THE STATE OF A WOMAN'S HEART:

Women and Heart Disease and Why We Need Specialized Care

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#WHVSymposium19
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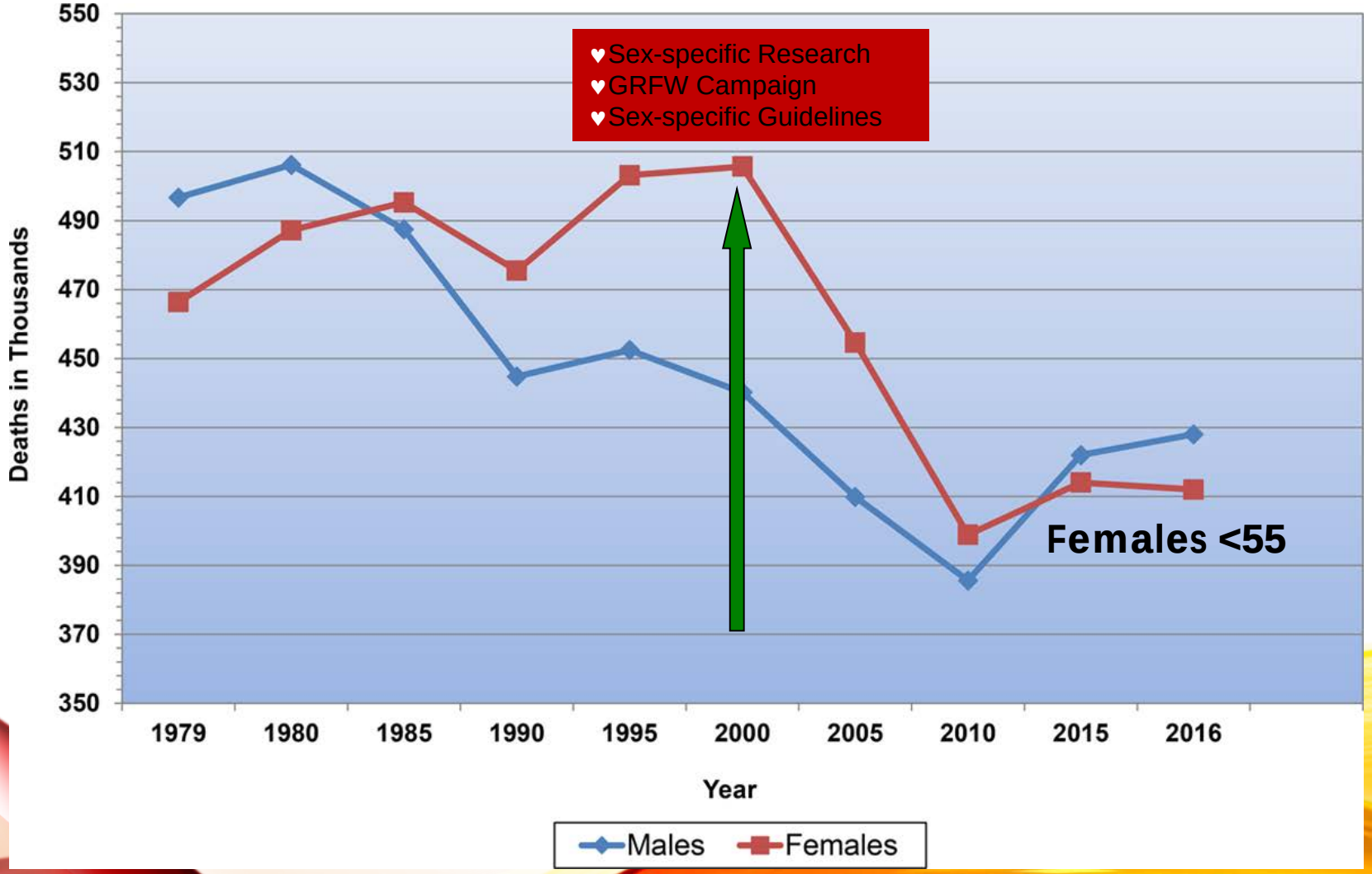
Presenter	**Disclosure**
Rachel M Bond, MD	None

Cardiovascular Disease (CVD) mortality trends for males and females (United States: 1979–2016)



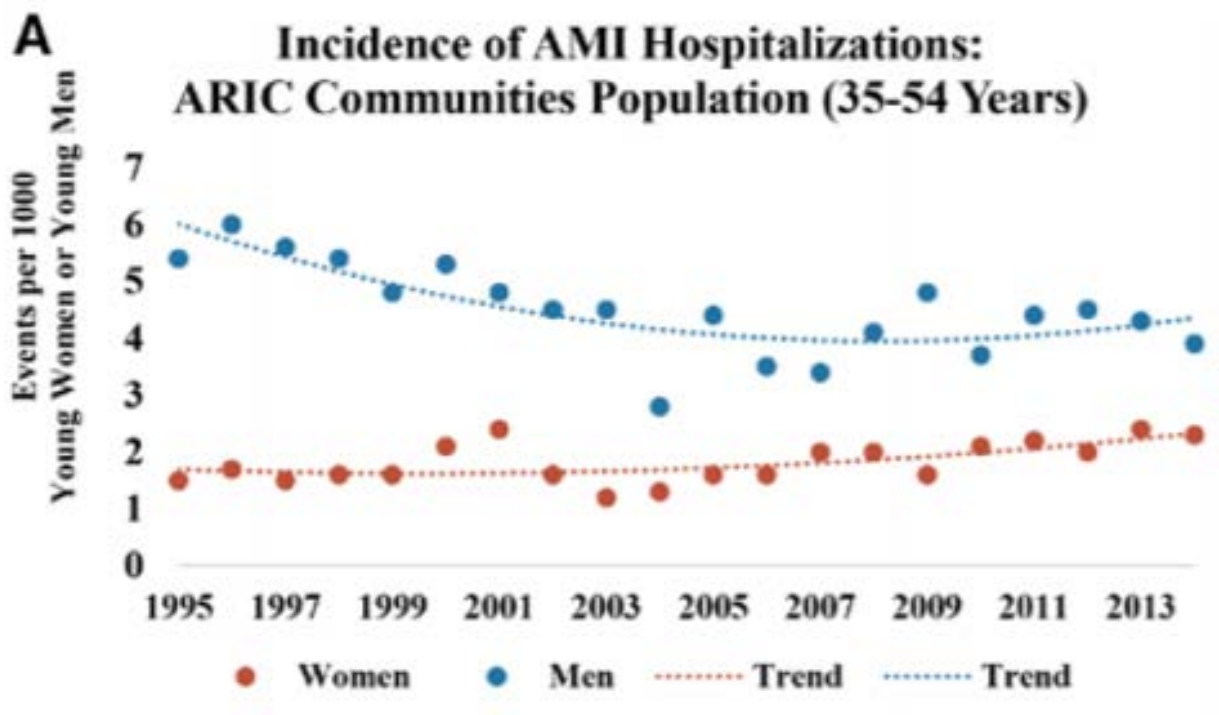
Emelia J. Benjamin. Circulation. Heart Disease and Stroke Statistics—2019 Update: A Report From the American Heart Association, Volume: 137, Issue: 12, Pages: e67-e492, DOI: (10.1161/CIR.0000000000000558)

THE STATE OF A WOMAN'S HEART

Women should be treated similar to men, but are they?

Lets Review the Guidelines (ACS).

