Revios

Your Heart

Would you get Standard Rates?

Dr Jeremy Sayer
Consultant Cardiologist
St. Bartholomew's Hospital

Revios

Summary

- Cardiovascular Risk
  Estimation of cardiovascular risk

  Further risk assessment
  - ECG, Exercise ECG, EBCT, MSCT
  - The Future

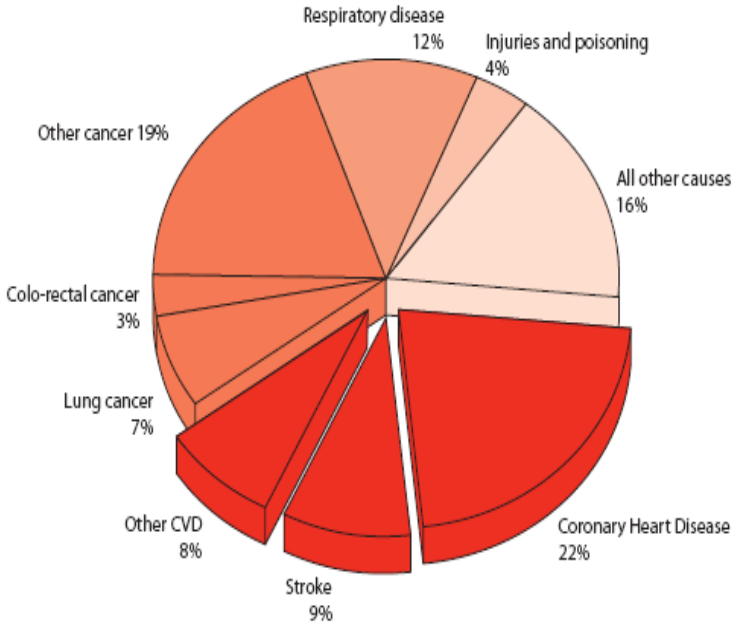
  Hypercholesterolaemia

- Valvular Disorders
  The natural history

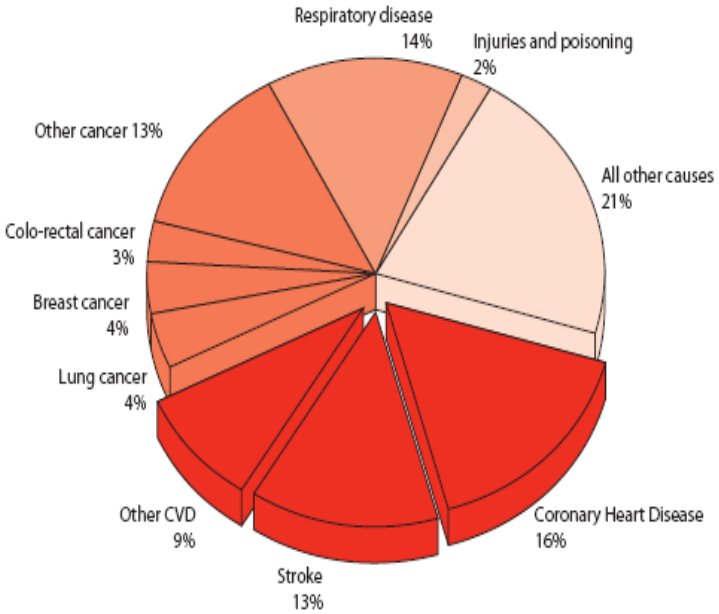
- Cardiomopathy
  HCM, LVH or Athlete's Heart?

- Ventriclular ectopics
  Should you worry?

Heart disease in UK



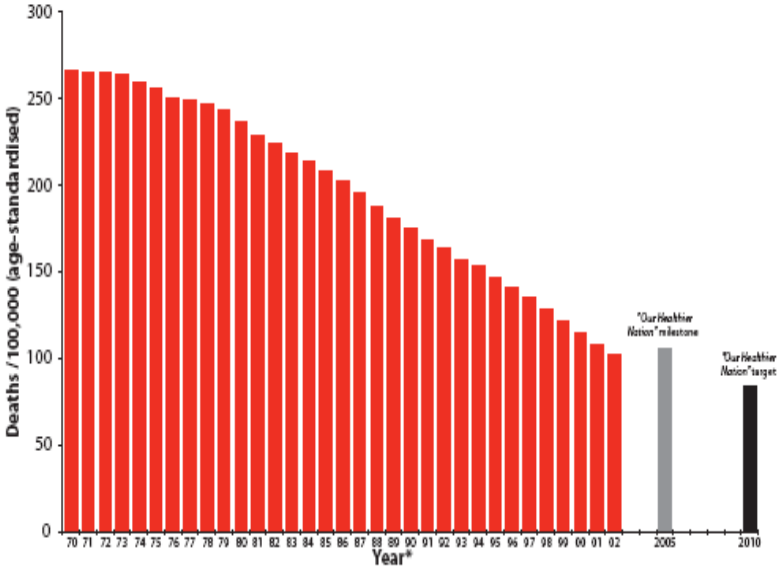
Men



Women

Causes of deaths, 2003, United Kingdom

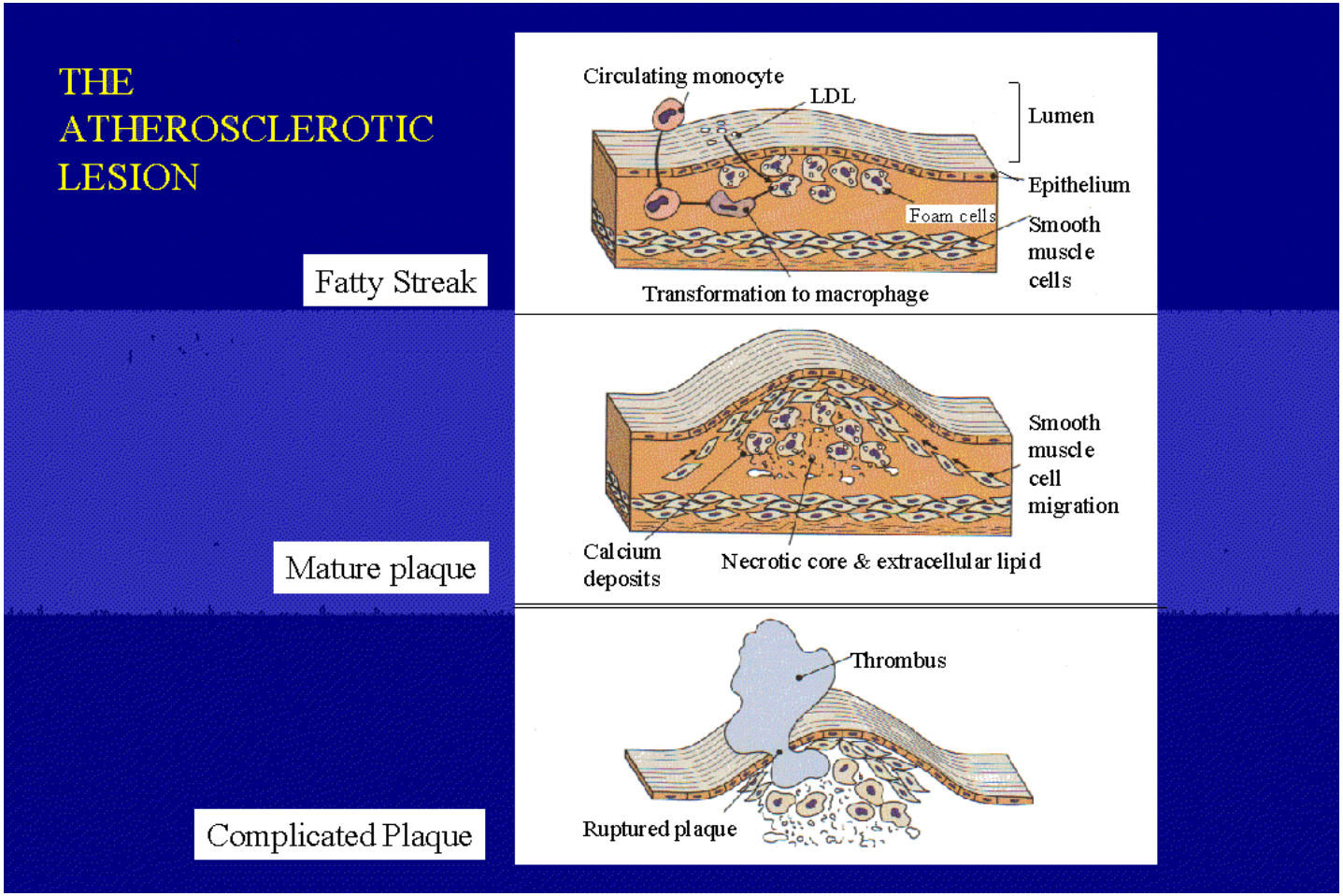
Fig 1.1a *Death rates from CHD, stroke and all other diseases of the circulatory system, people aged under 75, 1970-2002, England, with Our Healthier Nation milestone and target*



Data are three year moving averages plotted against middle year. ICD9 data have been adjusted to be comparable with ICD10 data. Data from 1984-1992 have been adjusted due to the effects of coding medical enquiries and WHO Rule 3.

Sources: Data from Office for National Statistics (2004); analysis by Central Health Monitoring Unit, Department of Health.

Pathology


THE ATHEROSCLEROTIC LESION
Fatty Streak
Circulating monocyte
LDL
Lumen
Epithelium
Foam cells
Smooth muscle cells
Transformation to macrophage
Mature plaque
Smooth muscle cell migration
Calcium deposits
Necrotic core & extracellular lipid
Complicated Plaque
Thrombus
Ruptured plaque

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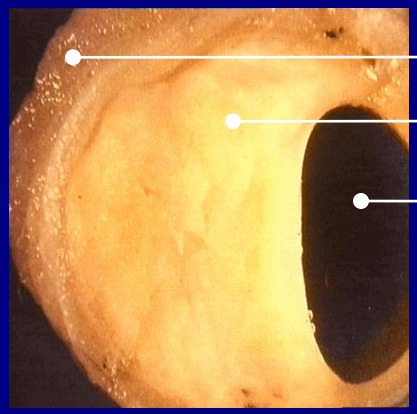
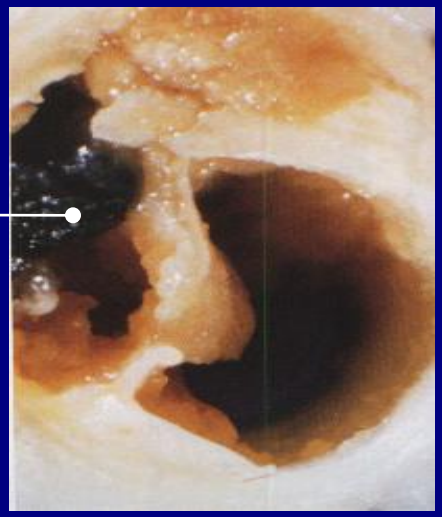
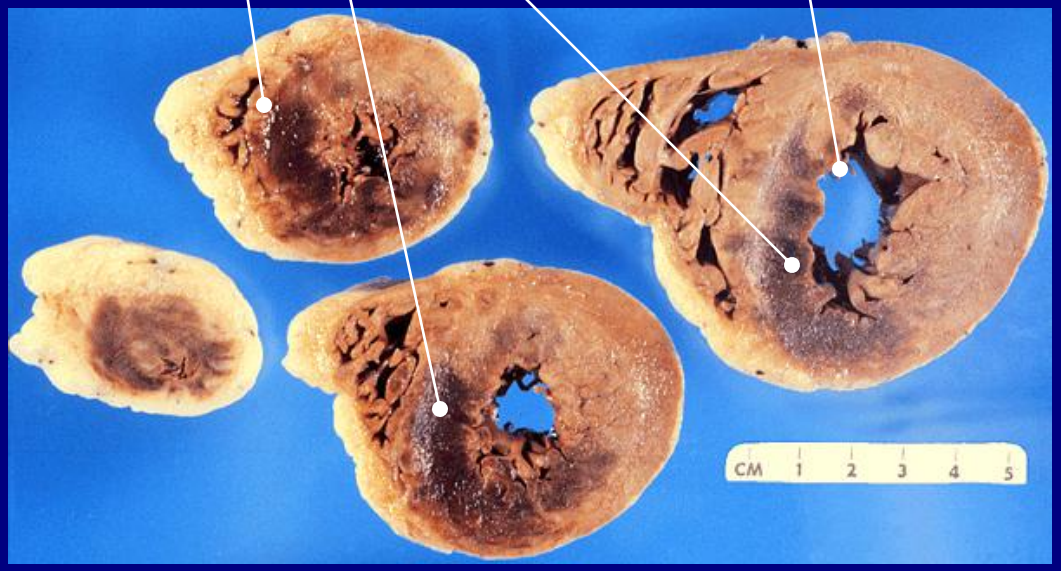
Coronary artery plaque
and its consequences







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Risk factors for Coronary Artery Disease

Age	Fibrinogen	Lipoprotein (a)
Alcohol	Gender	Obesity
C-reactive protein	Homocysteine	Personality
D-dimer	Hypercholesterolaemia	Serum amyloid
Depression	Hypertension	Smoking
Diabetes	Inactivity	Stress
Family history	Interleukin-6	Soft water

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Risk factors for Coronary Artery Disease
Markers

Fibrinogen

Lipoprotein (a)

C-reactive protein

Homocysteine

D-dimer

Serum amyloid

Interleukin-6

Risk factors for Coronary Artery Disease
Those difficult to measure

Personality

Depression

Inactivity

Soft water

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Risk factors for Coronary Artery Disease
'Standard measures'

Age

Gender

Obesity

Hypercholesterolaemia

Hypertension

Smoking

Diabetes

Family history

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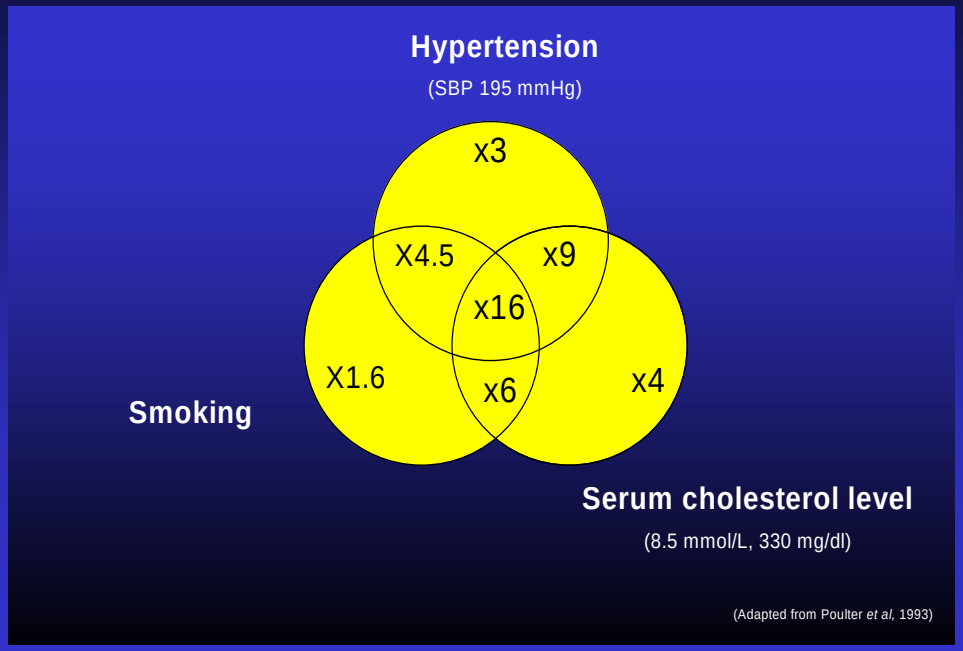
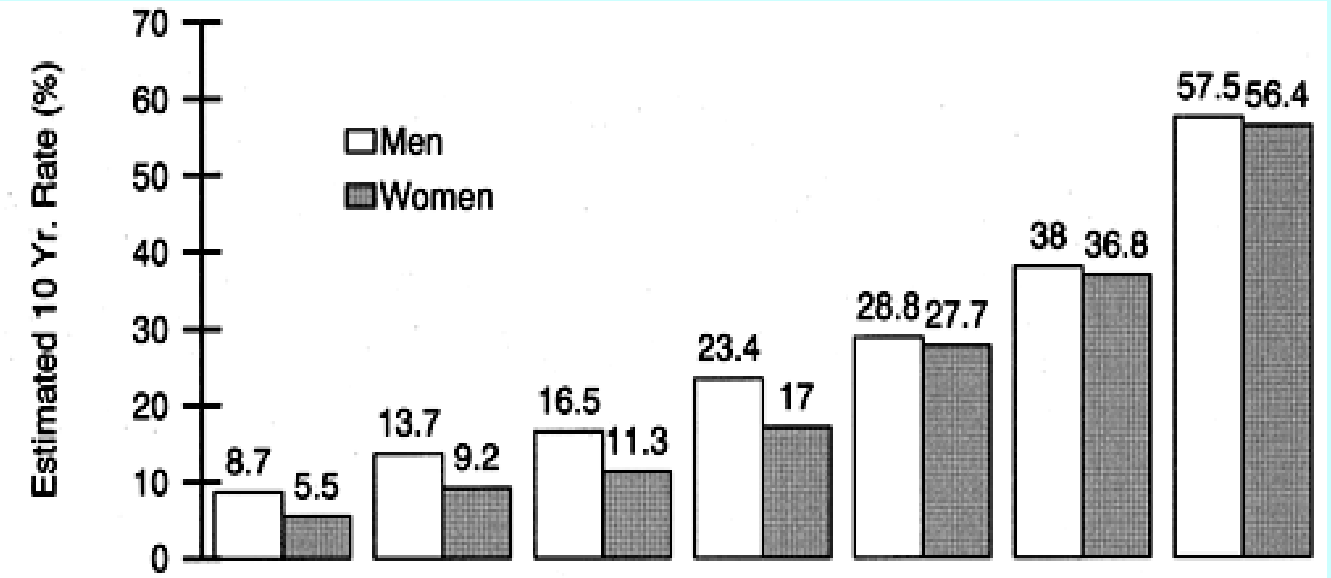
Levels of risk associated with smoking, hypertension and hypercholesterolaemia



