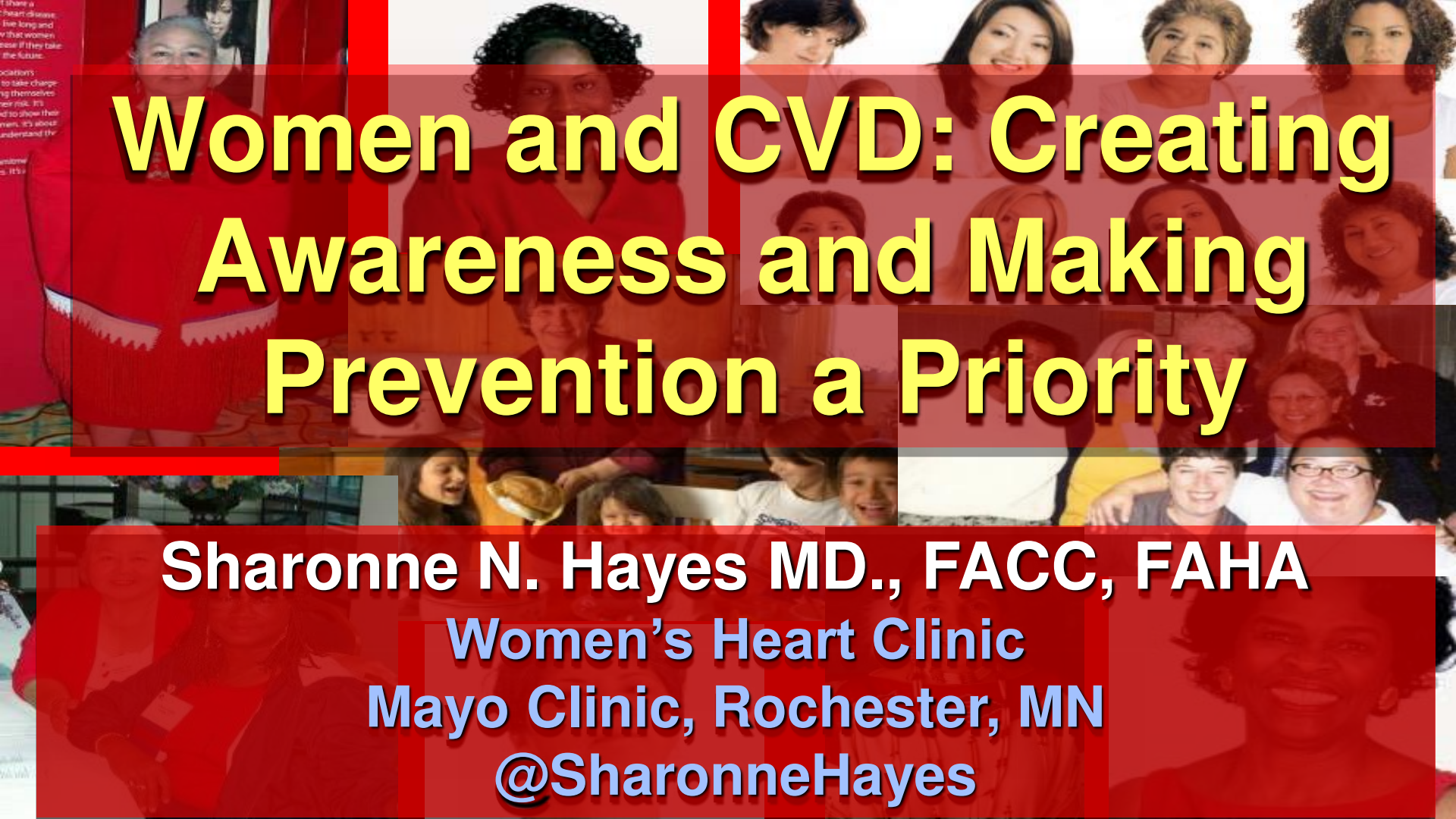


Women and CVD: Creating Awareness and Making Prevention a Priority

Sharonne N. Hayes MD., FACC, FAHA

Women's Heart Clinic

Mayo Clinic, Rochester, MN

@SharonneHayes

Relevant Financial Relationship(s)

