بسم الله الرحمن الرحيم
Prevention of CAD: Update

By

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Overview

- Introduction
- Burden of CVD
- Atherosclerosis risk factors
- Global risk assessment
- Preventive strategies
- Conclusions
Introduction

Historical medical recordings as early as 2500 BC referred to the practice of Prevention. References to the importance of prevention are found in the writings of Hippocrates and Osler, thus rendering the prevention concept important and certainly “not new” in the practice of medicine.
Major Clinical Manifestations of Atherothrombosis

- Ischemic stroke
- Transient ischemic attack
- Myocardial infarction
- Angina:
  - Stable
  - Unstable
- Peripheral arterial disease:
  - Intermittent claudication
  - Rest Pain
  - Gangrene
  - Necrosis

Adapted from: Drouet L. Cerebrovasc Dis 2002; 13(suppl 1): 1–6.
Atherothrombosis is Commonly Found in More Than One Arterial Bed*¹

Cerebrovascular disease

- 24.7%
- 7.4%
- 3.3%
- 19.2%

Coronary disease

- 29.9%
- 3.8%
- 11.8%

Peripheral arterial disease

- 3.3%

*¹ Data from CAPRIE study (n=19,185)

Atherothrombosis* is the Leading Cause of Death Worldwide†

- Atherothrombosis*: 52%
- Cancer: 24%
- Infectious Disease: 19%
- Pulmonary disease: 14%
- Violent death: 12%
- AIDS: 5%

*Mortality (%)

*Cardiovascular disease, ischemic heart disease and cerebrovascular disease
†Worldwide defined as Member States by WHO Region (African, Americas, Eastern Mediterranean, European, South East Asia and Western Pacific).

Atherothrombosis Will Remain the Leading Cause of Disease Burden

The ten leading causes of disease burden in developed countries 1990–2020

<table>
<thead>
<tr>
<th>1990 disease or injury(^1)</th>
<th>Rank order</th>
<th>2020 disease or injury(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic heart disease</td>
<td>1</td>
<td>Ischemic heart disease</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>2</td>
<td>Cerebrovascular disease</td>
</tr>
<tr>
<td>Road traffic accidents</td>
<td>3</td>
<td>Unipolar major depression</td>
</tr>
<tr>
<td>Bronchus and lung cancers</td>
<td>4</td>
<td>Bronchus &amp; lung cancers</td>
</tr>
<tr>
<td>Self-inflicted injuries</td>
<td>5</td>
<td>Road traffic accidents</td>
</tr>
<tr>
<td>Conditions arising during perinatal period</td>
<td>6</td>
<td>Alcohol use</td>
</tr>
<tr>
<td>Lower respiratory infections</td>
<td>7</td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>8</td>
<td>Dementia and other CNS disorders</td>
</tr>
<tr>
<td>Colon and rectal cancers</td>
<td>9</td>
<td>Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>Stomach cancer</td>
<td>10</td>
<td>Self-inflicted Injuries</td>
</tr>
</tbody>
</table>

Note: Disease burden is measured in disability adjusted life years (DALYs), a measure that combines the impact on health of years lost due to premature death and years lived with a disability. One DALY is equivalent to one lost year of healthy life.

Atherothrombosis Significantly Reduces Life Expectancy

Analysis of data from the Framingham Heart Study

- More than 60% of patients aged >40 develop cardiovascular disease
- Cardiovascular disease reduces life expectancy by 11–12 years for patients aged >50

<table>
<thead>
<tr>
<th>Average Life Expectancy at Age 60 (Men)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>20.0 years</td>
</tr>
<tr>
<td>History of CVD</td>
<td>12.3 years</td>
</tr>
<tr>
<td>History of AMI</td>
<td>10.8 years</td>
</tr>
<tr>
<td>History of stroke</td>
<td>7.98 years</td>
</tr>
</tbody>
</table>

CVD = cardiovascular disease
AMI = acute myocardial infarction

Source: Peeters et al. Eur Heart J 2002; 23: 458
**Risk of Myocardial Infarction and Stroke Greatly Increases With Atherothrombotic Disease**

<table>
<thead>
<tr>
<th></th>
<th>Increased risk of MI</th>
<th>Increased risk of stroke$^3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient with myocardial infarction</td>
<td>5–7 X greater risk$^1$</td>
<td>3–4 X greater risk (includes TIA)</td>
</tr>
<tr>
<td>Patient with ischemic stroke</td>
<td>2–3 X greater risk$^2$ (includes angina and CHD death)</td>
<td>9 X greater risk (major stroke)</td>
</tr>
<tr>
<td>Patient with peripheral arterial disease (PAD)</td>
<td>4 X greater risk$^4$ (includes fatal MI and other CHD death)</td>
<td>2–3 X greater risk (includes TIA)</td>
</tr>
</tbody>
</table>

*Data are versus the general population and measure the associated risk increase in events taken from different sources. The increase in risk of events was based on ten-year follow-up, except for risk of stroke following stroke, which measures subsequent annual risk. CHD = coronary heart disease. TIA = transient ischemic attack.

