Women and Heart Disease: The Yentl Syndrome 2013

C. Noel Bairey Merz, M.D., F.A.C.C, F.A.H.A
Women’s Guild Endowed Chair in Women’s Health
Barbra Streisand Women’s Heart Center
Preventive and Rehabilitative Cardiac Center
Cedars-Sinai Heart Institute
Los Angeles, California USA
merz@cshs.org
Women’s Heart Health (Bairey Merz)

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Stocks: None
New female majority Yentl and Yentl Syndrome

1984-1996: 12 years to recognize /take action

Source: CDC/NCHS and the American Heart Association
Compliments of Womenheart: the National Coalition for Women with Heart Disease
1718 M Street, NW - #330 • Washington, DC 20036
(www.womenheart.org)
The WISE Study: continuous NHLBI funding for 17 years

NHLBI-WISE 1996-

- Reference Cohort 1999- N=20
- Original Cohort 1997-2009 N=963
- WTH Case Match Cohort 2004 N=6,000

Univ of Florida
- Hormone Core CSMC 1997

UAB
- Biochemistry Core CSMC 1997

DCC Univ of Pgh
- Coronary Angiography Core RIIH 1997

Univ of Pgh
- Phytoestrogen Core CSMC 1997

Allegheny/ Hahneman
- Ambulatory ECG Core UF 1997

FEMHEART PD/Pfizer 1999 N=74

Genetics Core UPgh/UF-CSMC 2000

IVUS Substudy UF-CCF NHLBI- 2000 n=100

PMI MRS Core UAB 1999

QWISE WISE Pfizer-NHLBI 2001 N=78

RAAS RO1 UF NHLBI 2001 N=50

EWISE UF Pfizer 2002 N=50

PDE-5 Inhibition Trial Pfizer UF 2001

WISE Extension NHLBI 2001

Immune/Inflamm RO1 NHLBI UPgh 2001

WISE-ARIC UF Amersham/Fujisawa 2004 N=83

WISE-EPC Pilot UF-CSMC 2007 N=32

Androgen Core CSMC NHLBI 2003

WISE CMR RO1 CS-UF NHLBI 2009-14

R-WISE Gilead 2011-2014
The WISE Study: continuous NHLBI funding for 17 years

NHLBI-WISE
1996-

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N=20

Original
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WTH
Case Match Cohort
2004 N=6,000

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CSMC 1997

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Core UF 1997

Univ of Pgh

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Core CSMC 1997

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Angiography
Core RIH 1997

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PD/Pfizer 1999
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UPgh/UF-CSMC 2000

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Pfizer UF 2001

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NHLBI UPgh 2001

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Amersham/Fujisawa
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N=83

WISE-EPC Pilot
UF-CSMC 2007
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Androgen Core CSMC
NHLBI 2003

WISE-CMR ROI
CS-UF NHLBI 2003

R-WISE
Gilead 2011-2014
Paradox: Women have a two-fold increase in “normal” coronary arteries in the setting of ACS, nonSTE and STEMI

<table>
<thead>
<tr>
<th>Condition</th>
<th>No./Total (%)</th>
<th>Women</th>
<th>Men</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute coronary syndrome</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GUSTO²</td>
<td>343/1768 (19.4)</td>
<td>394/4638 (8.4)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>TIMI 18³</td>
<td>95/555 (17)</td>
<td>99/1091 (9)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Unstable angina²</td>
<td>252/826 (30.5)</td>
<td>220/1580 (13.9)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>TIMI IIIa²</td>
<td>30/113 (26.5)</td>
<td>27/278 (8.3)</td>
<td>&lt;.001</td>
<td></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>
<td></td>
</tr>
<tr>
<td>MI with ST-segment elevation²</td>
<td>50/492 (10.2)</td>
<td>119/1759 (6.8)</td>
<td>.02</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: GUSTO, Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries; MI, myocardial infarction; TIMI, Thrombosis In Myocardial Infarction.
WISE Study: Sex Differences in Heart Attack Plaques

Women erode

Men explode

Burke et al. Circ 1998
WISE Study

Male pattern fatty plaque:
Beer belly

Female pattern fatty plaque:
Cellulite

A schematic of mixed segmental and diffuse narrowings and associated pressure drops along the length of the artery at maximum flow. (A) Predominant, more severe single segmental stenoses with less diffuse narrowing, suitable for angioplasty or bypass surgery. (B) Predominantly diffuse disease or multiple stenoses with less segmental narrowing, not appropriate for angioplasty or bypass surgery. Reprinted with permission from Gould KL. Coronary artery stenosis and reversing atherosclerosis, 2nd ed. London: Arnold Publishing, 1999.
NHLBI-WISE
Microvascular Coronary Disease
Exertional angina

