

**Primary Prevention of  
Cardiovascular Disease in Diabetes:  
Treat as Secondary Prevention or Assess Individual  
Risks?**

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**Norwegian Postgraduate Course in Diabetes  
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# ANTIHYPERTENSIVE TREATMENT IN DIABETES

	Diabetic n	Rx	$\Delta$ SBP	$\Delta$ DBP	↓ Stroke	↓ CHD
SHEP	583	Thiazide	-9.8	-2.2	-22%	-56%
SYST.EUR	492	CCB	-8.6	-3.9	-69%	-57%
UKPDS	1148	$\beta$ blocker ACEI	-10	-5	-44%	-21%

# CARDIOVASCULAR EVENTS IN DIABETIC PATIENTS IN SHEP STUDY

Chlorthalidone ± atenolol for non-insulin treated patients with systolic BP  $\geq$ 160 mmHg, diastolic  $<$ 90 mmHg

	Diabetic (n=583)	Non-diabetic (n=4149)
Major CV events per 5yrs (%)	21.4 vs 31.5	13.3 vs 18.4
RR	0.66 (0.46-0.94)	0.66 (0.55-0.79)
Major CHD events per 5yrs (%)	9.2 vs 16.1	6.9 vs 7.6
RR	0.44 (0.25-0.77)	0.81 (0.62-1.05)

## HOT Study - diabetic subjects

Event	No. of events	Events/1000 patient-years	p for trend	Comparison	RR (95% CI)
<b><u>Major cardiovascular events</u></b>					
≤90 mmHg	45	24.4		90 vs 85	1.32 (0.843-2.06)
≤85 mmHg	34	18.6		85 vs 80	1.56 (0.91-2.67)
≤80 mmHg	22	11.9	0.005	90 vs 80	2.06 (1.24-3.44)
<b><u>All stroke</u></b>					
≤90 mmHg	17	9.1		90 vs 85	1.30 (0.63-2.67)
≤85 mmHg	13	7.0		85 vs 80	1.10 (0.50-2.40)
≤80 mmHg	12	6.4	0.34	90 vs 80	1.43 (0.68-2.99)

Events in patients with diabetes mellitus at baseline in relation to target blood pressure groups (n=501, 501 and 499 in the target groups ≤90 , ≤85 and ≤80 mmHg respectively)

# EFFECTS OF RAMIPRIL IN DIABETIC PATIENTS

## HOPE STUDY

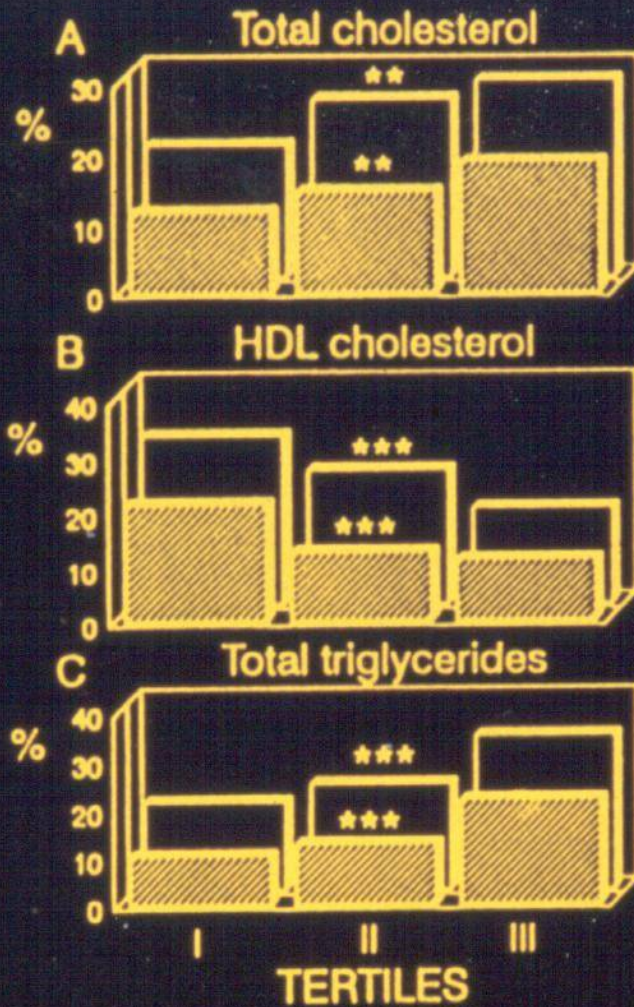
	<b>Ramipril (n = 1808)</b>	<b>Placebo (n = 1769)</b>	<b>Risk Reduction</b>	<b>P</b>
<b>MI, Stroke, CV Death</b>	15.3%	19.8%	25%	0.0004
<b>Total mortality</b>	10.8%	14.0%	24%	0.004
<b>CV death</b>	6.2%	9.7%	37%	0.0001
<b>Heart failure</b>	11.0%	13.3%	20%	0.019
<b>Overt nephropathy</b>	6.5%	8.4%	24%	0.027
<b>Laser therapy</b>	9.4%	10.5%	22%	0.24

<b>Blood pressure (mm Hg)</b>	<b>Baseline</b>	<b>Change at 1 month</b>	<b>Change at 2 years</b>	<b>Change at final visit</b>
<b>Systolic</b>				
Ramipril	141.7	-5.3	-2.7	-1.9
Placebo	142.3	-1.3*	0.6*	0.55†
<b>Diastolic</b>				
Ramipril	80.0	-2.6	-2.6	-3.3
Placebo	79.3	-0.3*	-1.05*	-2.3‡

\*p=0.0001. †p=0.0002. ‡p=0.008. p values for difference in change from baseline (ramipril vs placebo).