Coronary Heart Disease is a Major Health Burden

- A major health burden
  - Coronary heart disease is the leading cause of death in developed countries\(^1\)
  - Patients with cardiovascular disease consistently report worse quality of life than age- and sex-matched controls\(^2\)

- Key facts
  - In the USA: about 250,000 people a year die of CHD without being hospitalised\(^3\)
  - About every 29 seconds someone will suffer a coronary event in the USA\(^3\)

- Epidemiology:
  - Worldwide MI prevalence of 9.1 million in 2000 and rising\(^4\)
  - Prevalence of angina estimated to be 3.2% in men and 2.5% in women\(^5\)

\(^3\) American Heart Association. *2002 Heart and Stroke Statistical Update*. AHA, 2002
\(^4\) Guillot F, Moulard O. *Circulation* 1998: 98(abstr suppl 1): 1421
Coronary Heart Disease is Highly Prevalent

Prevalence of coronary heart disease by age and sex

Peripheral Arterial Disease is a Major Health Burden

Peripheral arterial disease (PAD)

- **A major health burden:**
  - Patients with PAD are six times more likely to die within ten years than those without PAD\(^1\)
  - Patients with PAD often have decreased quality of life because of pain during walking and limitations of mobility\(^2\)

- **Key facts:**
  - Survival rates are worse than for breast cancer or Hodgkin’s disease: patients with PAD have a five-year mortality rate of 28% compared with 15% for breast cancer and 18% for Hodgkin’s disease\(^1\)

- **Epidemiology:**
  - The prevalence of PAD is estimated at 27 million in Europe and North America\(^3\)

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Ischemic Stroke is a Major Health Burden

Ischemic stroke

- A major health burden in Western countries:
  - Stroke is the third most common cause of death\(^1\)
  - Stroke is the leading cause of disability in adults\(^1\)
  - Stroke is the second most important cause of dementia\(^1\)

- Key facts:
  - In the USA: every 53 seconds, someone suffers a stroke\(^2\)
  - In the UK: more than 47,000 working lives are lost (deaths before age of 65) each year and 8 million working days are lost\(^3\)

- Epidemiology:
  - Worldwide stroke prevalence of 7.1 million in 2000 and rising\(^4\)

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1. Leys D. Cerebrovascular Disease 2001: 11(suppl 2): 1–4
The Burden of Stroke Continues After the Acute Event

- Stroke progression during hospitalization
  - 24%
- Mortality
  - 30 days
    - 8–20%
  - 1 year
    - 15–25%
  - 5 years
    - 40–60%
- Complete or partial dependence
  - 27–53%
- Dementia persisting at 1 year
  - 34%

Stroke Has a Major Impact on Quality of Life

CVD: From Risk Factors to Clinical Presentation

Subclinical Disease
- Hypertension
- Diabetes
- Lipids
- Menopause
- Sex
- Age
- Obesity
- Inactivity
- Smoking
- Diet

Clinical Disease
- LVH
- Coronary Calcification
- Carotid Stenosis
- Inflammation
- Endothelial Dysfunction
- Stroke
- PVD
- Angina
- MI
- Sudden Death
- Heart Failure

Genes

Environment
Atherosclerosis: A Progressive Process

Normal → Fatty Streak → Fibrous Plaque → Occlusive Atherosclerotic Plaque → Plaque Rupture/ Fissure & Thrombosis

Clinically Silent → Effort Angina Claudication → Unstable Angina

Increasing Age → MI → Coronary Death → Stroke → Critical Leg Ischemia

Courtesy of P Ganz.
The Development of Atherothrombosis—a Generalized and Progressive Process

Acute syndrome:
- coronary
- cerebrovascular
- peripheral

Plaque rupture → Platelet activation and aggregation → Non-occlusive thrombus → Healing and resolution → Plaque growth

Adapted from: Drouet L. Cerebrovasc Dis 2002; 13(suppl 1): 1–6.
Atherothrombosis: Main Cause of Major Ischemic (Vascular) Events

- Atherothrombosis is characterized by a sudden (unpredictable) atherosclerotic plaque disruption (rupture or erosion) leading to platelet activation and thrombus formation.

- Atherothrombosis is the underlying condition that results in events leading to myocardial infarction, ischemic stroke, and vascular death.