(Adapted from Poulter *et al*, 1993)

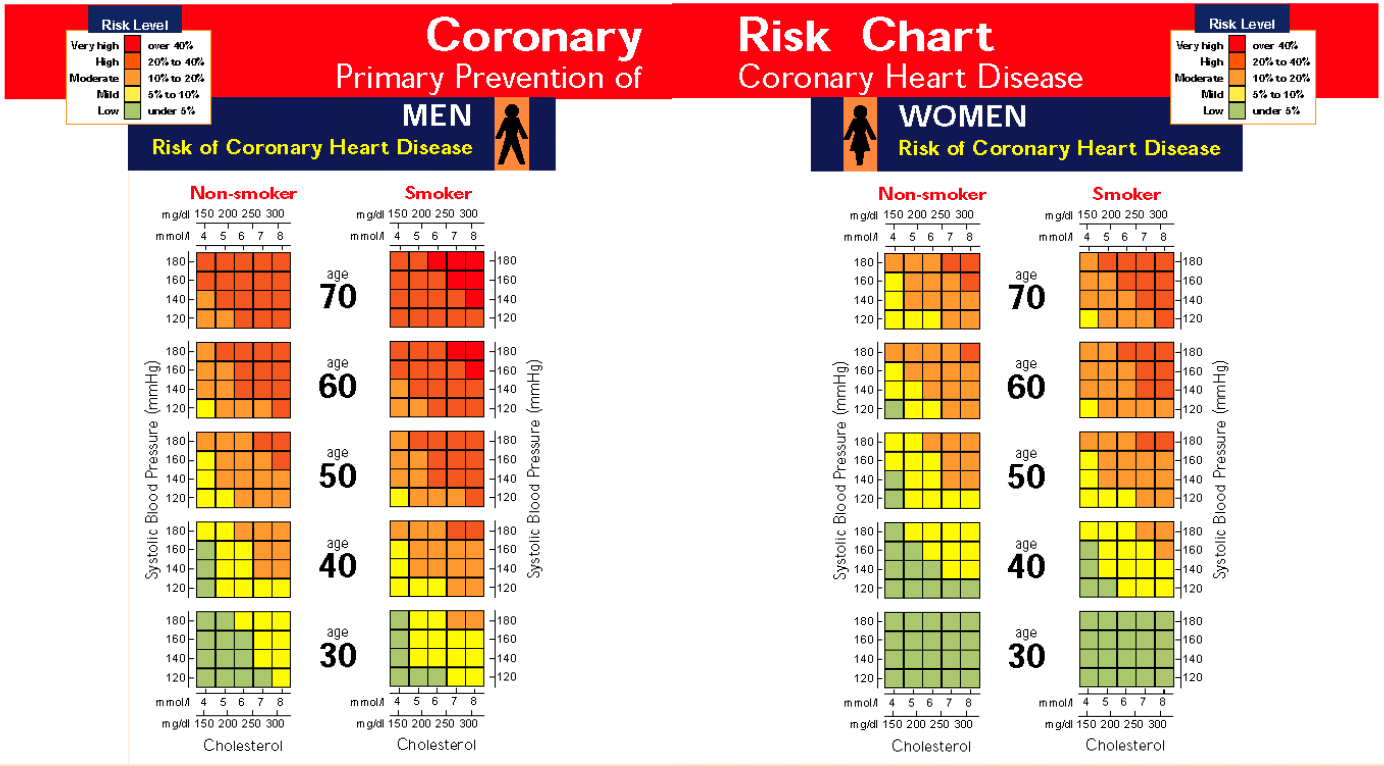
Estimated 10 year risk (%) of coronary artery disease in a 55 year old

Data from the Framingham Study. Am J Hypertens 1994;7:75



BP Systolic	120	160	160	160	160	160	160
Cholesterol	220	220	260	260	260	260	260
HDL-C	50	50	50	35	35	35	35
Diabetes	-	-	-	-	+	+	+
Cigarettes	-	-	-	-	-	+	+
LVH by ECG	-	-	-	-	-	+	+

Calculation of CHD Risk



How to use the Coronary Risk Chart for Primary Prevention

The chart is for estimating coronary heart disease (CHD) risk for individuals who have not developed symptomatic CHD or other atherosclerotic disease. Patients with CHD are already at high risk and require intensive lifestyle intervention and, as necessary, drug therapies to achieve risk factor goals.

- To estimate a person's absolute 10 year risk of a CHD event, find the table for their gender, smoking status and age. Within the table, find the cell nearest to their systolic blood pressure (mmHg) and total cholesterol (mmol/l or mg/dl).
- The effect of lifetime exposure to risk factors can be seen by following the table upwards. This can be used when advising younger people.
- High risk individuals are defined as those whose 10 year CHD risk exceeds 20% or will exceed 20% if projected to age 60.
- CHD risk is higher than indicated in the chart for those with:-
  - Familial hypercholesterolaemia
  - Diabetes: risk is approximately doubled in men and more than doubled in women
  - Those with a family history of premature cardiovascular disease
  - Those with low HDL cholesterol. These tables assume HDL cholesterol to be 1.0 mmol/l (39 mg/dl) in men and 1.1 (43) in women
  - Those with raised triglyceride levels >2.0 mmol/l (>180 mg/dl)
  - As the person approaches the next age category.
- To find a person's relative risk, compare their risk category with that for other people of the same age. The absolute risk shown here may not apply to all populations, especially those with a low CHD incidence. Relative risk is likely to apply to most populations.
- The effect of changing cholesterol, smoking status or blood pressure can be read from the chart.

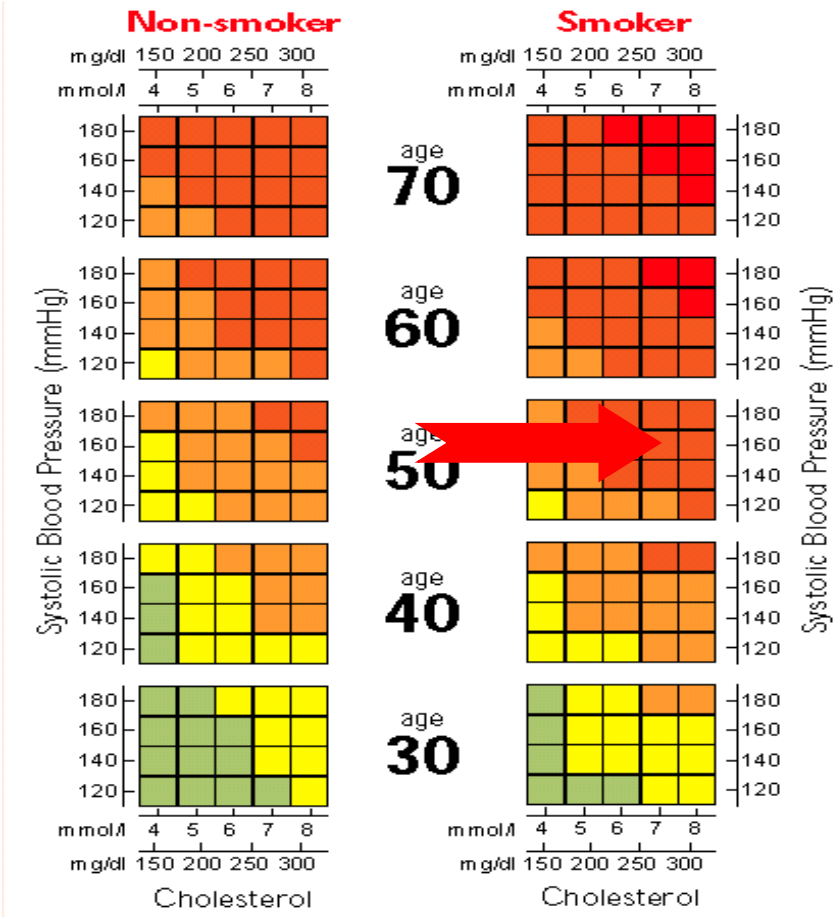
Figure 1 **Coronary risk chart for primary CHD prevention.**

Case 1 – a typical 55 year old male

- 55 year old
- Smoker
- Blood pressure 160 mmHg
- Cholesterol 7.5mmol/l
- Family history

The persons depicted in this presentation
are entirely fictitious.
Any resemblance to people living or dead
is purely coincidental

Case 1 – a typical 55 year old male



Very high	over 40%
High	20% to 40%
Moderate	10% to 20%
Mild	5% to 10%
Low	under 5%

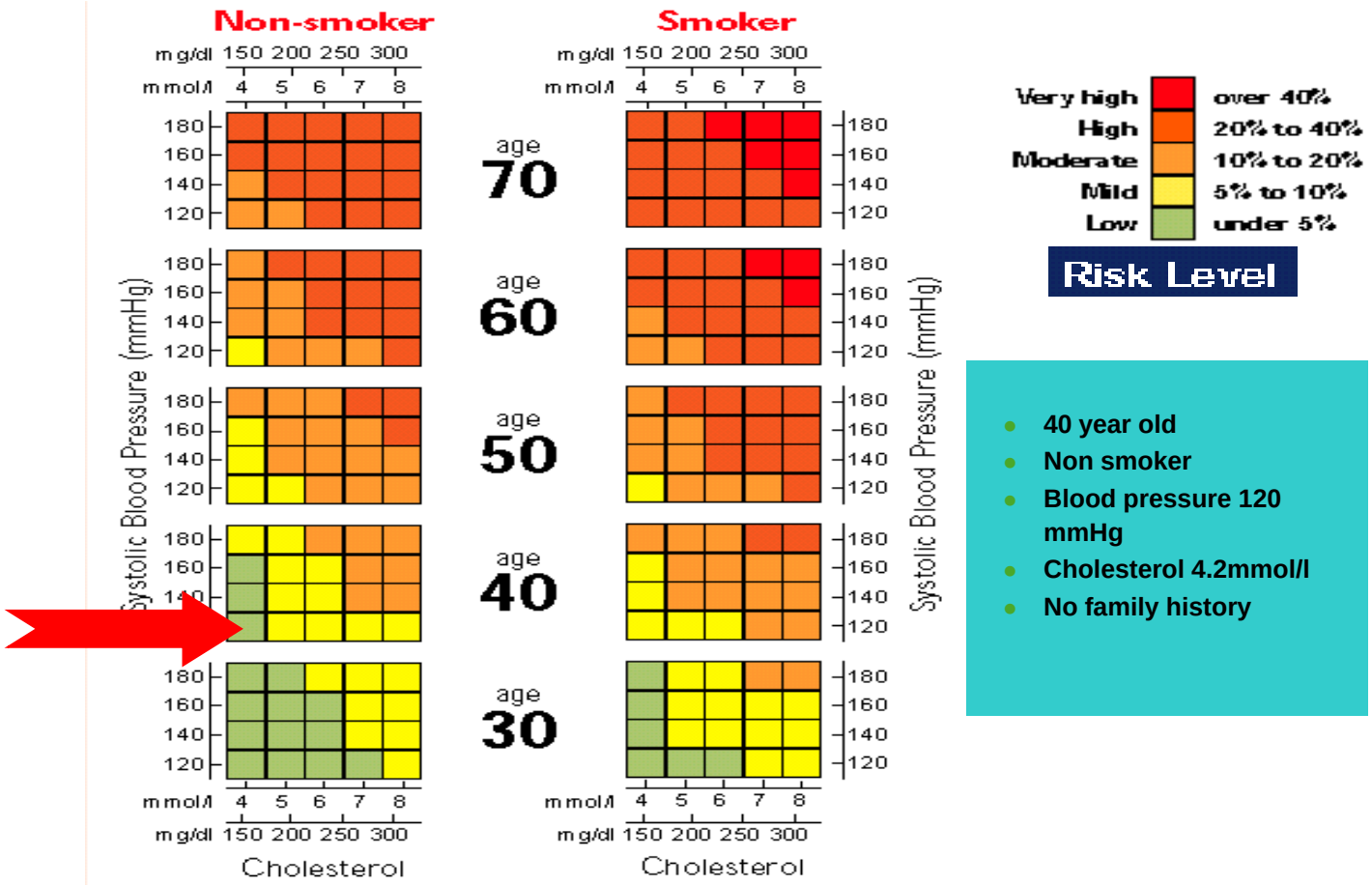
Risk Level

- 55 year old
- Smoker
- Blood pressure 160 mmHg
- Cholesterol 7.5mmol/l
- (Family history)

Case 2 – a healthy 40 year old male

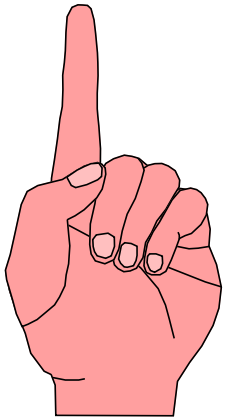
- 40 year old
- Non smoker
- Blood pressure 120 mmHg
- Cholesterol 4.2mmol/l
- No family history

Case 2 – a healthy 40 year old male



- 40 year old
- Non smoker
- Blood pressure 120 mmHg
- Cholesterol 4.2mmol/l
- No family history

Case 3 – single risk factor



- 40 year old
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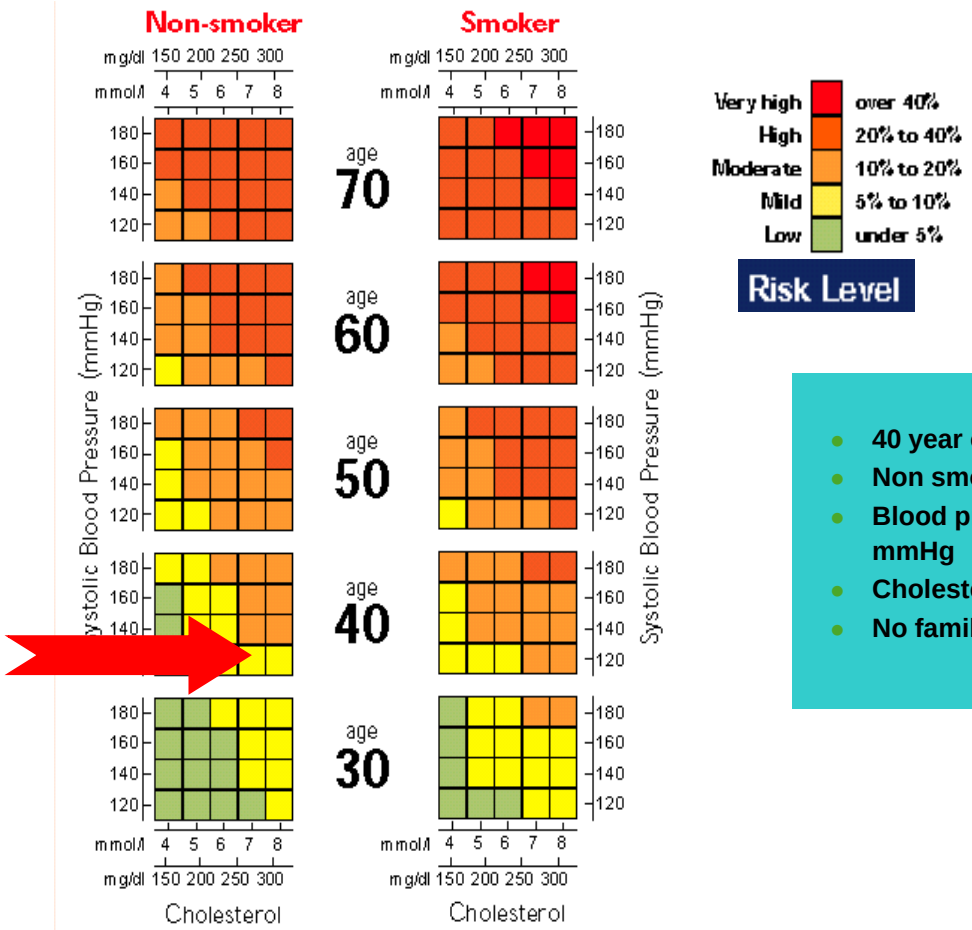
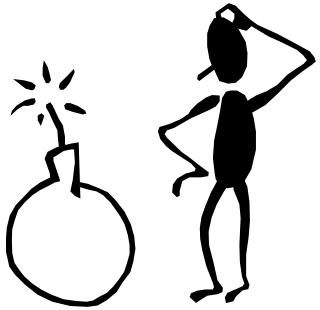
- No family history

Case 3 – single risk factor



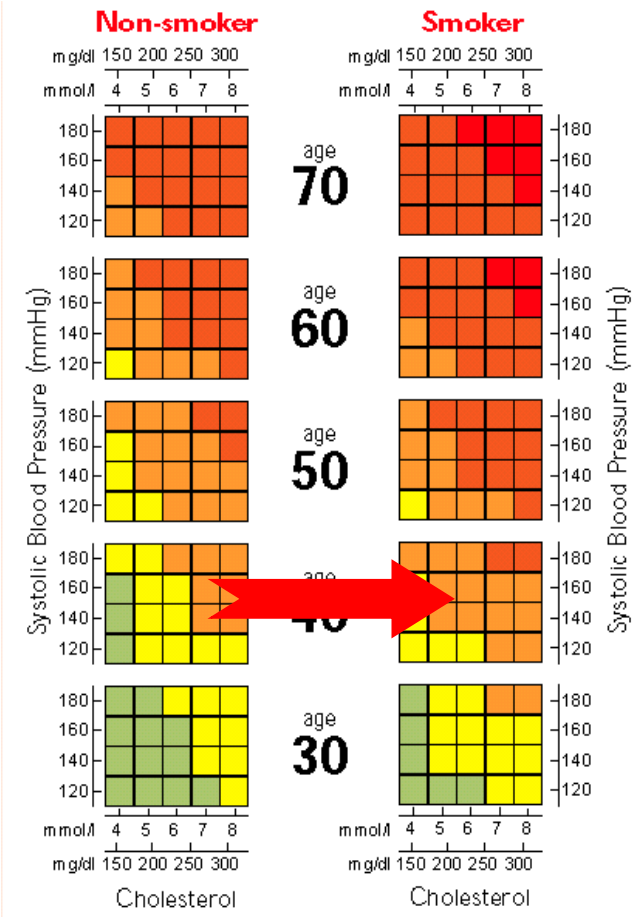
- 40 year old
- Non smoker
- Blood pressure 120 mmHg
- Cholesterol 7.5mmol/l
- No family history

