Cardiovascular Disease in Women: Scope of the Problem
2018 Update

Christina Economides, MD, MM, FSCAI
Cardiology & Cardiovascular Intervention
Disclosures:
Nothing to disclose
CC: Chest pain

HPI: 47 yo black woman w/ no significant known PMHx presented with chest pain characterized as dull, pressure and burning, in the epigastric and substernal area, 8/10 a/w nausea and vomiting, started @ 7 PM, it was now past midnight. She symptoms had been intermittent for the 2-3 days prior. She had presented to UC but was treated for GERD w/ Pepcid.

PMHx:
- HTN
- S/p Gastric Bypass Surgery

Meds: None
All: Ibuprofen, Avocados

SHx: Smokes 3 cig/day, drinks socially, uses marijuana
ER Course

- Given Aspirin & Heparin IV load
- Pt became unresponsive
- VF arrest -> shocked -> NSR
- Intubated for airway protection
- VF again -> shocked -> NSR
PE

VS- T 97.5  P 56  R 16  BP 98/60  97% 2L
NC, 92 kg, BMI 36.0
Gen: Obese woman intubated
Neck: Supple
Chest: Bilaterally CTA
CV:  RRR, Nl S1, S2, No r/m/g, No JVD
Abd: Large, +BS, Soft, NT
Ext:  No c/c/e,  2+ bilateral fem/DP/radial pulses
Most women in America die from cancer.

Heart disease is a man’s problem.

Only older women have heart disease.

Most doctors know about women’s risk of heart disease.

Heart disease in women is the same as heart disease in men and should be treated the same.
Objectives

• Review the epidemiology of CVD in women
• Identify barriers to cardiovascular care in women
• Discuss gender specific differences in presentation of CVD
• Review gender disparities in current management of ACS
Social & Economic Impact

- CVD is the leading cause of death in the US
- Someone has a heart attack every 43 seconds in the US
- Each minute, someone dies from a heart disease-related event
- Coronary heart disease alone costs the US $108.9 billion each year
  - Total includes the cost of health care services, medications, and lost productivity
Facts

• CVD leading cause of death of American women
• Causes 1 in 3 female deaths in the US
• That’s ~ one female death every minute!
• But it doesn’t affect all women alike,
• the warning signs for women aren’t the same in men
Cardiovascular disease and other major causes of death for all males and females (United States: 2014).


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Top 10 Most Common Causes of Death in US Women

- Diseases of heart: 329,238
- Cerebrovascular diseases: 86,993
- Lung and bronchus cancer: 69,078
- Chronic lower respiratory disease: 68,497
- Alzheimer’s disease: 51,039
- Accidents (unintentional injury): 41,426
- Diabetes mellitus: 41,116
- Influenza and pneumonia: 38,581
- Colorectal cancer: 34,949
- 26,224

Source: Breast Cancer and Statistics by STATISTICA, November 2009
WHERE WE DONATE VS. DISEASES THAT KILL US

**MONEY RAISED**
- **Heart Disease**: $257,895M
- **Diabetes**: $147M
- **Motor Neuron Disease (Including ALS)**: $54.1M
- **Chronic Obstructive Pulmonary Disease**: $22.9M
- **$14M
- **$7M
- **$4.2M
- **$3.2M

**DEATHS (US)**
- **Breast Cancer**: 596,577
- **Suicide**: 142,942
- **HIV / AIDS**: 73,831
- **Prostate Cancer**: 41,374
- **Chronic Obstructive Pulmonary Disease**: 39,618
- **Cancer**: 21,176
- **Diabetes**: 7,683
- **Heart Disease**: 6,849

Source: Death statistics from 2011 CDC report. Money raised from listed charities.
Health Status of Minority Women

Mortality rates for major causes of death for females by ethnicity

- **Asian-American**
  - Chronic lower respiratory diseases: 113.8
  - Cerebrovascular diseases: 113.8
  - Malignant neoplasms: 103
  - Diseases of the heart: 48.6

- **Native American**
  - Chronic lower respiratory diseases: 109.1
  - Cerebrovascular diseases: 109.1
  - Malignant neoplasms: 24.9
  - Diseases of the heart: 39.1

- **Hispanic**
  - Chronic lower respiratory diseases: 137.1
  - Cerebrovascular diseases: 137.1
  - Malignant neoplasms: 100.6
  - Diseases of the heart: 36.4

- **White**
  - Chronic lower respiratory diseases: 207.5
  - Cerebrovascular diseases: 207.5
  - Malignant neoplasms: 168.7
  - Diseases of the heart: 57.8

- **Non-Hispanic White**
  - Chronic lower respiratory diseases: 210.4
  - Cerebrovascular diseases: 210.4
  - Malignant neoplasms: 172.5
  - Diseases of the heart: 58.6

- **African-American**
  - Chronic lower respiratory diseases: 284.1
  - Cerebrovascular diseases: 284.1
  - Malignant neoplasms: 196.6
  - Diseases of the heart: 78.1

# of deaths per 100,000 persons

US Pharm. 2006;31(9):8.

Percentage breakdown of deaths attributable to cardiovascular disease (United States: 2014).