Characteristics of Plaques Prone to Rupture

- T lymphocyte
- Macrophage foam cell (tissue factor+)
- "Activated" intimal SMC (HLA-DR+)
- Normal medial SMC

Identifying Those at Risk of Atherothrombosis\textsuperscript{1,2}

Local factors:
- Elevated prothrombotic factors: fibrinogen, CRP, PAI-1
- Blood flow patterns, vessel diameter, arterial wall structure

Generalised disorders
- Obesity
- Diabetes

Atherothrombosis manifestations
(myocardial infarction, stroke, vascular death)

Genetic
- Genetic traits
- Gender
- Age

Lifestyle
- Smoking
- Diet
- Lack of exercise

Systemic conditions
- History of vascular events
- Hypertension
- Hyperlipidemia
- Hypercoagulable states
- Homocystinemia

2. 2. Drouet L. Cerebrovasc Dis 2002;
Established Risk Factors of CAD

- Dyslipidemia
- Cigarette Smoking
- DM & Metabolic Syndrome
- Physical Inactivity
- Obesity
- HTN
- Male sex
- Age
- Family History

New Risk Factors:
- Homocystinemia
- LP (a)
- Fibrinogen

- Modifiable
- Non-modifiable

ATP III JAMA, 2001
Homocysteine: Role in Atherogenesis

- Linked to pathophysiology of arteriosclerosis in 1969
- CVD patients have elevated levels of plasma homocysteine
- May cause vascular damage to intimal cells
- Elevated levels linked to:
  - genetic defects
  - exposure to toxins
  - diet
- Increased dietary intake of folate and vitamin B6 may reduce CVD morbidity and mortality

McCully KS. *JAMA.* 1998;279:392-393.
Dyslipidemia
Cholesterol and CHD: Seven Countries Study

Early Primary-Prevention Trials: Overview

- WHO: Clofibrate
  - N=15,745, P<0.05
- Oslo: Diet/smoking cessation
  - N=1,232, P=0.02
- Upjohn: Colestipol
  - N=2,278, P≤0.02
- LRC-CPPT: cholestyramine
  - N=3,806, P<0.05
- HHS: Gemfibrozil
  - N=4,081, P<0.02

N=number enrolled.

* Net difference between treatment and control groups (P values are for events).

Early Secondary-Prevention Trials: Overview

-6 -10 -13 -23 -9 -13 -29 -35

TC * CHD events *

CDP: Niacin (n=1,119)
N=8,341, P=ns

CDP: Clofibrate (n=1,103)
N=8,341, P=ns

Stockholm: Clofibrate + niacin
N=555, P=ns

POSCH: Partial ileal bypass
N=838, P<0.001

N=number enrolled; ns=not significant.

* Net difference between treatment and control groups (P values are for events).

Summary of Effects of Lipid Lowering on Lipids and Clinical Events in Recent Statin Trials

- TC: Total Cholesterol
- LDL-C: Low-Density Lipoprotein Cholesterol
- HDL-C: High-Density Lipoprotein Cholesterol
- Nonfatal MI/CHD death
- CHD death
- All-cause mortality

WOSCOPS (N=6,595)
4S (N=4,444)
CARE (N=4,159)

N=number enrolled.
4S: Effect of LDL-C Lowering on Coronary Events in Secondary Prevention Trial in Men and Women

Subjects: 4,444 (81% men, 19% women)
Age range: 35-70 yr
Mean baseline TC: 261 mg/dL
Mean baseline LDL-C: 188 mg/dL
Duration: 5 yr
Intervention: Simvastatin 20-40 mg/day

Subjects: 4,444 (81% men, 19% women)
Age range: 35-70 yr
Mean baseline TC: 261 mg/dL
Mean baseline LDL-C: 188 mg/dL
Duration: 5 yr
Intervention: Simvastatin 20-40 mg/day

*P<0.00001.
†95% CI: -27 to -54.
‡P=0.003.

**SIMVASTATIN: CAUSE-SPECIFIC MORTALITY**

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>SIMVASTATIN</th>
<th>PLACEBO</th>
<th>Rate ratio &amp; 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(10269)</td>
<td>(10267)</td>
<td></td>
</tr>
<tr>
<td>Vascular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary</td>
<td>587</td>
<td>707</td>
<td>STATIN better</td>
</tr>
<tr>
<td>Other vascular</td>
<td>194</td>
<td>230</td>
<td>PLACEBO better</td>
</tr>
<tr>
<td>ANY VASCULAR</td>
<td>781 (7.6%)</td>
<td>937 (9.1%)</td>
<td>17% SE 4 reduction (2P&lt;0.0001)</td>
</tr>
<tr>
<td>Non-vascular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neoplastic</td>
<td>359</td>
<td>345</td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>90</td>
<td>114</td>
<td></td>
</tr>
<tr>
<td>Other medical</td>
<td>82</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>Non-medical</td>
<td>16</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>NON-VASCULAR</td>
<td>547 (5.3%)</td>
<td>570 (5.6%)</td>
<td>5% SE 6 reduction (NS)</td>
</tr>
<tr>
<td>ALL CAUSES</td>
<td>1328 (12.9%)</td>
<td>1507 (14.7%)</td>
<td>13% SE 4 reduction (2P&lt;0.001)</td>
</tr>
</tbody>
</table>
**SIMVASTATIN: MAJOR VASCULAR EVENTS**

