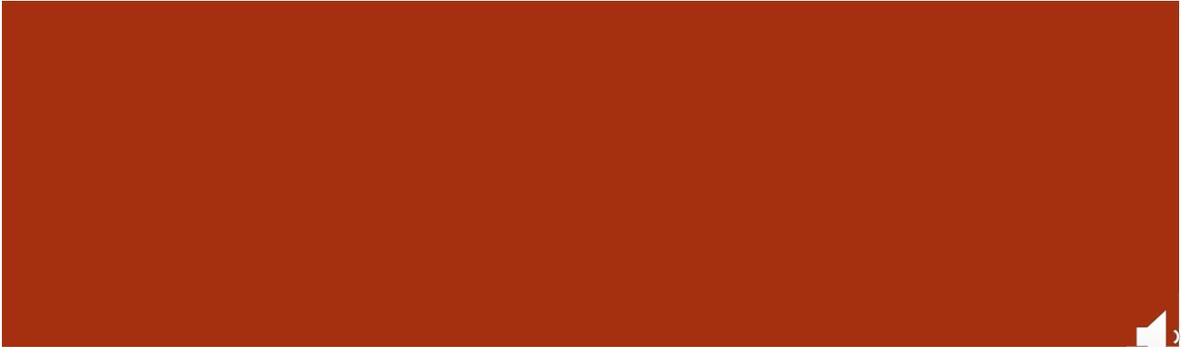

HEART DISEASE IN WOMEN: FACTS AND FICTION

APRIL 2022

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TODAY'S TALK

- Do we treat heart disease differently in women?
- Should we be treating heart disease differently in women?



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COMMON MYTHS ABOUT WOMEN & HEART DISEASE

I've been a smoker for so long, quitting now won't make a difference

It can't happen to me

I've been a smoker for so long, quitting now won't make a difference

Heart attacks in men and women are treated the same way

Heart attacks in men and women occur with the same symptoms

I'm more likely to get breast cancer than heart disease

I'm more likely to get breast cancer than heart disease

CURRENT RESEARCH APPLIES EQUALLY TO MEN AND WOMEN

My doctor regularly assesses my heart risk

Heart disease runs in my family there's **nothing** I can do



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WOULD IT SURPRISE YOU TO KNOW THAT IN 2022

Women with acute coronary syndromes are:

- Less likely to be treated with guideline-directed medical therapies
- Less likely to undergo cardiac catheterization
- Less likely to receive timely reperfusion
- More likely to die in the hospital
- Less likely to be discharged on medications that are known to improve survival



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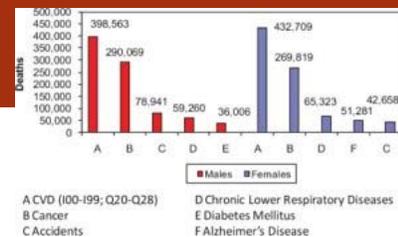
“IT CAN’T HAPPEN TO ME”

- 2012 AHA survey:
- Just over half of women are able to identify heart disease/heart attack as the greatest threat to their health