- Coronary Heart Disease: 45.1%
- Stroke: 16.5%
- Heart Failure*: 8.5%
- High Blood Pressure: 9.1%
- Diseases of the Arteries: 3.2%
- Other: 17.6%

* Includes congenital heart disease

Figure 1. Decline in Deaths from Cardiovascular Disease in Relation to Scientific Advances.
Figure 1. Decline in Deaths from Cardiovascular Disease in Relation to Scientific Advances.
Significant Differences Between Men and Women

• In aspects of epidemiology, recognition, diagnosis and treatment

• Women are not referred as often as men for appropriate tests and/or therapeutic procedures by physicians

• Women under-represented in clinical trials
  – Only in the last 15 yrs have women been included, but they are still only represent ~27% of populations in most trials
Barriers to Cardiovascular Care in Women

- Confusion due to mixed messages from the media
- Tendency to underestimate the problem by women themselves
- Lack of awareness on part of patients and healthcare providers
Twelve-Year Follow-Up of American Women’s Awareness of Cardiovascular Disease Risk and Barriers to Heart Health
Lori Mosca, MD, MPH, PhD; Heidi Mochari-Greenberger, MPH, RD; Rowena J. Dolor, MD, MHS;
L. Kristin Newby, MD, MHS; Karen J. Robb, MBA

Figure. Overall trends in awareness that coronary heart disease is the leading cause of death in women.
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2009 (n=127)</td>
<td>1997 (n=188)</td>
<td>2009 (n=159)</td>
<td>1997 (n=294)</td>
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<tr>
<td>Leading cause of death</td>
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<tr>
<td>Breast cancer</td>
<td>14</td>
<td>19[^c^,d]</td>
<td>10</td>
<td>17[^d]</td>
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<tr>
<td>Cancer (general)</td>
<td>27</td>
<td>38</td>
<td>18</td>
<td>33</td>
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<tr>
<td>Heart disease/heart attack</td>
<td>50</td>
<td>16 (&lt;0.001)</td>
<td>59</td>
<td>28[^a]</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>12</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Don’t know/no answer</td>
<td>7</td>
<td>15[^c]</td>
<td>7</td>
<td>12[^c]</td>
</tr>
<tr>
<td>Greatest health problem</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast cancer</td>
<td>34[^d]</td>
<td>41[^d]</td>
<td>29</td>
<td>40[^d]</td>
</tr>
<tr>
<td>Cancer (general)</td>
<td>9</td>
<td>19</td>
<td>15</td>
<td>26</td>
</tr>
<tr>
<td>Heart disease/heart attack</td>
<td>12</td>
<td>4</td>
<td>20</td>
<td>5</td>
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<tr>
<td>Obesity</td>
<td>9</td>
<td>...</td>
<td>7</td>
<td>...</td>
</tr>
<tr>
<td>Other</td>
<td>29[^a,d]</td>
<td>13</td>
<td>21</td>
<td>16</td>
</tr>
<tr>
<td>Don’t know/no answer</td>
<td>7</td>
<td>23[^b,c]</td>
<td>9</td>
<td>13</td>
</tr>
</tbody>
</table>

Telephone results are presented for comparability between 1997 and 2009 surveys.
All values are weighted percentages. Superscript letters denote significant differences at \(P<0.05\) between age groups. \(P\) values are for tests of proportion between 1997 and 2009. Ellipses indicate response not surveyed in 1997.
## Table 6. Barriers to Living a Heart-Healthy Lifestyle by Race/Ethnicity and Age Group

<table>
<thead>
<tr>
<th>Barriers (Aided)</th>
<th>Overall (n=1158)</th>
<th>White (n=634)</th>
<th>Nonwhite (n=524)</th>
<th>Age &lt;50 y (n=683)</th>
<th>Age &gt;50 y (n=475)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>I have family obligations and other people to take care of</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>God or some higher power ultimately determines my health</td>
<td>37</td>
<td>35</td>
<td>44</td>
<td>33</td>
<td>42</td>
<td>0.03</td>
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<tr>
<td>I am not confident that I can successfully change my behavior</td>
<td>33</td>
<td>33</td>
<td>34</td>
<td>36</td>
<td>30</td>
<td>0.13</td>
</tr>
<tr>
<td>There is too much confusion in the media about what to do</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I am stressed to do the things that need to be done</td>
<td>28</td>
<td>28</td>
<td>27</td>
<td>33</td>
<td>21</td>
<td>0.002</td>
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<tr>
<td>I do not want to change my lifestyle</td>
<td>28</td>
<td>30</td>
<td>25</td>
<td>32</td>
<td>24</td>
<td>0.04</td>
</tr>
<tr>
<td>My health care professional does not think I need to worry about heart disease</td>
<td>27</td>
<td>26</td>
<td>28</td>
<td>29</td>
<td>24</td>
<td>0.18</td>
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<tr>
<td>I do not have time to take care of myself</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15</td>
<td>&lt;0.001</td>
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<tr>
<td>I do not know what I should do</td>
<td>29</td>
<td>27</td>
<td>27</td>
<td>28</td>
<td>30</td>
<td>0.007</td>
</tr>
<tr>
<td>I am fearful of change</td>
<td>22</td>
<td>22</td>
<td>20</td>
<td>25</td>
<td>18</td>
<td>0.04</td>
</tr>
<tr>
<td>I am confused by what I am supposed to do to change my lifestyle</td>
<td>21</td>
<td>22</td>
<td>18</td>
<td>24</td>
<td>17</td>
<td>0.04</td>
</tr>
<tr>
<td>I feel the changes required are too complicated</td>
<td>20</td>
<td>20</td>
<td>22</td>
<td>23</td>
<td>17</td>
<td>0.08</td>
</tr>
<tr>
<td>My health care professional does not explain clearly what I should do</td>
<td>19</td>
<td>18</td>
<td>21</td>
<td>21</td>
<td>17</td>
<td>0.23</td>
</tr>
<tr>
<td>My friends/family have told me that I do not need to change</td>
<td>16</td>
<td>17</td>
<td>15</td>
<td>18</td>
<td>15</td>
<td>0.34</td>
</tr>
<tr>
<td>I do not think changing my behavior will reduce my risk of developing heart disease</td>
<td>13</td>
<td>14</td>
<td>10</td>
<td>12</td>
<td>14</td>
<td>0.48</td>
</tr>
<tr>
<td>I am too ill/old to make changes</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>6</td>
<td>10</td>
<td>0.08</td>
</tr>
<tr>
<td>My health care professional does not speak my language</td>
<td>8</td>
<td>8</td>
<td>9</td>
<td>6</td>
<td>8</td>
<td>0.67</td>
</tr>
</tbody>
</table>

