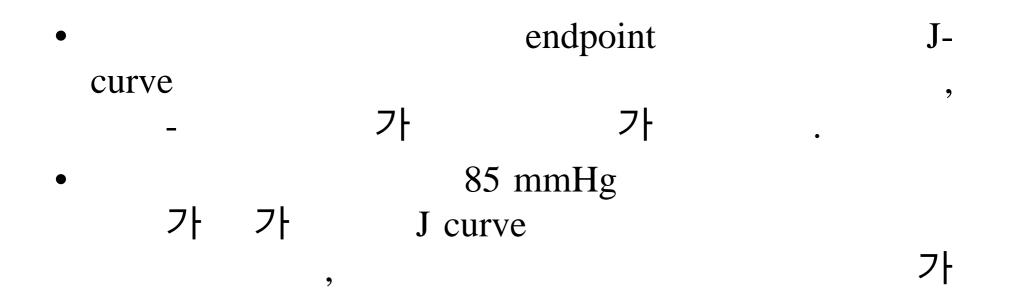
Arch Intern Med 1999;159:2004

### Rates of Events and Diastolic Blood Pressure in Active Treatment and Control Groups - Meta-Analysis of 7 RCTs -



Boutitie F Ann Intern Med. 2002;13

# Summary



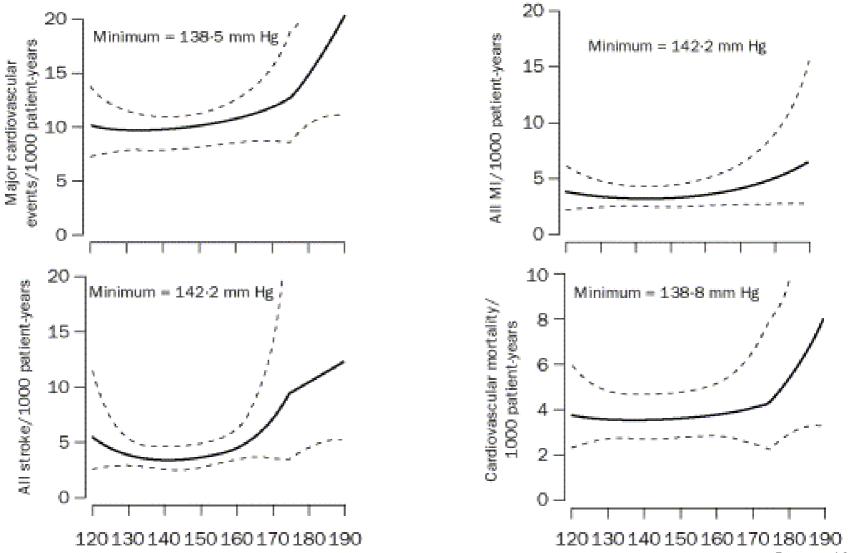
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Cruickshank J. The J-curve in hypertension. Curr Cardiol Rep. 2003 Nov;5(6):441-52. Review

It is now reasonable to conclude that for nonischemic hypertensive subjects the therapeutic lowering of diastolic blood pressure (DBP) to the low 80s mm Hg is beneficial, but it is safe (though unproductive) to go lower.

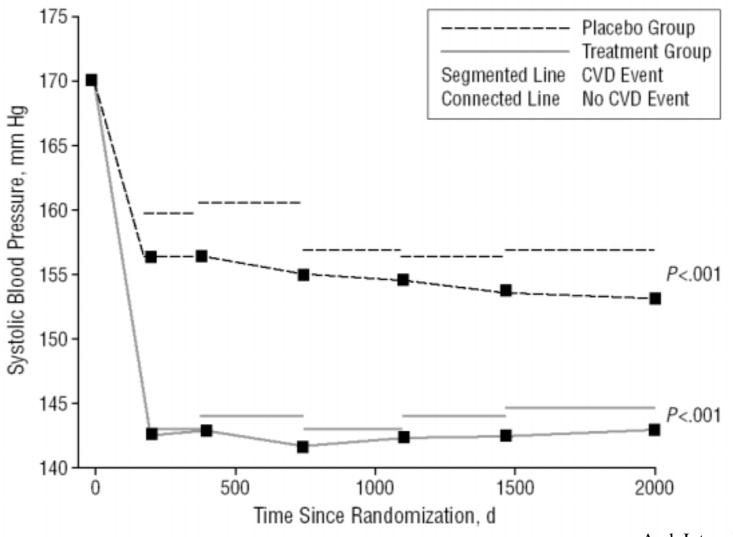
However, in the presence of coronary artery disease (limited coronary flow reserve) there is a J-curve relationship between treated DBP and myocardial infarction, but not for stroke. In such high-risk (for myocardial infarction) cases it would be prudent to avoid lowering DBP to below the low 80s mm Hg.

