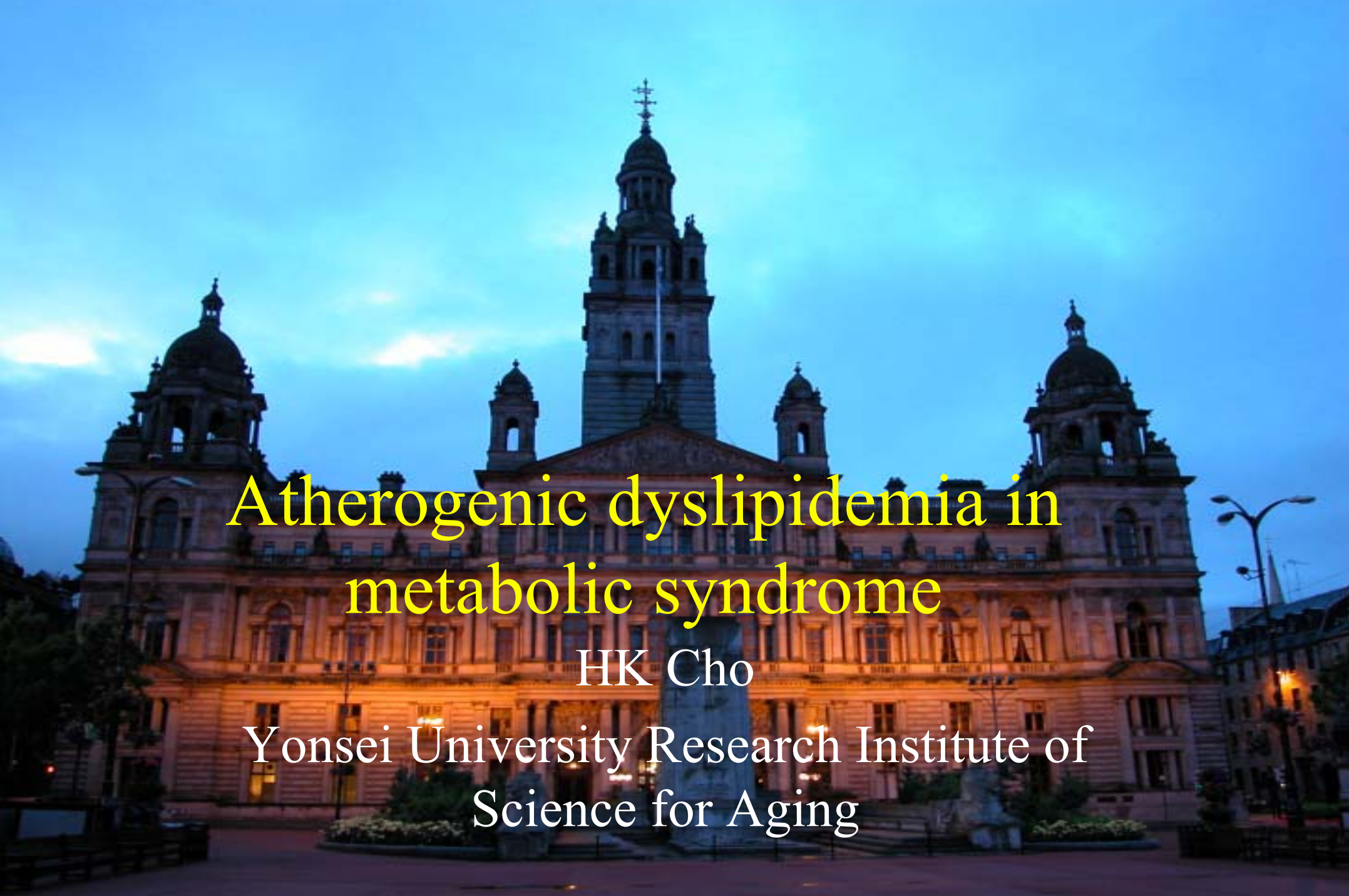
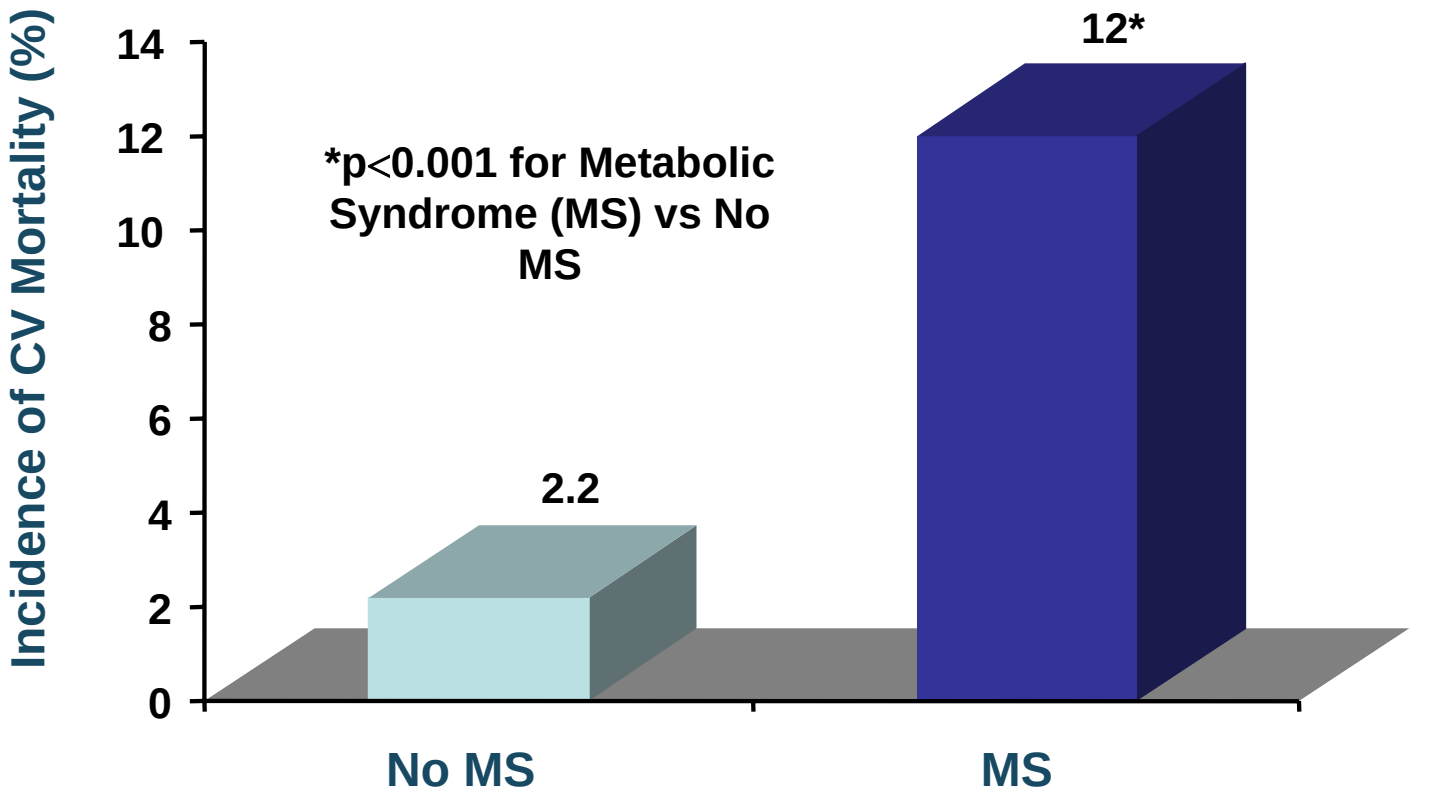


Atherogenic dyslipidemia in metabolic syndrome

HK Cho

Yonsei University Research Institute of Science for Aging

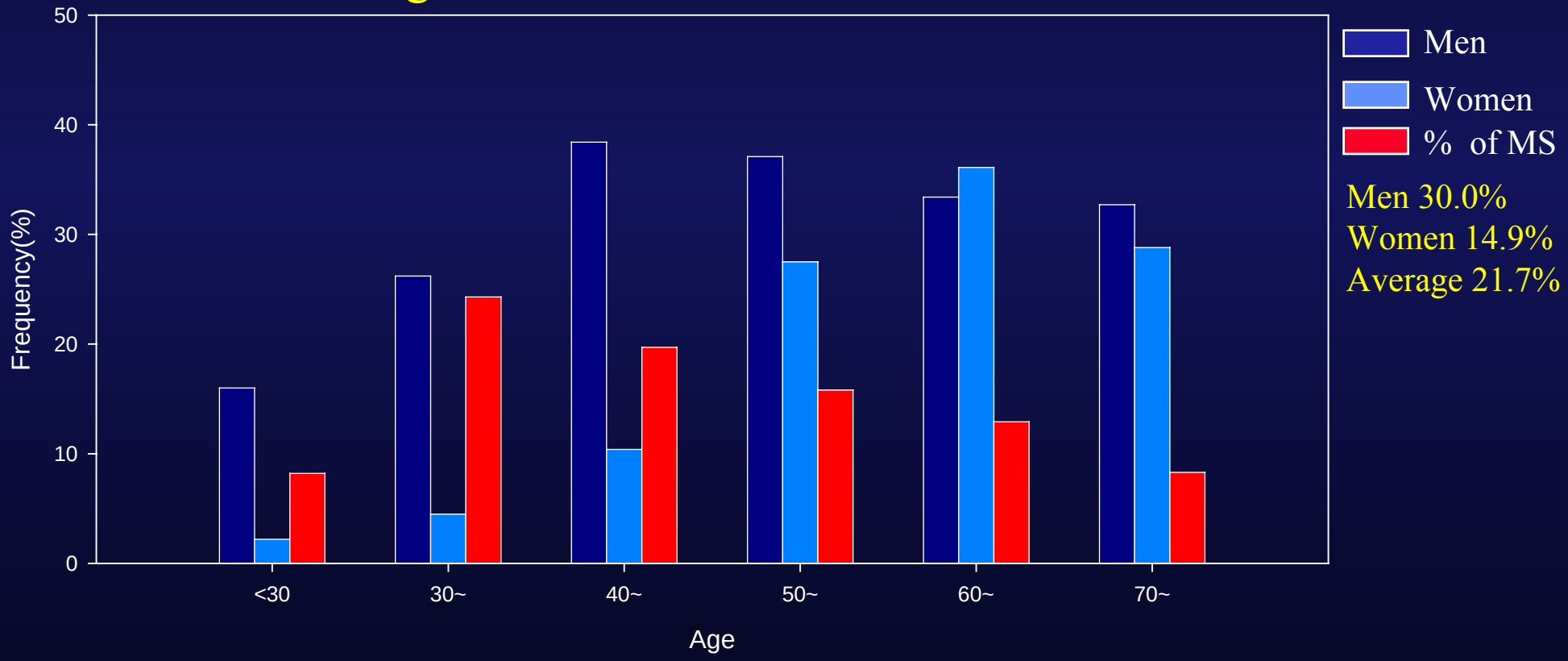
Cardiovascular Mortality and Metabolic Syndrome



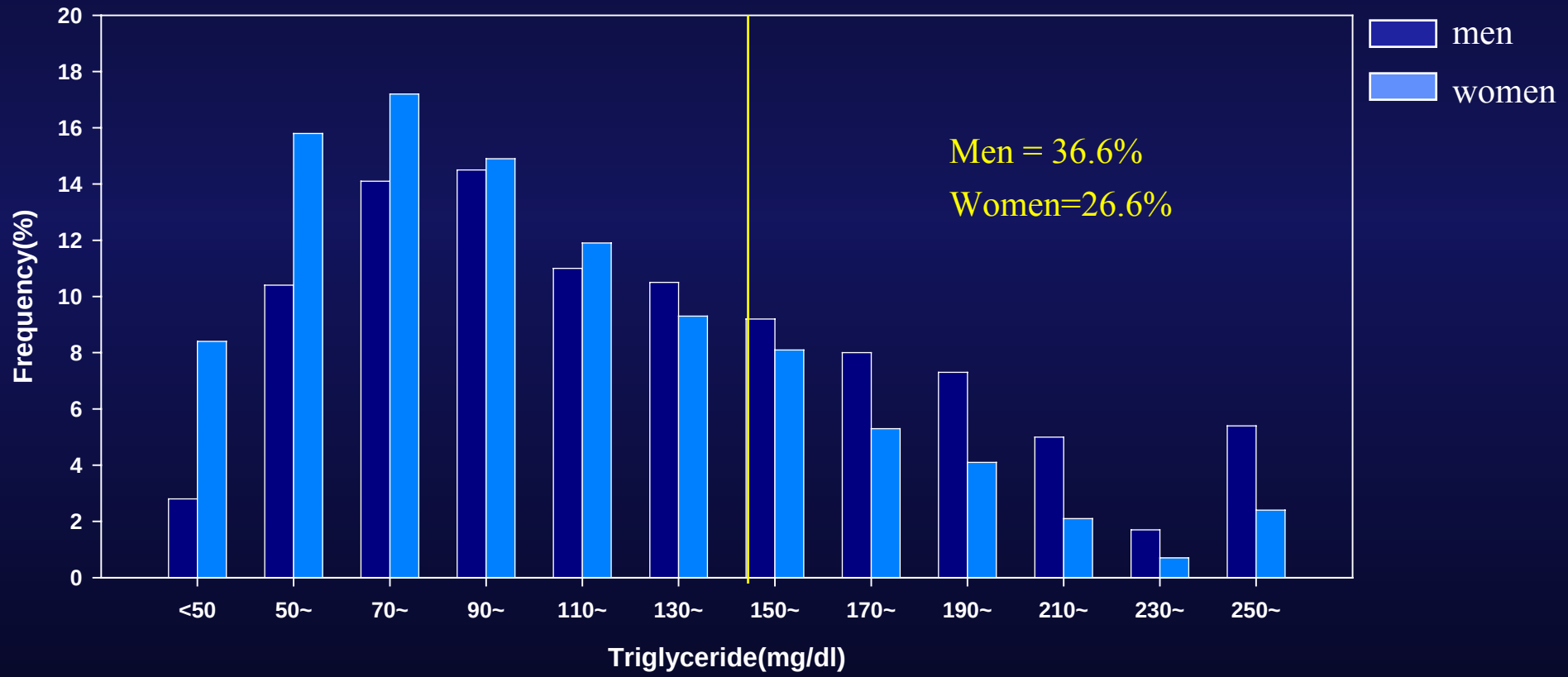
Isomaa B et al. *Diabetes Care*. 2001;24:683