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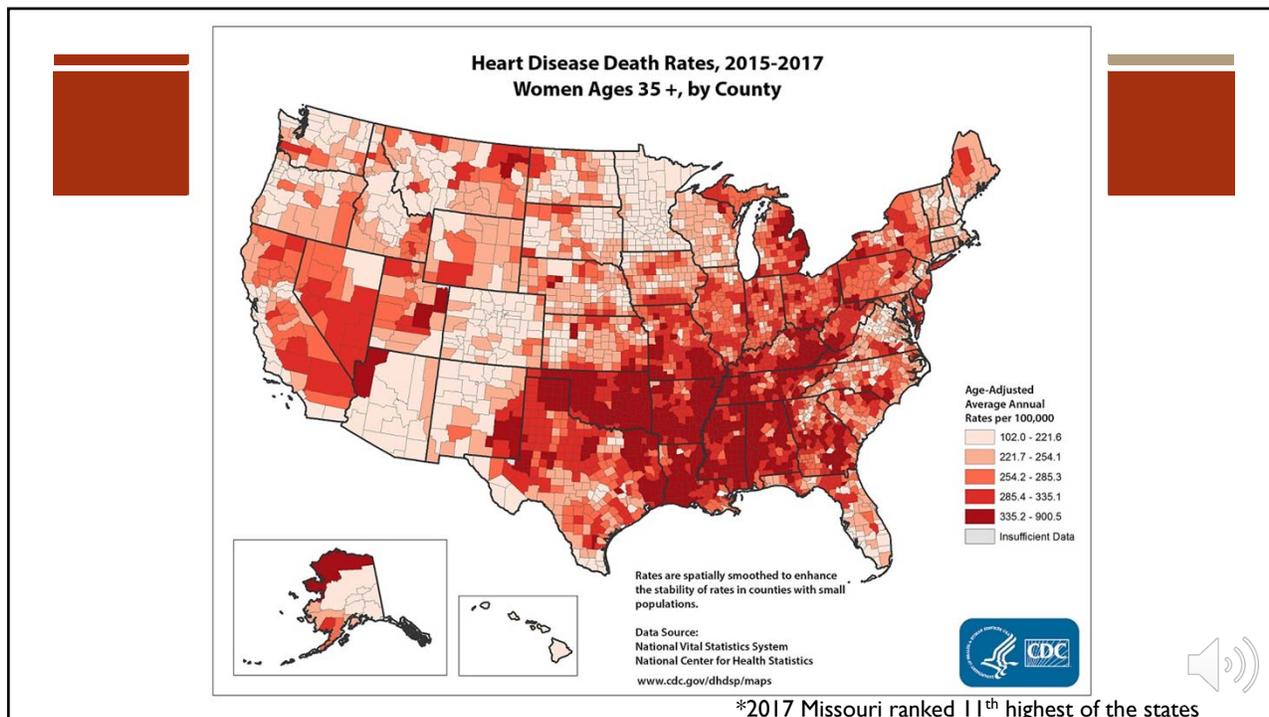
BY THE NUMBERS



- Heart disease is the leading killer of women
- More than 1 in 3 adult women has some form of cardiovascular disease
- 5 times as many women die from cardiovascular disease each year as from breast cancer
- In 2011, cardiovascular disease caused 1 death per minute among females
- That's about the same as all deaths from cancer, chronic lower respiratory disease and diabetes **combined!**



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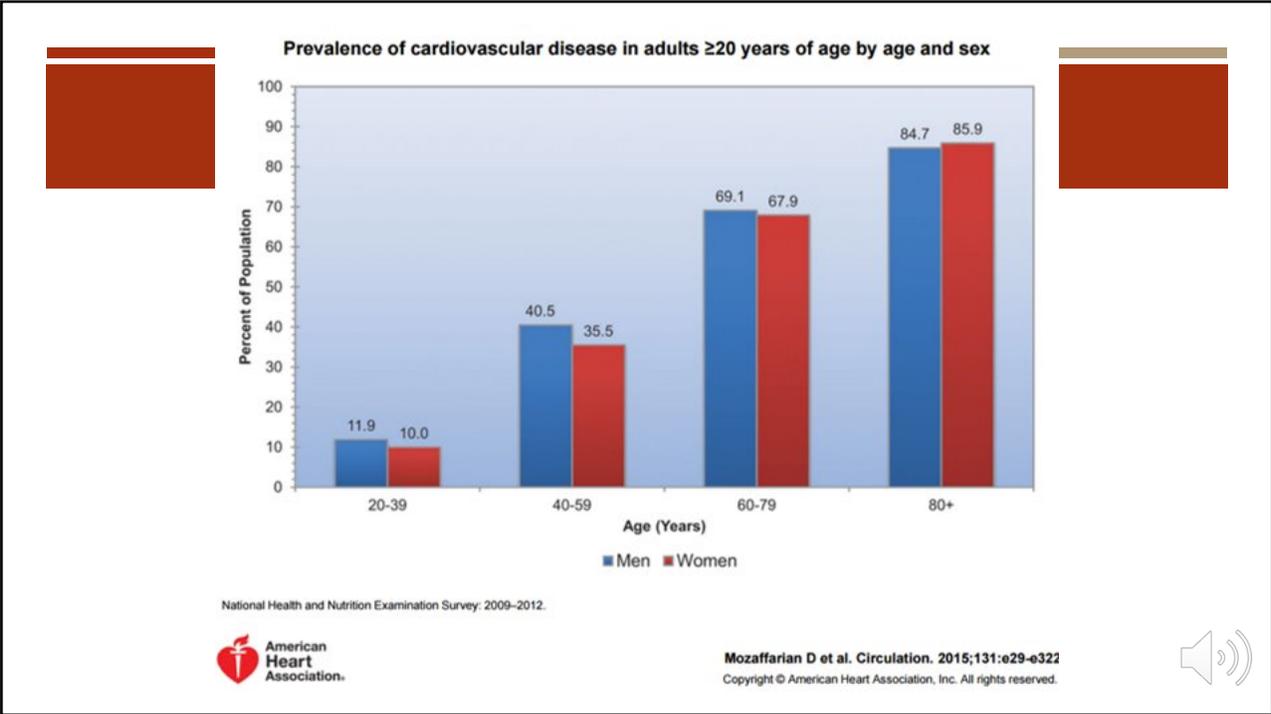


