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Primary and Secondary Prevention of Coronary Artery Disease
This figure depicts the tiered approach to preventing CVD. Primordial prevention makes up the base and optimizes health behaviors to reduce the development of CVD risk factors. The second tier is primary prevention, which targets CVD risk factors to prevent the development of CVD. Last, the apex is secondary and tertiary prevention, where CVD is targeted to prevent progression and development of additional CVD. Adapted with permission from Vaduganathan et al. (5). CAD = coronary artery disease; CVD = cardiovascular disease; PVD = peripheral vascular disease.
### Table 3. Risk-Enhancing Factors for Clinician-Patient Risk Discussion

<table>
<thead>
<tr>
<th>Risk-Enhancing Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• <strong>Family history of premature ASCVD</strong> (males, age &lt;55 y; females, age &lt;65 y)</td>
</tr>
<tr>
<td>• <strong>Primary hypercholesterolemia</strong> (LDL-C 160–189 mg/dL [4.1–4.8 mmol/L]; non–HDL-C 190–219 mg/dL [4.9–5.6 mmol/L])*</td>
</tr>
<tr>
<td>• <strong>Metabolic syndrome</strong> (increased waist circumference [by ethnically appropriate cutpoints], elevated triglycerides [&gt;150 mg/dL, nonfasting], elevated blood pressure, elevated glucose, and low HDL-C [&lt;40 mg/dL in men; &lt;50 mg/dL in women] are factors; a tally of 3 makes the diagnosis)</td>
</tr>
<tr>
<td>• <strong>Chronic kidney disease</strong> (eGFR 15–59 mL/min/1.73 m² with or without albuminurinia; not treated with dialysis or kidney transplantation)</td>
</tr>
<tr>
<td>• <strong>Chronic inflammatory conditions</strong>, such as psoriasis, RA, lupus, or HIV/AIDS</td>
</tr>
</tbody>
</table>

ABI indicates ankle-brachial index; AIDS, acquired immunodeficiency syndrome; apoB, apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; HIV, human immunodeficiency virus; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein (a); and RA, rheumatoid arthritis.
### Table 3. Risk-Enhancing Factors for Clinician-Patient Risk Discussion (cont’d)

<table>
<thead>
<tr>
<th>Risk-Enhancing Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>- History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk, such as preeclampsia</td>
</tr>
<tr>
<td>- High-risk race/ethnicity (e.g., South Asian ancestry)</td>
</tr>
<tr>
<td>- Lipids/biomarkers: associated with increased ASCVD risk</td>
</tr>
<tr>
<td>- Persistently elevated,* primary hypertriglyceridemia (≥175 mg/dL, nonfasting);</td>
</tr>
<tr>
<td>- If measured:</td>
</tr>
</tbody>
</table>
  - Elevated high-sensitivity C-reactive protein (≥2.0 mg/L) |
  - Elevated Lp(a): A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥50 mg/dL or ≥125 nmol/L constitutes a risk-enhancing factor, especially at higher levels of Lp(a). |
  - Elevated apoB (≥130 mg/dL): A relative indication for its measurement would be triglyceride ≥200 mg/dL. A level ≥130 mg/dL corresponds to an LDL-C >160 mg/dL and constitutes a risk-enhancing factor |
  - ABI (<0.9) |

*Optimally, 3 determinations.
INTERHEART: Impact of multiple risk factors on CV risk

### Age and Gender Difference in Deaths Prevented as a Result of Primary and Secondary Prevention (1980-2000)

<table>
<thead>
<tr>
<th>Age</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 25-54 M</td>
<td>1380</td>
</tr>
<tr>
<td>Age 25-54 F</td>
<td>38490</td>
</tr>
<tr>
<td>All ages M</td>
<td>39,870</td>
</tr>
<tr>
<td>Age 25-54 F</td>
<td>715</td>
</tr>
<tr>
<td>Age 55-84 F</td>
<td>24345</td>
</tr>
<tr>
<td>All ages F</td>
<td>25,080</td>
</tr>
<tr>
<td>All ages M&amp;F</td>
<td>64,930</td>
</tr>
</tbody>
</table>