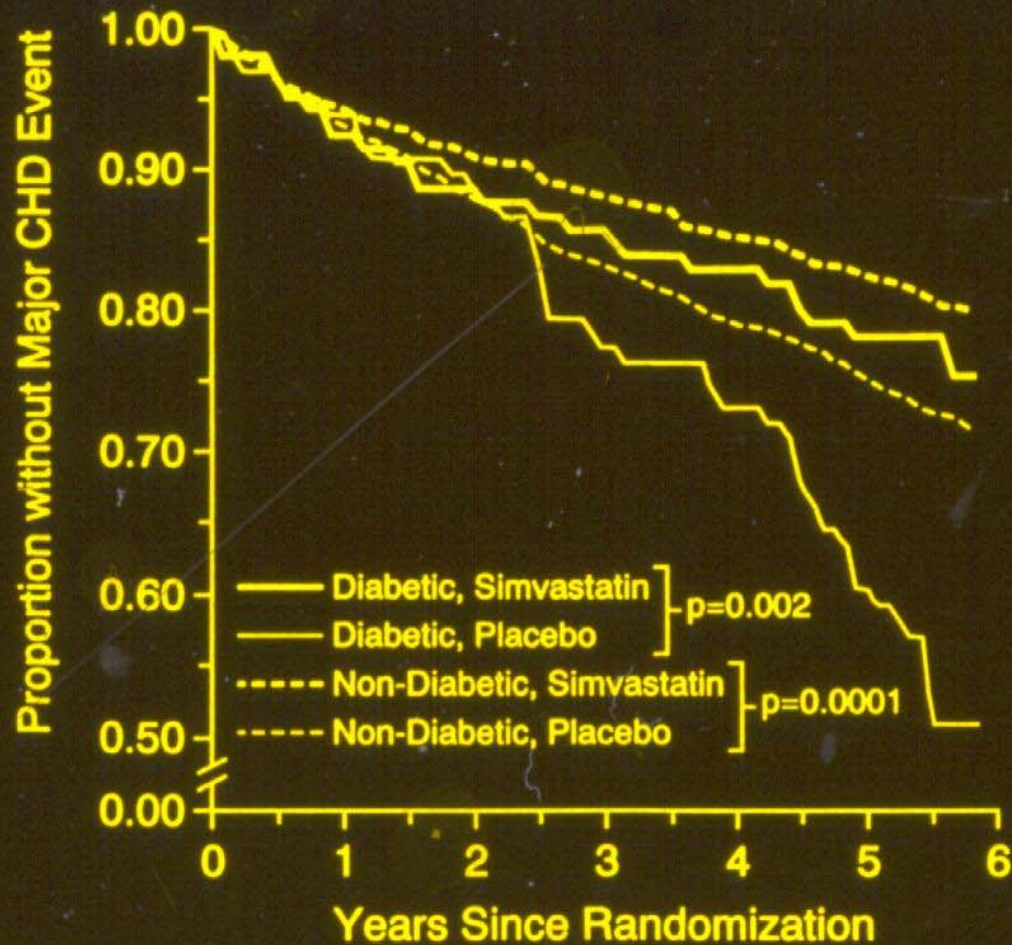
**Change in blood pressure with ramipril and placebo**

**HOPE Study, 2000**



**The 7-year age-adjusted incidence (%) of CHD mortality (▨) and all CHD events (CHD death or nonfatal myocardial infarction) (□) with respect to the tertiles of serum lipids**

Lehto et al, 1997



*Kaplan-Meier survival curves for the probability of remaining free of a major CHD event during follow-up in nondiabetic and diabetic patients treated with placebo or simvastatin in the 4S.*



# EFFECT OF LIPID LOWERING THERAPY ON CHD EVENTS IN DIABETIC PATIENTS

## PRIMARY PREVENTION

STUDY	DIABETIC (n)	DRUG	CHD REDUCTION	P VALUE
Helsinki Heart	125	Gemfibrozil	60%	NS
AFCAPS/TEXCAPS	155	Lovastatin	33%	NS

## SECONDARY PREVENTION

4S	202	Simvastatin	55%	0.002
CARE	586	Pravastatin	25%	0.05
LIPID	782	Pravastatin	19%	NS
VA-HIT	627	Gemfibrozil	24%	0.05

## THE EFFECT OF GEMFIBROZIL IN SECONDARY PREVENTION OF CHD EVENTS IN 2531 MEN WITH LDL-CHOLESTEROL <3.6 MMOL/L

Subgroup	Placebo	Gemfibrozil	Risk Reduction	P Value
<b>Diabetes</b>				
Yes	116/318 (36%)	88/309 (28%)	24 (-0.1 to 43)	0.05
No	214/949 (23%)	170/955 (18%)	24 (6 to 30)	0.009

