



By

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- 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

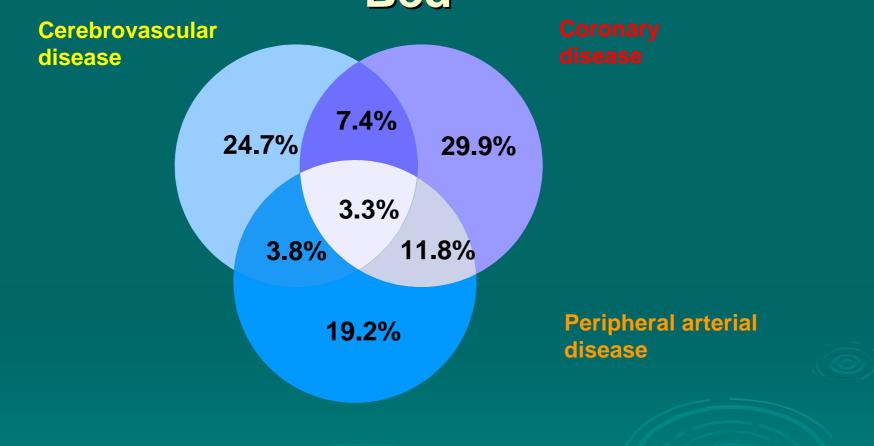
- Ischemic stroke Myocardial infarction

- Transient
- Angina: • Stable • Unstable

- Peripheral arterial disease: • Intermittent claudication
  - Intermittent claudication
     Rest Pain
  - Gangrene
  - Necrosis

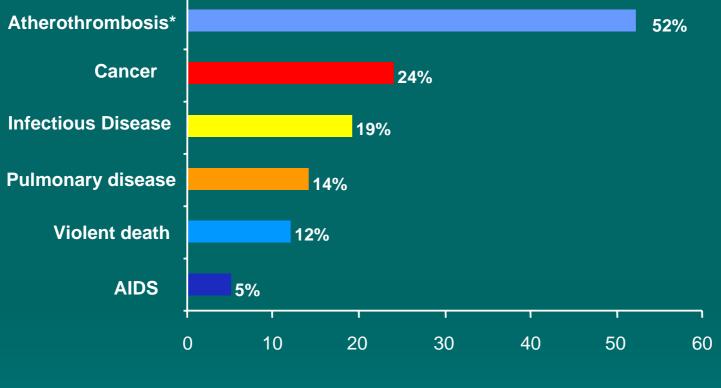
Adapted from: Drouet L. Cerebrovasc Dis 2002; 13(suppl 1): 1–6.

## Atherothrombosis is Commonly Found in More Than One Arterial Bed<sup>\*1</sup>



\*Data from CAPRIE study (n=19,185) 1. Coccheri S. *Eur Heart J* 1998; 19(suppl): P1268.

## Atherothrombosis<sup>\*</sup> is the Leading Cause of Death Worldwide<sup>†1</sup>



#### Mortality (%)

\*Cardiovascular disease, ischemic heart disease and cerebrovascular disease <sup>†</sup>Worldwide defined as Member States by WHO Region (African, Americas, Eastern Mediterranean, European, South Est Asia and Western Pacific). 1. World Health Organization. The World Health Report 2001. Geneva: WHO; 2001.

# Atherothrombosis Will Remain the Leading Cause of Disease Burden

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

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

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

1. Murray and Lopez. Global Burden of Disease Study. 1996

2. Murray and Lopez. Global Burden of Disease Study. 1997

## 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

| Average Life Expectancy<br>at Age 60 (Men) |            |  |
|--|------------|--|
| Healthy                                    | 20.0 years |  |
| History of CVD                             | 12.3 years |  |
| History of AMI                             | 10.8 years |  |
| History of stroke                          | 7.98 years |  |

CVD = cardiovascular disease AMI = acute myocardial infarction

Source: Peeters et al. Eur Heart J 2002; 23: 458 466

## Risk of Myocardial Infarction and Stroke Greatly Increases With Atherothrombotic Disease

|  | Increased risk of MI   | Increased risk of stroke <sup>3</sup>       |
|--|--|---|
| Patient with myocardial infarction                   | <b>5–7 X</b><br>greater risk <sup>1</sup>  | <b>3–4 X</b><br>greater risk (includes TIA) |
| Patient with<br>ischemic stroke                      | <b>2–3 X</b><br>greater risk <sup>2</sup> (includes<br>angina and CHD death)       | <b>9 X</b><br>greater risk (major stroke)   |
| Patient with<br>peripheral arterial<br>disease (PAD) | <b>4 X</b><br>greater risk <sup>4</sup> (includes fatal<br>MI and other CHD death) | <b>2–3 X</b><br>greater risk (includes TIA) |

\*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

- 1. Rossouw JE et al. N Eng J Med 1990; 323: 1112–1119
- 2. Kannel WB. J Cardiovasc Risk 1994; 1: 333-339
- 3. Wilterdink JL, Easton JD. Arch Neurol 1992; 49: 857-863
- 4. Criqui MH et al. N Eng J Med. 1992; 326: 381-386

## Coronary Heart Disease is a Major Health Burden

Myocardial infarction (MI) and unstable angina

>A major health burden

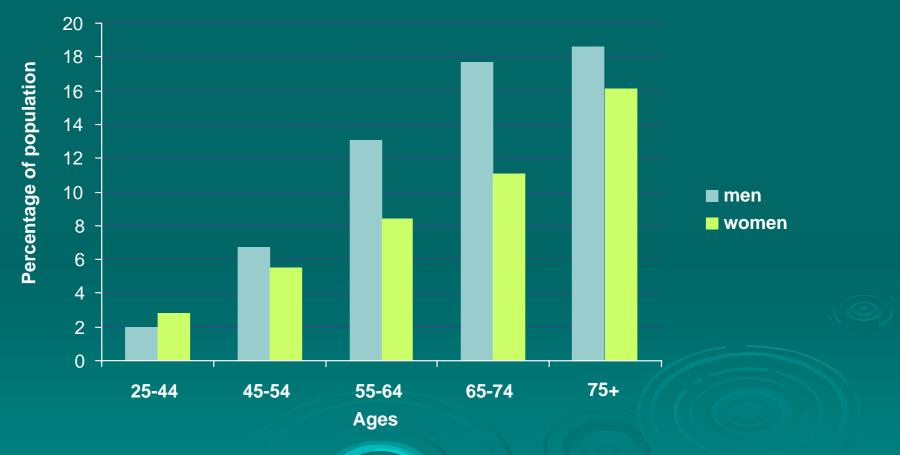
- Coronary heart disease is the leading cause of death in developed countries<sup>1</sup>
- Patients with cardiovascular disease consistently report worse quality of life than age- and sex-matched controls<sup>2</sup>

≻Key facts

- In the USA: about 250.000 people a year die of CHD without being hospitalised<sup>3</sup>
- About every 29 seconds someone will suffer a coronary event in the USA<sup>3</sup>
- > Epidemiology:
  - Worldwide MI prevalence of 9.1 million in 2000 and rising<sup>4</sup>
  - Prevalence of angina estimated to be 3.2% in men and 2.5% in women<sup>5</sup>
- 1. Murray CJL, Lopez AD. In: Murray CJL, Lopez AD, eds. Global Burden of Disease. Vol 1. 1996
- 2. Brown N et al. Heart 1999; 81: 352-358
- 3. American Heart Association. 2002 Heart and Stroke Statistical Update. AHA, 2002
- 4. Guillot F, Moulard O. Circulation 1998: 98(abstr suppl 1): 1421
- 5. Department of Health. Health Survey for England: cardiovascular disease. London: DoH, 1999

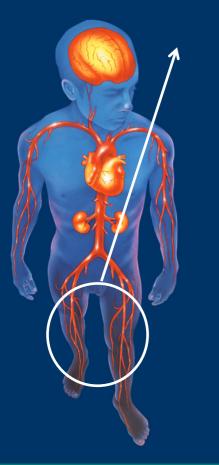
## Coronary Heart Disease is Highly Prevalent

Prevalence of coronary heart disease by age and sex<sup>1</sup>



1. American Heart Association. 2002 Heart and Stroke Statistical Update. AHA, 2002

## 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<sup>1</sup>
- Patients with PAD often have decreased quality of life because of pain during walking and limitations of mobility<sup>2</sup>