Case 4 – mildly raised risk factors



- 40 year old
- Smoker
- Blood pressure 145 mmHg
- Cholesterol 5.4mmol/l
- No family history

Case 4 – mildly raised risk factors



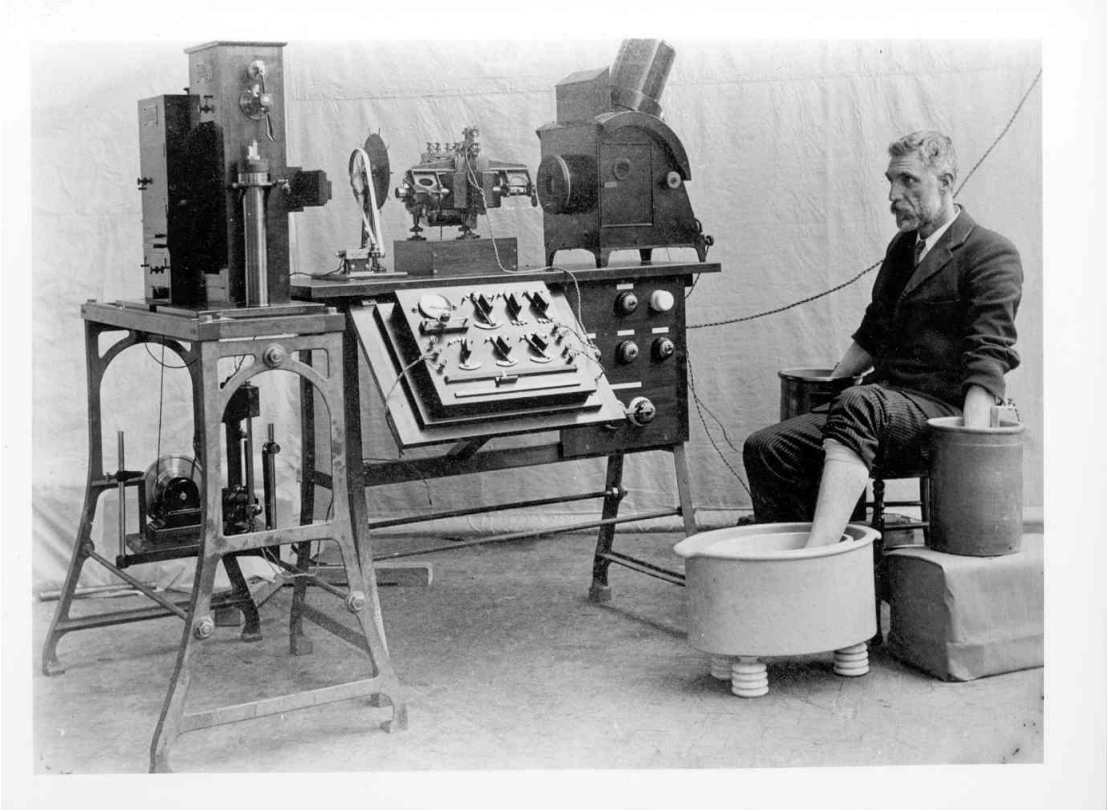
Very high	over 40%
High	20% to 40%
Moderate	10% to 20%
Mild	5% to 10%
Low	under 5%

Risk Level

- 40 year old
- Smoker
- Blood pressure 145 mmHg
- Cholesterol 5.4mmol/l
- No family history

Further Risk Stratification

The Resting ECG

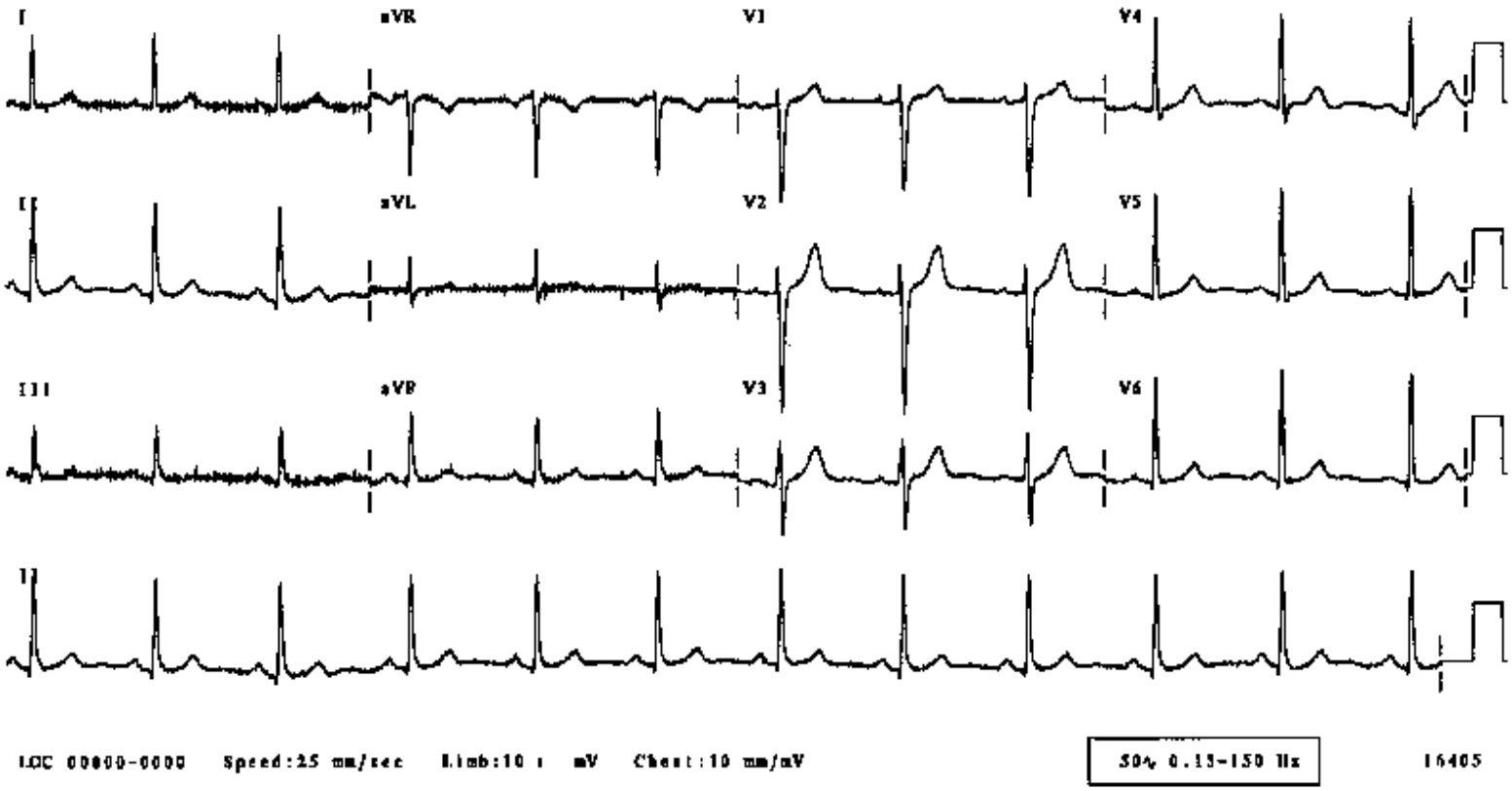


Further Risk Assessment

Sensitivity and Specificity

True positive (TP)	**Abnormal test in individual with disease**
False positive (FP)	**Abnormal test in individual without disease**
True negative (TN)	**Normal test in individual without disease**
False negative (FN)	**Normal test in individual with disease**
Sensitivity	**% with disease who have an abnormal result (TP/TP + FN)**
Specificity	**% without disease who have an normal result (TN/TN + FP)**

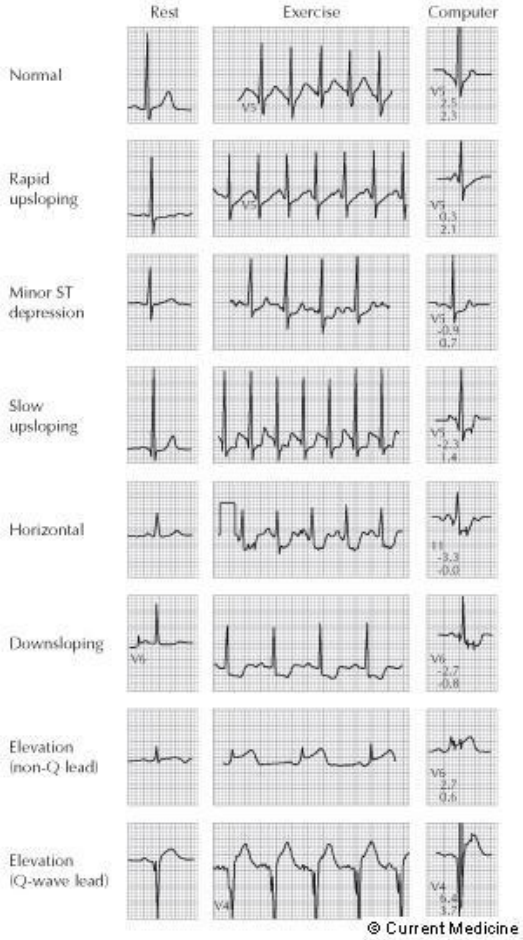
Normal ECG



Normal in 50% on patients with chronic stable angina

The Exercise ECG

Sensitivity	50 - 60%
Specificity	~ 70%



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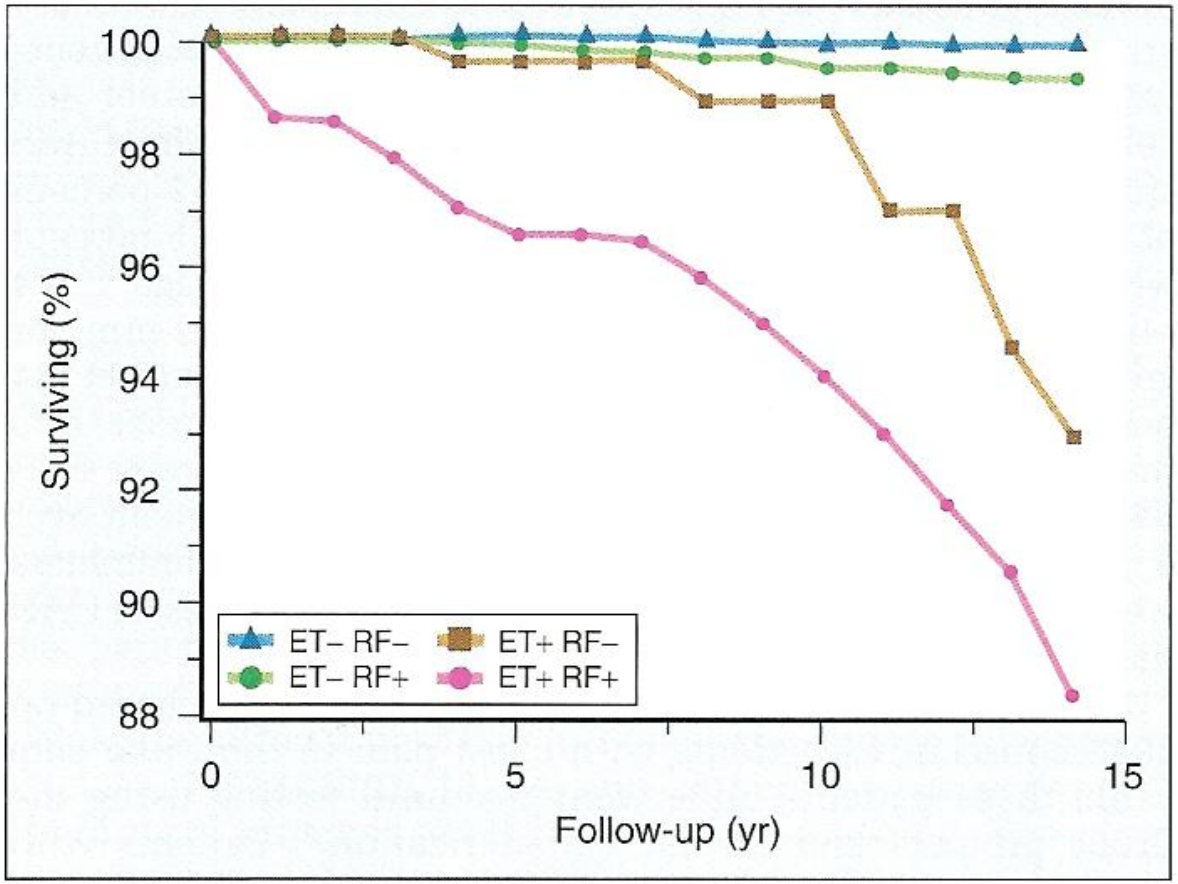
Outcome of 25,927 asymptomatic men undergoing ETT



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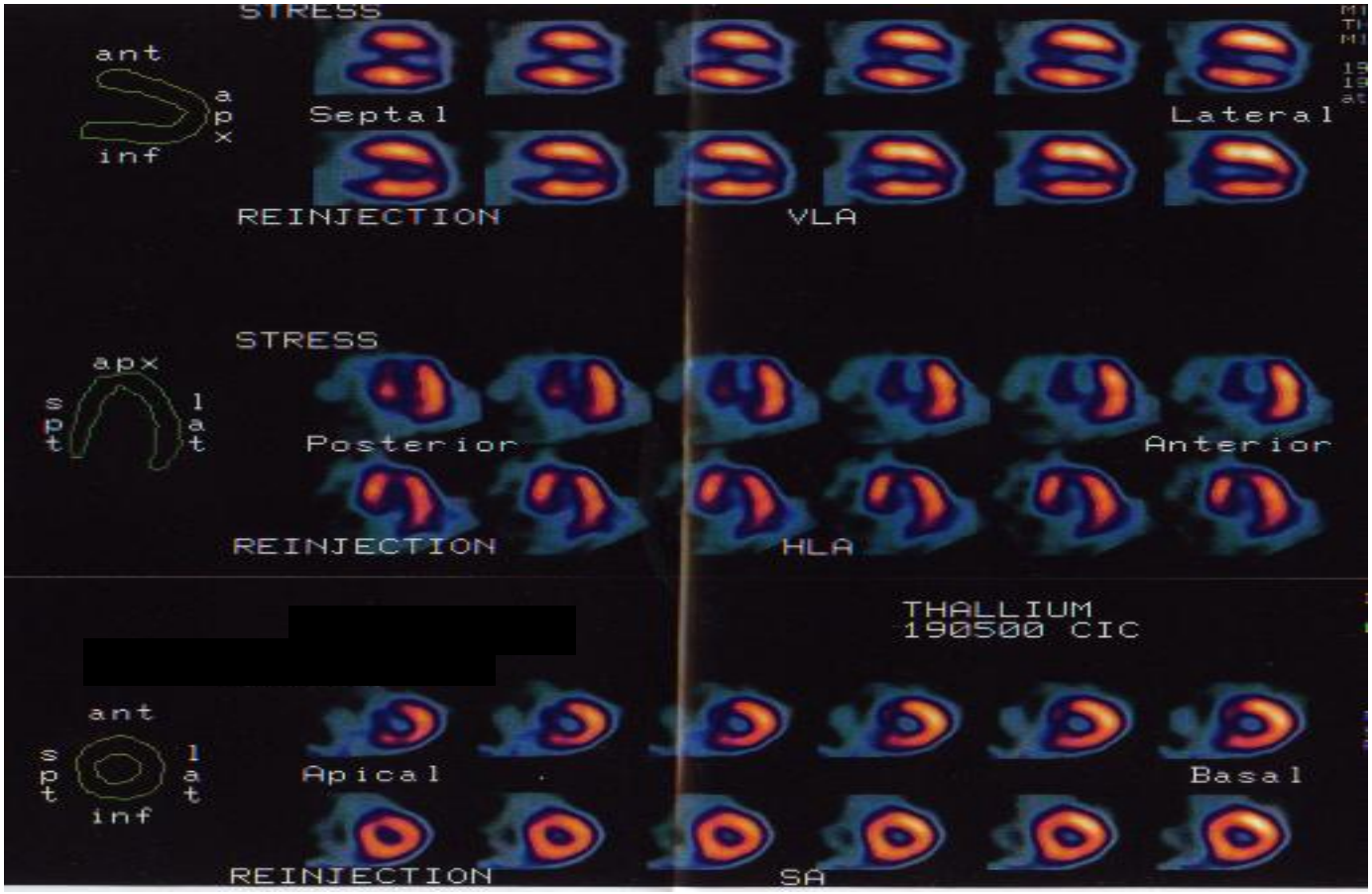
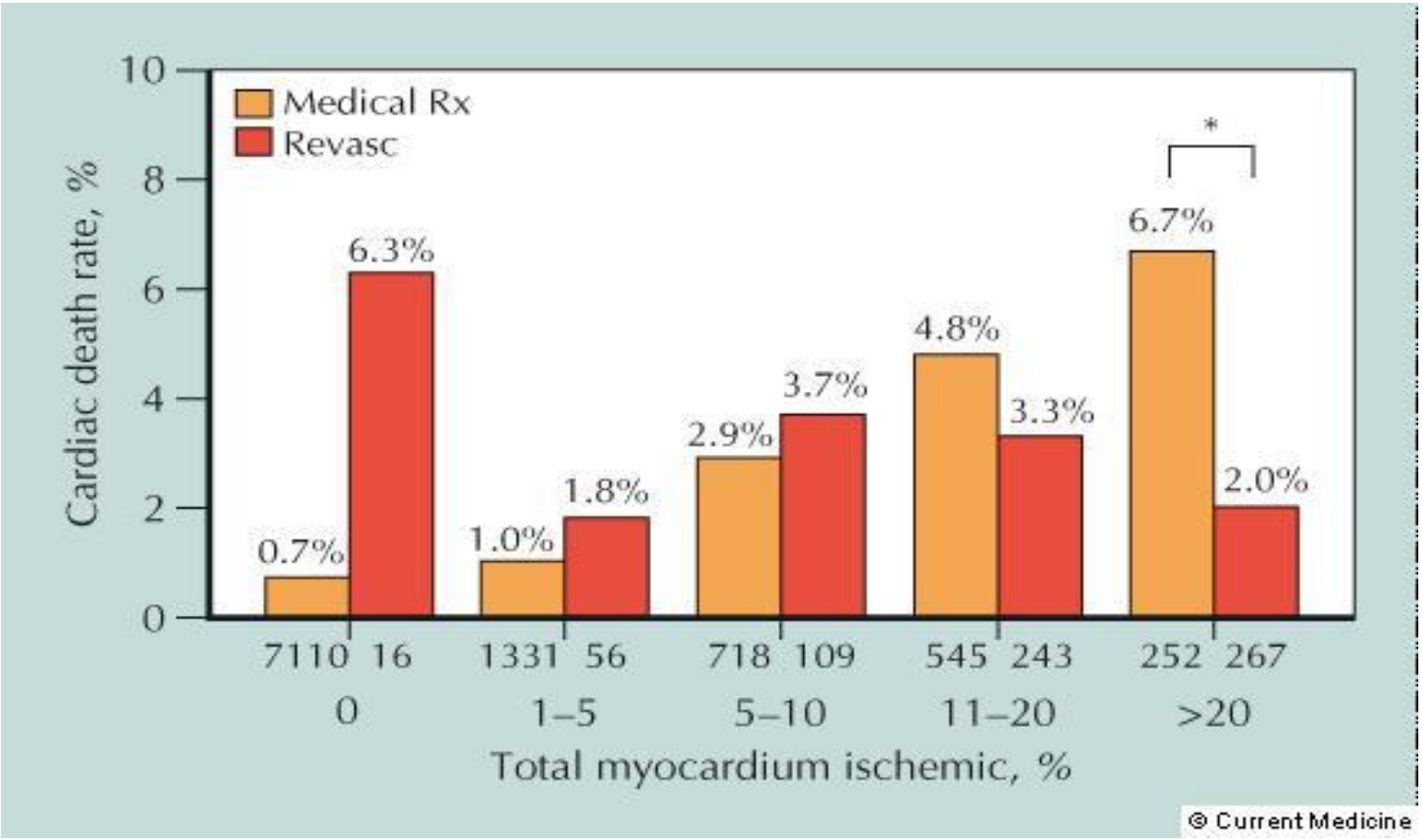
Further Risk Assessment