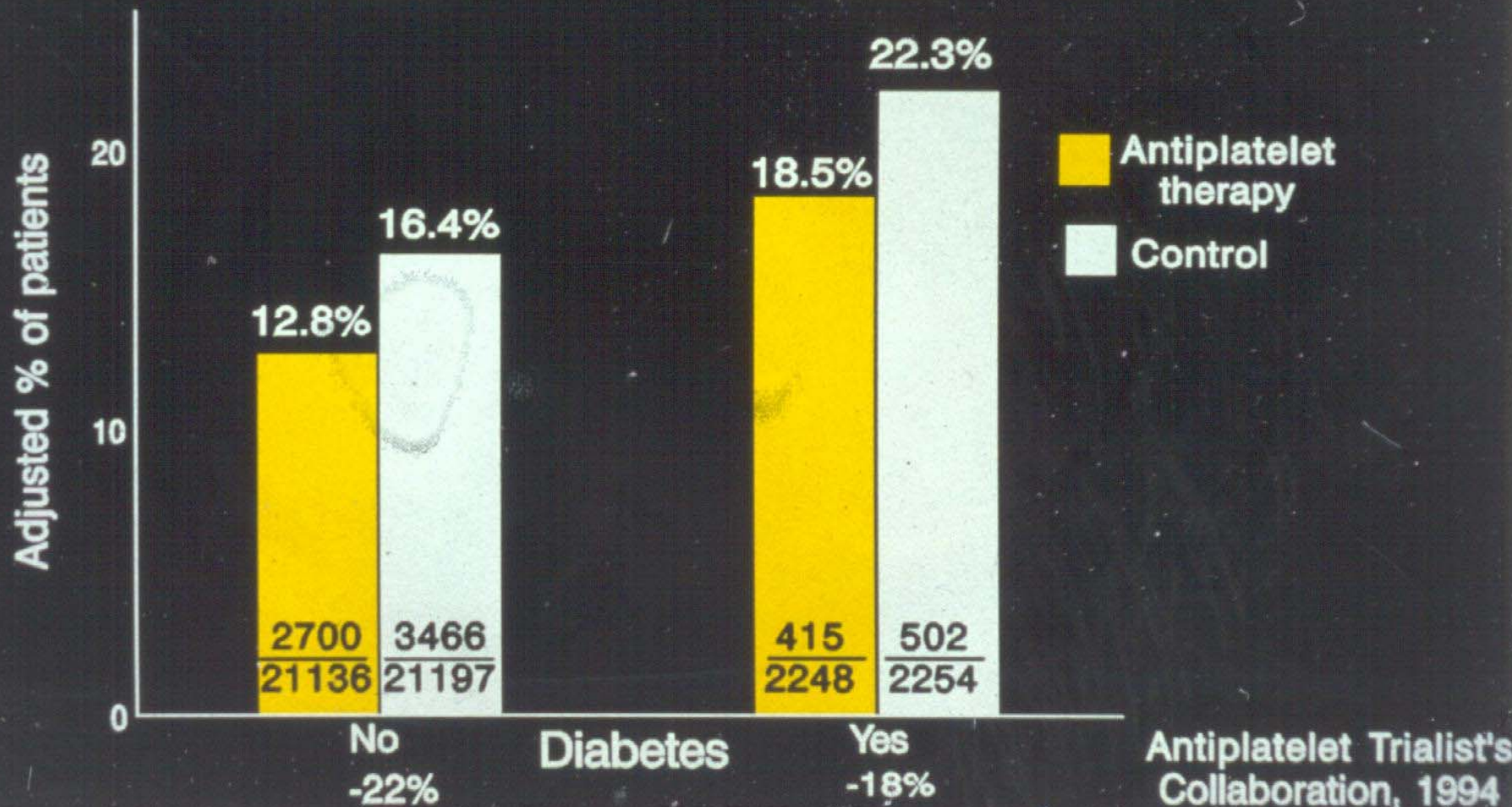
VA-HIT Study, 1999

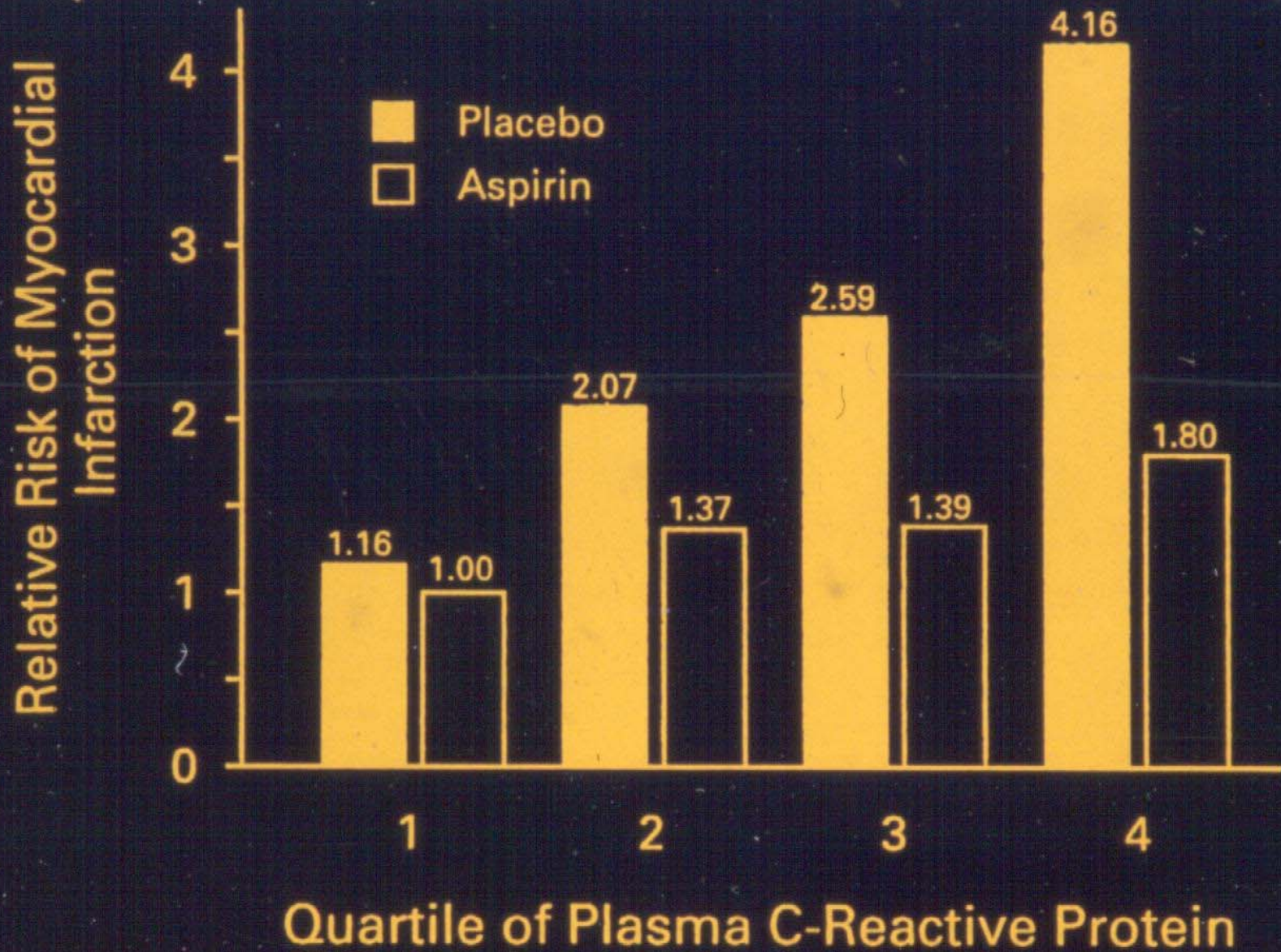
# ANTIPLATELET THERAPY IN DIABETIC PATIENTS