INCIDENCE OF AMI
ARIC STUDY



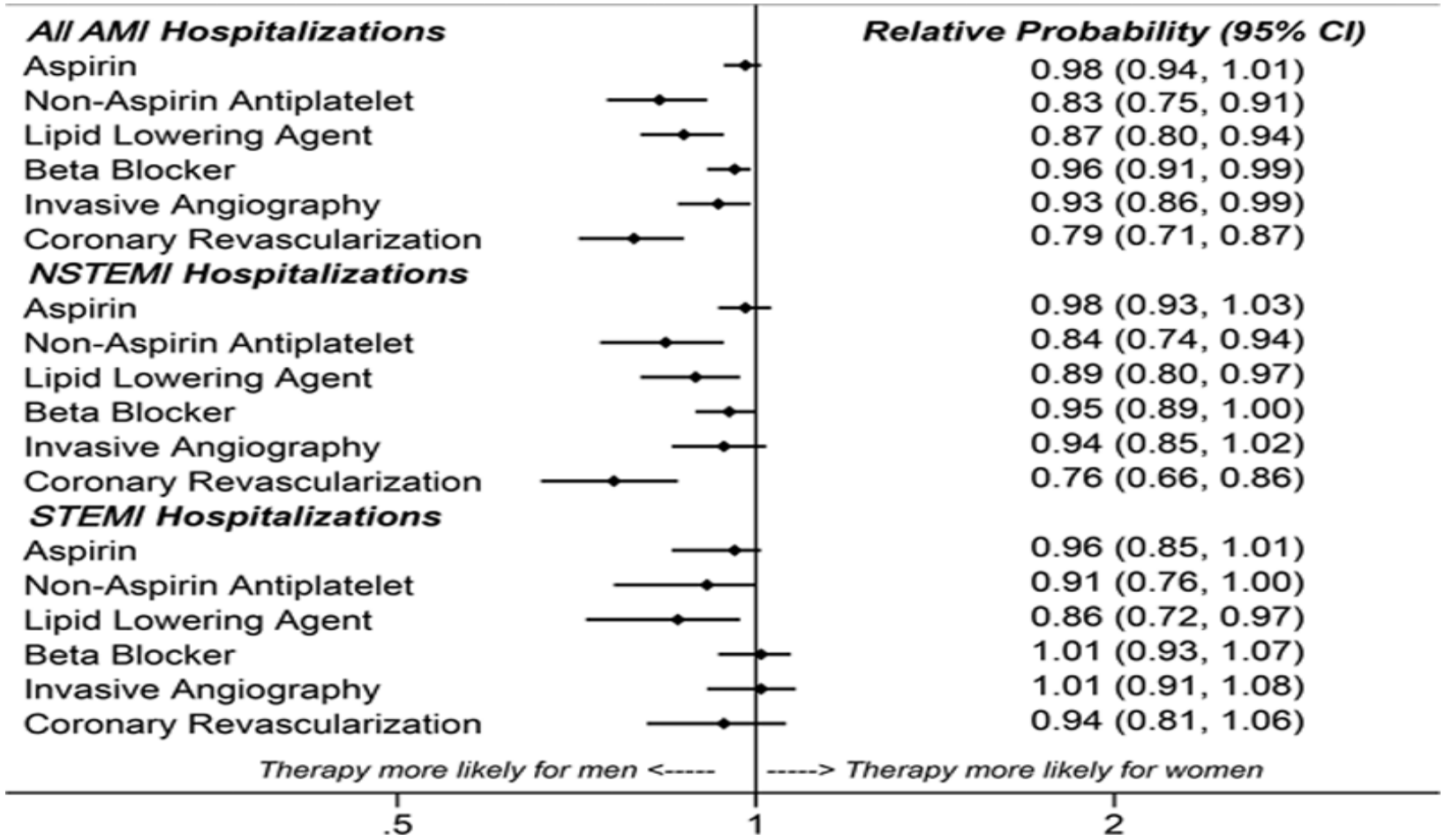
- From 1995 to 2014, 28,732 patients aged 35-74 years of age were evaluated.
  - Of these, 8,737 (30%) were young.

- **Conclusion**: significant increase in patients presenting with AMI who were <55 years of age from 1995 to 2014 (**age 35-54 years**).
  - Most pronounced in **young women**

- Young women had a **higher comorbidity burden** and were more likely to be **Black**.

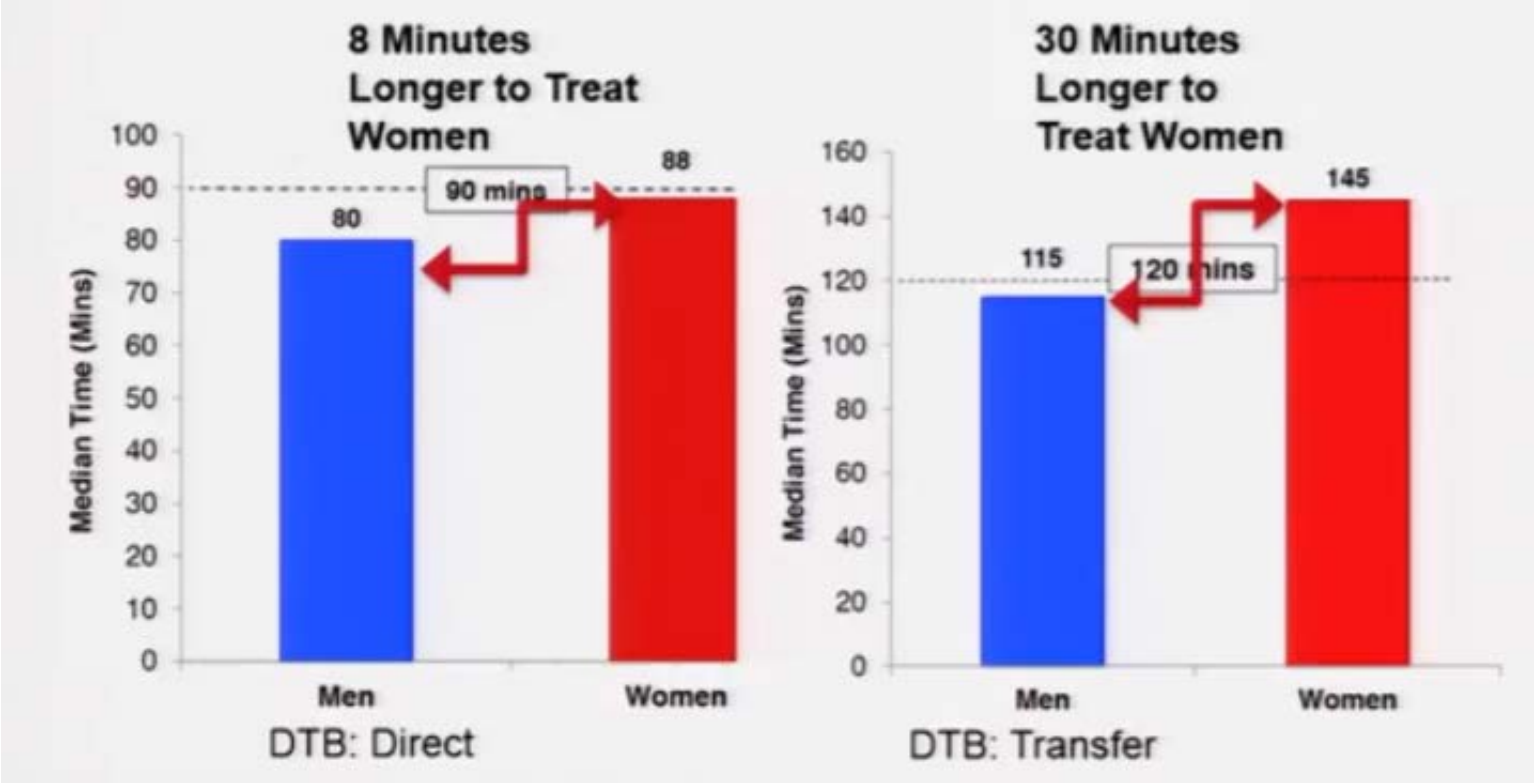
Arora S, et al. The ARIC Community Surveillance Study. Circulation. Circulation. 2019;139:1047–1056

Young women were less likely to undergo invasive strategy or to be managed with guideline-based AMI medications.



Sameer Arora. Circulation. Twenty Year Trends and Sex Differences in Young Adults Hospitalized With Acute Myocardial Infarction, Volume: 139, Issue: 8, Pages: 1047-1056, DOI: (10.1161/CIRCULATIONAHA.118.037137)

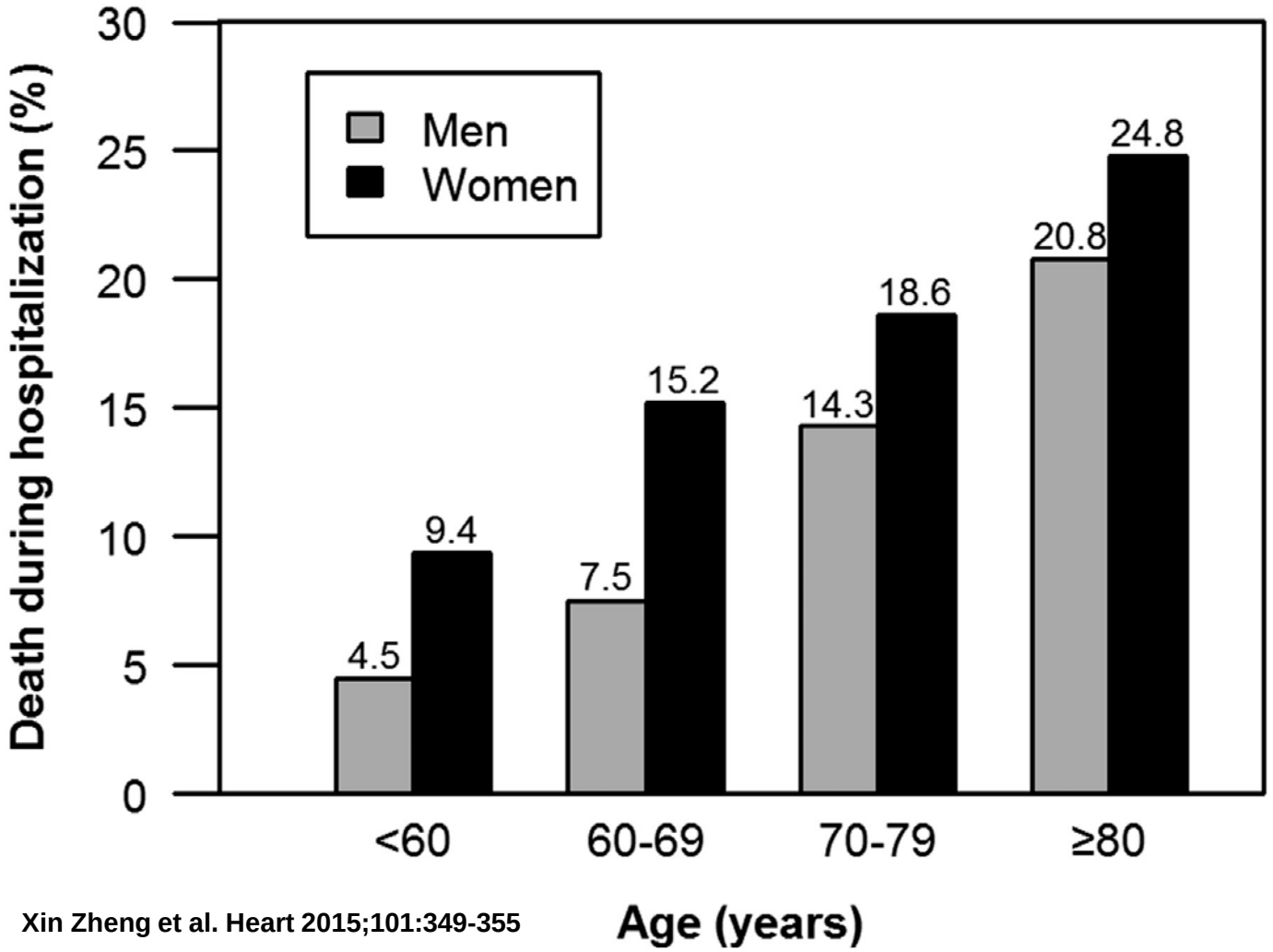
VIRGO TRIAL: DOOR-TO-BALLOON DELAYS IN WOMEN WITH STEMI



