Chronic ischemic heart disease
Background

- Acute MI is the leading cause of death in North America and Europe. Each year, an estimated 785,000 Americans will sustain a new MI, and another 470,000 will have a recurrent MI.
- An American has an acute MI every 25 seconds, and someone dies of an MI every minute.
- In 2007, Coronary Heart Disease caused one out of every six deaths.
CVD and other major causes of death in US 2013

Chart 13-9. Cardiovascular disease and other major causes of death for all males and females (United States: 2013). A indicates cardiovascular disease (International Classification of Diseases, 10th Revision codes I00–I99); B, cancer (C00–C97); C, accidents (V01–X59 and Y85–Y86); D, chronic lower respiratory disease (J40–J47); E, diabetes mellitus (E10–E14); and F, Alzheimer disease (G30). Source: National Center for Health Statistics and National Heart, Lung, and Blood Institute.
Death rates attributable to CV dz, 2000-2013

Chart 2-14. US age-standardized death rates* attributable to cardiovascular diseases, 2000 to 2013. CHD indicates coronary heart disease; and CVD, cardiovascular disease. *Directly standardized to the age distribution of the 2000 US standard population. †Total CVD: International Classification of Diseases, 10th Revision (ICD-10) I00 to I99, Q20 to Q28. §Stroke (all cerebrovascular disease): ICD-10 I60 to I69. ¶CHD: ICD-10 I20 to I25. **Other CVD: ICD-10 I00 to I15, I26 to I51, I70 to I78, I80 to I89, I95 to I99. Source: Centers for Disease Control and Prevention, National Center for Health Statistics.
Chart 3-3. Long-term trend in current cigarette smoking prevalence (%) for adults ≥18 years of age by sex (National Health Interview Survey [NHIS], 1965-2014, selected years). Data derived from the Centers for Disease Control and Prevention/National Center for Health Statistics, Health, United States, 2014 (NHIS).a


↓ Smoking  ↑ Obesity
Tobacco ban for people born after the year 2000 passes Tasmanian upper house

Doctors vote for ban on UK cigarette sales to those born after 2000

British Medical Association hails vote as step towards achieving goal of a tobacco-free society by 2035, but critics call it 'illiberal'
What is ischemia?

- Blood supply ≠ Blood demand
- Leading cause is obstructive CAD (plaque formation in response to inflammation)
Other (Type II) causes of ischemia

- Anemia: Transfuse to hemoglobin of 10
- HTN: Important cause of subendocardial ischemia
- Tachycardia: Decrease HR below 100 bpm before ordering echo
- Sepsis: Demand ischemia
- Aortic stenosis: Pressure overload
- Volume overload: Decreased coronary perfusion pressure
Factors affecting supply/demand

1. Heart Rate
2. Coronary Tone
3. Intraluminal obstruction/plaque
4. Coronary Perfusion Pressure
   (AoDP – LVEDP)
Pathophysiology: AS

- Valve obstruction → ↑intraventricular pressure to maintain CO
- Ventricular wall hypertrophy (to reduce wall stress)
- LVH → ↓Compliance, Impaired passive filling, ↑preload dependence on atrial contraction
- ↑LVEDP → Subendocardial ischemia (↓myocardial perfusion pressure)
- Progressive valvular obstruction & increasing wall stress
- Angina, Syncope, Dyspnea → ↑Filling pressure, ventricular dilatation, contractile dysfunction, ischemia, arrhythmia
Abnormalities Evolving During Myocardial Ischemia

- Symptoms occur at end of ischemic cascade
- Approximately 50% of patients with angina also experience episodes of asymptomatic (silent) ischemia
- Many episodes of ischemia never become painful

Dual Goals for Management of Stable Ischemic Heart Disease (SIHD)

- Prevent MI and Death (Disease Modification) → Survival
- Reduce Ischemia and Relieve Anginal Symptoms → Symptoms
Patients with stable CAD are still at risk of cardiovascular events

**REACH registry**

Annual event rates in stable CAD outpatients (n=38602), 1-year follow-up

- **Non-fatal MI**: 1.4%
- **UA**: 6.44%
- **CABG**: 1.4%
- **PCI**: 3.8%
- **CHF**: 4.9%
- **CV death**: 1.8%
- **Death/MI/Stroke/Hosp**: 15.2%

3 of 20 patients with established CAD had a major event or had been hospitalized within a year.

