Women's Heart Health: Prevention, Diagnosis and Treatment of Heart Disease in Women

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32 y/o AA female with history of obesity and HTN presents with chest pressure

- Sitting at rest when developed acute onset of stabbing chest pain which radiated to her back. The pain waxed and waned and after 30 minutes her husband called 911. Her pain resolved with sl TNG and ASA.
- Transported to MGH ED arrived 1/9 11:50 pm
- PMH: Obesity, HTN since first pregnancy (no preeclampsia, on no meds) GERD
- FH: HTN in parents, cousin w SCD MI age 35
• BP 200/100
• Handheld echo in the ED: no effusion, overall normal LV function
• TnT 0.8, K 2.9 Mg 1.3
• ECG:

• CTA chest, abd and pelvis no abnormalities
• TnT 0.45
• Patient painfree and admitted to SDU on ASA, statin, metoprolol, heparin drip
• Echo obtained:
• Although often considered to be a man’s disease, heart disease should be equally concerning to women

• Cardiovascular disease is the leading cause of death in women
  – Worldwide 8.6 million women die from heart disease annually
  – In the US Nearly 500,000 women die from cardiovascular disease each year
  – This is nearly twice the death rate from all forms of cancer
  – Although the death rate from heart disease has been steadily declining for men, the death rate has not been declining for women
Cardiovascular Disease Death Rate Trends

Cardiovascular Disease Mortality Trends for Males and Females United States: 1979–2009

Source: NCHS.

Prevalence of Cardiovascular Disease in Americans Age 20 and Older by Age and Sex
NHANES III: 1988-94

Source: © American Heart Association 2004
Acute MI Mortality by Age and Sex

![Graph showing mortality by age and sex.]

Source: Adapted from Vaccarino 1999

WHY DO WE NEED A DIFFERENT APPROACH IN WOMEN?

Diagnostic Challenges:
- Lack of awareness
- Women present with atypical symptoms
- Less sensitivity and specificity of routine ETT in women

Treatment Challenges:
- Women present later than men with acute MI
- Women are less likely to receive PCI, aggressive medical therapies following MI
- More co-morbidities
- Smaller hearts, smaller arteries.

Source: American Heart Association 2004
Evaluation of Heart Disease Risk in Women-
High Risk

- Evidence of coronary arterial, cerebrovascular or peripheral vascular disease disease (CAD)
- Abdominal aortic aneurysm
- End-stage or chronic kidney disease
- Diabetes mellitus
- 10-y Predicted CVD risk >10%

Evaluation of Heart Disease Risk in Women- At Risk (> 1 of the following)

- Cigarette smoking
- SBP >120 mm Hg, DBP >80 mm Hg, or treated HTN
- Total cholesterol >200 mg/dL/5.2 mmol/L, HDL-C <50mg/dl/1.29 mmol/L
- Treated for dyslipidemia
- Obesity, particularly central adiposity
- Poor diet
- Physical inactivity
- Family history of premature CVD
- Metabolic syndrome
- Evidence of advanced subclinical atherosclerosis
- Poor exercise capacity on treadmill test and/or Abnormal heart rate recovery
- Systemic autoimmune collagen-vascular disease (eg, lupus or rheumatoid arthritis)
- History of preeclampsia, gestational diabetes, or Pregnancy-induced HTN
Evaluation of Heart Disease Risk in Women-Optimal Risk

• Total cholesterol <200 mg/dL/5.2 mmol/L (untreated), HDL>50 mg/dL/1.29 mmol/L
• BP <120/80 mm Hg (untreated)
• Fasting blood glucose <100 mg/dL/5.5 mmol/L (untreated)
• Body mass index <25 kg/m2
• Abstinence from smoking
• Physical activity at goal for adults 20 y of age:
  – 150 min/wk moderate intensity, 75 min/wk vigorous intensity, or combination
• Healthy (DASH-like) diet

Important CV Risk Considerations in Women

• History of pre-eclampsia, gestational hypertension, diabetes
• History of Raynaud’s, migraine headaches
• Premature menopause
• Functional capacity- strong predictor of overall mortality
• Include questions in your screening questionnaire
My Life Check

HOW TO USE MY LIFE CHECK

STEP 1: Answer questions about your Simple 7
• Three measurements of your blood characteristics
• Four things you do every day that impact your health

STEP 2: Choose your action plan
• Compare your current Simple 7 with what is recommended for you
• Select the actions for your Simple 7 that are right for your health

STEP 3: Discover your heart score
• This number (0-10) is an indication of your overall cardiovascular health based on the information you’ve given.