Prevalence of metabolic syndrome in Korean population

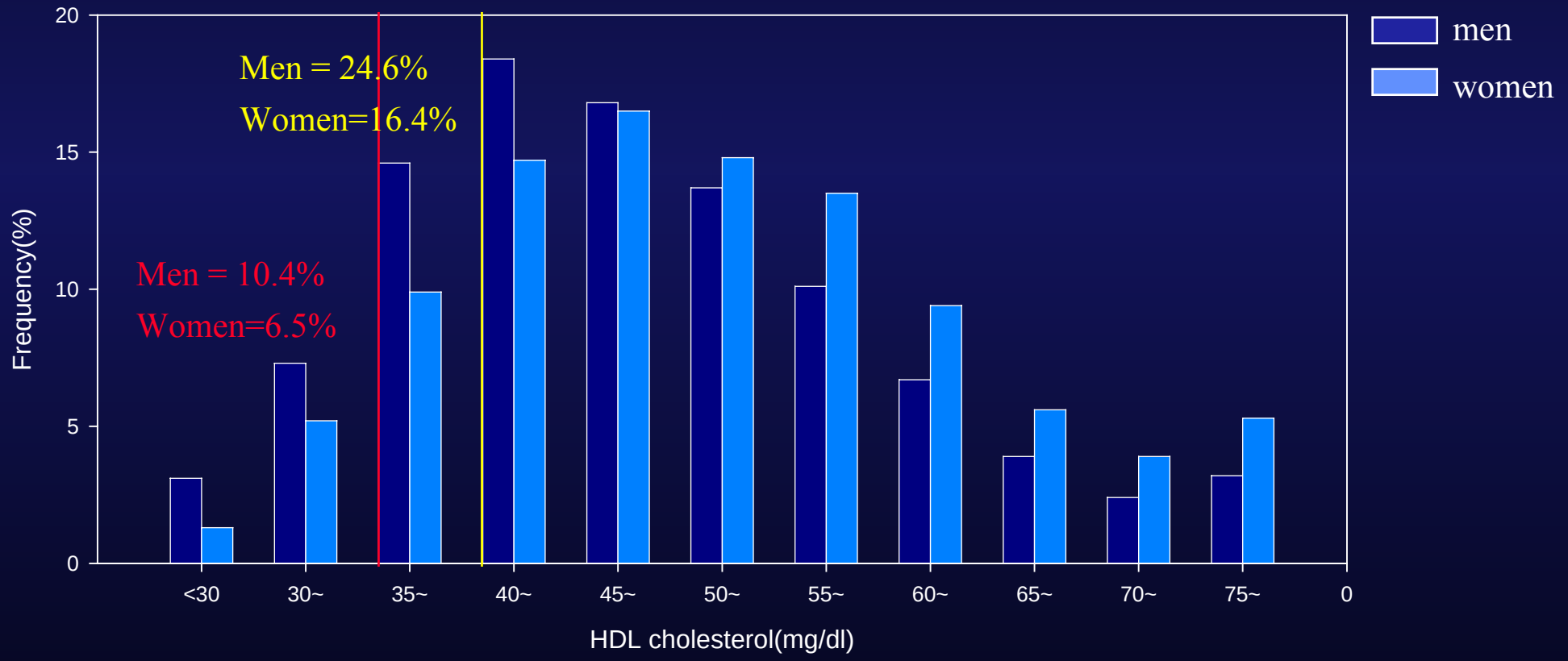
Asian-Pacific guideline



Distribution of triglyceride in Korean population



Distribution of HDLc in Korean population



Atherogenic dyslipidemia

Hypertriglyceridemia

Low HDLc

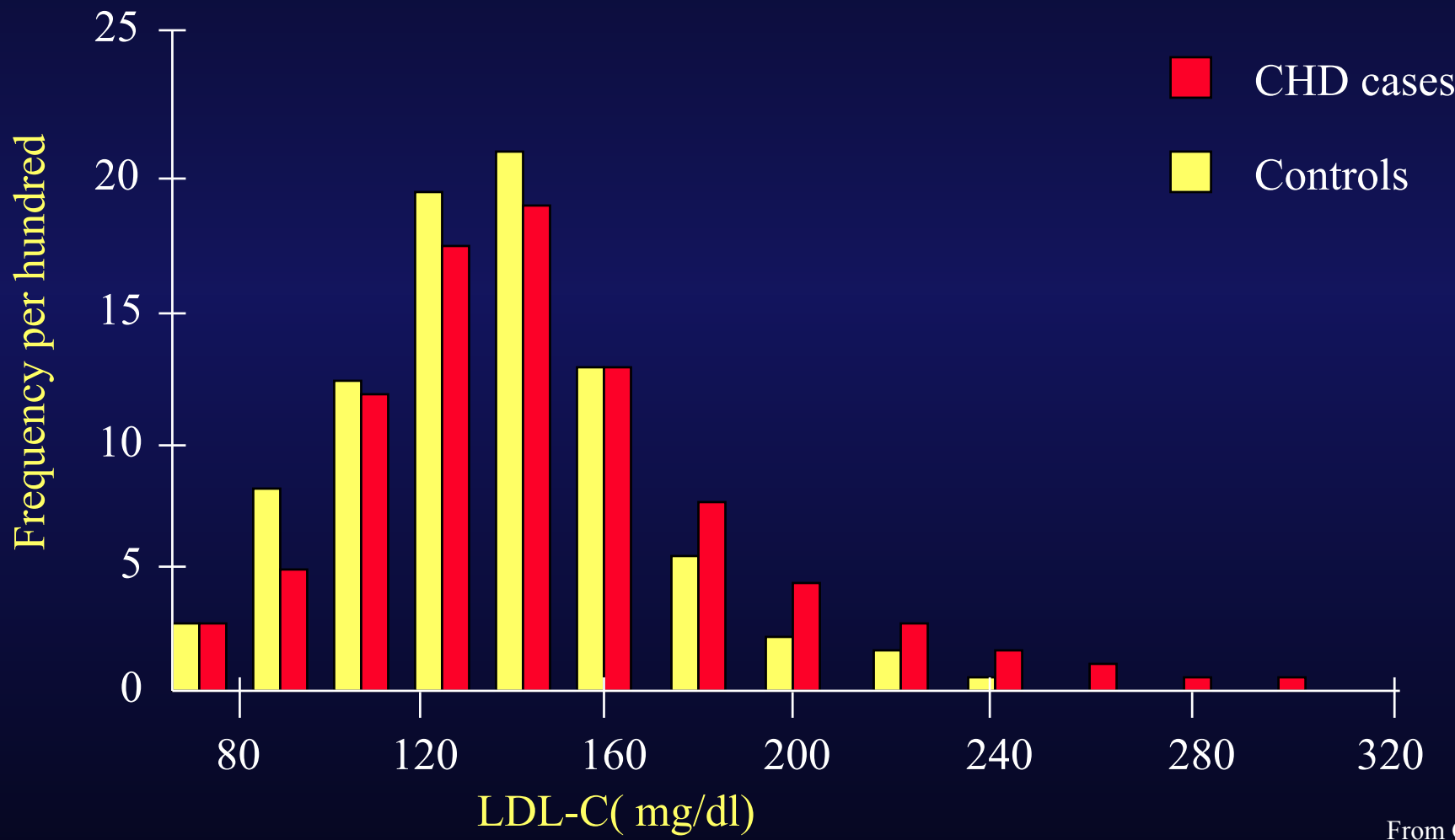
Modest increased LDLc

Small, dense LDL (apoB) ⬆

Cardioprotective HDL (apoA-1) ⬇

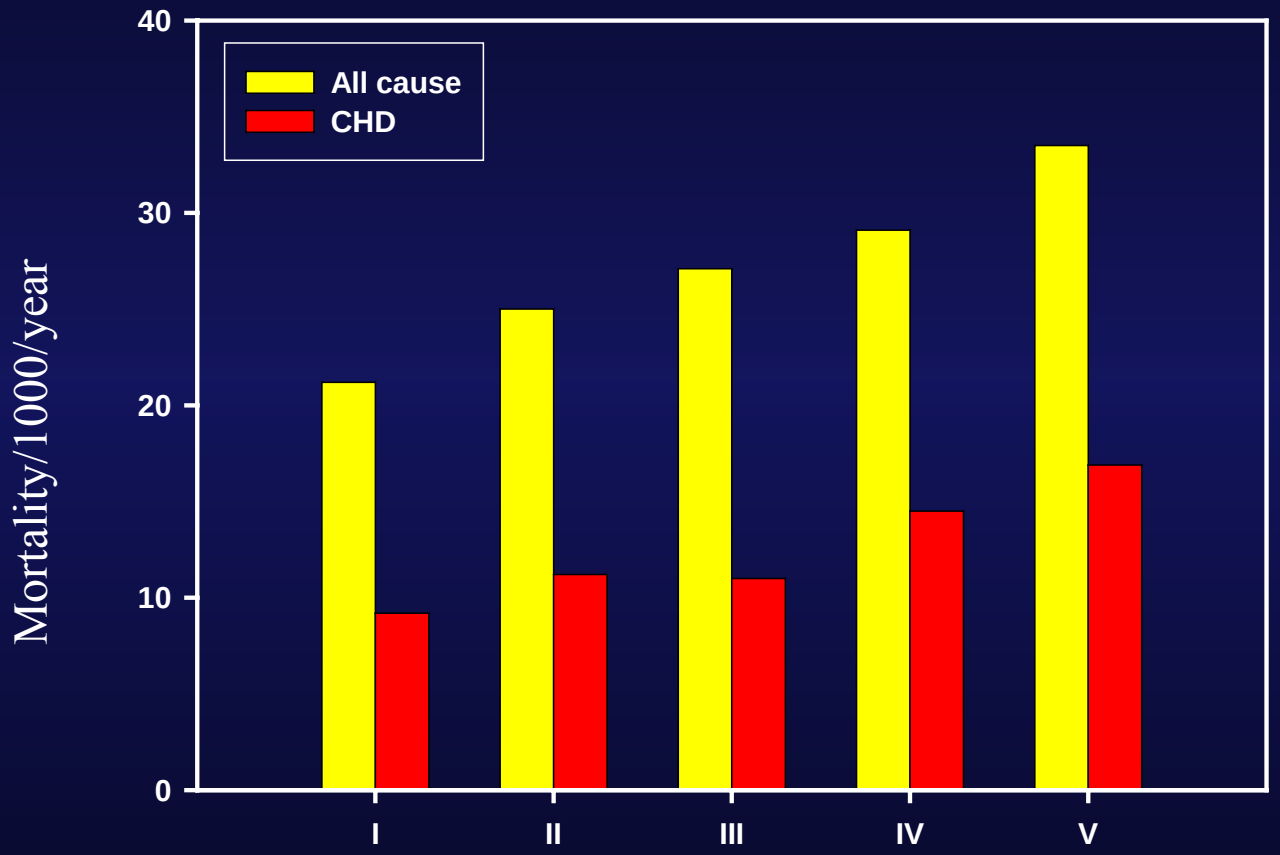
Coronary Heart Disease

LDL cholesterol distribution



From Genest, JACC 1992

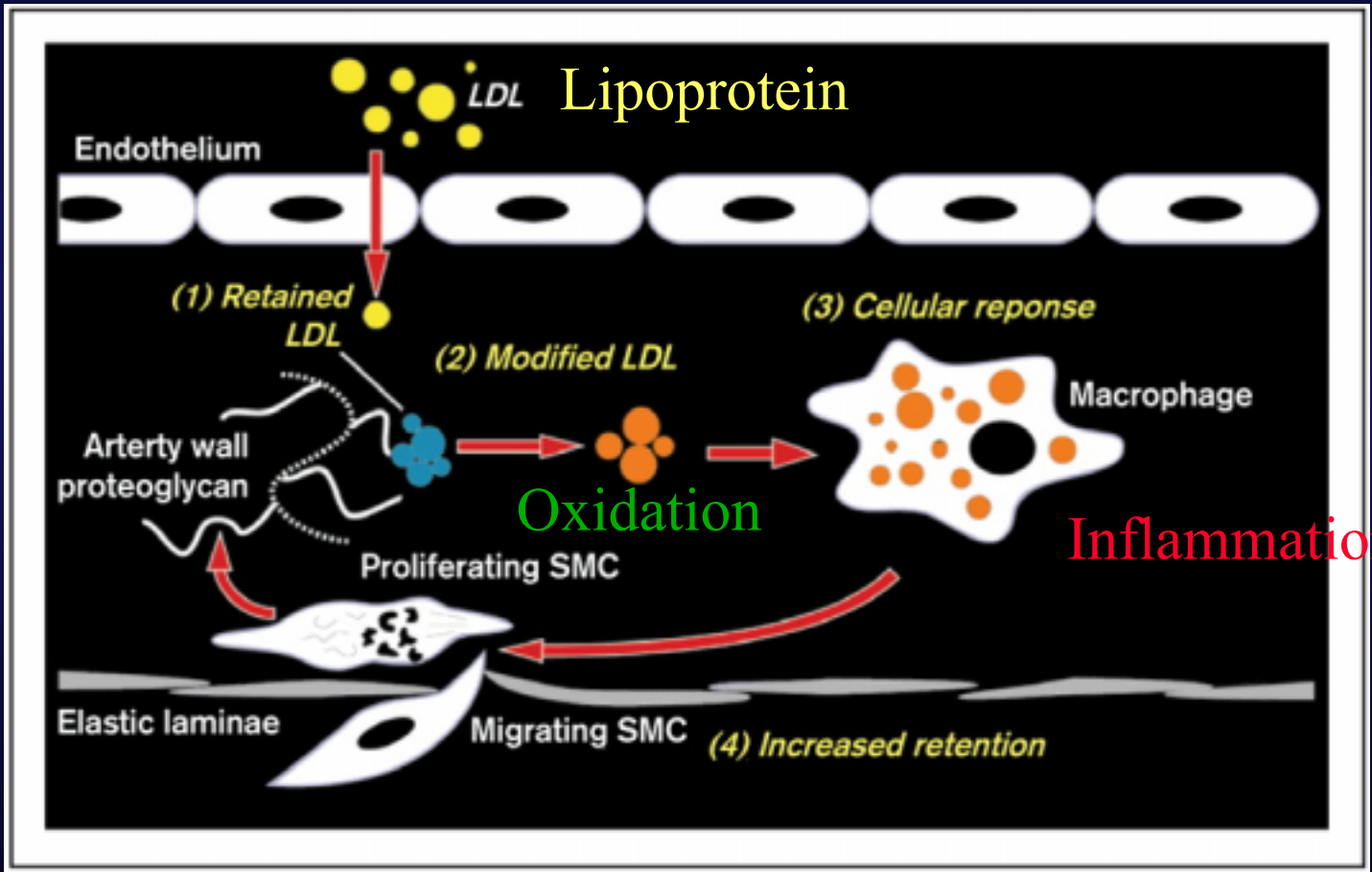
TG and mortality in CHD



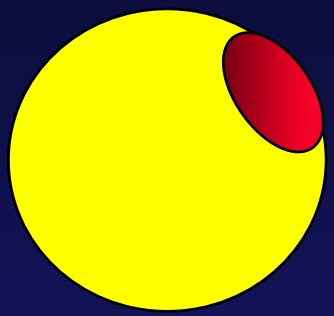
Age adjusted all cause and CHD mortality per 1000 persons in male
TG I<94.3, II 94.3~124.4, III 124.4~160.7, IV 160.7~217, V>217 mg/dl