### **CV Events in Relation to Achieved SBP** -HOT-



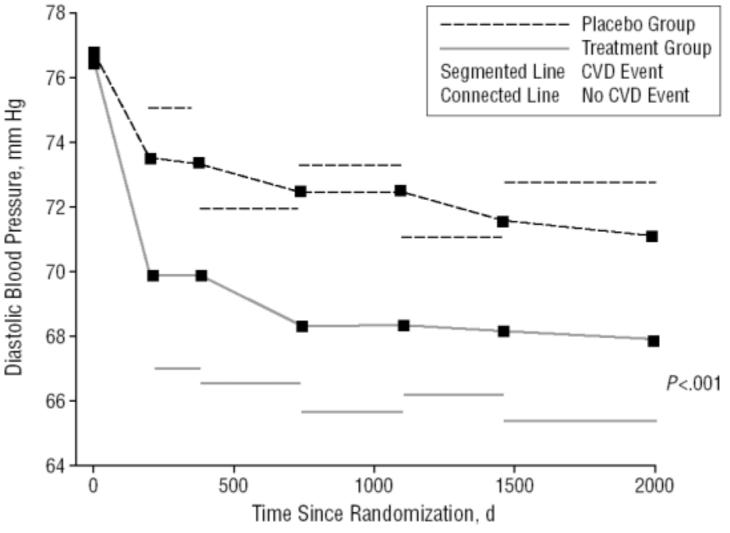
Lancet 1998;351:1755

### Systolic BP in Patient with/without CVD -SHEP-



Arch Intern Med 1999;159:2004

### **Diastolic BP in Patient with/without CVD** -SHEP-



Arch Intern Med 1999;159:2004

# RR of Events for 5 mmHg Decrease of Pressure -SHEP-

	Stroke		CI	HD	CVD		
Event	Active Treatment (n = 103)	Placebo (n = 159)	Active Treatment (n = 139)	Placebo (n = 183)	Active Treatment (n = 287)	Placebo (n = 413)	
SBP†	0.90‡ (0.85-0.95)	0.96 (0.92-1.01)	0.98 (0.93-1.04)	0.95§ (0.91-1.00)	0.94‡ (0.91-0.97)	0.95‡ (0.93-0.98)	
DBP†	1.14‡ (1.05-1.22)	0.92§ (0.85-1.00)	1.08§ (1.00-1.16)	1.00 (0.93-1.08)	1.11‡ (1.05-1.16)	1.00 (0.95-1.05)	
Composite variable	2.16‡	1.56§	1.81‡	2.50‡	2.05‡	1.97‡	
Age	1.13	1.33‡	1.05	1.04	1.09	1.12‡	
Sex (men)	1.28	1.27	2.16‡	1.74‡	1.69‡	1.49‡	
Race (black)	1.10	1.41	0.56	0.87	0.72	0.99	
Medication	1.03	1.30	0.82	1.00	0.93	1.18	
Smoker (ever)	1.00	0.99	1.15	1.13	1.13	1.13	

\*CHD indicates coronary heart disease; CVD, cardiovascular disease; SBP, systolic blood pressure; and DBP, diastolic blood pressure.