#### 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<sup>1</sup>

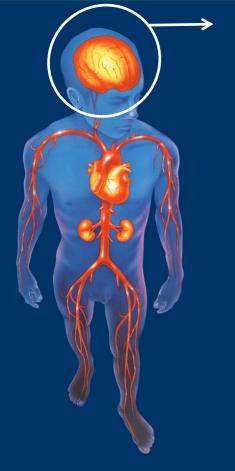
#### >Epidemiology:

 The prevalence of PAD is estimated at 27 million in Europe and North America<sup>3</sup>

1. Criqui MH et al. N Eng J Med 1992; 326: 381–386 2. Belch JJF et al. Arch Int Med 2002. In press 3. Weitz JI et al. Circulation 1996; 94: 3026–3049

# <u>Ischemic Stroke is a Major Health</u>





#### Ischemic stroke

- A major health burden in Western countries:
  - Stroke is the third most common cause of death<sup>1</sup>
  - Stroke is the leading cause of disability in adults<sup>1</sup>
  - Stroke is the second most important cause of dementia<sup>1</sup>
  - Key facts:
    - In the USA: every 53 seconds, someone suffers a stroke<sup>2</sup>
    - 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<sup>3</sup>
- Epidemiology:
  - Worldwide stroke prevalence of 7.1 million in 2000 and rising<sup>4</sup>
- 1. Leys D. Cerebrovascular Disease 2001: 11(suppl 2): 1-4
- 2. American Heart Association. 2002 Heart and Stroke Statistical Update. AHA, 2002
- 3. NHS Executive. Burdens of Disease: a discussion document. London: Department of Health, 1996
- 4. Guillot F, Moulard O. Circulation 1998: 98(abstr suppl 1): 1421

## The Burden of Stroke Continues After the Acute Event

- Stroke progression during hospitalization 24%
- > Mortality

30 days 1 year

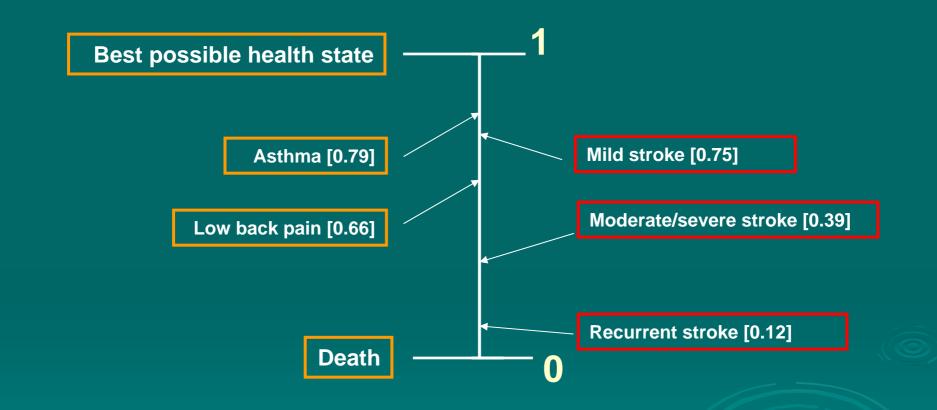
**5** years

- Complete or partial dependence 27–53%
- Dementia persisting at 1 year 34%

8–20% 15–25% 40–60%

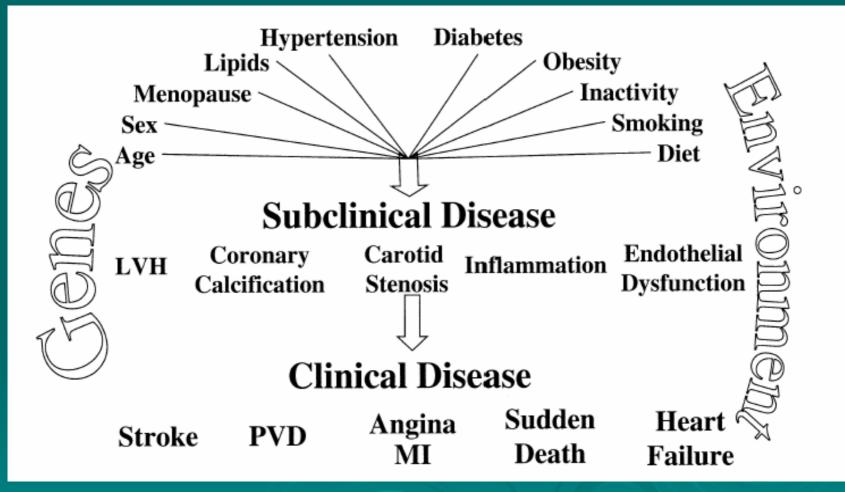
Source: Sacco. Neurology. 1997; 49 (Suppl 4): S39-S44

# Stroke Has a Major Impact on Quality of Life



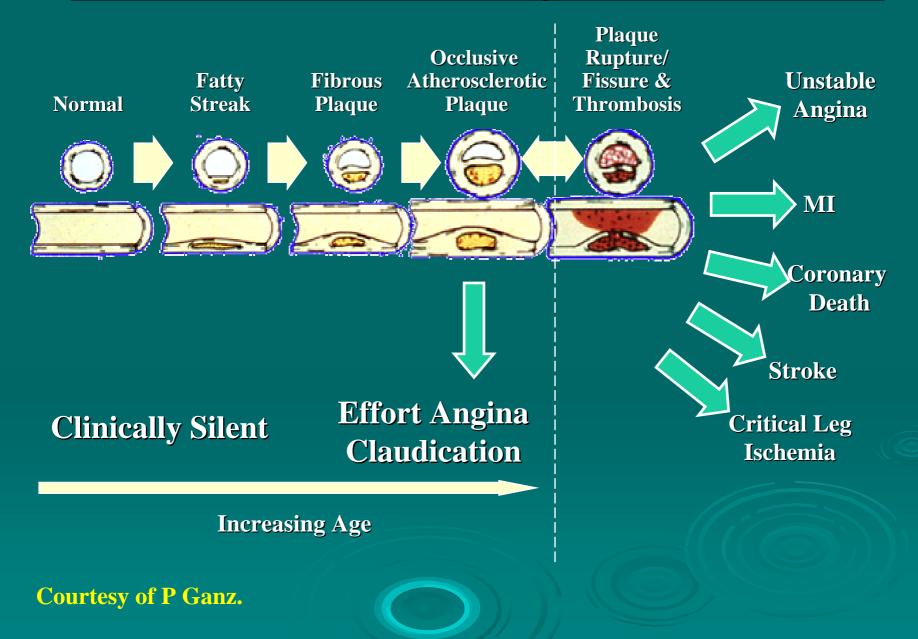
- 1. Gage BF et al. JAMA 1995; 274: 1839–1845
- 2. Burstrom K et al. Qual Lif Res 2001; 10: 621-635

# <u>CVD: From Risk Factors to</u> <u>Clinical Presentation</u>

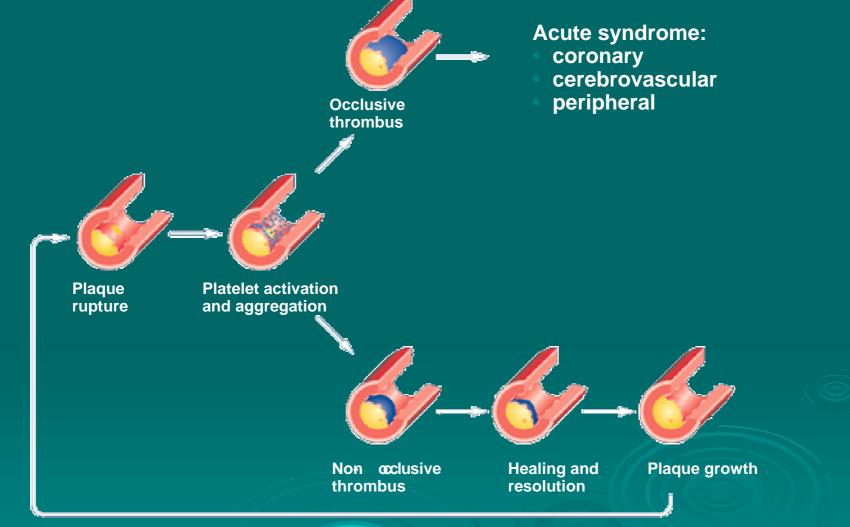


JACC Vol. 40, No. 4, 2002:579–651

## **Atherosclerosis: A Progressive Process**



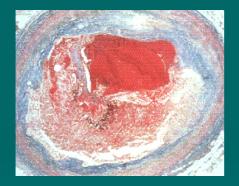
## The Development of Atherothrombosisa Generalized and Progressive Process