Values represent the weighted percent of women surveyed online who strongly or somewhat agreed that they experienced each barrier to living a heart healthy lifestyle.

*P* value for difference in proportion by race/ethnic group or by age group.
Other Significant Findings

- Only 53% of women would call 911 if they thought they were having symptoms of a heart attack.
- Awareness of atypical symptoms of heart disease was low.
- Majority of women cited therapies to prevent CVD that are not evidence-based.

Circ Cardiovasc Qual Outcomes. 2010
Racial/Ethnic and Age Differences in Women’s Awareness of Heart Disease

Heidi Mochari-Greenberger, M.P.H., Ph.D., Kerri L. Miller, M.A., and Lori Mosca, M.D., M.P.H., Ph.D.
Awareness

- Black and Hispanic women 66% less likely than white women to be aware (odds ratio [OR] 0.34, 95% CI 0.23-0.50) after multivariable adjustment for significant confounders
- 65% of white women were aware
- Awareness did not differ between black and Hispanic women (37% vs. 38%)
- Other significant multivariable predictors included <high school education and income <$35,000/year
Awareness

- Younger women (age < 55 years)
  - Less likely to be aware (OR 0.66, 95% CI 0.50-0.87)
  - Less likely to report being very well/well informed about heart disease (OR 0.53, 95% CI 0.41-0.68) compared to older women

- Awareness of heart attack signs, SOB (34%), nausea (15%), and fatigue (7%), was low among all women

- Awareness was low among racial/ethnic minority status and age < 55 years

- These groups should be targeted for educational programs
Physicians’ Awareness of CVD

- 2005 American Heart Association study
- Only 8% of primary care physicians and 17% of cardiologists knew that heart disease kills more women than men

| Table 8. Physician's Agreement With Statements About CVD Prevention and Guidelines |
|---------------------------------|-------------------|-------------------|
|                                 | Physician Specialty |
|                                 | PCP (A) (n=300)    | OBGyn (B) (n=100) |
| More women than men die each year of CVD. | 8.3<sup>C</sup>     | 13.0<sup>C</sup>    |
|                                 | 17.0<sup>A</sup>    |                   |
| I am willing to seek additional training that will allow me to better engage in preventive health treatments for CVD in women. | 28.0<sup>B</sup>     | 43.0<sup>AC</sup>    |
|                                 | 25.0<sup>B</sup>     |                   |
| By and large, the results of clinical research to determine optimal risk-reducing interventions in men generalize to women. | 8.3<sup>C</sup>   | 4.0<sup>C</sup>    |
|                                 | 14.0<sup>B</sup>     |                   |

Values are percentages. Superscript letters indicate statistically significant differences at P<0.05 using a t test of proportions.

*Physicians who stated that they agree or strongly agree on a 10-point Likert scale.
History of Women’s Health Research

• 1977, US FDA issued a guideline: “General Considerations for the Clinical Evaluation of Drugs”

  Restricted women of childbearing potential from participating in phase 1 and early phase 2 clinical studies until reproductive toxicity studies had been conducted in animals and some evidence of human effectiveness had become available.

• Policy emerged in the aftermath of the discovery of birth defects resulting from fetal exposure to thalidomide and diethylstilbestrol.
1985, The Public Health Service Task Force on Women’s Health Issues:

The “historical lack of research focus on women’s health concerns has compromised the quality of health information available to women as well as the health care they receive”.

Government Response

• National Institutes of Health established
  – Office of Research on Women’s Health

• US Department of Health and Human Services (HHS) established
  – Office on Women’s Health (OWH) to promote the inclusion of women in clinical research.

• 2001, Institute of Medicine (IOM) published a report: “Exploring the Biological Contributions to Human Health: Does Sex Matter?”
  – Approach to women’s health research was transformed to address sex and gender differences in disease development and progression, as well as response to therapies
When do gender differences become gender disparities?

