Coronary artery disease Prevention to cure

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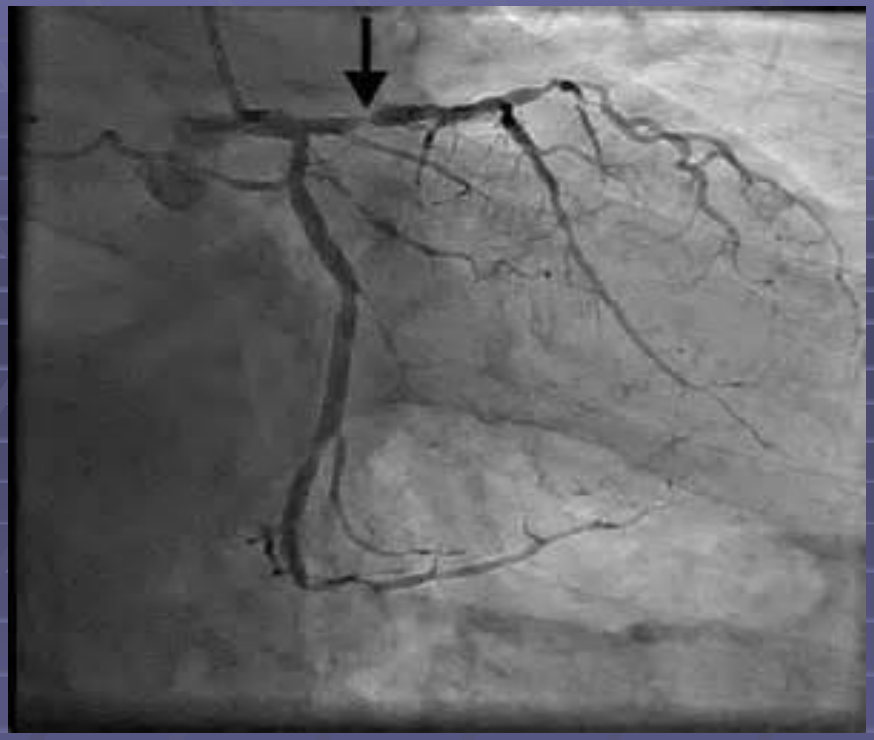

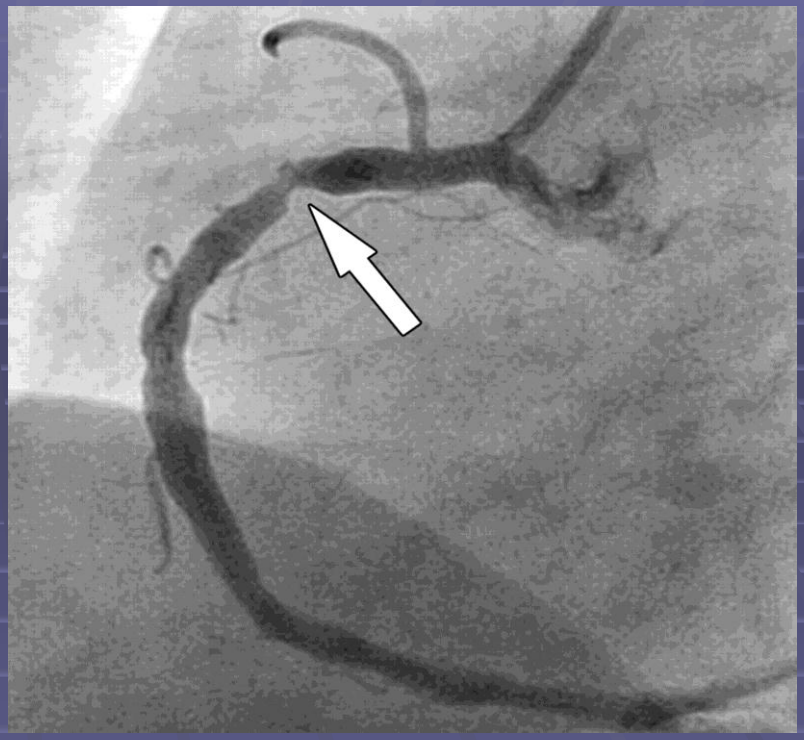

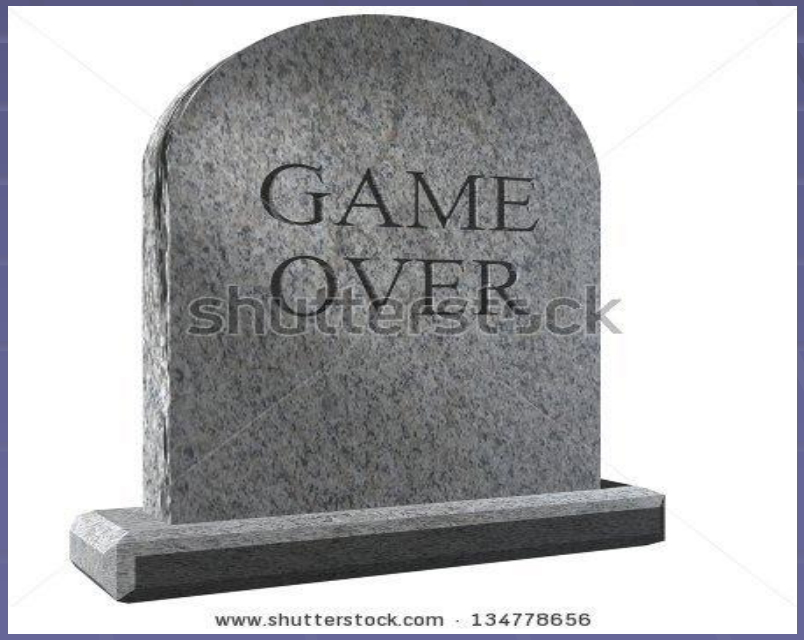
GAME
OVER
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- Coronary artery disease cannot be prevented
- Coronary artery disease cannot be cured

- **Coronary artery disease cannot be prevented**
  - Risk can be reduced
- **Coronary artery disease cannot be cured**
  - Excellent interventions to improve symptoms and prognosis

That's no good!

- We don't know what causes CAD in an individual patient.

- There is a relationship between risk factors and disease, but
- some patients with many risk factors have no CAD;
- others with little to no known risk factors have severe CAD.

- We don't know why coronary artery lesions occur when they do and where they do

- Some people have symptoms (angina), others have none (sudden death).

- Some coronary lesions progress rapidly; others remain stable for a long time.

- Severe lesions often stented, but may remain stable for years;
- Mild lesions not stented, but may cause acute MI in a few weeks.

Some good news!

- We do know which risk factors increase the likelihood of development of CAD
- Addressing these risk factors reduce the risk of cardiac events (and other complications).
- However
  - Relationship between risk factors and CAD is not good enough to advise a patient what is going to happen to them - which is what they want to now!
- How well are we doing – can we do better?
  - Cause
  - Risk stratification
  - Investigations
  - Treatment

3 cases in the last week

- Prevention
- Cure
- Risk stratification

Case 1

- 43 year old man
- Smoker
- No other risk factors
- No illnesses

- Acute anterior MI (no warning)
- Coronary angiogram shows occluded LAD, severe RCA, severe circumflex disease
- Acute stent to LAD

- Dies a few hours later of cardiogenic shock

- Could this have been prevented and how?

Case 2

- 65 year old man
- Hypertension, dyslipidaemia – well treated
- 4 weeks abdominal and chest pain, worse after meals and walking, ? Angina, ?GORD
- Normal resting ECG, but markedly positive ETT
- Admitted from clinic

- Coronary angiogram – 95% Left main stenosis and occluded right coronary artery.
- Echo shows normal LV function

- Undergoes successful CABG with excellent recovery

- Is he cured?

Case 3

- 55 year old woman
- TC: 6.5
- LDL: 4.5
- HDL 1.2
- Strong family history of elevated cholesterol and CAD
- Normal ETT
- Coronary calcium score 0

- What is her risk for developing CAD and can we reduce the risk?

Coronary Artery Disease

- Major cause of morbidity and mortality
- CVD has been the leading cause for death in the USA for the past 100 years.
- 500 000 Americans die annually from CHD
- Expected health care costs of CHD by 2030 - $1 trillion.
- ***Significant decline in mortality due to ASCVD past decade***.

Why do we get CAD?

- ***No single cause***
- ***Interplay between:***
  - Risk factors
  - Environmental exposures
  - Genetic susceptibility

Rise in CVD in the mid 20th century

- Framingham
- Warts and all, still forms the cornerstone for risk assessment

Risk factors

- ***Modifiable***
- Hypertension
- Dyslipidaemia
- Diabetes
- Smoking
- Obesity
- Physical activity
- Diet
- Alcohol

Non-modifiable

Age

Gender

Genetics

Family History

Risk Factors

- Hs-CRP
- Fibrinogen
- Homocysteine
- Lipoprotein a
- Small, dense LDL
- Ankle brachial index
- Coronary calcification

Prevalence of coronary risk factors in the USA

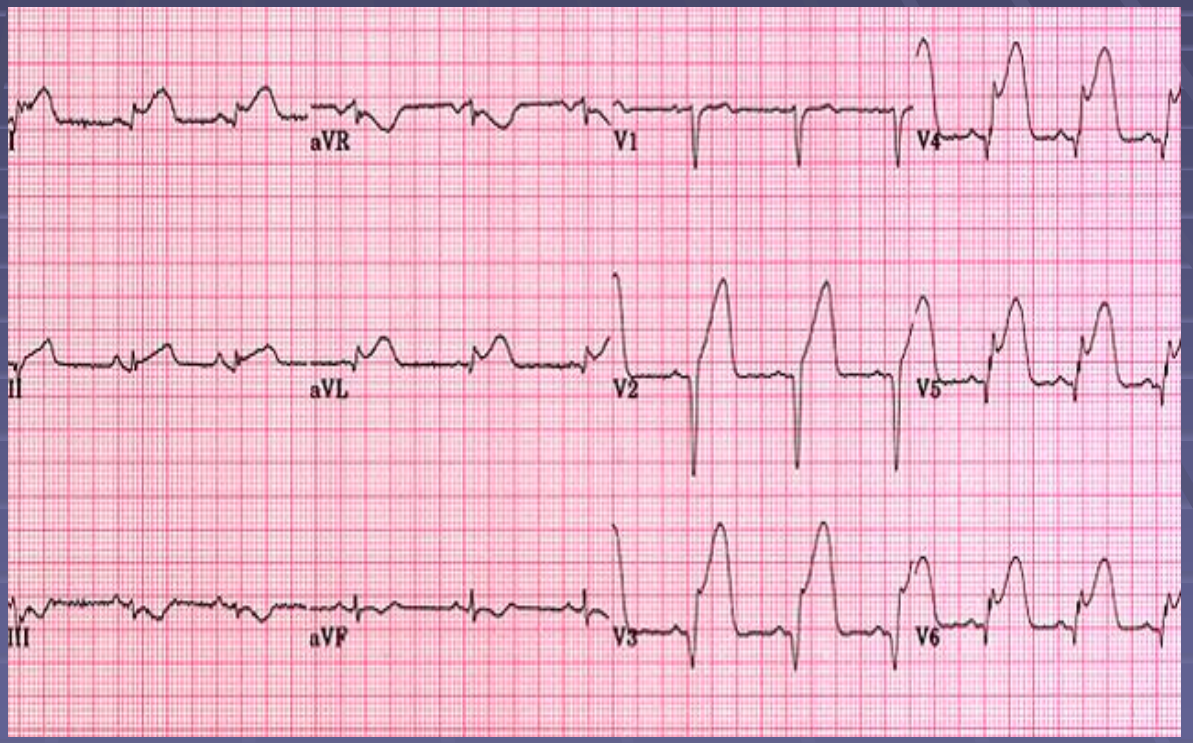
Elevated LDL	46%
Reduced HDL	26%
Prehypertension	22%
Hypertension	25%
Smoking	25%
Diabetes	8%
Overweight or obese	65%
Physically inactive	38%
Metabolic syndrome	24%