Goals for Therapy in SIHD, 2016
Reduce/stabilize atherosclerotic plaque (ACS/MI/SCD)

- Antiplatelet Therapy: ASA 81, ADP antagonist if recent ACS or stent
- ACEI / ARB (esp if DM, HF, EF < 40%, HTN)
- Statin – High intensity - ↓↓ LDL by > 50%
  - Atorvastatin 40-80mg,
  - Rosuvastatin 20-40mg
- Secondary Prevention Measures
  - Smoking cessation
  - BP < 140/90
  - HbA1c < 7%
  - BMI = 18.5-24.9
  - Physical Exercise: 30-60 min ≥ 5 days / week
  - Influenza Vaccine
Goals of Therapy in SIHD, 2016
Reduce Symptoms

- Medications to reduce HR, BP, contractility, preload
  - B-blockers
  - Ca++ blockers
  - Nitrates
  - Ivabradine

- Medication that affect myocardial calcium homeostasis
  - Ranolazine
Ivabradine in Stable Coronary Artery Disease without Clinical Heart Failure

Kim Fox, M.D., Ian Ford, Ph.D., Philippe Gabriel Steg, M.D., Jean-Claude Tardif, M.D., Michal Tendera, M.D., and Roberto Ferrari, M.D., for the SIGNIFY Investigators*

Presented at ESC Congress 2014 Hotline 2

ABSTRACT

BACKGROUND
An elevated heart rate is an established marker of cardiovascular risk. Previous analyses have suggested that ivabradine, a heart-rate–reducing agent, may improve outcomes in patients with stable coronary artery disease, left ventricular dysfunction, and a heart rate of 70 beats per minute or more.
Ivabradine in Stable Coronary Artery Disease without Clinical Heart Failure

Kim Fox, M.D., Ian Ford, Ph.D., Philippe Gabriel Steg, M.D., Jean-Claude Tardif, M.D., Michal Tendera, M.D., and Roberto Ferrari, M.D.,

- 19,102 patients who had both stable CAD without clinical heart failure and a heart rate of 70 beats per minute or more.

- After a median follow-up of 27.8 months, there was no significant difference between the ivabradine group and the placebo group in the incidence of the primary end point, death from CV causes and nonfatal Myocardial Infarction.
Effect of ivabradine on symptoms

(angina population: CCS class ≥ II, n=12,049)

**Elective revascularization**
- Ivabradine 2.8%
- Placebo 3.5%
- HR 0.82 (p=0.058)

*P < 0.01*

Ranolazine: Mechanism of Action

- Ischemia
  - $\uparrow$ Late $I_{Na}$
    - Na$^+$ Overload
      - Ca$^{++}$ Overload
        - Diastolic relaxation failure (Increased diastolic tension)
        - Extravascular compression
  - Ranolazine: Inhibits the late inward Na$^+$ current
Patient-reported angina severity before and after taking ranolazine

N = 92 respondents

Patient-reported changes in quality of life on the Patient Global Impression of Change scale since initiating ranolazine treatment.

Optimize risk factors to prolong life.

Optimal medical therapy should be given for all patient whether they have epicardial disease or not, but whether they have angina and ischemic symptoms. (Microvascular disease)

Relieve symptoms, individualized for patient. Trial and error is needed. Constant reassessment of symptoms and side-effects is required because “stable” ischemic heart disease is actually a dynamic disease.
Ischemic Heart Disease in Women

Less obstructive CAD in women undergoing angiography vs. men

Patients undergoing elective diagnostic angiography for angina

Women | Men
---|---
<40  | 40-49  | 50-59  | 60-69  | 70-79  | >79  
0% | 0% | 0% | 0% | 0% | 0%  
20% | 20% | 20% | 20% | 20% | 20%  
40% | 40% | 40% | 40% | 40% | 40%  
60% | 60% | 60% | 60% | 60% | 60%  
80% | 80% | 80% | 80% | 80% | 80%  
100% | 100% | 100% | 100% | 100% | 100%  