- **Secondary**:
  - Age 25-54 M: 28400
  - Age 25-54 F: 148245
  - All ages M: 176645
  - Age 55-84 F: 7200
  - All ages F: 67315
  - All ages M&F: 74520

- **Primary**: 251165

*Young et al. Am J Prev Medicine 2010*
# Risk Factors for Heart Disease

<table>
<thead>
<tr>
<th>Non Modifiable Risk Factors</th>
<th>Modifiable Risk Factors</th>
<th>Novel Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td>SMOKING</td>
<td>C REACTIVE PROTEIN</td>
</tr>
<tr>
<td>GENDER</td>
<td>HYPERLIPIDEMIA</td>
<td>FIBRINOGEN</td>
</tr>
<tr>
<td>ETHNICITY</td>
<td>HYPERTENSION</td>
<td>CORONARY ARTERY CALCIFICATION</td>
</tr>
<tr>
<td>FAMILY HISTORY</td>
<td>DIABETES</td>
<td>HOMOCYSTEINE</td>
</tr>
<tr>
<td>PREVIOUS CARDIOVASCULAR EVENT</td>
<td>OBESITY</td>
<td>LIPOPROTEIN A</td>
</tr>
<tr>
<td></td>
<td>PHYSICAL INACTIVITY</td>
<td>SMALL DENSE LDL</td>
</tr>
<tr>
<td></td>
<td>APOB / APOA1 RATIO</td>
<td>RENAL DISEASE</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HIV</td>
</tr>
</tbody>
</table>
Abdominal obesity: a major risk factor for diabetes and cardiovascular disease

- Endothelial dysfunction
- Atherogenic dyslipidemia
- Hypertension
- Inflammatory profile
- Insulin resistance
- Pro-thrombotic state
How high stress can cause disease

STRESS
Adrenal glands release cortisol, the stress hormone.

BIOLOGICAL IMPACT
Cortisol works to reduce the inflammatory response that stress produces.

CHRONIC STRESS
Body builds resistance to inflammation-reducing cortisol.

CHRONIC INFLAMMATION RESPONSE
Inflammation causes or worsens various diseases, including cardiovascular and infectious diseases, among others.

Source: Sheldon Cohen, Carnegie Mellon University

James Hilston/Post-Gazette
Fig. 2. Treatment of T2DM for Primary Prevention of CVD

HbA1c > 6.5% consistent with T2DM

- Dietary counseling regarding key aspects of a heart-healthy diet (Class I)
- At least 150 minutes/week of moderate to vigorous physical activity (Class I)
- Aggressive treatment of other CVD risk factors
- Consideration of metformin as first-line pharmacologic therapy to improve glycemic control and reduce CVD risk (Class IIa)

HbA1c < 7.0% after lifestyle therapies and metformin?

- NO
  - Does the patient have other CVD risk factors?
    - NO
      - Further management of diabetes per primary care provider or endocrinology
    - YES
      - Consideration may be given to an SGLT-2 inhibitor or a GLP-1R agonist to improve glycemic control and reduce CVD risk (Class IIb)
  - YES
    - Reinforce the importance of diet and physical activity and continue current management
Fig. 3.

Primary Prevention: Assess ASCVD Risk in Each Age Group
Emphasize Adherence to Healthy Lifestyle

- **Age 0-19 y**
  - Lifestyle to prevent or reduce ASCVD risk
  - Diagnosis of Familial Hypercholesterolemia → statin

- **Age 20-39 y**
  - Estimate lifetime risk to encourage lifestyle to reduce ASCVD risk
  - Consider statin if family history premature ASCVD and LDL-C ≥160 mg/dL (≥4.1 mmol/L)

- **Age 40-75 y** and LDL-C ≥70-<190 mg/dL (≥1.8-<4.9 mmol/L) without diabetes mellitus
  - 10-year ASCVD risk percent begins risk discussion

- **Age >75 y**
  - Clinical assessment, Risk discussion

### ASCVD Risk Enhancers:

- Family history of premature ASCVD
- Persistently elevated LDL-C ≥160 mg/dL (≥4.1 mmol/L)
- Chronic kidney disease
- Metabolic syndrome
- Conditions specific to women (e.g., preeclampsia, premature menopause)
- Inflammatory diseases (especially rheumatoid arthritis, psoriasis, HIV)
- Ethnicity (e.g., South Asian ancestry)