Overlap of risk factors with other bad things

- Smoking – lung cancer
- Alcohol – cirrhosis
- Diabetes – renal failure, blindness etc

Risk factors

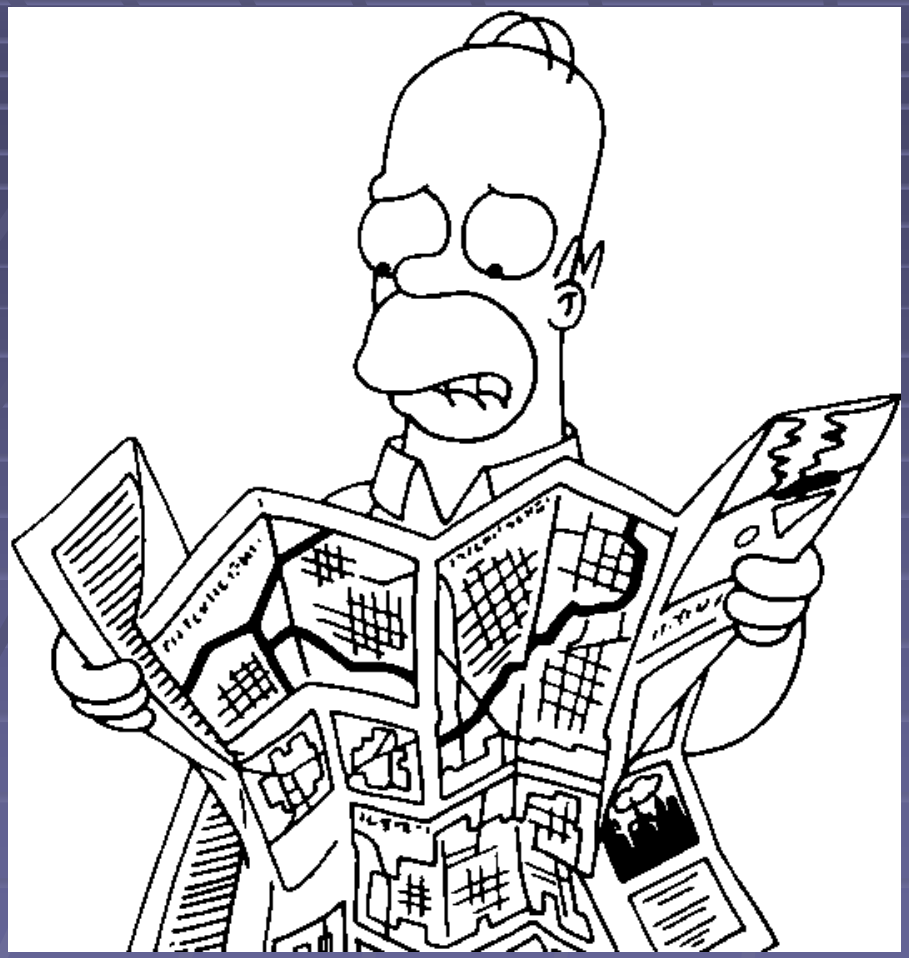
- Hypertension
- Dyslipidaemia
- Diabetes
- Smoking
- Obesity
- Physical activity
- Diet
- Alcohol



“The faster you drive the bigger the mess”

- Speed
- Alcohol
- Texting/Talking
- Tired

Guidelines




GUIDELINES ASSIST AND DO NOT REPLACE
DO YOU NEED A HAND?
GUIDELINES FOR EXPERTS

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Neil J. Stone, Jennifer Robinson, Alice H. Lichtenstein, C. Noel Bairey Merz, Conrad B. Blum, Robert H. Eckel, Anne C. Goldberg, David Gordon, Daniel Levy, Donald M. Lloyd-Jones, Patrick McBride, J. Sanford Schwartz, Susan T. Shero, Sidney C. Smith, Jr, Karol Watson and Peter W.F. Wilson

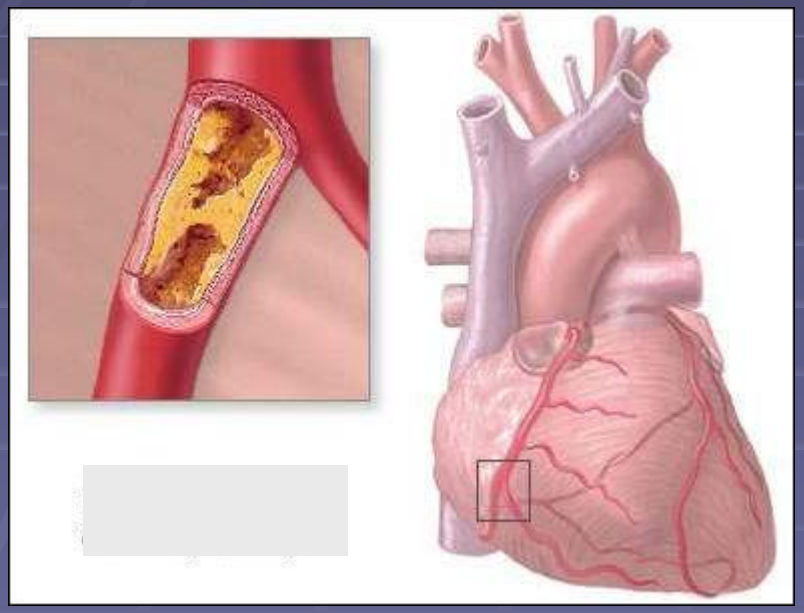
Circulation. published online November 12, 2013;

2.1. Lifestyle as the Foundation for ASCVD Risk Reduction Efforts

It must be emphasized that lifestyle modification (i.e., adhering to a heart healthy diet, regular exercise habits, avoidance of tobacco products, and maintenance of a healthy weight) remains a critical component of health promotion and ASCVD risk reduction, both prior to and in concert with the use of cholesterol-lowering drug therapies. Healthy diet or lifestyle modifications were recommended as background therapy for the RCTs of cholesterol-lowering drug therapy. See the 2013 Lifestyle Management Work Group Guideline (10) for lifestyle recommendations for healthy adults.


EAT MORE FRUITS
EXERCISE
DRINK MORE WATER
READ SPIRATIONAL BOOKS
HEALTHY LIFESTYLE
PEACE OF MIND
MEDITATION
WALK MORE
EAT WELL

Statins




Mevacor® 20
(Lovastatin)
Lipitor
10 mg*
Lescol® XL
UNIT DOSE
100 tablets
CRESTOR
rosuvastatin calcium
10 mg tablets
Rx only
CRESTOR
rosuvastatin calcium
10 mg tablets

