CORONARY HEART DISEASE IN WOMEN

Nazanin Azadi, MD

Disclosures: none
• 63 year old lady, non-smoker, with no medical history.

• 4/28/2014 After returning from dinner with her sister and family, begins to feel chest burning/discomfort. Attempts to take a cold/hot shower with no relief. Lays down on the ground of her sister’s home and tells her family she believes she is having a heart attack. She feels as though, ‘an elephant is sitting my chest.’ Tells her sister to call 911.

• EMS arrives at which point she tells them, ‘I am having a heart attack, I feel like I am going to die.’ ‘I want to rip my heart out of my chest.’
• An EKG is performed.

• No Aspirin is given.

• No NTG is administered.

• EMS tells her, ‘YOU ARE NOT HAVING A HEART ATTACK, YOU ARE HAVING AN ANXIETY ATTACK. STOP BREATHING SO HARD AND CALM DOWN’

• She tells them, ‘I feel like I am going to die. An elephant is sitting on my chest. I am having a heart attack. Please take me to the emergency room.’

• No Aspirin is given. No NTG is given. She is not placed on a gurney. She is instructed to walk to the ambulance and is taken to the emergency room.
Coronary Angiogram
Heart Disease
The leading killer of women
Heart Disease

The leading killer of women at all ages

LEADING CAUSES OF DEATH FOR AMERICAN WOMEN (2000)

One in three women dies from heart disease. It’s the #1 killer of women, regardless of race or ethnicity. It also strikes at younger ages than most people think, and the risk rises in middle age. And, two-thirds of women who have heart attacks never fully recover.

To learn more, visit www.nhlbi.nih.gov/health/hearttruth


*Numbers of deaths are rounded to the nearest thousand.
Death Rates in Women

At Every Age, More Women Die of Heart Disease Than Breast Cancer

Coronary Artery Disease
Stroke
Lung Cancer
Breast Cancer
Colon Cancer
Endometrial Cancer

Cardiovascular Disease Deaths: Trends for Males and Females
United States: 1979-2001

Source: CDC/NCHS © AHA, 2004
• More than one in three female adults has some form of cardiovascular disease (CVD).

• Since 1984, the number of CVD deaths for females has exceeded those for males.

• In 2010, CVD was the cause of death in 400,332 females. Females represented 51.0% of deaths from CVD.

• In 2010, CVD was the first listed diagnosis of 2.8 million females discharged from short-stay hospitals.

• In 2010, 25.1% of bypass and 32.9% of PCI patients were female.
Major Causes of Death for Males and Females, 2010

A indicates cardiovascular disease plus congenital cardiovascular disease (ICD-10 I00-I99, Q20-Q28); B, cancer (C00-C97); C, accidents (V01-X59, Y85-Y86); D, chronic lower respiratory disease (J40-J47); E, diabetes mellitus (E10-E14); F, Alzheimer disease (G30).
• About 6.6 million females alive today have CHD.

• Each year new and recurrent MI and fatal CHD will impact an estimated 385,000 women.

• 26% of women age 45 and older who have an initial recognized MI (heart attack) die within a year compared with 19% of men.

• 64% of women who died suddenly of CHD had no previous symptoms.

• 518,000 females diagnosed with CHD were discharged from short-stay hospitals in 2010.
Differences in the Management and Prognosis of Women and Men Who Suffer From Acute Coronary Syndromes

Sonia S. Anand, MD, PhD, FRCPC,* Chang Chun Xie, MSc, PhD,* Shamir Mehta, MD, MSc, FRCPC,* Maria Grazia Franzosi, BSc ScD,† Campbell Joyner, MD, FRCPC,‡ Susan Chrolavicius, BSc,* Keith A. A. Fox, MD, FRCP,§ Salim Yusuf, DPhil, FRCPC,* for the CURE Investigators