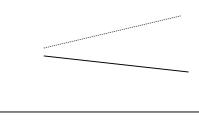
+For 5-mm Hg decrease; values are relative risk (95% confidence interval).

§P<.05.

Includes diabetes, previous heart attack, or stroke.

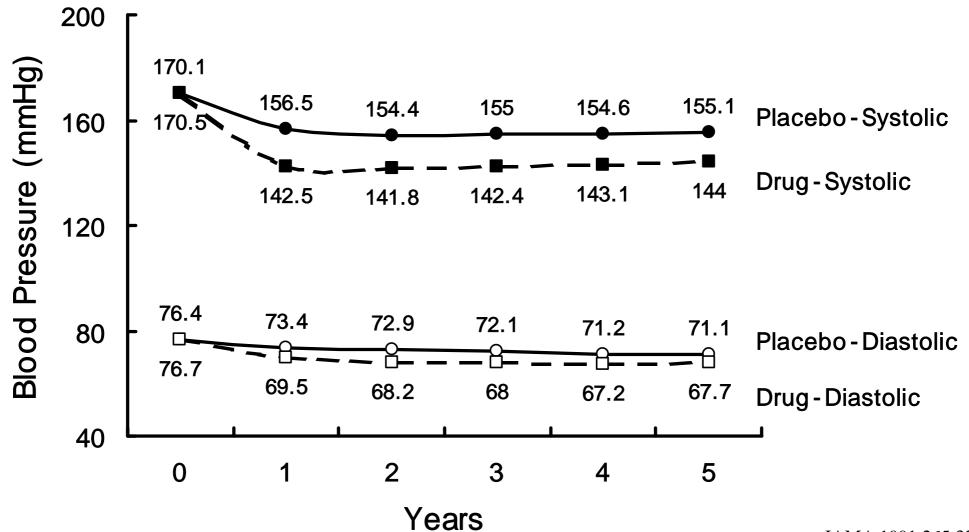
**¶**For 5 years.

Events



<sup>‡</sup>P<.01.

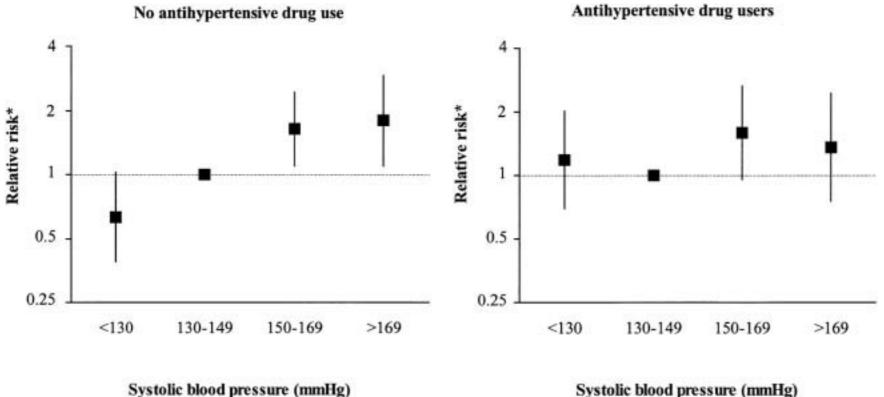
# Systolic and Diastolic Pressure during Follow-up in SHEP



# **Comparison of Treatment Groups between Old Meta-analysis and HOT**

	Collins et al. 1990 (n=18487)	HOT, 1998 (n=18790)
Age (years)	52.0	61.5
Initial DBP (mmHg)	99	105
Achieved DBP (mmHg)	93	83.2
DBP reduction (mmHg)	6	20-24
F/U duration (years)	5	3.8
Events (/1000 person-year	<i>:</i> )	
MI	7.8	3.0
CV Mortality	6.5	3.8