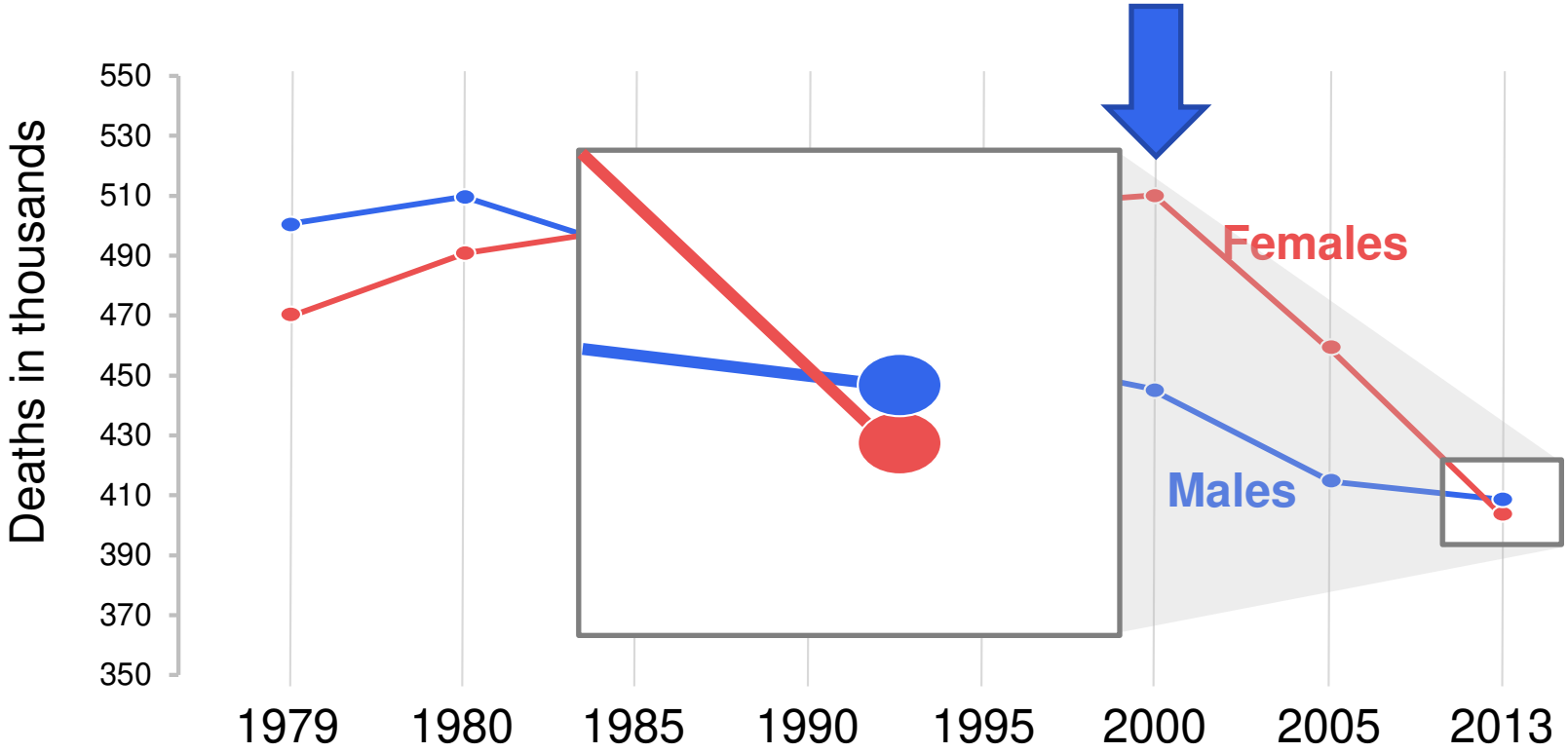
None

Off Label Usage

None

Your Heart Journey | WOMENHEART | Get Involved | Our Story | Blog

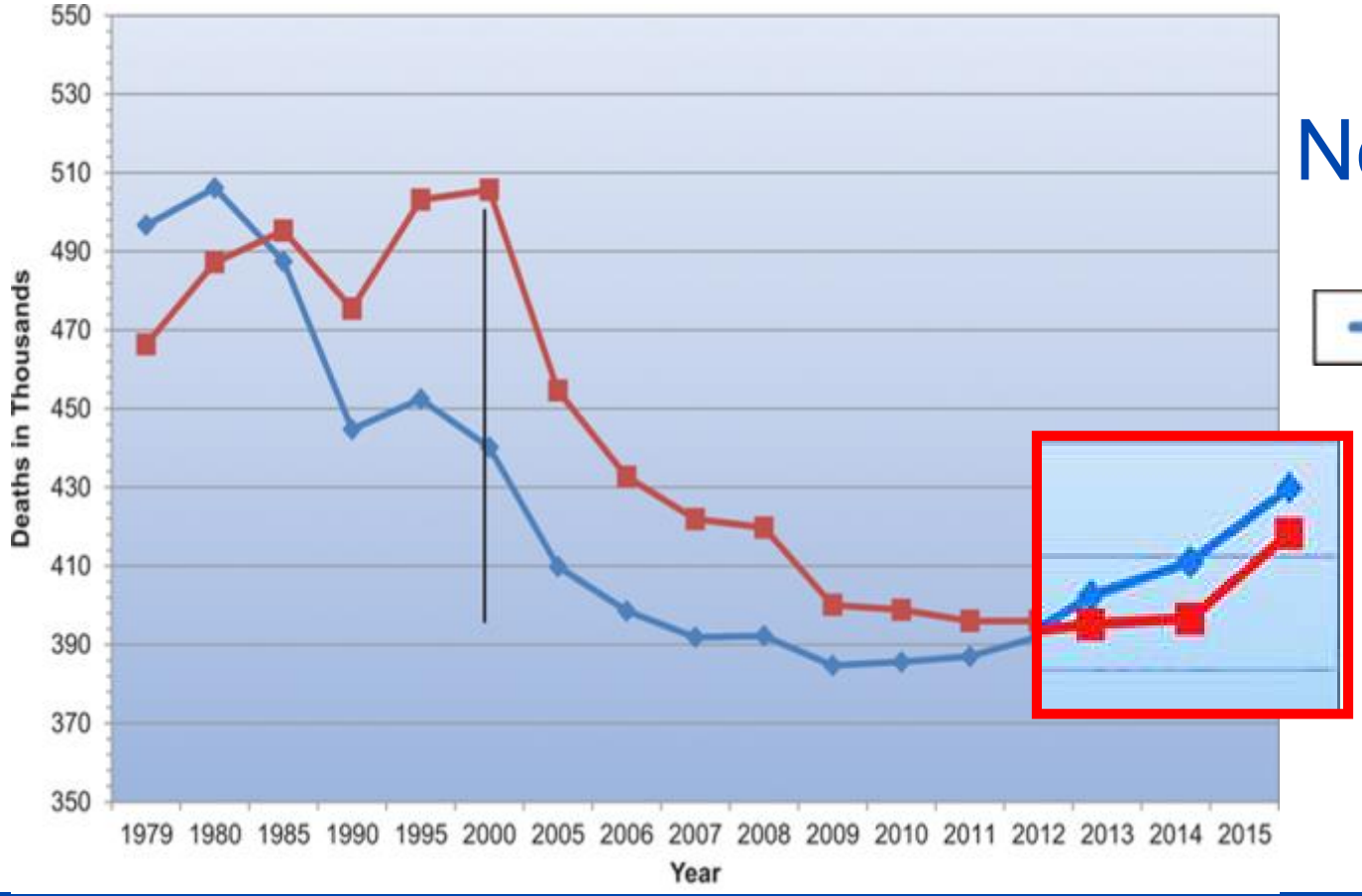
CVD Mortality Trends



CVD mortality trends for males and females (United States: 1979–2013)