Myocardial Perfusion Scanning



Further Risk Assessment

Myocardial Perfusion Scanning



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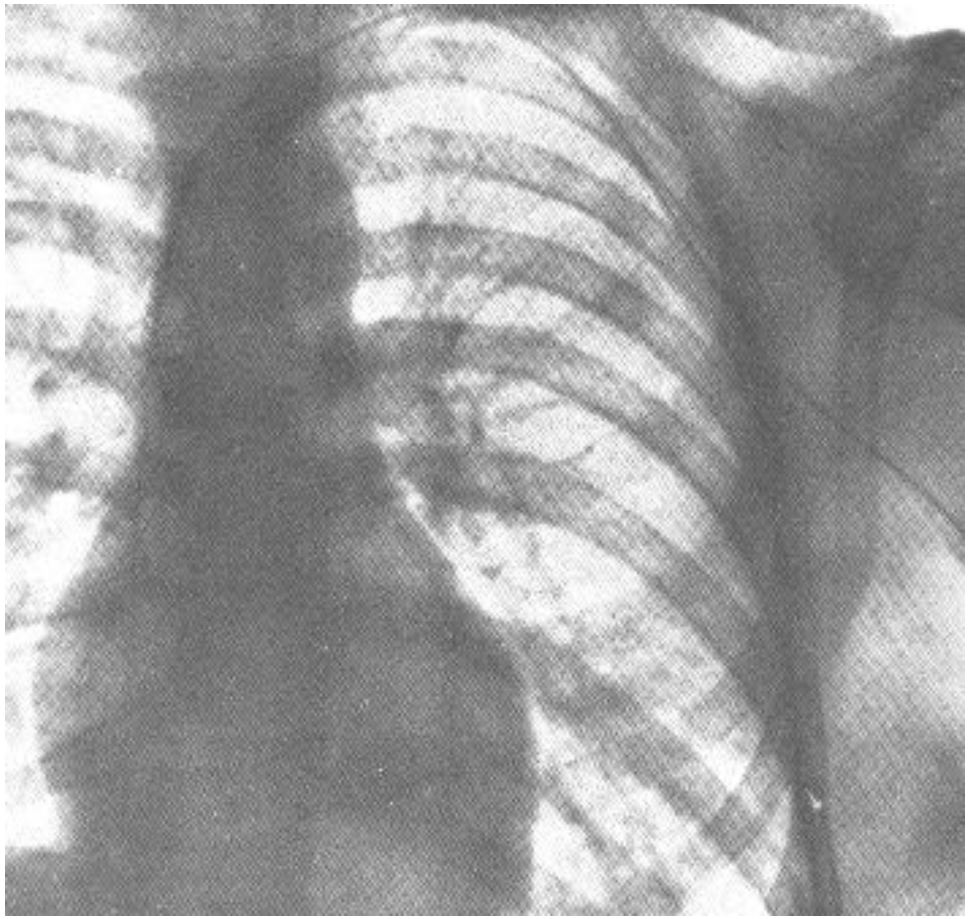
Comparison of Noninvasive Exercise Tests: Meta-analyses

Study	Test	N (% female)	Sensitivity	Specificity
Fleischmann[11]	ECG	2456 (34%)	52%	71%
	SPECT	3237 (30%)	87%	64%
Kwok[12] (gender-specific)	ECG	3721 (100%)	61%	70%
	SPECT	842 (100%)	78%	64%
AHRQ[62] (gender-specific)	SPECT	1249 (44%)	77%	69%

Further Risk Assessment

Coronary Angiography

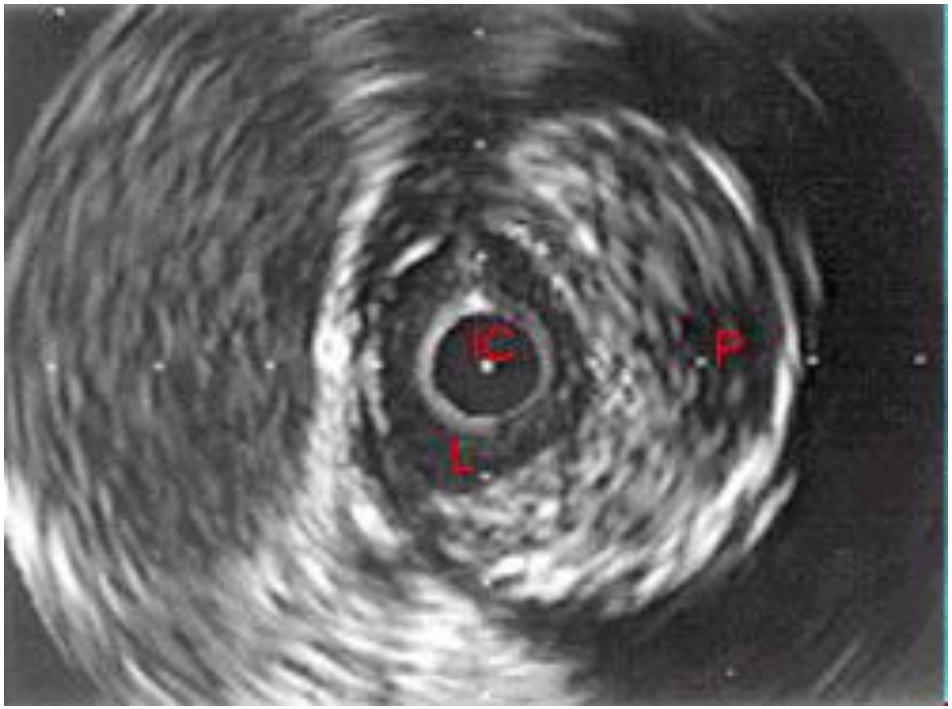


Forssmann 1929
Right heart catheter

Further Risk Assessment

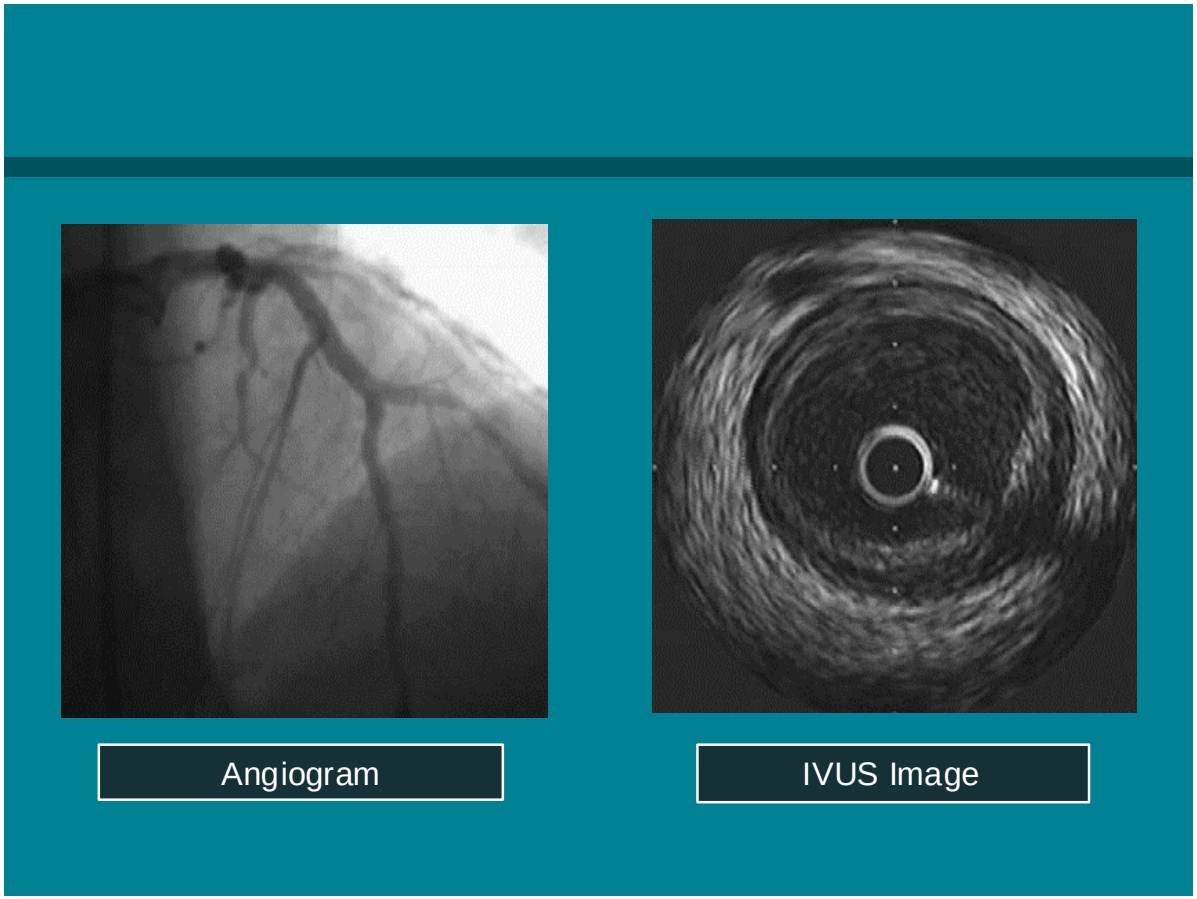
Coronary Angiography

Intravascular Ultrasound (IVUS)



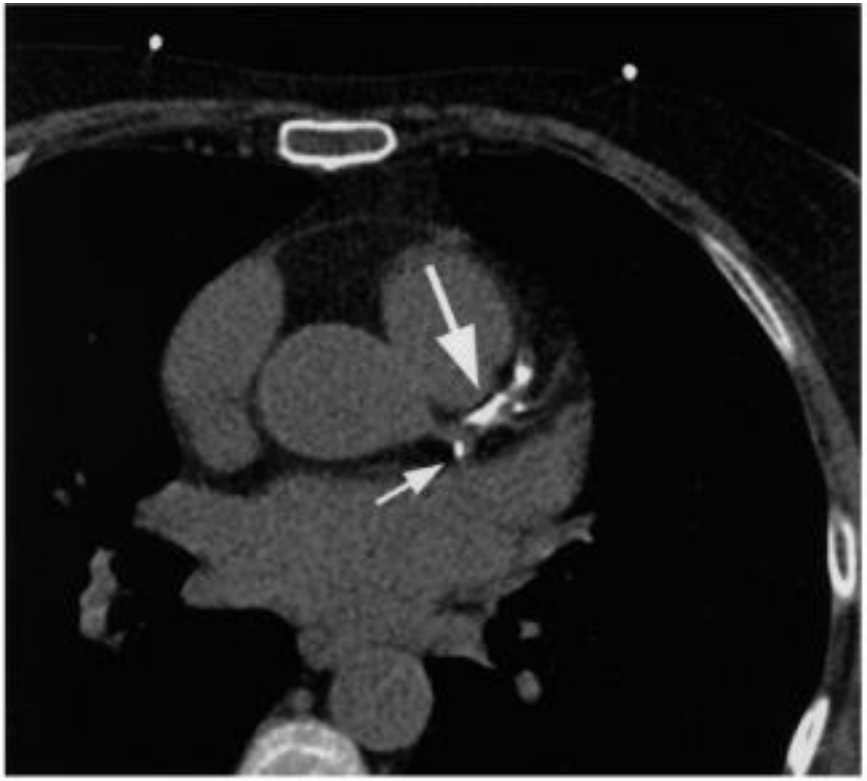
IVUS image of inside a coronary artery.
IC=IVUS catheter, L=lumen, P=plaque

Intravascular Ultrasound (IVUS)



Nissen SE et al. JAMA 2004; 291(9)1071-1080

Electron Beam CT and Calcium Scoring



Calcification of the left anterior descending coronary artery (large arrow) and left circumflex coronary artery (small arrow)

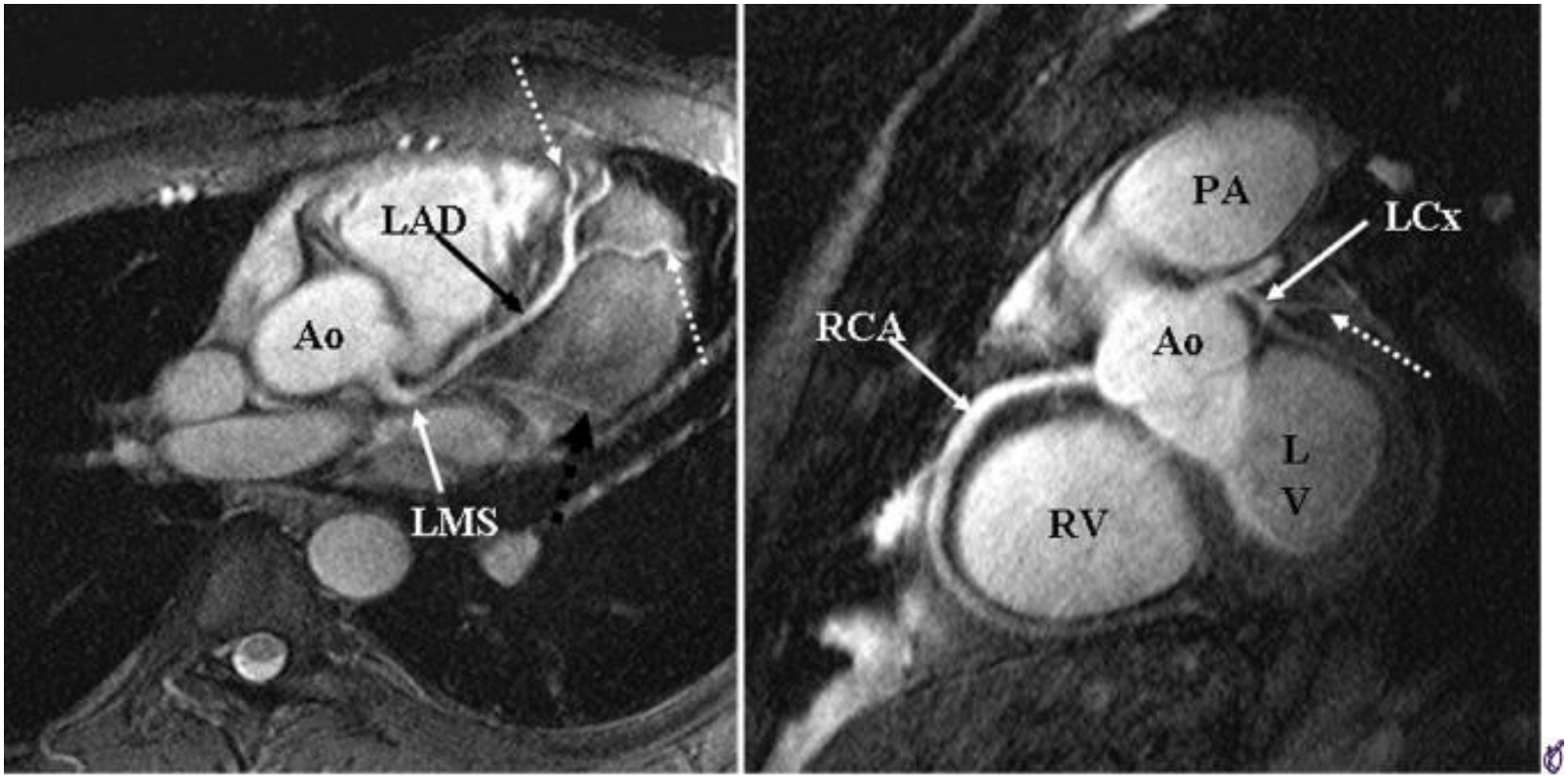
Test	Sensitivity (%)	Specificity (%)
Stress ECG	68	77
EBCT	84	84
Cardiac Catheterisation	100	100