Haim et al, Circulation 1999;100:475

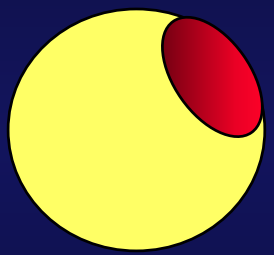
Lipoproteins and atherosclerosis



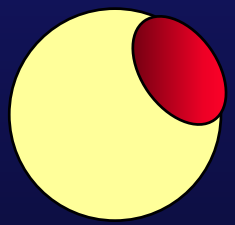
3 kinds of LDL



Large, buoyant LDL
LDL1

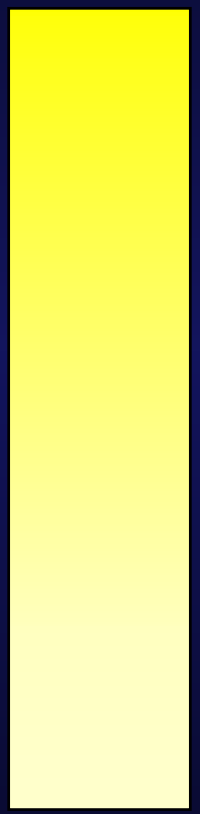


Intermediate LDL
LDL2



Small, dense LDL
LDL3

cholesterol



triglyceride

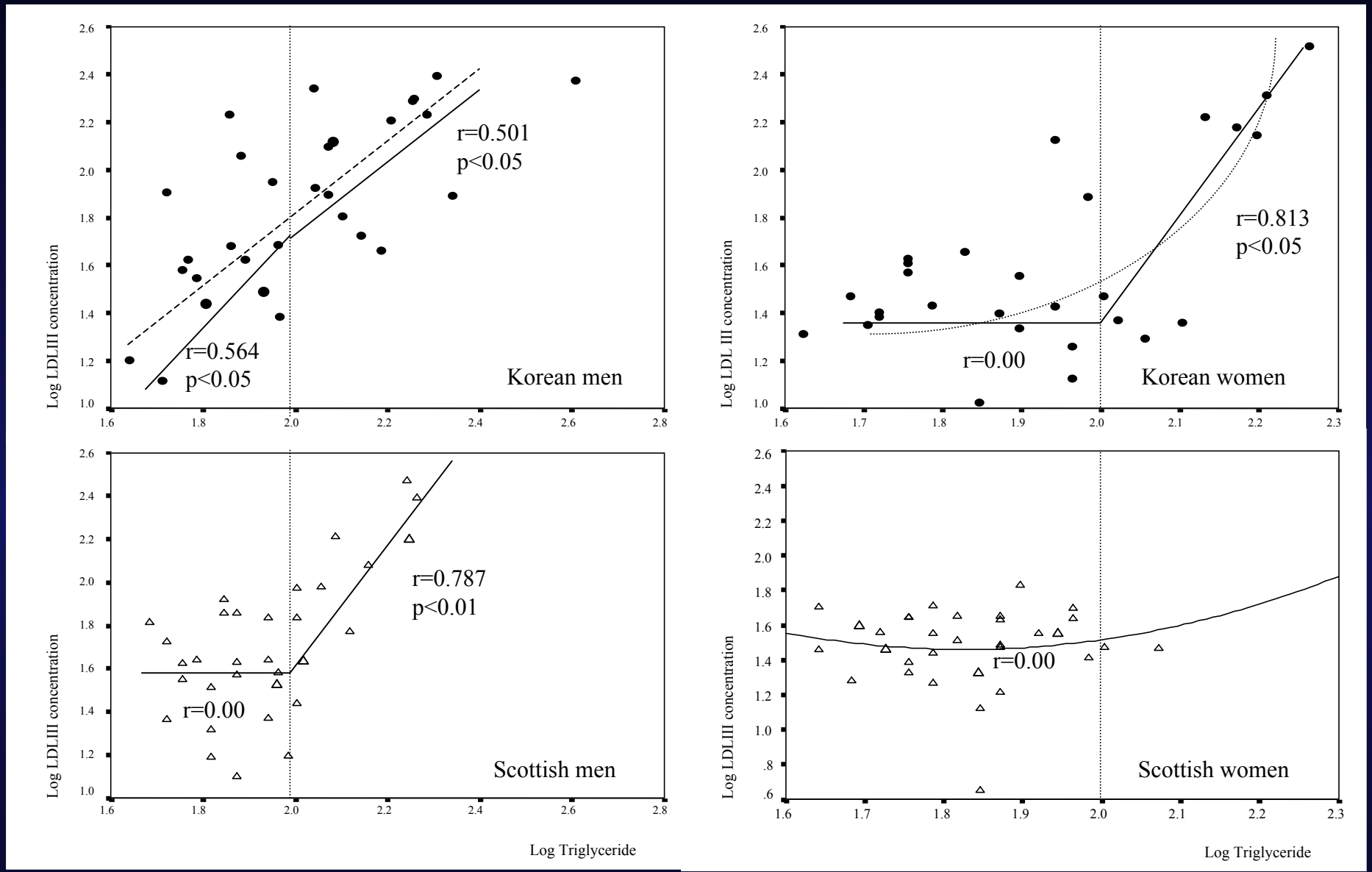
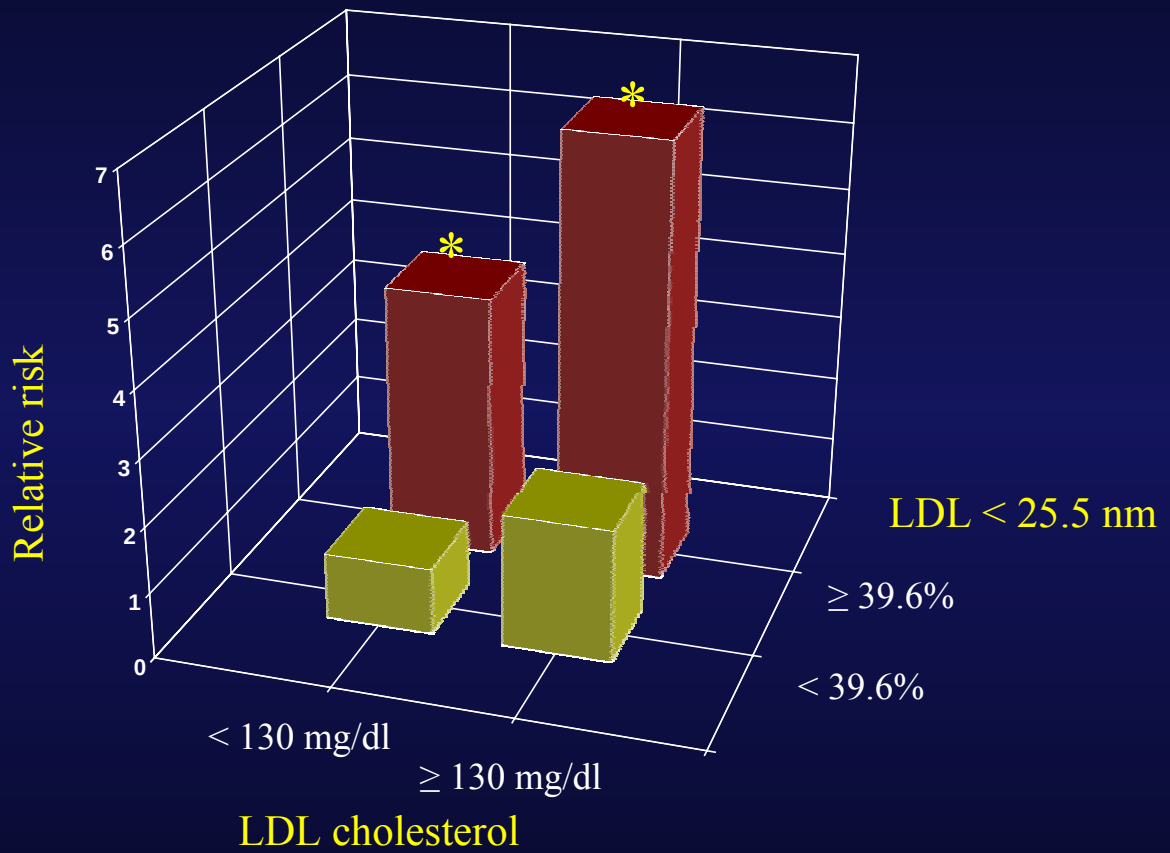


Fig. 2. Scattergrams of log LDL III concentration versus log triglyceride concentration in Korean and Scottish population. Broken line of the Korean population were drawn from total population of men and women from this study.

Cho et al Atherosclerosis 2002;164:187-193

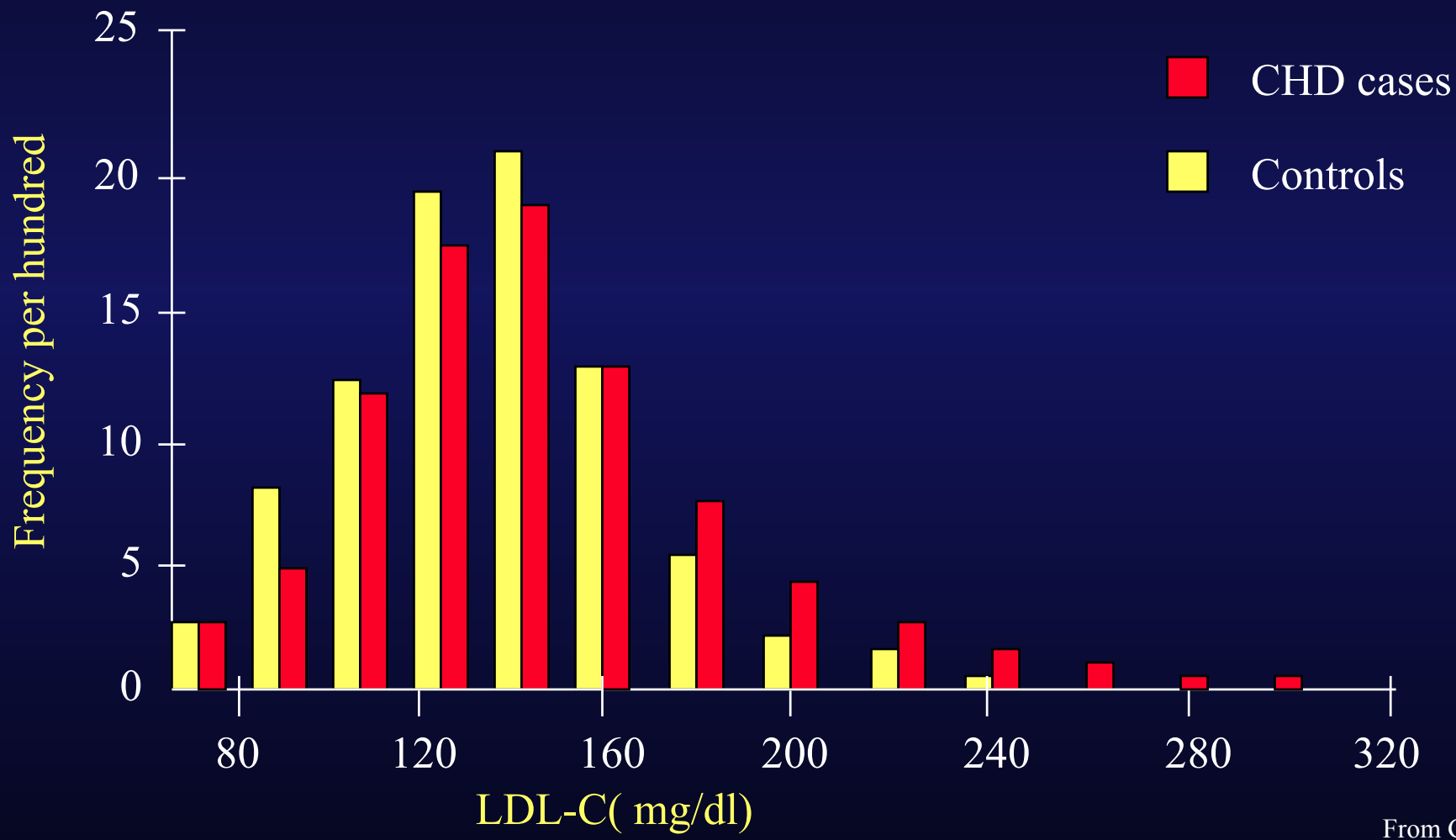
Small dense LDL and CHD
-LDL cholesterol-



Relative risk and p level according to baseline plasma LDL cholesterol and proportion of LDL < 25.5 nm. Relative risks were adjusted for age, BMI, systolic blood pressure, type II DM, medication use at baseline, family history of IHD, and smoking habits.

Modified from St-Pierre et al. Circulation 2001;104

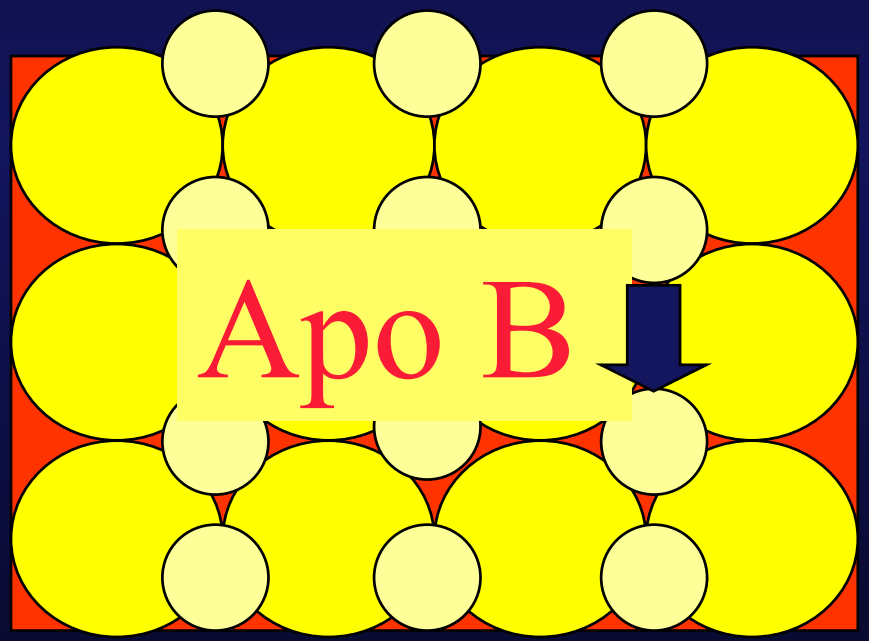
LDL cholesterol distribution



From Genest, JACC 1992

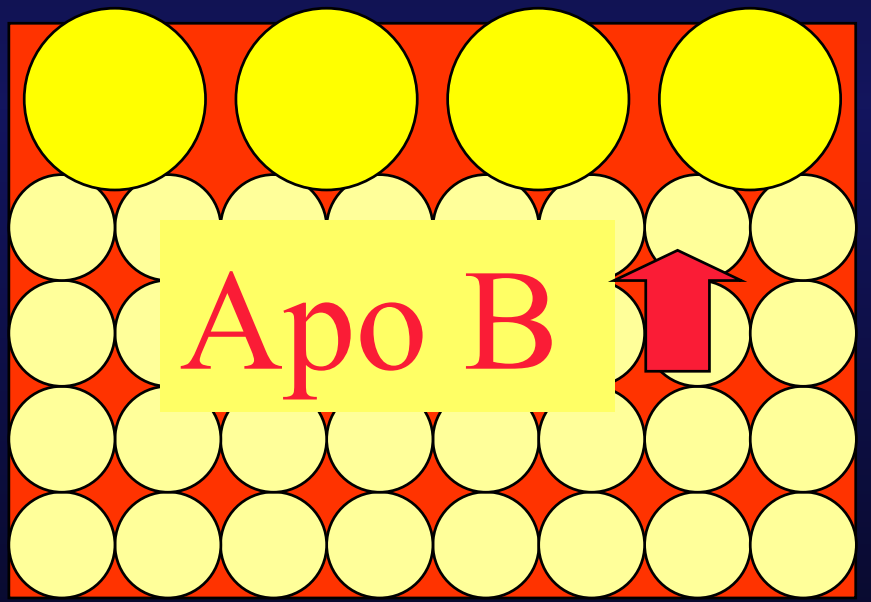
Myth of LDL cholesterol

LDLc = 140 mg/dl, TG=90 mg/dl



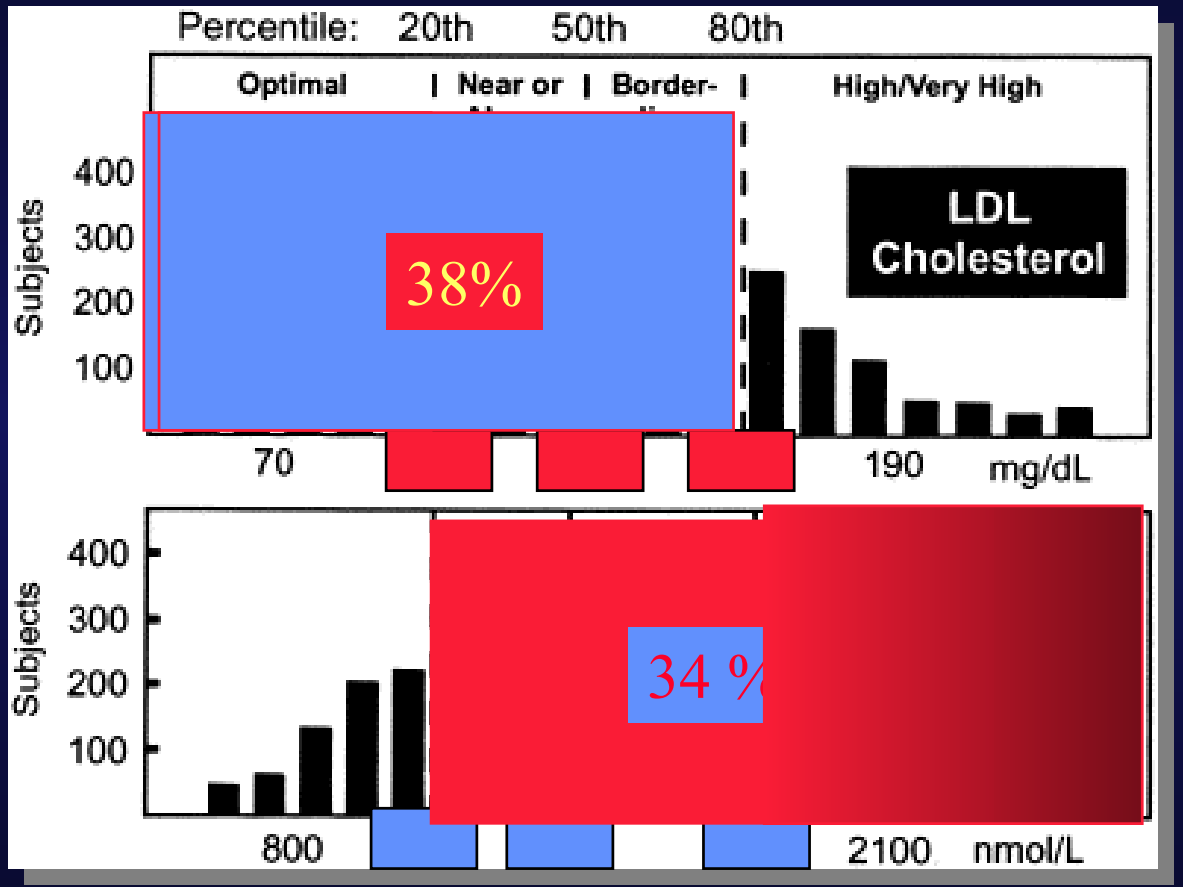
LDL particle number =24
Small dense LDL = 12