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>4,836</td>
<td>7,726</td>
</tr>
<tr>
<td>Angiography (overall) (%)</td>
<td>39.4</td>
<td>45.5</td>
</tr>
<tr>
<td>In-hospital (%)</td>
<td>25.4</td>
<td>29.5</td>
</tr>
<tr>
<td>Out of hospital (%)</td>
<td>14.0</td>
<td>16.0</td>
</tr>
<tr>
<td>No diseased vessels (%)</td>
<td>499 (26.7)</td>
<td>480 (13.2)</td>
</tr>
<tr>
<td>Significant coronary artery disease by angiography (triple-vessel disease or left main &gt;50%) (%)</td>
<td>652 (34.9)</td>
<td>1,621 (44.7)</td>
</tr>
<tr>
<td>Angioplasty or CABG (%)</td>
<td>29.8</td>
<td>40.4</td>
</tr>
<tr>
<td>Angioplasty or CABG among patients with significant coronary artery disease (%)</td>
<td>451/652 (69.2%)</td>
<td>1,178/1,621 (72.7%)</td>
</tr>
<tr>
<td>CV death, MI, stroke at 30 days (%)*</td>
<td>4.4</td>
<td>4.9</td>
</tr>
<tr>
<td>CV death, MI, stroke at end of follow-up (%)*</td>
<td>9.7</td>
<td>11.1</td>
</tr>
<tr>
<td>Refractory angina or rehospitalization for angina (%)*</td>
<td>16.6</td>
<td>13.9</td>
</tr>
<tr>
<td>CVD, MI, stroke, refractory angina, or rehospitalization (%)*</td>
<td>23.6</td>
<td>22.5</td>
</tr>
</tbody>
</table>
### Differences in the Management and Prognosis of Women and Men Who Suffer From Acute Coronary Syndromes

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<table>
<thead>
<tr>
<th>CV death, MI, stroke or refractory ischemia (adjusted for treatment allocation, region)</th>
<th>TIMI Low</th>
<th>TIMI Intermediate</th>
<th>TIMI High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>193/1,268 (15.2%)</td>
<td>681/2,818 (24.2%)</td>
<td>273/750 (36.4%)</td>
</tr>
<tr>
<td>Men</td>
<td>322/2,006 (16.0%)</td>
<td>1,056/4,479 (23.6%)</td>
<td>360/1,239 (29.1%)</td>
</tr>
</tbody>
</table>

| Angiography |  |
| --- | --- | --- | --- |
| Women | 538/1,268 (42.4%) | 1,042/2,818 (37.0%) | 286/750 (38.1%) |
| Men | 987/2,006 (49.2%) | 2,074/4,479 (46.3%) | 564/1,239 (45.5%) |

\[ p < 0.001 \text{ within each risk strata} \]
Gender Disparities in the Diagnosis and Treatment of Non–ST-Segment Elevation Acute Coronary Syndromes: Large-Scale Observations From the CRUSADE

<table>
<thead>
<tr>
<th>Variable</th>
<th>(n = 21,323)</th>
<th>(n = 14,552)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment within 24 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>91.6%</td>
<td>89.6%</td>
</tr>
<tr>
<td>Heparin, any</td>
<td>84.0%</td>
<td>80.0%</td>
</tr>
<tr>
<td>Unfractionated heparin</td>
<td>54.8%</td>
<td>48.5%</td>
</tr>
<tr>
<td>Low molecular weight heparin</td>
<td>35.9%</td>
<td>37.7%</td>
</tr>
<tr>
<td>Glycoprotein Ilb/IIIa inhibitor, any</td>
<td>38.6%</td>
<td>28.7%</td>
</tr>
<tr>
<td>Troponin-positive</td>
<td>39.9%</td>
<td>30.5%</td>
</tr>
<tr>
<td>Troponin-negative</td>
<td>29.0%</td>
<td>19.4%</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>77.7%</td>
<td>75.8%</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitor</td>
<td>42.2%</td>
<td>42.4%</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>41.0%</td>
<td>35.6%</td>
</tr>
<tr>
<td>Discharge medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>90.4%</td>
<td>87.5%</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>82.7%</td>
<td>80.5%</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitor</td>
<td>55.5%</td>
<td>55.3%</td>
</tr>
<tr>
<td>Statin</td>
<td>63.4%</td>
<td>55.9%</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>53.2%</td>
<td>48.0%</td>
</tr>
</tbody>
</table>
Temporal trends in patient and treatment delay among men and women presenting with ST-elevation myocardial infarction

Padma Kaul, PhD, a Paul W. Armstrong, MD, a Sunil Sookram, MD, b, c Becky K. Leung, BSc, a Neil Brass, MD, a and Robert C. Welsh, MD a Alberta, Canada
Temporal trends in patient and treatment delay among men and women presenting with ST-elevation myocardial infarction

Padma Kaul, PhD, Paul W. Armstrong, MD, Sunil Sookram, MD, Becky K. Leung, BSc, Neil Brass, MD, and Robert C. Welsh, MD Alberta, Canada
About 50% of women sent home with “normal coronaries” continue to experience disabling symptoms