Figure 2. Major recommendations for statin therapy for ASCVD prevention

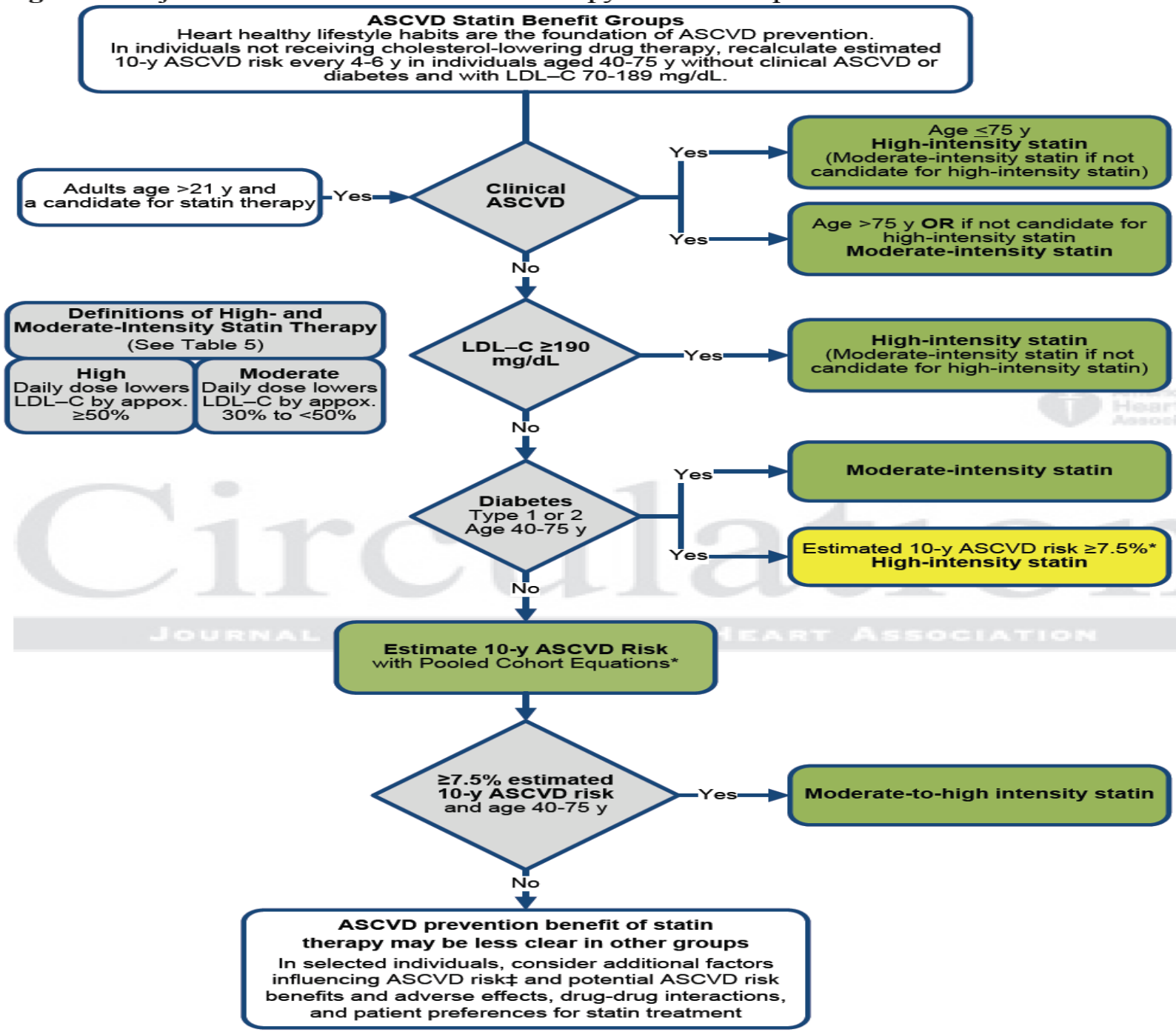


Figure 3. Initiating statin therapy in individuals with clinical ASCVD

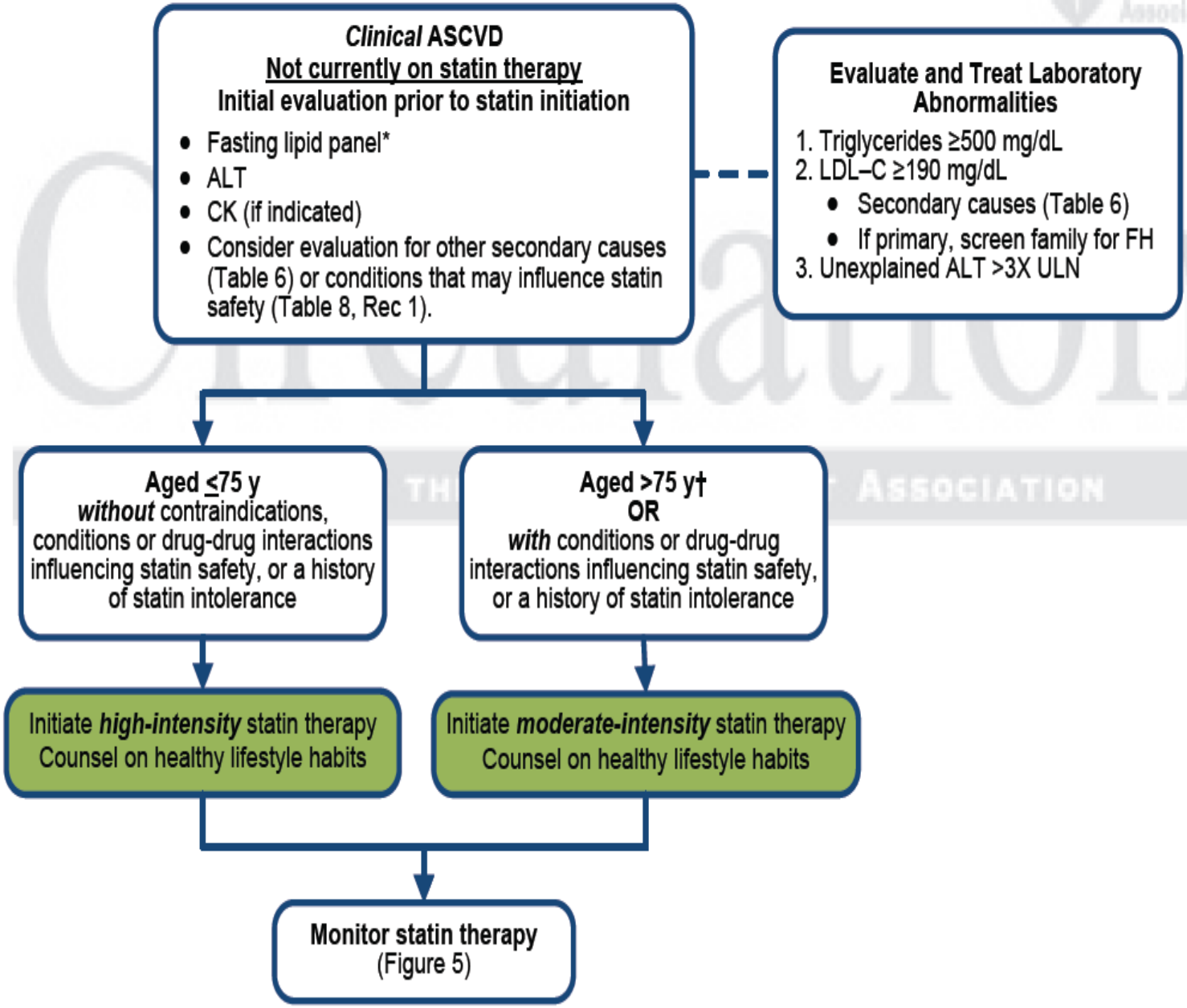
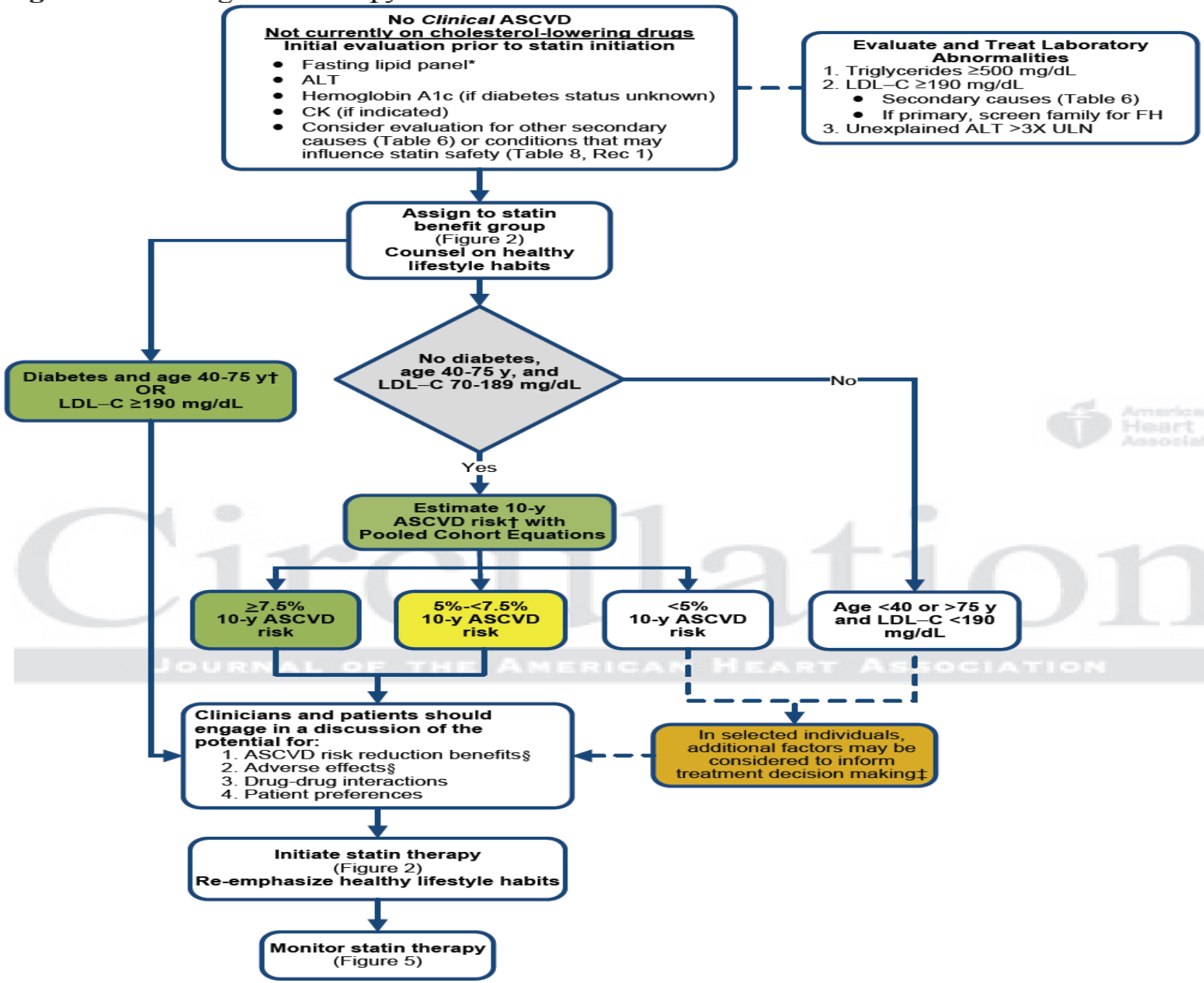
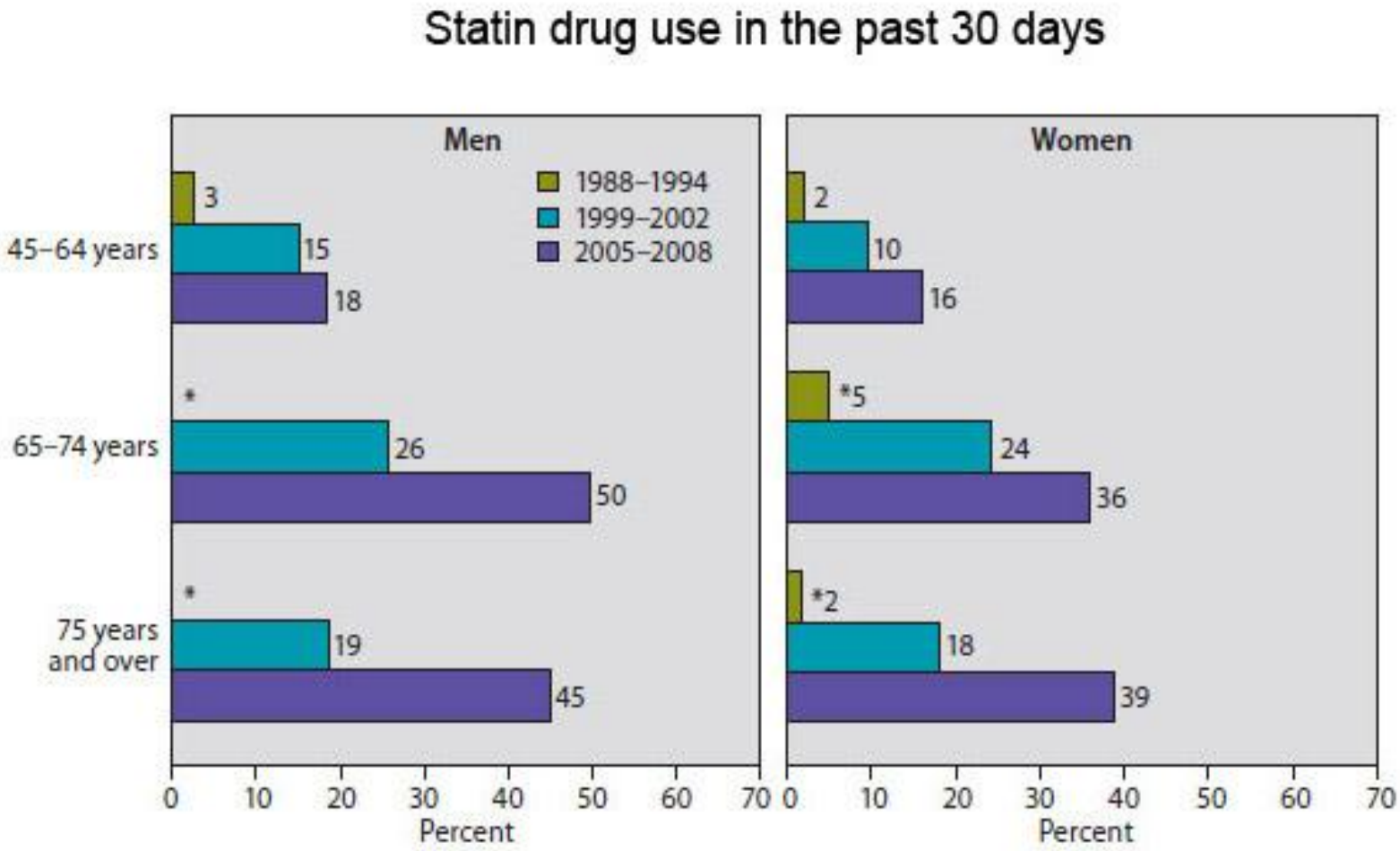
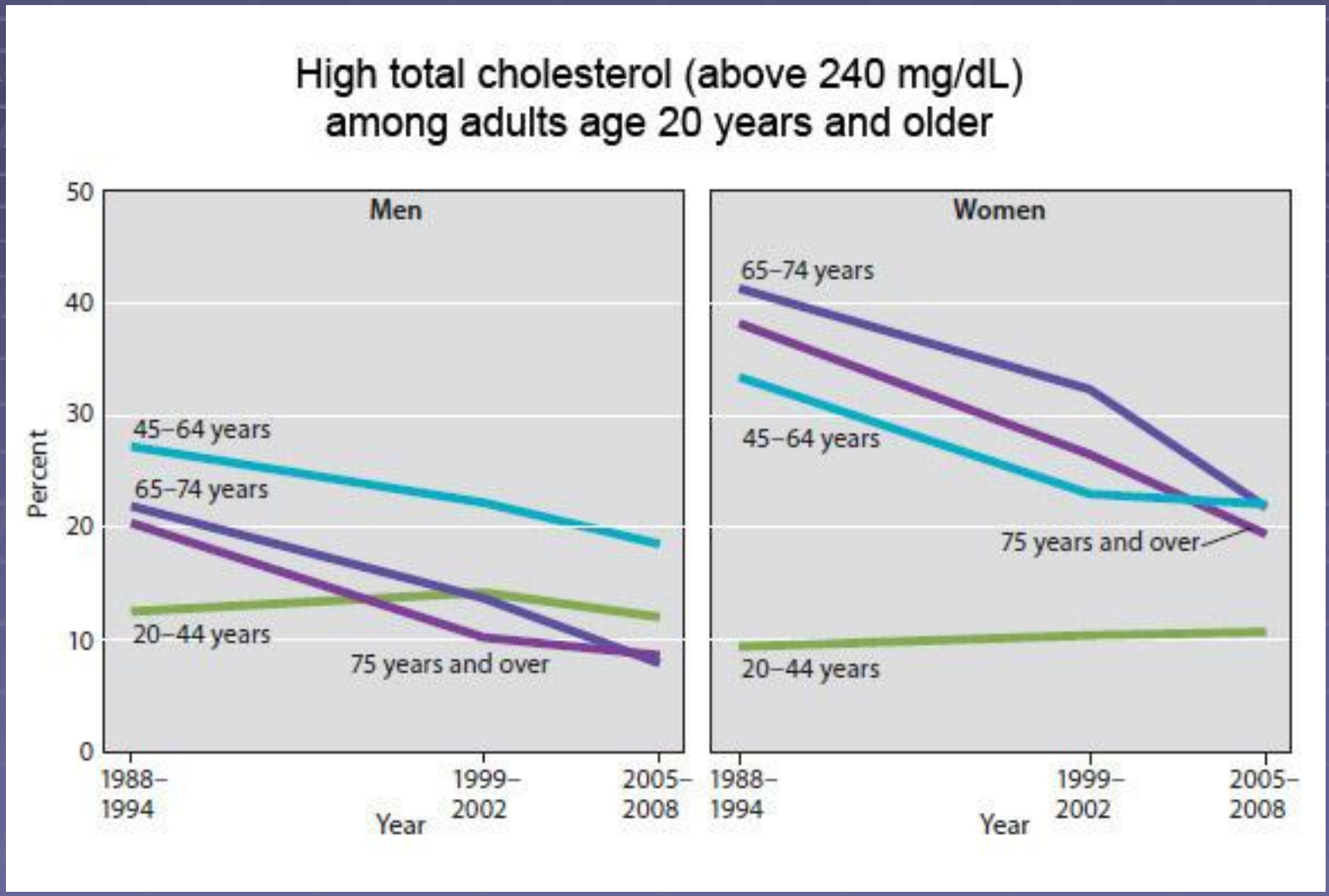