Adapted from Am J Cardiac Imaging 1996;10:180-6

Multi-slice CT

Further Risk Assessment

Cardiac MR



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The 'Activated' Endothelium

activated endothelium

cytokines (eg. IL-1, TNF-α)

chemokines (eg.MCP-1, IL-8)

growth factors (eg. PDGF, FGF)

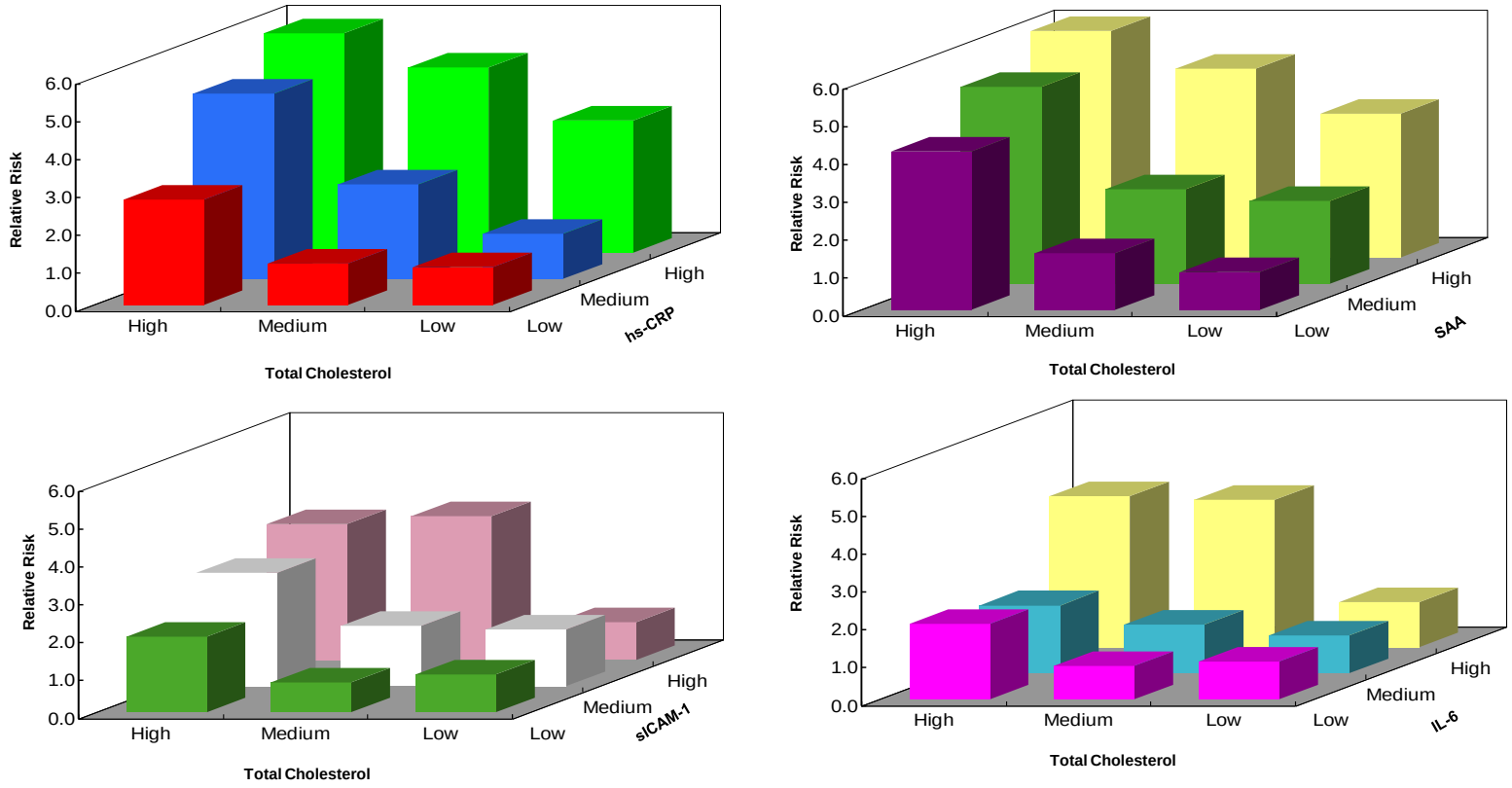
attracts monocytes and T lymphocytes which adhere to endothelial cells

CELLULAR ADHESION MOLECULES

induces cell proliferation and a prothrombic state

Adapted from Koenig W. *Eur Heart J* 1999;**1**(Suppl T);T19-26.

Markers of Inflammation in the Prediction of Cardiovascular Disease in Women



hs-CRP, high-sensitivity C-reactive protein; SAA, serum amyloid A; sICAM, serum intracellular adhesion molecule; IL, interleukin.
Ridker PM, et al. *N Engl J Med.* 2000;342:836-843. (with permission)

Hypercholesterolaemia and IHD

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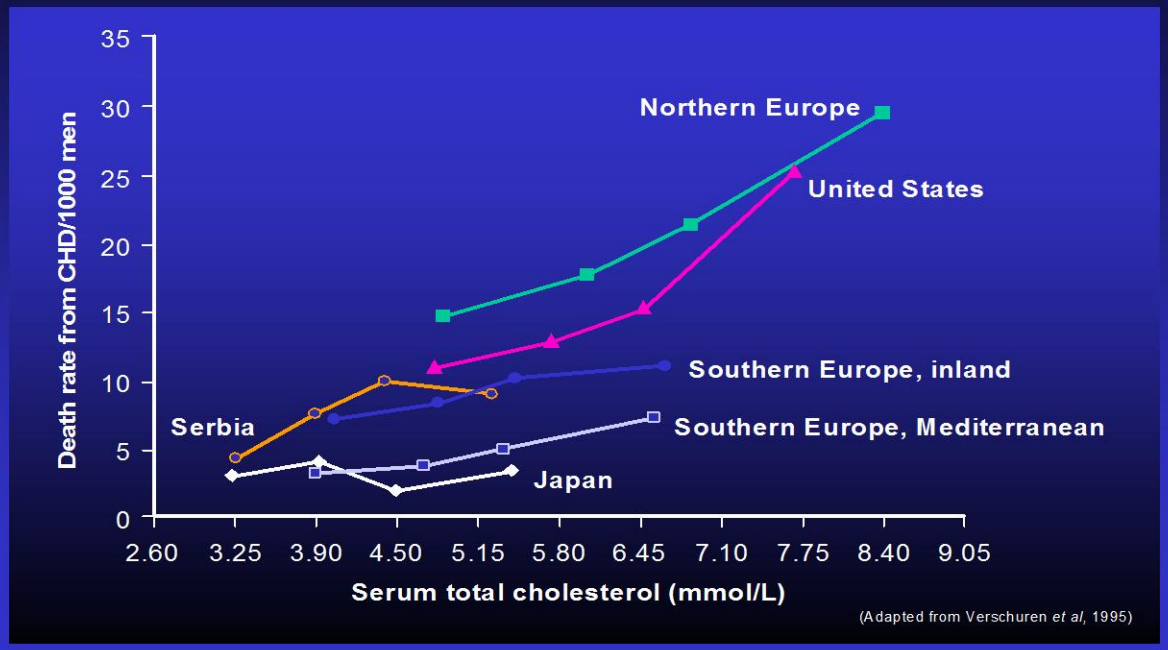
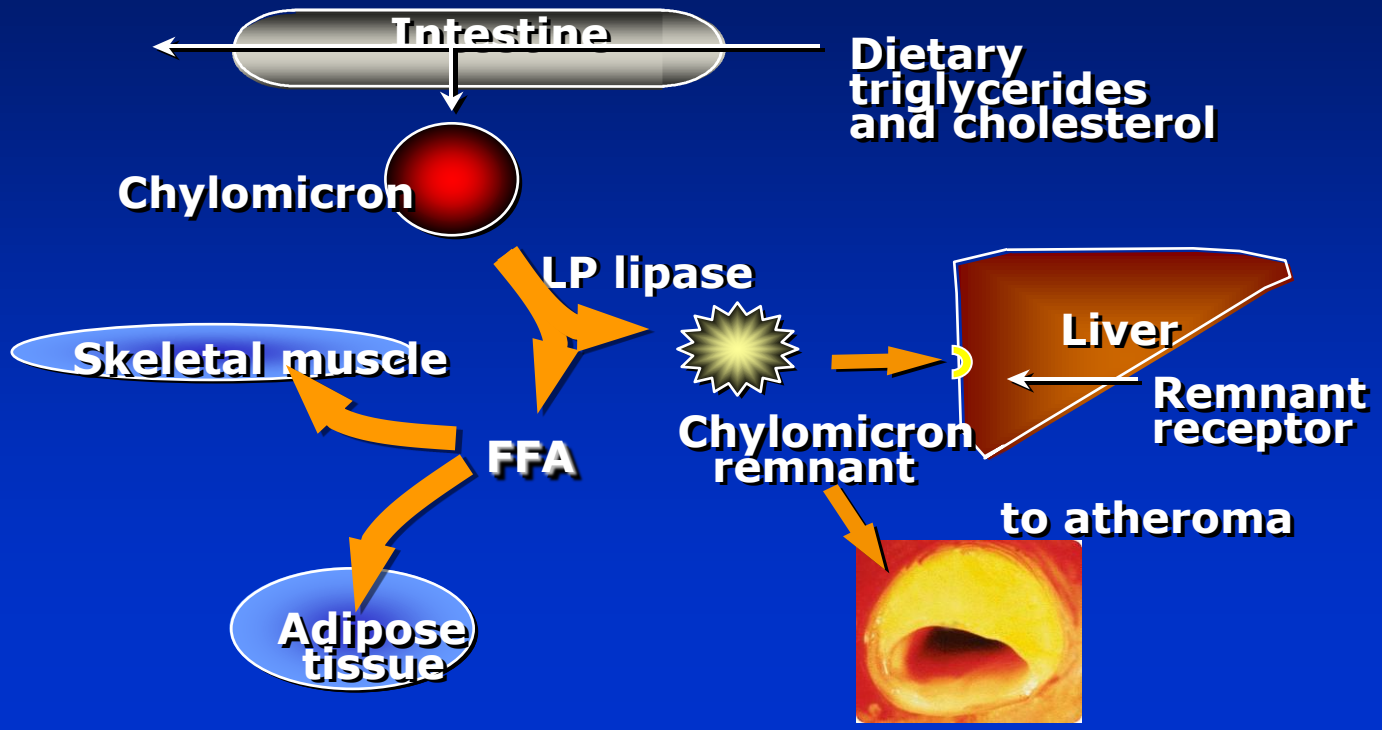
Relationship of serum cholesterol to mortality

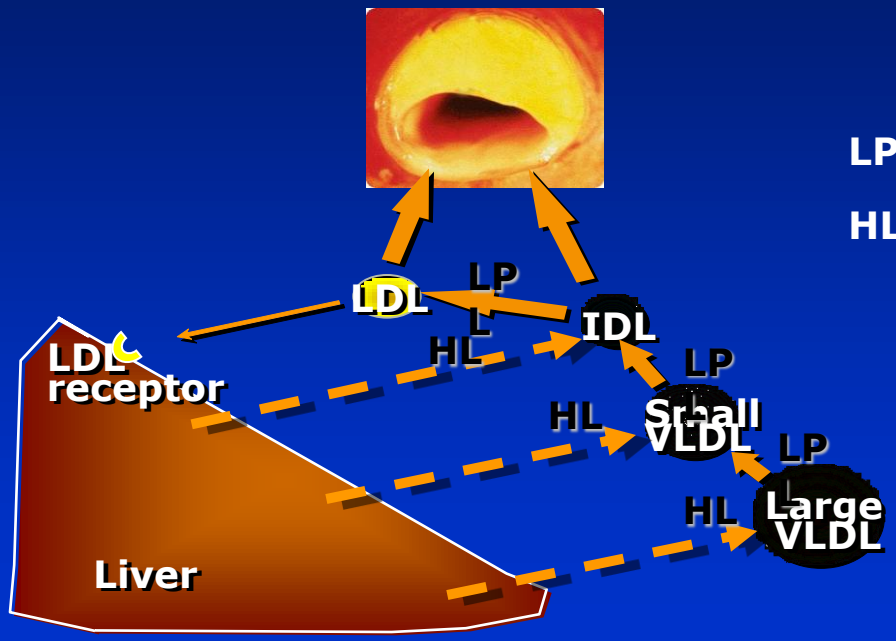
(Seven Countries Study)



Exogenous Pathway of Lipid Metabolism



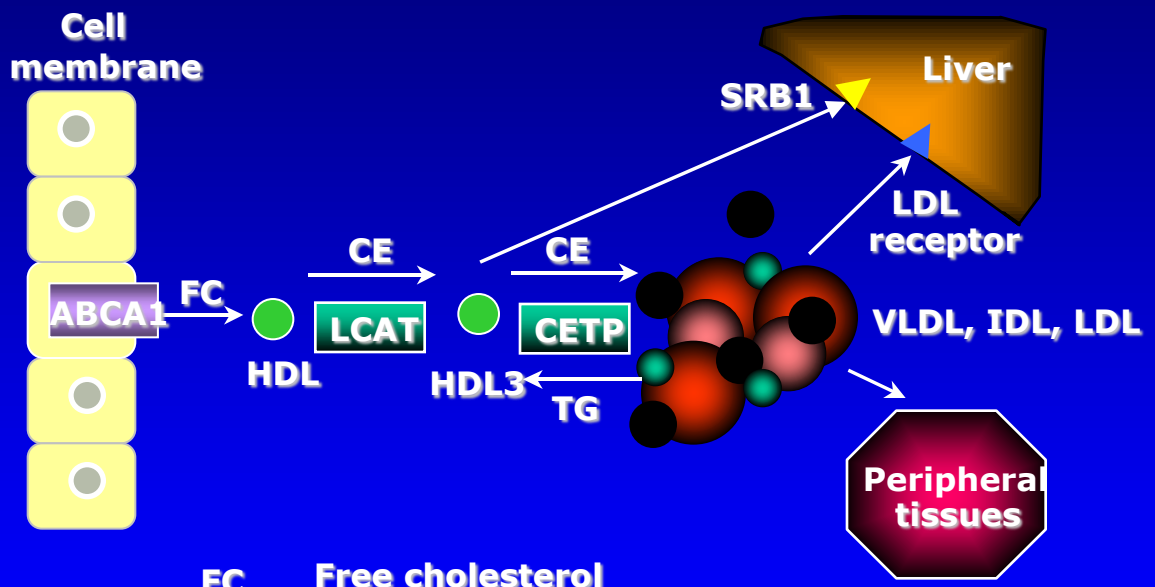
Endogenous Pathway of Lipid Metabolism



LPL Lipoprotein lipase

HL Hepatic lipase

Reverse Cholesterol Transport



FC	Free cholesterol
TG	Triglycerides
CE	Cholesterol esters
LCAT	Lecithin cholesterol acyl transferase
CETP	Cholesteryl ester transfer protein

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Classification of Dyslipidaemias
Fredrickson (WHO) Classification

Phenotype	Lipoprotein elevated	Serum cholesterol	Serum triglyceride	Atherogenicity	Prevalence
I	Chylomicrons	Normal to ↑	↑↑↑↑	None seen	Rare
IIa	LDL	↑↑	Normal	+++	Common
IIb	LDL and VLDL	↑↑	↑↑	+++	Common
III	IDL	↑↑	↑↑↑	+++	Intermediate
IV	VLDL	Normal to ↑	↑↑	+	Common
V	VLDL and chylomicrons	Normal to ↑	↑↑↑↑	+	Rare

LDL – low-density lipoprotein; IDL – intermediate-density lipoprotein; VLDL – very low-density lipoprotein. (High-density lipoprotein (HDL) cholesterol levels are not considered in the Fredrickson classification.)

(Adapted from Yeshurun *et al.*, 1995)

(a) Achilles tendon xanthoma; (b) tendon xanthomata on the dorsum of a hand (heterozygous familial hypercholesterolaemia); and (c) planar xanthoma in the antecubital fossa (homozygous familial hypercholesterolaemia). Courtesy of Professor PN Durrington.