Percent of patients with >50% stenosis

Age (years)

ACC-National Cardiovascular Data Registry™. J Am Coll Cardiol. 2006

Women with ACS more likely to have “normal” coronary arteries than men

Table. Prevalence of “Normal” and Nonobstructive Coronary Arteries in Women Compared With Men

<table>
<thead>
<tr>
<th></th>
<th>No/Total (%)</th>
<th></th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Women</td>
<td>Men</td>
<td></td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>343/1768 (19.4)</td>
<td>394/4638 (8.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>TIMI 1b</td>
<td>95/555 (17)</td>
<td>99/1091 (9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Unstable angina²</td>
<td>252/826 (30.5)</td>
<td>222/1580 (13.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>TIMI IIIa³</td>
<td>30/113 (26.5)</td>
<td>27/278 (8.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>MI without ST-segment elevation²</td>
<td>41/450 (9.1)</td>
<td>55/1299 (4.2)</td>
<td>.001</td>
</tr>
<tr>
<td>MI with ST-segment elevation²</td>
<td>50/492 (10.2)</td>
<td>119/1789 (6.8)</td>
<td>.02</td>
</tr>
</tbody>
</table>

Abbreviations: GUSTO, Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries; MI, myocardial infarction; TIMI, Thrombolysis In Myocardial Infarction.

JAMA. January 26, 2005, Vol 293, No. 4
Ischemic Heart Disease in Women

- Coronary *dysfunction* relative to obstruction
- Vasospasm
- Endothelial dysfunction
- Microvascular dysfunction

*(60% of total coronary blood flow)*
Microvascular dysfunction assessed by positron emission tomography (PET)

Non-obstructive CAD

MACE 57/901, follow up 1.5 years

<table>
<thead>
<tr>
<th>CAC 0</th>
<th>CAC 1-399</th>
<th>CAC ≥400</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=214</td>
<td>188</td>
<td>163</td>
</tr>
<tr>
<td>1.4%</td>
<td>5.2%</td>
<td>4.8%</td>
</tr>
<tr>
<td>1.8%</td>
<td>7.5%</td>
<td>3.6%</td>
</tr>
</tbody>
</table>

P=0.24, CAC
P=0.002, CFR

Image from Prof. P. Camici

Ischemic Heart Disease in Women

Coronary Angiograms for Patients with Chest Pain
Women are more likely to have minor or no obstruction

Diffuse atherosclerosis
Most often seen in younger women with IHD

Obstructive atherosclerosis
Most often seen in men and older women

Generalized narrowing

Generalized pressure drop

Localized stenosis
Sudden pressure drop

Pressure

Pressure

Adapted with permission from (K. Lance Gould, 1999).
Case Presentation

- 54 year old post menopausal female presented to the ER with prolonged chest pain x 12 hour at rest
- PMH:
  - Gestational DM
  - HTN
  - Dyslipidemia
- Family history: father with stroke at 59, and MI at 66
- Meds: HRT, HCTZ 12.5mg daily
Case presentation

- **Vitals:** BP: 150/65, HR: 62, O2sat: 100% on RA, BMI: 31 kg/m2
- **Physical exam:** Unremarkable cardio-pulmonary exam
- **Troponin I:** 2.98 →4.29→2.64
- **Fasting lipids:** TC 164, LDL 95, HDL 50, TG 93
- **Rest Myocardial Perfusion SPECT:** 3% perfusion defect of the anterior wall
- **Echo:** Normal LV function, LVEF 64%, no WMA, mild diastolic dysfunction
- **Coronary angiogram:** LVEDP 19, no obstructive CAD, no vasospasm or myocardial bridging reported
What is the Diagnosis?

1. Non-cardiac
2. Pericarditis or myocarditis
3. Ischemic heart disease (IHD) s/p ACS/AMI
Should she have any further evaluation?