Figure 4. Initiating statin therapy in individuals ***without*** *clinical* ASCVD

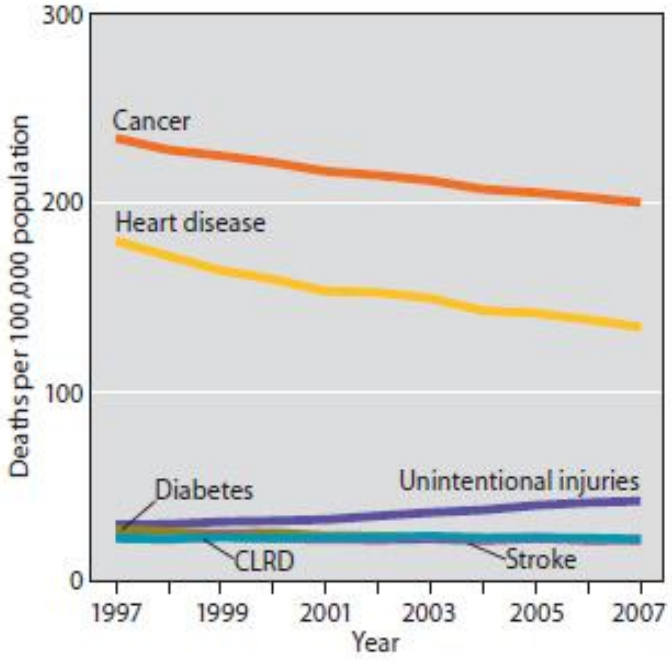


Statin use in the past 30 days USA



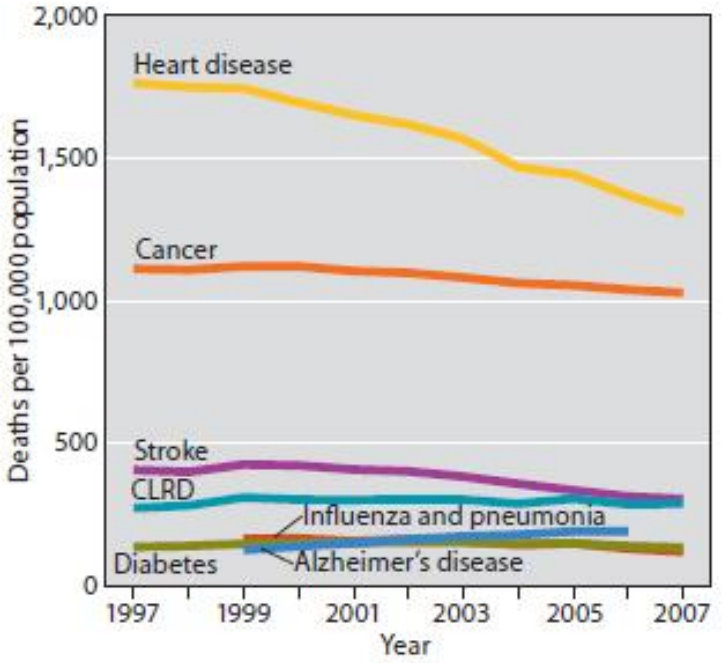

High total cholesterol (above 240 mg/dL)
among adults age 20 years and older
Men
Women
Percent
50
40
30
20
10
0
45–64 years
65–74 years
20–44 years
75 years and over
1988–1994
1999–2002
2005–2008
Year

Death rates for leading causes among persons 45-64, 1997-2007



CLRD = chronic lower respiratory disease

Death rates for leading causes among persons 65 and older, 1997-2007



CLRD = chronic lower respiratory disease

Primary prevention – tough sell!