STEP 4: Print or save your results

STEP 5: Return periodically to take the assessment again
• Compare your results to measure your improvement

REAL HEART SCORE

10.0

What you need to know to use this health assessment
• Anti-Privacy Policy
• Terms and Conditions

If you can achieve an Excellent rating in all of the simple 7 areas, you will reach your "ideal" cardiovascular health.

Tell me more

MASSACHUSETTS GENERAL HOSPITAL
HEART CENTER
Hyperlipidemia: Statin therapy

4 Statin Benefit Groups:
1. Individuals with clinical ASCVD
2. Individuals with primary elevations of LDL-C ≥190 mg/dL
3. Individuals 40 to 75 years of age with diabetes and LDL-C 70 to 189 mg/dL, without clinical ASCVD
4. Individuals without clinical ASCVD or diabetes who are 40 to 75 years of age with LDL-C 70 to 189 mg/dL, and have a calculated 10-year ASCVD risk of 7.5% or higher.

Individuals in the last group can be identified by using the Pooled Cohort Equations for ASCVD risk prediction developed by the Risk Assessment Work Group. Lifestyle counseling should occur at the initial and follow-up visits as the foundation for statin therapy and may improve the overall risk factor profile.

Figure 1. 2013 American College of Cardiology–American Heart Association Guidelines for Use of Statin Therapy in Patients at Increased Cardiovascular Risk.

Patients ≥21 yr of age without heart failure (NYHA class II, III, or IV) or end-stage renal disease (undergoing hemodialysis) Screen for cardiovascular risk factors Measure LDL cholesterol

Clinical atherosclerotic CVD
High-intensity statin therapy

Diabetes mellitus (type 2 or type 1) and age of 46-75 yr and LDL cholesterol 70-189 mg/dL
Calculate 10-yr risk of atherosclerotic CVD
If risk >7.5%, moderate-intensity statin therapy
If risk ≤7.5%, high-intensity statin therapy

No diabetes mellitus and age of 46-75 yr and LDL cholesterol ≥190 mg/dL
Calculate 10-yr risk of atherosclerotic CVD
If risk >7.5%, moderate-intensity statin therapy
If risk ≤7.5%, high-intensity statin therapy

LDL cholesterol <190 mg/dL
High-intensity statin therapy
Hypertension:

- HTN increases risk of a heart attack, heart failure, stroke, kidney disease, and blood vessel disease, including aortic dissection and peripheral blood vessel disease
- Of the 67.9% of people with hypertension who are being treated, a full 50% still do not have their blood pressure under control
- Risk factor for HTN, Afib and CHF
- >70% post-menopausal women have HTN

Benefits of Statins

- High intensity therapy – lowering LDL cholesterol by >50%.
- Moderate intensity therapy - lowering LDL cholesterol by 30-50%.
- Reduces ASCVD events across the spectrum of baseline LDL-C levels > 70 mg/dL.
- Relative reduction in ASCVD risk is consistent for primary and secondary prevention.

✓ Absolute reduction in ASCVD events is proportional to baseline absolute ASCVD risk.

