Coronary artery disease
Prevention to cure

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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 know 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 20\textsuperscript{th} 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?


*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.
Healthy lifestyle:
- Eat more fruits
- Exercise
- Drink more water
- Read spiritual books
- Meditation
- Walk more
- Eat well
- Peace of mind
Figure 2. Major recommendations for statin therapy for ASCVD prevention

ASCVD Statin Benefit Groups
Heart healthy lifestyle habits are the foundation of ASCVD prevention. In individuals not receiving cholesterol-lowering drug therapy, recalculate estimated 10-y ASCVD risk every 4-6 y in individuals aged 40-75 y without clinical ASCVD or diabetes and with LDL-C 70-189 mg/dL.

Adults age >21 y and a candidate for statin therapy

Yes

Clinical ASCVD

Yes

Age ≤75 y
High-intensity statin
(Moderate-intensity statin if not candidate for high-intensity statin)

No

Yes

Age >75 y OR if not candidate for high-intensity statin
Moderate-intensity statin

No

LDL-C ≥190 mg/dL

Yes

High-intensity statin
(Moderate-intensity statin if not candidate for high-intensity statin)

No

No

Definition of High- and Moderate-Intensity Statin Therapy
(See Table 5)

High Daily dose lowers LDL-C by approx. ≥50%

Moderate Daily dose lowers LDL-C by approx. 30% to <50%

Yes

Diabetes Type 1 or 2 Age 40-75 y

Yes

High-intensity statin
(Moderate-intensity statin if not candidate for high-intensity statin)

No

Yes

Moderate-intensity statin

No

Yes

Estimated 10-y ASCVD risk ≥7.5%*
High-intensity statin

No

Yes

Moderate-to-high intensity statin

ASCVD prevention benefit of statin therapy may be less clear in other groups
In selected individuals, consider additional factors influencing ASCVD risk and potential ASCVD risk benefits and adverse effects, drug-drug interactions, and patient preferences for statin treatment
Figure 3. Initiating statin therapy in individuals with clinical ASCVD

Clinical ASCVD
Not currently on statin therapy
Initial evaluation prior to statin initiation
• Fasting lipid panel*
• ALT
• CK (if indicated)
• Consider evaluation for other secondary causes (Table 6) or conditions that may influence statin safety (Table 8, Rec 1).

Evaluate and Treat Laboratory Abnormalities
1. Triglycerides ≥500 mg/dL
2. LDL-C ≥190 mg/dL
   - Secondary causes (Table 6)
   - If primary, screen family for FH
3. Unexplained ALT >3X ULN

Aged ≤75 y
without contraindications, conditions or drug-drug interactions influencing statin safety, or a history of statin intolerance

Initiate high-intensity statin therapy
Counsel on healthy lifestyle habits

Aged >75 y†
OR
with conditions or drug-drug interactions influencing statin safety, or a history of statin intolerance

Initiate moderate-intensity statin therapy
Counsel on healthy lifestyle habits

Monitor statin therapy
(Figure 5)
**Figure 4. Initiating statin therapy in individuals without clinical ASCVD**

**No Clinical ASCVD**
- Not currently on cholesterol-lowering drugs
- Initial evaluation prior to statin initiation
  - Fasting lipid panel
  - ALT
  - Hemoglobin A1c (if diabetes status unknown)
  - CK (if indicated)
  - Consider evaluation for other secondary causes (Table 6) or conditions that may influence statin safety (Table 8, Rec 1)

**Assign to statin benefit group** (Figure 2)
- Counsel on healthy lifestyle habits

**Diabetes and age 40-75 y†**
- **OR**
- LDL-C ≥190 mg/dL

**No diabetes, age 40-75 y, and LDL-C 70-189 mg/dL**

**Estimate 10-y ASCVD risk†** with Pooled Cohort Equations

- ≥7.5% 10-y ASCVD risk
- 5%<7.5% 10-y ASCVD risk
- <5% 10-y ASCVD risk
- Age <40 or >75 y and LDL-C <190 mg/dL

**Clinicians and patients should engage in a discussion of the potential for:**
1. ASCVD risk reduction benefits§
2. Adverse effects§
3. Drug-drug interactions
4. Patient preferences

**Initiate statin therapy** (Figure 2)
- Re-emphasize healthy lifestyle habits

**Monitor statin therapy** (Figure 5)

**Evaluate and Treat Laboratory Abnormalities**
1. Triglycerides ≥250 mg/dL
2. LDL-C ≥190 mg/dL
   - Secondary causes (Table 6)
   - If primary, screen family for FH
3. Unexplained ALT >3X ULN

†: The term “†” is used to indicate information that is essential for understanding the flowchart.
Statin use in the past 30 days USA

Statin drug use in the past 30 days

Men
- 45–64 years: 3%, 15%, 18%
- 65–74 years: 26%, 50%
- 75 years and over: 19%, 45%

Women
- 45–64 years: 2%, 10%, 16%
- 65–74 years: 24%, 36%
- 75 years and over: 18%, 39%

* Denotes significant difference.
High total cholesterol (above 240 mg/dL) among adults age 20 years and older

Men

- 45–64 years
- 65–74 years
- 20–44 years
- 75 years and over

Women

- 65–74 years
- 45–64 years
- 75 years and over
- 20–44 years
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**

**No Clinical ASCVD**
- Not currently on cholesterol-lowering drugs
- Initial evaluation prior to statin initiation
  - Fasting lipid panel*
  - ALT
  - Hemoglobin A1c (if diabetes status unknown)
  - CK (if indicated)
  - Consider evaluation for other secondary causes (Table 6) or conditions that may influence statin safety (Table 8, Rec 1)

**Assign to statin benefit group (Figure 2)**
- Counsel on healthy lifestyle habits

**Diabetes and age 40-75 y† OR LDL-C ≥190 mg/dL**

**No diabetes, age 40-75 y, and LDL-C 70-189 mg/dL**

**Estimate 10-y ASCVD risk† with Pooled Cohort Equations**

- **≥7.5% 10-y ASCVD risk**
  - Clinicians and patients should engage in a discussion of the potential for:
    1. ASCVD risk reduction benefits§
    2. Adverse effects§
    3. Drug-drug interactions
    4. Patient preferences

- **<5% 10-y ASCVD risk**
  - In selected individuals, additional factors may be considered to inform treatment decision making†

**Initiate statin therapy (Figure 2)**
- Re-emphasize healthy lifestyle habits

**Monitor statin therapy (Figure 5)**

**Evaluate and Treat Laboratory Abnormalities**
1. Triglycerides ≥250 mg/dL
2. LDL-C ≥190 mg/dL
   - Secondary causes (Table 6)
   - If primary, screen family for FH
3. Unexplained ALT >3X ULN
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
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
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 risk factors and elevated CAC: 17/1000 person-years
- ≥ 3 risk factors 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 $\geq 3$RF’s have CAC 0
- Thus NNS to detect CAC of 0 = 3
- Estimated 10 year event rate 3.1%
Number needed to treat (NNT)

- $\geq 3$ 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
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 or 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 4.65 mmol/l
- HDL 0.90 mmol/L
- TG 1.7 mmol/L
- LDL 3.00 mmol/L
- Blood pressure 130/85 mmHg
- 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 4.65 mmol/l
- HDL 0.90 mmol/L
- TG 1.7 mmol/L
- LDL 3.00 mmol/L
- Blood pressure 130/85 mmHg
- 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
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.