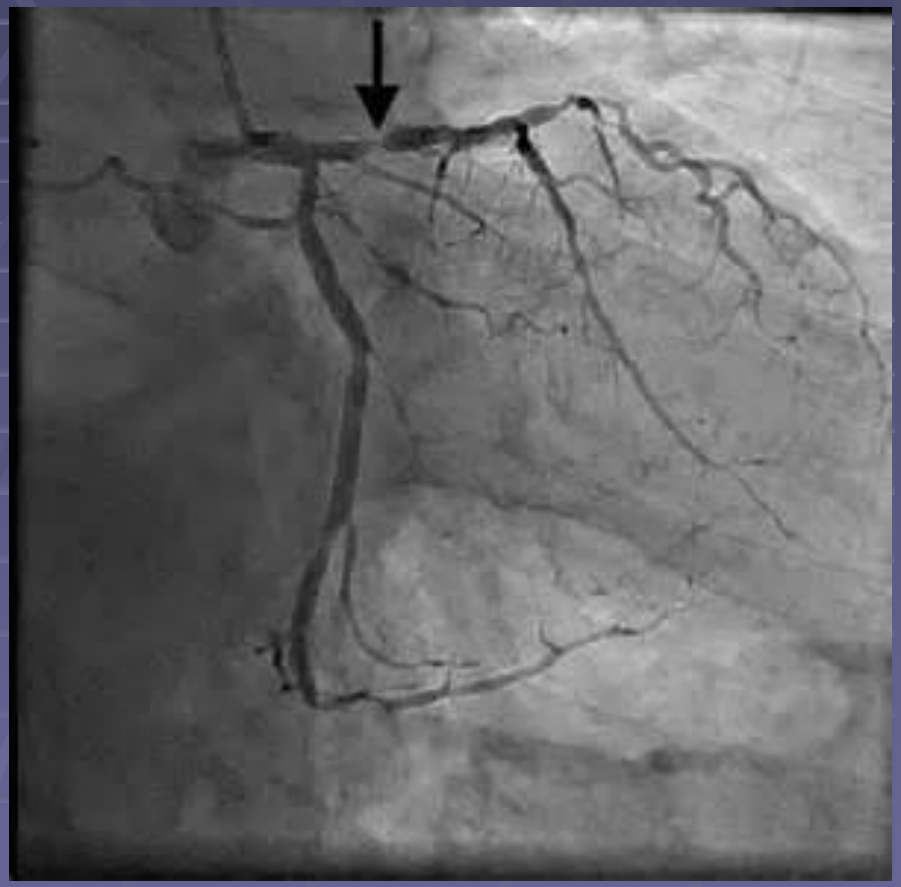
Cancer screening

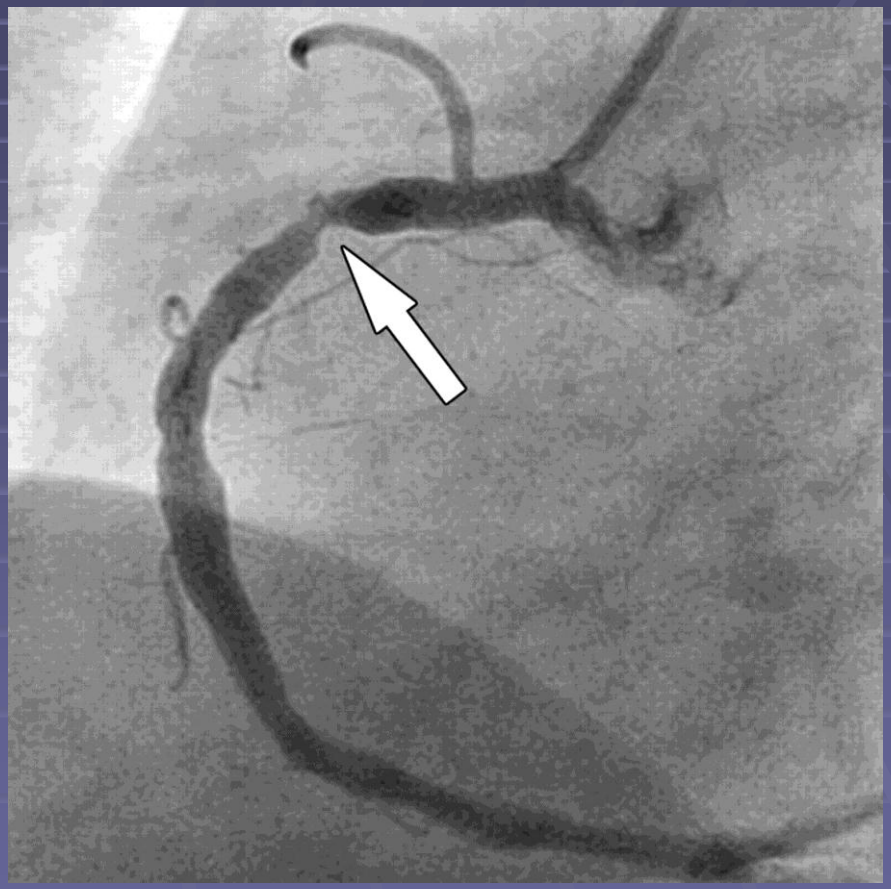
- Mammogram
- Pap smear
- Colonoscopy
- PSA

- Aimed at confirming or excluding presence of disease and if present, detecting early.

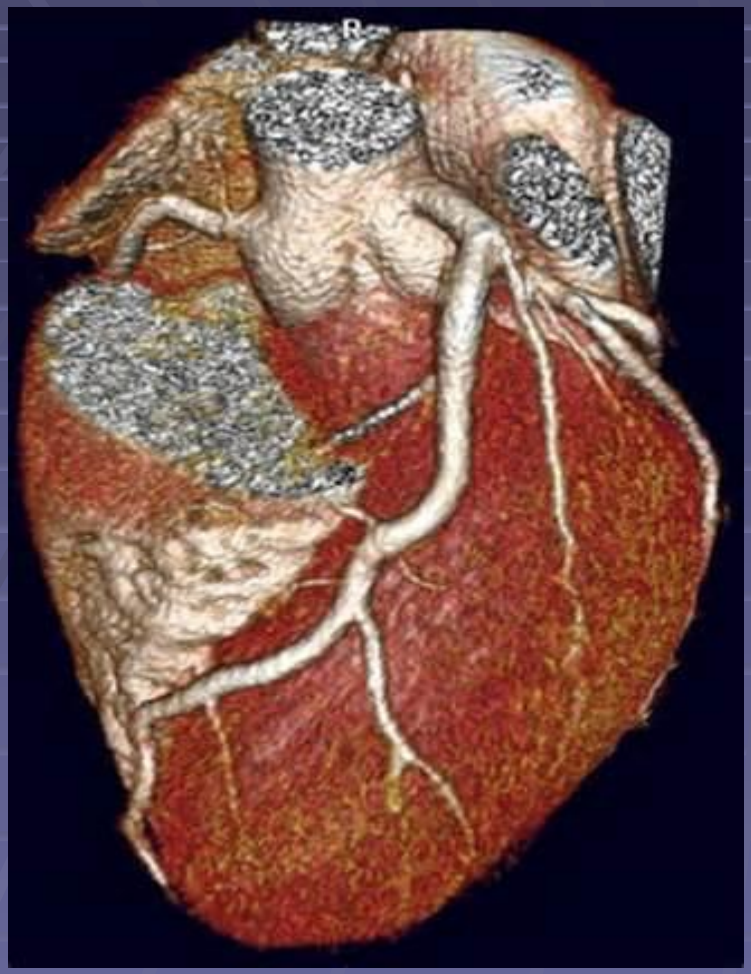
Tests to diagnose CAD (significant)

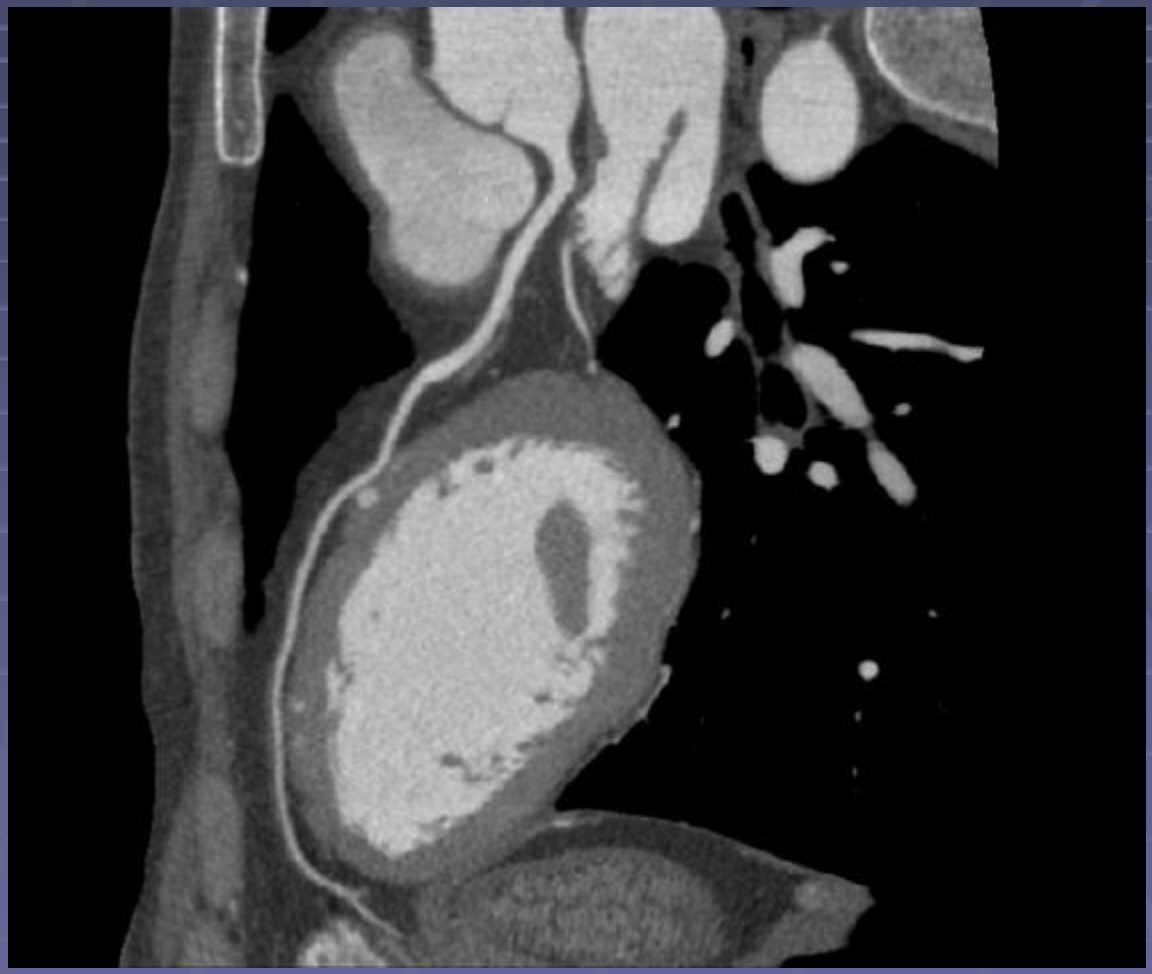
- History
- Clinical exam
- ECG
- ETT
- ESE, nuclear, MRI
- CT
- Angiogram
- FFR, IVUS, OCT