Young women (age <55) with STEMI are less likely to receive reperfusion therapy and experience more delays in treatment than men.

D'Onofrio et al. Circulation. 2015;131: 1324-1332.

In-hospital mortality rate following STEMI among women and men by age.



Xin Zheng et al. Heart 2015;101:349-355

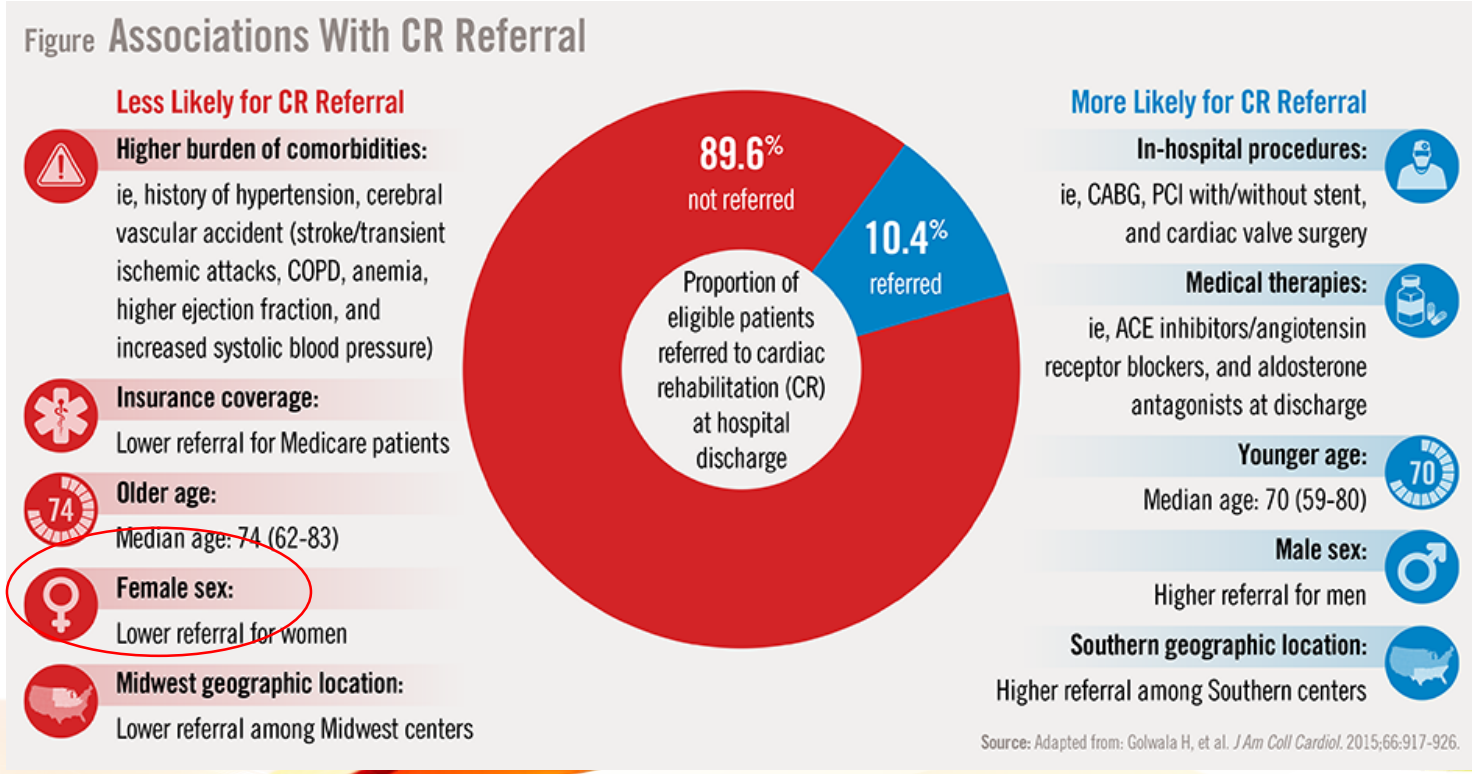
More complications of (all age groups):

- cardiogenic shock
- heart failure
- renal failure
- stroke
- re-infarction
- bleeding

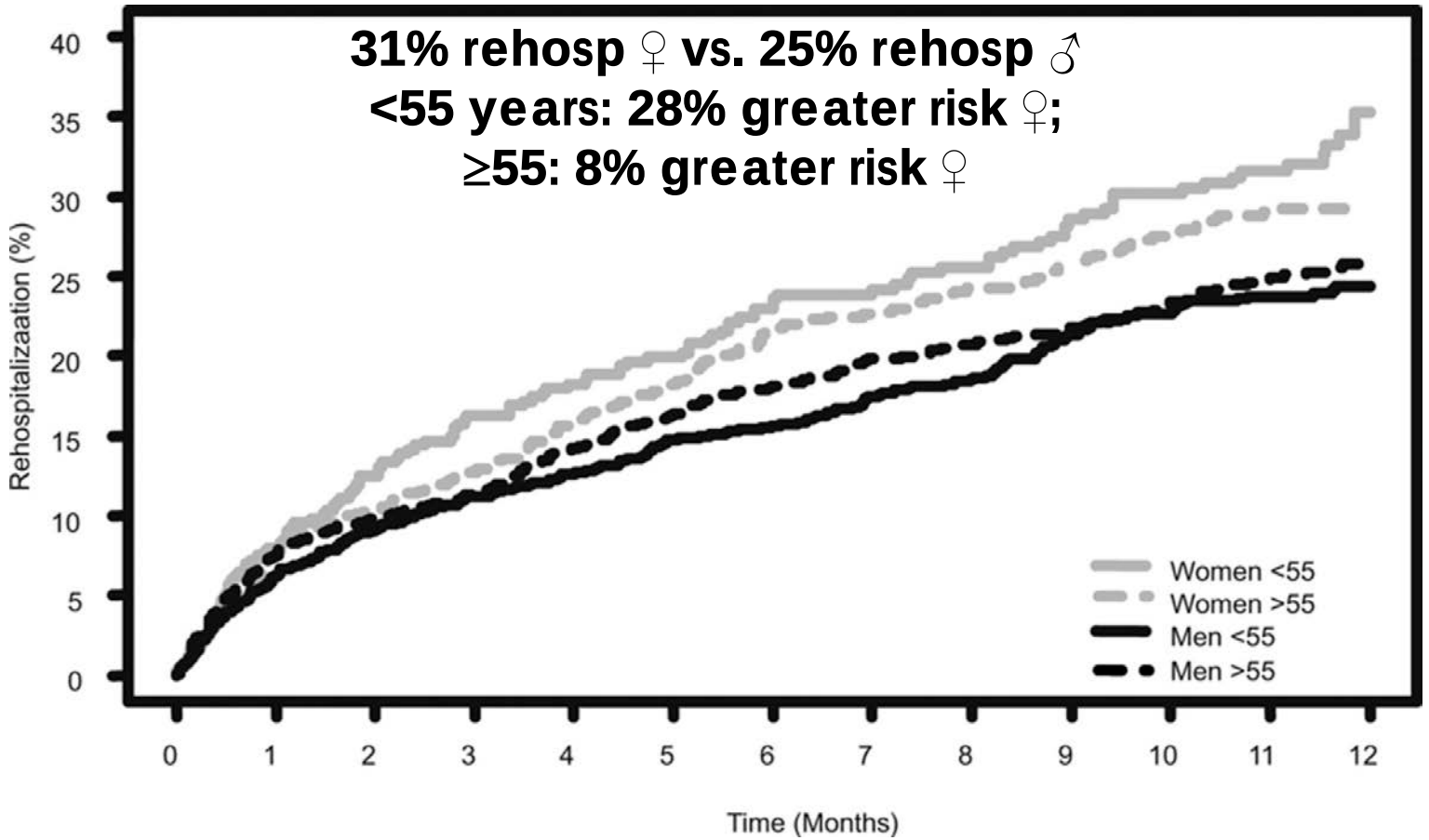
LESS CAD TREATMENT ALSO AT DISCHARGE

- Post-ACS, women less likely to be discharged on ASA, ACEI, statin, and to meet BP goal.
- Cardiac rehab (CR) significantly ↓ mortality in ACS, PCI, CABG, cardiac valve surgery and CHF, but **men** are a **1/3 more likely to be enrolled.**

When women are referred, they are **more likely to dropout**.