Mozaffarian et al. Circulation. 2016;133:e38-e360

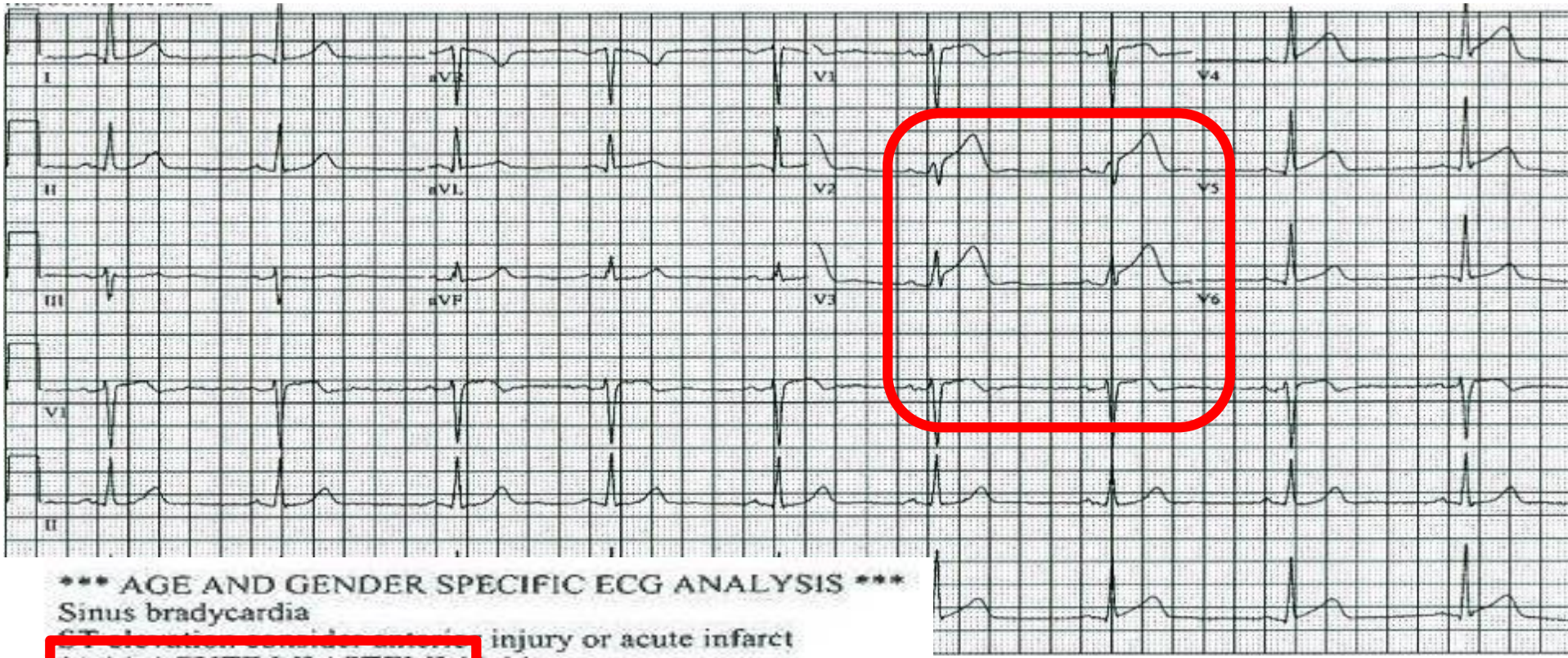
Not So Fast…



Males Females

Prevention Alert!

39 y/o Headache, Chest Pain, Dyspnea



*** AGE AND GENDER SPECIFIC ECG ANALYSIS ***
Sinus bradycardia
injury or acute infarct
** ** ACUTE MI / STEMI ** **
Abnormal ECG

What is the next step in care?

1. Start a nitro drip, admit to cardiology
2. Call in the STEMI cath lab team
3. Start a beta blocker and send to the CCU
4. GI cocktail and a nitro, then overnight observation in the chest pain unit

What is the next step in care?

1. Start a nitro drip, admit to cardiology
2. **Call in the STEMI cath lab team**
3. Start a beta blocker and send to the CCU
4. GI cocktail and a nitro, then overnight observation in the chest pain unit

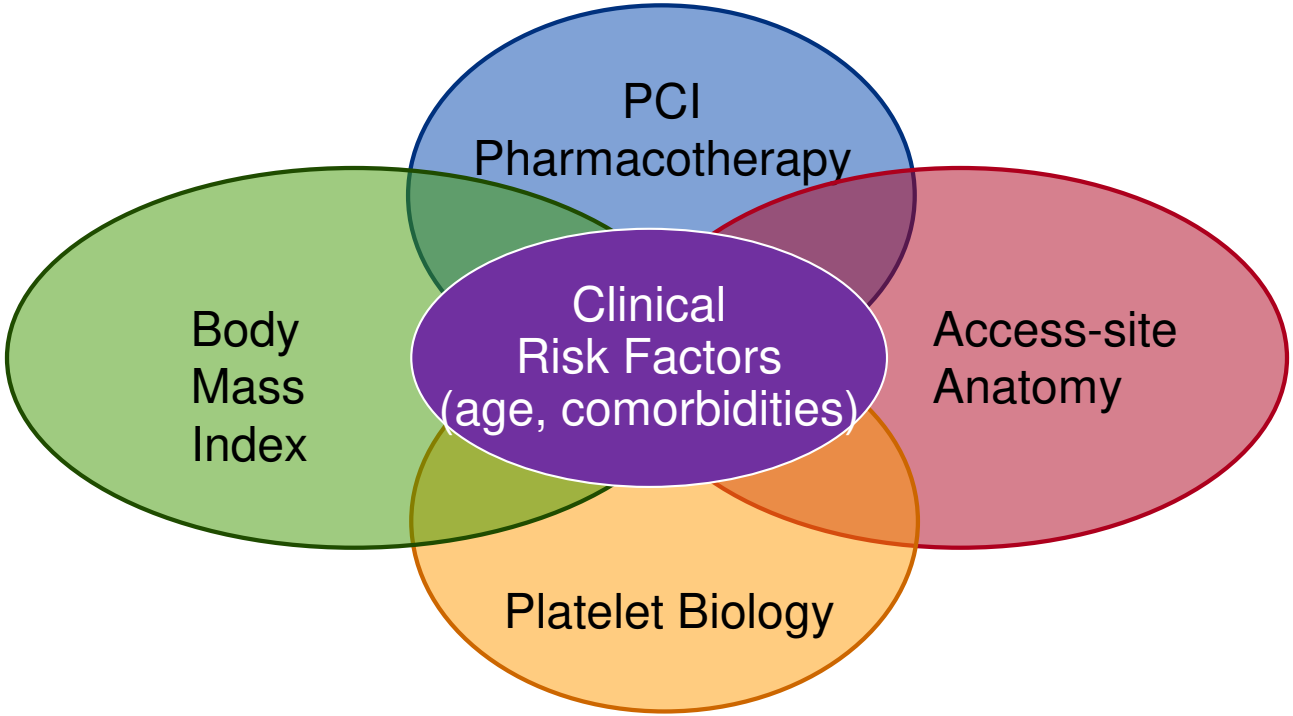
Gender Disparities in MI Care

- 1238 pts ***w/STEMI*** (18-55 yr; 695 women)
- Women (vs. men):
  - Less likely to receive reperfusion (4% vs 9%)
  - Exceeded door-to-needle time (67% vs. 37%)
- Sex: Major factor in exceeding reperfusion guidelines - OR 1.72 (95% CI 1.28–2.33)