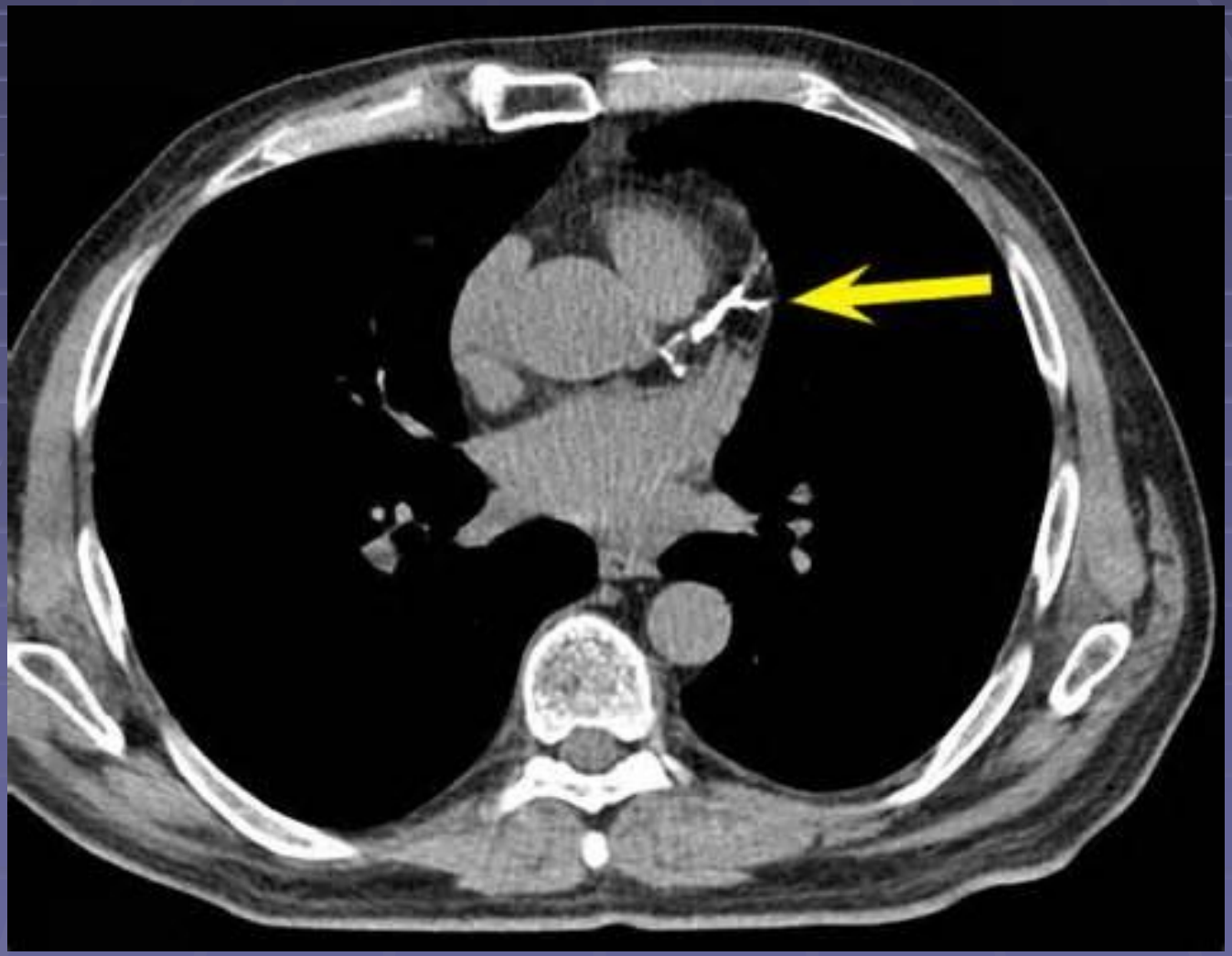


CT Coronary angiogram





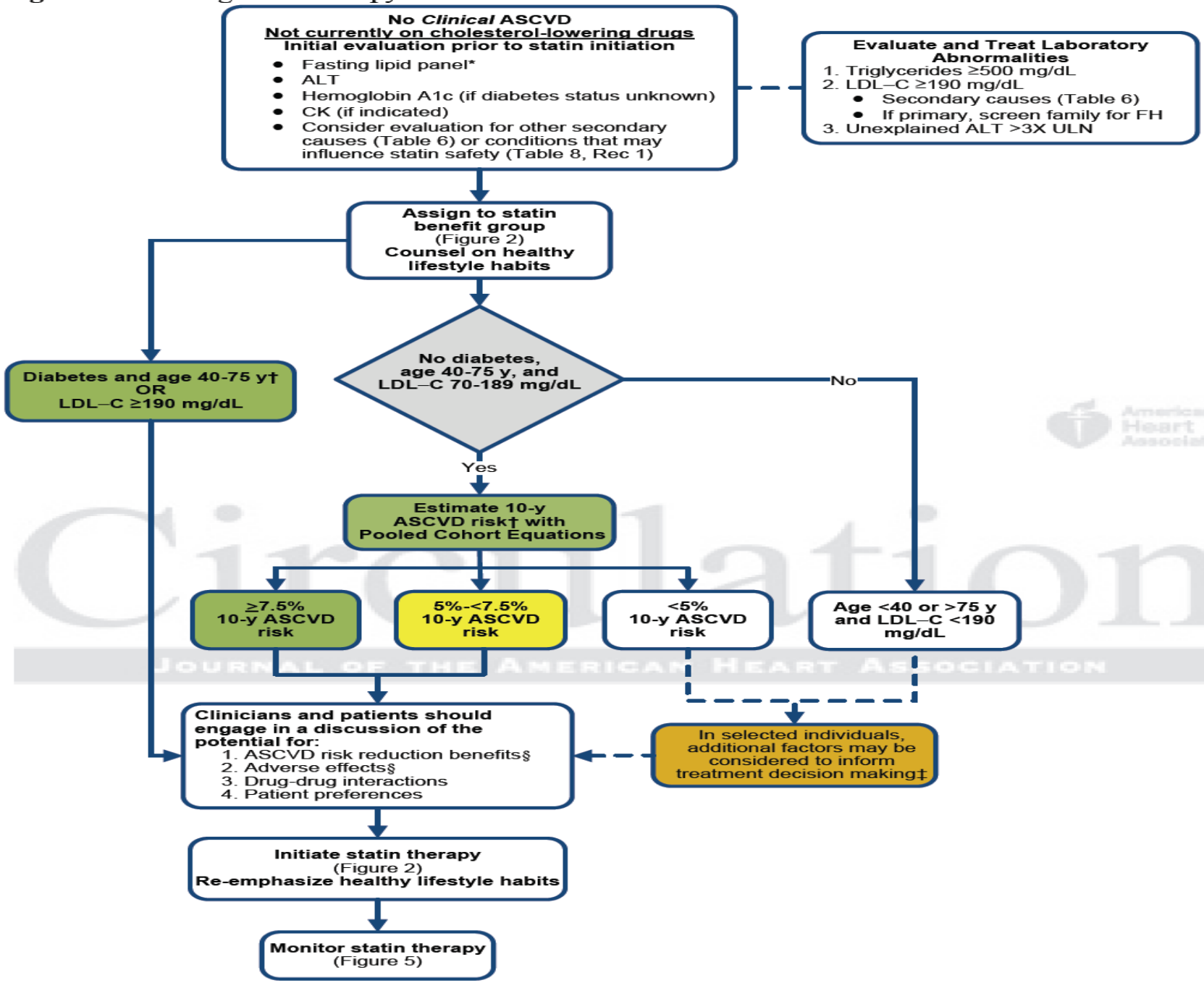
CT coronary calcium score Paradigm shift in early detection of coronary artery disease



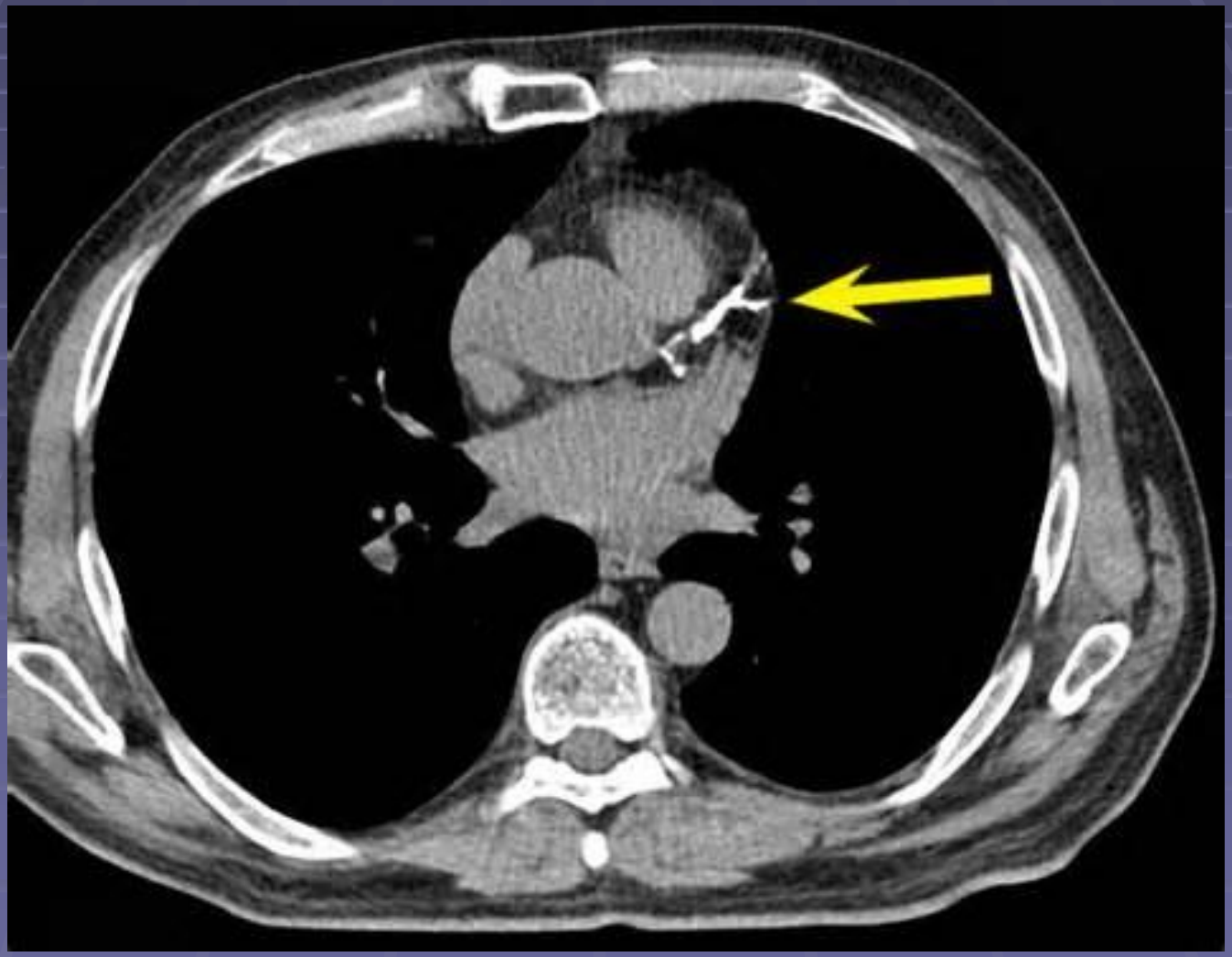
Risk stratification

- **What is an easier sell?**
  - Medication for life to improve risk factors (LDL)
  - Medication for disease already present (visible) with associated increased CVD risk