SEX DIFFERENCES IN REHOSPITALIZATION AFTER AMI- TRIUMPH STUDY



- Women of **all age groups** have higher crude risk of rehospitalization over the first year after AMI

Rachel P. Dreyer et al. Circulation. 2017;135:521-531

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THE STATE OF A WOMAN'S HEART

Steps to Improve This?

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STEPS TO IMPROVE OUTCOMES

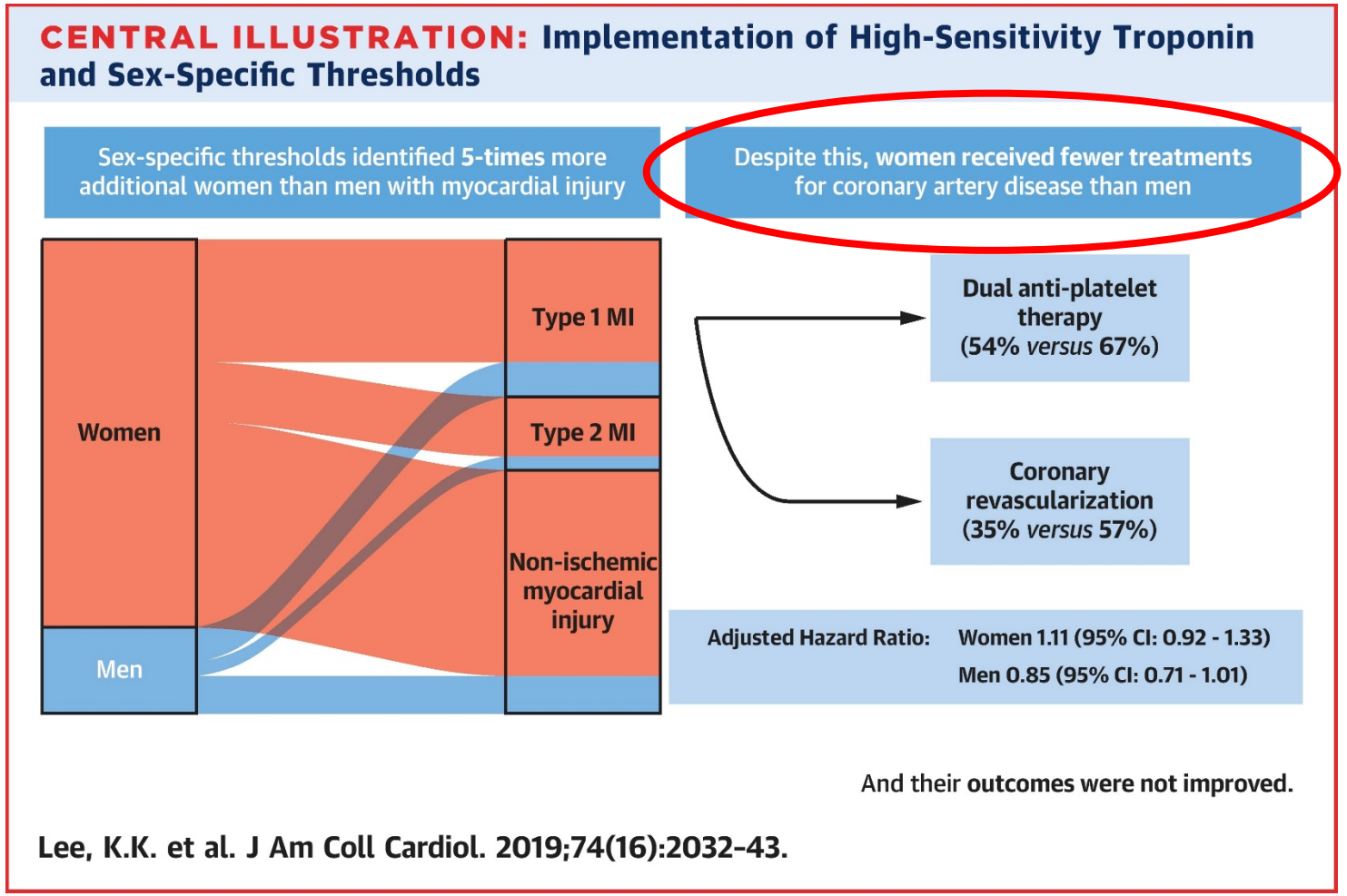
Steps to Improve Outcomes in Women with STEMI

- Increase Awareness and Need for Timely Care Targeting Women
- Increase Awareness and Need for Timely Care Targeting Healthcare Providers
- Implementation of Standardized Protocols
- Artificial Intelligence to improve Timeliness and Adherence of Care
- Increase Research to Understand Sex Disparities in STEMI Care & Continued Surveillance by Sex

Martha Gulati. Journal of the American Heart Association. Yentl's Bikini: Sex Differences in STEMI, Volume: 8, Issue: 10, DOI: (10.1161/JAHA.119.012873)

SEX-SPECIFIC THRESHOLDS

HS-TROPONIN



The use of an hs-cTnI assay and sex-specific thresholds **increased**:

- **Type 1 MI in women by 25%** vs. by 6% in men.
- The diagnosis of **type 2 MI in women by 39%** vs. 9% in men.
- Diagnosis of **nonischemic myocardial injury in women by 67%** vs 12% in men.
- The use of coronary angiography, revascularization and prescriptions for preventive therapies increased

Lee KK, et al. Sex-Specific Thresholds of High-Sensitivity Troponin in Patients with Suspected Acute Coronary Syndrome. JACC 74 (16) 22 October 2019; 2032-2043.

THE STATE OF A WOMAN'S HEART

Women should be treated similar to men, but are they?.

Reviewing the Guidelines (Non-ACS).

THE STATE OF A WOMAN'S HEART: CONGESTIVE HEART FAILURE

Less CHF Treatment

- **HFrEF:** less likely to receive evidence-based therapies
  - Guideline-Directed Medical Therapy (GDMT)
  - ICD
  - CRT- despite better response
  - VAD- referred much later in clinical course
  - Heart transplant

- **HfpEF:** more common in women, no guidelines for diagnosis, treatment

Bogaev, RC Gender Disparities Across the Spectrum of Advanced Cardiac Therapies: Real or Imagined? Curr Cardiol Rep (2016) 18:108.

THE STATE OF A WOMAN'S HEART: ARRHYTHMIAS

Less Arrythmia Treatment (Atrial Fibrillation, most common)

♥**AF**: Higher mortality and stroke rates, worse quality of life

♥**Women are less likely to:**

- See an electrophysiologist
- Receive oral anticoagulation
- Undergo catheter ablation although both sexes report similar success & improvement in QOL.
- Have TEE or DCCV
- Be prescribed rhythm control meds if symptomatic

Bogaev, RC Gender Disparities Across the Spectrum of Advanced Cardiac Therapies: Real or Imagined? Curr Cardiol Rep (2016) 18:108.

THE STATE OF A WOMAN'S HEART: PERIPHERAL ARTERY DISEASE

Less PAD Treatment

- **Asymptomatic PAD twice as common in women as men but women have**
- Greater functional impairment
- Lower rates of revascularization
- Increased likelihood of emergent procedures

Gulati M. Circulation 2017 135: 495-49.

THE STATE OF A WOMAN'S HEART: VALVULAR HEART DISEASE

- **Valvular disease**:
- Aortic Valve Disease (Aortic Stenosis)
  - Women have **higher 30 day operative mortality from SAVR** after adjustment for other factors.
  - Women have more upfront risk of complications with TAVR, **but > or equivalent long-term survival depending on studies.**
    - Sex-specific outcomes of TAVR with the **newer generation valves** showed higher major vascular complications, but **no sex-differences in survival or stroke** at 30 day or 1 year.
      - More sizes to choose from and more accurate valve sizing.

Bogaev, RC Gender Disparities Across the Spectrum of Advanced Cardiac Therapies: Real or Imagined? Curr Cariol Rep (2016) 18:108
Szerlip M, et al. Sex-specific Outcomes of TAVR with the Sapien 3 Valve. Insight from the PARTNER II S3 high-risk and intermediate-risk cohorts. JACC: Cardiovascular Interventions 11:1): January 1 2018.

THE STATE OF A WOMAN'S HEART

Do women and men experience CVD alike?

Spectrum of Pathophysiology.

YENTL SYNDROME

274 THE NEW ENGLAND JOURNAL OF MEDICINE July 25, 1991

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THE YENTL SYNDROME

Yentl, the 19th-century heroine of Isaac Bashevis Singer's short story,[1] had to disguise herself as a man to attend school and study the Talmud. Being "just like a man" has historically been a price women have had to pay for equality. Being different from men has meant being second-class and less than equal for most of recorded time and throughout most of the world. It may therefore be sad, but not surprising, that women have all too often been treated less than equally in social relations, political endeavors, business, education, research, and health care.

