Tamara Horwich, MD, MS is an attending cardiologist and Health Sciences Associate Clinical Professor of Medicine/Cardiology at the David Geffen School of Medicine at UCLA. She is Medical Director of UCLA's Cardiac Rehabilitation Program, including the Dr. Dean Ornish Comprehensive Lifestyle Program for Reversing Heart Disease, Co-Director of the UCLA Women's Cardiovascular Health Center, and an active member of the Ahmanson-UCLA Cardiomyopathy Center. Dr. Horwich's clinical interests include treating and preventing heart disease in women, cardiac rehabilitation, treating patients with heart failure, and performing and interpreting echocardiograms. Dr. Horwich's main research interests include studying obesity, body composition and cardiovascular disease, as well as risk factors and novel therapies for patients with heart disease, with a focus on women. She has been a grant recipient from the National Institutes of Health, the Heart Failure Society of America, as well as the Iris Cantor Women's Center at UCLA. Dr. Horwich is a Fellow of the American College of Cardiology and American Heart Association and has helped draft national guidelines on management of heart failure.
Women’s Heart Health: What We Know

Tamara Horwich, MD, MS
Associate Clinical Professor of Medicine / Cardiology
May 21, 2020
Canadian Physician Sir William Osler (1849-1919)

A typical heart attack patient is a “keen and ambitious man, the indicator of whose engine is always ‘full speed ahead’”

... a “well ‘set’ man from 45-55 years of age, with a military bearing, iron-gray hair, and a florid complexion.”
Frank Netter
1906 - 1991
Dr. Bernadine Healy (1944-2011)
Prevalence of cardiovascular disease in adults ≥20 years of age by age and sex


Mozaffarian D et al. Circulation. 2015;131:e29-e322
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Heart Disease - Leading Cause of Death

Deaths in Thousands

- 1980: Men 520, Women 470
- 1985: Men 510, Women 460
- 1990: Men 500, Women 450
- 1995: Men 490, Women 440
- 2000: Men 480, Women 430
- 2005: Men 470, Women 420
- 2010: Men 460, Women 410
- 2015: Men 450, Women 400
- 2020: Men 440, Women 390

Key Events:
- 1987: 1st statin released
- WHI
- HRT Stopped
- Awareness campaigns on women and heart disease
- Everyone losing ground

Salim S. Virani. Circulation. Heart Disease and Stroke Statistics—2020 Update: A Report From the American Heart Association, Volume: 141, Issue: 9, Pages: e139-e596,
Women and Heart Disease: What We Know

1. Coronary Artery Disease in Women
2. Heart Failure in Women
3. Unique Risk Factors in Women and Cardiovascular Syndromes Pertinent to Women
4. What We Are Doing
Coronary Artery Disease (CAD) in Women
Change in Coronary Artery Disease Incidence 1996-2005 in the UK

Davies A et al, Eur Heart J 2007
Young Women (ages 18 – 55 years) and Acute Myocardial Infarctions (Heart Attacks)

• Heart attacks are *decreasing* in the overall population but *increasing* in young women (<55 years)
• Women have LONGER hospital stays and HIGHER in-hospital mortality
• Women compared to men are LESS LIKELY to receive reperfusion therapy
• Women compared to men are MORE LIKELY to have delays in treatment including
  • Door to balloon time
  • Door to needle time

Women have “atypical” symptoms

- Chest pain or discomfort
- Unusual upper body discomfort
- Light-headedness or sudden dizziness
- Unusual or unexplained fatigue
- Shortness of breath
- Nausea
- Diaphoresis
Symptom Recognition and Healthcare Experiences of Young Women with Acute Myocardial Infarction (Age ≤ 55)

Symptom Recognition and Healthcare Experiences of Young Women with Acute Myocardial Infarction (Age ≤ 55)

“I felt so stupid laying in the ER...the nurse comes in and goes, ‘all your lab work, everything looks great’...and I burst into tears like I’m so embarrassed...The nurse comes in about 20 minutes later and goes, ‘we need to move you to ICU...you've had a heart attack.’ But it was a sense of relief...I was tryin’ to justify it. I was mortified...I felt like, oh my gosh, what are these people in the ER thinking of me? That here I am, a CRNA [Certified Registered Nurse Anesthetist], and I'm so stupid, you know, like a hypochondriac...
Symptom Recognition and Healthcare Experiences of Young Women with Acute Myocardial Infarction (Age ≤ 55)

“I remember callin’ a doctor and tellin’ him I was having these chest pains and all that stuff, and they just scheduled a regular appointment for me...I would not know that I’m havin’ a heart attack...I would consider that your [the doctor’s] responsibility...they should of pushed me in faster...
CAD may develop differently in women

MEN
- Focal Stenosis

WOMEN
- Diffuse Atherosclerosis
Women are More Likely to have **MINOCA** (Myocardial Infarction in the Absence of Coronary Artery Disease)