✓ Statin therapy only for individuals at increased ASCVD risk.
Hypertension

• Blood pressure: optimal level and lifestyle
  – An optimal blood pressure of <140/90 mm Hg should be encouraged through lifestyle approaches such as weight control, increased physical activity, alcohol moderation, Na restriction, and increased consumption of fruits, vegetables, and low-fat dairy products

• Blood pressure: pharmacotherapy
  – Pharmacotherapy is indicated when blood pressure is >140/90 mm Hg or 150/90 if > 60 years of age.
  – Thiazide diuretics first line

JNC 8 Recommendations

<table>
<thead>
<tr>
<th>Patient Subgroup</th>
<th>Target SBP (mm Hg)</th>
<th>Target DBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 years</td>
<td>&lt;130</td>
<td>&lt;80</td>
</tr>
<tr>
<td>&lt; 60 years</td>
<td>&lt;140</td>
<td>&lt;90</td>
</tr>
<tr>
<td>&gt; 60 years with CVD</td>
<td>&lt;140</td>
<td>&lt;90</td>
</tr>
<tr>
<td>&gt; 74 years with diabetes</td>
<td>&lt;140</td>
<td>&lt;90</td>
</tr>
</tbody>
</table>

CVD = chronic kidney disease; DBP = diastolic blood pressure; SBP = systolic blood pressure

JNC 8 Recommendations (continued)

• General nonblack population
  • Thiazides, CCB, ACEI, or ARB initially

• General black population
  • Thiazides or CCB initially

• CVD
  • Treatment should include ACEI or ARB
  • Up-titrate or add therapy after 1 mo if BP goal not achieved
  • Don’t use ACEI and ARB together
  • If > 3 drugs needed, refer to hypertension specialist

Physical Activity

• Important predictor of overall risk
• Previous studies in men-strongest predictor of death in both normal subjects and patients with CV disease
• Women Take Heart Study
  – Exercise capacity predicted all cause death in asymptomatic women
  – Persisted after adjustment for traditional risk factors
  – For each 1 MET ↑ a 17% ↓ in mortality rate was observed

Assessment of Functional Capacity

• Duke Activity Status Index
  – 12-item self-reported questionnaire that captures a person's ability to perform routine activities

Hlatky MA, et al. Am J Cardiol 1989;64:651-44
DASI

- Accurate estimate of peak oxygen consumption
- DASI/3.5 = Estimated MET levels
- DASI < 20 (5.7 METS) are considered functionally impaired

### TABLE I

<table>
<thead>
<tr>
<th>Activity</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Can You:</td>
<td></td>
</tr>
<tr>
<td>1. Take care of yourself, that is, eating, dressing, bathing or using the toilet?</td>
<td>2.75</td>
</tr>
<tr>
<td>2. Walk indoors, such as around your house?</td>
<td>1.75</td>
</tr>
<tr>
<td>3. Walk a block or 2 on level ground?</td>
<td>2.75</td>
</tr>
<tr>
<td>4. Climb a flight of stairs or walk up a hill?</td>
<td>5.60</td>
</tr>
<tr>
<td>5. Run a short distance?</td>
<td>8.00</td>
</tr>
<tr>
<td>6. Do light work around the house like dusting or washing dishes?</td>
<td>2.70</td>
</tr>
<tr>
<td>7. Do moderate work around the house like vacuuming, sweeping floors, or carrying in groceries?</td>
<td>3.50</td>
</tr>
<tr>
<td>8. Do heavy work around the house like scrubbing floors, or lifting or moving heavy furniture?</td>
<td>8.00</td>
</tr>
<tr>
<td>9. Do yardwork like raking leaves, weeding, or pushing a power mower?</td>
<td>4.50</td>
</tr>
<tr>
<td>10. Have sexual relations?</td>
<td>5.25</td>
</tr>
<tr>
<td>11. Participate in moderate recreational activities like golf, bowling, dancing, doubles tennis, or throwing a baseball or football?</td>
<td>6.00</td>
</tr>
<tr>
<td>12. Participate in strenuous sports like swimming, singles tennis, football, basketball or skiing?</td>
<td>7.50</td>
</tr>
</tbody>
</table>

### Annualized total CV event rates by ETT and DASI-estimated metabolic equivalents (METs) in 251 symptomatic women

**Modifiable Risk Factors: Sedentary Lifestyle**

- 30% of women report no leisure time physical activity
- Exercise is less prevalent among white women compared to white men
- African American and Hispanic women have the lowest prevalence of leisure time physical activity
- Work with women to utilize personalized exercise options within their community