Benefit per 1000 patients (SD):  
 P: <0.00001

36 (3)  
 <0.00001

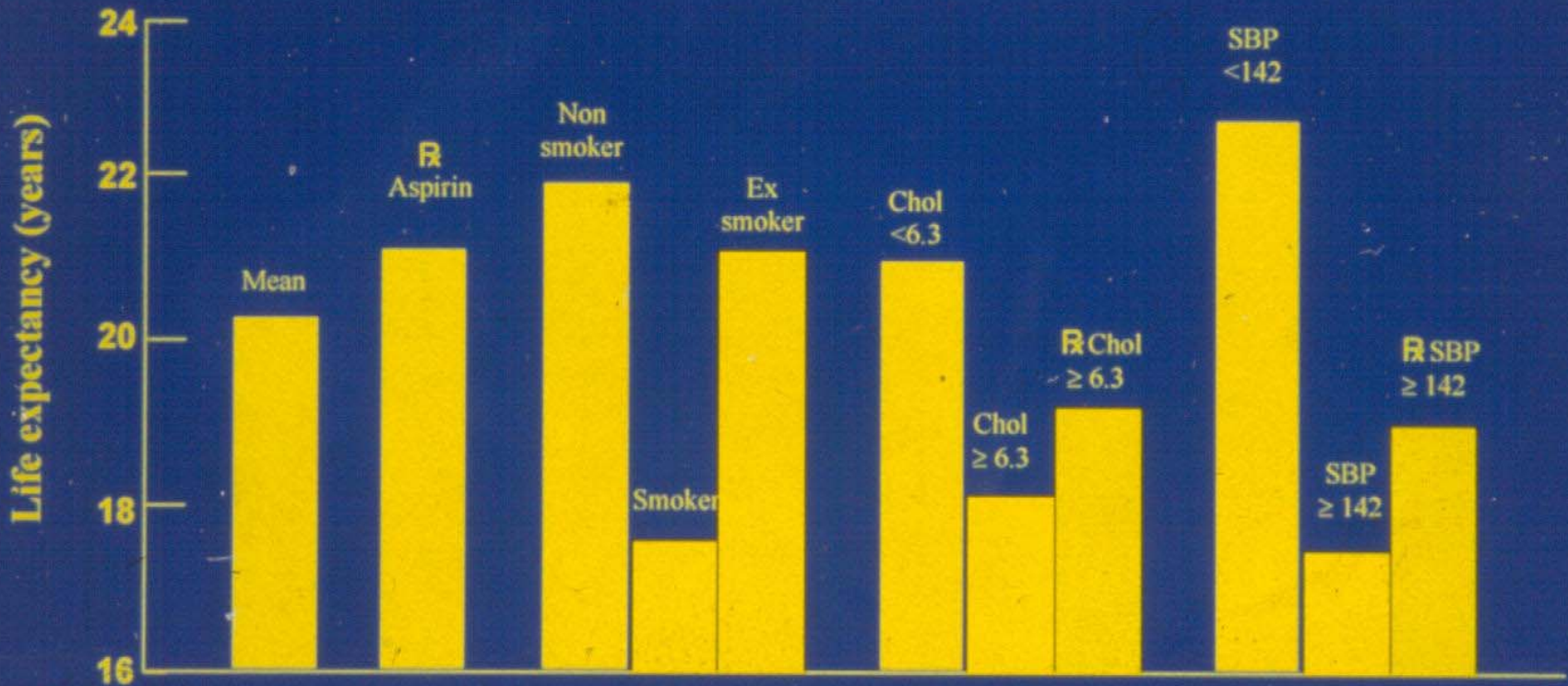
38 (12)  
 <0.002

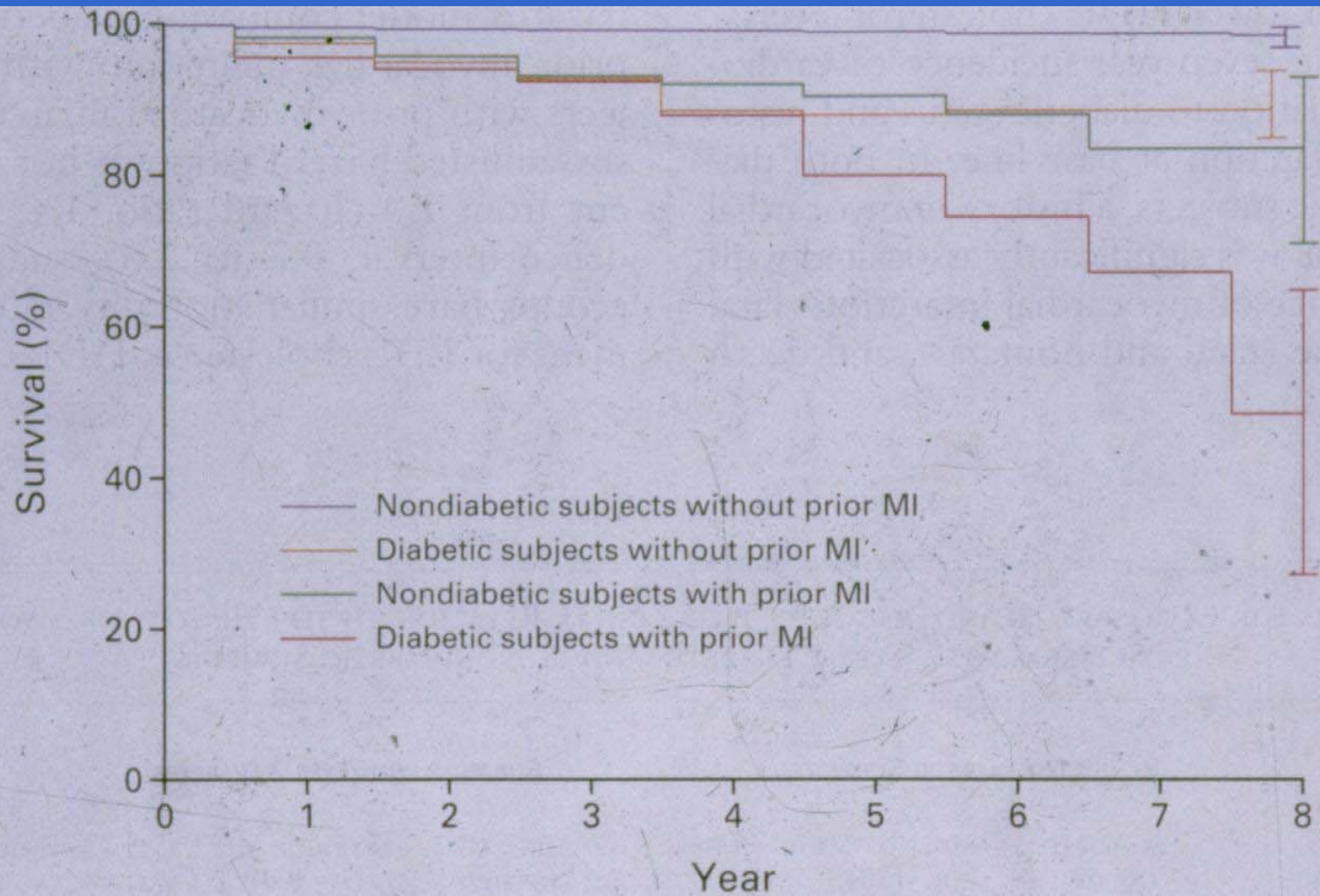




Ridker et al, 1997

# EFFECTS OF RISK FACTORS AND INTERVENTIONS ON LIFE EXPECTANCY IN A 45 YEAR OLD DIABETIC MAN



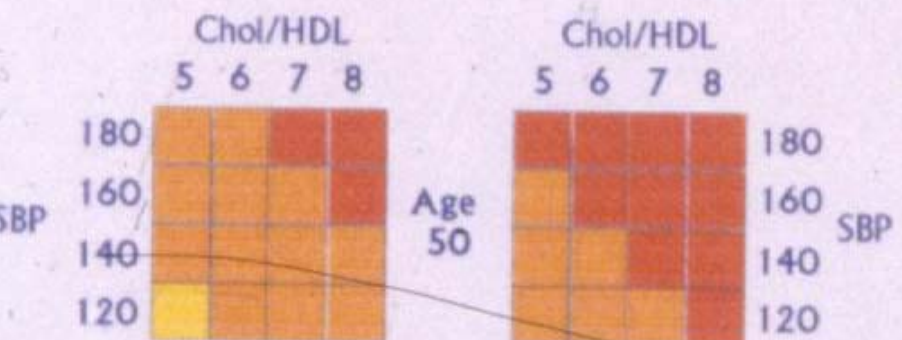
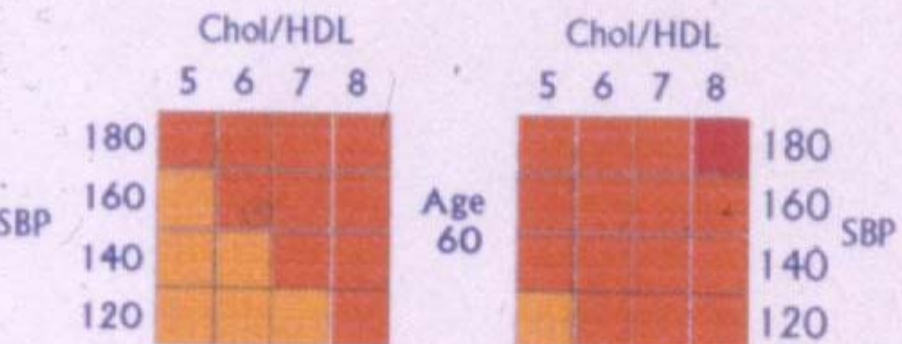
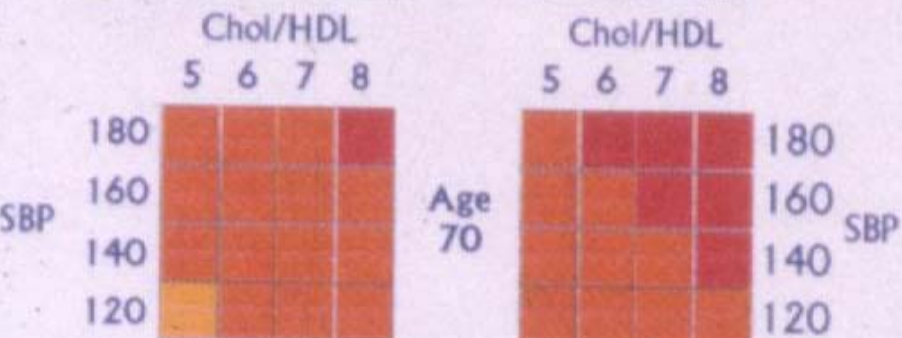