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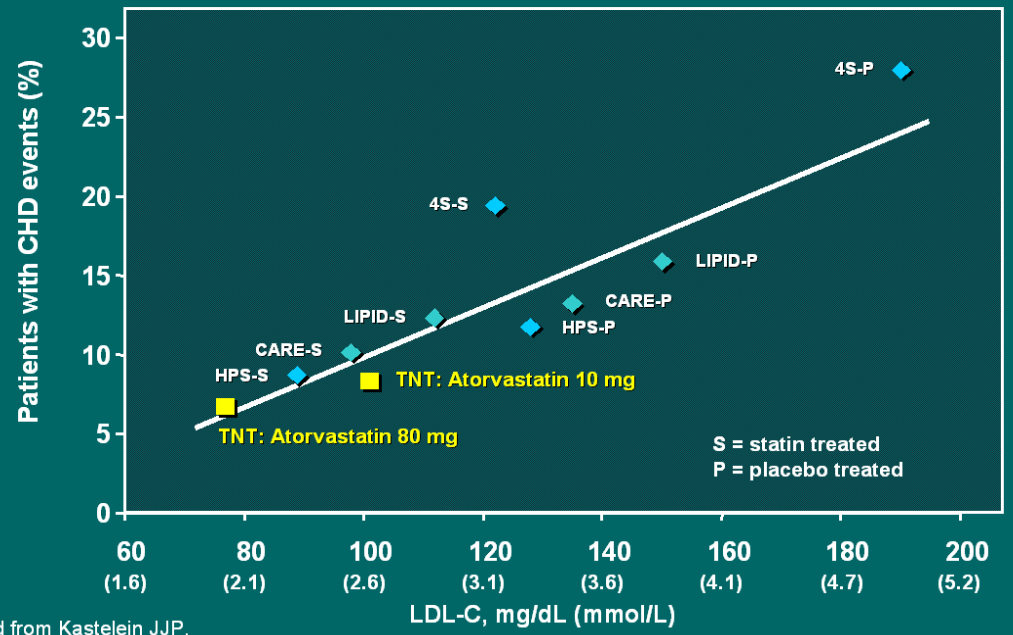
Significant Benefit in Lowering LDL-C Levels to Below Current Treatment Guidelines



Modified from Kastelein JJP.
Atherosclerosis. 1999;143(suppl 1):S17-S21

Lipitor is licensed to reduce cholesterol in hyperlipidaemic patients

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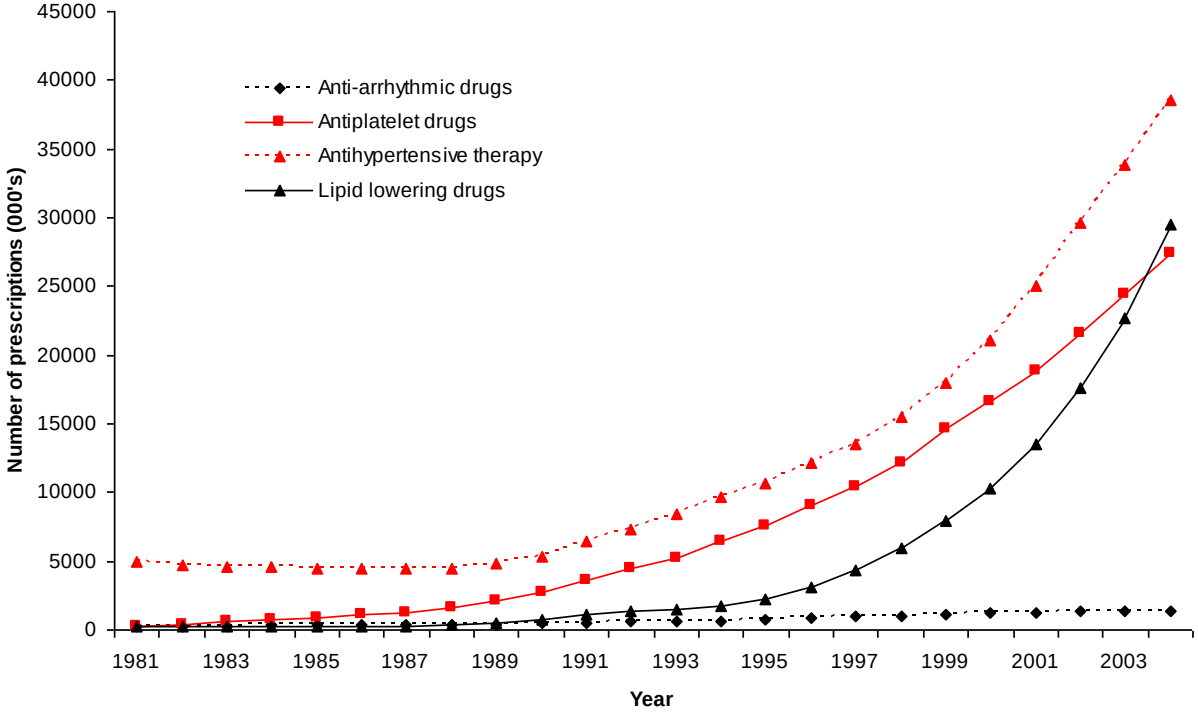
Prescriptions used in the prevention and treatment of diseases of the circulatory system, selected BNF paragraphs, 1981-2004, England

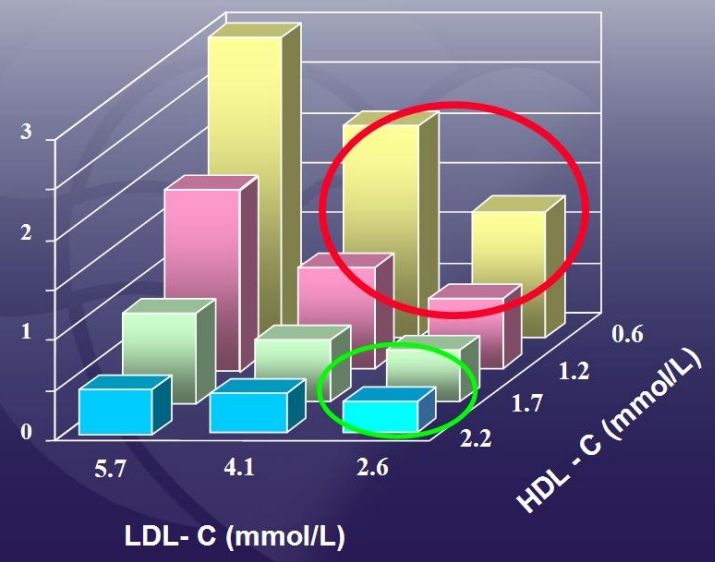


FIELD

Framingham: HDL and LDL as a predictor of CHD Risk

FOURNIER PHARMA

Risk of CAD over 4 yrs of follow-up*



* Men aged 50-70

Gordon T et al. Am J Med 1977;62:707-714.

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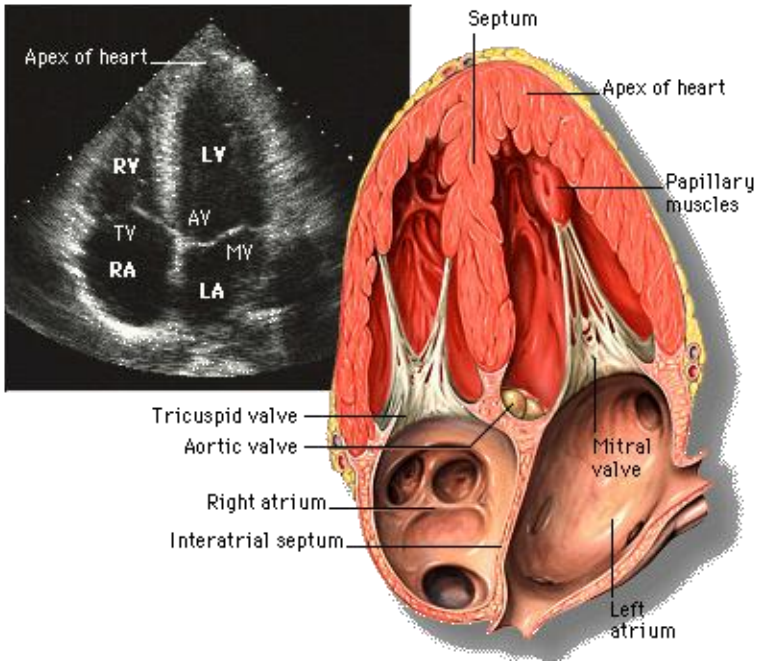
Risk of CHD with increasing triglycerides

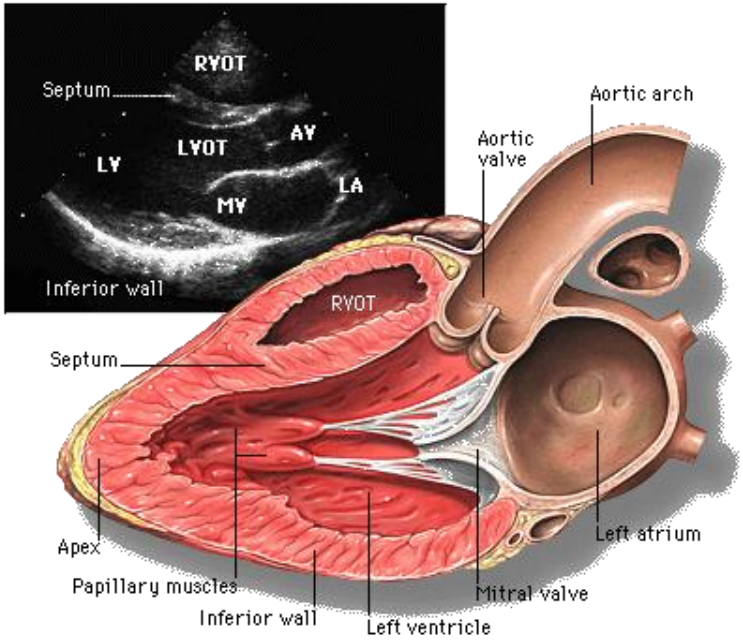
	Relative risk*	
	Men	**Women**
Univariate analysis	1.33	2.02
Adjusted for HDL-C	1.24	1.57

*Risk ratio for CHD in middle-aged persons for each 1.1 mmol/L (97 mg/dL) rise in serum triglycerides. Data based on meta-analysis of 14 prospective studies.

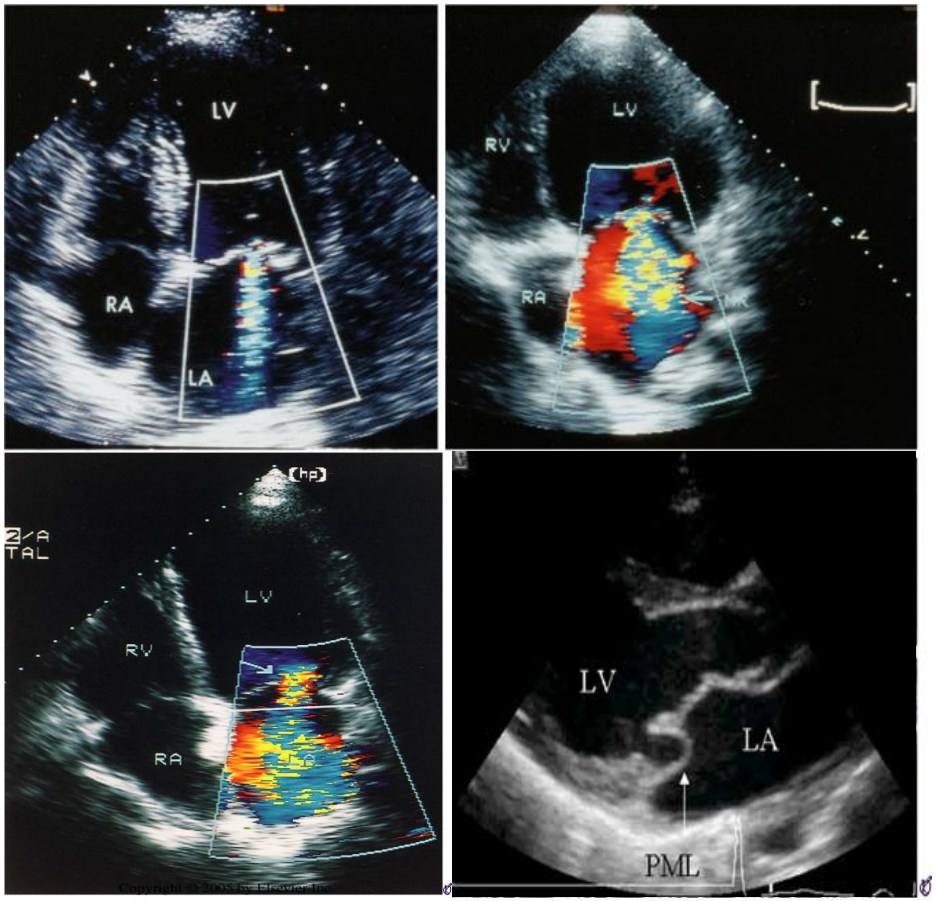
……..and the rest...

Valve Disease





Mitral Regurgitation



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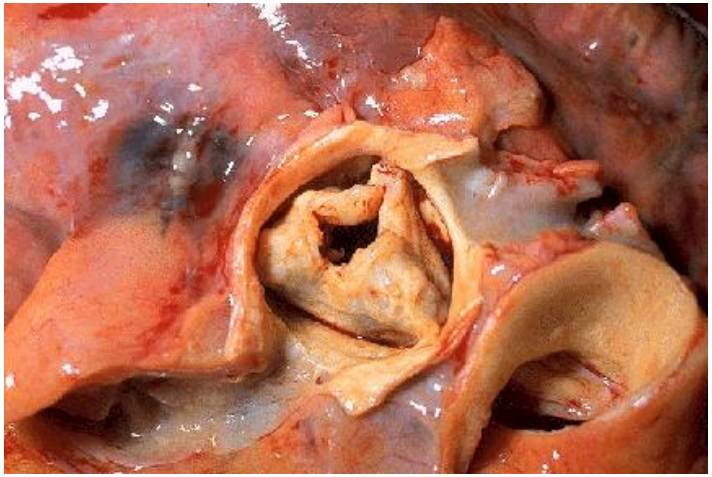
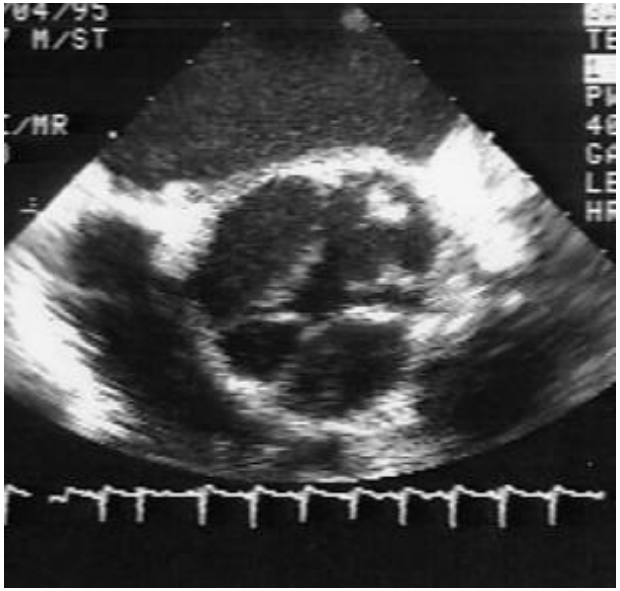
Aortic valve Disease





Mild and moderate aortic stenosis

Natural history and risk stratification by echocardiography

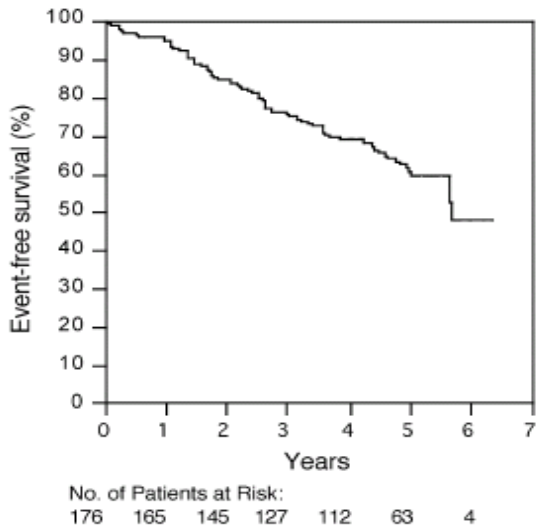


Fig. 1 Kaplan–Meier event-free survival (events: aortic valve replacement n=33, death n=34).

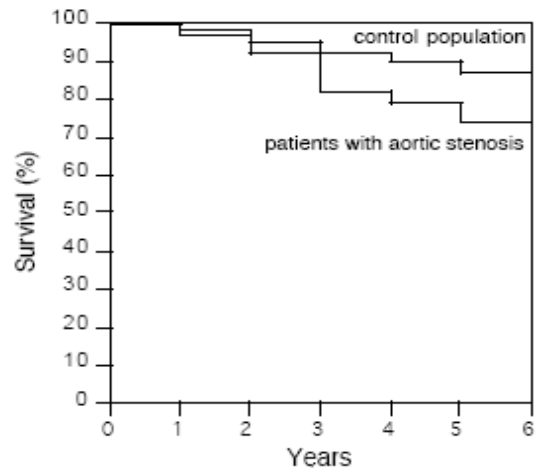


Fig. 2 Kaplan–Meier overall survival of patients compared with survival for age- and gender-matched control subjects (P=0.004). This analysis includes perioperative and postoperative deaths for those patients who required valve replacement during follow-up. The data were taken from the Austrian life tables of 1992 that are provided by the Austrian Statistical Institute and represent the survival of the general Austrian population.