Two studies published in this issue of the *Journal* provide evidence that there is sex bias in the management of coronary heart disease. In one study, Ayanian and Epstein[2] show that in Massachusetts and Maryland women were significantly less likely to undergo coronary angiography, percutaneous transluminal coronary angioplasty, or coronary surgery when admitted to the hospital with a diagnosis of myocardial infarction, unstable or stable angina, chronic ischemic heart disease, or chest pain. These differences were evident even after the investigators controlled for age, race, heart failure, diabetes, and economic status. Steingart et al.[3] used a prospective postinfarction intervention trial to examine a similar hypothesis. They determined that women had angina before myocardial infarction as frequently and with more debilitating effect than men, yet women underwent cardiac

- Yentl was the heroine of a 19th century short story by Issac Bashevis Singer
  - She had to disguise herself as a man to study the Talmud.
  - Being "just like a man" has historically been a price women had to pay for equality
- 1991 Dr. Bernadine Healy noted discrepancy in inclusion in women in research, particularly CVD
- For decades women were treated either as **"second class"** when it came to medical care ***or*** assumed to be **"little men"**

Suffering from Yentl Syndrome: Sex Differences in Symptoms of IHD

Chest Pain, Discomfort, Pressure or Squeezing, Like there's a ton of weight on your chest

Upper body pain, or discomfort in one or both arms, back, shoulder, neck, jaw or upper part of the stomach

Shortness of Breath

1/3 of the time atypical symptoms!

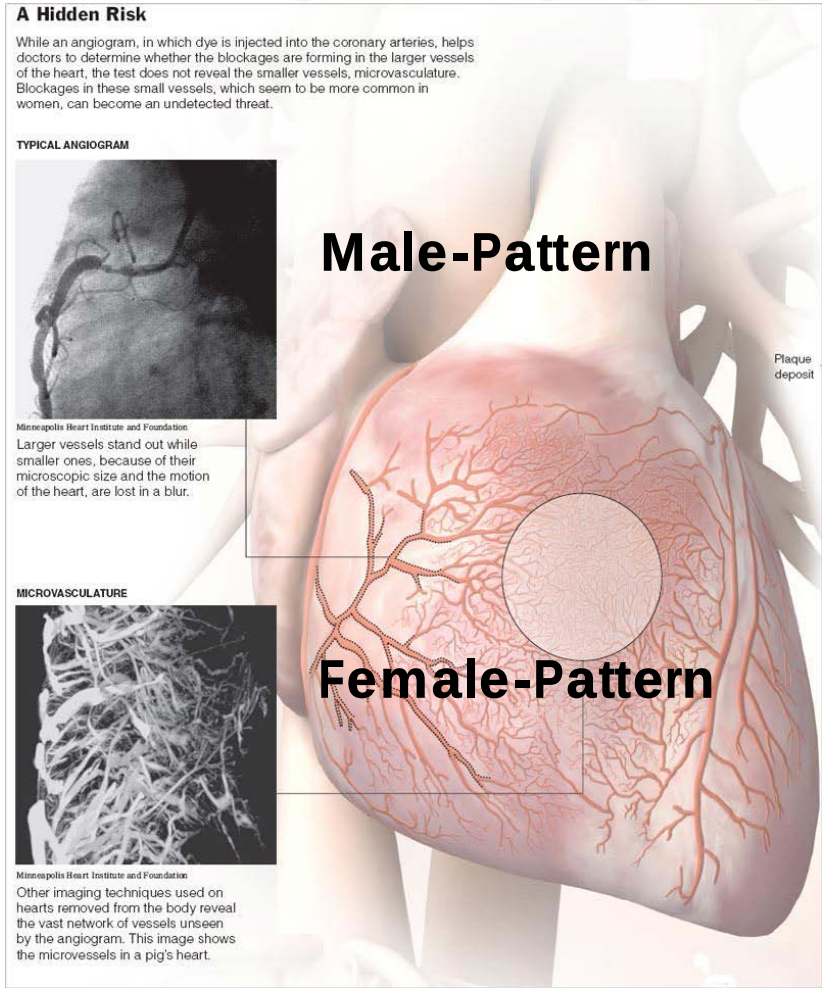
Women are more likely to experience shortness of breath, nausea/vomiting, back or jaw pain, and excessive fatigue than men

Source: Womenhealth.gov/heartattack

SEX DIFFERENCES IN SYMPTOMS MAY TRANSLATE INTO DIFFERENCES IN PATHOPHYSIOLOGY

"Inconvenient" Angiographic Truths

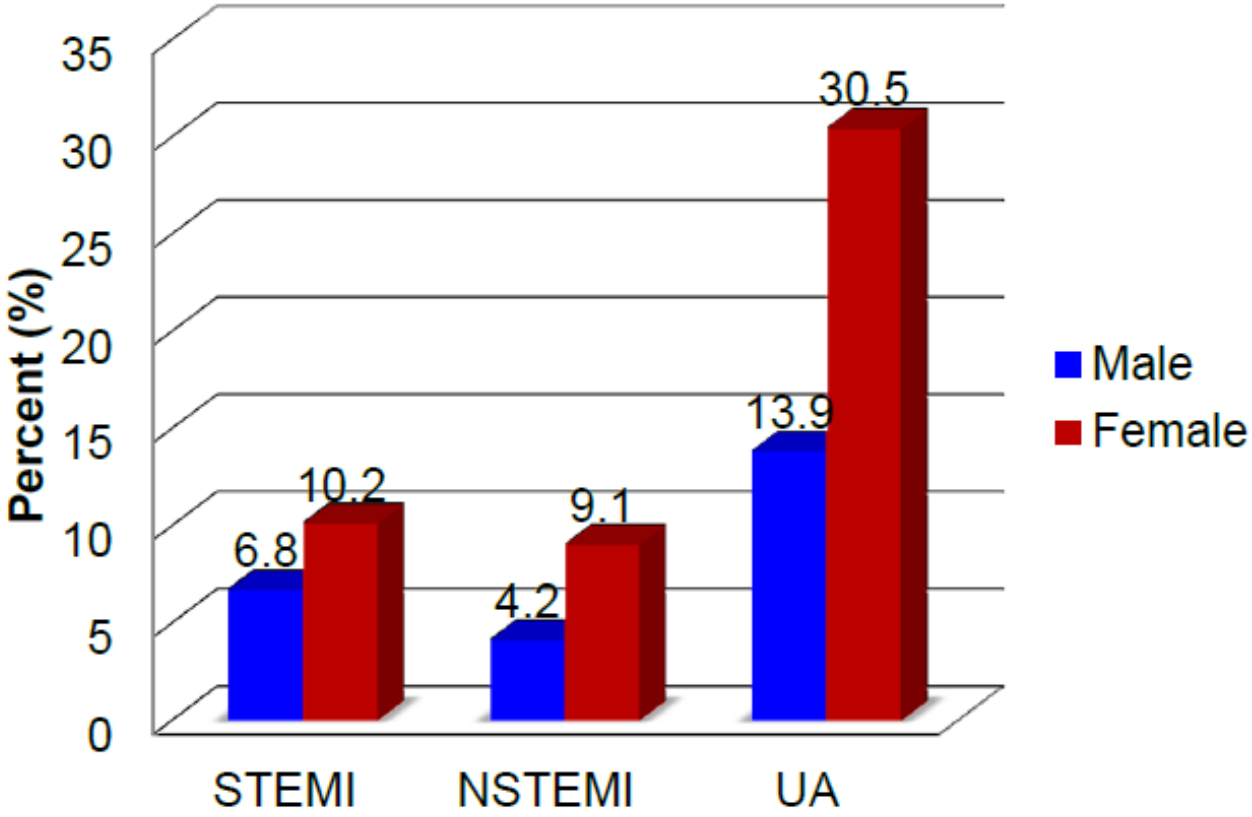
- Men are ~3X more likely to have obstructive CAD
- **Women** are ~**2-3X** more likely to have **no or nonobstructive CAD** despite angina
  - -**INOCA** (ischemia with nonobstructive coronary arteries)
  - -**MINOCA** (MI with nonobstructive coronary arteries)
- Women with chronic persistent angina, and without obstructive CAD have a worse prognosis with ↑adverse event rates, poor QOL, repeat hospitalization & coronary angiography, consumption of health-care resources compared to those without angina



Patel MR, N Engl J Med 2010; 362:886-895 (ACC National Cardiovascular Data Registry)
Johnson BD Eur Heart J. 2006 Jun;27(12):1408-15
Gulati M, Arch Intern Med 2009; 843–850

PERCENTAGE OF PATIENTS WHO HAD IHD BUT NO OBSTRUCTIVE CAD: GUSTO IIB

- **MINOCA** has higher mortality than the general population (**up to 5% one year mortality**).
- NOT as high as obstructive disease (6.7%)