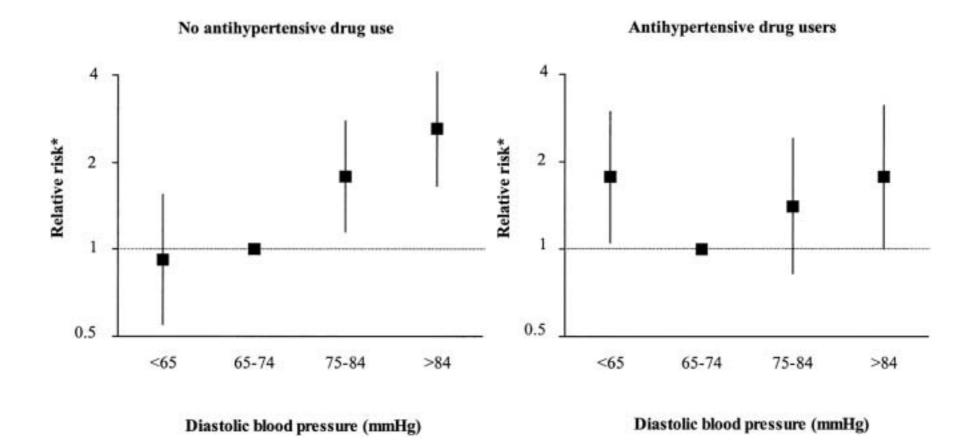
### Systolic BP and Risk of Stroke according to **Antihypertensive Treatment** -Rotterdam Study-



Systolic blood pressure (mmHg)

Hypertension 1999;34:1181

### Diastolic BP and Risk of Stroke according to Antihypertensive Treatment -Rotterdam Study-



Hypertension 1999;34:1181

### **Events in Patients without Diabetes Mellitus** -HOT-

Target BP*		/ents te**	p for trend		Target BP*	Number of events	Events rate**	p for trend
U	rdiovascular ev	ents			Cardiovas	cular mort	ality	
90 mm H					90 mm Hg	66	3.1	
85 mm Hg					85 mm Hg	69	3.2	
80 mm H					80 mm Hg		4.1	0.061
All myoca 90 mm Hg	ardial infarction g 70	n			Total mor			0.001
85 mm H					90 mm Hg	158		
80 mm H					85 mm Hg	165		
All strok					80 mm Hg	190		
90 mm H	g 77			_				

85 mm Hg

80 mm Hg

97

77

\*: actual BP; 85.2, 83.2, 81.1 mmHg respectively \*\*; per 1000 patient-year

# **Report of the European Working Party on High Blood Pressure in the Elderly (EWPHE)**

• Patients with low blood pressure had decreased values for body mass index and hemoglobin—two indicators of poor health

# **CVD vs Systolic and Diastolic BP** Framingham Study

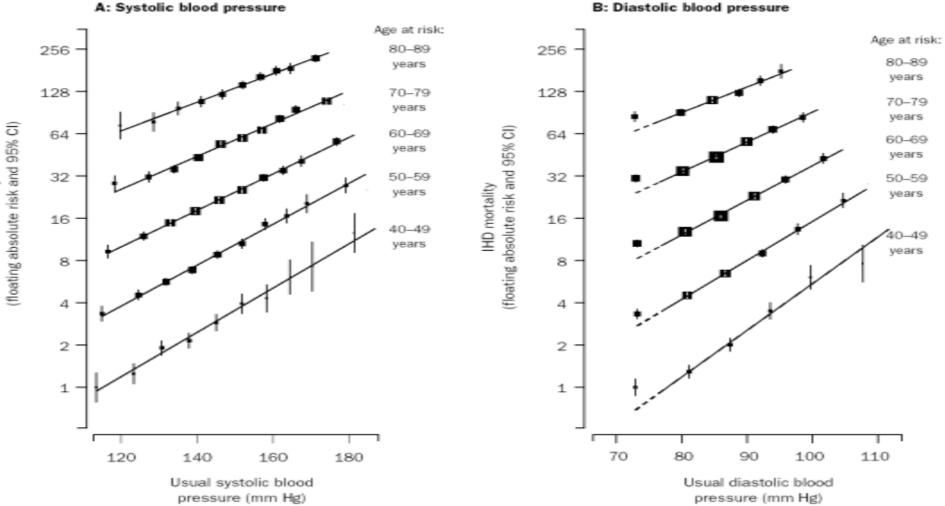
**TABLE 4** Incidence of Nonfatal Cardiovascular Events by Diastolic Pressure at