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

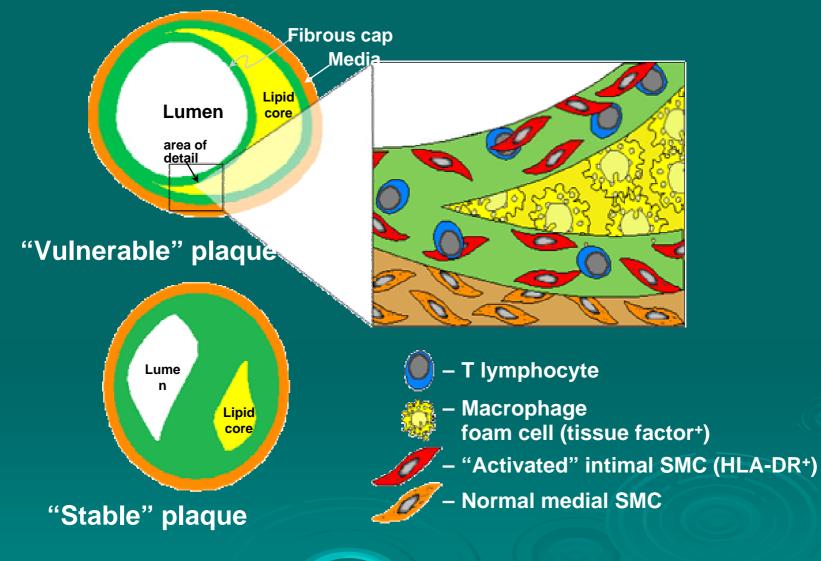




Plaque rupture<sup>1</sup>
 Plaque erosion<sup>2</sup>
 Atherothrombosis is the underlying condition that results in events leading to myocardial infarction, ischemic stroke, and vascular death

1. Falk E et al. Circulation 1995; 92: 657–71. 2. Arbustini E et al. Heart 1999; 82: 269–272

### **Characteristics of Plaques Prone to Rupture**

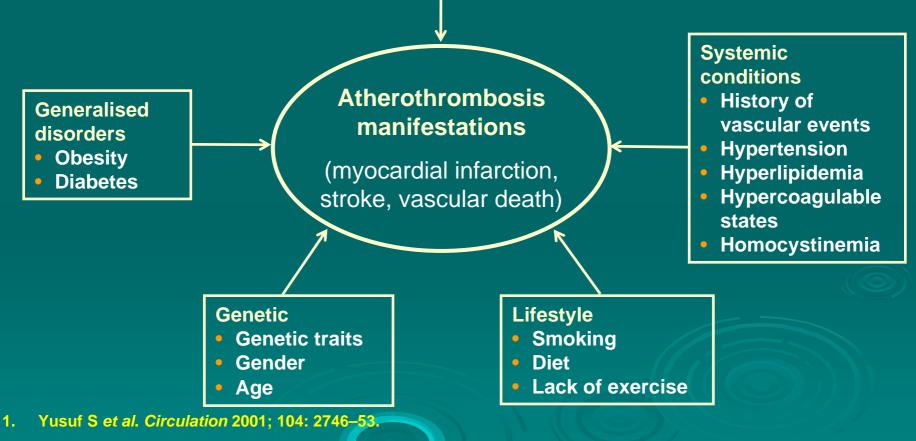


Libby P. Circulation. 1995;91:2844-2850



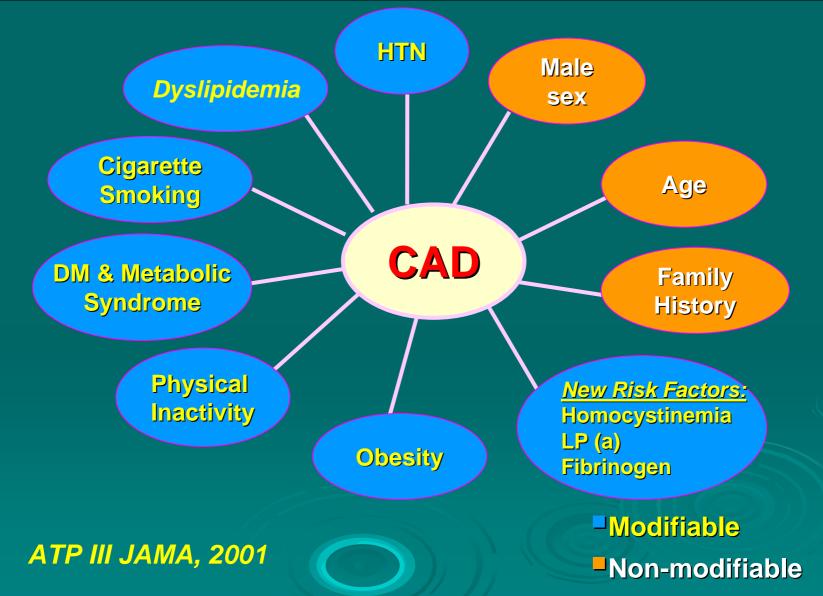
Local factors:

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



2. 2. Drouet L. Cerebrovasc Dis 2002;

## **Established Risk Factors of CAD**



# Homocysteine:

## **Role in Atherogenesis**

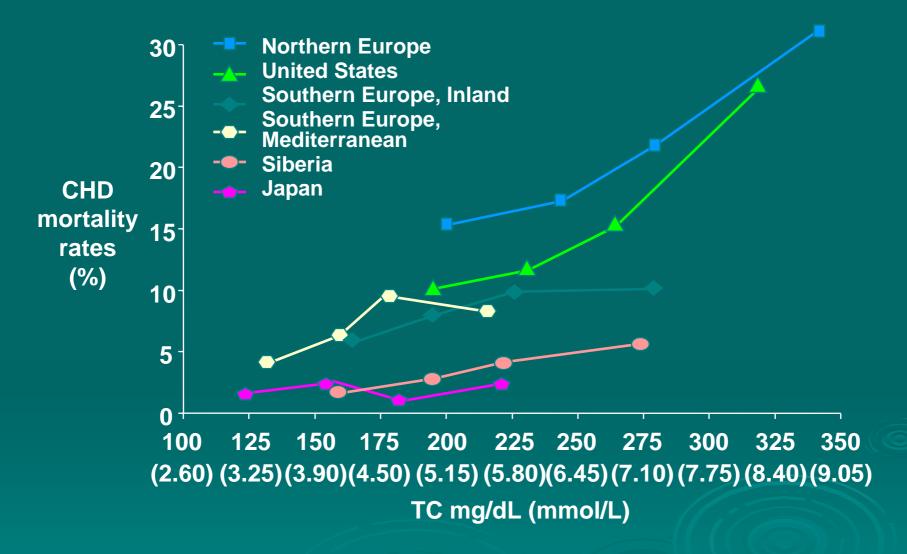
- Linked to pathophysiology of arteriosclerosis in 1969
- CVD patients have elevated levels of plasma homocysteine
- May cause vascular damage to intimal cells
- Elevated levels linked to:
  - genetic defects
  - exposure to toxins
  - diet

Increased dietary intake of folate and vitamin B6 may reduce CVD morbidity and mortality

McCully KS. *Am J Pathol.* 1969;56:111-128. McCully KS. *JAMA*. 1998;279:392-393. Rimm EB et al. *JAMA*. 1998;279:359-364.