Kaplan - Meier Estimates of the Probability of Death from Coronary Heart Disease in 1059 Subjects with Type 2 Diabetes and 1378 Nondiabetic Subjects with and without Prior Myocardial Infarction. MI denotes myocardial infarction. I bars indicate 95% confidence intervals. Haffner et al, 1998.

# NON-DIABETIC MEN

## NON-SMOKERS

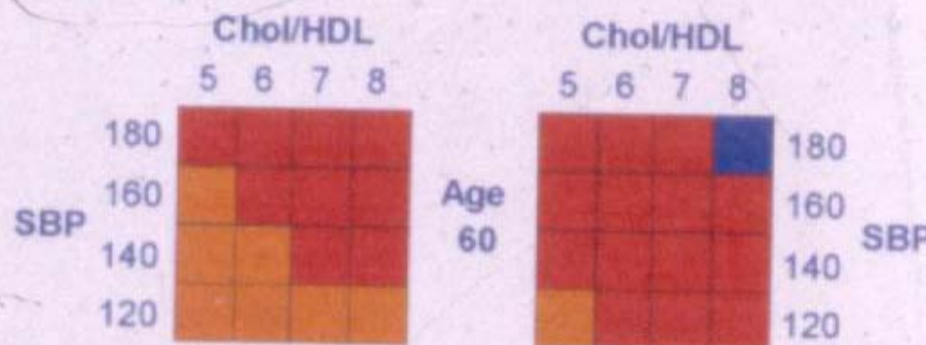
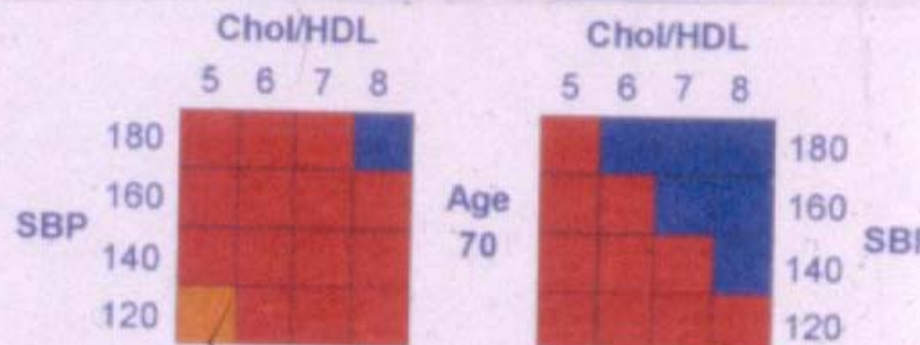
## SMOKERS