- **Disparity:**
  - The lack of equality or the presence of inequity

- **World Health Organization (WHO)**
  - **Health inequity:**
    - Differences in health, which are not only unnecessary and avoidable but, in addition, are considered unfair and unjust

  - **Equity in healthcare:**
    - Equal access to available care for equal need
    - Equal utilization for equal need, and
    - Equal quality of care for all
Healthcare Access Disparities

• Women are more likely than men to have forgone needed healthcare due to cost
• 1 in 5 women (~19 million women) between the ages of 18 and 64 are uninsured
  – More likely to have inadequate access to care
  – Get a lower standard of care when they are in the health system
  – Have poorer health outcomes
Risk Factors in Common with Men

- Personal history of CVD
- Age > 55
- Family hx of premature CHD
- HTN
- Diabetes
- Dyslipidemia
- CKD
- Metabolic Syndrome
- Lifestyle factors: smoking, diet, obesity, excess, alcohol, sedentary lifestyle, psychosocial
- Inflammatory Markers
Risk Scores in Women

• Traditional risk score, Framingham, includes:
  – Age, gender, total and HDL cholesterol, cigarette smoking, and systolic blood pressure

• Does not include
  – Diabetes, family history

• This underestimates risk
  – Considers >75% of women “low risk”
Diabetes Mellitus

- **Vascular disease**
  - Large arteries: heart, carotids
  - Small arteries: eyes, kidneys, extremities
- **#1 reason for blindness, ESRD/HD, amputations in US**
- **10.6 million women have diabetes (8% of all women >20 yrs)**
- **3 million women who have diabetes are undiagnosed**
- **34.4 million women have pre-diabetes**
Mortality from Coronary Heart Disease in Subjects with Type 2 Diabetes and in Nondiabetic Subjects with and without Prior Myocardial Infarction

Steven M. Haffner, M.D., Seppo Lehto, M.D., Tapani Rönnemaa, M.D., Kalevi Pyörälä, M.D., and Markku Laakso, M.D.

Diabetes increases coronary mortality with and without a prior MI.

Figure 1. Kaplan–Meier Estimates of the Probability of Death from Coronary Heart Disease in 1059 Subjects with Type 2 Diabetes and 1378 Nondiabetic Subjects with and without Prior Myocardial Infarction. MI denotes myocardial infarction. I bars indicate 95 percent confidence intervals.
ASCVD Risk Score 2014

- Atherosclerotic Cardiovascular Disease
- New threshold of 7.5% 10-year risk for men and women
- Clinical calculation
- App is free
http://tools.acc.org/ASCVD-Risk-Estimator/
ASCVD Risk Estimator

10-Year ASCVD Risk

24.9% calculated risk

8.8% risk with optimal risk factors

Lifetime ASCVD Risk

Lifetime Risk Calculator only provides lifetime risk estimates for individuals 20 to 59 years of age.

Gender

Male  Female

Age

72

Note: Lifetime risk is only calculated for the 20 to 59 year range

Total Cholesterol (mg/dL)

278

HDL - Cholesterol (mg/dL)

46

Race

White  African American  Other

Systolic Blood Pressure

162

Diabetes

Yes  No

Smoker

Yes  No

*Intended for use if there is not ASCVD and the LDL cholesterol is <190 mg/dL.

**Optimal risk factors include: Total cholesterol of 170 mg/dL, HDL-cholesterol of 50 mg/dL, Systolic BP of 110 mm Hg, Not taking medications for hypertension, Not a diabetic, Not a smoker.
Based on the data entered (assuming no clinical ASCVD and LDL-C 70-189 mg/dL):

- Gender: Female
- Age: 72
- Race: African American
- Total Cholesterol: 278
- HDL-Cholesterol: 46
- Systolic Blood Pressure: 162
- Hypertension Treatment: No
- Diabetes: No
- Smoker: No

**Moderate to High-Intensity Statin Recommended**

Before initiating statin therapy, it is reasonable for clinicians and patients to engage in a discussion which considers the potential for ASCVD risk reduction benefits and for adverse effects, for drug-drug interactions, and patient preferences for treatment. (IIa C)

Adults 40 to 75 years of age with LDL-C 70 to 189 mg/dL with no diabetes and estimated 10-year ASCVD risk ≥7.5% should be treated with moderate to high-intensity statin therapy. (I A)

In individuals for whom after quantitative risk assessment a risk-based treatment decision is uncertain, additional factors may be considered to inform treatment decision making. These factors may include primary LDL-C ≥160 mg/dL or other evidence of genetic hyperlipidemias, family history of premature ASCVD with onset <55 years of age in a first degree male relative or <65 years of age in a first degree female relative, high-sensitivity C-reactive protein ≥2 mg/L, CAC score ≥300 Agatston units or ≥75 percentile for age, sex, and ethnicity, ankle-brachial index <0.9, or elevated lifetime risk of ASCVD. Additional factors may be identified in the future. (IIib C)

**Lifestyle Recommendations**

AHA/ACC guidelines stress the importance of lifestyle modifications to lower cardiovascular disease risk. This includes eating a heart-healthy diet, regular aerobic exercises, maintenance of desirable body weight and avoidance of tobacco products.
Clinician References

Understanding Cardiovascular Risk

Lifestyle Recommendations

Groups that Benefit from Statin Therapy

Blood Cholesterol Recommendation Summary

Recommendations for Initiation of Statin Therapy

Intensities of Statin Therapy

Recommendations to Monitor Response to Statin Therapy

Statin Safety Recommendations

External Links to Full Guidelines & More Information
Intensities of Statin Therapy