Possibly d/t coronary microvascular or macrovascular endothelial dysfunction

673/936 enrolled in WISE had persistent chest pain (PChP)

PChP-w no obstructive disease is not a benign condition

2x the number of CV events (MIs, strokes, CHF and CV deaths) than those w/o PChP.
Telephone survey of a nationally representative random sample of women; 1024 respondents age ≥ 25 years

46% identified heart disease as the leading cause of death in women, up from 30% in 1997 and 34% in 2000

Black, Hispanic, and younger women (<45 years old) had lower awareness of heart disease

Only 38% of women reported that their doctors had ever discussed heart disease with them.
Plaque Erosion and Outward (Positive) Remodeling

- Plaque erosion and thrombus formation 2x likely in women (men have more plaque rupture)
- Outward (positive) remodeling- atherosclerotic lesion protrudes outward than impinging on the lumen

Adapted from Bellasi et al, New insights into ischemic heart disease in women. Cleveland Clinic Journal of Medicine; 74: 585-594
Women suffer more plaque erosions (above) compared to plaque explosions in men (below), leading to more acute coronary syndromes (unstable angina) and non-Q MI in women, making diagnosis more difficult and leading to delays in treatment.
Major Risk Factors

- Cigarette smoking (passive smoking?)
- Elevated total or LDL-cholesterol
- Hypertension (BP $\geq 140/90$ mmHg or on antihypertensive medication)
- Low HDL cholesterol ($<40$ mg/dL)$^\dagger$
- Family history of premature CHD
  - CHD in male first degree relative <55 years
  - CHD in female first degree relative <65 years
- Age (men $\geq 45$ years; women $\geq 55$ years)

$^\dagger$ HDL cholesterol $\geq 60$ mg/dL counts as a “negative” risk factor; its presence removes one risk factor from the total count.
Other Recognized Risk Factors

- Obesity: Body Mass Index (BMI)
  - Weight (kg)/height (m²)
  - Weight (lb)/height (in²) x 703
- Obesity BMI ≥30 kg/m² with overweight defined as 25-<30 kg/m²
- Abdominal obesity involves waist circumference >40 in. in men, >35 in. in women
- Physical inactivity: most experts recommend at least 30 minutes moderate activity at least 4-5 days/week
Diabetes as a CHD Risk Equivalent

- 10-year risk for CHD $\cong 20\%$
- High mortality with established CHD
  - High mortality with acute MI
  - High mortality post acute MI
- Prevalence has increased over 25% in past 15 years in California, paralleling
  - 50% increase in overweight/obesity
Menopause and the Risk of Coronary Heart Disease

(modified data from “Menopausal status as a risk for coronary artery disease”
Arch Intern Med 1995;155:57-61)
Changes with Menopause

Lipids
- Total-Cholesterol ↑
- HDL-Cholesterol ↓

Prevalence Differences
- Hypertension ↑
- Metabolic Syndrome ↑

Risk Factor, Disease, or Outcome Risk
- Triglycerides ↑
- Diabetes Mellitus ↑
- Obesity (BMI ≥30)*** ↑
- Waist Circumference >35” ↑

***Obesity ~25% of women - BMI ≥30, Less leisure-time physical activity - Greater functional decline -

Adapted from Bellasi et al, New insights into ischemic heart disease in women. cleveland clinic journal of medicine; 74: 585-594
Probability of Death From CHD in Patients With NIDDM and in Nondiabetic Patients, With and Without Prior MI

- Nondiabetic subjects without prior MI
- Diabetic subjects without prior MI
- Nondiabetic subjects with prior MI
- Diabetic subjects with prior MI
Framingham Heart Study 30-Year Follow-Up: CVD Events in Patients With Diabetes (Ages 35-64)

<table>
<thead>
<tr>
<th>Risk ratio</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total CVD</td>
<td>38</td>
<td>30</td>
</tr>
<tr>
<td>CHD</td>
<td>20</td>
<td>19</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Intermittent claudication</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>6</td>
<td>3*</td>
</tr>
</tbody>
</table>

Age-adjusted annual rate/1,000

P<0.001 for all values except *P<0.05.