LDLc = 100 mg/dl, TG=150 mg/dl



LDL particle number =36
Small dense LDL = 32

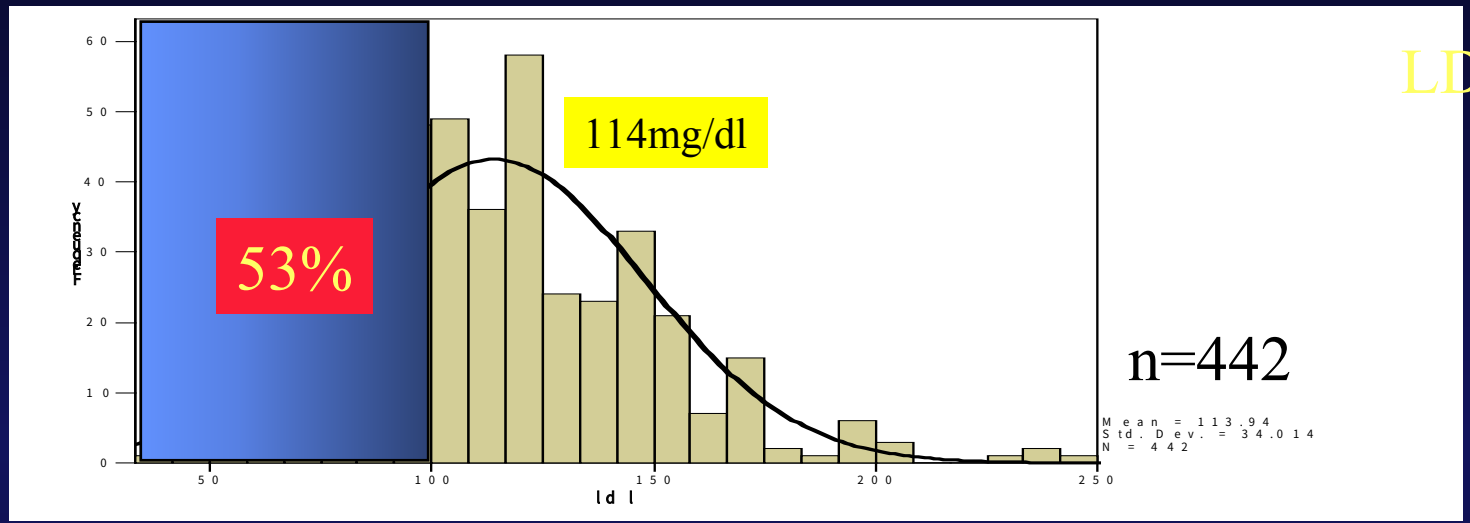
Discrepancy between LDLc and LDL particles



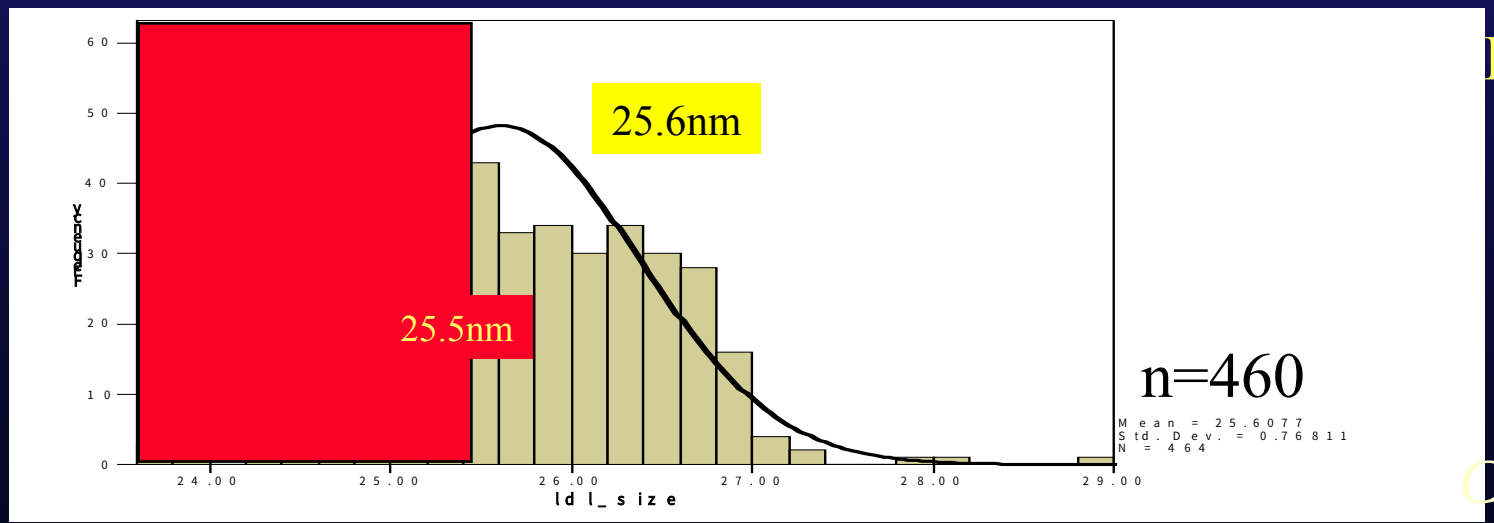
Histogram of LDLc and nuclear magnetic resonance-measured LDL particle concentration from the Framingham Offspring Study(n=3,437)

Otvos et al. Am J Cardiol 2002;90(suppl):22i

LDLc- Particle discrepancy
-DM or CHD-



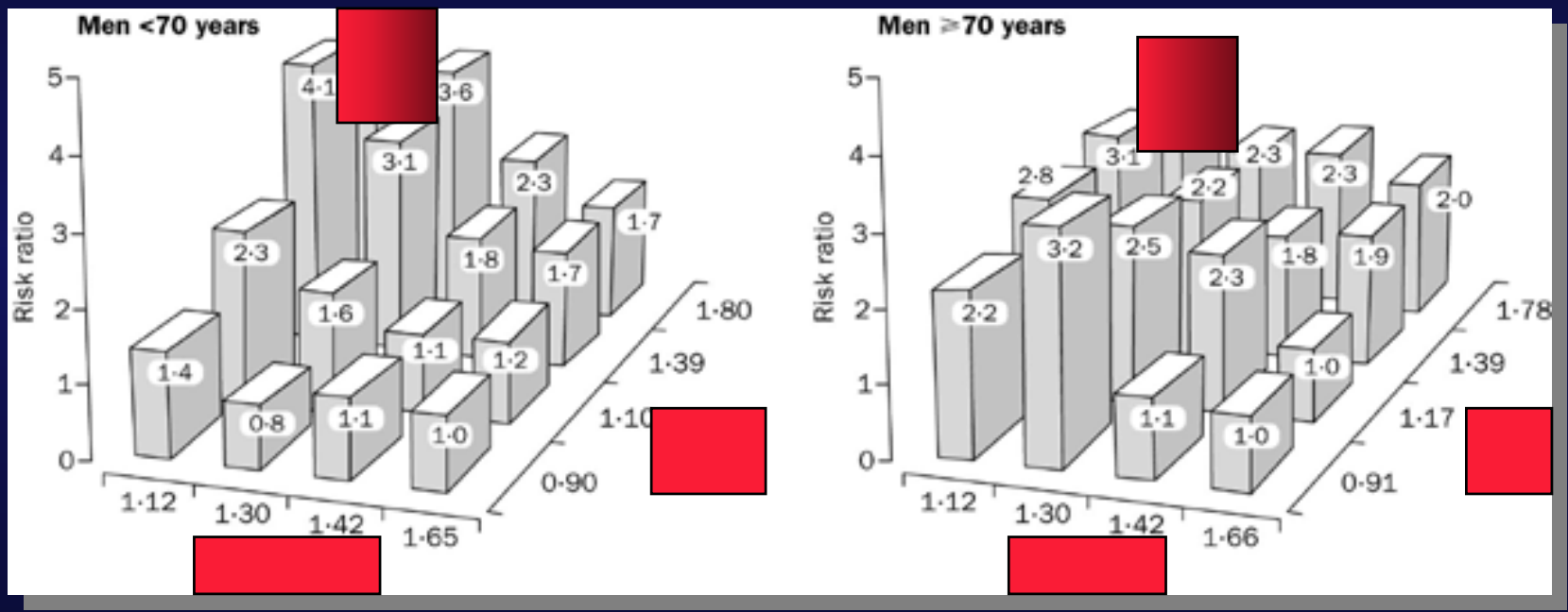
LDLc (mg/dl)



L particle size (nm)

Cho, unpublished

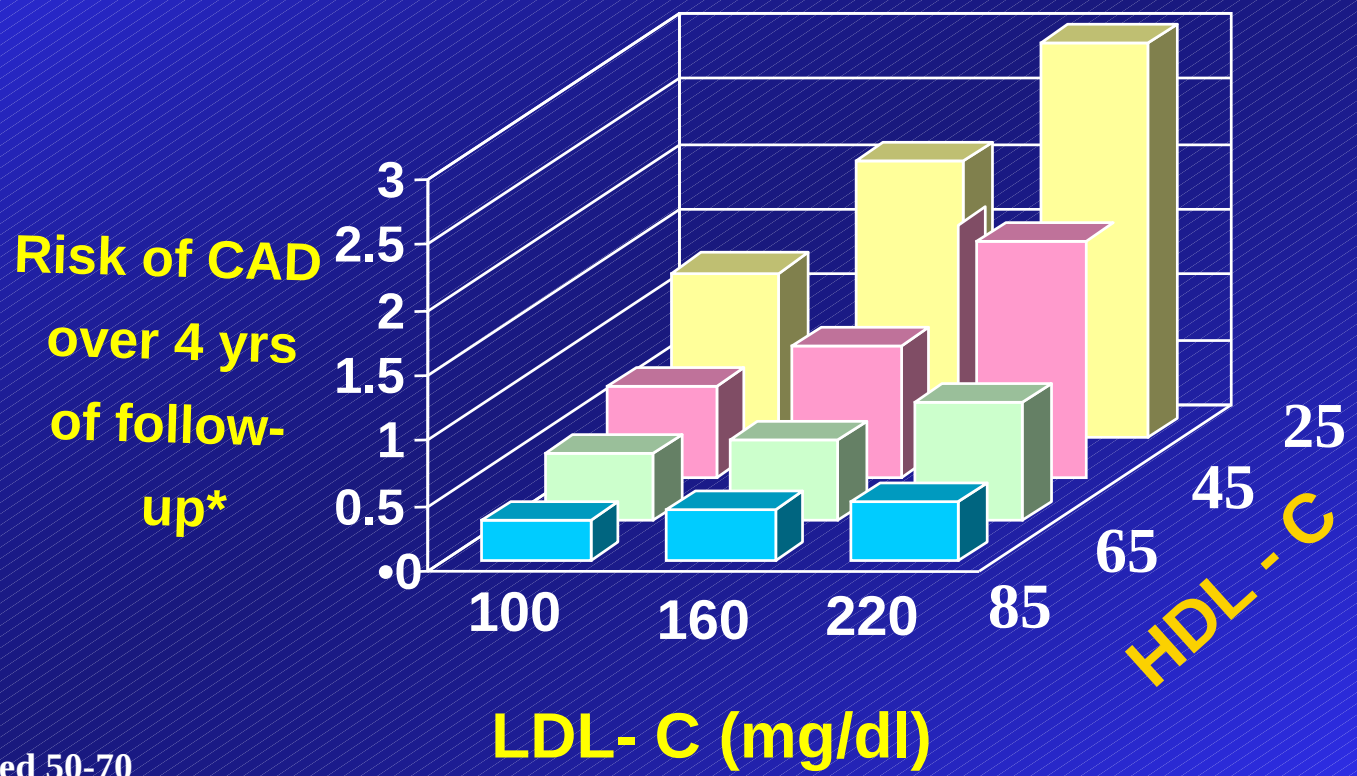
AMORIS
(Apoprotein-related Mortality Risk Study)



Relative risk ratios of fatal MI by quartiles of Apo B and Apo A-1 in men. Adjusted for age, total cholesterol, and triglycerides by the Cox model. From 175 553 individuals for 67 ms. 98 722 men and 76 831 women were included.

Wallidus et al. Lancet 2001;358:2026

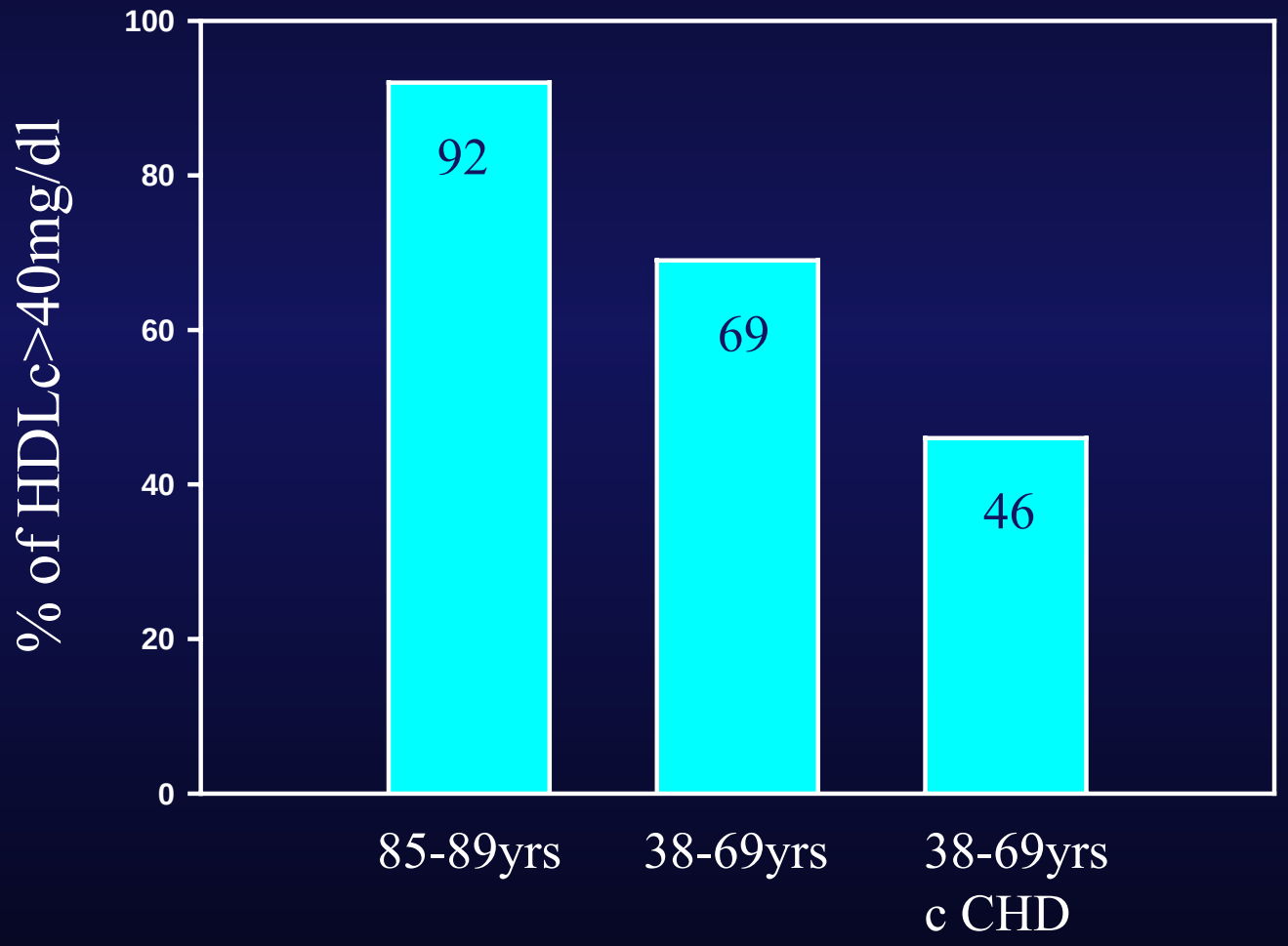
Framingham: HDL vs LDL as a predictor of CHD risk