Source: CDC, U.S. Surgeon General 1996

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**Diabetes**

- 5-7 times ↑ risk of heart disease
  - Higher in women than in men
- Risk ↑ even in pre-diabetes
- Diabetics are much more likely to be obese, have other risk factors
- 3X ↑ risk in women gestational diabetes
- High risk for heart disease
- Lifetime risk of developing DM in children born after 2000
  - 1/5
  - 1/3 in Hispanic children
Coronary Disease Mortality and Diabetes in Women

116,000 subjects age 30-55 followed 8 years

Definition of Metabolic Syndrome in Women

- Abdominal obesity - waist circumference ≥ 35 in.
- High triglycerides ≥ 150mg/dL/1.69 mmol/L
- Low HDL cholesterol < 50mg/dL/1.29 mmol/L
- Elevated BP ≥ 130/85mm Hg
- Fasting glucose ≥ 100mg/dL/6.1 mmol/L

Source: AHA/NHLBI 2005
Early Research: Metabolic Syndrome Project

Take Home Points
MetSyn is significantly more common among women in lower socioeconomic classes. MetSyn is grossly under diagnosed in all women, regardless of socioeconomic class.

Figure 2: Model of Microvascular Angina in Women

- Hemorrhage: Acute injury
- Neointimal hyperplasia
- Vascular dysfunction
- Hypo- and hyper-perfusion
- Neovascularization

Shaw et al. 2009, JACC 1567

Figure 2. Model of Microvascular Angina in Women.
Cigarette Smoking

- Number one cause of heart attacks in premenopausal women
- Cigarette smoking is the **single most preventable cause of premature death** in the United States.
- Smokers 2-3 times more likely to die from coronary heart disease
- Women should be advised not to smoke and to avoid environmental tobacco smoke.
- Provide counseling at each encounter, nicotine replacement, and other pharmacotherapy as indicated in conjunction with a behavioral program or formal smoking cessation program.

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**Obesity Trends* Among U.S. Adults**


*(BMI ≥ 30, or about 30 lbs. overweight for 5’4” person)*

<table>
<thead>
<tr>
<th>Year</th>
<th>&lt;10%</th>
<th>10%-14%</th>
<th>15%-19%</th>
<th>20%-24%</th>
<th>25%-29%</th>
<th>≥30%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>No Data</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Weight Maintenance/Reduction Goals

- BMI between 18.5 and 24.9
- Waist circumference < 35 inches
- Weight loss goals
  - 10% of body weight over six months or 1-2 pounds weight loss/week
  - Reduce calories by 500-1,000 per day

Source: Mosca 2011
Obesity Runs Through Social Networks
(Christakis, et al)

- Framingham Heart Study: highly interconnected social network
- 12,067 people assessed repeatedly from 1971 to 2003
- They examined whether weight gain in one person was associated with weight gain in friends, siblings, spouse, and neighbors.
- Obesity likes company! clusters of obese persons (BMI>30) at all timepoints
- Obesity extended up to three degrees of separation
- Influence of social ties on likelihood of becoming obese:
  - Friend: 57%
  - Sibling: 40%
  - Spouse: 37%
  - Neighbor no increase
- Greater influence in same gender connections

Current Research: Psychological Analysis

- Psychological Stress and Heart Disease
  - Depression predicts the development of CHD in healthy people\[19]\n  - Depression increases the risk of mortality in CHD patients\[20]\n  - Stress is associated with a higher risk of ischemic heart disease in women and men\[21,22]\n  - Prevalence of CHD is increased among persons with anxiety disorders\[23]\n- SO… Among low income and minority women, what is the relationship between psychological and cardiovascular health?