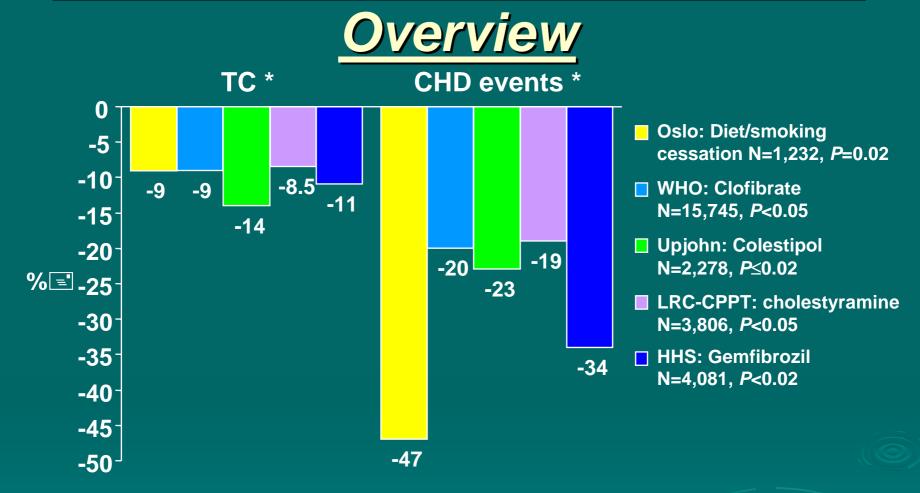


### **Cholesterol and CHD: Seven Countries Study**



Verschuren WMM et al. JAMA. 1995;274:131-136.

## **Early Primary-Prevention Trials:**



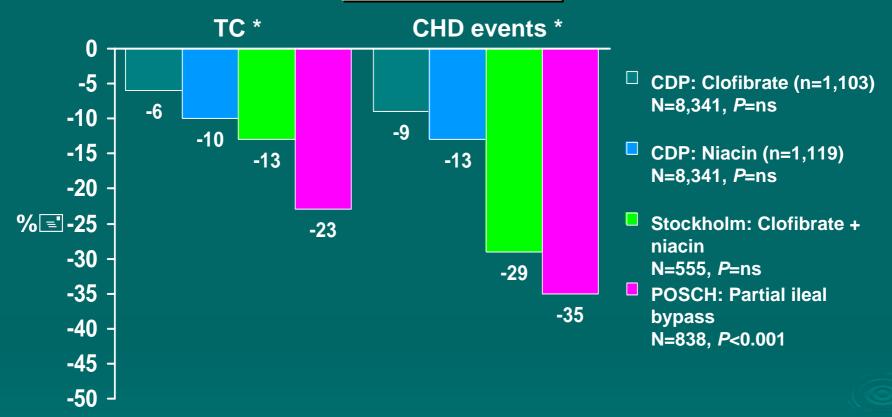
#### N=number enrolled.

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

Adapted from Levine GN et al. N Engl J Med. 1995;332:512-521.

## **Early Secondary-Prevention Trials:**

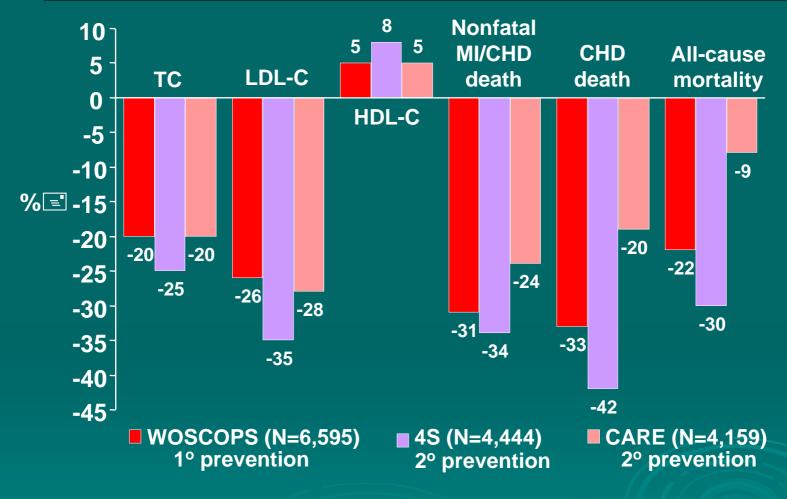
<u>Overview</u>



N=number enrolled; ns=not significant.

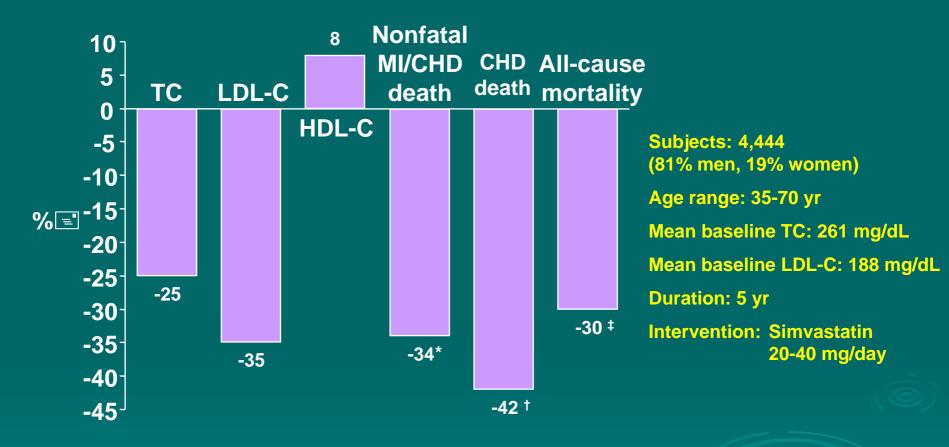
\* Net difference between treatment and control groups (*P* values are for events). Adapted from Levine GN et al. *N Engl J Med.* 1995;332:512-521.

## <u>Summary of Effects of Lipid Lowering on Lipids</u> and Clinical Events in Recent Statin Trials



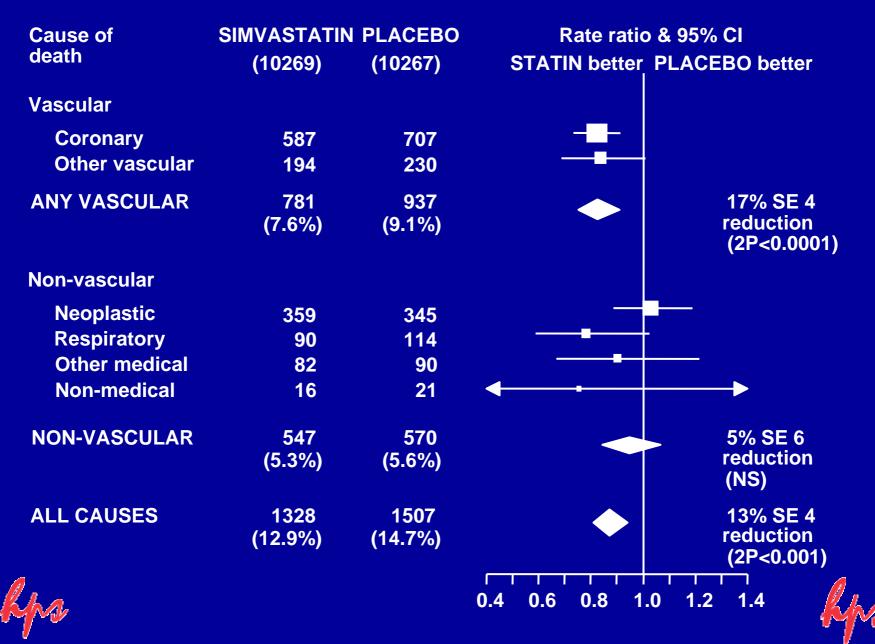
N=number enrolled.