<table>
<thead>
<tr>
<th>Vascular event</th>
<th>SIMVASTATIN (10269)</th>
<th>PLACEBO (10267)</th>
<th>Rate ratio &amp; 95% CI</th>
<th>STATIN better</th>
<th>PLACEBO better</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major coronary</td>
<td>898</td>
<td>1212</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any stroke</td>
<td>444</td>
<td>585</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Revascularisation</td>
<td>939</td>
<td>1205</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANY OF ABOVE</td>
<td>2033 (19.8%)</td>
<td>2585 (25.2%)</td>
<td>24% SE 3 reduction (2P&lt;0.00001)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
SIMVASTATIN: MAJOR VASCULAR EVENT by YEAR

Benefit/1000 (SE): 5(3)  20(4)  35(5)  46(5)  54(7)  60(18)
SIMVASTATIN: Main conclusions

After allowance for non-compliance, 40mg daily simvastatin safely reduces the risk of heart attack, of stroke, and of revascularisation by about one-third

5 years of statin treatment typically prevents these “major vascular events” in about:

- 100 of every 1000 people with previous MI
- 80 " " " other CHD
- 70 " " " cerebrovascular disease
- 70 " " " other arterial disease
- 70 " " " diabetes (age 40+)

irrespective of cholesterol level (or age, or sex, or other treatments)
### ATP III: LDL-C, HDL-C, TC Classification

<table>
<thead>
<tr>
<th>LDL-C (mg/dL)</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td>Optimal</td>
</tr>
<tr>
<td>100–129</td>
<td>Above, near optimal</td>
</tr>
<tr>
<td>130–159</td>
<td>Borderline high</td>
</tr>
<tr>
<td>160–189</td>
<td>High</td>
</tr>
<tr>
<td>≥190</td>
<td>Very high</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HDL-C (mg/dL)</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>Low</td>
</tr>
<tr>
<td>≥60</td>
<td>High</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TC (mg/dL)</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;200</td>
<td>Desirable</td>
</tr>
<tr>
<td>200–239</td>
<td>Borderline high</td>
</tr>
<tr>
<td>≥240</td>
<td>High</td>
</tr>
</tbody>
</table>

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## Risk Stratification for Primary Prevention in Adults: Classification Based on Total Cholesterol and HDL-C

<table>
<thead>
<tr>
<th>Cholesterol level</th>
<th>HDL-C</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desirable blood cholesterol &lt;200 mg/dL</td>
<td>≥35 mg/dL</td>
<td>Repeat testing within 5 yr</td>
</tr>
<tr>
<td>Borderline-high blood cholesterol</td>
<td></td>
<td>Perform fasting lipoprotein analysis</td>
</tr>
<tr>
<td>200-239 mg/dL</td>
<td>≥35 mg/dL and</td>
<td>Reevaluate risk status in 1-2 yr</td>
</tr>
<tr>
<td></td>
<td>&lt;2 other risk factors</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;35 mg/dL or</td>
<td>Perform fasting lipoprotein analysis</td>
</tr>
<tr>
<td></td>
<td>≥2 other risk factors</td>
<td></td>
</tr>
<tr>
<td>High blood cholesterol ≥240 mg/dL</td>
<td></td>
<td>Perform fasting lipoprotein analysis</td>
</tr>
</tbody>
</table>

For persons *without* known CHD, other forms of atherosclerotic disease, or diabetes:

- Count the number of risk factors.
- Use Framingham scoring for persons with ≥2 risk factors* to determine the absolute 10-year CHD risk.

*For persons with 0–1 risk factor, Framingham calculations are not necessary.