High-Intensity Statin
Daily dose lowers LDL-C, on average by approximately ≥50%

- Atorvastatin 40-80 mg
- Rosuvastatin 20-(40) mg

Moderate-Intensity Statin
Daily dose lowers LDL-C, on average by approximately 30% to <50%

- Atorvastatin 10-(20) mg
- Fluvastatin 40 mg bid
- Fluvastatin XL 80 mg
- Lovastatin 40 mg
- Pitavastatin 2-4 mg
- Pravastatin 40-(80) mg
- Rosuvastatin (5)-10 mg
- Simvastatin 20-40 mg

Low-Intensity Statin
Daily dose lowers LDL-C, on average by approximately <30%

- Fluvastatin 20-40 mg
- Lovastatin 20 mg
- Simvastatin 10 mg
- Pitavastatin 1 mg
- Pravastatin 10-20 mg

*Evidence from 1 RCT (down-titration if unable to tolerate atorvastatin 80 mg)
Risk Factors Unique to Women

• Early menarche
• Premature menopause
• Pregnancy complications:
  – HTN in pregnancy/Pre-eclampsia
  – Gestational Diabetes
  – Spontaneous pregnancy loss
  – Preterm birth
• Women with chronic inflammatory disease:
  – Systemic Lupus Erythematosus
  – Rheumatoid Arthritis
  – Systemic Vasculitis
Psychosocial Risk Factors

- Women drastically **underestimate** their own risk
- Linked to adverse cardiovascular outcomes in women
- Depression
- Anxiety
- Inadequate social and economic resources
- Adversities early in life
- Caregiver stress
- Marital stress
  - *Marriage reduces CV risk in men,*
  - *but increases the risk in women!*

Marital Stress Worsens Prognosis in Women With Coronary Heart Disease
The Stockholm Female Coronary Risk Study

Kristina Orth-Gomér, MD, PhD
Sarah P. Wamala, PhD
Myriam Horsten, PhD
Karin Schenck-Gustafsson, MD, PhD
Neil Schneiderman, PhD
Murray A. Mittleman, MD, DrPH

Context  Psychosocial stress has been associated with incidence of coronary heart disease (CHD) in men, but the prognostic impact of such stress rarely has been studied in women.

Objective  To investigate the prognostic impact of psychosocial work stress and marital stress among women with CHD.

Design and Setting  Population-based, prospective follow-up study conducted in the city of Stockholm, Sweden.
Study

• Investigate prognostic impact of psychosocial work stress and marital stress among women with CHD

• Population-based, prospective follow-up study conducted in Stockholm, Sweden

• Participants:
  – 292 consecutive female pts 30-65 years (n = 279 working or cohabiting w/ a male partner)
  – Who were hospitalized for acute MI or unstable angina btw February 1991 and February 1994
  – Followed for a median of 4.8 years)
Main Outcome Measures

• Recurrent coronary events, including cardiac death, acute MI, and revascularization procedures by:
  – Marital stress (assessed using the Stockholm Marital Stress Scale, a structured interview) and by
  – Work stress (assessed using the ratio of work demand to work control)
Results

- Married/cohabiting women w/ a male partner (n = 187), marital stress a/w a 2.9-fold (95% CI, 1.3-6.5) increased risk of recurrent events
  - After adjustment for age, estrogen status, education level, smoking, diagnosis at index event, diabetes mellitus, systolic blood pressure, smoking, triglyceride level, high-density lipoprotein cholesterol level, and left ventricular dysfunction

- Working women (n = 200), work stress did not significantly predict recurrent coronary events (hazard ratio, 1.6; 95% CI, 0.8-3.3).

- Marital stress but not work stress predicts poor prognosis in women 30-65 yrs w/ CHD
Presenting Symptoms
Subtle Symptoms in Men and Women

- Chest pain – still the most common in both genders
- Shortness of breath, often without chest pain
  - 17% of women recognized chest tightness
  - 29% recognized shortness of breath as a symptom of a heart attack
- Pain in upper back, shoulder blades, neck or jaw
- Unusual/unexplained fatigue, sleeplessness, weakness or dizziness
- Flu-like symptoms: nausea, clamminess or cold sweats, hot flushes
- Feelings of anxiety
<table>
<thead>
<tr>
<th>Typical Symptoms</th>
<th>Atypical Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain/discomfort (pressure, tightness, squeezing)</td>
<td>Chest pain: sharp, pleuritic, burning, aching, soreness, reproducible</td>
</tr>
<tr>
<td>Additional symptoms with chest pain</td>
<td>Other symptoms excluding chest pain</td>
</tr>
<tr>
<td>Radiation of pain to jaw, neck, shoulders, arm, back, epigastrium</td>
<td>Unusual fatigue</td>
</tr>
<tr>
<td>Associated symptoms: dyspnea, nausea, vomiting, lightheadedness, diaphoresis</td>
<td>Unusual shortness of breath</td>
</tr>
<tr>
<td></td>
<td>Upper back/chest pain</td>
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<tr>
<td></td>
<td>Neck, jaw, arm, shoulder, back, epigastric pain</td>
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<tr>
<td></td>
<td>Flu-like symptoms</td>
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<tr>
<td></td>
<td>Dizziness</td>
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<tr>
<td></td>
<td>Generalized scared/anxiety feeling</td>
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<tr>
<td></td>
<td>Generalized weakness</td>
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<tr>
<td></td>
<td>Indigestion</td>
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<td></td>
<td>Palpitations</td>
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</tbody>
</table>