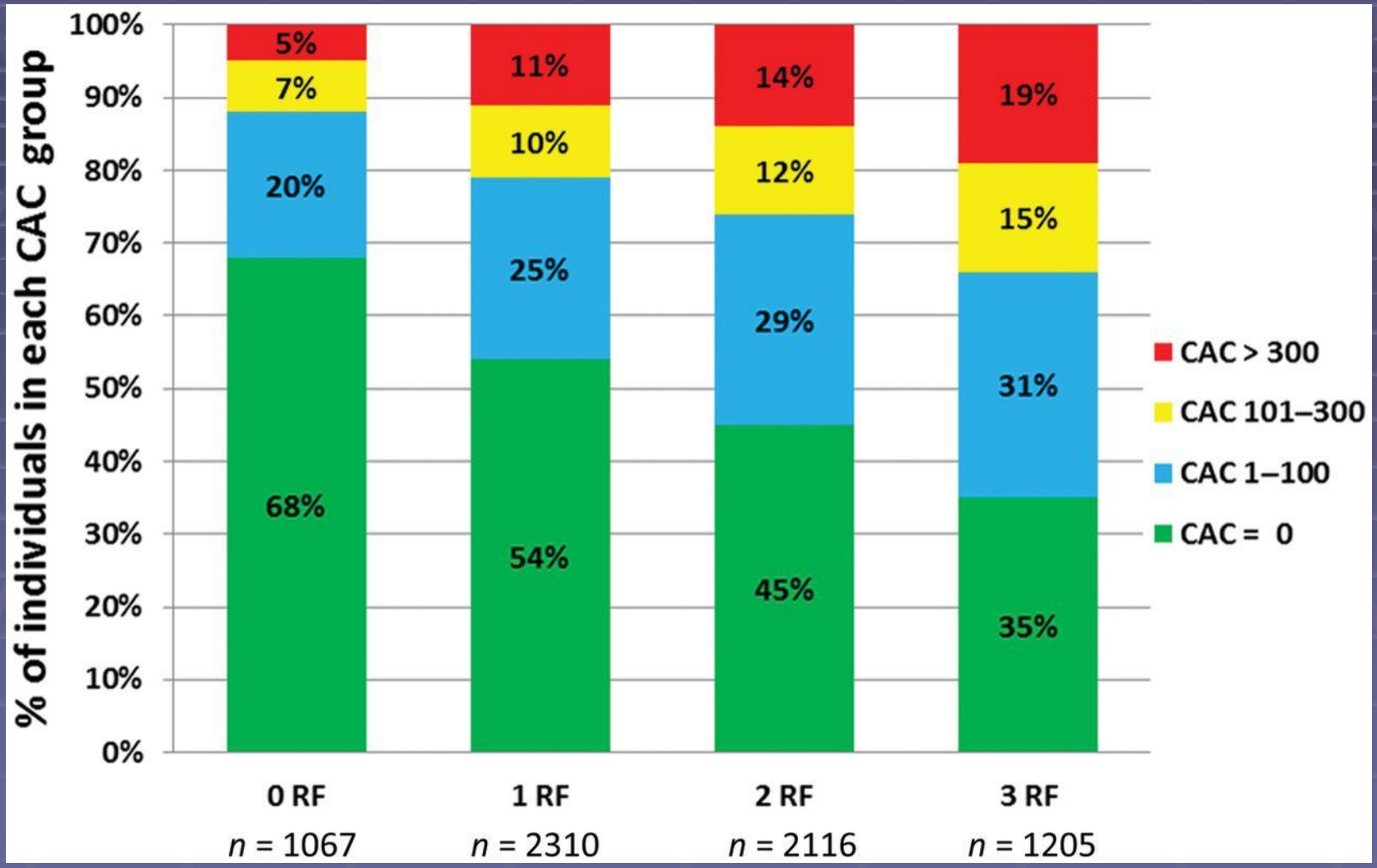
Figure 4. Initiating statin therapy in individuals ***without*** *clinical* ASCVD



Paradigm shift in thinking of coronary artery disease prevention



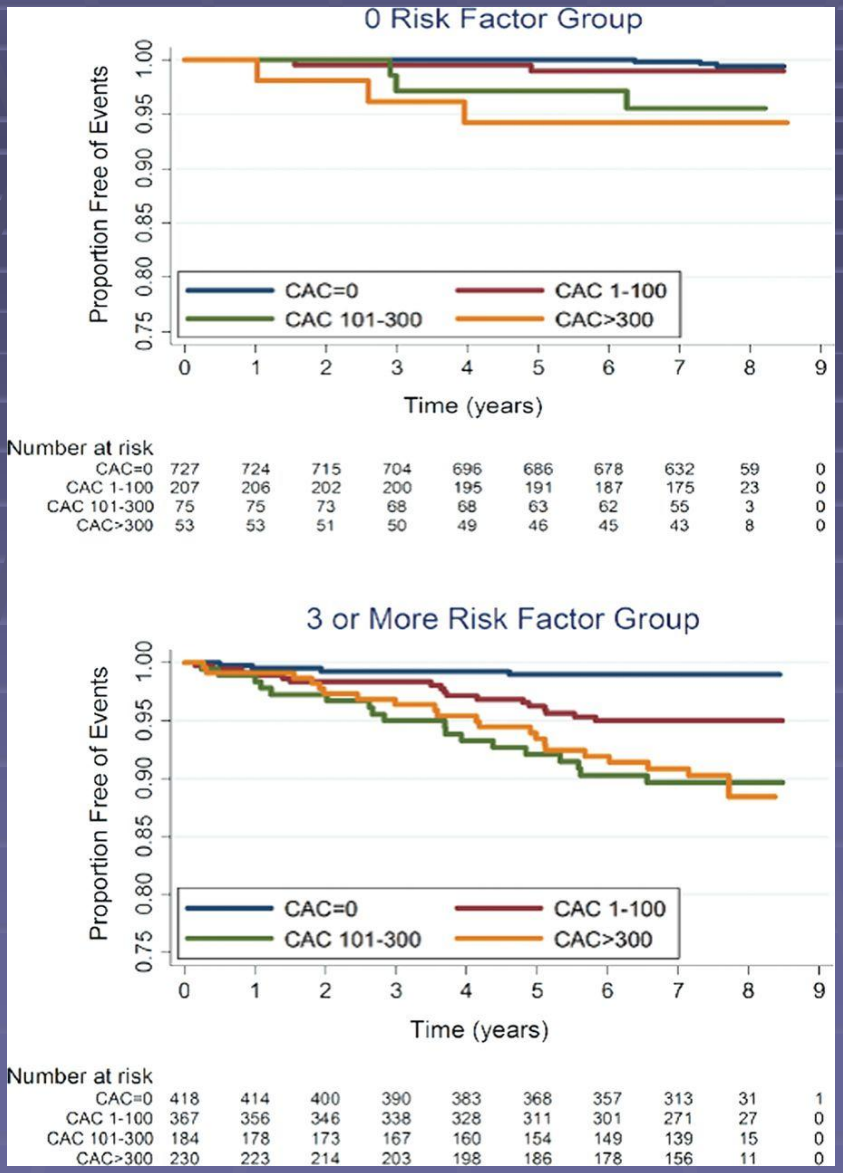
Distribution of coronary artery calcium by risk factor burden.



Michael G. Silverman et al. Eur Heart J 2014;35:2232-2241

European Heart Journal

Kaplan-Meier estimates of coronary heart disease event free survival by coronary artery calcium score in individuals with 0 and ≥3 risk factors.



Michael G. Silverman et al. Eur Heart J 2014;35:2232-2241

European Heart Journal

Coronary calcification

- ≥ 3 risk factors, 35% of individuals had CAC score 0

- No risk factors
  - >10% had CAC >100
  - 7% had CAC score 101-300
  - 5% had CAC score >300.

- RF's associated with higher relative risk but low absolute risk
- 0 RF 0.6
- 1RF 1.6 per 1000 person years
- 2RF 2.5

- ***Age – dominant risk factor***
  - Less important when CAC is known
- ***Lipids***
  - Significant discordance between LDL and CAC score with events at follow up.
    - *20% with normal lipids had CAC>100*
      - ASCVD event rate of >20/1000 person years
    - *50% with all lipids abnormal had CAC of 0*
      - ASVCD event rate of 6/1000 person years.

- ***Obesity, metabolic syndrome, DM***

- 50% of obese individuals had CAC = 0.
  - Non DM with high CAC much higher risk than DM with CAC score = 0.

- ***CRP***
  - Additional predictive power but still need to treat many people who don't develop CVD.
  - CAC influenced NNT

- **Lifestyle factors**

- >33% with poor lifestyle had CAC = 0

- >15% with ≥ 4 healthy lifestyle factors have CAC >100

Coronary Calcification

- 44 000 asymptomatic people self referred for CAC screening
  - All cause mortality over 5 years

- **0 RF and elevated CAC - 17/1000 person-years**

- **≥ 3 RF's and CAC 0 - 3/1000 person-years**

Number need to scan (NNS)

- 0 RF's to detect CAC >300, NNS = 20.
  - 10 year event rate 11%
- 0 RF's to detect CAC >100 = 8
  - 10 year event rate 9%.
- Current guidelines:
  - Screen moderate and low-intermediate risk
  - ? Low risk as well for future guidelines

Number need to scan (NNS)

- 1/3 of individuals with ≥ 3RF's have CAC 0
- Thus NNS to detect CAC of 0 = 3
- Estimated 10 year event rate 3.1%

Number needed to treat (NNT)

- ≥ 3 RF's and CAC 0 = treat 222 people to prevent a single ACVD event

- 0 RF's and CAC >300 = treat 36 people to prevent a single ACVD event

?Need for a paradigm shift

- Risk factor based
- +
- Detection of subclinical atherosclerosis

What to do with no or few RF and elevated CAC?