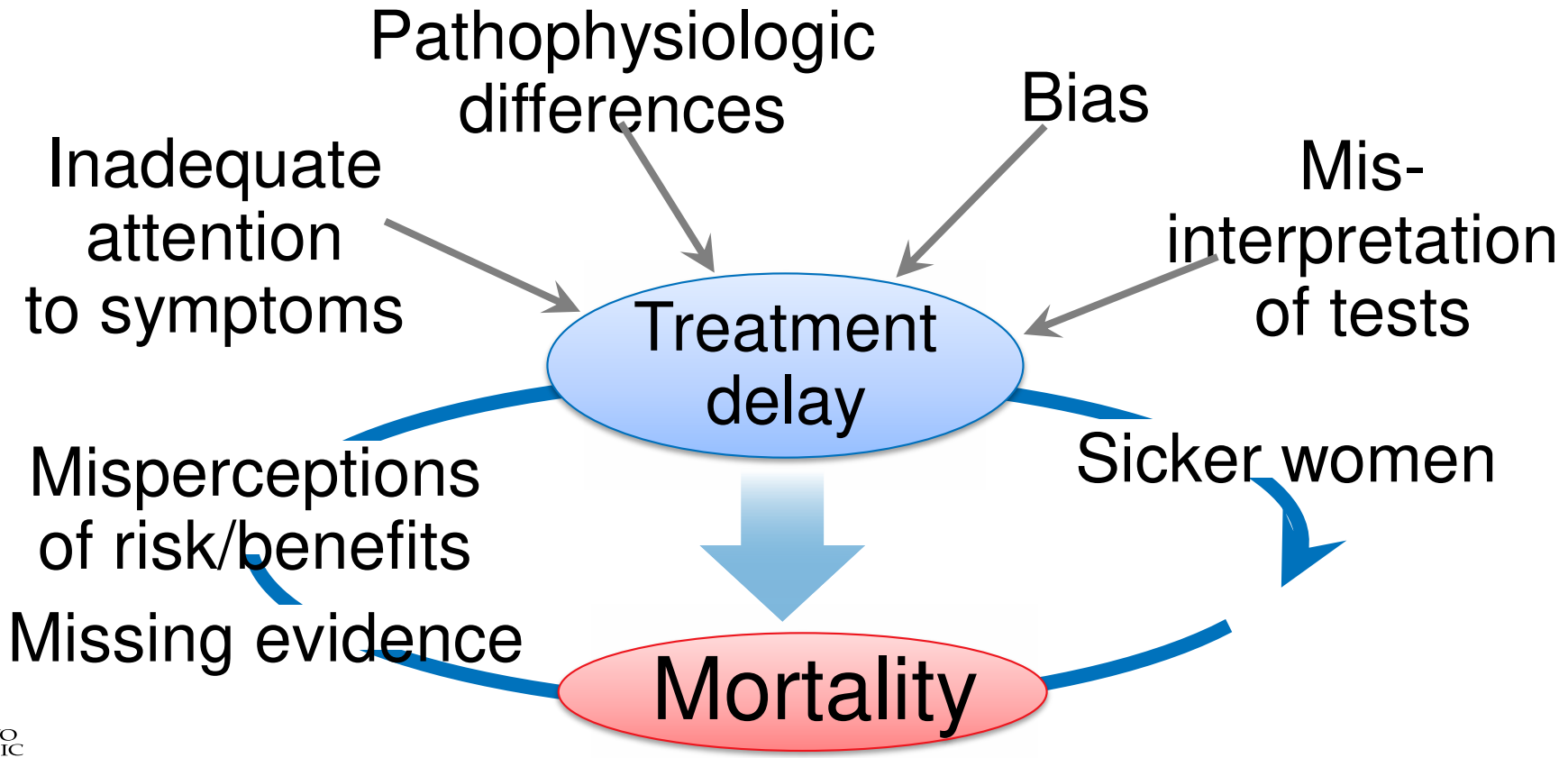
VIRGO: D'Onofrio G; Circulation. 2015;131:1324-1332