AMI indicates acute myocardial infarction.
Sex Differences in Clinical Presentation

• Consequences for
  – Timely identification of ischemic symptoms
  – Appropriate triage
  – Judicious diagnostic testing and management

• Detrimental consequences for women
  – Misdiagnosis
  – Delayed revascularization
  – Higher AMI mortality rates
During Presentation

• Compared to men, women are less likely to:
  – Undergo an electrocardiogram, cardiac monitoring, or cardiac blood tests
  – Receive a cardiology consult
  – Be admitted to a coronary care or telemetry unit

• Women are more likely to:
  – Receive controlled substances and anti-anxiety medications in the ER, suggesting that they were being treated for psychiatric or psychosomatic complaints
• Women were older, presented later, and had a higher mortality rate than men
• Women were less likely to receive aspirin, heparin, and beta-blockers
• When treated with thrombolytic therapy, women received therapy an average of almost 14 min later than men and had a higher incidence of major bleeding
• Women were less likely to undergo cardiac catheterization, percutaneous transluminal coronary angioplasty, and coronary artery bypass surgery

Women with STEMI

- Pooled data from 22 randomized trials of primary PCI vs thrombolysis in pts w/ STEMI, women had lower 30-day mortality w/ primary PCI than w/ thrombolysis, 2006
- Confirmed in Gusto II-B angioplasty substudy 2004
Benefits of direct angioplasty for women and men with acute myocardial infarction: Results of the Global Use of Strategies to Open Occluded Arteries in Acute Coronary Syndromes (GUSTO II-B) Angioplasty Substudy

Jacqueline E. Tamis-Holland, MD, A Angela Palazzo, MD, A Amanda L. Stebbins, MS, A James N. Slater, MD, A Jean Boland, MD, A Stephen G. Ellis, MD, A and Judith S. Hochman, MD, A for the GUSTO II-B Angioplasty Substudy Investigators New York, NY, Durham, NC, Liège, Belgium, and Cleveland, Ohio

Conclusions

The GUSTO II-B PTCA substudy was a large randomized trial comparing direct PTCA to t-PA. The results of this study demonstrated that although the relative benefit of PTCA to t-PA for women and men appeared similar with a similar adjusted OR for reaching the 30-day clinical end point of death, nonfatal MI, and nonfatal disabling stroke, women derived a greater absolute benefit from this therapy. We therefore conclude that in institutions where PTCA is readily available, women with acute ST-segment elevation MI who are at higher risk for ICH following thrombolytic therapy should be referred for direct PTCA.
Temporal Trends and Sex Differences in Revascularization and Outcomes of ST-Segment Elevation Myocardial Infarction in Younger Adults in the United States

Sahil Khera, MD,* Dhaval Kolte, MD, PhD,* Tanush Gupta, MD,* Kathir Selvan Subramanian, MD,* Neel Khanna, MD,* Wilbert S. Aronow, MD,* Chul Ahn, PhD,† Robert J. Timmermans, MD,* Howard A. Cooper, MD,* Gregg C. Fonarow, MD,† William H. Frishman, MD,* Julio A. Panza, MD,* Deepak L. Bhatt, MD, MPH†
Study

- Determine temporal trends and sex differences in revascularization and in-hospital outcomes of younger pts with STEMI.
- 2004 to 2011 Nationwide Inpatient Sample databases
- All patients age 18 to 59 years hospitalized with STEMI
- Analyzed temporal trends and sex differences in revascularization strategies, in-hospital mortality, and length of stay
- 1,363,492 younger adults (age <60 years) with acute myocardial infarction
- 632,930 (46.4%) had STEMI
- Younger women with acute myocardial infarction were less likely than men to present with STEMI (adjusted odds ratio [OR]: 0.74; 95% confidence interval [CI]: 0.73 to 0.75)
Younger women with STEMI were 26% less likely to receive reperfusion as compared with younger men (percutaneous coronary intervention adjusted OR: 0.74.)
Thrombolysis

PCI

CABG

**Figure 2:** Temporal trends in use of thrombolysis, PCI, and CABG among younger men and women with STEMI.

- **A:** Men ($P_{trend} < 0.001$) vs. Women ($P_{trend} < 0.001$) for thrombolysis (lytic) across years.
- **B:** Men ($P_{trend} < 0.001$) vs. Women ($P_{trend} < 0.001$) for PCI across years.
- **C:** Men ($P_{trend} < 0.001$) vs. Women ($P_{trend} < 0.001$) for CABG across years.

Temporal trends in use of (A) thrombolysis (lytic), (B) percutaneous coronary intervention (PCI), and (C) coronary artery bypass grafting (CABG) among younger men and women with STEMI. $P_{trend} < 0.001$ for all. Abbreviations as in Figure 1.
In-hospital mortality was significantly higher in younger women compared with men (4.5% vs. 3.0%; adjusted OR: 1.11; 95% CI: 1.07 to 1.15).
Use of PCI for STEMI and in-hospital mortality have increased, whereas length of stay has decreased in both sexes over the past several years. Younger women are less likely to receive revascularization for STEMI and have higher in-hospital mortality as compared with younger men.
Women with NSTEMI

• Experience more complications than men:
  – Cardiogenic shock
  – Heart failure
  – Renal failure
  – Stroke
  – Re-infarction
  – Bleeding
  – Readmission

• 2014 ACC/AHA NSTEMI guidelines:
  Early invasive strategy as a class I indication (Level of Evidence: A) for women with high-risk features
Women and CABG

• Review of 23 CABG studies with outcomes stratified by sex:
  – Women patients were older and had more comorbidities than the men
  – Early mortality was significantly higher in the women, even after risk adjustment for comorbidities, use of internal mammary grafts, age, and body surface area

Meta-analysis of 20 CABG Studies

• Pts who underwent isolated CABG
• Short-term mortality higher in women
  – Who were older
  – Had greater comorbidities
  – Were more likely to undergo urgent CABG than men
• Short-term mortality persisted at mid- and long-term follow-up

Gender-specific predictors of early mortality after coronary artery bypass graft surgery.