### 4S: Effect of LDL-C Lowering on Coronary Events in Secondary Prevention Trial in Men and Women

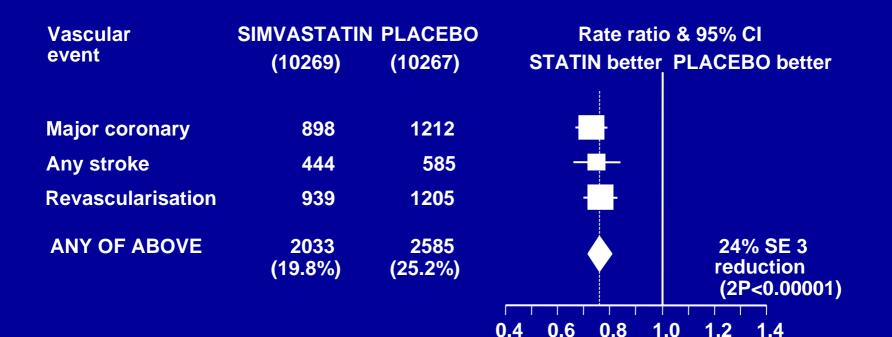


\**P*<0.00001. <sup>†</sup>95% CI: -27 to -54. <sup>‡</sup>*P*=0.003. **4S Group.** *Lancet.* **1994;344:1383-1389.** 

### **SIMVASTATIN: CAUSE-SPECIFIC MORTALITY**



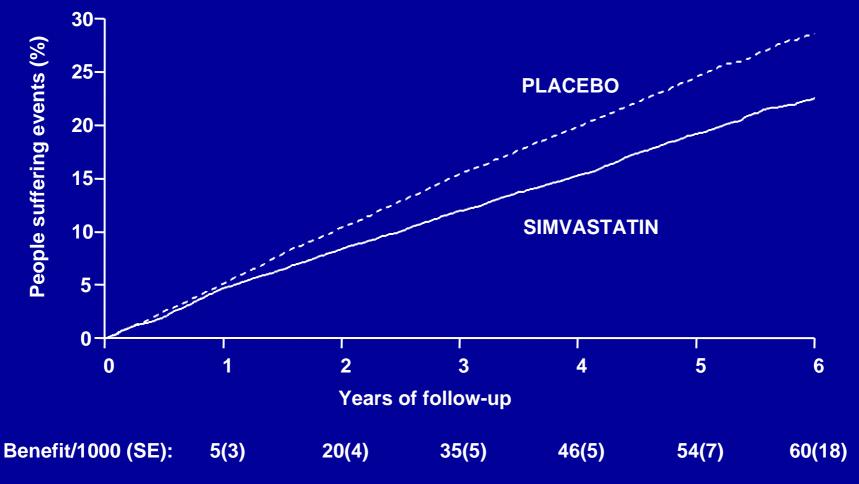
## **SIMVASTATIN: MAJOR VASCULAR EVENTS**



kps



#### SIMVASTATIN: MAJOR VASCULAR EVENT by YEAR







## 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 | " | "   | "  |
|----|---|-----|----|
| 70 |   | II. | II |
| 70 |   | II. | II |
| 70 |   | II. | 11 |

other CHD cerebrovascular disease

- other orterial diagona
- other arterial disease

diabetes (age 40+)

irrespective of cholesterol level (or age, or sex, or other treatments)





# <u>ATP III: LDL-C, HDL-C, TC</u> <u>Classification</u>

| LDL-C (mg/dL) |                     |  |
|---------------|---------------------|--|
| <100          | Optimal             |  |
| 100–129       | Above, near optimal |  |
| 130–159       | Borderline high     |  |
| 160–189       | High                |  |
| ≥190          | Very high           |  |
| HDL-C (mg/dL) |                     |  |
| <40           | Low                 |  |
| ≥60           | High                |  |
| TC (mg/dL)    |                     |  |
| <200          | Desirable           |  |
| 200–239       | Borderline high     |  |
| ≥240          | High                |  |

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*, 2001;285:2486-2497.

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

| Cholesterol level                                  | HDL-C                                 | Follow-up                            |
|--|---------------------------------------|--------------------------------------|
| Desirable blood cholesterol                        | ≥35 mg/dL                             | Repeat testing within 5 yr           |
| <200 mg/dL   | <35 mg/dL                             | Perform fasting lipoprotein analysis |
| Borderline-high blood cholesterol<br>200-239 mg/dL | ≥35 mg/dL and <2 other risk factors   | Reevaluate risk status in<br>1-2 yr  |
| -  | <35 mg/dL or<br>≥2 other risk factors | Perform fasting lipoprotein analysis |
| High blood cholesterol<br>≥240 mg/dL               |                                       | Perform fasting lipoprotein analysis |

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 1993;269:3015-3023.

## ATP III: Assessment of Risk

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.

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*, 2001;285:2486-2497.

## <u>ATP III:</u>

# **Risk Categories, LDL-C Goals**

| Risk Category  | LDL-C Goal (mg/dL) |
|--|--------------------|
| CHD and CHD risk<br>equivalents<br>(10-year risk >20%) | <100               |
| ≥2 risk factors<br>(10-year risk ≤20%)                 | <130               |
| 0–1 risk factor*                                       | <160               |

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

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 2001;285:2486-2497.

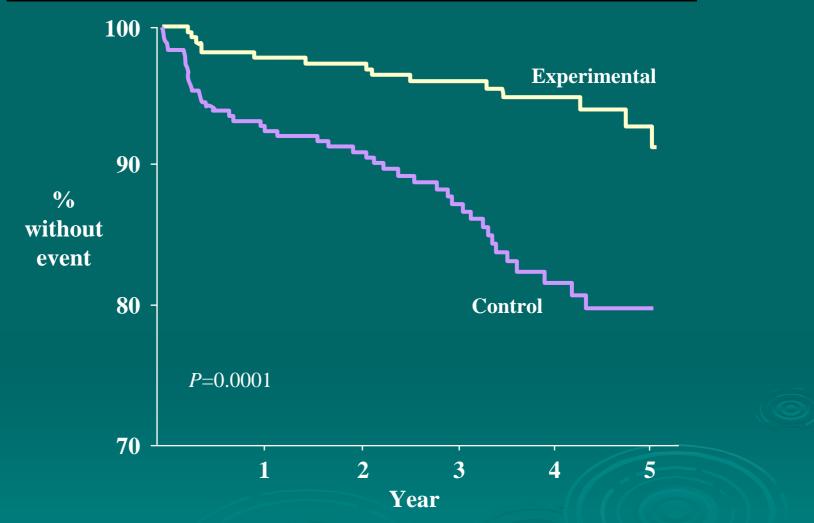
## Dietary Therapy for Elevated Blood Cholesterol

| Nutrient*   |                         | Recommended intake                       |                       |
|---|-------------------------|--|-----------------------|
|   | Step I Diet             |  | Step II Diet          |
| Total fat   | · · · · · ·             | <30% of total calories                   |                       |
| <ul> <li>Saturated fatty acids</li> </ul>           | 8-10% of total calories |  | <7% of total calories |
| <ul> <li>Polyunsaturated<br/>fatty acids</li> </ul> |                         | ≤10% of total calories                   |                       |
| <ul> <li>Monounsaturated<br/>fatty acids</li> </ul> |                         | $\leq$ 15% of total calories             |                       |
| Carbohydrates                                       |                         | $\geq$ 55% of total calories             |                       |
| Protein   |                         | ~15% of total calories                   |                       |
| Cholesterol   | <300 mg/day             |  | <200 mg/day           |
| Total calories                                      |                         | To achieve and maintain desirable weight |                       |

\*Calories from alcohol not included.

Expert Panel on Detection, Evaluation, and Treatment of High Blood cholesterol in Adults, JAMA 1993

#### <u>Lyon Diet Heart Study: Cumulative Survival</u> <u>Without Cardiac Death and Nonfatal MI</u>



de Lorgeril M et al. Circulation. 1999;99:779-785.

### LDL-C Treatment Cut points and Targets for Therapy Primary and Secondary Prevention

|   | Initiatio  | n LDL | -C target |
|---|------------|-------|-----------|
| Patient category                          | level (mg/ | dL)   | (mg/dL)   |
|   | Diet Dr    | ug    |           |
| No CHD, <2 other RF                       | ≥160 ≥1    | 90    | <160      |
| No CHD, ≥2 other RF                       | ≥130 ≥1    | 60    | <130      |
| With CHD or other atherosclerotic disease | >100 ≥1    | 30    | ≤100      |

RF = risk factors.

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. JAMA. 1993;269:3015-3023.