Relation between Smoking, Use of Birth Control Pills and the Risk of a Heart Attack

(modified data from Rosenberg L et al. Myocardial infarction and cigarette smoking in women younger than 50 years of age. JAMA 1985;253:2965-2969)
Perhaps the most important risk factor for coronary heart disease is the misperception that coronary heart disease is a man’s disease.
Chest pain or Angina

**Typical Angina:**

heaviness, pressure or squeezing sensation behind the breastbone with radiation across the chest, up the neck or down the left arm or “strangling” or “suffocating” sensation. caused or worsened by exercise and eased by rest usually lasts two to five minutes

**Atypical Angina (frequently encountered in women):**

shortness of breath extreme fatigue lightheadedness or fainting nausea and/or indigestion
Women’s Early Warning Signs of a Heart Attack

- **Weeks before Heart Attack (95% of women)**
  - Unusual fatigue (70.7%)
  - Sleep disturbance (47.8%)
  - Shortness of breath (42.1%)
  - Indigestion (39.4%)
  - Chest pain (29.7%)

- **At time of Heart Attack**
  - Shortness of breath (57.9%)
  - Weakness (54.8%)
  - Fatigue (42.9%)
  - Chest pain (57%)

McSweeney, JC et al. Circulation 2003; 2619-2623
Assessing Ischemic Disease

- Stress EKG may be less useful in looking for ischemia
  - Guidelines still support for women with normal resting 12 lead EKG
- Decreased functional capacity may predict poor outcomes
  - WISE showed that women who could not achieve 4.7 METS of work had a risk of death or nonfatal MI 3.7x higher than others with better functional capacity
- Stress ECHO and SPECT are good options in women
Drawbacks of Diagnostic Imaging in Women

- Low exercise capacity – ↓likelihood of reaching adequate pressure rate product
  - Solution: Pharmacologic stress testing
- Breast attenuation artifact – higher false positive imaging studies
  - Solution: Gated acquisition; attenuation correction for nuclear imaging
  - Solution: Echocardiography
- Lower pretest probability of CAD – higher false positive rate
  - Solution: Integrate clinical variables, risk factors, into decision-making process
Women and CHD: What Test to Order When

- For women at high or intermediate risk of coronary artery disease, consider treadmill echocardiography or nuclear perfusion imaging
- For women unable to exercise, consider dobutamine stress echocardiography or adenosine or dipyridamole nuclear imaging
- In high risk women with typical symptoms of coronary artery disease, consider referral to a cardiologist
- For high risk women, consider cardiac catheterization if symptoms persist despite negative non-invasive imaging

A stepwise approach beginning with conventional exercise testing may be considered for women who:

- Are at low or intermediate risk for coronary artery disease
- Are able to exercise
- Have an electrocardiogram that can be interpreted during stress testing

An image-enhanced test may be more predictive in women than conventional electrocardiogram stress testing, and may also be more cost effective in women at intermediate risk for CHD

Evidence-Based Guidelines for Cardiovascular Disease Prevention in Women

Expert Panel/Writing Group*
Lori Mosca, MD, PhD (Chair)†; Lawrence J. Appel, MD‡; Emelia J. Benjamin, MD‡;
Kathy Berra, MSN, ANP‡§; Nisha Chandra-Strobos, MD†; Rosalind P. Fabunmi, PhD‡;
Deborah Grady, MD, MPH†; Constance K. Haan, MD¶; Sharonne N. Hayes, MD‡;
Debra R. Judelson, MD§; Nora L. Keenan, PhD‡§; Patrick McBride, MD, MPH†;
Suzanne Oparil, MD†; Pamela Ouyang, MD†; Mehmet C. Oz, MD†;
Michael E. Mendelsohn, MD‡; Richard C. Pasternak, MD†; Vivian W. Pinn, MD §§;
Rose Marie Robertson, MD†; Karin Schenck-Gustafsson, MD, PhD†; Cathy A. Sila, MD‡;
Sidney C. Smith, Jr, MD¶¶; George Sopko, MD, MPH‡‡; Anne L. Taylor, MD**;
Brian W. Walsh, MD‖; Nanette K. Wenger, MD†; Christine L. Williams, MD, MPH†

*Representing the following participating organizations and major cosponsors: the American Heart Association†; American College of Cardiology‡; American College of Nurse Practitioners§; American College of Obstetricians and Gynecologists¶; American College of Physicians¶¶; American Medical Women’s Association§; Association of Black Cardiologists**; Centers for Disease Control and Prevention††; National Heart, Lung and Blood Institute‡‡; Office of Research on Women’s Health§§; Society of Thoracic Surgeons¶¶; and World Heart Federation||. 
Assessment of CHD Risk