- No randomised trials

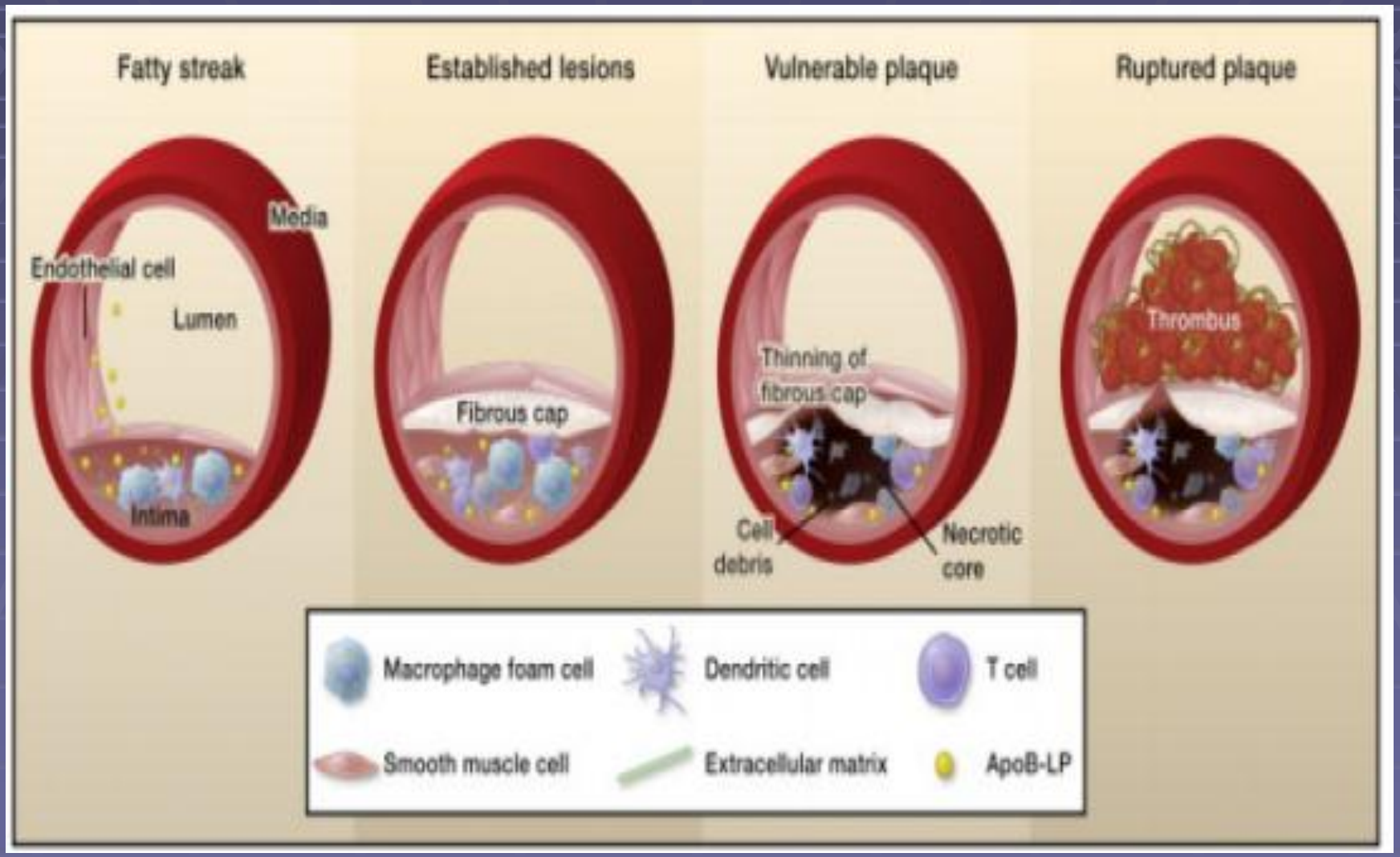
What to do with RF's and CAC = 0

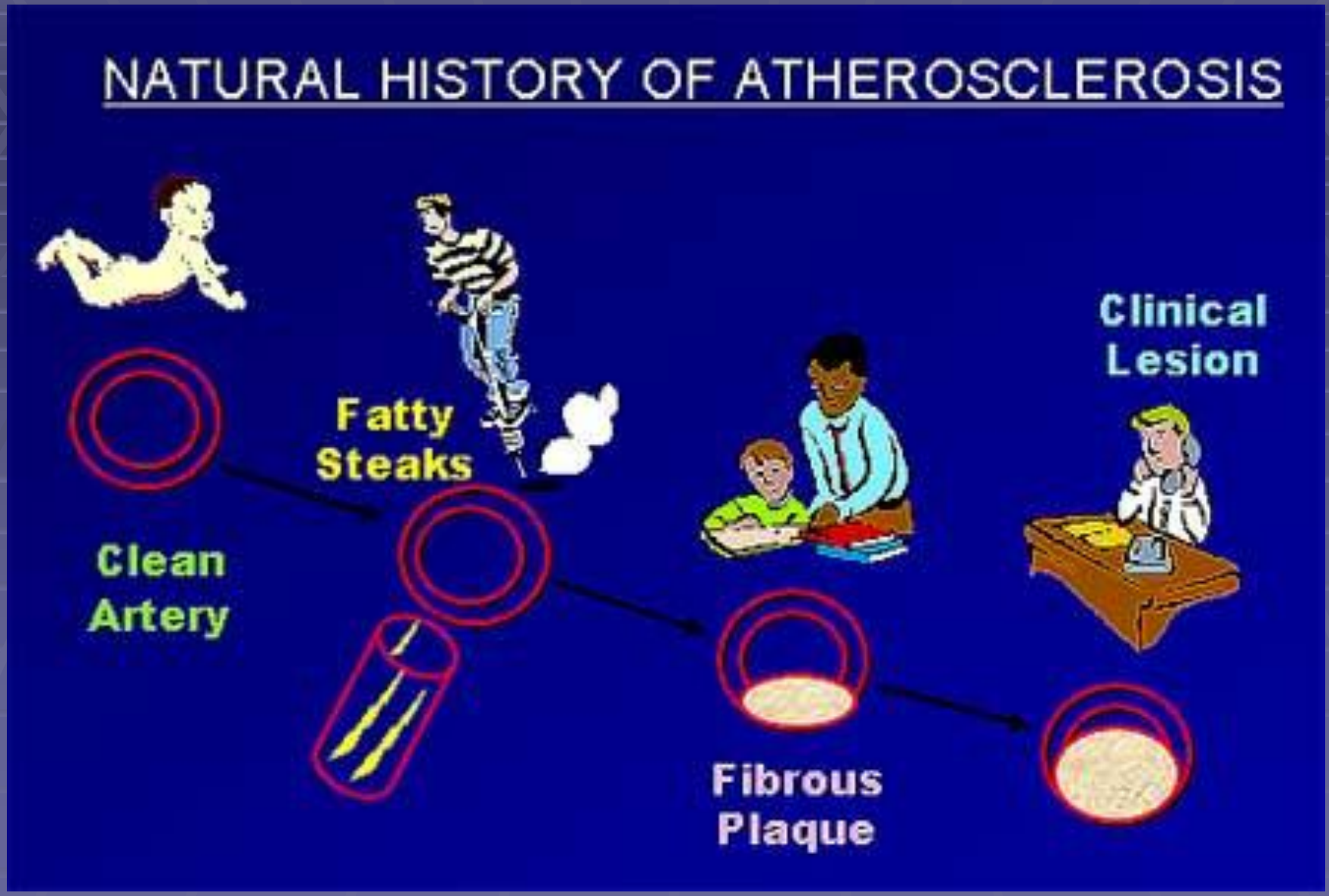
- Sarwar et al (meta-analysis)
  - 30 000 individuals with CAC = 0
  - 0.5% had a cardiovascular event during mean fu of 4 years

- MESA
  - 38% of diabetics had no CAC and those had minimal CHD events over 6 year follow up.

When does CAD start?

- ***Not at the time of diagnosis***
  - Screening
  - Mild symptoms
  - Myocardial infarction
  - Death


Fatty streak
Established lesions
Vulnerable plaque
Ruptured plaque
Media
Endothelial cell
Lumen
Intima
Fibrous cap
Thinning of fibrous cap
Cell debris
Necrotic core
Thrombus
Macrophage foam cell
Dendritic cell
T cell
Smooth muscle cell
Extracellular matrix
ApoB-LP


NATURAL HISTORY OF ATHEROSCLEROSIS
Clean Artery
Fatty Steaks
Fibrous Plaque
Clinical Lesion

Many opportunities for intervention – you just need to know where to look

Many opportunities for intervention – you just need to know where to look

- “The harder I practice the luckier I seem to get”

Important concept

- Primary prevention versus secondary prevention

Cure / Intervention

- Depends on the presentation
- Often PCI with ACS
- CABG or PCI ort med for non ACS
- PCI deals with a lesion = acne
- PCI or CABG does not obviate the need for medical management; often more!
- ICD, CRT, remodelling surgery etc

2013 Guidelines

- Risk for developing a first atherosclerotic cardiovascular disease over a 10 year period
  - Nonfatal MI
  - Death from CHD
  - Stroke (fatal or nonfatal)

diet

- Table 25 european guidelines

Coronary calcification

- Figure 1 of paper Silverman EHJ
- Figure 2 same paper
- Figure 3 same paper

All figures!

- 52 year old accountant
- Jogger – 5 km/day
- BMI 25
- Smokes 10 cigarettes a day during tax season
- Total cholesterol 4.65mmol/l
- HDL 0.90 mmol/L
- TG 1.7 mmol/L
- LDL 3.00 mmol/L
- Blood pressure 130/85mmHg
- Father has diabetes

Guidelines

- Clinical atherosclerotic cardiovascular disease
- LDL > 4.9mmol/L
- Diabetes and LDL ≥ 1.8mmol/L
- 10-year risk of cardiovascular disease is ≥ 7.5% and LDL ≥ 1.8mmol/L.

- 52 year old accountant
- Jogger – 5 km/day
- BMI 25
- Smokes 10 cigarettes a day during tax season
- Total cholesterol 4.65mmol/l
- HDL 0.90 mmol/L
- TG 1.7 mmol/L
- LDL 3.00 mmol/L
- Blood pressure 130/85mmHg
- Father has diabetes

Guidelines

- ***New guidelines:***
- 10 year risk of a cardiovascular event is 10.9% → Statin

- ***Old guidelines:***
- 10 year risk of a cardiovascular event is 13% → No Statin

- ✓ Do not start statin therapy
- ✓ Start statin therapy and monitor LDL level
- ✓ Start statin therapy without monitoring LDL level

- ✓ **Do not start statin therapy (57%)**
  - ✓ Quitting smoking reduces his risk to just over 5%
  - ✓ Consider measurement of hs-CRP, LDL particle analysis and Coronary Calcium CT scan, carotid ultrasound

- **Start statin therapy and monitor LDL level (26%)**
  - Aggressive life-style modification followed by a low-to-moderate dose of a statin if risk remains elevated. Monitor glucose, HBA1c and lipids
  - Metabolic syndrome and family history of diabetes
  - Metabolic syndrome doubles cardiovascular disease risk and increases risk for diabetes by a factor of 5
  - Acknowledged concern for increase risk for diabetes with statin
  - Greatest benefit with lower LDL and increased side effects with higher statin dose

- ✓ **Start statin therapy without monitoring LDL level (17%)**
  - ✓ Best way to reduce risk is to quit smoking
  - ✓ Statin treatment may reduce risk of cardiovascular disease and stroke by 20%, regardless of the baseline lipid profile. Overall risk, rather than initial LDL level determines the magnitude of statin benefit.
  - ✓ NNT for 10 years to avoid a cardiovascular event is 50
  - ✓ Put another way, among people with his medical profile, 98% will have the same outcome, whether or not they take a statin.
  - ✓ Intensely personal and depends on patient preferences
  - ✓ Shared decision making
  - ✓ Remind patient that whatever he chooses, sensible people with similar profiles may make a different choice

Comments / Feedback

- **Lifestyle modification**
  - Improved diet
  - Exercise
  - Stress management
  - Smoking cessation
  - "Statins should not be considered to be a **substitute** for interventions that, if adopted, would contribute much more substantially to lifelong health for Stephen".
  - "The new guidelines recommend a **thorough discussion** about risk discussion before a statin is prescribed".
  - "Statin treatment may reduce the **motivation** to adopt a healthier lifestyle".
  - "**Shared decision making** with the patient".

Get on with starting a statin because

- Sustained lifestyle modifications, although desirable, are often difficult to achieve.

Obesity can help heart attack victims survive - study

Risk ≠ Disease

- Risk ⟶ CAC ⟶ Symptoms ⟶ ASCVD events

- Graded association between increasing CAC score and ASCVD events.

- Risk for disease vs disease already present
- Speeding vs. accident

Coronary calcium score

- **Major studies**
  - MESA – USA
  - HNR study – European

- **Greatest value is “power of zero”**
  - Event rates generally 0.5% (CHD events or all cause mortality).

CAC vs CTCA

- Ref 25Cho I,
- NCP in 4500 individuals with CAC 0 = 7% and no events over follow up.