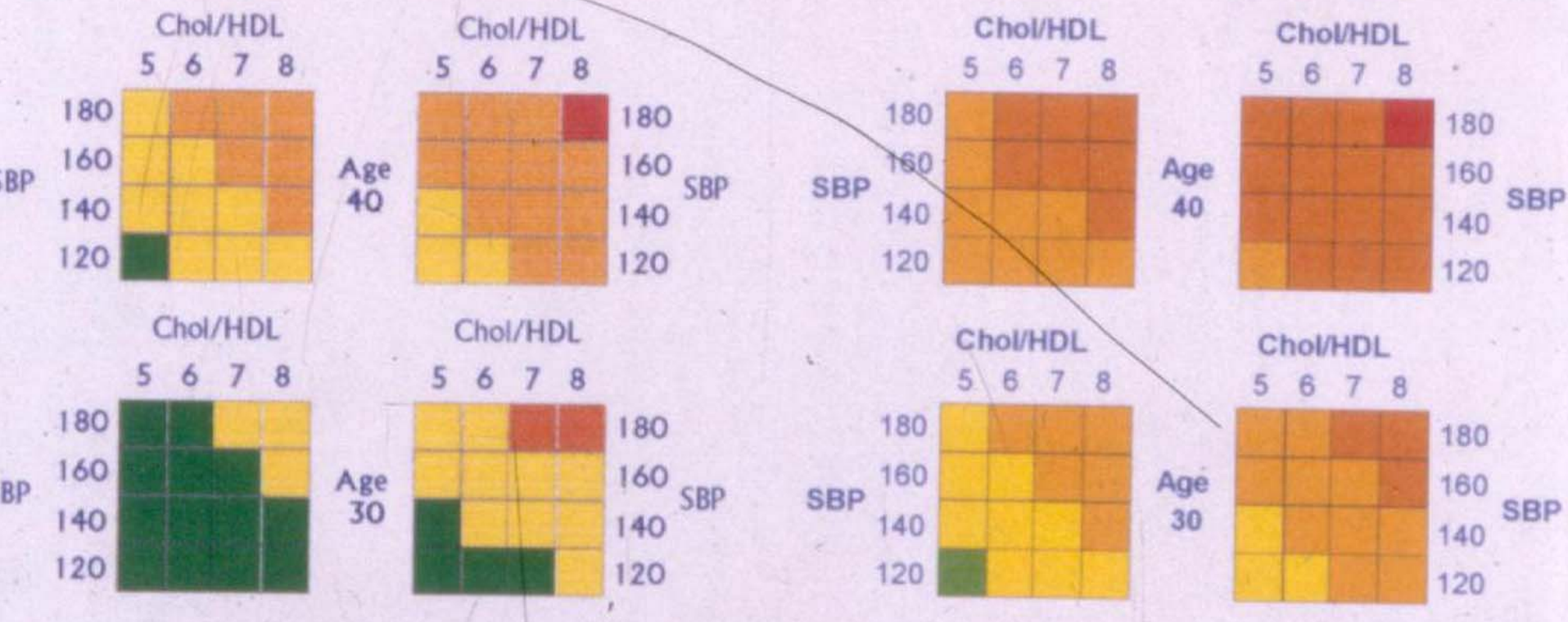


# MICROALBUMINURIC DIABETIC MEN

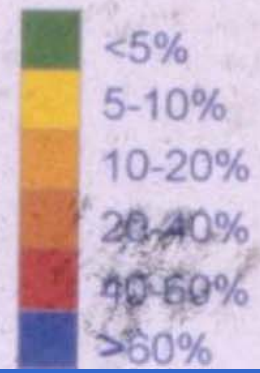
## NON-SMOKERS

## SMOKERS





**% Risk of CHD event in 10 yrs**



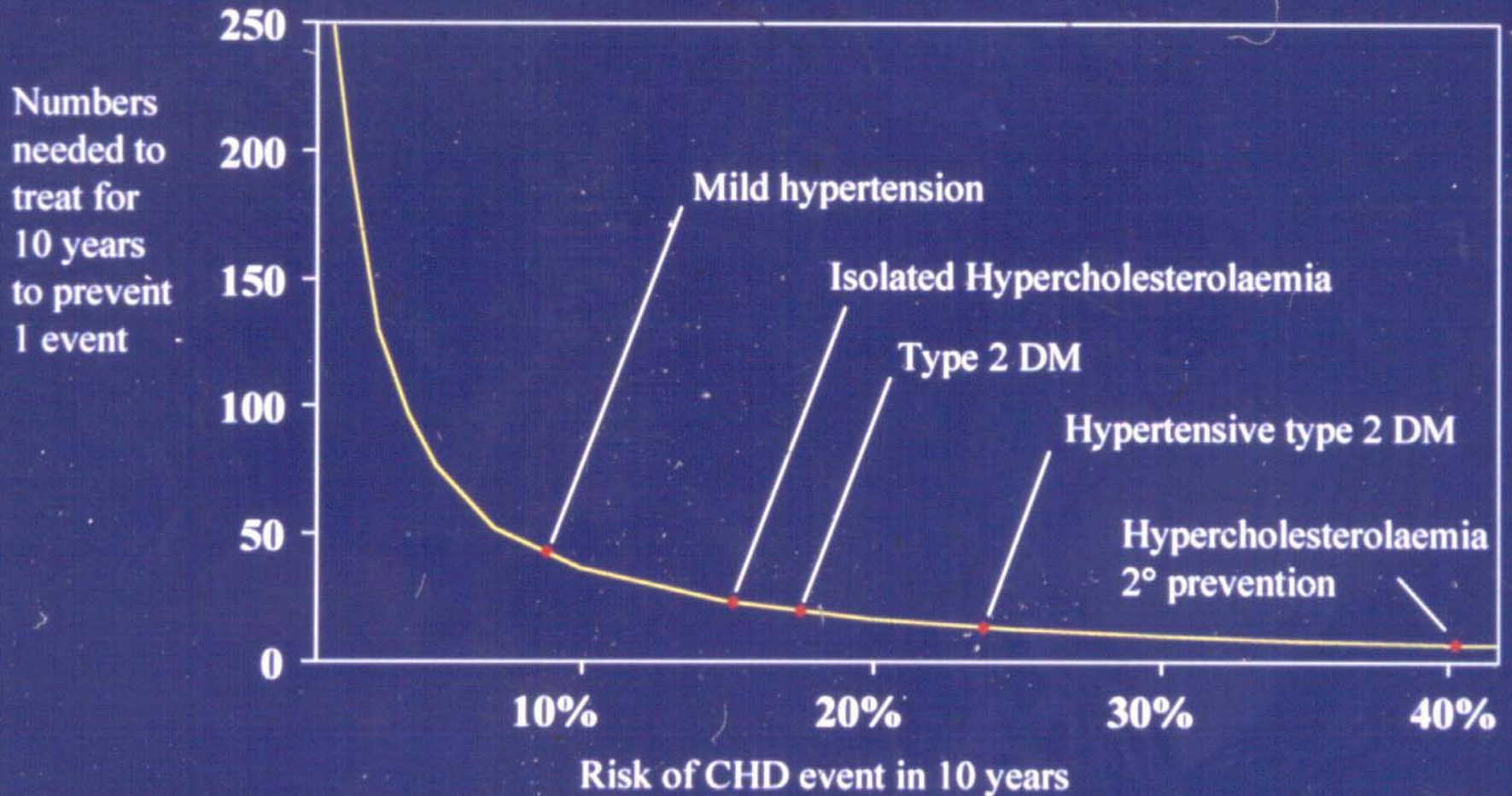


# **NUMBERS NEEDED TO TREAT FOR 10 YEARS TO PREVENT 