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

• Count the number of risk factors.
• Use Framingham scoring if ≥2 risk factors* to determine the absolute 10-year CHD risk.
• Determine risk status: high (>20% 10-year risk or CHD risk equivalents), intermediate (10-20% 10-year risk), or low (<10% risk)

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

# ATP III Framingham Risk Scoring

## Assessing CHD Risk in Women

### Step 1: Age

<table>
<thead>
<tr>
<th>Years</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-34</td>
<td>-7</td>
</tr>
<tr>
<td>35-39</td>
<td>-3</td>
</tr>
<tr>
<td>40-44</td>
<td>0</td>
</tr>
<tr>
<td>45-49</td>
<td>3</td>
</tr>
<tr>
<td>50-54</td>
<td>6</td>
</tr>
<tr>
<td>55-59</td>
<td>8</td>
</tr>
<tr>
<td>60-64</td>
<td>10</td>
</tr>
<tr>
<td>65-69</td>
<td>12</td>
</tr>
<tr>
<td>70-74</td>
<td>14</td>
</tr>
<tr>
<td>75-79</td>
<td>16</td>
</tr>
</tbody>
</table>

### Step 2: Total Cholesterol

<table>
<thead>
<tr>
<th>TC (mg/dL)</th>
<th>Points at Age 20-39</th>
<th>Points at Age 40-49</th>
<th>Points at Age 50-59</th>
<th>Points at Age 60-69</th>
<th>Points at Age 70-79</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;160</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>160-199</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>200-239</td>
<td>8</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>240-279</td>
<td>11</td>
<td>8</td>
<td>5</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>≥280</td>
<td>13</td>
<td>10</td>
<td>7</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

### Step 3: HDL-Cholesterol

<table>
<thead>
<tr>
<th>HDL-C (mg/dL)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥60</td>
<td>-1</td>
</tr>
<tr>
<td>50-59</td>
<td>0</td>
</tr>
<tr>
<td>40-49</td>
<td>1</td>
</tr>
<tr>
<td>&lt;40</td>
<td>2</td>
</tr>
</tbody>
</table>

### Step 4: Systolic Blood Pressure

<table>
<thead>
<tr>
<th>Systolic BP (mm Hg)</th>
<th>Points if Untreated</th>
<th>Points if Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;120</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>120-129</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>130-139</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>140-159</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>≥160</td>
<td>4</td>
<td>6</td>
</tr>
</tbody>
</table>

### Step 5: Smoking Status

<table>
<thead>
<tr>
<th></th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsmoker</td>
<td>0</td>
</tr>
<tr>
<td>Smoker</td>
<td>9</td>
</tr>
</tbody>
</table>

### Step 6: Adding Up the Points

<table>
<thead>
<tr>
<th>Age</th>
<th>Total cholesterol</th>
<th>HDL-cholesterol</th>
<th>Systolic blood pressure</th>
<th>Smoking status</th>
<th>Point total</th>
</tr>
</thead>
</table>

### Step 7: CHD Risk

<table>
<thead>
<tr>
<th>Point Total</th>
<th>10-Year Risk Risk</th>
<th>Point Total</th>
<th>10-Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;9</td>
<td>&lt;1%</td>
<td>20</td>
<td>11%</td>
</tr>
<tr>
<td>9</td>
<td>1%</td>
<td>21</td>
<td>14%</td>
</tr>
<tr>
<td>10</td>
<td>1%</td>
<td>22</td>
<td>17%</td>
</tr>
<tr>
<td>11</td>
<td>1%</td>
<td>23</td>
<td>22%</td>
</tr>
<tr>
<td>12</td>
<td>1%</td>
<td>24</td>
<td>27%</td>
</tr>
<tr>
<td>13</td>
<td>2%</td>
<td>≥25</td>
<td>≥30%</td>
</tr>
<tr>
<td>14</td>
<td>2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>3%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>8%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Risk estimates were derived from the experience of the Framingham Heart Study, a predominantly Caucasian population in Massachusetts, USA.