 Specified Levels of Systolic Blood Pressure\*

Diastolic BP (mm Hg)	10-Yr Incidence Rate (%)									
	Systolic BP (mm Hg): <140			140-159			>160			
	At risk	Events	Rate	At risk	Events	s Rate	At risk	Events	Rate	
Men										
<80	1,147	129	11.3%	65	29	44.6%	12	6	50.0%	
80-90	1,219	139	11.4%	211	44	20.9%	42	19	45.2%	
>90	288	56	19.4%	414	79	19.1%	230	76	33.0%	
Women										
<80	1,918	92	4.8%	133	30	22.6%	38	12	31.6%	
90	1,023	68	6.7%	267	36	13.5%	89	19	21.4%	
>90	163	17	10.4%	289	42	14.5%	250	58	23.2%	
Both										
<80	3,065	221	7.2%	198	59	29.8%	50	18	36.0%	
80-89	2,242	207	9.2%	478	80	16.7%	131	38	29.0%	
>90	451	73	16.2%	703	121	17.2%	480	134	27.9%	

Kannel. Am J Cardiol 2004;94:380

### Age-Specific Relevance of Usual Blood Pressure to Vascular Mortality: a Meta-Analysis



**HD** mortality

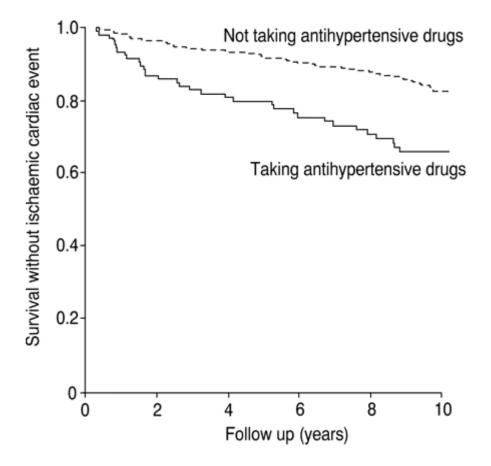
Lancet 2002; 360: 1903-13

### **Randomized Trials of Drug Therapy in AMI** (Beat-blocker)

Agents	No. of Patients	Duration of Study	RR of Death (95% CI)	р
)n				
Atenolol	16,027	7 days	0.85 (0.73-0.99)	0.04
Metoprolol	5,778	15 days	0.87 (0.67-1.08)	0.29
Metoprolol	1,434	6 days	1.00‡	0.98
Timolol	1,884	33 mo	0.61 (0.46-0.80)	0.001
Propranolol	3,837	25 mo	0.72 (0.64-0.80)	0.005
	on Atenolol Metoprolol Metoprolol Timolol	Patients Patients Patients Timolol 16,027 S,778 Patients	Patients of Study on Atenolol 16,027 7 days Metoprolol 5,778 15 days Metoprolol 1,434 6 days Timolol 1,884 33 mo	Patients       of Study       (95% CI)         on       Atenolol       16,027       7 days       0.85 (0.73-0.99)         Metoprolol       5,778       15 days       0.87 (0.67-1.08)         Metoprolol       1,434       6 days       1.00‡         Timolol       1,884       33 mo       0.61 (0.46-0.80)

### Incidence of myocardial infarction in elderly men being treated with antihypertensive drugs

- 484 men born in 1914 and living in Malmo, Sweden during 1982 and follow up for up to 10 years
- Among men with diastolic blood pressure >90 mm Hg, the risk was increased twofold but disappeared when adjustments were made for other cardiovascular risk factors
- Among those with diastolic blood pressure </=90 mm Hg, the risk associated with taking antihypertensive drugs was four times higher and remained after adjustment for other cardiovascular risk factors



BMJ 1996;313:457-461