Bleeding Risk in AMI

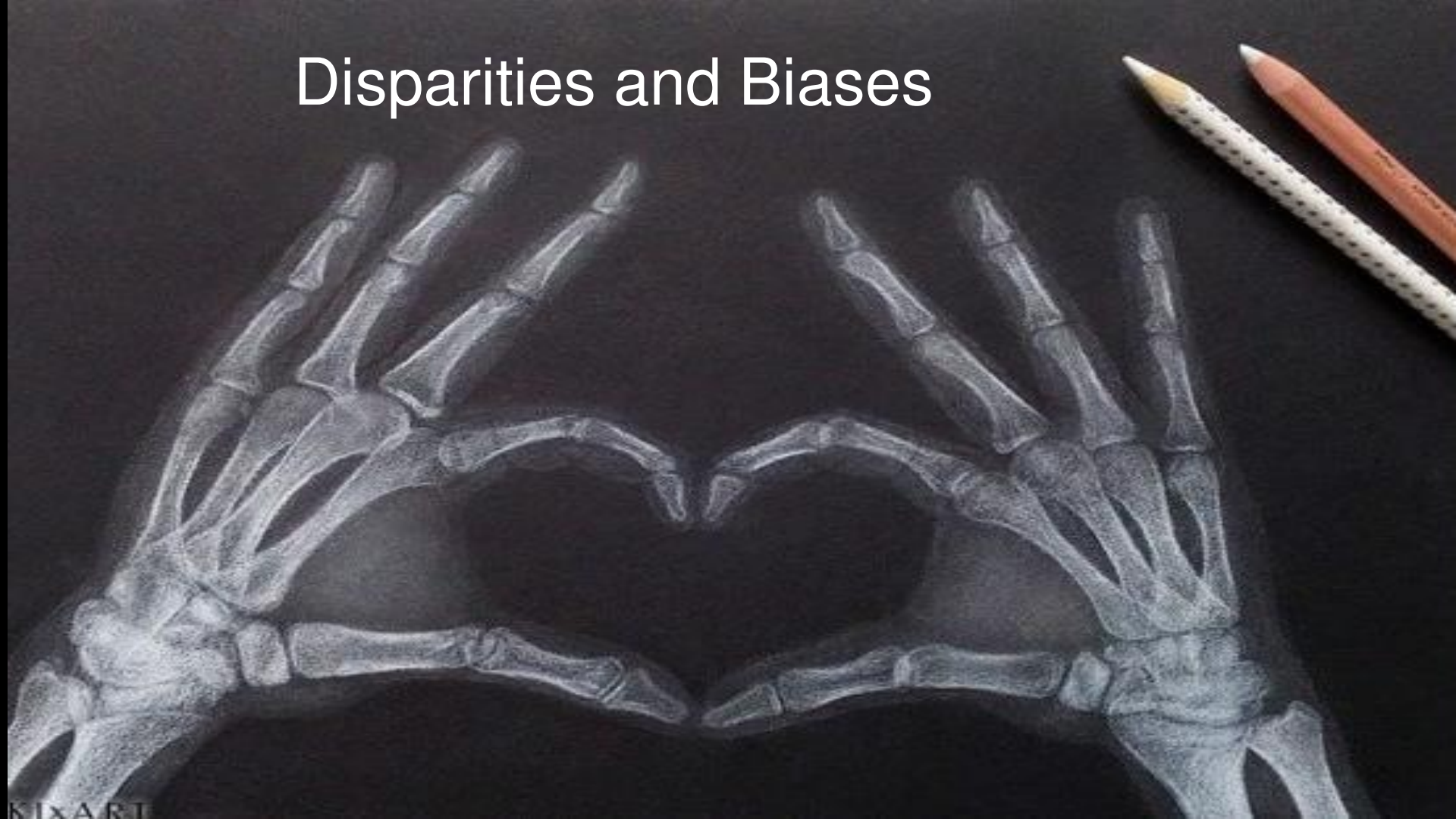
Sex and Gender Considerations



Sex/Gender Differences in Survival



Disparities and Biases

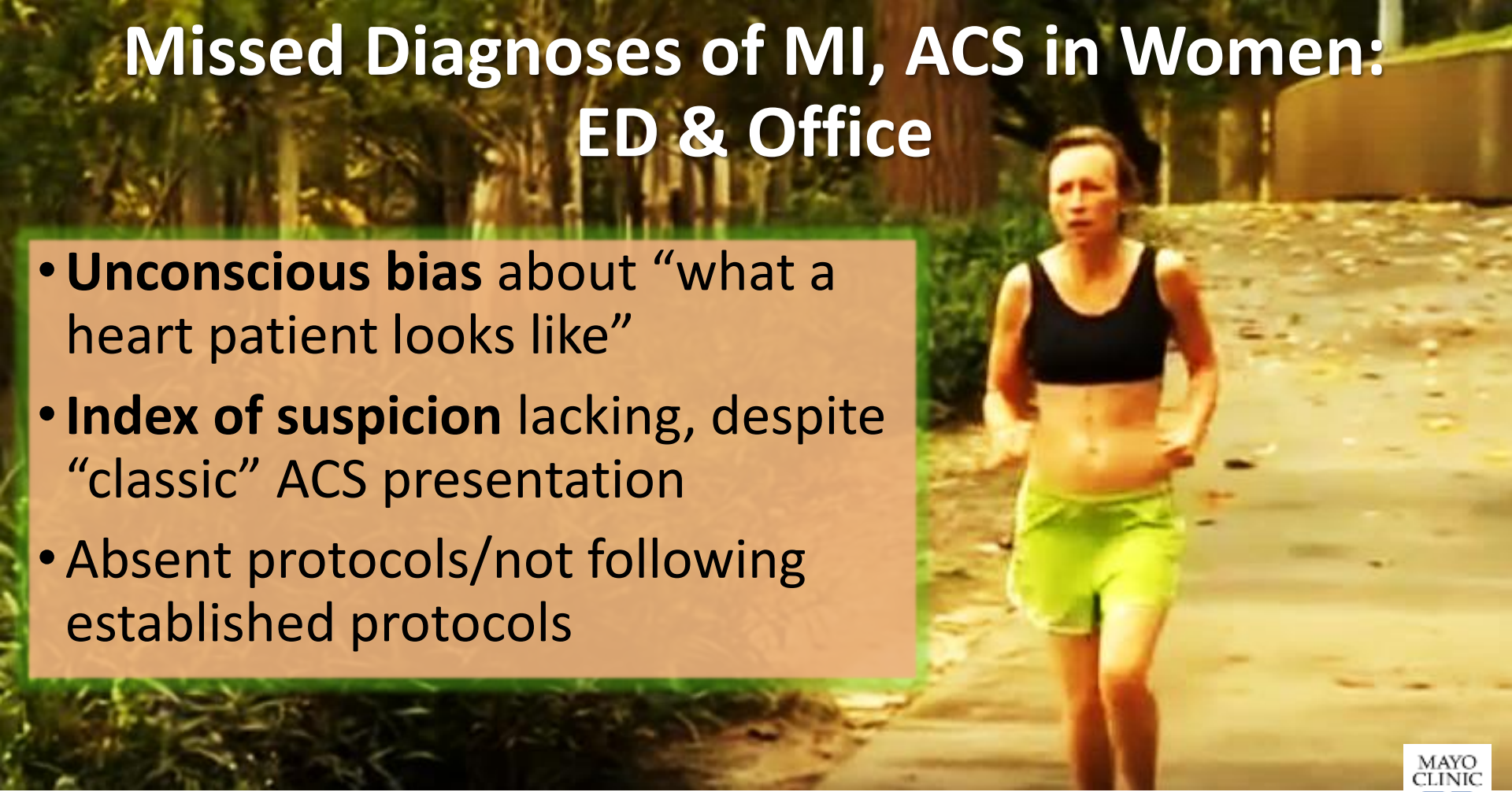


Why The Differences? Disparities?

- Sex-based physiological differences (unexplored)
- Psychosocial influences
- Provider knowledge & research gaps
- Provider bias (unconscious)
- Non-aligned policies
- Unenforced recs and best practices

When women are valued and well, families, children, and communities will benefit

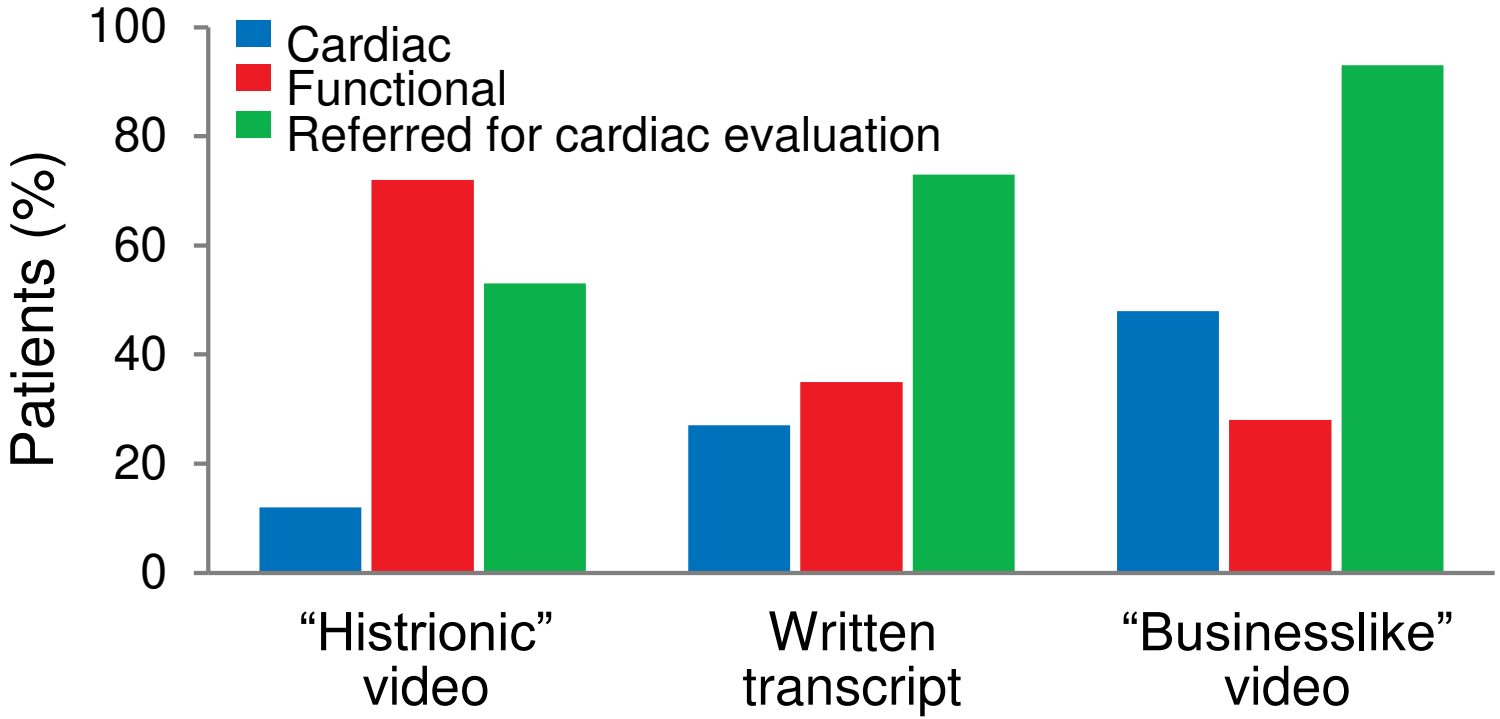
Missed Diagnoses of MI, ACS in Women: ED & Office