High Risk:

- Established coronary heart disease
- Cerebrovascular disease
- Peripheral arterial disease
- Abdominal aortic aneurysm
- End-stage or chronic renal disease
- Diabetes mellitus
- 10-year Framingham global risk >20%
Classification of CVD Risk in Women (Mosca et al., Circ 2007)

- **At Risk:**
  - Evidence of subclinical vascular disease (e.g., coronary calcium)
  - Metabolic Syndrome
  - Poor exercise capacity on treadmill and/or abnormal heart rate recovery
  - >=1 major risk factor for CVD including:
    - Cigarette smoking
    - Poor diet
    - Physical inactivity
    - Obesity (esp central obesity)
    - Family history of premature CVD (<55 male or <65 female relative)
    - Hypertension
    - Dyslipidemia

- **Optimal risk:** Framingham global risk <10% and a healthy lifestyle with no risk factors
# Priorities for Prevention in Practice According to Risk Assessment

<table>
<thead>
<tr>
<th>Class I recommendations</th>
<th>High-Risk Women (&gt;20% Risk)</th>
<th>Intermediate-Risk Women (10% to 20% Risk)</th>
<th>Lower-Risk Women (10% Risk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking cessation</td>
<td></td>
<td>Smoking cessation</td>
<td></td>
</tr>
<tr>
<td>Physical activity</td>
<td></td>
<td>Physical activity</td>
<td></td>
</tr>
<tr>
<td>Card rehab</td>
<td></td>
<td>Heart-healthy diet</td>
<td></td>
</tr>
<tr>
<td>Diet therapy</td>
<td></td>
<td>Weight maint/reduct</td>
<td></td>
</tr>
<tr>
<td>Weight maint/reduct</td>
<td></td>
<td>BP control</td>
<td></td>
</tr>
<tr>
<td>BP control</td>
<td></td>
<td>Cholesterol control</td>
<td></td>
</tr>
<tr>
<td>Aspirin therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Blocker therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitor (ARBs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mgmt/control of DM</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class IIa recommendation</th>
<th>Treatment for depression</th>
<th>Aspirin therapy</th>
<th></th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Class IIb recommendations</th>
<th>Omega 3 fatty-acid supplementation</th>
<th>Folic acid supplementation</th>
<th>Mosca, L “Heart Disease Prevention in Women” Circulation, 2004</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>
Lifestyle Change: First Line of Defense Against Heart Disease

- The AHA expert panel rated the following as Class I recommendations:
  - Stop cigarette smoking and avoid secondhand tobacco smoke
  - Get at least 30 minutes of physical activity most or preferably all days (60-90 minutes for those needing to lose or sustain weight)
  - Start a risk-reduction or cardiac rehabilitation program if recent acute coronary syndrome or cardiovascular event
  - Eat a heart-healthy diet (consistent with NCEP/ATP III TLC)
  - Maintain healthy weight by balancing caloric intake with caloric expenditure to achieve BMI between 18.5-24.9 kg/m²

Mosca et al. Circulation 2004 and 2007
Essential Components of NCEP Therapeutic Lifestyle Change (TLC)

- Decrease in saturated fats (<7% of total calories) and trans fatty acids\(^1\)
- Increased dietary and supplemental fiber\(^1\)
  - High-fiber breakfast cereals, supplements, and so forth
- Plant sterols and stanols (2 g/d)\(^1\)
  - Spreads, pills, added to yogurt or other foods, or combined with aspirin
- Soy protein\(^2\)
- Flavonoids (nuts)\(^3\)
- Weight loss\(^1\)
- Exercise\(^1\)

**ATP III: Nutritional Components of the TLC Diet**

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Recommended Intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saturated fat*</td>
<td>&lt;7% of total calories</td>
</tr>
<tr>
<td>Polyunsaturated fat</td>
<td>Up to 10% of total calories</td>
</tr>
<tr>
<td>Monounsaturated fat</td>
<td>Up to 20% of total calories</td>
</tr>
<tr>
<td>Total fat</td>
<td>25%–35% of total calories</td>
</tr>
<tr>
<td>Carbohydrate (esp. complex carbs)</td>
<td>50%–60% of total calories</td>
</tr>
<tr>
<td>Fiber</td>
<td>20–30 g/d</td>
</tr>
<tr>
<td>Protein</td>
<td>~15% of total calories</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>&lt;200 mg/d</td>
</tr>
</tbody>
</table>

*Trans fatty acids also raise LDL-C and should be kept at a low intake.

Note: Regarding total calories, balance energy intake and expenditure to maintain desirable body weight.