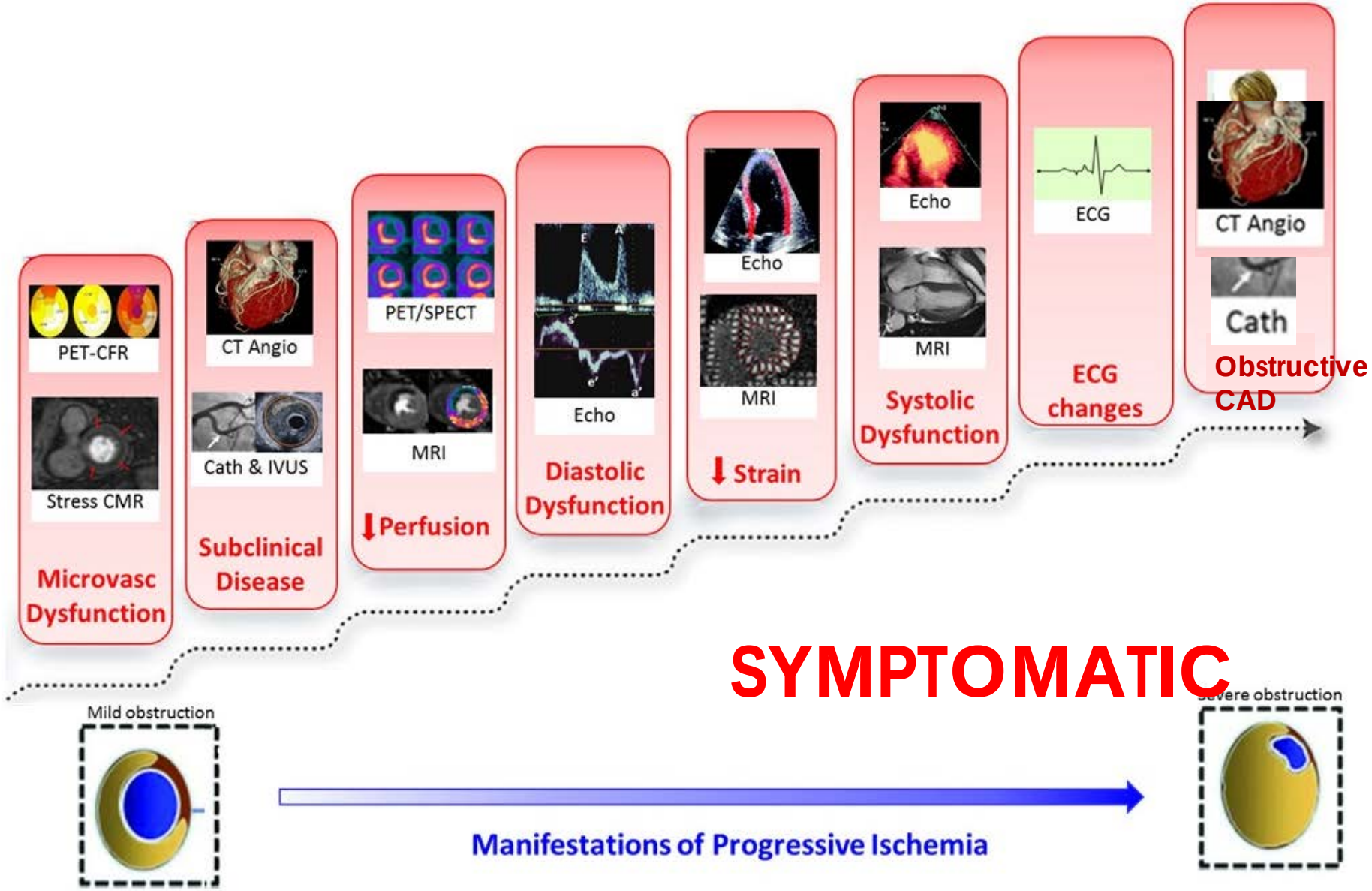
GUSTO IIb (Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes IIb) study

J Am Coll Cardiol. 2012;60(11):951-956. doi:10.1016/j.jacc.2012.02.082

WHAT DO WOMEN WITH MINOCA HAVE?

- **Coronary plaque rupture** (both sexes)
- **Coronary plaque erosion** (more commonly ♀)
- **Spontaneous coronary artery dissection** (SCAD)
- **Takotsubo** or stress-induced cardiomyopathy
- **Type II MI** (supply-demand mismatch)
- **Coronary Vasospasm**
- **Intracoronary thromboembolism**
- **Myocarditis**
- **Microvascular disease**

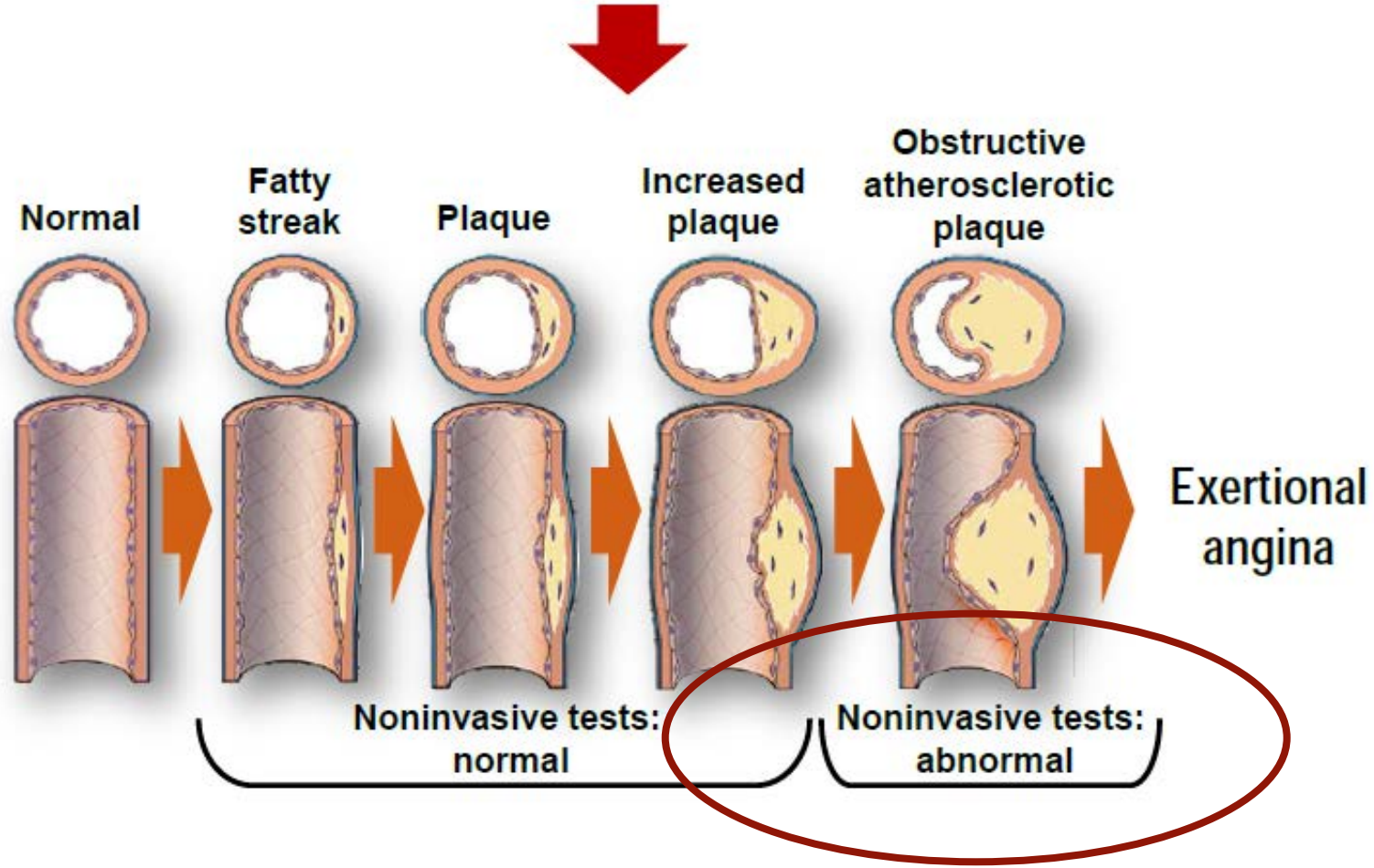
WORKING MODEL OF IHD



Aggrawal N, Bond R, et al. The Role of Imaging in Women With Ischemic Heart Disease. Clinical Cardiology 2018 Feb;41(2):194-202.