* Men aged 50-70

Gordon, Castelli, *et al*. *Am J Med* 1977

HDLc and Longevity

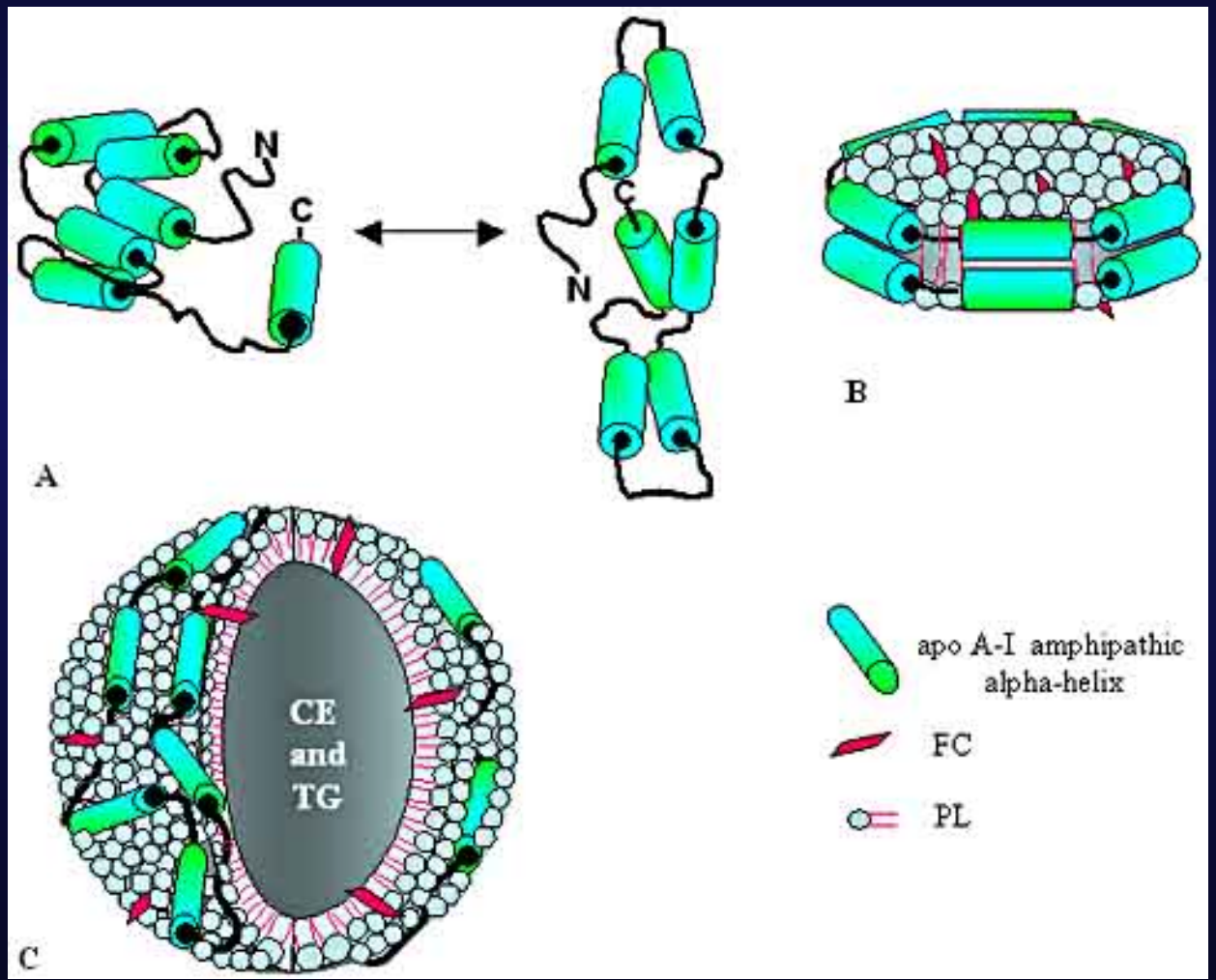


Nikkila M et al. Age Aging 1990;19:119-24

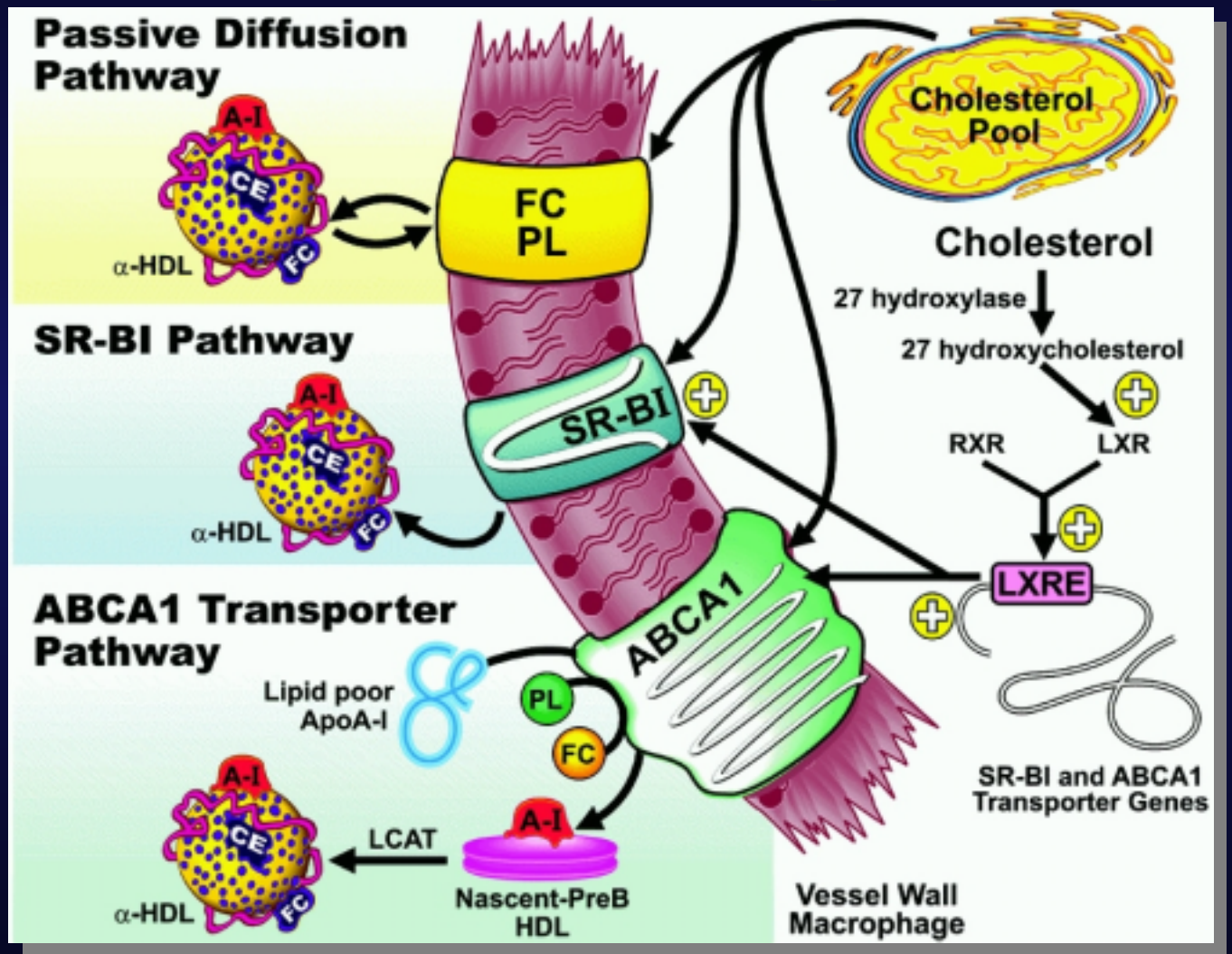
Role of HDL

- Reverse cholesterol transport
- Anti-inflammation
- Anti-oxidation

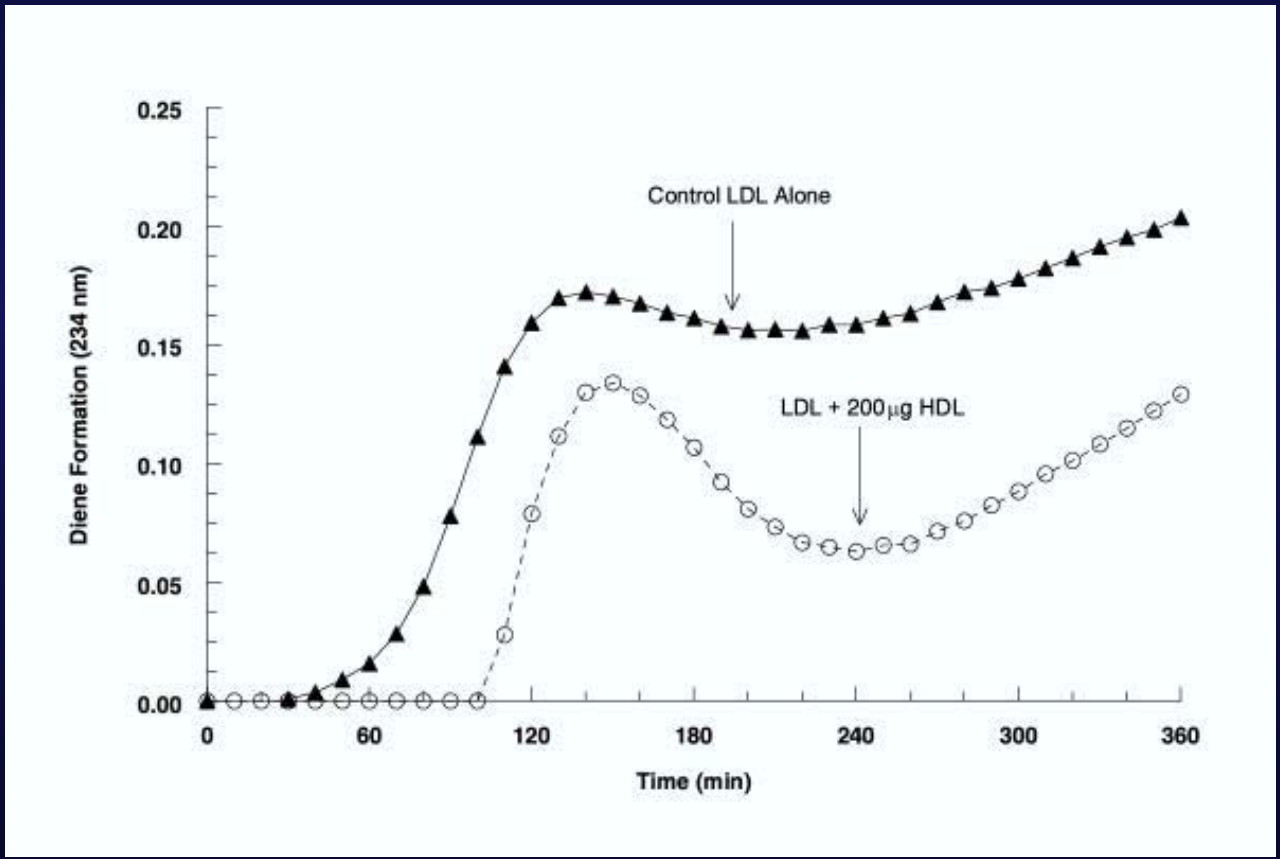
HDL structure



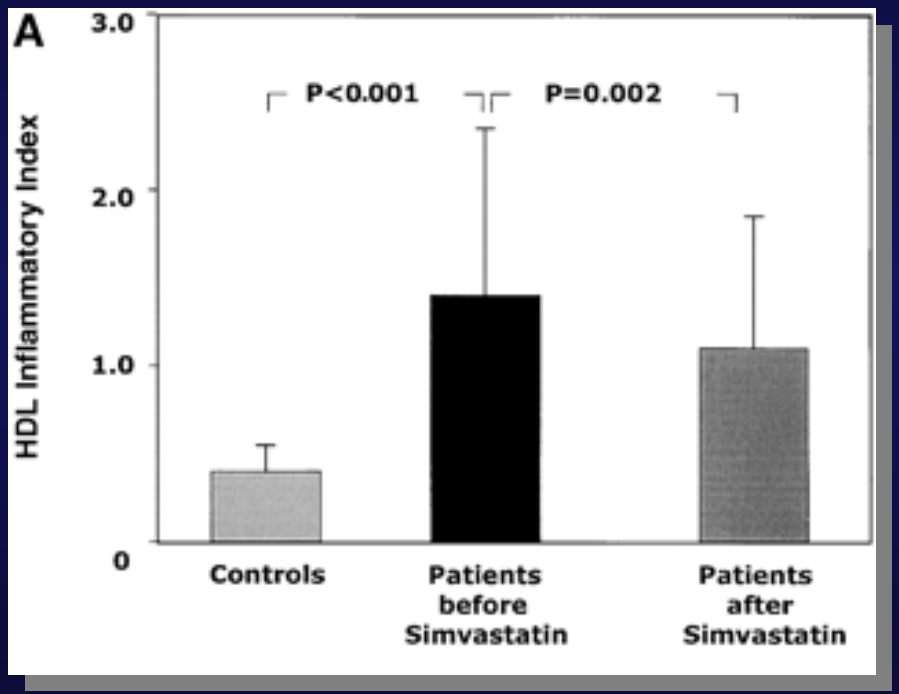
Reverse transport



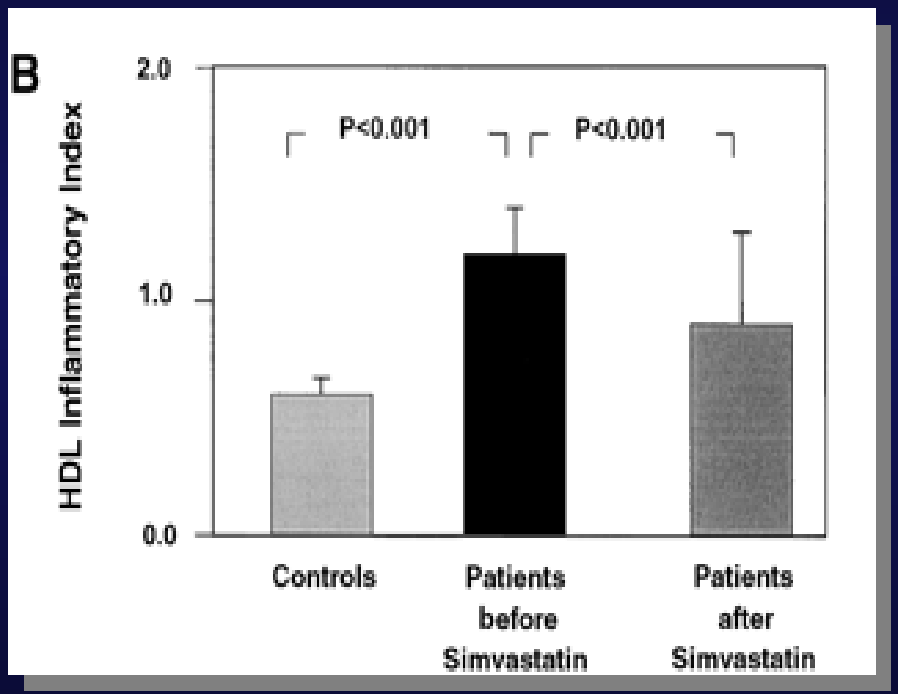
Anti-oxidation role of HDL



Anti-inflammatory role of HDL