### ATP III: Risk Categories, LDL-C Goals

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>LDL-C Goal (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD and CHD risk equivalents (10-year risk &gt;20%)</td>
<td>&lt;100</td>
</tr>
<tr>
<td>≥2 risk factors (10-year risk ≤20%)</td>
<td>&lt;130</td>
</tr>
<tr>
<td>0–1 risk factor*</td>
<td>&lt;160</td>
</tr>
</tbody>
</table>

*Almost all people with 0–1 risk factor have a 10-year risk <10%; thus, Framingham risk calculations are not necessary.*

**Dietary Therapy for Elevated Blood Cholesterol**

<table>
<thead>
<tr>
<th>Nutrient*</th>
<th>Recommended intake</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Step I Diet</td>
</tr>
<tr>
<td>Total fat</td>
<td>&lt;30% of total calories</td>
</tr>
<tr>
<td>• Saturated fatty acids</td>
<td>8-10% of total calories</td>
</tr>
<tr>
<td>• Polyunsaturated fatty acids</td>
<td>≤10% of total calories</td>
</tr>
<tr>
<td>• Monounsaturated fatty acids</td>
<td>≤10% of total calories</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>≥55% of total calories</td>
</tr>
<tr>
<td>Protein</td>
<td>~15% of total calories</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>&lt;300 mg/day</td>
</tr>
<tr>
<td>Total calories</td>
<td>To achieve and maintain desirable weight</td>
</tr>
</tbody>
</table>

*Calories from alcohol not included.

*Expert Panel on Detection, Evaluation, and Treatment of High Blood cholesterol in Adults, JAMA 1993*
Lyon Diet Heart Study: Cumulative Survival Without Cardiac Death and Nonfatal MI

Experimental

Control

% without event

Year

1
2
3
4
5

P=0.0001

100
90
80
70

P=0.0001

<table>
<thead>
<tr>
<th>Patient category</th>
<th>Initiation level (mg/dL)</th>
<th>LDL-C target (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diet</td>
<td>Drug</td>
</tr>
<tr>
<td>No CHD, &lt;2 other RF</td>
<td>≥160</td>
<td>≥190</td>
</tr>
<tr>
<td>No CHD, ≥2 other RF</td>
<td>≥130</td>
<td>≥160</td>
</tr>
<tr>
<td>With CHD or other atherosclerotic disease</td>
<td>&gt;100</td>
<td>≥130</td>
</tr>
</tbody>
</table>

RF = risk factors.

### ATP III: LDL-C Treatment Cutpoints for Therapy

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Initiate TLC*</th>
<th>Consider Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD and CHD risk equivalents</td>
<td>≥100 mg/dL</td>
<td>≥130 mg/dL (100–129 mg/dL: drug optional)†</td>
</tr>
<tr>
<td>≥2 risk factors</td>
<td>≥130 mg/dL</td>
<td>10-year risk 10%–20%: ≥130 mg/dL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10-year risk &lt;10%: ≥160 mg/dL</td>
</tr>
<tr>
<td>0–1 risk factor</td>
<td>≥160 mg/dL</td>
<td>≥190 mg/dL (160–189 mg/dL: drug optional)</td>
</tr>
</tbody>
</table>

*Therapeutic lifestyle changes
†Some authorities use LDL-C–lowering drugs if TLC does not achieve LDL-C <100 mg/dL; others use drugs to modify HDL-C and TG.

# ATP III Pharmacologic Treatment

<table>
<thead>
<tr>
<th></th>
<th>Statins</th>
<th>Fibrates</th>
<th>Niacin</th>
<th>BAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C</td>
<td>↓↓↓↓</td>
<td>↓</td>
<td>↓</td>
<td>↓↓↓</td>
</tr>
<tr>
<td>HDL-C</td>
<td>↑</td>
<td>↑↑↑</td>
<td>↑↑↑↑↑↑</td>
<td>↑</td>
</tr>
<tr>
<td>TG</td>
<td>↓↓</td>
<td>↓↓↓↓</td>
<td>↓↓↓↓</td>
<td>↓↑</td>
</tr>
</tbody>
</table>

**BAS**: Bile acid sequestrant
ATP III: 
Management of Very High LDL-C

- LDL-C $\geq 190$ mg/dL usually traced to genetic forms of hypercholesterolemia
- Recommended actions:
  - Early detection in young adults through cholesterol screening to prevent premature CHD
  - Family cholesterol testing to identify affected relatives
  - Combination drug therapy usually required to achieve target LDL-C levels

ATP III:
New Features of Guidelines—Updated Lipid/Lipoprotein Classifications

- Optimal LDL-C level: identified as <100 mg/dL
- Categorical low HDL-C: raised to <40 mg/dL to more accurately define patients at increased risk
- TG classification cutpoints: lowered to focus more attention on moderate elevations
  - normal: <150 mg/dL
  - borderline high: 150–199 mg/dL
  - high: 200–499 mg/dL
  - very high: ≥500 mg/dL

Effects of Drug Therapy and Diet on Lipids

* 84% reached NCEP LDL target (<130 mg/dL).
† 63% reached NCEP LDL-C target (<100 mg/dL).

Community and societal barriers to the prevention of CVD

Medical setting barriers.