<table>
<thead>
<tr>
<th>ACUTE CORONARY SYNDROME</th>
<th>WOMEN</th>
<th>MEN</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>GUSTO (overall)</td>
<td>19.4%</td>
<td>8.4%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GUSTO (unstable angina)</td>
<td>30.5%</td>
<td>13.9%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GUSTO (NSTEMI)</td>
<td>9.1%</td>
<td>4.2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GUSTO (STEMI)</td>
<td>10.2%</td>
<td>6.8%</td>
<td></td>
</tr>
<tr>
<td>TIMI 18 (USA or NSTEMI)</td>
<td>17%</td>
<td>9.0%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TIMI IIIa (USA or NSTEMI)</td>
<td>26.5%</td>
<td>8.3%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Buargini and Bairey-Merz. JAMA. January 26, 2005, Vol 293, No. 4
Coronary Angiogram: the Gold Standard

What we see on an angiogram

What’s really there
Treatment of MINOCA

Statins, ACE/ARBs and β-blockers improve outcomes in MINOCA. Dual antiplatelet therapy does not.

Women and Heart Failure
Hospital discharges for heart failure by sex (United States: 1980–2010).

- Majority is HFrEF (low LVEF)
- Therapies: Beta-blockers, ACEI/ARBs, AAs, CRT / ICD, Ivabradine, Neprilysin inhibitors, SGLT2 inhibitors
- Majority is HFpEF ("Diastolic HF")
Common Characteristics of HFpEF Patients

Compared to HFrEF patients, HFpEF patients were more likely to be, or have, the following characteristics:

- Female
- Older
- Obese
- Higher New York Heart Association class
- More cardiovascular comorbidities: hypertension, diabetes, atrial fibrillation, valvular disease
- More noncardiovascular comorbidities: anemia, chronic kidney disease, chronic pulmonary disease, hypothyroidism, cancer, peptic ulcer, psychiatric disorders

HFpEF: Heart Failure with Preserved Ejection Fraction

Typical Patient

Female
Older
High BMI
Hypertension
Atrial Fibrillation
NO epicardial CAD

Peripartum cardiomyopathy

- Peripartum cardiomyopathy is marked by loss of cardiac contractile function in women late in pregnancy or soon after delivery. PPCM affects approximately 1:1000 births worldwide.
Incidence of PPCM

South Africa
Nigeria
Niger

India
China
Pakistan

USA
California
USA
Tennessee
Kentucky
Chicago
Georgia
HAITI

Blauwet et. al. Heart 97:23 2011
Women have Unique Risk Factors for Coronary Artery Disease

Traditional ASCVD Risk Factors

- Diabetes
- Smoking
- Obesity and overweight
- Physical inactivity
- Hypertension
- Dyslipidemia

Emerging, Nontraditional ASCVD Risk Factors

- Preterm delivery
- Hypertensive disorders of pregnancy
- Gestational diabetes
- Autoimmune disease
- Breast cancer treatment
- Depression
CVD Events in Patients With Diabetes: Framingham 30-Year Follow-Up
Women with DM have ~40% greater risk of developing Cardiovascular Disease compared to Men with DM

- Hazard ratio 2.68 in women vs 1.85 in men
Women, Obesity, and Coronary Artery Disease

Recent Research from the UCLA Women’s Cardiovascular Center

- Men: 4% increased probability of coronary artery calcium per 10 kg increase in fat mass
- Women: No increased risk of coronary artery calcification with increasing levels of body fat mass
Incidence of Cardiovascular Disease: Relation to age and Menopausal Status

The Menopause Bump

Pre and Post Menopause Changes

• Cross-sectional study of 3,636 women
• (40–59 years old)

<table>
<thead>
<tr>
<th>Variable</th>
<th>PRE</th>
<th>POST</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td>49.7</td>
<td>55.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Activity (METS)</td>
<td>5502</td>
<td>2458</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>26.9</td>
<td>28.1</td>
<td>0.001</td>
</tr>
<tr>
<td>% BF</td>
<td>34.1</td>
<td>36.2</td>
<td>0.001</td>
</tr>
<tr>
<td>HTN (%)</td>
<td>55.2</td>
<td>60.4%</td>
<td>0.01</td>
</tr>
<tr>
<td>LDL-c</td>
<td>121.6</td>
<td>132.2</td>
<td>0.001</td>
</tr>
<tr>
<td>HDL-c</td>
<td>63.7</td>
<td>62.5</td>
<td>NS</td>
</tr>
<tr>
<td>TG</td>
<td>100.8</td>
<td>113.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Glucose</td>
<td>92.0</td>
<td>95.8</td>
<td>0.001</td>
</tr>
</tbody>
</table>
Adverse *Pregnancy* Outcomes Which are Associated 1.8 – 4.0x Greater Risk of Future CVD