### ATP III:

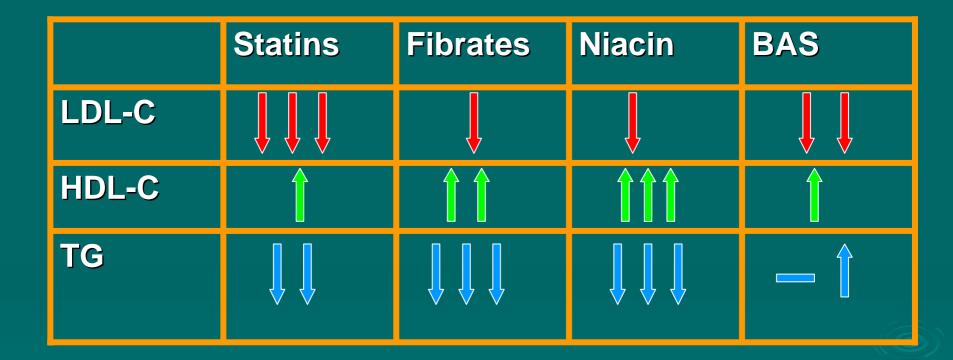
LDL-C Treatment Cutpoints for Therapy

|                              | Initiate   |  |
|------------------------------|------------|--|
| Risk Category                | TLC*       | Consider Drug Therapy  |
| CHD and CHD risk equivalents | ≥100 mg/dL | ≥130 mg/dL<br>(100–129 mg/dL: drug optional) <sup>†</sup>            |
| ≥2 risk factors              | ≥130 mg/dL | 10-year risk 10%–20%: ≥130<br>mg/dL<br>10-year risk <10%: ≥160 mg/dL |
| 0–1 risk factor              | ≥160 mg/dL | ≥190 mg/dL<br>(160–189 mg/dL: drug optional)                         |

\*Therapeutic lifestyle changes <sup>†</sup>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.

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 2001;285:2486-2497.

### **ATP III Pharmacologic Treatment**



**BAS: Bile acid sequestrant** 

## <u>ATP III:</u>

## Management of Very High LDL-C

- LDL-C ≥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

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 2001;285:2486-2497.

### ATP III:

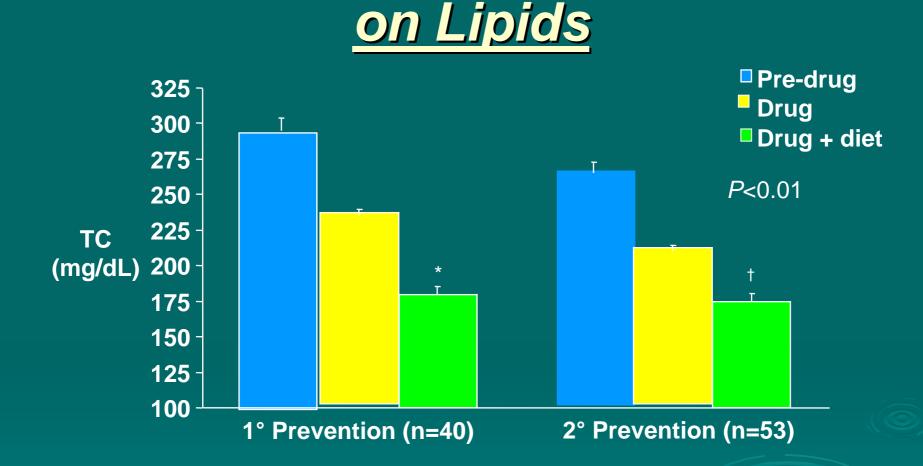
New Features of Guidelines—

### **Updated Lipid/Lipoprotein Classifications**

- Optimal LDL-C level: identified as <100 mg/dL</p>
- 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</li>
  - borderline high: 150–199 mg/dL
  - high: 200–499 mg/dL
  - very high: ≥500 mg/dL

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 2001;285:2486-2497.

### **Effects of Drug Therapy and Diet**



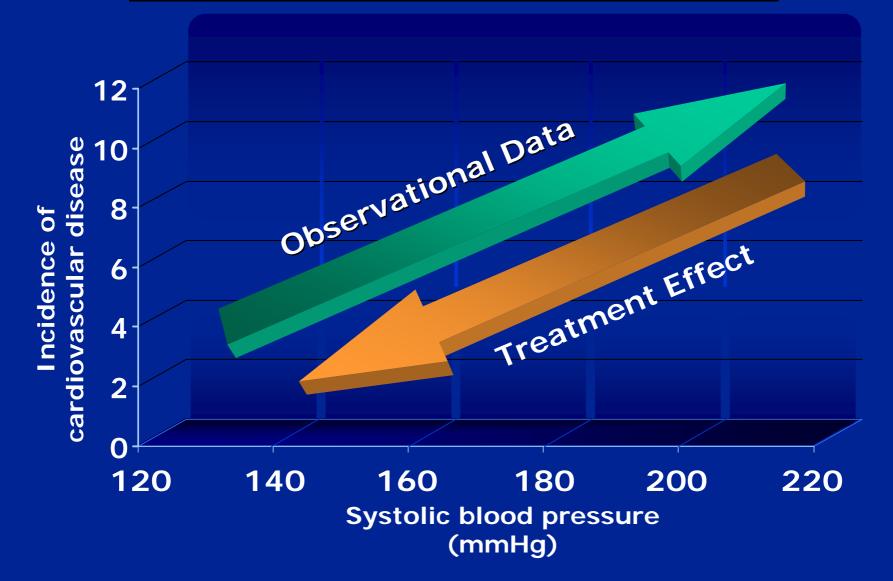
\* 84% reached NCEP LDL target (<130 mg/dL).</li>
† 63% reached NCEP LDL-C target (<100 mg/dL).</li>
Barnard RJ, et al. *Exerpta Medica Brief Reports*. 1997;1112-1114.

## **BARRIERS TO ACHIEVING RISK-FACTOR REDUCTION**

- 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



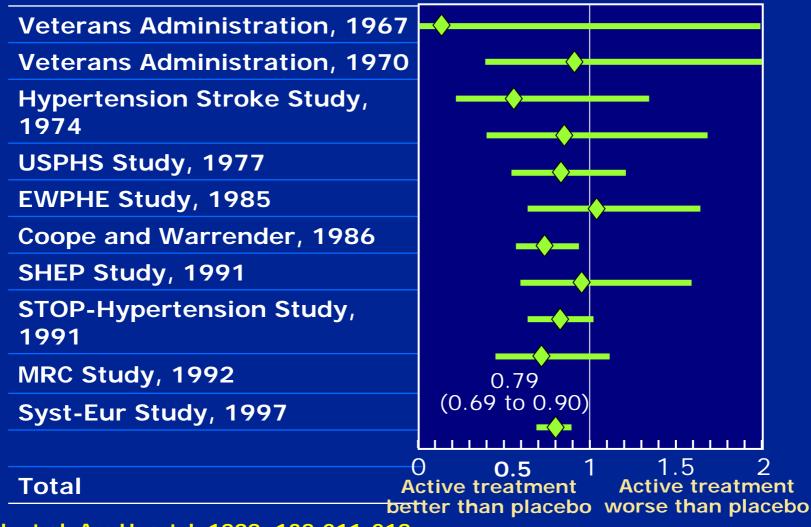
#### <u>Hypertension Treatment Effect</u> <u>Mirrors Observational Data</u>



#### **Relative Risk for Coronary Heart**

<u>Disease</u>

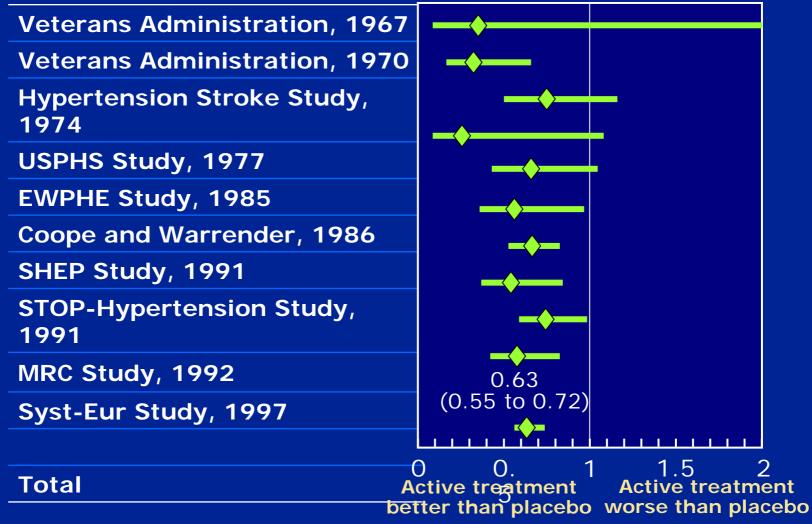
Odds ratios and 95% confidence intervals



He J, et al. Am Heart J. 1999; 138:211-219.