Diagnosis: Evaluation for Obstructive CAD in Women

- Difficult because:
  - greater co morbidities
  - higher rates of false positives
  - greater functional disability
  - the workup may be limited or prematurely terminated
  - atypical symptoms

- Chest pain is experienced by most women with CHD, but non-chest pain presentations are more common in women than men

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The Ischemic Cascade

- Time From Onset of Ischemia
- Flow Maldistribution
  - Hypoperfusion
  - Diastolic Dysfunction
  - Systolic Dysfunction
  - ECG Changes
  - Angina

- Nuclear
- Echo
Exercise Stress Testing

- Limited to those with normal EKG
- Limited to those able to exercise
- Diminished accuracy in part related to:
  - lower obstructive CAD prevalence
  - lower QRS voltage
  - hormonal factors
- Endogenous estrogen may cause a digoxin-like effect on EKG
- Ischemia may vary during the menstrual cycle, more likely to demonstrate ischemia when estradiol levels are low
- Hormone Replacement Therapy promote peripheral vasoreactivity causing a decrease in ischemia

NUCLEAR STRESS TESTING

Sensitive in men and women
Can use pharmacologic stress test if unable to exercise
Factors that appear to affect diagnostic accuracy in women include small heart size and relatively lower cardiac mass relative to men
Photon attenuation due to breast artifact on SPECT imaging in women ↓ specificity
The lower prevalence of epicardial CAD in women affects accuracy of all non-invasive diagnostic modalities in women.
ETT vs. SPECT in women, Shaw et al. Circulation 2011

WOMEN trial

- First RCT comparing effectiveness of standard ETT compared to imaging
- 824 women randomized to ETT vs. exercise MPI
- Eligible if: typical/atypical chest pain
  - interpretable EKG
  - over 40
  - intermediate pre test probability
  - capable of performing 5 METS

WOMEN study

- Crossover to MPI in 18% women with ETT alone
- 6% total underwent coronary angiography
- Costs were 48% lower in ETT group
Differences in 2-year primary end points by randomized test assignment in patients with normal and abnormal test results.


Copyright © American Heart Association

Angina-free status during follow-up by randomization to an exercise treadmill test (ETT) vs exercise myocardial perfusion imaging (MPI).


Copyright © American Heart Association
Limitations of Study

- 27% of patients had nonspecific chest pain
- Event rate low
- Study population was likely low risk
- Did not use other variables of ETT to improve diagnostic and prognostic features
- Limited power to detect outcome differences
Stress Echocardiography

- Wall motion abnormalities occur early in ischemic cascade
  - ↑ Specificity with echocardiography
  - Less expensive
  - Absent radiation exposure
  - Ability to image wall motion and cardiac function
Published Meta-Analyses Diagnostic Accuracy of Exercise Electrocardiography, Stress Echocardiography, and Stress SPECT Imaging in Women

<table>
<thead>
<tr>
<th>Author, Year (Ref.)</th>
<th>Exercise ECG</th>
<th>Stress Echo</th>
<th>Stress SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fleischmann et al., 1998</td>
<td>—</td>
<td>—</td>
<td>85%</td>
</tr>
<tr>
<td>(143)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kwok et al., 1999 (146)</td>
<td>61%</td>
<td>70%</td>
<td>86%</td>
</tr>
<tr>
<td>Beattie et al., 2003 (143)</td>
<td>—</td>
<td>—</td>
<td>81%</td>
</tr>
<tr>
<td>Average</td>
<td>61%</td>
<td>70%</td>
<td>84%</td>
</tr>
</tbody>
</table>

Cardiac CT

- **EBCT**
  - Yields a calcium score
- **MDCT**
  - Able to accurately quantify the coronary calcium plaque burden
Cardiac CT

• Several RCT ongoing to compare initial strategy of cardiac CT to functional testing
  PROMISE trial
  RESCUE trial