**Conditions:**
- Hypertensive disorders of pregnancy (chronic hypertension, gestational hypertension, preeclampsia, eclampsia, HELLP syndrome)
- Gestational diabetes mellitus
- IUGR (intrauterine growth retardation)
- Preterm birth (idiopathic/spontaneous)
- Placental abruption
- Obesity/excessive pregnancy weight gain/post-partum weight retention
- Sleep disorders; moderate-to-severe obstructive sleep apnea
- Maternal age older than 40 years
Pregnancy – a Stress Test for the Heart


Women, Stress, And Heart Disease: Tako-Tsubo Cardiomyopathy

“BROKEN HEART” Syndrome

- Acute heart attack and heart failure presentation with normal coronary arteries
- Preceding emotional stressor, “lifetime crisis”
- 90% post-menopausal females

**Spontaneous Coronary Artery Disease (SCAD)**

- First described in 1931
- A non-atherosclerotic form of acute coronary syndrome
- Underdiagnosed and often not considered in younger women presenting with chest pain

Previously considered rare, SCAD now recognized to cause 2–4% of all ACS, 24–36% of MIs in women <50y, and the most common cause of pregnancy-associated MI
What are We Going to Do?
Recent Research from UCLA Women’s CVD Center: Urinary Stress Hormones in Women vs Men

Epinephrine
Norepinephrine
Dopamine

No difference
<0.0001
<0.0001

ng/dl

women
men

## Arterial Stiffness

### Baseline Characteristics of Men and Women in MESA

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>3097 (52.0%)</td>
<td>2862 (48.0%)</td>
<td>--</td>
</tr>
<tr>
<td>Age</td>
<td>62.1 (10.26)</td>
<td>62.2 (10.21)</td>
<td>0.7832</td>
</tr>
<tr>
<td>Augmentation Index (AIx)</td>
<td>15.5 (2.30)</td>
<td>14.3 (1.88)</td>
<td>&lt;0.000001</td>
</tr>
<tr>
<td>Pulse Pressure Amplification (PPA)</td>
<td>11.0 (0.48)</td>
<td>11.5 (0.50)</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Reflection Magnitude (RM)</td>
<td>8.41 (0.83)</td>
<td>8.38 (1.07)</td>
<td>&lt;0.00001</td>
</tr>
</tbody>
</table>

Healthy Lifestyle in Women = Heart Disease Prevention!

<table>
<thead>
<tr>
<th>Optimal Lifestyle Factor</th>
<th>Reduced Risk of Coronary Heart Disease*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not Smoking</td>
<td>↓ 71%</td>
</tr>
<tr>
<td>Exercise ≥ 2.5 hours / week</td>
<td>↓ 28%</td>
</tr>
<tr>
<td>Healthy Eating Index (top 40%)</td>
<td>↓ 31%</td>
</tr>
<tr>
<td>Alcohol ≤ 1 drink / day</td>
<td>↓ 33%</td>
</tr>
<tr>
<td>Normal Body Weight (BMI)</td>
<td>↓ 32%</td>
</tr>
<tr>
<td>TV watching &lt; 7 hours / week</td>
<td>-</td>
</tr>
</tbody>
</table>

*After adjustment for all other potential risk factors
Study of >88,000 women followed for 20 years

Chomistek et al. JACC 2015

- Women who engaged in all 6 healthy lifestyles had a **92% lower risk** of getting coronary heart disease
How Much Exercise? *Moderate* Physical Activity Reduces Cardiovascular Risk in Women

Study of 1.3 million women in the UK. Armstrong et al. Circulation Cardiovascular Outcomes 2015
Ornish Intensive Cardiac Rehab: Four key elements working in concert ...

- **Exercise**: 1 hour of group exercise
- **Stress Management**: 1 hour of stress management techniques
- **Community**: 1 hour of group support
- **Nutrition**: Group meal
ECHOS: Research Effort Aimed at Decreasing Stress and Increasing Wellness in UCLA undergraduates. PI Kimberly Uehisa, UCLA undergrad
Meta-analysis of Primary Prevention Statin Trials in Women

<table>
<thead>
<tr>
<th>Trial</th>
<th>Year</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFCAPS/ TexCAPS</td>
<td>1998</td>
<td>0.67</td>
<td>(0.34-1.31)</td>
</tr>
<tr>
<td>MEGA</td>
<td>2006</td>
<td>0.73</td>
<td>(0.49-1.10)</td>
</tr>
<tr>
<td>JUPITER</td>
<td>2008</td>
<td>0.54</td>
<td>(0.37-0.80)</td>
</tr>
<tr>
<td>Combined</td>
<td></td>
<td>0.63</td>
<td>(0.49-0.82)</td>
</tr>
</tbody>
</table>

p < 0.001
What are the optimal doses for medications in women with Heart Failure?
Summary

• More women die of CVD every year than all cancers combined
• Ischemic heart disease may present differently in men compared to women and can be more difficult to diagnose
• Young women presenting with MI have higher in-hospital mortality
• Women tend to have HFpEF while men tend to have HFrEF
• There are unique risk factors for heart disease in women compared to men, including gestational diabetes and menopause. Risk factors with more impact in women compared to men include stress, anxiety, depression, diabetes
Thank you