- 1. Nothing further is needed
- 2. Stress testing
- 3. Coronary flow reserve testing
Coronary Reactivity Testing

**Baseline**
- mid LAD bridging and minimal plaque on IVUS

**Adenosine**
- CFR 1.8, adenosine-induced vasoconstriction, chest pain but no ST-T changes
  - Normal CFR is > 2.5

**Nitroglycerin**
- Resolution of vasoconstriction
  - LVEDP = 18
How should she be treated?

- 1. Current treatment is fine
- 2. Treatment for pericarditis or myocarditis
- 3. Start ACS guidelines medication (ASA, bb, ACEi/ARB and high intensity statin) and angina management
Case presentation Conclusion after CRT

- **DX**
  - Ischemic Heart Disease with coronary microvascular dysfunction and epicardial coronary vasospasm
  - Mid-LAD bridging without any significant systolic compression
  - NSTEMi with nonobstructive CAD
  - Diastolic dysfunction

- **RX**
  - ASA 81mg
  - Amlodipine 5mg daily
  - Coreg 3.125mg bid
  - Atorvastatin 80mg daily
  - Quinapril 40mg daily
  - sL NTG prn
  - HCTZ
  - Stop HRT
  - Cardiac Rehab
Thank you!!!
Beta-Blocker Use: CV Death, Nonfatal MI, Nonfatal Stroke in Patients with Known CAD but Without MI

REACH Registry

[Graph showing event rate for primary outcome with beta-blocker vs. no beta-blocker]

CHARISMA Trial

<table>
<thead>
<tr>
<th>Outcome</th>
<th>B-blocker Better</th>
<th>B-blocker Worse</th>
<th>HR (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Outcome</td>
<td>1.06</td>
<td>0.82</td>
<td>1.38</td>
<td>0.640</td>
</tr>
<tr>
<td>All-cause Mortality</td>
<td>0.93</td>
<td>0.67</td>
<td>1.30</td>
<td>0.672</td>
</tr>
<tr>
<td>CV Mortality</td>
<td>0.83</td>
<td>0.54</td>
<td>1.27</td>
<td>0.389</td>
</tr>
<tr>
<td>MI</td>
<td>1.11</td>
<td>0.66</td>
<td>1.87</td>
<td>0.692</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.12</td>
<td>0.79</td>
<td>1.60</td>
<td>0.525</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>1.06</td>
<td>0.87</td>
<td>1.29</td>
<td>0.580</td>
</tr>
</tbody>
</table>

[Table showing numbers at risk by study group]

# Meta-Analysis: β-Blockers, Calcium Channel Blockers, and Nitrates for Stable Angina

<table>
<thead>
<tr>
<th></th>
<th>Cardiac Death</th>
<th>Angina Episodes</th>
<th>Nitro Use</th>
<th>Total Exercise Time</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>β-blockers vs. CCB</strong></td>
<td>0.97 (0.67-1.38)</td>
<td>-0.31 (-0.62-0.0)</td>
<td>-0.14 (-0.41-0.32)</td>
<td>-0.10 (-0.20-0.0)</td>
</tr>
<tr>
<td>(72 trials)</td>
<td><em>P</em>=0.97</td>
<td><em>P</em>=0.06</td>
<td><em>P</em>=0.32</td>
<td><em>P</em>=0.06</td>
</tr>
<tr>
<td><strong>Long-acting nitrates vs. CCB</strong></td>
<td>NA</td>
<td>0.52 (-0.12-0.60)</td>
<td>-0.19 (-0.50-0.11)</td>
<td>-0.11 (-0.36-1.40)</td>
</tr>
<tr>
<td>(12 trials)</td>
<td></td>
<td><em>P</em>=0.10</td>
<td><em>P</em>=0.22</td>
<td><em>P</em>=0.39</td>
</tr>
<tr>
<td><strong>Nitrates vs. β-blocker</strong></td>
<td>1.0 (0.21-4.70)</td>
<td>-0.83 (-4.70-3.10)</td>
<td>-1.90 (-0.40-0.20)</td>
<td>0.29 (-0.90-0.32)</td>
</tr>
<tr>
<td>(6 trials)</td>
<td>*P&gt;*0.99</td>
<td><em>P</em>=0.68</td>
<td><em>P</em>=0.08</td>
<td><em>P</em>=0.29</td>
</tr>
</tbody>
</table>

*Reference: 1.0.