1 CHD EVENT IF BACKGROUND RISK IS 30%**

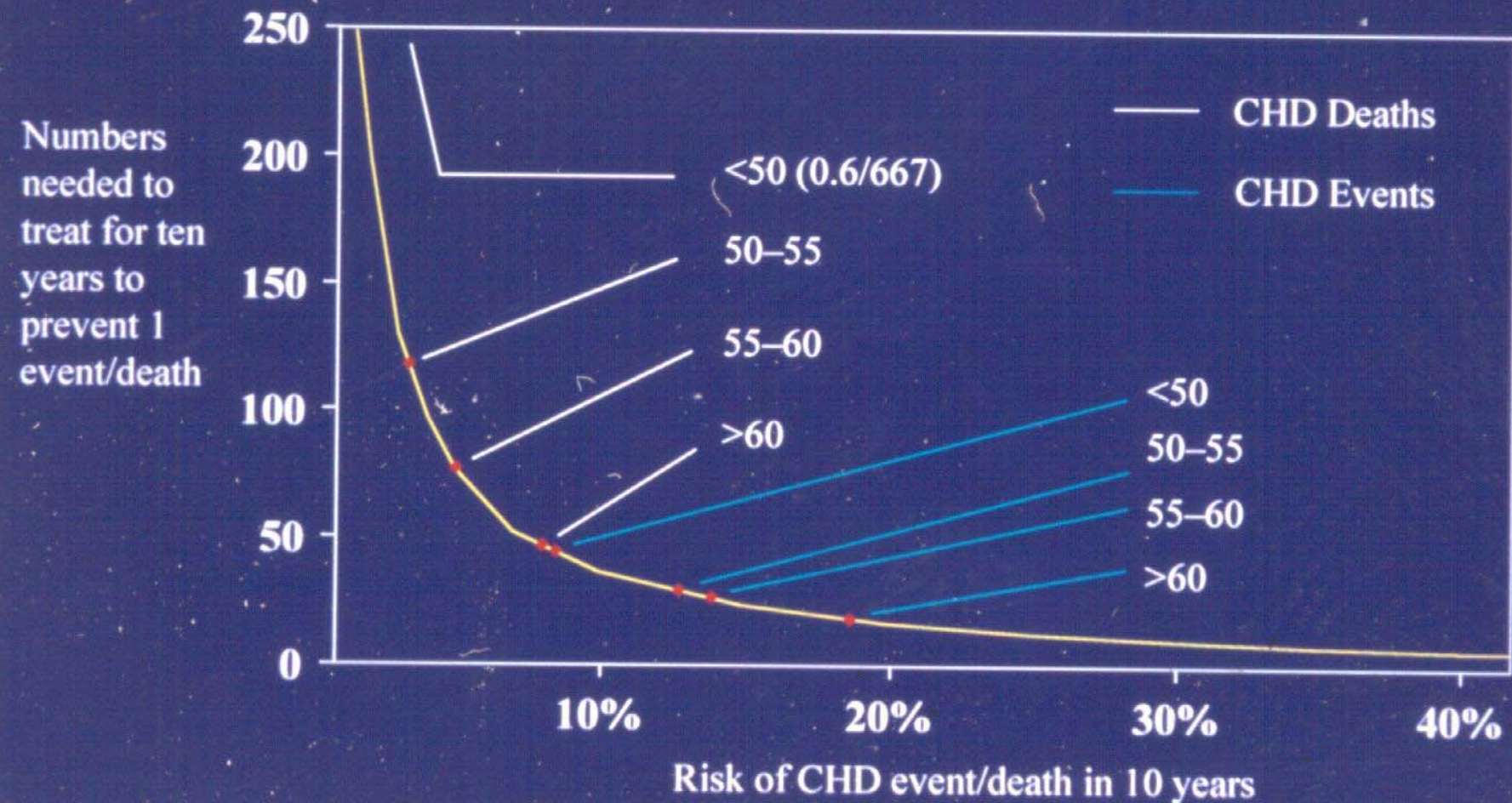
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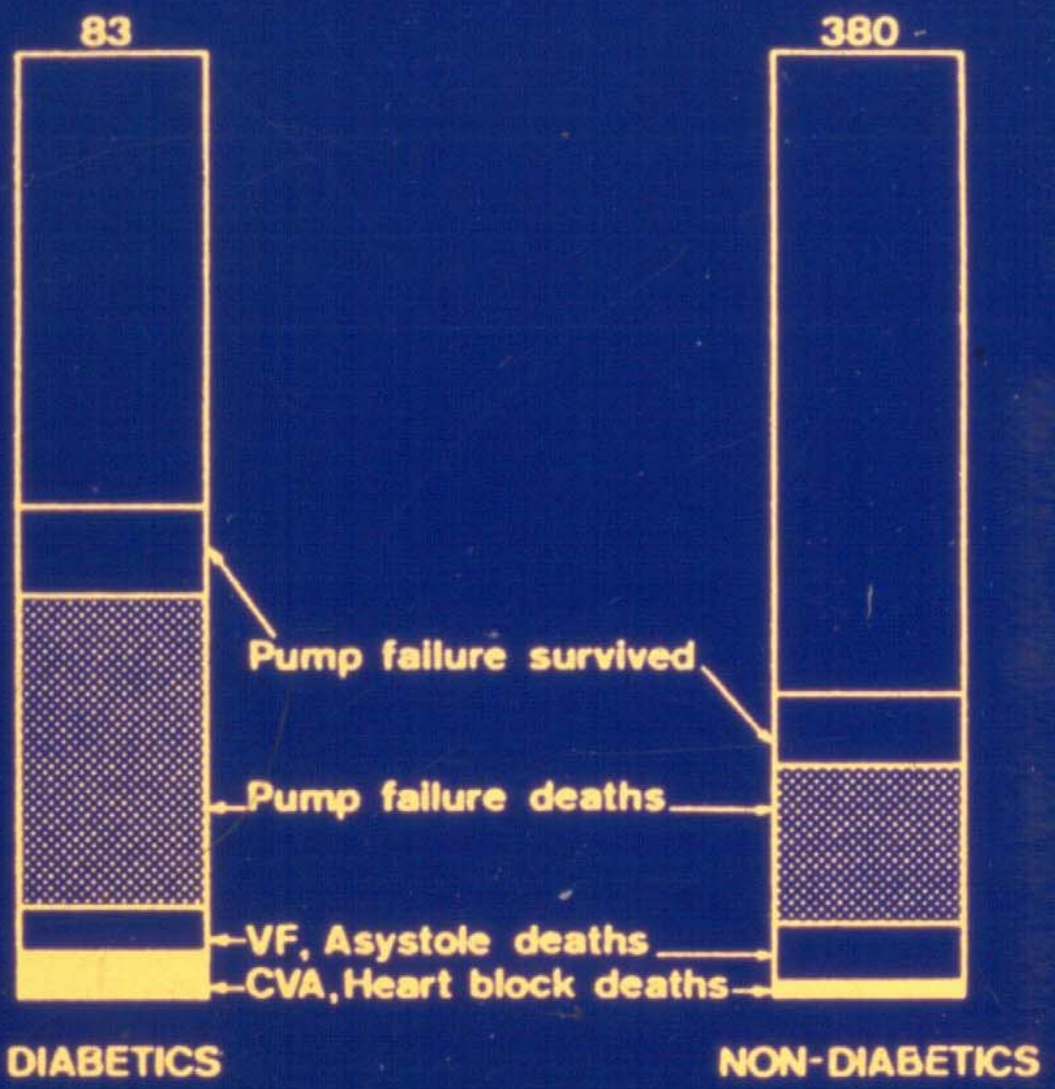
Glucose lowering	20.8
Blood pressure	15.9
Cholesterol lowering	29.8
Aspirin	15.2
Stopping smoking	17.4