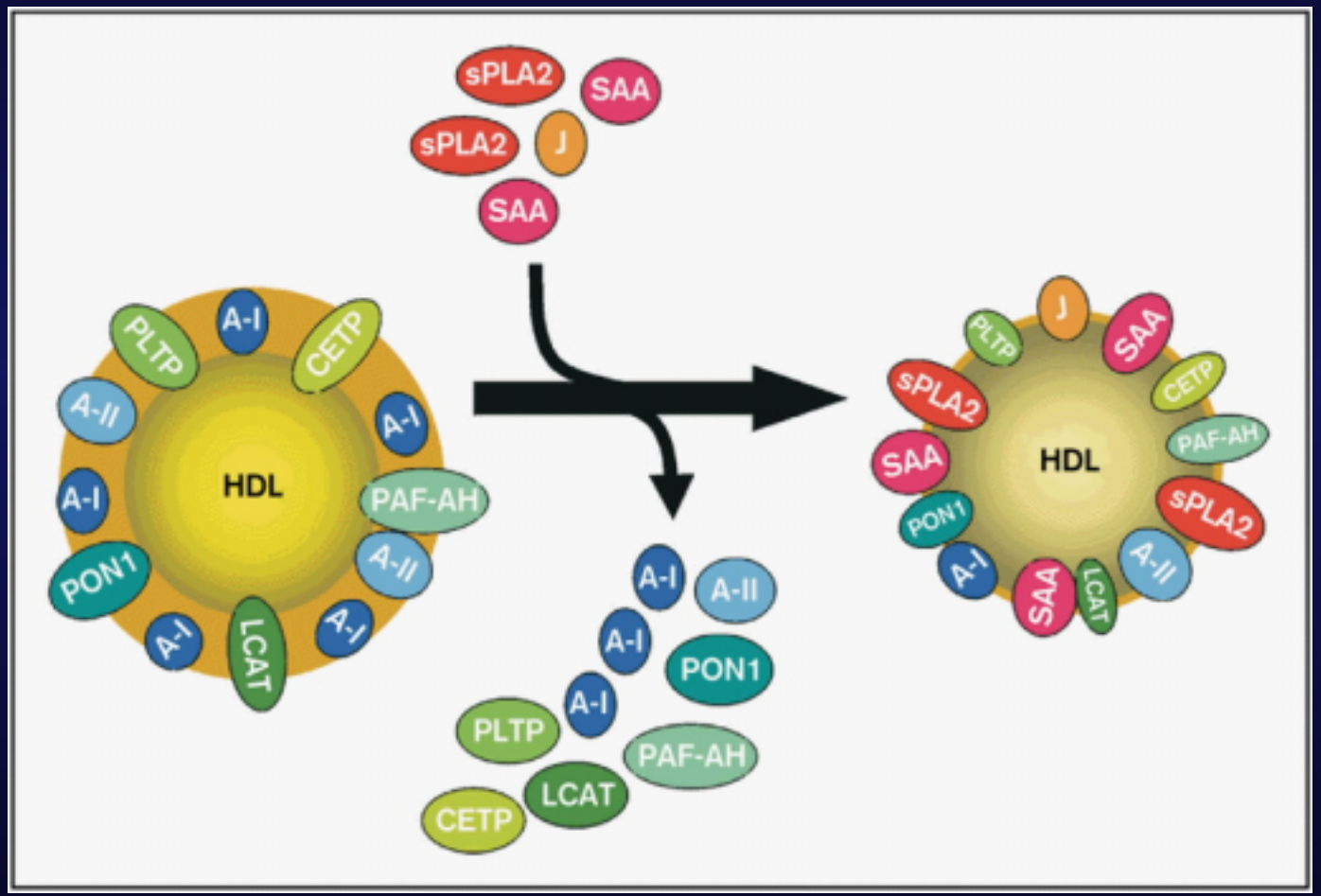


CHD equivalent with normal HDLc



CHD with high HDLc(>70 mg/dl)

Impact of inflammation on HDLc



Atherogenic dyslipidemia

Hypertriglyceridemia

Low HDLc

Modest increased LDLc

Small, dense LDL (apoB) ⬆

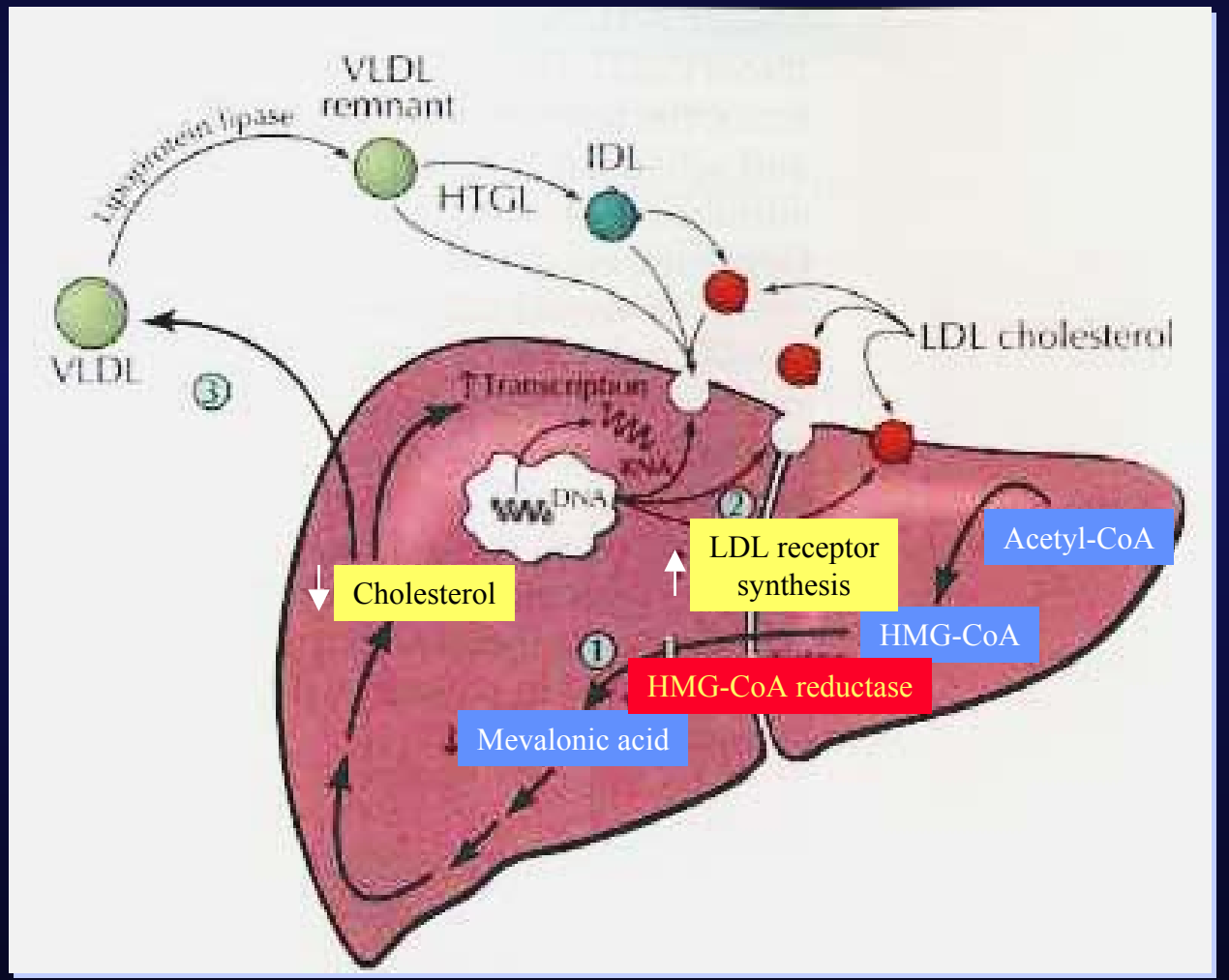
Cardioprotective HDL (apoA-1) ⬇

Coronary Heart Disease

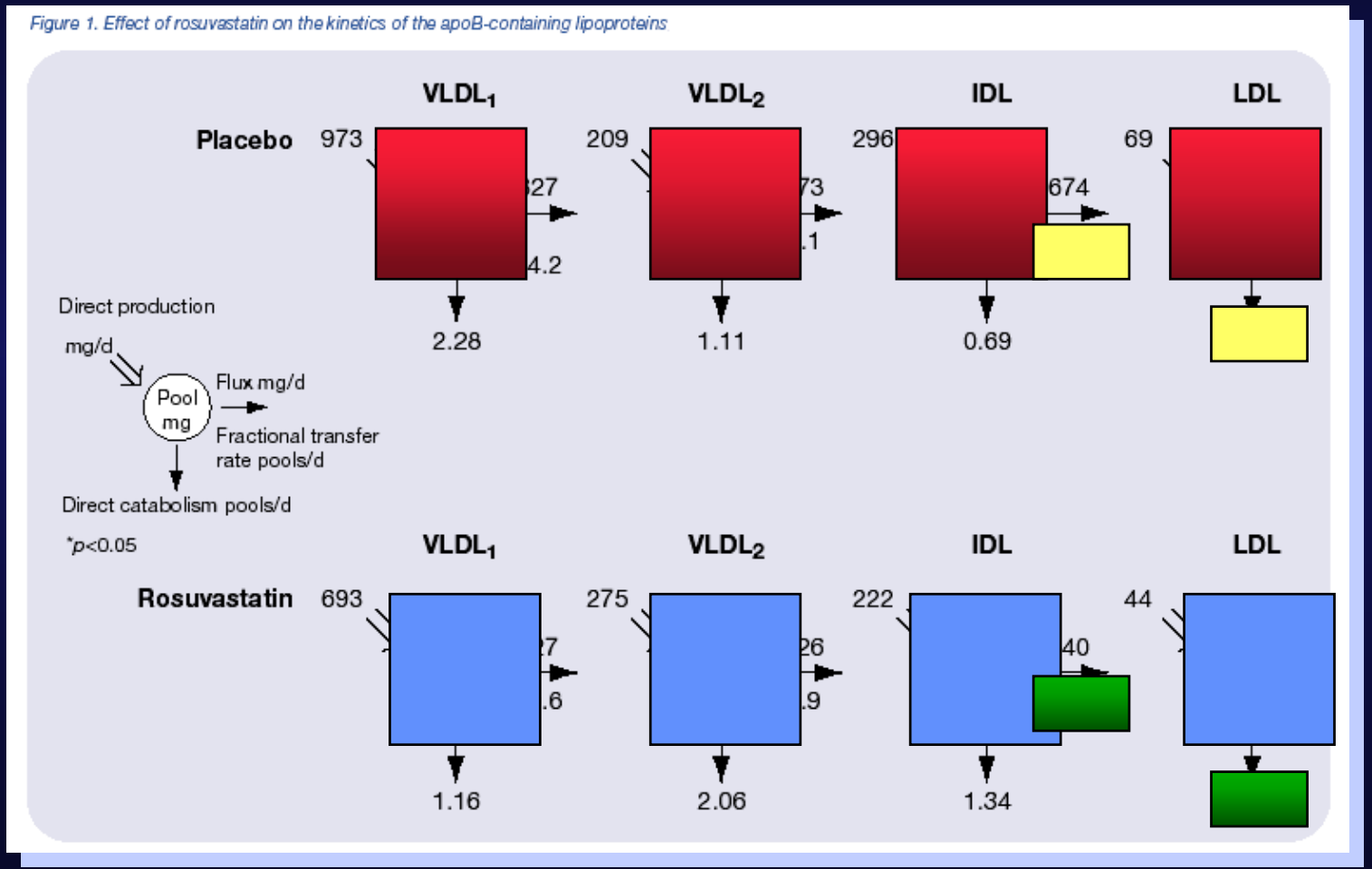
INTERHEART study

• ApoB/ApoA1 ratio	49.2%
• Smoking	35.7%
• Psychosocial factors	32.5%
• HiBP	17.9%
• Abdominal obesity	20.1%
• DM	9.9%