- Prospective study of 1559 pts admitted to the German Heart Institute Berlin, 2005 – 2008
- Key mediators of excess mortality in women
  - Older age
  - Lower physical functioning
  - Postoperative complications, including low cardiac output syndrome, respiratory insufficiency, and resuscitation
- These sex-specific differences in outcomes persist with modern off-pump CABG techniques, Emmert MY et al, 2010.
Sex Differences in Cardiac Risk Factors, Perceived Risk, and Health Care Provider Discussion of Risk and Risk Modification Among Young Patients With Acute Myocardial Infarction

The VIRGO Study

Erica C. Leifheit-Limson, PhD,* Gail D’Onofrio, MD, MS,† Mitra Daneshvar, MPH,* Mary Geda, MSN,‡ Héctor Bueno, MD, PhD,‖ John A. Spertus, MD, MPH,‖ Harlan M. Krumholz, MD, SM,‖ Judith H. Lichtman, PhD, MPH*‖
VIRGO (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients)

• Compared prevalence of 5 cardiac risk factors by sex (DM, DL, HTN, Obesity, Smoking)
• Risk perceptions
• Health care provider feedback on heart disease and risk modification between young women and men hospitalized w/AMI
  – 3,501 AMI patients age 18 to 55 years
  – 2349 women, 1152 men
  – U.S. and Spanish hospitals
  – August 2008 and January 2012
98% of pts had ≥1 risk factor
64% had ≥3 risk factors
Percentage of women and men reporting that before their index acute myocardial infarction event, they considered themselves at risk for heart disease, were told by a health care professional that they were at risk, or had a health care provider talk to them about heart disease and ways to modify their risk. *p Values for comparisons by sex within the overall, U.S., and Spanish cohorts were calculated with chi-square tests.
Sex Differences in Treatments, Relative Survival, and Excess Mortality Following Acute Myocardial Infarction: National Cohort Study Using the SWEDHEART Registry

Oras A Alabas, BSc, MSc, PhD; Chris P Gale, BSc(HONS), MBBS, PhD, MEd, MSc; Marlous Hall, MSc, PhD; Mark J. Rutherford, BSc(HONS), PhD; Karolina Szummer, MD, PhD; Sofia Sederholm Lawesson, MD, PhD; Joakim Alfredsson, MD, PhD; Bertil Lindahl, MD, PhD; Tomas Jemberg, MD, PhD

Clinical Trial Registration—URL: https://www.clinicaltrials.gov. Unique identifier: NCT02952417. (J Am Heart Assoc. 2017;6: e007123. DOI: 10.1161/JAHA.117.007123.)
Odds of receipt of guideline-indicated care for women compared with men, by (A) ST-segment–elevation myocardial infarction and (B) non–ST-segment–elevation myocardial infarction.

<table>
<thead>
<tr>
<th></th>
<th>STEMI OR (95% CI)</th>
<th>NSTEMI OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>0.61 (0.57–0.64)</td>
<td>0.71 (0.69–0.74)</td>
</tr>
<tr>
<td>Aspirin*</td>
<td>0.84 (0.79–0.89)</td>
<td>0.85 (0.82–0.88)</td>
</tr>
<tr>
<td>β-blockers</td>
<td>0.67 (0.64–0.70)</td>
<td>0.83 (0.81–0.86)</td>
</tr>
<tr>
<td>β-blockers*</td>
<td>0.88 (0.84–0.93)</td>
<td>0.97 (0.93–1.00)</td>
</tr>
<tr>
<td>Statin</td>
<td>0.47 (0.45–0.49)</td>
<td>0.54 (0.53–0.56)</td>
</tr>
<tr>
<td>Statin*</td>
<td>0.76 (0.72–0.80)</td>
<td>0.75 (0.73–0.77)</td>
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<tr>
<td>ACEi or ARB</td>
<td>0.68 (0.65–0.71)</td>
<td>0.83 (0.81–0.85)</td>
</tr>
<tr>
<td>ACEi or ARB*</td>
<td>0.78 (0.74–0.81)</td>
<td>0.86 (0.84–0.89)</td>
</tr>
<tr>
<td>P2Y12 inhibitors</td>
<td>0.59 (0.57–0.61)</td>
<td>0.70 (0.69–0.72)</td>
</tr>
<tr>
<td>P2Y12 inhibitors*</td>
<td>0.83 (0.80–0.87)</td>
<td>0.87 (0.85–0.89)</td>
</tr>
<tr>
<td>Revascularization</td>
<td>0.46 (0.44–0.48)</td>
<td>0.46 (0.45–0.47)</td>
</tr>
<tr>
<td>Revascularization*</td>
<td>0.66 (0.63–0.69)</td>
<td>0.57 (0.55–0.58)</td>
</tr>
<tr>
<td>Reperfusion</td>
<td>0.57 (0.55–0.59)</td>
<td></td>
</tr>
<tr>
<td>Reperfusion*</td>
<td>0.80 (0.77–0.84)</td>
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</tbody>
</table>
Risk of death at 6 months, 1 year, and 5 years for women compared with men by (A) ST-segment–elevation myocardial infarction (STEMI) and (B) non–ST-segment–elevation myocardial infarction (NSTEMI).