European Heart Journal (2004) **25**, 199–205

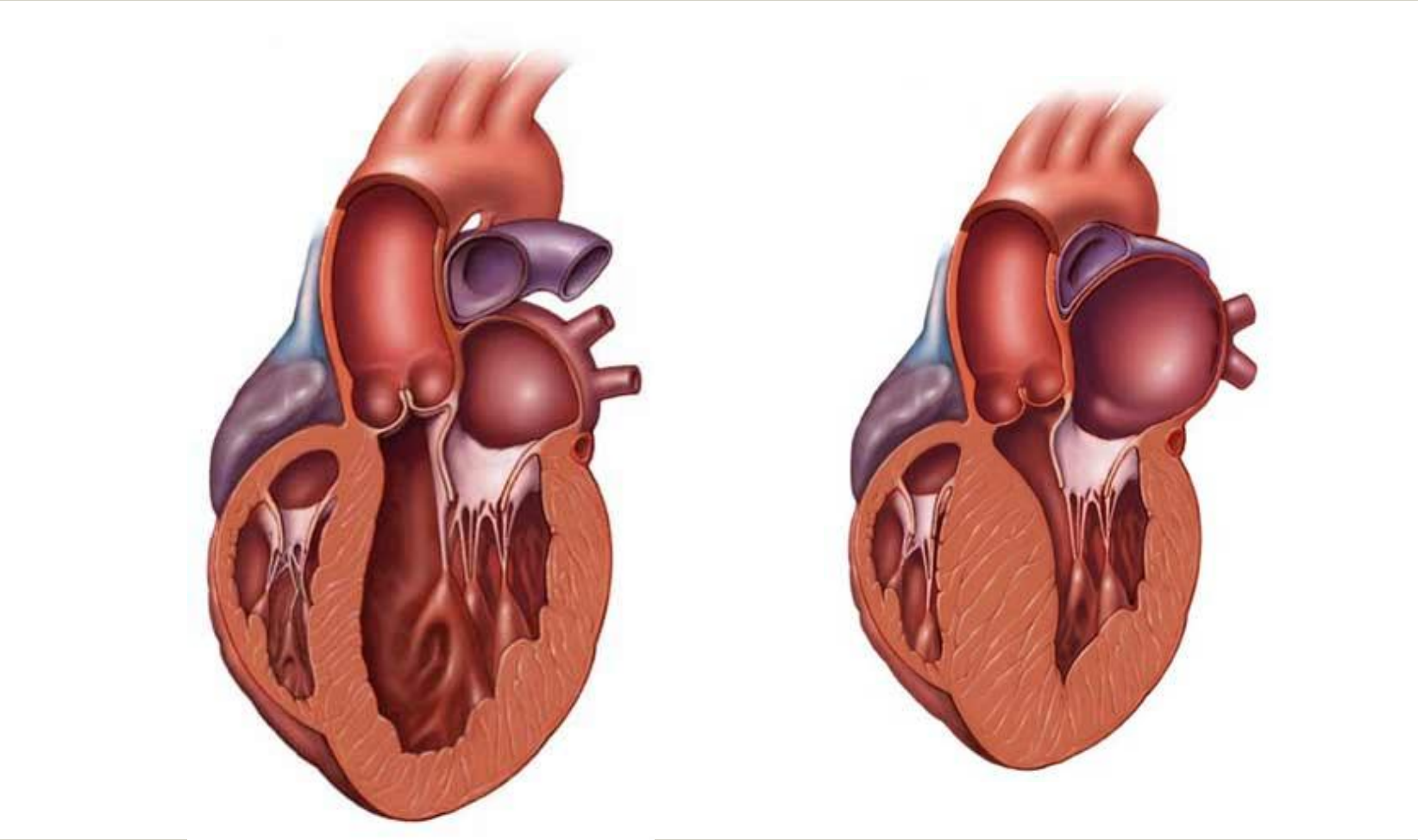
Aortic Regurgitation

BONOW ET AL., ACC/AHA TASK FORCE REPORT
JACC Vol. 32, No. 5, November 1998:1486-1588

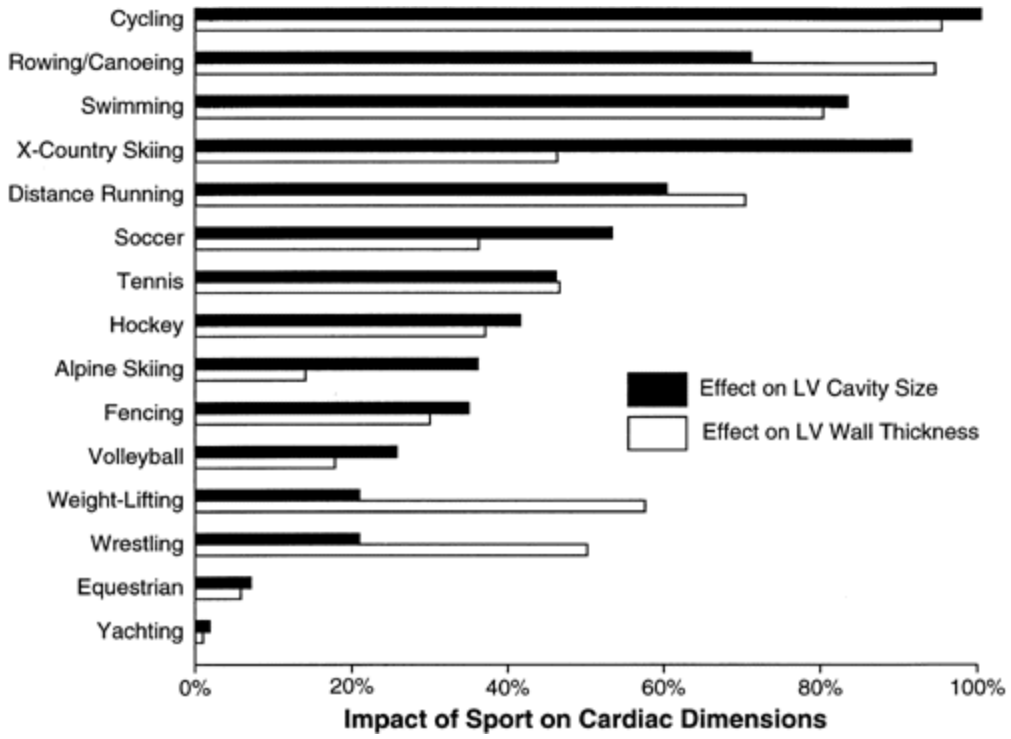
Table 15. Natural History of Aortic Regurgitation

Asymptomatic patients with normal LV systolic function (190–197):	
· Progression to symptoms and/or LV dysfunction	<6%/y
· Progression to asymptomatic LV dysfunction	<3.5%/y
· Sudden death	<0.2%/y
Asymptomatic patients with LV systolic dysfunction (204–206):	
· Progression to cardiac symptoms	>25%/y
Symptomatic patients (207–209):	
· Mortality rate	>10%/y

Left Ventricular Hypertrophy, Hypertrophic Cardiomyopathy and Athletes Heart



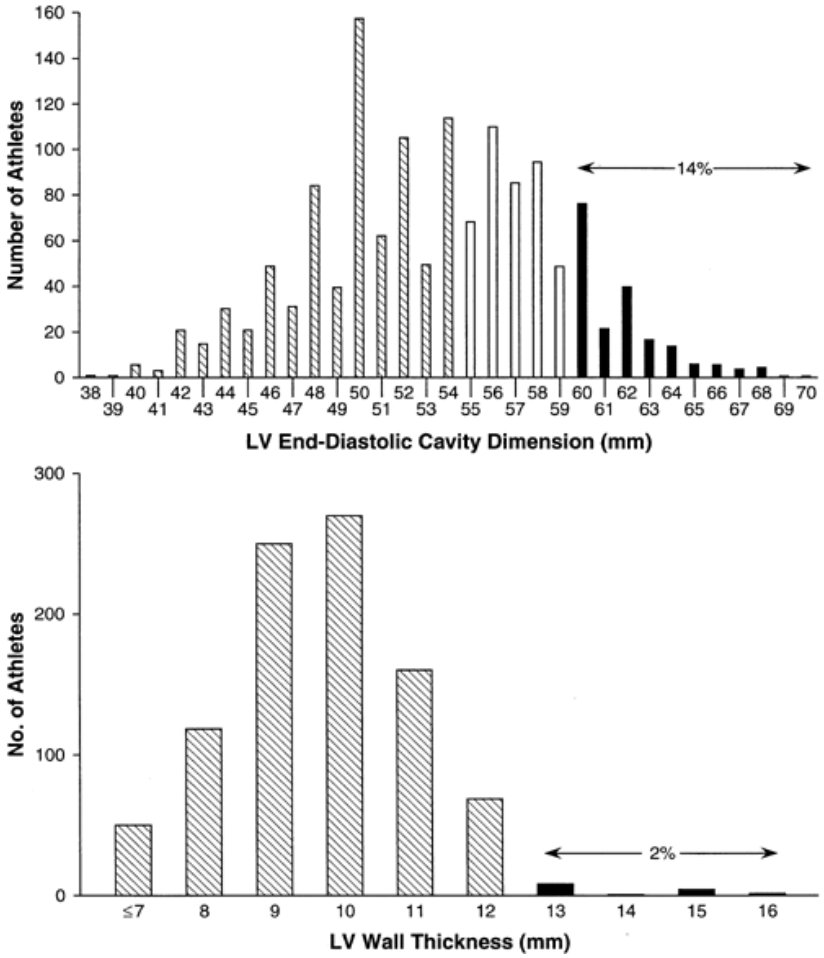
Left Ventricular Dimensions and Athletes Heart



Relative impact of different types of sports training on left ventricular (LV) cavity dimension and wall thickness (expressed as a percentage of maximum)

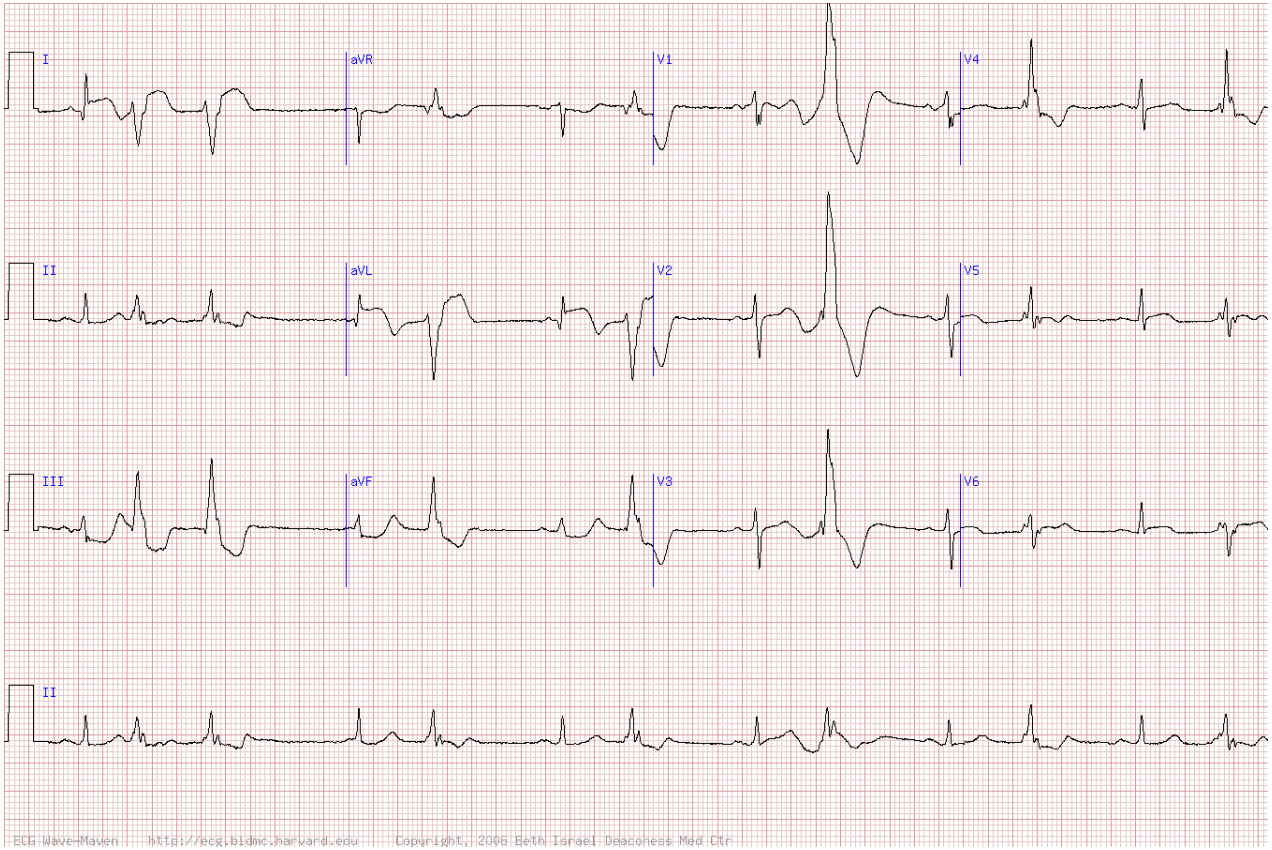
Left Ventricular Dimensions and Athletes Heart

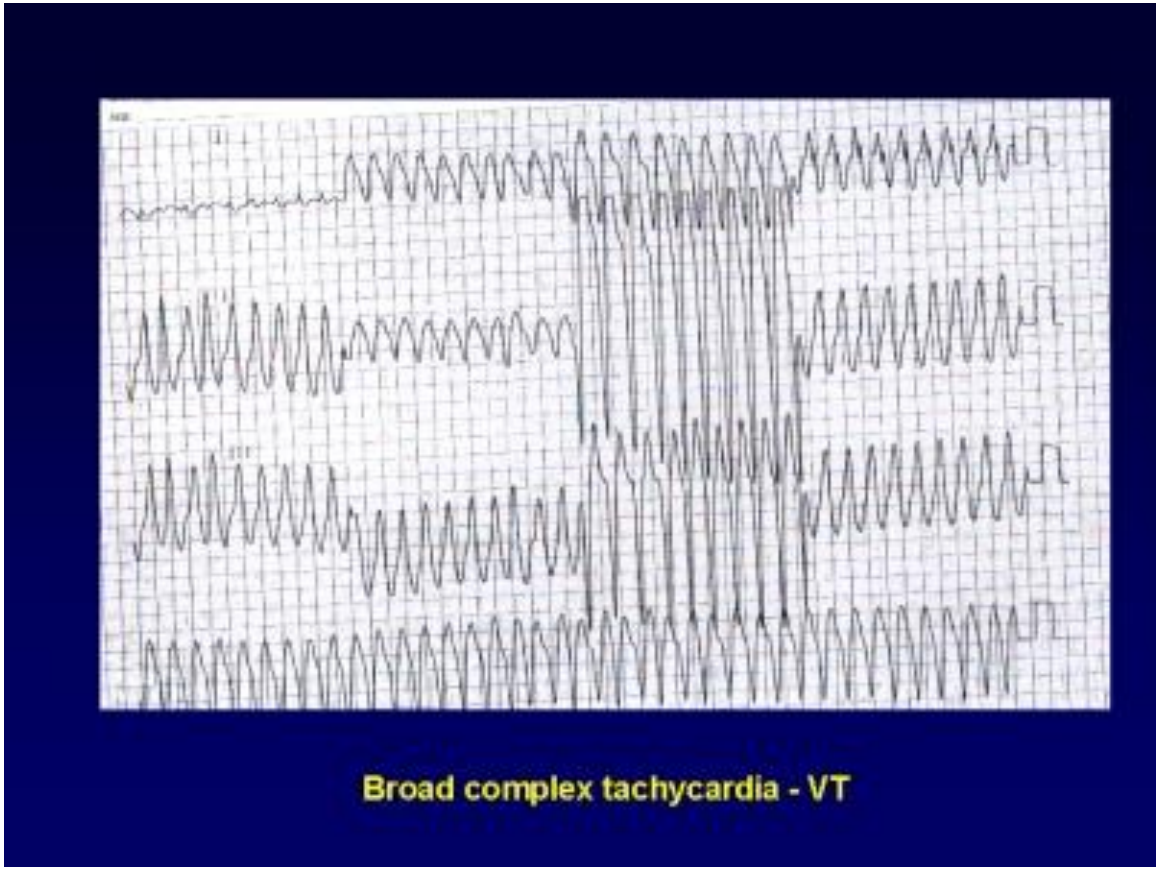
Distribution of LV dimensions in trained athletes

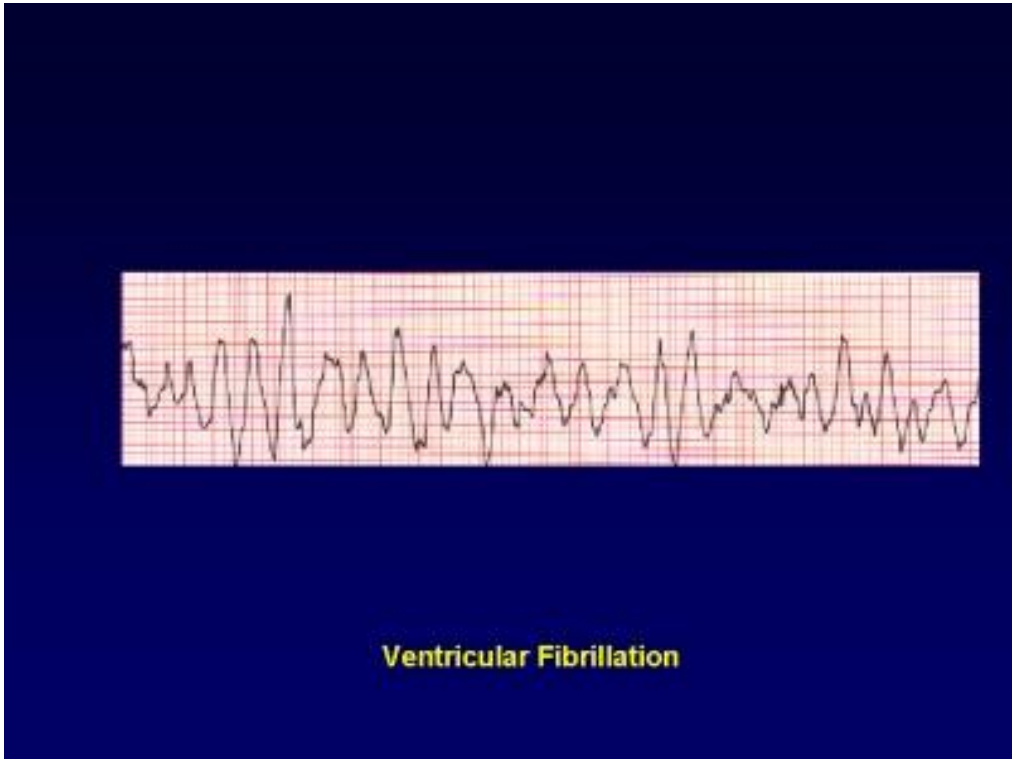


N Engl J Med 1991; 324:295–301

Ventricular ectopics




Broad complex tachycardia - VT


Ventricular Fibrillation

THANK YOU

ADDITIONAL SLIDES

DEFINITION

OF

MYOCARDIAL INFARCTION

Definition of Myocardial Infarction

World Health Organisation (WHO) definition:

Two out of three of

- **Typical symptoms**
- **Typical enzyme rise**
- **Typical ECG (with the development of Q waves)**

Revios

Definitions of Myocardial Infarction

Pathological diagnosis - loss of cardiac myocytes (necrosis) by prolonged ischaemia

WHO	2 out of 3 of	Typical symptoms Enzyme rise Typical ECG pattern

European Heart Journal (2000) **21,** 1502–1513
doi:10.1053/euhj.2000.2305, available online at http://www.idealibrary.com on

Consensus Document

Myocardial infarction redefined — A consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the Redefinition of Myocardial Infarction

The Joint European Society of Cardiology/American College of Cardiology Committee**

Revios

SUMMARY
Definition of MI

Criteria for acute, evolving or recent MI
Either one of the following criteria satisfies the diagnosis for an acute, evolving or recent MI:

(1) Typical rise and gradual fall (troponin) or more rapid rise and fall (CK-MB) of biochemical markers of myocardial necrosis with at least one of the following:
(a) ischemic symptoms;
(b) development of Q waves
(c) ECG changes indicative of ischemia (ST segment elevation or depression)
(d) coronary artery intervention (e.g., coronary angioplasty).
(2) Pathologic findings of an acute MI.