Patient-related barriers to CVD prevention.

CV Myths:
1. Heart disease is going away
2. Living with heart disease is not so bad
3. Heart disease is a good way to die
4. Only older people have strokes
5. Women do not get heart disease
6. No more research is needed
Hypertension
Hypertension Treatment Effect Mirrors Observational Data

Incidence of cardiovascular disease vs. Systolic blood pressure (mmHg)

Observational Data

Treatment Effect
# Relative Risk for Coronary Heart Disease

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds ratios and 95% confidence intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Veterans Administration, 1967</td>
<td></td>
</tr>
<tr>
<td>Veterans Administration, 1970</td>
<td></td>
</tr>
<tr>
<td>Hypertension Stroke Study, 1974</td>
<td></td>
</tr>
<tr>
<td>USPHS Study, 1977</td>
<td></td>
</tr>
<tr>
<td>EWPHE Study, 1985</td>
<td></td>
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<tr>
<td>Coope and Warrender, 1986</td>
<td></td>
</tr>
<tr>
<td>SHEP Study, 1991</td>
<td></td>
</tr>
<tr>
<td>STOP-Hypertension Study, 1991</td>
<td></td>
</tr>
<tr>
<td>MRC Study, 1992</td>
<td></td>
</tr>
<tr>
<td>Syst-Eur Study, 1997</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>0.79 (0.69 to 0.90)</strong></td>
</tr>
</tbody>
</table>

### Relative Risk for Stroke

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio and 95% Confidence Intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Veterans Administration, 1967</td>
<td>Active treatment better than placebo</td>
</tr>
<tr>
<td>Veterans Administration, 1970</td>
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<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
</tr>
</tbody>
</table>

# Blood Pressure Classification

<table>
<thead>
<tr>
<th>BP Classification</th>
<th>SBP mmHg</th>
<th>DBP mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
<td>&lt;80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120–139</td>
<td>80–89</td>
</tr>
<tr>
<td>Stage 1 Hypertension</td>
<td>140–159</td>
<td>90–99</td>
</tr>
<tr>
<td>Stage 2 Hypertension</td>
<td>≥160</td>
<td>≥100</td>
</tr>
</tbody>
</table>

*JNC VII JAMA 2003*
<table>
<thead>
<tr>
<th>Condition</th>
<th>Average Percent Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke incidence</td>
<td>35–40%</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>20–25%</td>
</tr>
<tr>
<td>Heart failure</td>
<td>50%</td>
</tr>
</tbody>
</table>

JNC VII JAMA 2003
Goals of Therapy

- Reduce CVD and renal morbidity and mortality.
- Treat to BP <140/90 mmHg or BP <130/80 mmHg in patients with diabetes or chronic kidney disease.
- Achieve SBP goal especially in persons ≥50 years of age.

JNC VII JAMA 2003
## Classification and Management of BP for adults

<table>
<thead>
<tr>
<th>BP classification</th>
<th>SBP* mmHg</th>
<th>DBP* mmHg</th>
<th>Lifestyle modification</th>
<th>Initial drug therapy</th>
<th>Without compelling indication</th>
<th>With compelling indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
<td>and &lt;80</td>
<td>Encourage</td>
<td></td>
<td>No antihypertensive drug indicated.</td>
<td>Drug(s) for compelling indications. ‡</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120–139</td>
<td>or 80–89</td>
<td>Yes</td>
<td></td>
<td></td>
<td>Drug(s) for compelling indications. ‡</td>
</tr>
<tr>
<td>Stage 1 Hypertension</td>
<td>140–159</td>
<td>or 90–99</td>
<td>Yes</td>
<td>Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination.</td>
<td>Drug(s) for the compelling indications. ‡</td>
<td></td>
</tr>
<tr>
<td>Stage 2 Hypertension</td>
<td>&gt;160</td>
<td>or &gt;100</td>
<td>Yes</td>
<td>Two-drug combination for most† (usually thiazide-type diuretic and ACEI or ARB or BB or CCB).</td>
<td>Other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed.</td>
<td></td>
</tr>
</tbody>
</table>

*Treatment determined by highest BP category.

†Initial combined therapy should be used cautiously in those at risk for orthostatic hypotension.