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TODAY'S TALK

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- Should we be treating heart disease differently in women?

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EVEN IN 2022...

- From prevention to presentation and through all treatment stages, there are gender disparities

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Physicians, including cardiologists, consistently perceive ASCVD risk as being lower in women than men despite similar calculated risk scores



10-year ASCVD 18.7%

- *aspirin
- *moderate-intensity statin
- *BP control
- *lifestyle recs



10-year ASCVD 18.7%



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PRIMARY PREVENTION

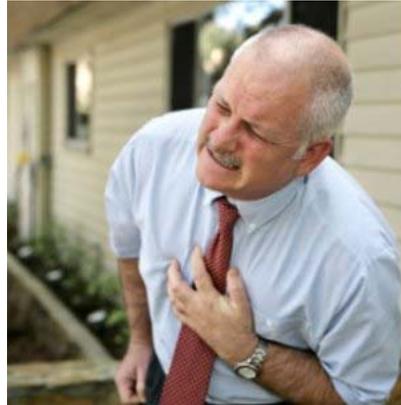
- Women are less likely than men to be prescribed preventive lipid-lowering therapy, aspirin and therapeutic lifestyle changes
- When medications are prescribed, treatment is less likely to be aggressive or to achieve optimal effects
 - women with hypertension are less likely to have their blood pressure at goal
 - hyperlipidemic women, especially those with coexisting diabetes, are less likely to be treated with statins to lower low-density lipoprotein (LDL) cholesterol.



Garcia et al. Cardiovascular Disease in Women: Clinical Perspectives. Circ Res. 2006 Apr 15; 188(8): 1273-1293.

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THIS IS WHAT A HEART ATTACK LOOKS LIKE



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SYMPTOMS

Women are less likely than men to experience chest pain, in some series up to 40% acute MI without chest pain

- Pain in upper back, jaw or neck
- Shortness of breath
- Flu-like symptoms: nausea (49%) or vomiting, cold sweats
- Fatigue or weakness
- Feelings of anxiety, fear (31%), loss of appetite, discomfort
- Shoulder pain and arm pain are twice as predictive of an acute coronary syndrome in women compared to men

- *These are more subtle and easier to overlook or attribute to other causes!*



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SYMPTOMS

Survey 2003

95% of women reported early warning symptoms up to a month before their MI

These were:

- Unusual fatigue in 70%
- Sleep disturbance in 48%
- Shortness of breath in 42%
- Indigestion in 39%
- Anxiety in 35%
- Only 30% of women reported chest discomfort as a prodromal symptom, and they described it as aching, tightness, or pressure rather than as pain



McSweeney Acute and Prodromal Myocardial Infarction Symptom Survey (MAPMISS)

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PRESENTATION OF ACUTE MI

- Women are more likely than men to attribute symptoms to a gastrointestinal illness, stress or anxiety
- Women wait longer than men to go to an emergency room when having an acute coronary event
- In one study, median delay time was 53.7 hours for women and 15.6 hours for men
- Younger women more likely to wait longer (35% >6 hours after onset)



Source: Women's Heart Foundation, derived from statistics compiled from the National Center on Health Statistics, National Heart Lung and Blood Institute, the American Heart Association, HANES III and the World Heart Federation.