### ACCURACY OF NON-INVASIVE TESTING VERSUS CORONARY ANGIOGRAPHY IN DIAGNOSING CAD IN WOMEN WITH NO KNOWN CAD

<table>
<thead>
<tr>
<th>Modality</th>
<th>Quality of Studies</th>
<th>Number of Studies</th>
<th>Number of Patients</th>
<th>Total Women</th>
<th>Summary Sensitivity, % (95% CI)</th>
<th>Summary Specificity, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG</td>
<td>All</td>
<td>29</td>
<td>8,825</td>
<td>3,392</td>
<td>62 (68 – 68)</td>
<td>68 (63 – 73)</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td>10</td>
<td>3,821</td>
<td>1,410</td>
<td>70 (58 – 79)</td>
<td>62 (53 – 69)</td>
</tr>
<tr>
<td>ECHO</td>
<td>All</td>
<td>14</td>
<td>2,538</td>
<td>1,286</td>
<td>79 (74 – 85)</td>
<td>83 (74 – 89)</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td>5</td>
<td>1,227</td>
<td>561</td>
<td>79 (69 – 87)</td>
<td>85 (68 – 94)</td>
</tr>
<tr>
<td>SPECT</td>
<td>All</td>
<td>14</td>
<td>1,340</td>
<td>1,000</td>
<td>81 (78 – 86)</td>
<td>78 (69 – 84)</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td>4</td>
<td>484</td>
<td>394</td>
<td>83 (52 – 95)</td>
<td>72 (37 – 92)</td>
</tr>
<tr>
<td>CMR</td>
<td>All</td>
<td>5</td>
<td>580</td>
<td>501</td>
<td>72 (55 – 85)</td>
<td>84 (69 – 93)</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td>5</td>
<td>580</td>
<td>501</td>
<td>72 (55 – 85)</td>
<td>84 (69 – 93)</td>
</tr>
<tr>
<td>Coronary CTA</td>
<td>All</td>
<td>5</td>
<td>1,298</td>
<td>474</td>
<td>83 (69 – 96)</td>
<td>77 (54 – 91)</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td>3</td>
<td>312</td>
<td>124</td>
<td>65 (28 – 99)</td>
<td>73 (17 – 97)</td>
</tr>
</tbody>
</table>

95% CI = 95-percent confidence interval; CMR = cardiac magnetic resonance imaging; CTA = computed tomography angiography; ECG = electrocardiography; ECHO = exercise/stress echocardiography; SPECT = single photon emission computed tomography.
Women with chest pain and normal coronary arteries

- Lower prevalence of obstructive CAD but leading killer of women needs to be explained
- Up to 50% of women undergoing coronary angiography have ‘normal arteries’
- Despite less epicardial coronary obstruction women have symptoms, ischemia and worse prognosis
- This paradox needs to be explained
Coronary Macro and Microvascular Disease

A

B

Table 2. Five-Year Rates of Cardiovascular Outcomes in Asymptomatic Women Compared With Symptomatic Women With Normal and Obstructive CAD

<table>
<thead>
<tr>
<th></th>
<th>Asymptomatic Women (N=1000)</th>
<th>Symptomatic Women (WISE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal Coronary Arteries (n=218)</td>
<td>Obstructive CAD (n=152)</td>
</tr>
<tr>
<td>Ml. %</td>
<td>0.7</td>
<td>0.9</td>
</tr>
<tr>
<td>Hospitalization for CHF. %</td>
<td>0.3</td>
<td>2.6</td>
</tr>
<tr>
<td>Stroke, %</td>
<td>1.3</td>
<td>2.4</td>
</tr>
<tr>
<td>Death due to CV. %</td>
<td>0.5</td>
<td>1.5</td>
</tr>
<tr>
<td>All-cause mortality, %</td>
<td>2.1</td>
<td>2.0</td>
</tr>
<tr>
<td>Primary composite endpoint, %</td>
<td>2.3</td>
<td>2.8</td>
</tr>
<tr>
<td>Secondary composite endpoint, %</td>
<td>5.9</td>
<td>6.1</td>
</tr>
</tbody>
</table>

Abbreviations: CAD, coronary artery disease; CHF, congestive heart failure; CV, cardiovascular causes; MI, myocardial infarction; WISE, Women's Ischemia Syndrome Evaluation; WTHR, B. James Women's Heart Project.