†Reference: 0.0

Case presentation conclusion after CRT

- Final Diagnosis:
  - Ischemic Heart Disease with coronary microvascular dysfunction and epicardial coronary vasospasm
  - Mid-LAD bridging without any significant systolic compression
  - NSTEMI with nonobstructive CAD
  - Diastolic Dysfunction
Which patients with SIHD are candidates for revascularization with either CABG or PCI?

- Survival advantage
  - Left main or complex CAD
  - >50% stenosis of LM
  - >70% in 3 major coronary arteris
  - >70% in prox LAD and one other major coronary
  - Survivor of SCD (presumed ischemia-mediated VT from >70% stenosis in major coronary artery)

- To relieve sx if persist despite OMT
  - All the above patients, plus other patient with >70% stenosis in ≥ 1 coronary artery
Case presentation

- Patient was diagnosed with an NSTEMI with no obstructive CAD
- Differential diagnosis:
  - Coronary vasospasm
  - Myocarditis
  - Coronary microvascular dysfunction
- Her symptoms persisted and she was referred to the tertiary heart center for further evaluation 2 months post ACS
Coronary Reactivity Testing

### Diagnostic test in suspected vasospastic Angina

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>A</th>
</tr>
</thead>
<tbody>
<tr>
<td>An ECG is recommended during angina if possible.</td>
<td>I</td>
<td>C</td>
<td>I</td>
</tr>
<tr>
<td>Coronary arteriography is recommended in patients with characteristic episodic resting chest pain and ST-segment changes that resolve with nitrates and/or calcium antagonists to determine the extent of underlying coronary disease.</td>
<td>I</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Ambulatory ST-segment monitoring should be considered to identify ST-deviation in the absence of an increased heart rate.</td>
<td>IIA</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Intracoronary provocative testing should be considered to identify coronary spasm in patients with normal findings or non obstructive lesions on coronary arteriography and the clinical picture of coronary spasm to diagnose the site and mode of spasm.</td>
<td>IIA</td>
<td>C</td>
<td></td>
</tr>
</tbody>
</table>

### Investigation in patients with suspected coronary Microvascular disease

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise or dobutamine echocardiography should be considered in order to establish whether regional wall motion abnormalities occur in conjunction with angina and ST-changes.</td>
<td>IIA</td>
<td>C</td>
<td>I</td>
</tr>
<tr>
<td>Transthoracic doppler echocardiography of the LAD with measurement of diastolic coronary blood flow following intravenous adenosine and at rest may be considered for non invasive measurement of coronary flow reserve.</td>
<td>IIB</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Intracoronary acetylcholine and adenosine with Doppler measurements may be considered during coronary arteriography, if the arteriogram is visually normal, to assess endothelium dependent and non-endothelium dependent coronary flow reserve, and detect microvascular/epicardial vasospasm.</td>
<td>IIB</td>
<td>C</td>
<td></td>
</tr>
</tbody>
</table>

FFR = fractional flow reserve; LAD = left anterior descending.

* Class of recommendation.