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PRESENTATION OF ACUTE MI

- Once in contact with EMS or ED, providers are slower to recognize the presence of MI in women because “characteristic” patterns of chest pain are less frequently present
- Once recognized, women are less likely to be referred for appropriate treatment and more likely to have longer delays in transfer to a PCI-capable facility
- In STEMI, door-to-balloon times are consistently longer for women; women are 1.7x more likely to exceed reperfusion time goals

Dreyer R et al. *Heart Lung Circ.* 2013 Oct;22(10):861-9
Brodie et al. *JACC* 2006 Jan;47(2):289-95
Circulation. 2008;doi:10.1161/CIRCULATIONAHA.108.789800



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TREATMENT OF ACUTE STEMI

- **Treatment guidelines do not differ between sexes**
- Despite this, women are consistently less likely than men to receive beta blockers, ACE inhibitors, statins and aspirin - therapies known to improve survival
- This contributes to a higher rate of complications after MI in women, even after adjusting for age
- Women are half as likely to be referred for cardiac rehab on discharge

Source: Women's Heart Foundation, derived from statistics compiled from the National Center on Health Statistics, National Heart Lung and Blood Institute, the American Heart Association, HANES III and the World Heart Federation.



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TREATMENT

- 25% of coronary bypass surgery patients are women
- 35% of PCI patients are women
- 30.3% of heart transplant patients are women



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TREATMENT

- Women are significantly less likely to be referred for implanted cardiac defibrillators when clinically indicated

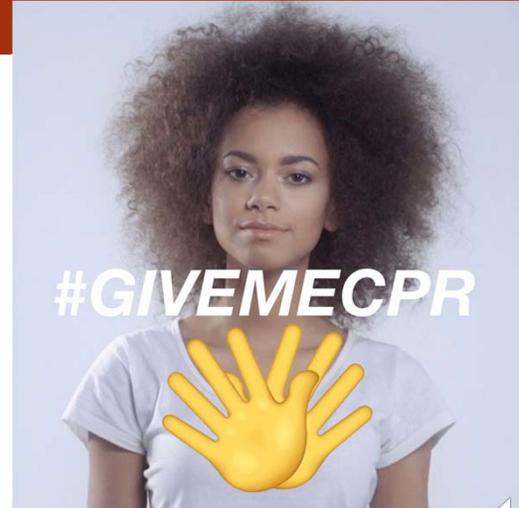


Johnson et al. Pacing Clin Electrophysiol. 2018 Sep;41(9):1150-1157

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CARDIAC ARREST...YEP, EVEN CPR!

- Women are 27% less likely to receive bystander CPR in out of hospital cardiac arrest
- Men's odds of survival were 23% higher
- 19,000 arrests; October 2019
- A virtual reality study found that even female avatars were less likely to receive CPR from bystanders in a virtual simulation



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WHY?????

- Potentially inappropriate touching or exposure;
- Fear of being accused of sexual assault;
- Fear of causing physical injury;
- Poor recognition of women in cardiac arrest -- specifically a perception that women are less likely to have heart problems, or may be overdramatizing or "faking" an incident; or
- The misconception that breasts make CPR more challenging



Perman et al. Circulation 2019 Feb 19;139(8):1060-1068

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Womanikin



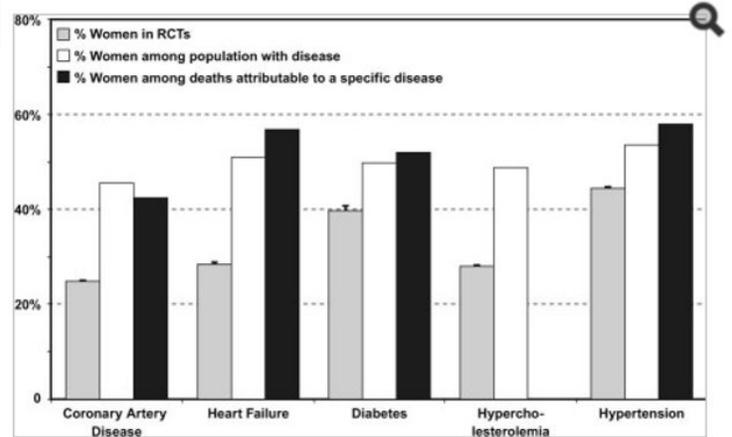
A **universal** attachment to challenge biased CPR training.