1 Indicates 0% stenosis.
2 Indicates 75% to 80% stenosis.
3 Adjusted for age, race, body mass index, systolic blood pressure, diabetes mellitus, education, employment, family history of CAD, smoking history, and theographic symptoms.
4 Comparison with cohort with the WISE cohort who had normal coronary arteries.
5 Consists of MI, hospitalization for heart failure, stroke, or cardiovascular death.
6 Consists of MI, hospitalization for heart failure, stroke, or death due to any cause.
Mechanism for microvascular disease

- Altered resting smooth muscle tone
- Altered responses to vasoconstrictors or dilators
- Reduced number of arterioles/capillaries
- Structural alterations that cause reduced lumen size, increased wall/lumen ratio, increased stiffness and remodeling
Diagnosis

• Difficult and often questioned
• Cannot be visualized by angiography
• As abnormality may not involve all coronary microvessels of a coronary branch uniformly, therefore may be ‘scattered’ throughout myocardium
• Limitations of current methods to detect small burden of ischemia
• Intermittent nature

STRESS CARDIAC MR – SUBENDOCARDIAL ISCHEMIA
PANTING ET AL. NEJM 2002;346:1948-53

Figure 3. Images of Myocardium at Peak Myocardial Enhancement during the First Pass of Gadolinium in a Patient with Syndrome X at Rest (Panel A) and during Stress (Panel B), Showing a Ring of Delayed Subendocardial Enhancement (Arrows in Panel B).
Treatment Goals

- Reduce angina and improve QOL
- Reduce adverse cardiac event risk
- Current angina guidelines do not specifically address microvascular disease
- High prevalence of atherosclerosis and adverse prognosis recommend: aspirin, statins

Limited trial data

- NO RCT showing reduction of adverse cardiac events
- Hormone therapy
- L-arginine
- Beta blocker superior to nitrates and calcium antagonists
  - 10 patient study, crossover double-blind randomized study
Ranolazine

- Pilot study – Women’s Heart Center Cedars-Sinai LA
- J Am Coll Cardiol Img 2011;4:514–22
- 20 patients, randomized to ranolazine or placebo

- Better Seattle Angina Questionnaire at follow-up
- Trend towards improved MPRI on cardiac MR
Treatment of Heart Disease in Women

- Guidelines for treatment of CAD, CHF, arrhythmias, valve disease not gender specific
  - Women of childbearing age should avoid statins if at all possible
  - Avoidance of ACE-I in pregnancy
- Women exhibit survival c/w men in specific therapies
  - Cardiac resynchronization for heart failure
  - TAVR for aortic stenosis
- Women are still under-referred for these therapies

Study Design: Overview

- What is this “HAPPY” Heart?
  - Who: Overworked, underpaid, middle age woman
  - What: Cardiovascular “lifestyle intervention” program
  - When: Currently in its 3rd year
  - Where: Revere Health Center (complete with AWESOME beach front views, seriously!)
  - Why: WISEWOMAN suggest this will work, but will it work in OUR population
  - How: The amazing, tireless work of the HAPPY Heart team
Study Design: Overview

• Goals of the HAPPY Heart Program
  – Screening program for CVD risk factors
    • Identify at-risk patients
    • Motivation
  – Individualized approach to risk factor reduction
    • Identify barriers such as income/education
  – Examine potential benefits of a lifestyle risk reduction program
    • Stress
    • Anxiety
    • Depression

Study Design: Study Design

• Prospective Cohort Study
  – Randomize women to "usual care" vs. enrollment in lifestyle intervention program
  – Original design RCT

• So now, Onto “Plan B”
  – Prospective, cohort study
  – Current enrollment is N=64, ALL enrolled in program
  – Focus on community service and outreach
Study Design: Inclusion/Exclusion