- **Unconscious bias** about “what a heart patient looks like”
- **Index of suspicion** lacking, despite “classic” ACS presentation
- Absent protocols/not following established protocols

MAYO CLINIC

Physician Attitude and Women's Communication Styles



Birdwell, Arch Int Med 1993

MAYO CLINIC

Prevention Alert!

Patient-Level Gender Differences: Young Women & Acute MI

- Prodromal symptoms vary: nature, duration
- Inaccurate assessment of personal CVD risk, attribute Sx to noncardiac causes
- Competing/conflicting priorities influence decisions about seeking acute care (e.g., caregiving)
- Healthcare system inconsistently responsive to women: delayed eval, Diagnosis
- Women do not **routinely** access primary care & preventive care for heart disease

Circ Cardiovasc Qual Outcomes. 2015;8:S31-S38

Sex Matters….

"Every cell has a sex"

Understanding sex-based differences is critical to optimal prevention, diagnosis, and treatment of men *and* women

Sex ≠ Gender

- **Sex: *biology* of human and animal subjects**
- **Gender: *self-identity and/or social representation* of an individual**

Women's Unique CVD Risks
Individualized *("Precision")* Cardiology

- Lifetime hormonal fluxes (puberty, pregnancy, menopause)
- Peripartum vascular remodeling
- HTN disorders of pregnancy
- Gestational diabetes
- Delivering a thin baby
- PCOS
- Post menopausal hormone therapy
- Coronary/aortic root dissection
- Sex-specific effects of conventional risk factors

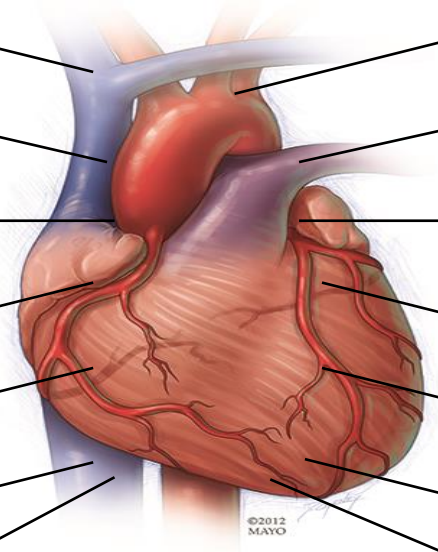
MAYO CLINIC

"I'd like some of that preventive medicine I've heard so much about."


HEEL THYSELF...

Traditional ASCVD Risk Factors

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



Emerging, Nontraditional ASCVD Risk Factors

- Preterm delivery
- Hypertensive disorders of pregnancy
- Gestational diabetes
- Autoimmune disease
- Breast cancer treatment
- Depression
- Menopause

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

Smoking in Women

Prevention Alert!

"Social" (non-daily) smoking kills

- 50% ↑ death
- 3X ↑ heart disease
- 5X ↑ lung cancer

} *vs. never smokers*

Bjartveit: BMJ, 2005; Inoue-Choi: AJPM, 2019 (NHIS data)
Karachi: Arch Int Med, 1994 (NHS)

Sex Differences in Modifiable Risk Factors in Young Adults at 1st MI

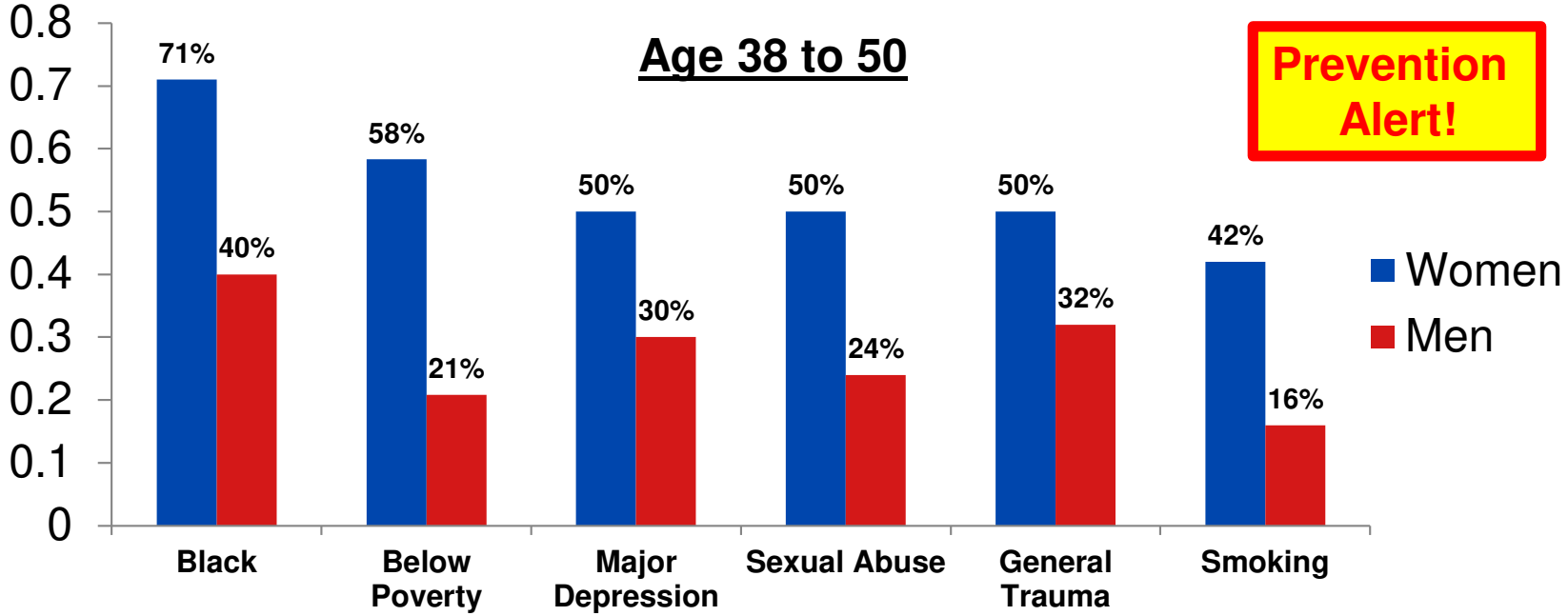
During a first myocardial infarction in young adults (18-59 years) in the U.S.