Nuts, Soy, Phytosterols, Garlic

- Nurses’ Health Study: five 1oz servings of nuts per week associated with 40% lower risk of CHD events; 2-4 servings/wk 25% lower risk
- Metaanalysis of 38 trials of soy protein showed 47g intake lowered total, LDL-C, and trigs 9%, 13%, and 11%, respectively; no effect on HDL-C.
- Phytosterol-supplemented foods (e.g., stanol ester margarine) lowers LDL-C avg. 10%
- Meta-analysis of garlic studies showed 9% total cholesterol reduction from 1/2-1 clove consumed daily for 6 months.
## Possible Benefits From Other Therapies

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Soluble fiber in diet (2–8 g/d) (oat bran, fruit, and vegetables)</td>
<td>↓ LDL-C 1% to 10%</td>
</tr>
<tr>
<td>• Soy protein (20–30 g/d)</td>
<td>↓ LDL-C 5% to 7%</td>
</tr>
<tr>
<td>• Stanol esters (1.5–4 g/d) (inhibit cholesterol absorption)</td>
<td>↓ LDL-C 10% to 15%</td>
</tr>
<tr>
<td>• Fish oils (3–9 g/d) (n-3 fatty acids)</td>
<td>↓ Triglycerides 25% to 35%</td>
</tr>
</tbody>
</table>

Aspirin in Primary Prevention: Effective Gender Differences

1.0

RR of MI Among Men

RR = 0.68 (0.54–0.86)

P = .001

RR of Stroke Among Men

RR = 1.13 (0.96–1.33)

P = .15

RR of MI Among Women

RR = 0.99 (0.83–1.19)

P = .95

RR of Stroke Among Women

RR = 0.81 (0.69–0.96)

P = .01

Aspirin Better

Placebo Better

BDT, 1988

PHS, 1989

HOT, 1998

PPP, 2001

HOT, 1998

PPP, 2001

HOT, 1998

PPP, 2001

WHS, 2005

Combined

Combined

Combined

Aspirin Better

Placebo Better

Blood Pressure Regulation in Women

- 3 of every 4 women with high blood pressure know they have it
- Fewer than 1 in 3 are controlling it
- All women must take steps to control their high blood pressure

AHA Guidelines for CVD Prevention in Women: Blood Pressure

- Encourage an optimal blood pressure of <120/80 mm Hg through lifestyle approaches (Class I, Level B)
- Pharmacotherapy when BP is 
  - ≥ 140/90 mm Hg
- Get BP even lower when
  - Target-organ damage
  - Diabetes
  - (Class I, Level A)

CHD Risk Equivalents

- > 20% 10-year risk of CHD
  - (Framingham projections) (downloadable risk algorithms at www.nhlbi.nih.gov)
- Diabetes
- Other forms of clinical atherosclerotic disease
  - Peripheral arterial disease (ABI <0.90)
  - Abdominal aortic aneurysm
  - Carotid artery disease (>=1mm CIMT?)

Other Interventions with Class I Recommendations

- Blood pressure – encourage optimal levels of <120/80 mmHg
- Cholesterol levels – optimal cholesterol levels <200 mg/dl, LDL-C < 100 mg/dl, HDL > 50 mg/dl, triglycerides <150 mg/dl
- Diabetes – recommend control to HgbA1c < 7%
When LDL-lowering drug therapy is employed in high-risk or moderately high risk patients, intensity of therapy should be sufficient to achieve a 30–40% reduction in LDL-C levels.
Highest Priority for Therapy is for Women at Highest Risk

- Those at highest risk, who already have pre-existing CVD, diabetes, or chronic kidney disease are most likely to benefit from preventive therapy involving the following Class I recommendations:
  - ACE inhibitor therapy (if coughing, subst. ARB)
  - Aspirin therapy (baby aspirin or maximum dose of 162 mg) unless contraindicated
  - Beta-blocker therapy in those with prior MI or current angina
  - Statin therapy
  - Niacin or fibrate therapy if low HDL present
  - Fibrates to lower triglycerides and improve HDL
  - Warfarin in those with atrial fibrillation unless contraindicated
**CHD Events: Results of Secondary Prevention Studies in Women**

<table>
<thead>
<tr>
<th></th>
<th>Placebo No. Events/Women</th>
<th>Intervention No. Events/Women</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4S</td>
<td>91/420</td>
<td>60/407</td>
<td>0.68 (0.51-0.91)</td>
</tr>
<tr>
<td>CARE</td>
<td>80/290</td>
<td>46/286</td>
<td>0.60 (0.37-0.97)</td>
</tr>
<tr>
<td>LIPID</td>
<td>104/760</td>
<td>90/756</td>
<td>0.87 (0.67-1.13)</td>
</tr>
<tr>
<td>HPS</td>
<td>282/1638</td>
<td>237/1628</td>
<td>0.85 (0.72-0.99)</td>
</tr>
<tr>
<td>Total and summary</td>
<td>557/3108</td>
<td>433/3077</td>
<td>0.80 (0.71-0.91)</td>
</tr>
</tbody>
</table>