‡Treat patients with chronic kidney disease or diabetes to BP goal of <130/80 mmHg.
7-Year Incidence of Fatal and Nonfatal MI

Incidence rate (%)

- No Prior MI* Nondiabetic (n=1,373) 4%
- Prior MI 19%
- No Prior MI* Diabetic (n=1,059) 20%
- Prior MI 45%

*At baseline
MI=myocardial infarction
P<0.001 for prior MI vs. no prior MI and for diabetes vs. no diabetes

OASIS Study Mortality by Diabetes and CVD Status

Diabetes/CVD (n=1,148)  RR=2.88 (2.37-3.49)
No Diabetes/CVD (n=3,503)  RR=1.99 (1.52-2.60)
Diabetes/No CVD (n=569)  RR=1.71 (1.44-2.04)
No Diabetes/No CVD (n=2,796)  RR=1.00

OASIS=Organization to Assess Strategies for Ischemic Syndromes  CVD=cardiovascular disease  RR=relative risk (95% confidence intervals)
Impact of Diabetes on Cardiovascular Mortality in MRFIT

MRFIT=Multiple Risk Factor Intervention Trial

*Risk factors analyzed: smoking, hypercholesterolemia, and hypertension.

Framingham Heart Study
CVD Events in Diabetics

CVD=cardiovascular disease  CHD=coronary heart disease *P<0.01 †P<0.05

Pathogenesis of Diabetic Macroangiopathy

- Dyslipidemia
- Insulin
- Thrombophilia
- Other Risk Factors

Macroangiopathy

- CAD
- CVD
- PAD
CVD In DM

Summary of Key Points

- Diabetics are at increased risk for all types of fatal and non-fatal cardiovascular (CV) events.
- The protection afforded nondiabetic women is lost in diabetic women.
- There is an increasingly negative impact on CV morbidity and mortality as the number of risk factors increases.
- The risk of myocardial infarction (MI) in a diabetic without prior MI is as great as the risk of MI in a nondiabetic with a previous MI.
- Microalbuminuria is a potent predictor of cardiovascular risk in diabetics, even more than in nondiabetics.
Continuum of Patients at Risk for a CHD Event

- Secondary Prevention
- Other Atherosclerotic Manifestations
- Subclinical Atherosclerosis
- Multiple Risk Factors
- Low Risk

Courtesy of CD Furberg.
CVD Prevention Pyramid

- **Primordial**
  - Activity
    - Healthy eating
    - Ideal weight
    - Psycho-social factors
    - Familial predisposition

- **Primary**
  - Lipids
    - Hypertension
    - Smoking cessation
    - Diabetes
    - + Primordial

- **Secondary**
  - ASA
  - ACE-I
  - Rehab
  - Beta-blockers
  - + Primary
# ACC Guidelines 2001 For Prevention of Atherosclerosis

<table>
<thead>
<tr>
<th>Goals</th>
<th>Intervention Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking: complete cessation</td>
<td>Assess tobacco use. Strongly encourage patient and family to stop smoking and to avoid secondhand smoke. Provide counseling, pharmacological therapy, and formal smoking cessation programs as appropriate.</td>
</tr>
<tr>
<td>BP control:</td>
<td></td>
</tr>
<tr>
<td>&lt;140/90 mm Hg or</td>
<td>Initiate lifestyle modification in all patients with blood pressure &gt;130 mm Hg systolic or 80 mm Hg diastolic.</td>
</tr>
<tr>
<td>&lt;130/85 mm Hg if heart failure or renal insufficiency</td>
<td>Add blood pressure medication, individualized to other patient requirements and characteristics (ie, age, race, need for drugs with specific benefits)</td>
</tr>
<tr>
<td>&lt;130/80 mm Hg if Diabetes</td>
<td></td>
</tr>
</tbody>
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## ACC Guidelines 2001 For Prevention of Atherosclerosis

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<tbody>
<tr>
<td><strong>Lipid management:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Primary goal</strong></td>
<td>Start dietary therapy in all patients</td>
</tr>
<tr>
<td>LDL &lt; 100 mg/dL</td>
<td>Promote physical activity and weight management.</td>
</tr>
<tr>
<td></td>
<td>Assess fasting lipid profile in all patients Add drug therapy according to the following guide:</td>
</tr>
<tr>
<td></td>
<td>- LDL &lt; 100 mg/Dl No LDL-lowering therapy</td>
</tr>
<tr>
<td></td>
<td>- LDL 100–129 mg/dL Therapeutic options:</td>
</tr>
<tr>
<td></td>
<td>- statin or resin</td>
</tr>
<tr>
<td></td>
<td>- Fibrate or niacin (if low HDL or high TG)</td>
</tr>
<tr>
<td></td>
<td>- Consider combined drug therapy</td>
</tr>
<tr>
<td></td>
<td>- LDL &gt;130 mg/dL</td>
</tr>
<tr>
<td></td>
<td>- Intensify LDL-lowering therapy</td>
</tr>
<tr>
<td></td>
<td>- Add or increase drug therapy</td>
</tr>
<tr>
<td></td>
<td>- with lifestyle therapies</td>
</tr>
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## ACC Guidelines 2001 For Prevention of Atherosclerosis