### Lipid/Biomarkers:

- Persistently elevated triglycerides (≥175 mg/dL, ≥2.0 mmol/L)

In selected individuals if measured:

- hs-CRP ≥2.0 mg/L
- Lp(a) levels ≥50 mg/dL or >125 nmol/L
- apoB ≥130 mg/dL
- Ankle-brachial index (ABI) <0.9

### Risk Discussion:

- **<5% “Low Risk”**
  - Emphasize lifestyle to reduce risk factors (Class I)

- **5% - <7.5% “Borderline Risk”**
  - Risk discussion: If risk enhancers present then risk discussion regarding moderate-intensity statin therapy (Class IIb)

- **≥7.5% - <20% “Intermediate Risk”**
  - Risk discussion: If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30% - 49% (Class I)

- **≥20% “High Risk”**
  - Risk discussion: Initiate statin to reduce LDL-C ≥50% (Class I)

**If risk decision is uncertain:**

- Consider measuring CAC in selected adults:
  - CAC = zero (lowers risk; consider no statin, unless diabetes, family history of premature CHD, or cigarette smoking are present)
  - CAC = 1-99 favors statin (especially after age 55)
  - CAC = 100+ and/or ≥75th percentile, initiate statin therapy
### Recommendations for Adults with High Blood Pressure or Hypertension

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| I   | A   | 1. In adults with elevated blood pressure (BP) or hypertension, including those requiring antihypertensive medications nonpharmacological interventions are recommended to reduce BP. These include:  
- weight loss,  
- a heart-healthy dietary pattern,  
- sodium reduction,  
- dietary potassium supplementation,  
- increased physical activity with a structured exercise program; and  
- limited alcohol. |
BP indicates blood pressure; and CVD, cardiovascular disease.
• Genesis of atherosclerosis is prolonged, multifactorial process
• Horus study 10 years back used CT to investigate arterial calcification in mummies as marker of atherosclerosis
• Wann & Colleagues studied 4 mummies of Inuit hunter-gatherer people (lived about 500 years ago, consumed a marine diet rich in omega-3-FA). 2 men and a woman who died by age 25 had calcified atheroma.
• Previous study showed that the CV death in this population was low, hypothesizing it was due to diet rich in Omega-3-FA
• Speculation is that exposure to particulate matter from smoky indoor fires may have played a role in atherosclerosis in this population with otherwise healthy lifestyle
• Autopsy study of young soldiers dying from trauma in Korean and Vietnam wars had extensive subclinical atherosclerosis (they might have developed clinical CVD decades later if they lived)
Intermittent Fasting

• Fasting for 14 hours with eating window of 10 hours
• Patients with metabolic synd., prediabetes, HTN, overweight
• There was lowering of LDL, Hemoglobin A1C, BP, weight
• Fasting depletes glucose body mobilizes energy from fat leading to lipolysis weight loss
• Fasting low grade ketosis lipolysis
• Flexibility, improvement in sleep quality, energy and endurance levels improved, felt better, long term adherence, aligning eating pattern with circadian rhythm
• Despite significant medical advances, CVD remains as leading cause of morbidity and mortality worldwide.

• Statins ↓ LDL by 20 to 60%, which corresponds to 30% reduction in CVD events.

• Despite the success of statins and other CV therapies, significant residual risk remains.

• In addition to treating standard risk factors, elevated TG have been relooked as therapeutic target.

• Several studies implicated elevated TG as an independent association with CVD risk.

• Older trials of Omega-3-FA suggested possible benefit. AHA recommended treatment as reasonable for secondary prevention of CHD and SCD in those with prevalent CAD. However, Omega-3-FA utilizing mixed DHA/EPA products and dosages of one gram or less per day failed to show CV benefit.
JELIS Study

- 18,645 Japanese pts (20% with CHD)
- Total chol > 243, predominantly on low intensity statin
- EPA 1.8 g daily → 19% RR in major CHD events at five years (2.8% vs 3.5%)
- Due to perceived biases (all Japanese pts, low intensity statin regimen, and open label design) these results had minimal clinical value
CHERRY Trial