<table>
<thead>
<tr>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female h/o CAD, PVD or stroke</td>
<td>h/o CKD (Cre ≥ 2)</td>
</tr>
<tr>
<td>≥ 2 CVD risk factors</td>
<td>h/o Chronic Hepatitis</td>
</tr>
<tr>
<td>Income &lt;200% FPL</td>
<td>h/o COPD</td>
</tr>
<tr>
<td>English/Spanish*</td>
<td>h/o valve disease</td>
</tr>
<tr>
<td>Able to give informed consent</td>
<td>h/o valve disease</td>
</tr>
<tr>
<td>MGH PCP</td>
<td>LVEF ≤ 50%</td>
</tr>
<tr>
<td>Age 40-60 (few exceptions)</td>
<td>Severe cognitive dysfunction</td>
</tr>
<tr>
<td></td>
<td>Current/planned pregnancy</td>
</tr>
</tbody>
</table>

Methods: Study Design

**HAPPY Heart Design**
- Patients are recruited/referred by PCP
- Phone screening, if eligible, appt. made
- At appointment, RN confirms eligibility
- IRB consent signed/formal enrollment
- *Baseline Testing
- Enrollment in the program

**Baseline Testing**
- BP, HR, Height, Weight, Waist/Hip Circ.
- Past Medical History
- Exercise/Activity Assessment
- Depression/Anxiety/Stress Assessment
- Lab Testing (BMP, Cholesterol, CRP, BNP)
- Echocardiography
- Electrocardiography
- Intimal Medical Thickness (IMT)
- 6 Minute Walk Test
- Framingham Risk Score
Methods: Study Design

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Nutrition</th>
<th>Psychological</th>
<th>Smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT Consult</td>
<td>Nutrition Consult</td>
<td>CESD-10</td>
<td>Offered cessation program</td>
</tr>
<tr>
<td>Individualized</td>
<td>Individual diet - Cost/Family</td>
<td>STAI</td>
<td>Offered free pharmacologic options</td>
</tr>
<tr>
<td>exercise plan</td>
<td>▼</td>
<td>PSS</td>
<td></td>
</tr>
<tr>
<td>Regular check in w/ Health Coach</td>
<td>▼</td>
<td>HAPPY Heart Relaxation &amp; Medication Classes</td>
<td></td>
</tr>
<tr>
<td>*HAPPY Heart</td>
<td>*HAPPY Heart Cooking Classes</td>
<td>▼</td>
<td></td>
</tr>
<tr>
<td>Exercise Classes</td>
<td></td>
<td>Regular check in w/ Health Coach</td>
<td></td>
</tr>
</tbody>
</table>

Enrollment
Year 0
N=64

Study Design
Year 1
Follow Up
N=57

Year 2
Follow Up
N=50

**FIG. 2.** Rates of meeting diagnostic criteria for metabolic syndrome, i.e. having 3 of 5 components of metabolic syndrome, at baseline, year 1 and year 2. This figure displays the significant decrease from baseline to year 1 and from baseline to year 2 in the rate of metabolic syndrome. *Denotes significant value.
Current Research: Year 1 and 2 Analysis

**Waist Circumference (cm)**

- Waist_0
- Waist_1
- Waist_2

**HbA1c**

- HbA1c_0
- HbA1c_1
- HbA1c_2

\( p < 0.001 \)
Conclusions

• More women than men are dying from heart disease in the US
• Knowledge gap exists on the part of physicians and patients regarding symptoms and treatment of CAD in women
• Prediction of risk of heart disease in women is different than that in men
  – New tools
• Women > 50 are the largest growing demographic
  – We must educate physician and policy makers
• Seize the teachable moment
Conclusions

- Many any factors that affect the accuracy of the noninvasive technologies (NITs) used to diagnose coronary artery disease (CAD) in women, making noninvasive CAD diagnosis challenging. Such factors include:
  - Symptoms of CAD in women being less predictive and more atypical when compared with men
  - Lower prevalence of obstructive epicardial CAD in women than in men
  - Higher prevalence of single-vessel disease
  - Smaller coronaries and LV size

Conclusions

- The HAPPY Heart Program Works
  - Decreases cardiovascular risk
  - Decreases psychological risk
  - REALLY difficult population to study and to treat

- We need MORE emphasis on primary prevention
  - PCP level
  - Specialty level
  - Primary Prevention Programs