25%	Diabetes Mellitus	>1 in 4	34%
6%	Drug Abuse	>1 in 20	5%
57%	Hypertension	>1 in 2	61%
58%	Dyslipidemia	>1 in 2	52%
16%	Obesity	>1 in 6	23%
54%	Smoking	>1 in 2	50%
92%	Any of these modifiable risk factors	>9 in 10	91%

Srikanth Yandrapalli et al. JACC 2019;73:573-584

Young Women with Recent MI Have More Psychosocial/Behavioral Risk Factors Than Men

Myocardial Infarction and Mental Stress Study (MIMS)



Vaccarino et al., Psychosom Med 2014

Prevention Alert!

Depression & Anxiety and CVD
Indirect Causal Effects

- Poor health behaviors – diet, activity
- Maladaptive coping styles – tobacco, alcohol
- Social isolation
- Chronic life stress
- Delays in seeking care
- Treatment nonadherence (meds, rehab)

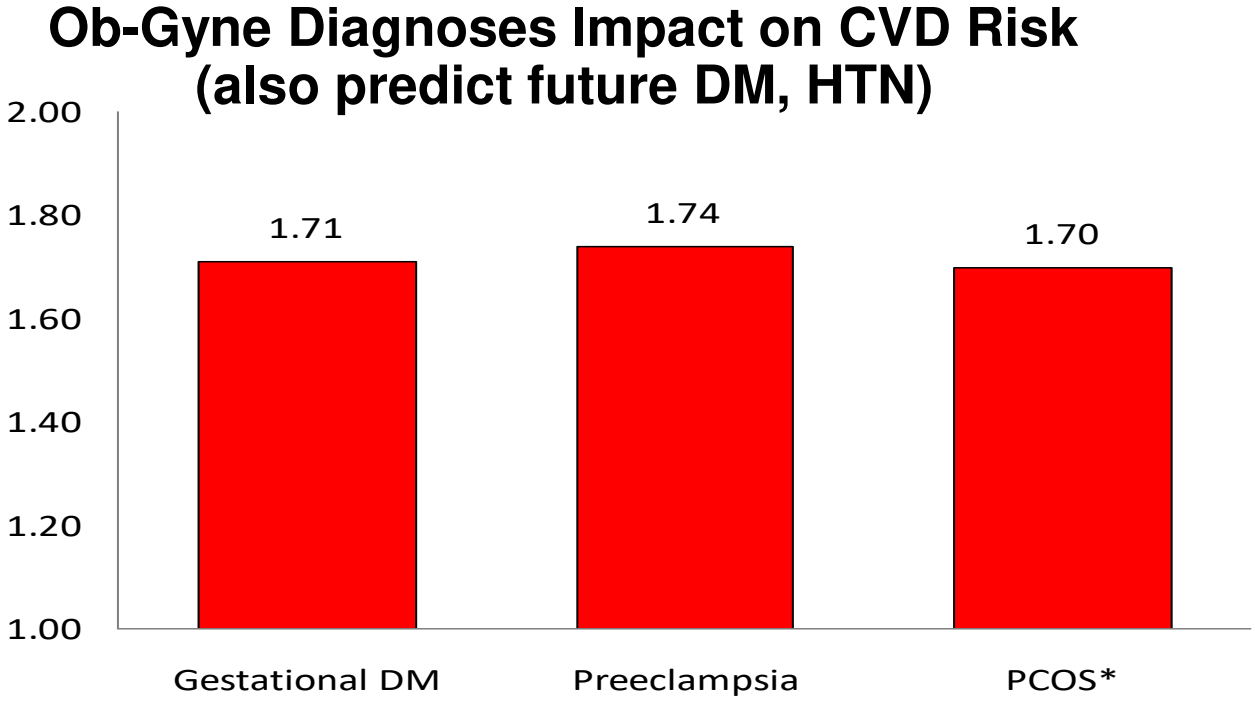
Physical inactivity accounts for ~ 25% of ↑ CVD mortality risk due to depression