- 193 post PCI Japanese pts
- Randomized to Pitavastatin + EPA 1.8 g daily vs. Pitavastatin monotherapy
- 6-8 month follow up
- Greater coronary plaque regression (81% vs 61% p=0.002)
3rd Trial

- 241 Japanese pts with ACS
- Randomized to Pitavastatin 2 mg + EPA 1.8 g daily vs. without EPA
- 58% risk reduction in CV death, non fatal MI, non fatal stroke and revascularization, 78% risk reduction in CV death in one year
REDUCE - IT

- Icosopent Ethyl (Vascepa) a purified ethyl ester of EPA
- 2g twice daily vs. mineral oil placebo on background of statin therapy in pts with CVD or diabetes + one additional risk factor
- LDL 41-100 mg/dl and TG 135-499 mg/dl
- 8179 pts (about 70% with established CVD, 30% for primary prevention)
- A striking reduction in first occurrence of primary endpoint (17.2% vs 22% decrease in CV death, MI, coronary revascularization, USA, stroke). All individual points were sig reduced
- 30% reduction in total (initial and recurrent) events related to primary endpoint on post ad-hoc analysis
- This magnitude of benefit is on par with statins, PCSK9 inhibitor.
• However, improvements in lipoprotein, inflammation parameters and even SCD did not predict the full range of benefit displayed, implying there are other factors involved

• Small increase in Afib/flutter and trend towards increased bleeding

• In Nov 2019, FDA unanimously voted CV risk reduction to label

• A month later, FDA approved Icosopent ethyl as a adjunctive therapy to reduce risk of CV events among adults with elevated TG of at least 150 mg

• Reduce – It demonstrated significant benefit of EPA to statin over statin monotherapy

• FDA month before approved: for CV risk reduction among adults already taking statin with TG level of 150 mg/dl or higher who have either established CAD or diabetes and two or more additional risk factors for CVD based on 25% risk reduction of events)

• Age, smoking, HTN, low HDL, elevated CRP, BMI > 25 kg/m^2, renal dysfunction, retinopathy, albuminuria, ABI < 0.9
• STRENGTH trial
• EPA + DHA
• Stopped early due to futility

• Non fasting lipids are about 50 mg/dl higher
LCD (low carb diet) and LFD (low fat diet)

• Diet recall study of 37,233 pts 1999-2014
• Avg age 50 yrs, 53% women
• No sig dif in LCD or LFD. Unhealthy or healthy components
• 20 percentile increase in unhealthy LCD linked with relative, total mortality ↑ by 7%, 11% in cancer death. For LFD, ↑ 6%, after adjusting to family history, DM, cancer, CHD
• 20 percentile increase in healthy LCD score relative, total mortality fell by 9% and 10% decrease in cancer deaths. For LFD, 15% relative decrease in cancer mortality and 11% relative drop in total mortality
• It is the type and quality of the fat and carbohydrates that matters for health
• LCD: high in plant protein, , Unsaturated fats, unprocessed carbs like whole grains, fruit, legumes, vegetables
• Low quality carbs (refined and added sugar) provide limited nutrition, has high glycemic load, ↑ inflammation, insulin resistance, dislipidemia)
Testosterone

• 1% topical gel
• > 65 yrs
• Double blind placebo control testosterone cardiovascular trial
• LV mass indexed to BSA showed significant increase in testosterone group
## Aspirin Use

### Recommendations for Aspirin Use

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIb</td>
<td>A</td>
<td>1. Low-dose aspirin (75-100 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk.</td>
</tr>
<tr>
<td>III: Harm</td>
<td>B-R</td>
<td>2. Low-dose aspirin (75-100 mg orally daily) should not be administered on a routine basis for the primary prevention of ASCVD among adults &gt;70 years of age.</td>
</tr>
<tr>
<td>III: Harm</td>
<td>C-LD</td>
<td>3. Low-dose aspirin (75-100 mg orally daily) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding.</td>
</tr>
</tbody>
</table>
• The most important way to prevent atherosclerotic vascular disease, heart failure, and atrial fibrillation is to promote a healthy lifestyle throughout life.

• Aspirin
• Statin
• PCSK9 inhibitors
• Icosopent Etyl
• ACE inhibitors
• Beta blockers
• Anti platlete agents
• Nitrates
• Cardiac rehab
Thank You

Prevention

Cure