### **Relative Risk for Stroke**

Odds ratios and 95% confidence intervals



He J, et al. Am Heart J. 1999; 138:211-219.



## **Blood Pressure Classification**

| BP Classification    | SBP mmHg        |     | DBP mmHg     |
|----------------------|-----------------|-----|--------------|
| Normal               | <120            | and | <80          |
| Prehypertension      | 120–139         | or  | 80–89        |
| Stage 1 Hypertension | 140–159         | or  | 90–99        |
| Stage 2 Hypertension | <u>&gt;</u> 160 | or  | <u>≥</u> 100 |

#### **JNC VII JAMA 2003**



### **Benefits of Lowering BP**



|                       | Average Percent Reduction |
|-----------------------|---------------------------|
| Stroke incidence      | 35–40%                    |
| Myocardial infarction | 20–25%                    |
| Heart failure         | 50%                       |

#### **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.

**JNC VII JAMA 2003** 



### Classification and Management of BP for adults

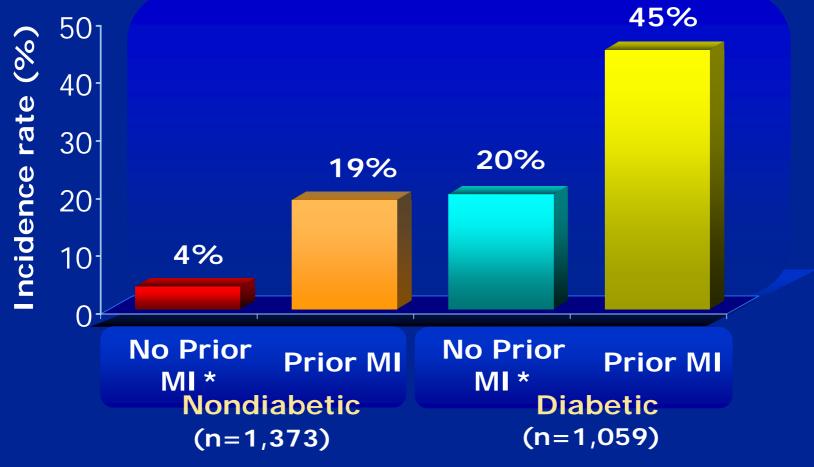
|                         | SBP*            | DBP* Lifestyle -                          |                                  | Initial drug therapy   |  |
|-------------------------|-----------------|---|----------------------------------|--|--|
| BP classification       | mmHg            | je se | Without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

\*Treatment determined by highest BP category.

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

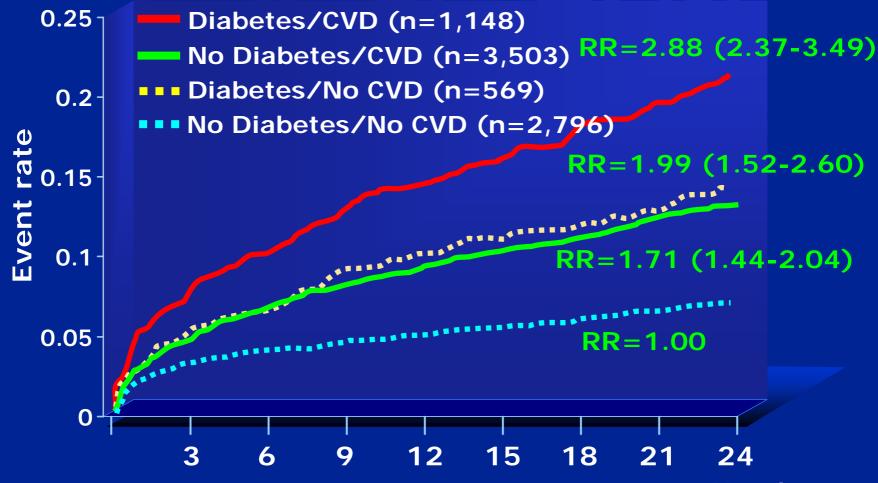
<sup>‡</sup>Treat patients with chronic kidney disease or diabetes to BP goal of <130/80 mmHg.

### <u>7-Year Incidence</u> of Fatal and Nonfatal MI



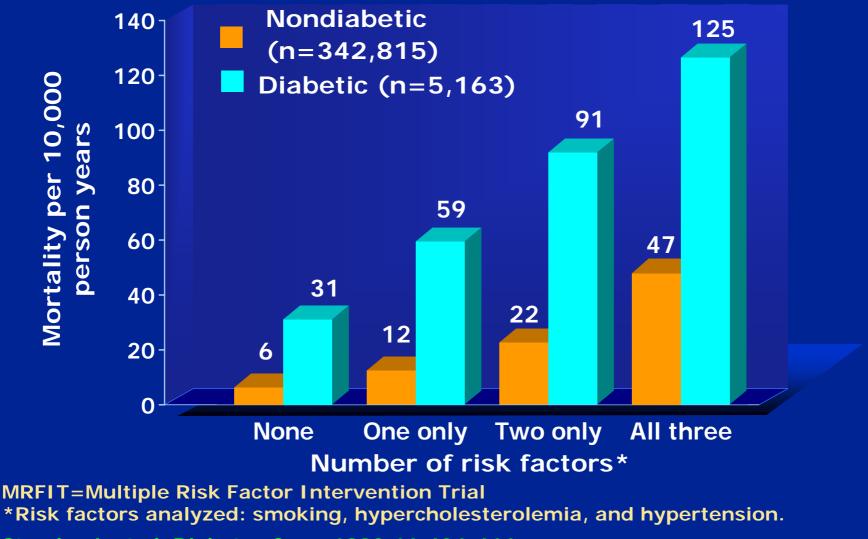
\*At baseline MI = myocardial infarction P<0.001 for prior MI vs. no prior MI and for diabetes vs. no diabetes Haffner SM, et al. N Eng J Med. 1998;339:229-234.

### <u>OASIS Study Mortality</u> by Diabetes and CVD Status



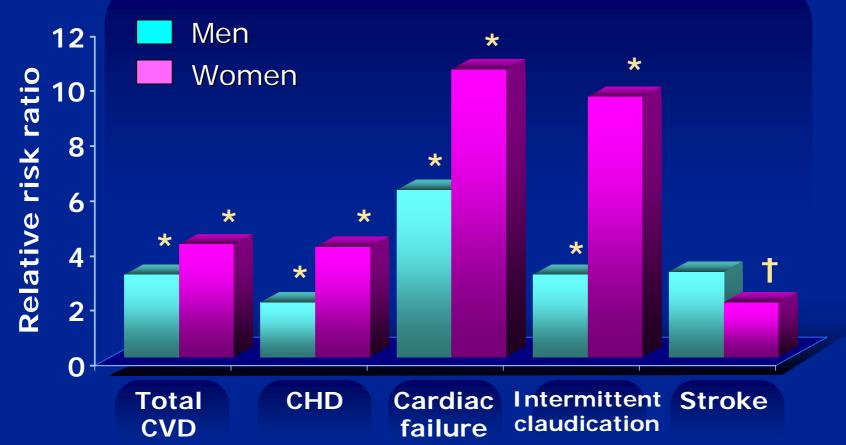
OASIS=Organization to Assess Strategies for Ischemic Syndromes Months CVD=cardiovascular disease RR=relative risk (95% confidence intervals) Malmberg K, et al. Circulation. 2000;102:1014-1019.