Criteria for established MI
Any one of the following criteria satisfies the diagnosis for established MI:
(1) Development of new pathologic Q waves on serial ECGs. The patient may or may not remember previous symptoms. Biochemical markers of myo-cardialnecrosis may have normalized, depending on the length of time that has passed since the infarct developed.
(2) Pathologic findings of a healed or healing MI.

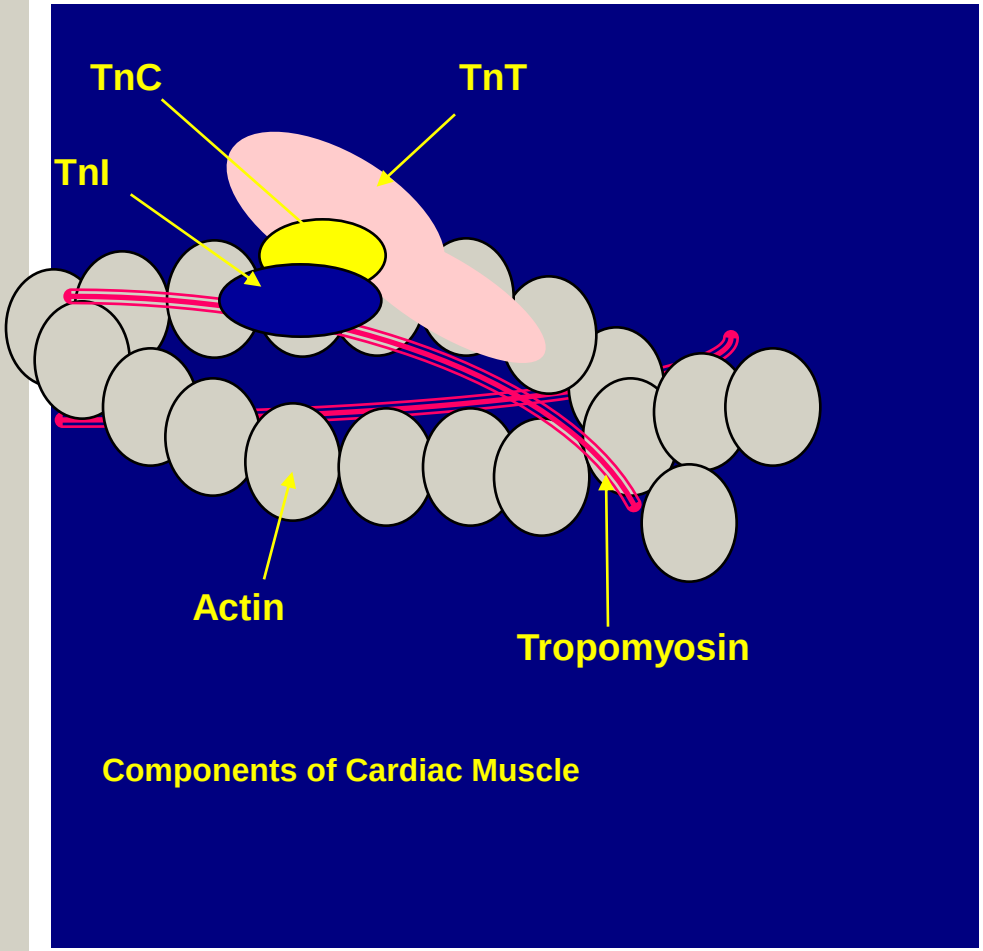
Troponin levels

Myocardial necrosis is detected if 'Maximal concentration of troponin T or I exceeds the decision limit (99th percentile of the values for a reference control group) on at least one occasion during the first 24 h after the index clinical event'

Implications

- Identification of more infarcts (but this would seem reasonable since any rise in Troponin is associated with adverse outcome)
- Allows appropriate secondary prevention in more cases
- Excludes previously mislabelled infarcts
- Social implications - HGV licenses, pilots licenses, life insurance, psychological

Cardiac Troponins



- 100% specific for myocardial damage
- Released within first few hours
- Peak at 12-24hours

- TnT detectable up to 14 days
- TnI detectable up to 5-7 days

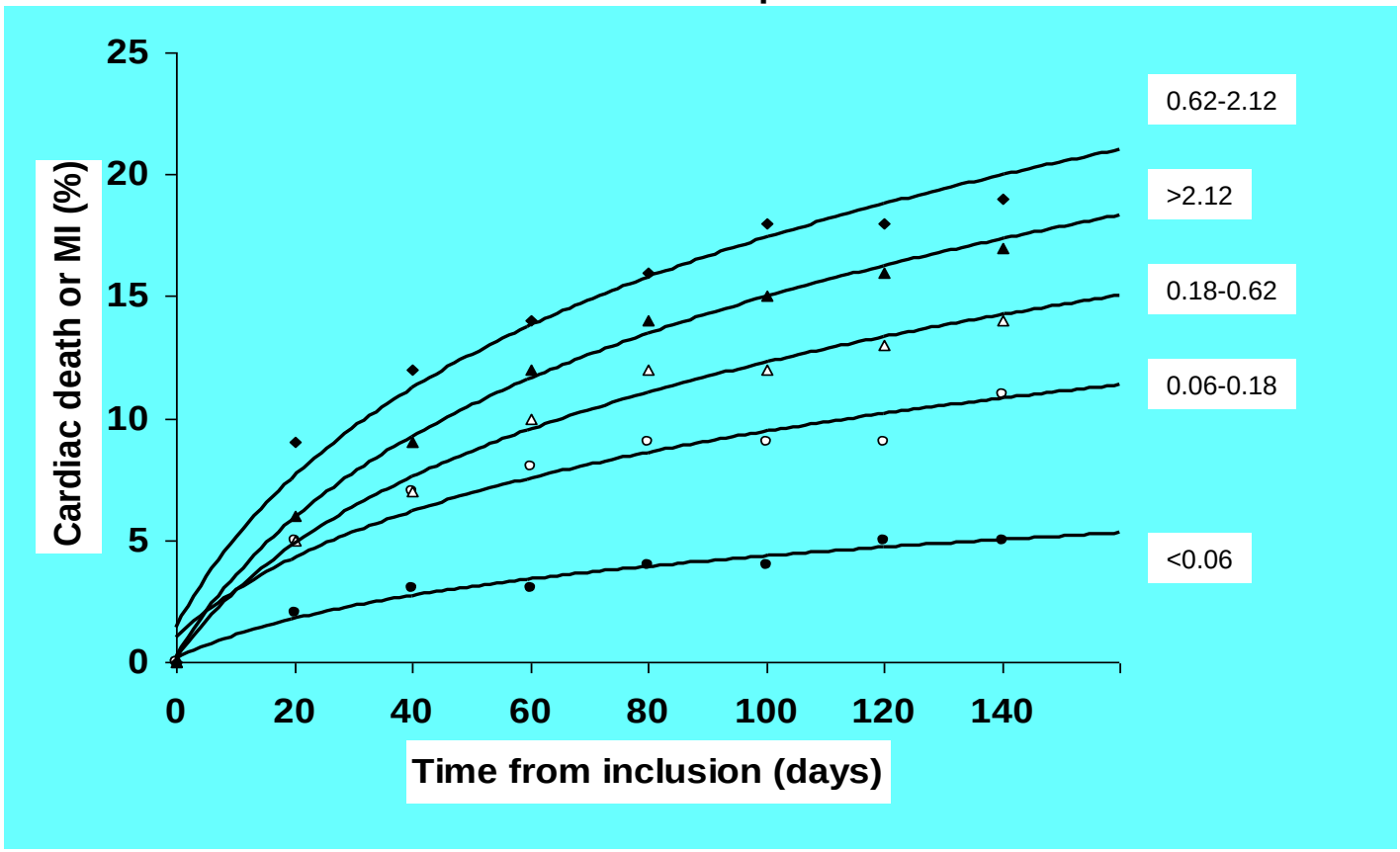
- Allow quantification of infarct size
- Prognostic indicators
- Guide therapy

	Sensitivity	Specificity
CK	90	90
AST	90	65
TnT	100	100

Revios

Risk Stratification in Unstable Angina

Role of Troponin T

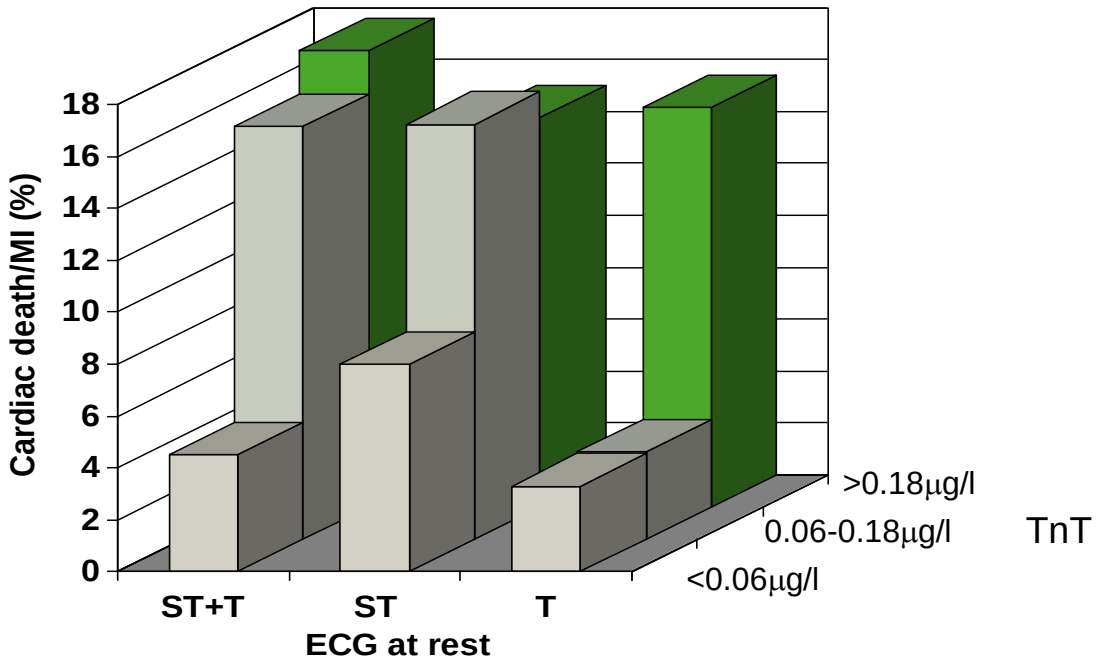


Cumulative risk of cardiac death or MI based on Tropnin T levels (µg/l)

Revios

Risk Stratification in Unstable Angina
Role of Troponin T and ECG Changes

Lindahl. Circulation 1996;93:1651

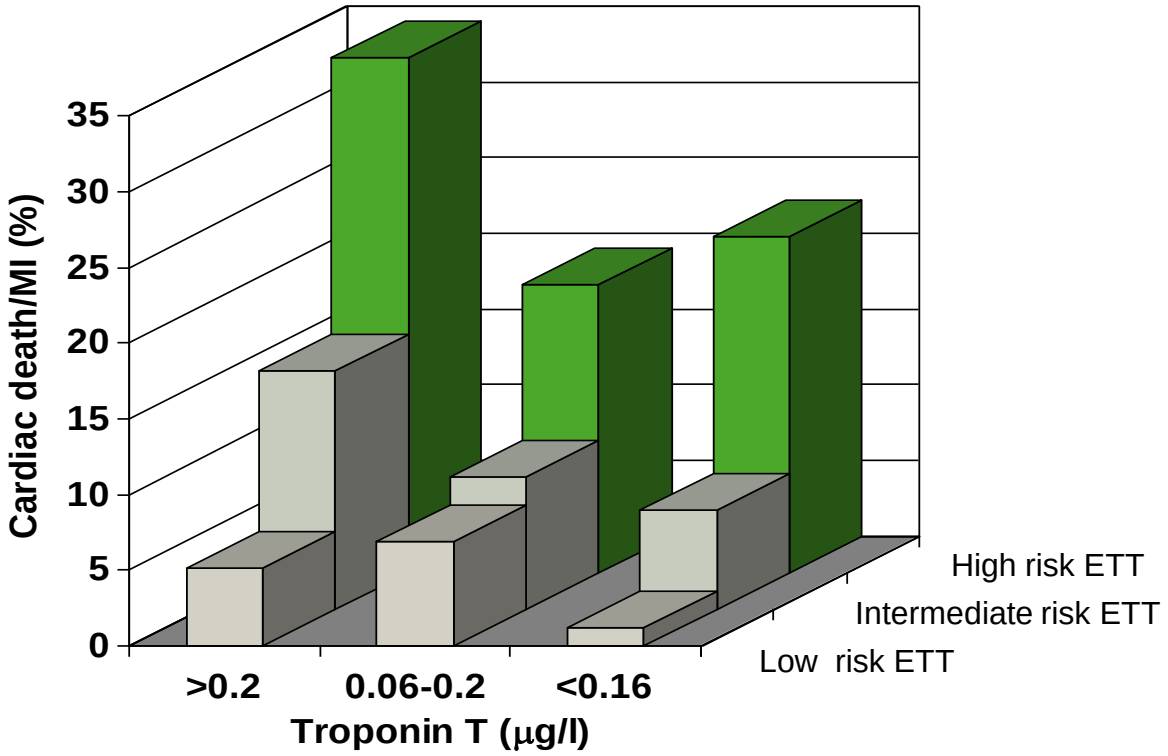


Five-months risk of cardiac death or MI in relation to resting ECG and tropnin T levels during the first 24h in the FRISC trial

Revios

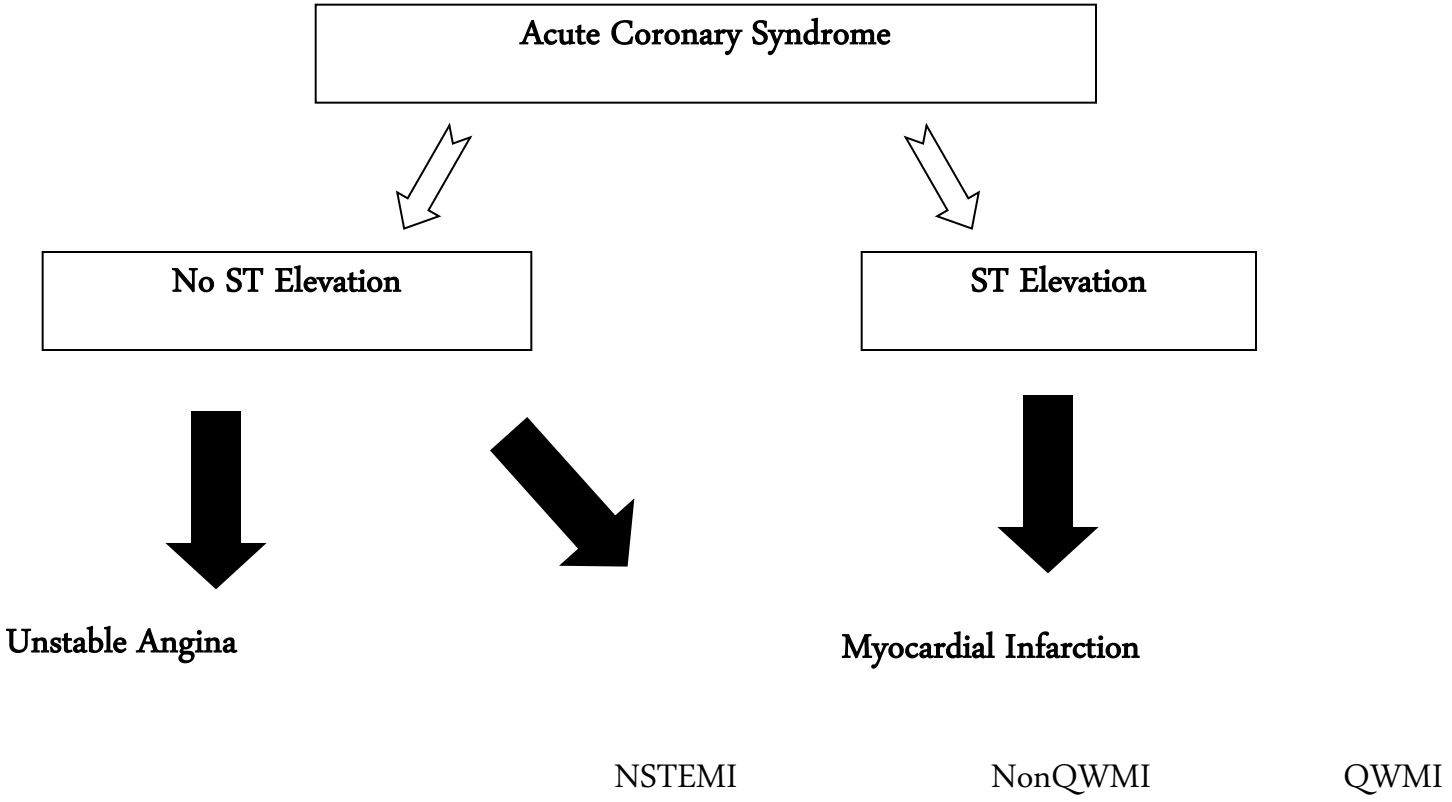
Risk Stratification in Unstable Angina
Role of Troponin T and Exercise Testing

Lindahl. Eur Heart J 1997;18:762



Five-months risk of cardiac death or MI in relation to exercise test response and tropnin T levels during the first 24h in the FRISC trial

Revios


Acute Coronary Syndrome
No ST Elevation
ST Elevation
Unstable Angina
Myocardial Infarction
NSTEMI
NonQWMI
QWMI