*P value for heterogeneity=.35
Walsh et al. JAMA 2004;291:2243-2252.*
Avoid “Class III” Interventions  
(Not proven useful or effective / may be harmful)

- Combined estrogen and progestin therapy, and *estrogen monotherapy since associated with increased risk of CVD
- Selective estrogen-receptor modulators (SERMs) also not recommended
- Antioxidant supplements including vitamin E, C, and beta-carotene
- Folic acid with or without B6 or B12 supplementation
- Aspirin for MI prevention in women aged <65 years
### Vitamins: Major Vascular Events

<table>
<thead>
<tr>
<th>Vascular Event</th>
<th>Vitamins (n = 10,269)</th>
<th>Placebo (n = 10,267)</th>
<th>Risk Ratio and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major coronary</td>
<td>1063</td>
<td>1047</td>
<td>1.00 (0.94–1.06)</td>
</tr>
<tr>
<td>Any stroke</td>
<td>511</td>
<td>518</td>
<td>P &gt; 0.9</td>
</tr>
<tr>
<td>Revascularization</td>
<td>1058</td>
<td>1086</td>
<td></td>
</tr>
<tr>
<td>Any of the above</td>
<td>2306</td>
<td>2312</td>
<td>1.00 (0.94–1.06)</td>
</tr>
</tbody>
</table>

(22.5%)

Heart and Estrogen/Progestin Replacement Study (HERS): Secondary Prevention of CHD in Women

- Randomized, placebo-controlled trial of E/P therapy vs. placebo in 2763 women with CHD; average age 67 years
- Treatment was 0.625 mg CEE + 2.5 mg medroxyprogesterone daily for 4 years
- Primary endpoint: nonfatal MI and CHD death
- Secondary endpoints: CABG, PTCA, unstable angina, CHF, PVD, TIA

JAMA 1998;280:605-613
HERS Results

• No statistically significant difference between HRT and placebo in both primary and secondary endpoints after 4 years.
• Within first year, greater incidence in CHD events in HRT group. In years 3 and 4, lower CHD events in HRT group compared to placebo.
• HRT lowered LDL 11% and increased HDL 10% compared to placebo.
• Approximately 50% of randomized women were on lipid-lowering drugs.
• Higher incidence of VTE and cholelithiasis in HRT group.

JAMA 1998;280:605-613
More Bad News: The Women’s Health Initiative

• Over 160,000 women nationwide, aged 50-79 and postmenopausal have participated in various components (observational, dietary modification, and HRT clinical trials)—over 3,000 at UCI

• The Estrogen/Progestin component of the HRT clinical trial involving 16,608 women nationwide was discontinued prematurely in Spring 2002 after 5.2 years of follow-up (instead of 8.5 years).
Those randomized to estrogen/progestin compared to placebo and statistically significant increased risks:

- Breast cancer 26% (8/10,000 person years)
- Total coronary heart disease 29% (7/10,000 person years)
- Stroke 41% (8/10,000 person years)
- Pulmonary embolism 2.1 X (8/10,000 person years)
- Protective for colorectal cancer (37% lower) and hip fracture (34% lower): no effect endometrial cancer or total mortality

Estrogen-only arm was also discontinued in December 2003 and was associated with a 39% increased risk of stroke (12 excess strokes per 10,000 person years) and 12% significant increased risk of cardiovascular events. JAMA. 2004 Apr 14;291(14):1701-12.
Heart Disease is the leading cause of death in women in the United States.

Most risk factors are the same for men and women, but women are at particularly high risk if they have diabetes mellitus. Genderspecific risks are menopause and intake of birth control pills while smoking.

Diagnosis of Heart Disease in women is very difficult since many women have atypical symptoms such as shortness of breath and extreme fatigue.
Prevention of heart disease is crucial

Almost 50% of heart disease problems can be avoided by lifestyle changes

Ineffective interventions such as antioxidants and hormone replacement therapy should be avoided
In order to reduce heart disease in women, the importance of heart disease in the female population has to be recognized.
THANK YOU