#### <u>Impact of Diabetes on</u> <u>Cardiovascular Mortality in MRFIT</u>



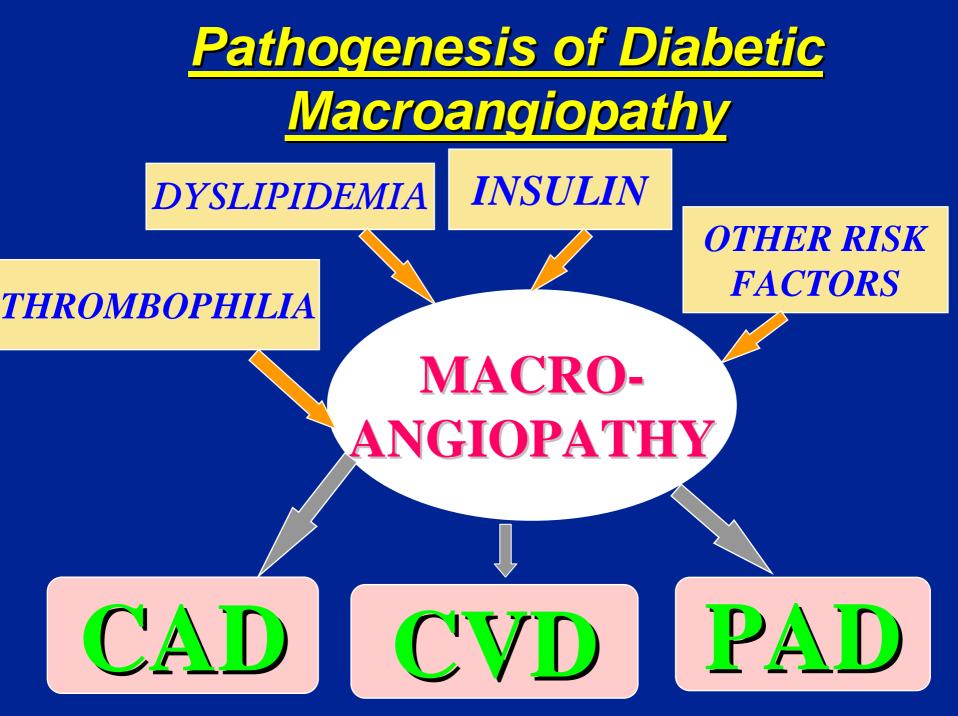
Stamler J, et al. Diabetes Care. 1993;16:434-444.

### <u>Framingham Heart Study</u> <u>CVD Events in Diabetics</u>



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

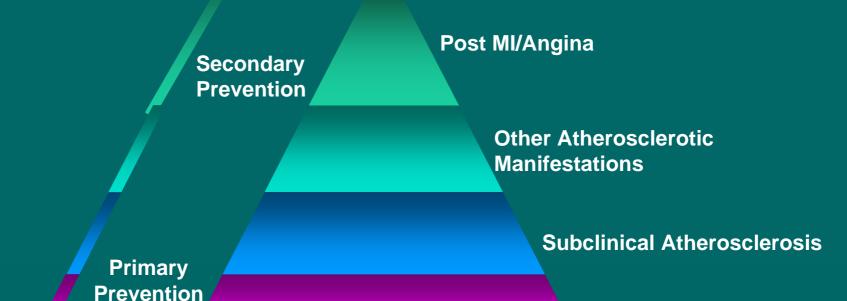
Wilson PWF, Kannel WB. In: Hyperglycemia, Diabetes and Vascular Disease. Ruderman N, et al. eds. Oxford;1992.





- 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

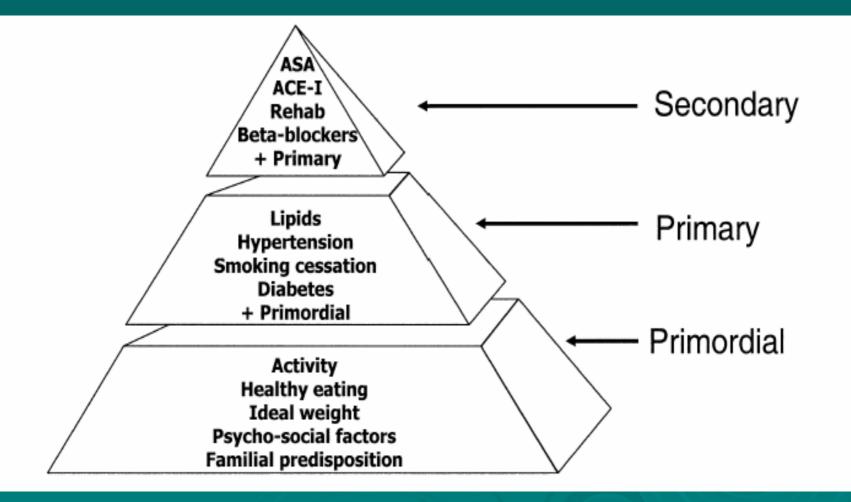


**Multiple Risk Factors** 

Low Risk

**Courtesy of CD Furberg.** 

## **CVD Prevention Pyramid**



## <u>ACC Guidelines 2001 For</u> <u>Prevention of Atherosclerosis</u>

| Goals  | Intervention Recommendations  |
|--|---|
| Smoking:<br>complete cessation   | 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.  |
| BP control:<br><140/90 mm Hg or<br><130/85 mm Hg if<br>heart failure or renal<br>insufficiency<br><130/80 mm Hg if<br>Diabetes | Initiate lifestyle modification in all patients<br>with blood pressure >130 mm Hg systolic or<br>80 mm Hg diastolic.<br>Add blood pressure medication,<br>individualized to other patient requirements<br>and characteristics (ie, age, race, need for<br>drugs with specific benefits) |

## <u>ACC Guidelines 2001 For</u> <u>Prevention of Atherosclerosis</u>

| Goals   | Intervention Recommendations   |
|---|--|
| Lipid management:<br>Primary goal<br>LDL ,100 mg/dL | Start dietary therapy in all patients<br>Promote physical activity and weight management.<br>Assess fasting lipid profile in all patients Add drug<br>therapy according to the following guide:<br>>LDL< 100 mg/DI No LDL-lowering therapy               |
|   | <ul> <li>&gt;LDL 100–129 mg/dL Therapeutic options:</li> <li>statin or resin</li> <li>Fibrate or niacin (if low HDL orhigh TG)</li> <li>Consider combined drug therapy</li> <li>&gt;LDL &gt;130 mg/dL</li> <li>Intensify LDL-lowering therapy</li> </ul> |
|   | <ul> <li>Add or increase drug therapy</li> <li>with lifestyle therapies</li> </ul>   |

## <u>ACC Guidelines 2001 For</u> Prevention of Atherosclerosis

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

## <u>ACC Guidelines 2001 For</u> <u>Prevention of Atherosclerosis</u>

| Goals                                     | Intervention Recommendations  |
|---|---|
| Weight management:<br>BMI 18.5–24.9 kg/m2 | <ul> <li>Calculate BMI and measure waist circumference</li> <li>Monitor response of BMI and waist circumference to therapy.</li> <li>Start weight management and physical activity as appropriate. When BMI \$25 kg/m2, goal for waist circumference is &lt;40 inches in men and &lt;35 inches in women.</li> </ul> |
| Diabetes<br>management:<br>Goal HbA1c ,7% | <ul> <li>Appropriate hypoglycemic therapy to achieve near-<br/>normal fasting plasma glucose, as indicated by HbA1c.</li> <li>Treatment of other risks (e g, physical activity, weight<br/>management, blood pressure, and cholesterol<br/>management).</li> </ul>  |

# ACC Guidelines 2001 For

### **Prevention of Atherosclerosis**

| Goals                                   | Intervention Recommendations   |
|---|--|
| Antiplatelet agents/<br>anticoagulants: | <ul> <li>Start and continue indefinitely aspirin 75 to 325 mg/d if<br/>not contraindicated.</li> <li>Consider clopidogrel 75 mg/d or warfarin if aspirin<br/>contraindicated. Manage warfarin to INR 2-3 for those not<br/>able to take aspirin or clopidogrel.</li> </ul> |
| ACE inhibitors:                         | <ul> <li>Treat all patients indefinitely post MI; start early in stable high-risk patients (anterior MI, previous MI, Killip class II)</li> <li>Consider chronic therapy for all other patients with coronary or other vascular disease unless contraindicated.</li> </ul> |
| B-Blockers:                             | <ul> <li>Start in all post-MI and acute ischemic syndrome patients. Continue indefinitely. Observe usual contraindications.</li> <li>Use as needed to manage angina, rhythm, or BP in all other patients.</li> </ul>   |

## 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

1. American Heart Association. 2002 Heart and Stroke Statistical Update. AHA, 2002

## 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 Bblocker 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