Abnormal SPECT

No obstructive CAD

Abnormal coronary flow reserve and elevated LVEDP

Diffuse atherosclerosis by IVUS

More men receive treatment

More women die

Obstructive CAD Male-pattern

Microvascular CAD Female-pattern

RX: ASA, BB, ACE, STATIN

DEATH/MI FOLLOWUP

Bairey Merz EHJ 2011
Clinical Practice Guidelines

- This slide set was adapted from the following 2004-6 ACC/AHA guidelines:
  - *Cardiovascular Disease Prevention in Women 2004, 2007, 2010*
  - *Management of Patients With ST-Elevation Myocardial Infarction*
  - *Management of Patients with Unstable Angina and Non-ST-Segment Elevation Myocardial Infarction*
  - *Preventing Heart Attack and Death in Patients with Atherosclerotic Cardiovascular Disease*
  - *Management of Patients with Chronic Stable Angina*
  - *Update for Coronary Artery Bypass Graft Surgery*
  - *Evaluation and Management of Chronic Heart Failure in the Adult*

- The full-text guidelines and executive summaries are also available on the
  - ACC and AHA websites at [www.acc.org](http://www.acc.org) and [www.americanheart.org](http://www.americanheart.org)

ACC=American College of Cardiology,
AHA=American Heart Association
Figure  Cox proportional hazard functions for 1-year survival at mean of covariates pre- and post-transition stratified by women vs men.

Novak et al Am J Medicine 2008;121:602
Guideline Implementation and ACS and the Sex Survival Gap

Following guideline implementation, mortality for women improves and the sex gap narrows (RED).
Guideline Implementation and ACS and the Sex Survival Gap

Following guideline implementation, mortality for women improves and the sex gap narrows (RED).

Persistent sex gap (BLUE) suggests more work still needed to understand sex-specific pathophysiology to improve outcomes for women and men.

Figure Cox proportional hazard functions for 1-year survival at mean of covariates pre- and post-transition stratified by women vs men.

Novak et al Am J Medicine 2008;121:602
Deaths in Thousands

Years

Males

Females

Source: NCHS and NHLBI
NHLBI Heart Truth/AHA, WISE and Guideline Campaigns

1997-2007: 43% ↓

Source: NCHS and NHLBI
Rate of Awareness of Heart Disease in Women Initially Doubled But Has Stalled

Results of 6 AHA National Surveys

Mosca et al, Circ Cardiovasc Qual Outcomes 2013;127:1254-1263
Women Remain the Majority of Victims and Still Receive Fewer Interventions to Prevent and Treat Heart Disease

- Less cholesterol screening 🚧
- Fewer lipid-lowering therapies 🚧
- Less use of heparin, beta-blockers and aspirin during myocardial infarction 🚧
- Less antiplatelet therapy for secondary prevention 🚧
- Fewer referrals to cardiac rehabilitation 🚧
- Fewer implantable cardioverter-defibrillators and heart transplants compared to men with the same recognized indications 🚧

Underrepresentation of Women in Cardiovascular Clinical Trials

Remains low compared to disease prevalence and death rates - Perseverates knowledge gaps which adversely impact women

Melloni, et al, Circ Cardiovasc Qual Outcomes 2010
Representation of Women in Cardiovascular Clinical Trials by cohort years of publication – trending up

Is 35% adequate with women the majority of victims?

Melloni, et al, Circ Cardiovasc Qual Outcomes 2010
Underreporting of Sex of Animals in Basic Science Studies – is this acceptable?

Animal articles in 2009 (%)

- General biology
- Immunology
- Neuroscience
- Physiology
- Pharmacology
- Endocrinology
- Reproduction
- Behavioral physiology
- Behavior
- Zoology

Unspecified: light grey
Both: medium green
Female: light blue
Male: dark red

Science 327:1572, 2010
Minority number of articles reporting data on women by year – is this appropriate?

17 percent of the articles comparing treatment strategies for CAD reported sex-specific outcomes

Sex-specific Issues in CAD
Pathophysiology and Presentation

The Barbra Streisand Women’s Heart Center:

a. Science – advocacy, philanthropy
b. Policy – research/publication, guidelines
c. Education – disparities, technology