# Numbers needed to treat with 25% risk reduction – men aged 55 to 60



# Effect of age on numbers needed to treat – Type 2 Diabetes



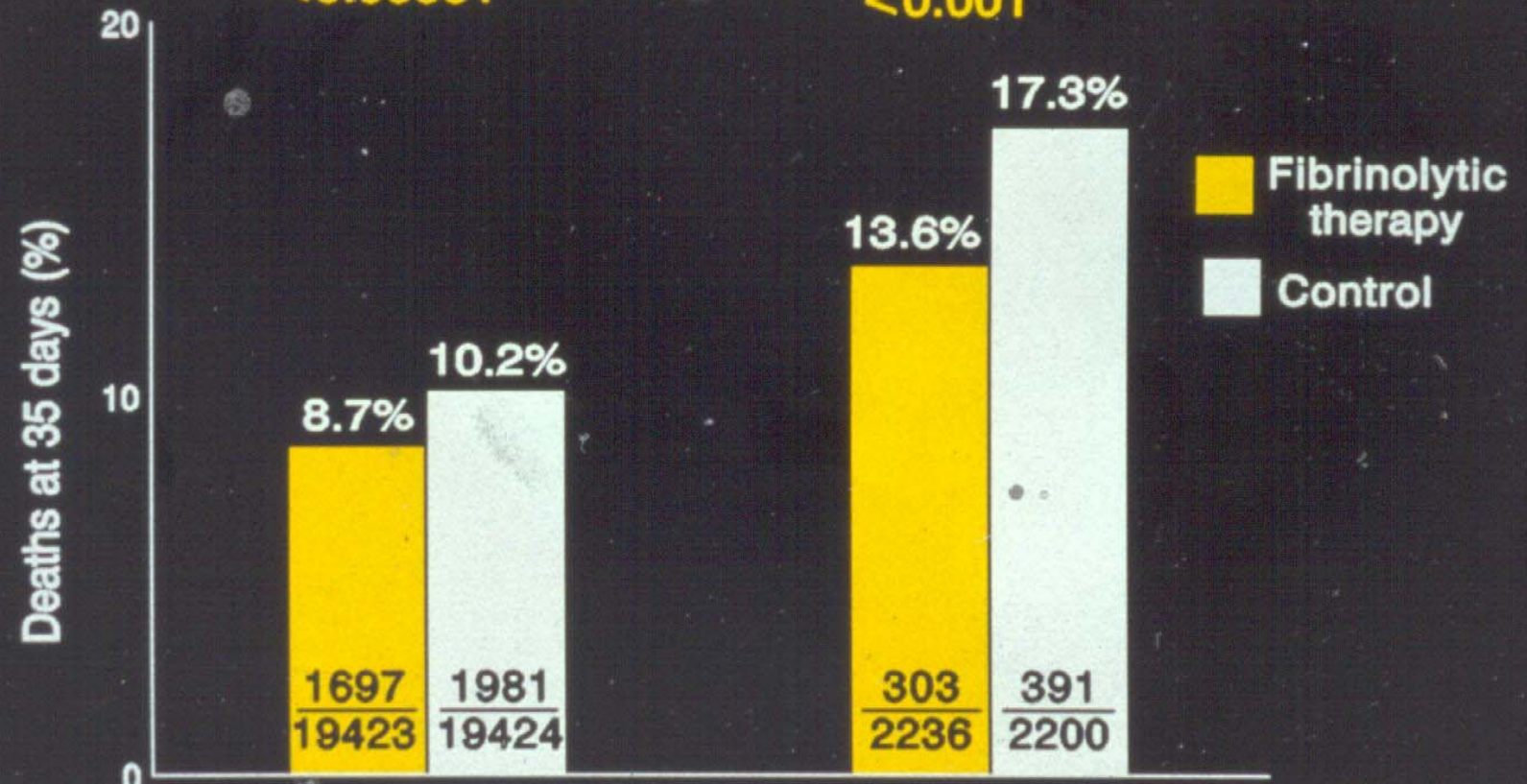


# THROMBOLYTIC THERAPY IN DIABETIC PATIENTS

Benefit per 1000 patients (SD)  
2P:

15 (3)  
<0.00001

37 (11)  
<0.001



No  
-15%

Diabetes

Yes  
-21%

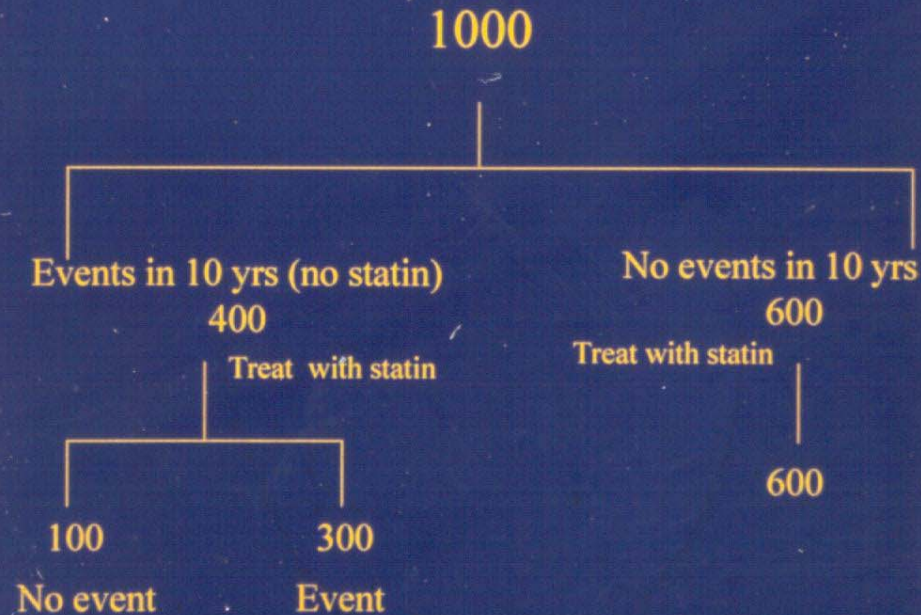
FTT Collaborative Group, 1994

# 1000 diabetic patients with hypercholesterolaemia

CHD risk approx 40% in 10 yrs

Effects of statins - ↓ risk by 1/4

No of Patients Treated



To prevent 100 myocardial infarctions need to treat 1000 men for 10 yrs

To prevent 1 myocardial infarction need to treat 10 men for 10 yrs

# Cost of Simvastatin

£1.11 = for 20mg

1 patient 20mg/day = £1.11 per day  
= £7.77 per week  
= £404.04 per year  
= £4,040 over  
10 years

10 patients 20mg/day for 10 years

£4,040 x 10 = £40,400

£40,400

# CONCLUSION

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- Assess overall risk - not “levels”
- Most diabetic patients need “2<sup>0</sup>” prevention
- Aggressive management of smoking
- Aggressive management of blood pressure
- Aggressive management of cholesterol
- Low threshold for aspirin