Statin-Mechanism of action



Effect of Rosuvastatin on Apo B kinetics



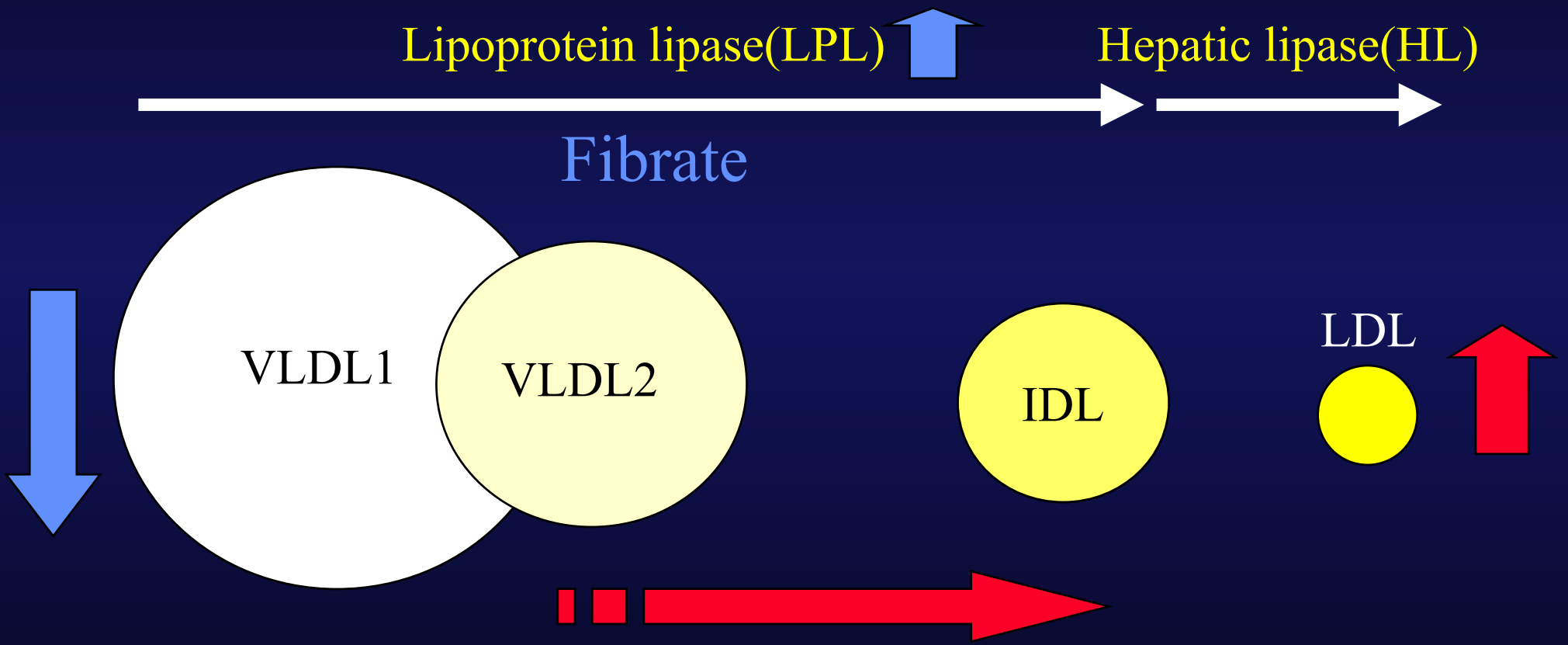
Total Apo B pool =3147

Total Apo B pool =1456

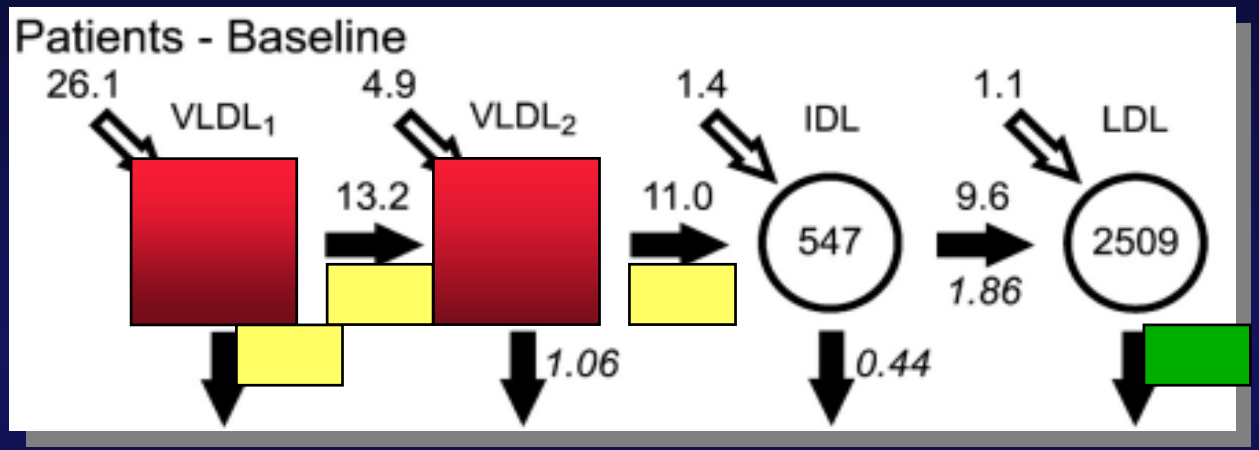
54% reduction

Caslake M et al. 13rd ISA, 2003, Kyoto, Japan

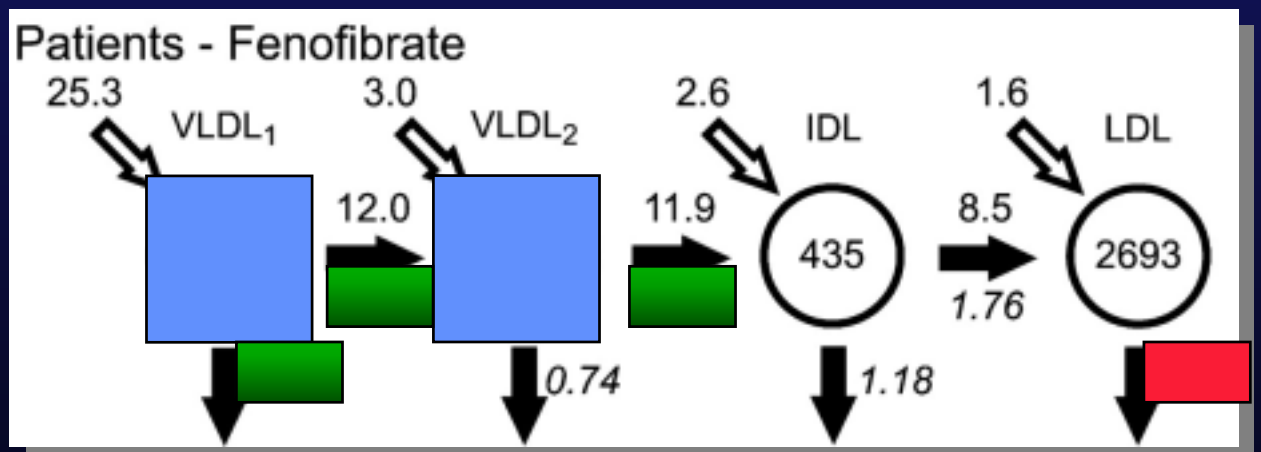
Fibrate and LDL



Effect of fenofibrate on Apo B kinetics



Total Apo B =4521

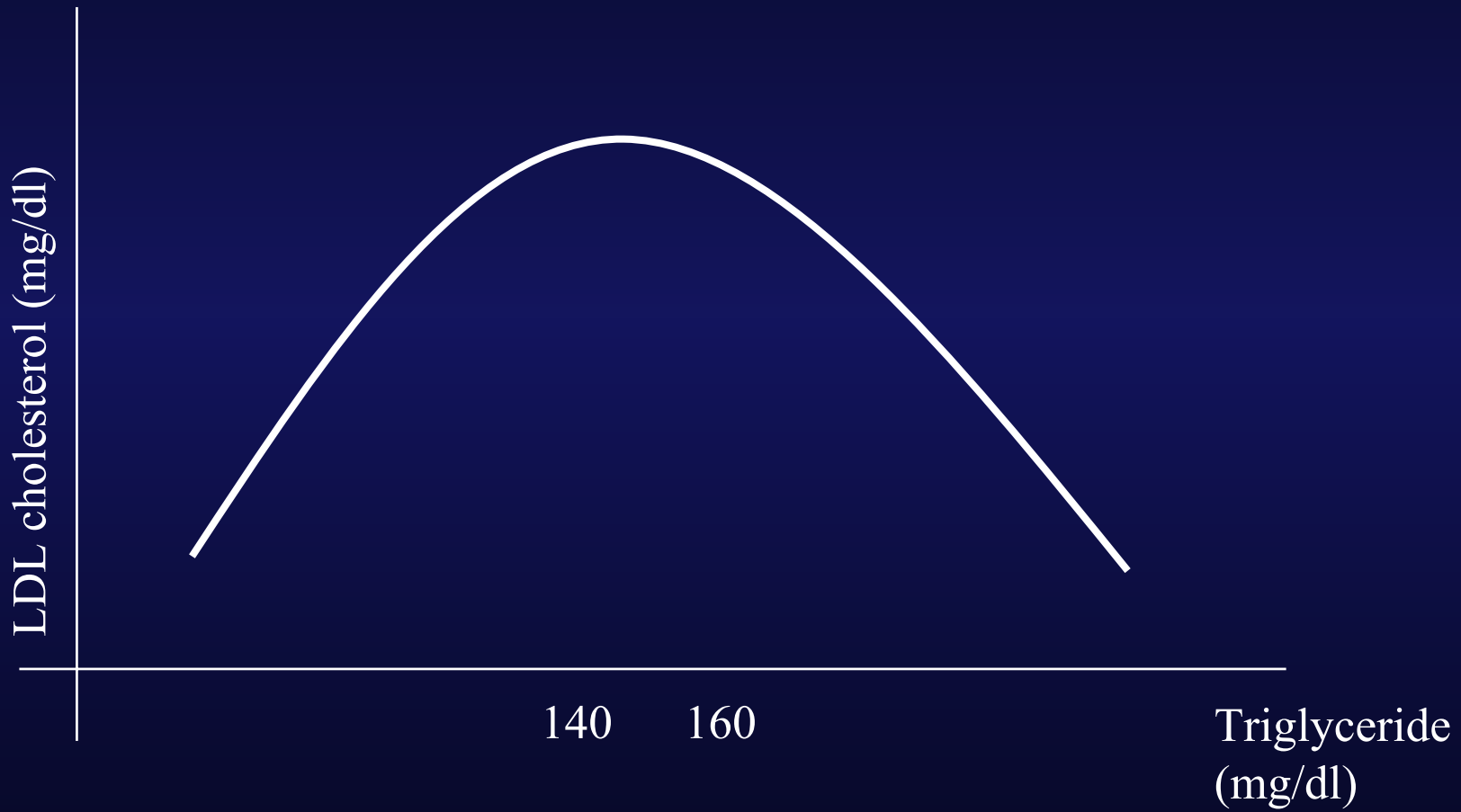


Total Apo B =3750

No significance

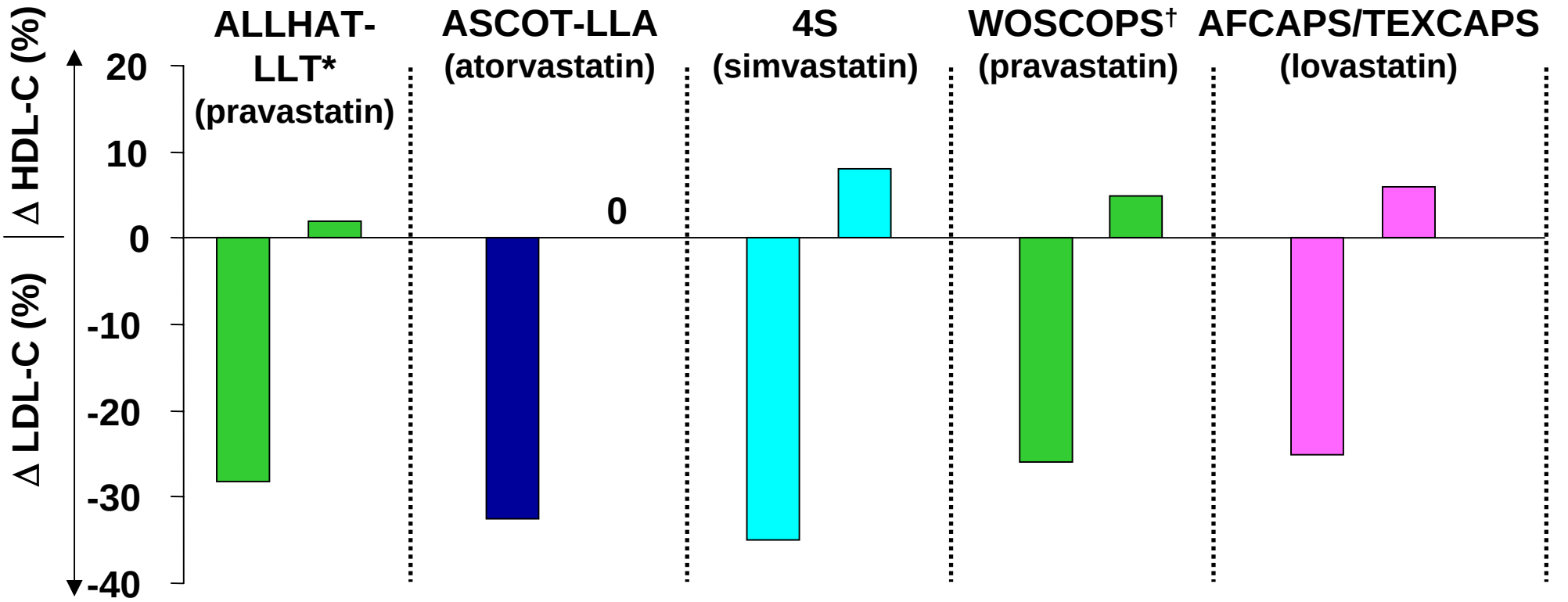
Bilz et al. J Lipid Res 2004.45:174

Triglyceride & LDL cholesterol



Caslake, PhD thesis

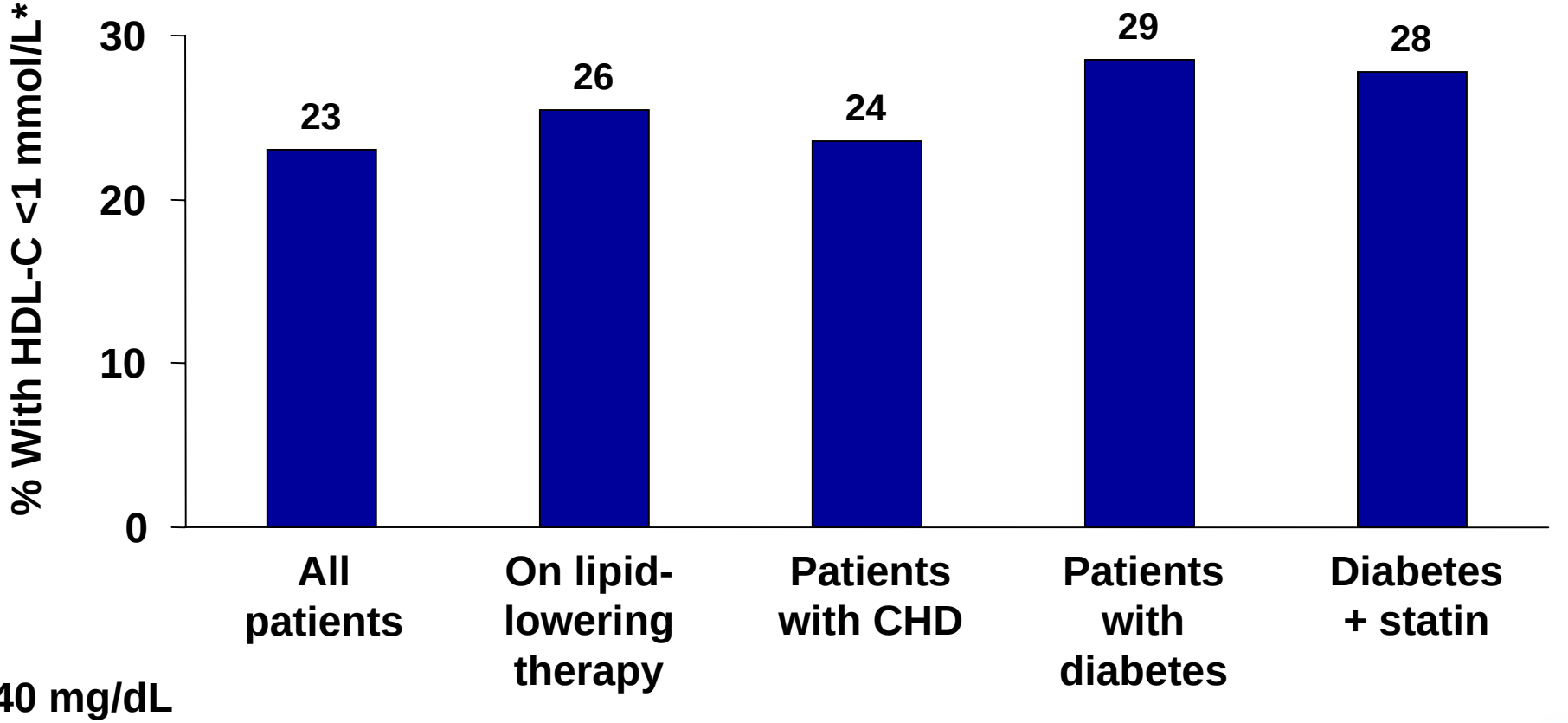
Limited effects of statins on HDL-C raising in major intervention trials



Control/placebo groups omitted for clarity
*4-year data; †Placebo-corrected

1. *JAMA* 2002;288:2998-3007; 2. *Lancet* 2003;361:1149-58;
3. *Lancet* 1994;344:1383-9; 4. *Circulation* 1999;99:216-23;
5. *JAMA* 1998;279:1615-22

Low HDL-C is common even among patients receiving a statin



*40 mg/dL

Patel JV et al. *Br J Cardiol* 2004;11:214-7

Limitations of Statin Monotherapy on CHD Events

Trial	Drug	N	Events,* n		Risk Reduction, %†	Events not Avoided, %
			Control Group	Statin Group		
4S WOSCOPS CARE AFCAPS LIPID	Simvastatin Pravastatin Pravastatin Lovastatin Pravastatin	30,817	2,042	1,490	26	74
HPS	Simvastatin	20,586	1,212	898	26	74
PROSPER	Pravastatin	5,804	356	292	19	81
ASCOT-LLA	Atorvastatin	10,305	154	100	36	64
Total		**67,462**	**3,764**	**2,780**	**27**	**73**

* Nonfatal MI and CHD death; AFCAPS also included unstable angina
† Weighted average