** Level of evidence.
Revascularization of SCAD Patients of OMT

<table>
<thead>
<tr>
<th>Indication</th>
<th>To improve prognosis:</th>
<th>To improve symptoms persistent on OMT:</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Heart Team approach to revascularization is recommended in patients with unprotected left main, 2-3 vessel disease, diabetes or comorbidities.</td>
<td>Class A Level C Class A Level C</td>
<td>Reference 266, 426-428</td>
</tr>
<tr>
<td>Left main &gt;50% diameter stenosis.</td>
<td>Class A Level A Class A Level A</td>
<td>Reference 172</td>
</tr>
<tr>
<td>Any proximal LAD &gt;50% diameter stenosis.</td>
<td>Class A Level A Class A Level A</td>
<td>Reference 172</td>
</tr>
<tr>
<td>2-3 vessel disease with impaired LV function / CHF.</td>
<td>Class B Level IIa Class B Level B</td>
<td>Reference 172</td>
</tr>
<tr>
<td>Single remaining vessel (&gt;50% diameter stenosis).</td>
<td>Class C Level A Class A Level A</td>
<td>Reference 172</td>
</tr>
<tr>
<td>Proven large area of ischaemia (&gt;10% LV)</td>
<td>Class B Level B Class B Level B</td>
<td>Reference 172</td>
</tr>
<tr>
<td>Any significant stenosis with limiting symptoms or symptoms non responsive/intolerant to OMT.</td>
<td>NA NA Class A Level A</td>
<td>Reference 172</td>
</tr>
<tr>
<td>Dyspnoea/cardiac heart failure with &gt;10% ischaemia/viability supplied by stenosis &gt;50%.</td>
<td>IIIb B&lt;ref, 418&gt; IIa Level B</td>
<td>Reference 172</td>
</tr>
<tr>
<td>No limiting symptoms with OMT in vessel other than left main or proximal LAD or single remaining vessel or vessel subtending area of ischaemia &lt;10% of myocardium or with FFR &gt;0.80.</td>
<td>III Level A Class III Level C</td>
<td>Reference 23, 25, 172, 400</td>
</tr>
</tbody>
</table>
Percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) in stable coronary artery disease without left main coronary artery involvement.

Number of coronary arteries with relevant stenosis* in proximal segment

1 or 2 vessel disease

Proximal LAD involvement

No

Yes

3 vessel disease

Syntax score ≤22

Syntax score ≥23

Heart Team Discussion®

Low surgical risk

PCI

CABG

Task Force Members et al. Eur Heart J 2013;eurheartj.eht296
Beta-Blocker Use: CV Death, Nonfatal MI, Nonfatal Stroke in Patients with Known CAD but Without MI

- Reach Registry showed no difference in outcomes in patient's with known CAD but no history of MI
- Charisma Trial also supports no difference if no h/o MI
- Post-MI patients with SIHD benefit from BB
Other Considerations when picking an anti-angina drug

- Carvedilol had improved HbA1C compared to Metoprolol in diabetics
- Ranexa significantly reduced HbA1c in patients with DM and CAD

### Definitions of risk for various test modalities

<table>
<thead>
<tr>
<th>Test Modalities</th>
<th>High Risk</th>
<th>Intermediate Risk</th>
<th>Low Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise stress ECG</td>
<td>CV mortality &gt; 2%/year.</td>
<td>CV mortality between 1 and 3%/year.</td>
<td>CV mortality &lt; 1%/year.</td>
</tr>
<tr>
<td>Ischaemia imaging</td>
<td>Area of ischaemia &gt; 10% (&gt;10% for SPECT; limited quantitative data for CMR = probably ≥2/16 segments with new perfusion defects or ≥2 dobutamine-induced dyssynchronous segments; ≥5 segments of LV by stress echo).</td>
<td>Area of ischaemia between 1 to 10% or any ischaemia less than high risk by CMR or stress echo.</td>
<td>No ischaemia.</td>
</tr>
<tr>
<td>Coronary CTA</td>
<td>Significant lesions of high risk category (three-vessel disease with proximal stenoses, LM, and proximal anterior descending CAD).</td>
<td>Significant lesions in large and proximal coronary artery(s) but not high risk category.</td>
<td>Normal coronary artery or plaques only.</td>
</tr>
</tbody>
</table>

CAD = coronary artery disease; CMR = cardiac magnetic resonance; CTA = computed tomography angiography; CV = cardiovascular; ECG = electrocardiogram; ICA = invasive coronary angiography; LM = left main; PTP = pre-test probability; SPECT = single photon emission computed tomography.
Annual Number of US Adults Diagnosed with Myocardial Infarction and fatal CHD by age and sex 1987-2004

Source: Adapted from Rosamond et al. Heart Disease and Stroke Statistic Circulation 2008