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RESEARCH

- Most of the research done includes studies on middle-aged men
- 27% of heart-related research participants are women



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PHYSICIANS

- Many of the physicians making treatment decisions are men
- The number of female physicians has been steadily increasing but the number of female cardiologists is steady at around 10-15%, and just 4% of interventional cardiologists



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TODAY'S TALK

- Do we treat heart disease differently in women?
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PRESENTATION

- Women are on average about 10 years older than men at presentation, although this gap narrows with older age
- Women are more likely than men to also have other risk factors like diabetes or hypertension



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RISK FACTORS

Traditional ASCVD Risk Factors	Emerging/nontraditional
Diabetes	Preeclampsia/gestational hypertension
Smoking	Gestational diabetes
Obesity/overweight	Breast cancer (chemotherapy, radiation)
Physical inactivity	Inflammatory disorders (SLE, RA)
Hypertension	Premature ovarian failure/early menopause (<45)
Dyslipidemia	Depression



Agarwala et al. Circulation. 2020;141:592-599.
Garcia et al. Circ Res. 2016;118(8):1273-1283.

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Stepping to Success: Reducing CVD Risk in Women

Step 1

Screen for Sex-specific Risk Factors:

- Prematurity
- Age at menarche
- Polycystic ovarian syndrome
- Hormone-based contraceptive use
- Recurrent spontaneous pregnancy loss
- Gestational diabetes
- Gestational HTN
- Pre-eclampsia
- Pre-term delivery
- Delivery of small for gestational age infant
- Early menopause/premature ovarian failure

Step 2

If sex-specific risk factors are present:

1. Assess for traditional CVD risk factors early and more frequently
2. Screen for, prevent, & treat intermediate phenotypes

Hypertension
Diabetes
Hyperlipidemia
Metabolic Syndrome

Step 3

Begin aggressive risk factor management

Implement lifestyle modifications with AHA's Life's Simple 7:

1. Manage blood pressure
2. Control cholesterol
3. Reduce blood sugar
4. Stay active
5. Eat Healthy
6. Lose weight
7. Stop Smoking

Step 4

Estimate risk & treat accordingly with consideration of sex-specific risk factors:

1. Assess 10-year ASCVD Risk/Lifetime risk
2. Treat early if borderline or intermediate risk and if sex-specific risk factors are present

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TRADITIONAL RISK FACTORS

- Diabetes: meta-analysis of 37 studies of almost 450,000 patients with type 2 diabetes: the summary relative risk for fatal CHD in patients with diabetes was 3.5 in women and 2.1 in men
- Smoking: women who smoke pack per day are 6x more likely to have an MI than nonsmokers, compared with 3x in men

Huxley et al. BMJ. 2006;332(7533):73

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STRESS TESTING

- Treadmill ECG without imaging is more likely to have a false positive in women
- Adding imaging, sensitivities and specificities are similar for men and women
 - European guidelines recommend stress echo
- Consider stress echo to limit radiation exposure to breast tissue, especially if younger



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ISCHEMIC HEART DISEASE IN WOMEN

- Women are less likely to have anatomically obstructive epicardial coronary artery disease
- Despite this, women have greater rates of angina and myocardial ischemia, and higher mortality compared with similarly aged men
- Women's Ischemia Syndrome Evaluation (WISE) study:
 - Abnormal coronary reactivity
 - Microvascular dysfunction
 - Plaque erosion/distal microembolization

Failure to recognize/treat these unique aspects of ischemic heart disease in women may contribute to the observed sex-based mortality gap



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10-YEAR WISE STUDY FOLLOW UP