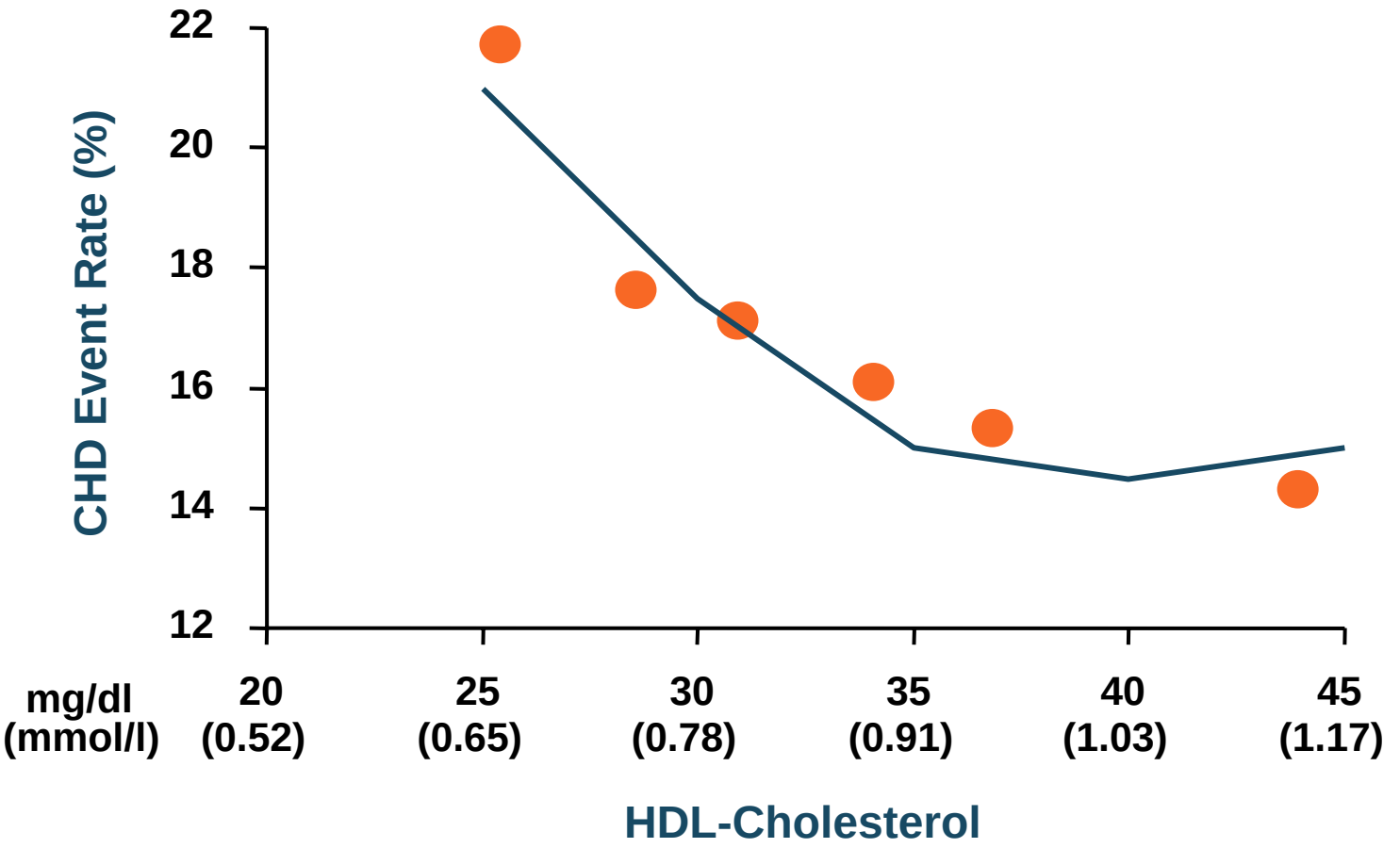
Bays H. *Expert Rev Cardiovasc Ther* 2004;2:89-105.

Metabolic syndrome & CHD

: Veterans Affairs High-Density Lipoprotein Intervention Trial(VA-HIT)

Trial	Drug	Baseline lipid		CAD event(%)			
		LDLc	HDLc	Placebo	Drug	RR	NNT
4S	Simvastatin	189	46	28.0	19.4	8.6	12
CARE	Pravastatin	139	39	13.2	10.2	3.0	33
LIPID	Pravastatin	150	37	15.9	12.3	3.6	28
VA-HIT	Gemfibrozil	111	32	21.7	17.3	4.4	23

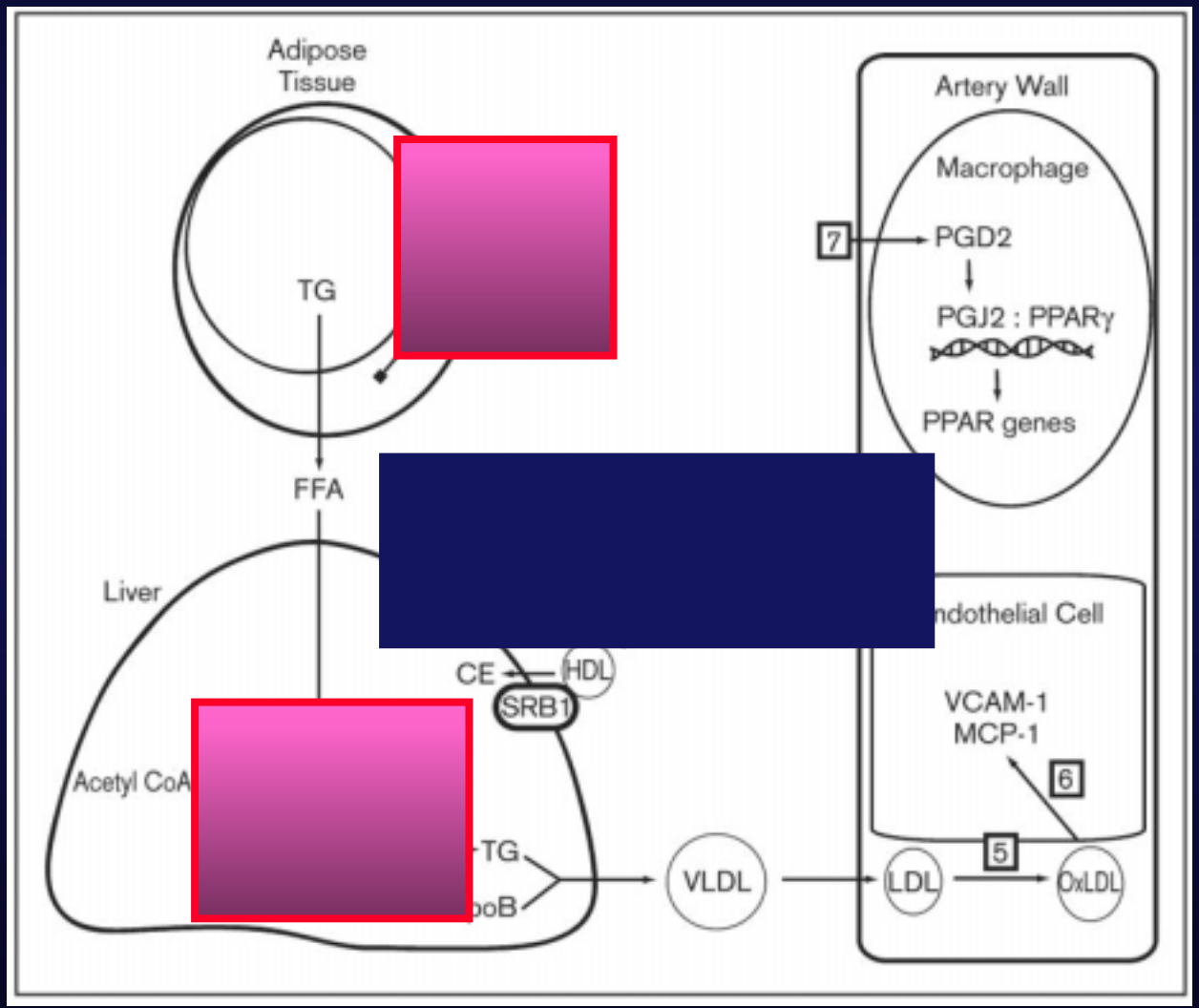
VA-HIT: Relation between CHD and HDL-C



Rubins HB et al. *N Engl J Med*. 1999;341:410; Sacks. *Am J Cardiol*. 2002;90:139

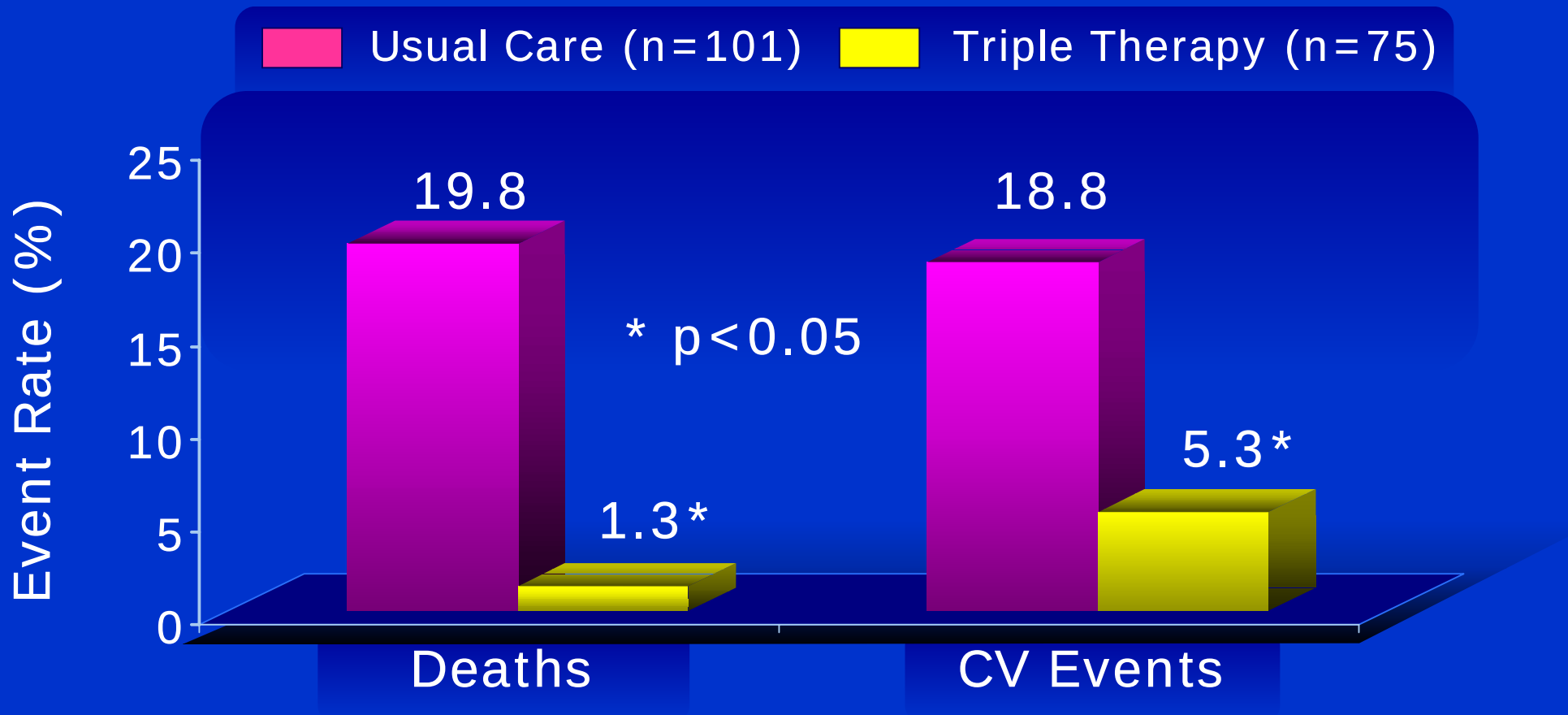
Niacin
-Mechanism-

TG



HDL

Familial Atherosclerosis Treatment Study (FATS): 10-Year Follow-up Results



LDL-C 188→166 mg/dL; HDL-C 38→40 mg/dL ; TG 208→220 mg/dL

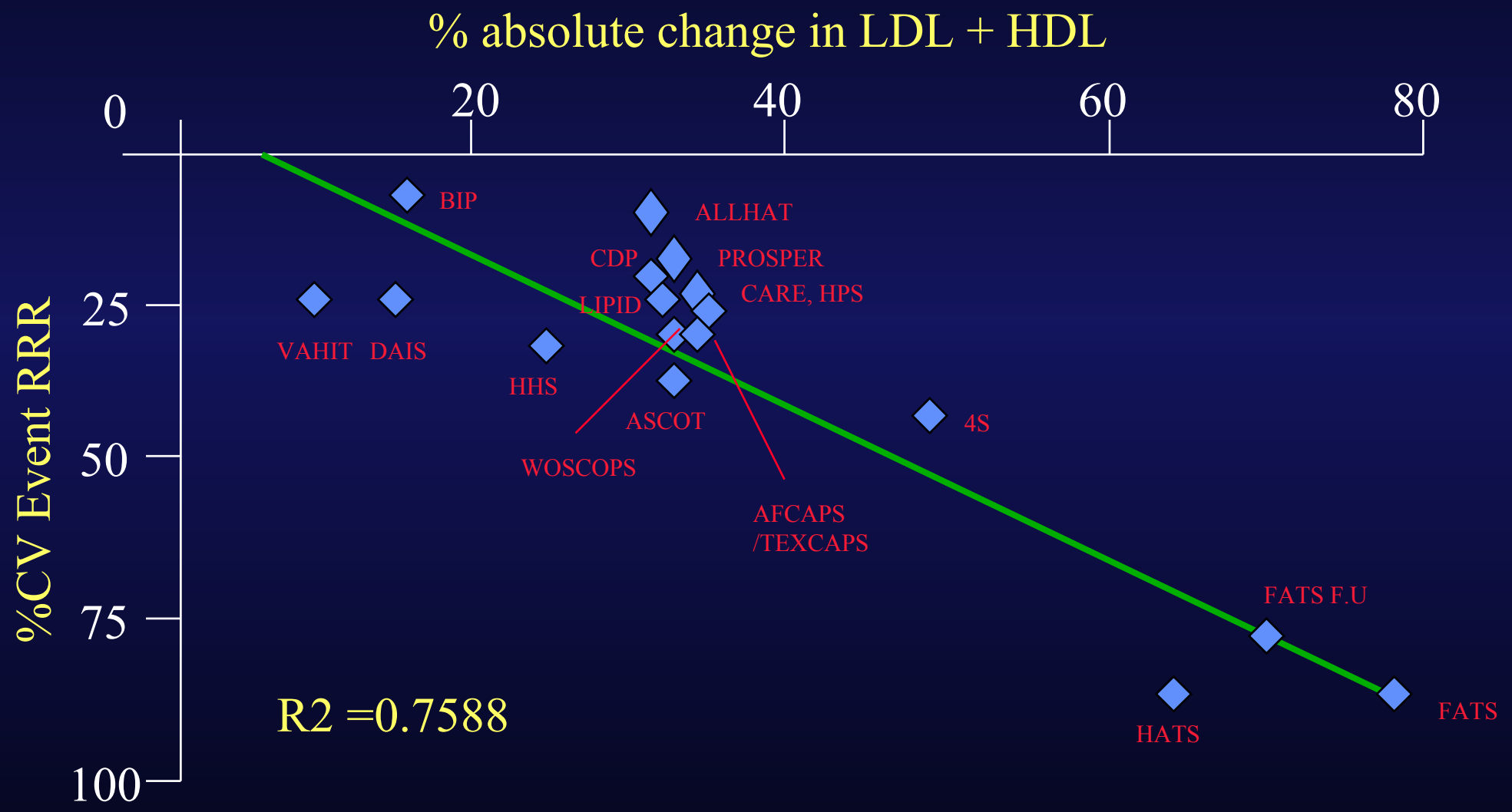
LDL-C 202→106 mg/dL; HDL-C 43→53 mg/dL; TG 210→134 mg/dL

Brown BG et al. *Circulation* 1998;98:I-635.

Fish Oils

Indications:	Adjunctive therapy to diet Hypertriglyceridemia (Type IV and V) With statins or other LDL-C–lowering drugs in mixed hyperlipidemia
Efficacy:	Decrease TG 30–40% LDL-C remains the same or increases No change in HDL-C
Side Effects:	GI upset and a “fish burp”
Intervention Trials:	Lyon Heart Study (dietary), GISSI Prevenzione Trial, others

HDLc and LDLc



Adapted from Am J Cardiol 2002;90(15B) 8K

Who is the best Statin mate?

Nice Statins

Niacin

W-3 FA

Fibrate

"It relieves watery eyes, runny nose, aching head, and scratchy throat. Side effects include runny eyes, watery nose, aching throat, and scratchy head."