OBJECTIVE OF ANTI-ANGINAL STRATEGIES

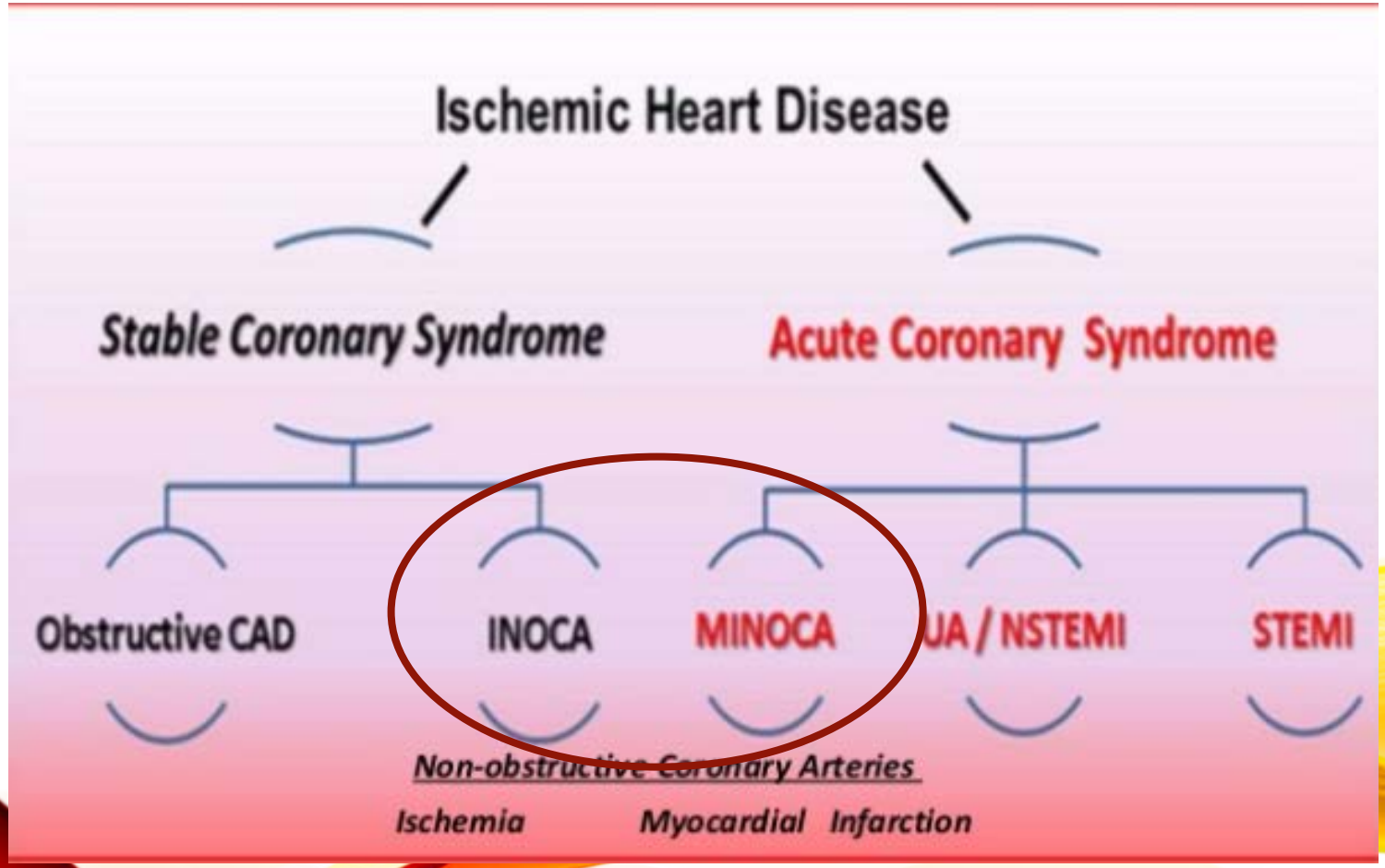
Reduce Ischemia & Relieve Symptoms



Gibbons ACC/AHA 2002 guidelines., www.acc.org/clinical/ guidelines/stable/stable.pdf., Abrams NEJM 2005;352:2524-33.

A CHANGING PHILOSOPHY

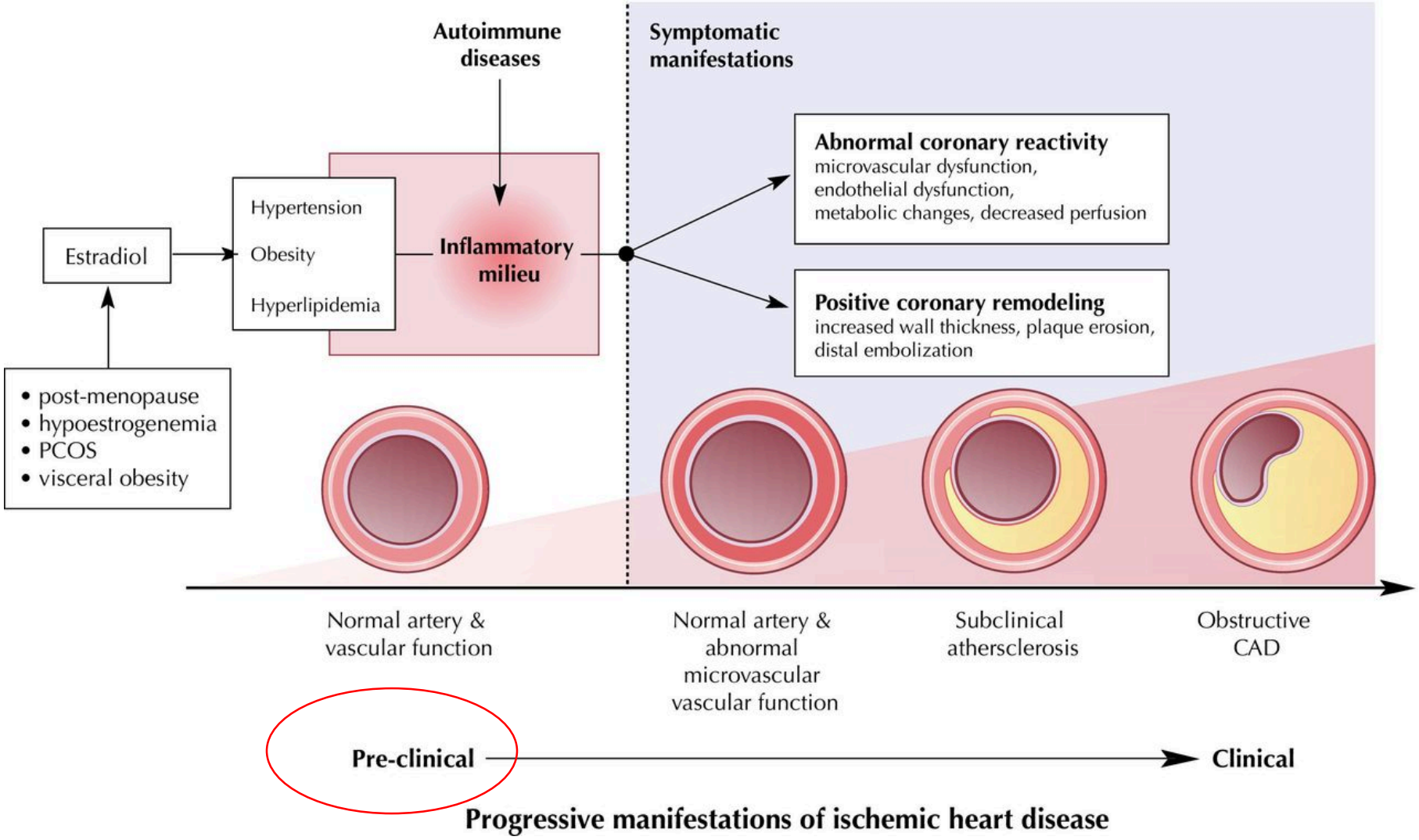
NONOBSTRUCTIVE DISEASE IS NOT ALWAYS FALSE POSITIVE. IT'S NOT BENIGN.



Colin Berry. Stable Coronary Syndromes: the Case for Consolidating the Nomenclature of Stable IHD. Circulation. 2017; 136: 437-439.