<table>
<thead>
<tr>
<th></th>
<th>STEMI</th>
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<th>NSTEMI</th>
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<tbody>
<tr>
<td></td>
<td>EMRR (95% CI)</td>
<td>EMRR (95% CI)</td>
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<tr>
<td>Model 1:</td>
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<tr>
<td>6 months</td>
<td></td>
<td>2.12 (1.85–2.42)</td>
<td>Model 1:</td>
<td></td>
<td>1.14 (1.10–1.18)</td>
</tr>
<tr>
<td>1 year</td>
<td></td>
<td>3.29 (2.40–4.51)</td>
<td>1 year</td>
<td></td>
<td>1.24 (1.19–1.29)</td>
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<tr>
<td>5 years</td>
<td></td>
<td>1.91 (1.73–2.10)</td>
<td>5 years</td>
<td></td>
<td>1.35 (1.28–1.42)</td>
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<tr>
<td>Model 2:</td>
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<tr>
<td>6 months</td>
<td></td>
<td>1.65 (1.50–1.81)</td>
<td>Model 2:</td>
<td></td>
<td>1.15 (1.11–1.19)</td>
</tr>
<tr>
<td>1 year</td>
<td></td>
<td>1.89 (1.66–2.16)</td>
<td>1 year</td>
<td></td>
<td>1.20 (1.16–1.24)</td>
</tr>
<tr>
<td>5 years</td>
<td></td>
<td>1.60 (1.48–1.72)</td>
<td>5 years</td>
<td></td>
<td>1.26 (1.21–1.32)</td>
</tr>
<tr>
<td>Model 3:</td>
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<td></td>
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<tr>
<td>6 months</td>
<td></td>
<td>1.26 (1.16–1.37)</td>
<td>Model 3:</td>
<td></td>
<td>0.97 (0.94–1.00)</td>
</tr>
<tr>
<td>1 year</td>
<td></td>
<td>1.43 (1.26–1.62)</td>
<td>1 year</td>
<td></td>
<td>1.01 (0.97–1.04)</td>
</tr>
<tr>
<td>5 years</td>
<td></td>
<td>1.31 (1.19–1.43)</td>
<td>5 years</td>
<td></td>
<td>1.07 (1.02–1.12)</td>
</tr>
</tbody>
</table>

Excess mortality

Oras A Alabas et al. J Am Heart Assoc 2017;6:e007123
What is New?

• We found a survival disadvantage for women with STEMI and NSTEMI who were followed for 10 years after acute MI

• These sex differences in excess mortality persisted after adjusting for age and comorbidities.

• However, the differences in excess mortality decreased or disappeared after adjusting for the use of evidence-based treatments.

• What Are the Clinical Implications?

• Our novel findings suggest that if treatments for acute MI were provided equally between sexes, then differences in deaths between men and women would be smaller and premature cardiovascular deaths among women would be reduced.
Studies/Course

- H/H 10/33, MCV 76, cre 1.26, LFTs 256/93, BNP 15
- Rapid troponin 0.13
- TC 118, Triglycerides 112, HDL 36, LDL 60
- HgbA1c 5.5
- Echo: EF 36%, Akinesis and thinning of most of the anterior wall, septum and apex c/w large anteroapical infarct. Apical aneurysm w/out obvious thrombus.
- Normal valves, Mild DD, IVC dilated.
- Extubated.
- Transferred to OSH.
Recommendations
2014 Guidelines

• ACC/AHA recommend that women with heart attacks and heart disease be treated in an equal manner to men with the same indications for noninvasive and invasive testing
STEMI: A Paradigm Shift

Adapted from Roger VL et al. *Circulation* 2011;123:e18-e209
STEMI -> Heart Failure

**Figure 2:** Projected *Heart Failure* direct medical costs and indirect (lost productivity) costs.

Adapted from Circulation 2011; 123:933–44
Women’s Awareness of Heart Disease 2012

- Barriers and motivators to engage in a heart healthy lifestyle are different for younger women, who also said their doctors were less likely to talk to them about heart disease.

- “This is a missed opportunity,” said Lori Mosca, M.D, M.P.H., Ph.D. “Habits established in younger women can have lifelong rewards. We need to speak to the new generation, and help them understand that living heart healthy is going to help them feel better, not just help them live longer. So often the message is focused on how many women are dying from heart disease, but we need to be talking about how women are going to live — and live healthier.”

- Mosca also said efforts need to be culturally sensitive to reach more minorities who are at high risk for heart disease.

Conclusions: CVD in Women

- There are real gender disparities that exist and contribute to elevated mortality rates for women with CVD
- Sustained educational efforts are needed to raise awareness in public and healthcare professionals
- Raise the index of suspicion during evaluation of women
- Further sex-specific research is warranted
- Prevention is paramount!