- 936 clinically stable women with symptoms and signs suggestive of ischemia referred for coronary angiography
- Mean age 58; 20% non-white, 25% diabetic, 59% hypertension, 55% hyperlipidemia, 59% BMI>30
- 20% had died at 10-year follow up; 60% of deaths were cardiovascular; 30% of these were in women without obstructive CAD (<50% stenosis)
- “in the absence of obstructive CAD on coronary angiography, women are most often provided reassurance rather than cardiovascular therapy” – despite 12% 10-year mortality (compared with 2.8% general population of women)
- But** when women’s ischemic heart disease looks like men’s, they are more likely to be treated appropriately

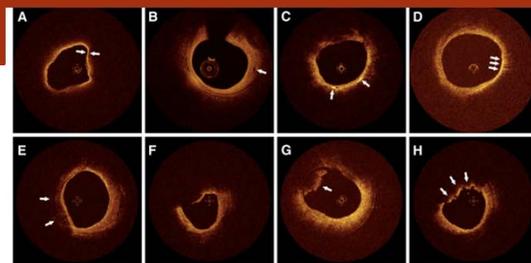


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WHAT DOES THE FUTURE HOLD?

Better diagnostic tools for ischemic heart disease in women

- Optical coherence tomography
- Cardiac CT and cardiac MRI
- PET-CT for microvascular dysfunction



Representative optical coherence tomography images. **a** TCFA, defined as a lipid-rich plaque with a fibrous cap thickness < 65 μm (arrows). **b** Microvessels are represented by black holes within the plaque (arrow). **c** Cholesterol crystals are reflected by thin, linear regions of high intensity within the plaque (arrows). **d** Macrophage accumulation on OCT images, defined as increased signal intensity within the fibrous cap, accompanied by heterogeneous backward shadows (arrows). **e** Calcification is reflected by an area with low backscatter signal and a sharp border (arrows). **f** Plaque disruption showing discontinuity of the fibrous cap. **g** White (platelet-rich) thrombus is represented by low and homogeneous backscattering with low signal attenuation (arrow). **h** Red (red blood cell-rich) thrombus is represented by high backscattering with high attenuation (arrows).



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WHAT DOES THE FUTURE HOLD?

- Gender-specific biomarkers?

Higher levels	Lower levels
high-density lipoprotein cholesterol	low-density lipoprotein cholesterol
leptin	lipoprotein-associated phospholipase A2 mass and activity
D-dimer	adiponectin
homoarginine	monocyte chemoattractant protein-1
N-terminal pro B-type natriuretic peptide	soluble endothelial cell adhesion molecule
	symmetrical dimethylarginine
	high-sensitivity troponin T
	cystatin C



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WHAT DOES THE FUTURE HOLD?

- As of June 2015, the National Institutes of Health now requires all animal research and human studies to include sex-specific reporting or to justify why this is not needed in a specific study.

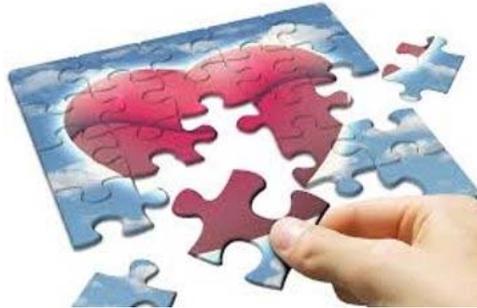


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WRAPPING IT UP

Heart disease in women is:

- Underrecognized
- Underdiagnosed
- Undertreated
- Understudied



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WRAPPING IT UP

- In 2012, 21% of women who were surveyed online reported that their doctor had *ever* discussed their risk for heart disease when discussing their health
 - 6% age 25-34 years
 - 16% age 35-44 years
 - 23% age 45-64 years
 - 33% age ≥ 65 years



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MORE RESOURCES

- **Acute Myocardial Infarction in Women**

- A Scientific Statement From the American Heart Association
- Circulation. 2016;133:916–947

- <https://www.cardiosmart.org/Heart-Conditions/Women-and-Coronary-Artery-Disease>

- <https://www.goredforwomen.org/>



American Heart Association.