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</tr>
</thead>
<tbody>
<tr>
<td><strong>Lipid management:</strong></td>
<td>➢ If TG &gt;150 mg/dL or HDL &lt;40 mg/dL: Emphasize weight management and physical activity. Advise smoking cessation.</td>
</tr>
<tr>
<td><strong>Secondary goal</strong></td>
<td>➢ If TG 200–499 mg/dL: Consider fibrate or niacin after LDL-lowering therapy*</td>
</tr>
<tr>
<td>If TG &gt;200 mg/dL, then non-HDL should be &lt;130 mg/dL</td>
<td>➢ If TG &gt;500 mg/dL: Consider fibrate or niacin before LDL-lowering therapy*</td>
</tr>
<tr>
<td></td>
<td>➢ Consider omega-3 fatty acids as adjunct for high TG</td>
</tr>
<tr>
<td><strong>Physical activity:</strong></td>
<td>➢ Assess risk, preferably with exercise test</td>
</tr>
<tr>
<td>Minimum goal</td>
<td>➢ Encourage minimum of 30 to 60 minutes of aerobic activity (walking, jogging, cycling)</td>
</tr>
<tr>
<td>30 minutes</td>
<td>➢ Increase in daily lifestyle activities (e.g., walking breaks at work, gardening, household work)</td>
</tr>
<tr>
<td>3 to 4 days/week</td>
<td>➢ Advise medically supervised programs for moderate to high-risk patients.</td>
</tr>
<tr>
<td>Optimal daily</td>
<td></td>
</tr>
</tbody>
</table>
# ACC Guidelines 2001 For Prevention of Atherosclerosis

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</tr>
</thead>
</table>
| Weight management: BMI 18.5–24.9 kg/m² | - Calculate BMI and measure waist circumference  
- Monitor response of BMI and waist circumference to therapy.  
- Start weight management and physical activity as appropriate. When BMI $25 kg/m², goal for waist circumference is <40 inches in men and <35 inches in women. |
| Diabetes management: Goal HbA1c ,7% | - Appropriate hypoglycemic therapy to achieve near-normal fasting plasma glucose, as indicated by HbA1c.  
- Treatment of other risks (e.g., physical activity, weight management, blood pressure, and cholesterol management). |
<table>
<thead>
<tr>
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</table>
| Antiplatelet agents/anticoagulants: | ➢ Start and continue indefinitely aspirin 75 to 325 mg/d if not contraindicated.  
➢ Consider clopidogrel 75 mg/d or warfarin if aspirin contraindicated. Manage warfarin to INR 2-3 for those not able to take aspirin or clopidogrel. |
| ACE inhibitors:             | ➢ Treat all patients indefinitely post MI; start early in stable high-risk patients (anterior MI, previous MI, Killip class II)  
➢ Consider chronic therapy for all other patients with coronary or other vascular disease unless contraindicated. |
| B-Blockers:                 | ➢ Start in all post-MI and acute ischemic syndrome patients. Continue indefinitely. Observe usual contraindications.  
➢ Use as needed to manage angina, rhythm, or BP in all other patients. |
Conclusions

- Atherothrombosis is:
  - leading cause of death worldwide
  - A leading cause of disability
  - A lifelong disease and occurrence of events is unpredictable
  - Adversely affects peoples’ quality of life

- The presence of multiple risk factors increases the risk of atherothrombotic events

- People with a history of atherothrombotic events i.e. myocardial infarction and stroke are at a far greater risk of having a subsequent event

Conclusions

- Lifestyle intervention to discontinue smoking, make healthier food choices, increase aerobic exercise and moderating alcohol consumption is important in all coronary and other atherosclerotic disease prevention programs.

- In patients with CHD, or other major atherosclerotic disease, rigorous control of BP, lipids, and glucose is recommended.

- Cardioprotective drug therapy should be considered and prescribed in selected patients:
  - Aspirin for all patients
  - B-blockers at the doses prescribed in the clinical trials following MI, particularly in high risk patients, and for at least three years. Verapamil or diltiazem should be considered as alternatives to B-blocker when this drug class is contraindicated.
Conclusions

- Cholesterol lowering therapy (statins) at the doses prescribed in the clinical trials
- ACE inhibitors at the doses prescribed in the clinical trials for patients with symptoms or signs of heart failure at the time of MI, or in those with persistent left ventricular systolic dysfunction (ejection fraction less than 40%)
- Anticoagulants for patients at risk of systemic embolisation with large anterior infarctions, severe heart failure, left ventricular aneurysm, or paroxysmal tachyarrhythmias.

- Integration of care of coronary and other atherosclerotic disease between hospital and general practice is essential by using common protocols to ensure optimal long term lifestyle, risk factor, and therapeutic management