A Changing Philosophy

Focus on Prevention



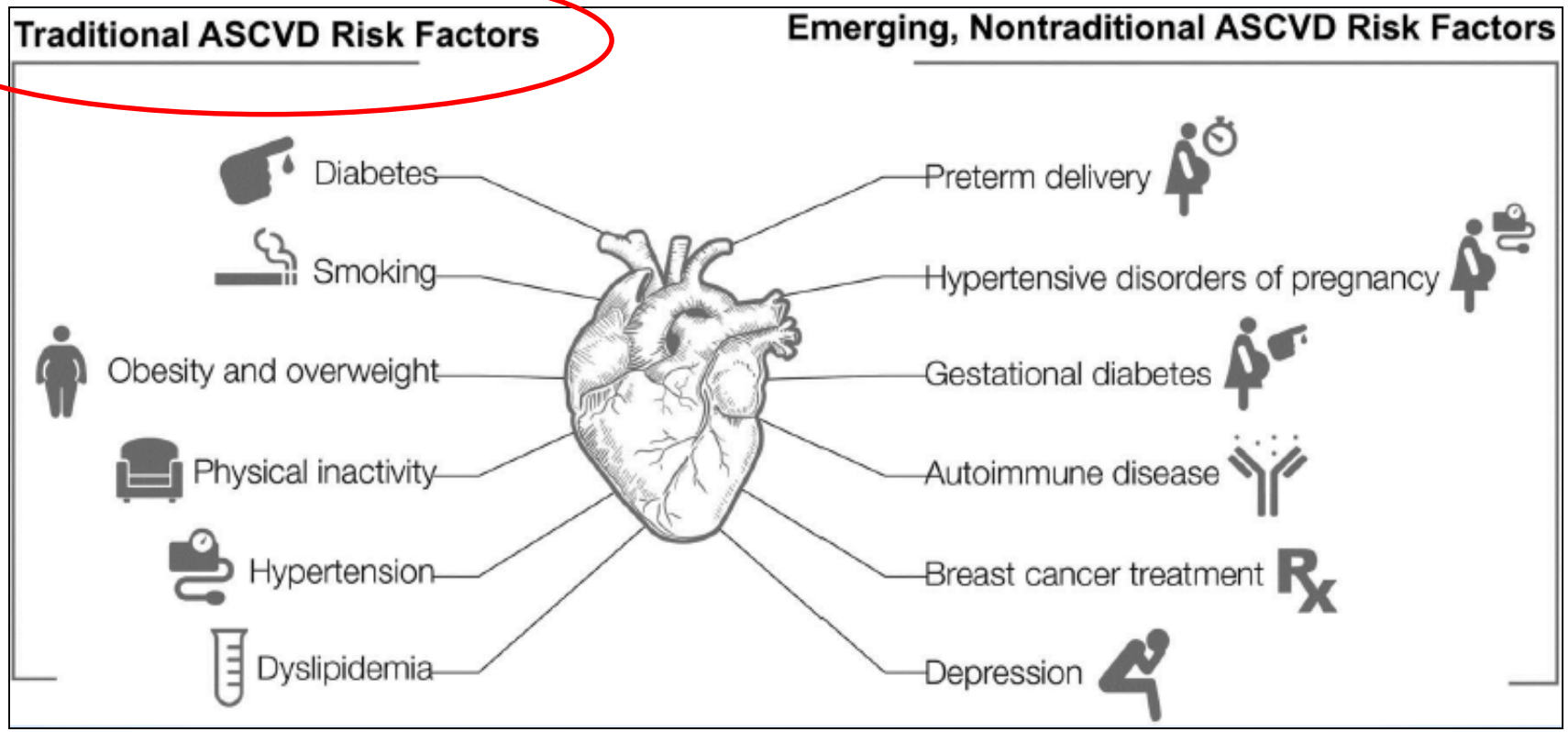
Progressive manifestations of ischemic heart disease

Leslee J. Shaw et al. JACC 2009;54:1561-1575

THE STATE OF A WOMAN'S HEART

Do CVD risk factors affect women in the same way as men?

GENDER SPECIFIC NOVEL RISK FACTORS



Mariana Garcia et al. Circ Res. 2016; 118: 1273-1293.

CVD RISK FACTORS IN WOMEN

	Prevalence vs Men	Relative Risk vs Men	Sex Specific
Smoking	↓	↑↑	
Diabetes/Metabolic Syndrome	↑	↑↑↑	Gestational DM PCOS
Hypertension	↑	↑	Preeclampsia Gestational HTN
Hyperlipidemia	-	-	
Physical Inactivity/ Poor Fitness	↑↑	↑	
Obesity	↑	-/↑	Postpartum Weight Gain
Depression	↑↑↑	?	
SLE/RA	↑↑↑	↑↑	

WHICH RISK FACTORS ARE MORE PREDICTIVE IN WOMEN?

- **Diabetes**
  - **DM confers a greater CVD risk for women than men**: 19.1% vs. 10.1%
  - metabolic syndrome, insulin resistance > risk in women compared to men
  - Diabetic women > men are less likely to be treated for CVD risks

- **Smoking**
  - associated with 50% of all coronary events in women (more prevalent in younger women)
  - Risk elevated even with minimal use (especially if used in combination with OCP)
  - **Women who smoke have a six-fold increased risk of MI** (vs. 3x in men)
    - incidence of PVD in smokers: women >>> men

- **Obesity**
  - **2 out of 3 women in the US are either obese or overweight**
  - Higher **CAD risk** at **64%** compared to **obese men at 46%**

Zuanetti G et al. JACC 1993;22:1788; Willett WC etal.NEJM 1987;317:1303

WHICH RISK FACTORS ARE MORE PREDICTIVE IN WOMEN?

♥Physical Inactivity

- ♥ **Most prevalent risk factor for women** in that **¼ of US women report no regular physical activity** and **¾ report less than the recommended** amount
- ♥ **Exercise provides greater protective effect for women than for men**
  - ♥ Nurse's Health Study identified ↓development of DM in women who exercise regularly and among diabetic women, a ↓ in the risk of CV events

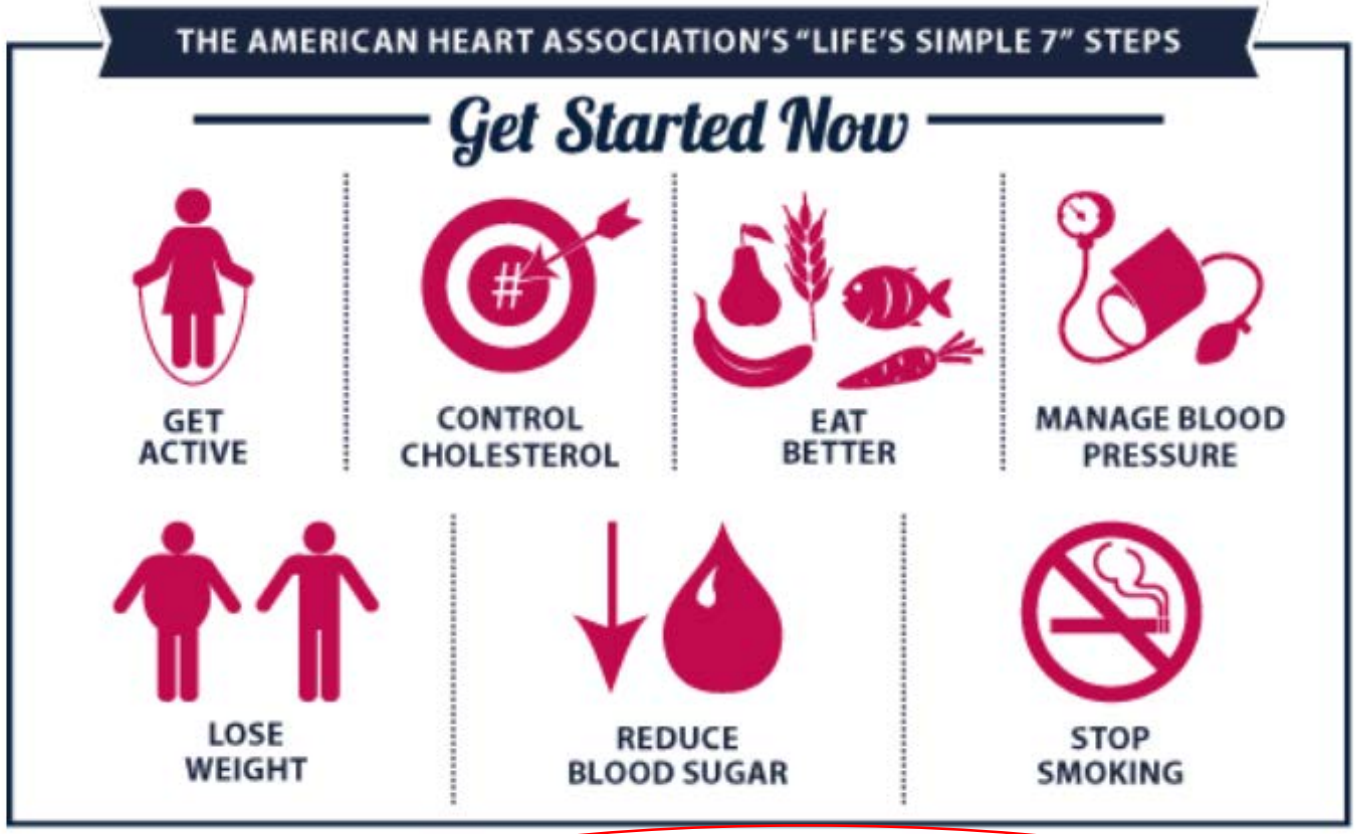
♥Hyperlipidemia

- ♥ The **highest population-adjusted CVD risk for women at 47%**
- ♥ Lp (a) can be more predictive in younger women
- ♥ TG can be more predictive in older women, especially if >400 mg/dL
- ♥ Benefits of statin therapy are similar for women and men
- ♥ Encourage use of ASCVD pooled cohort risk equation
  - ♥ Limitations for gender-specifics

Rich-Edwards, JW et al. NEJM 1995; 332:1758; Miller VT. Atherosclerosis 1994; 108 Suppl:S73; Orth-Gomer K. Circulation 1997;95:329

RECOMMENDATIONS FOR CVD PREVENTION

- Lifestyle counseling to improve CVD risk factors



AND mental health & stress reduction

CONCLUSION ON SEX DIFFERENCES IN CVD

- **Women have worse outcomes for AMI:**
  risk for women with obstructive CAD is increased compared with men, yet women **are less likely to receive guideline-indicated therapies**

- **Younger women at the greatest risk** for poor outcomes after AMI

- **"Normal" coronary angiograms** (luminal irregularities, <50% stenosis) with evidence of ischemia or infarct= **INOCA or MINOCA** and are seen more frequently in women vs. men with IHD and associated with increase adverse events
  - Pathophysiology needs to be better understood as does proper treatment.
  - Consider them a working diagnosis with need for emphasis on multimodality imaging

- CVD Risk Factors (Traditional)

THANK YOU!

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