Win S et al. Heart 2011

Pregnancy:
A Sex-Specific CVD Risk Factor

Pregnancy: "Metabolic Stress Test" That Predicts Future CVD

Relative Risk of Subsequent CVD

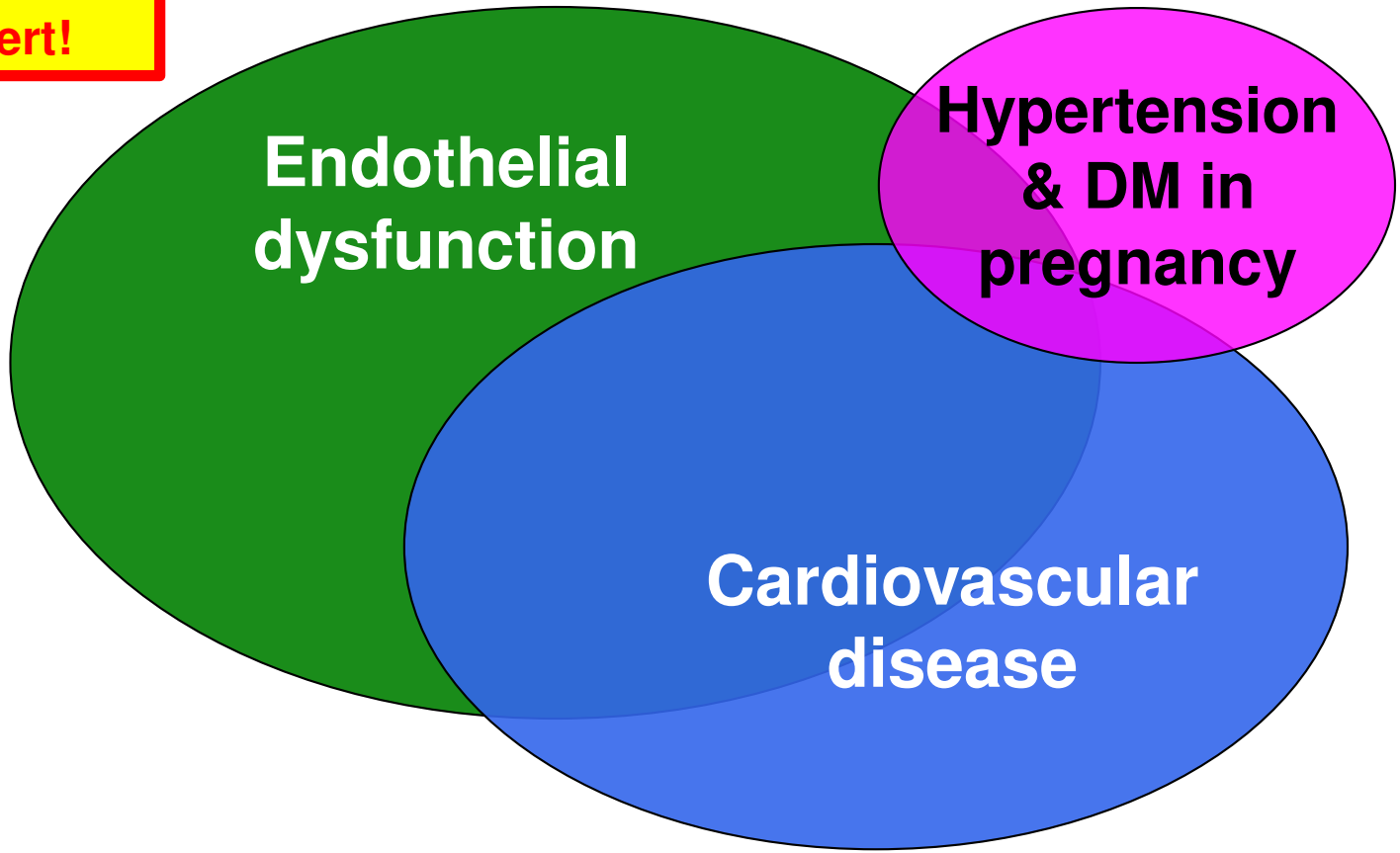


Shah 2008, Wild 2010, Hannaford 1997; Magnussen 2009, Kim 2002

*Polycystic Ovary Syndrome


WAITING ROOM
"Who was first?"
HARDIN

Prevention Alert!



Hierarchy of Female Concern

What's Important to Women?

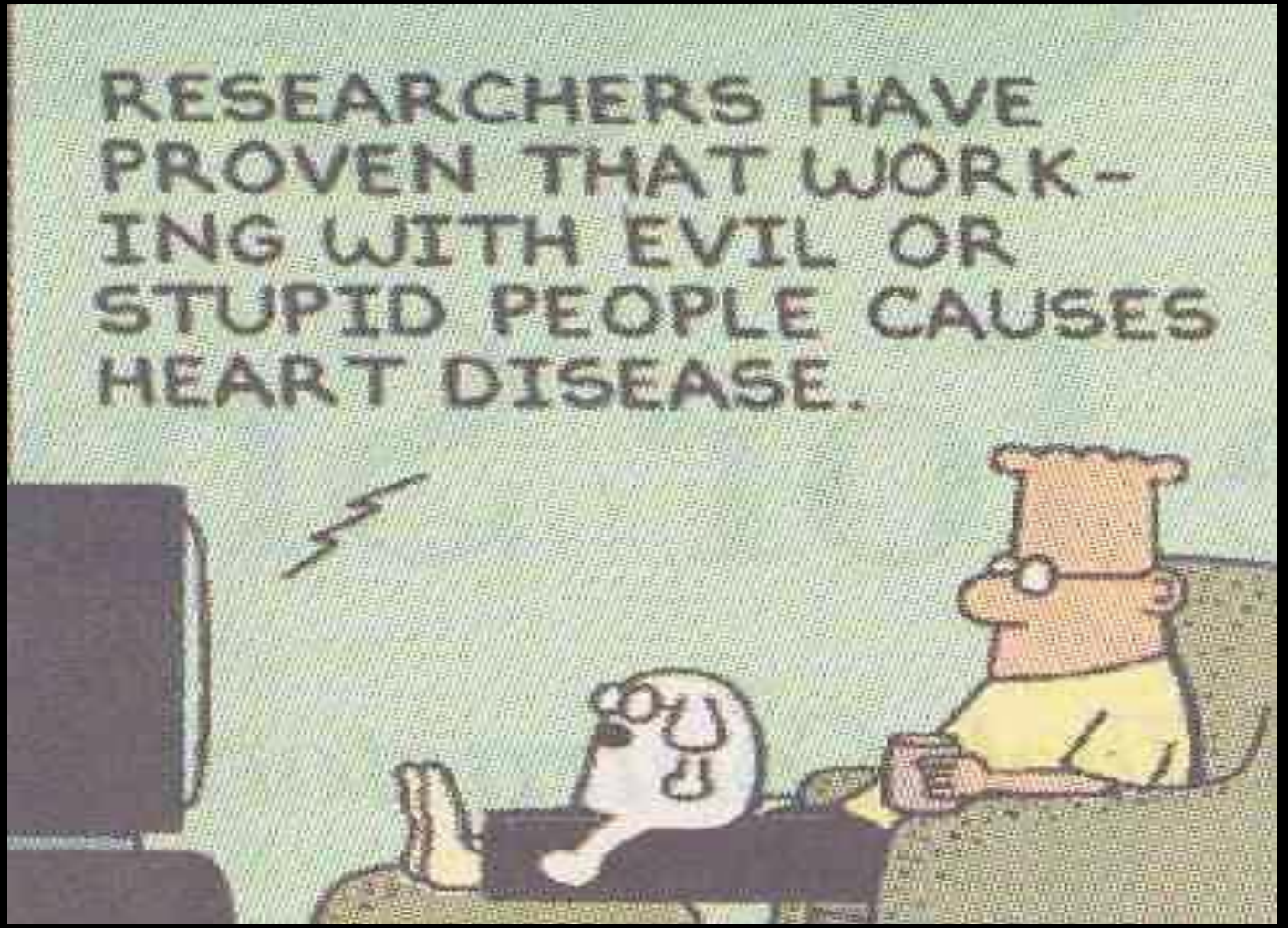
Ranking created from P&G 2000 Health Archetype Study

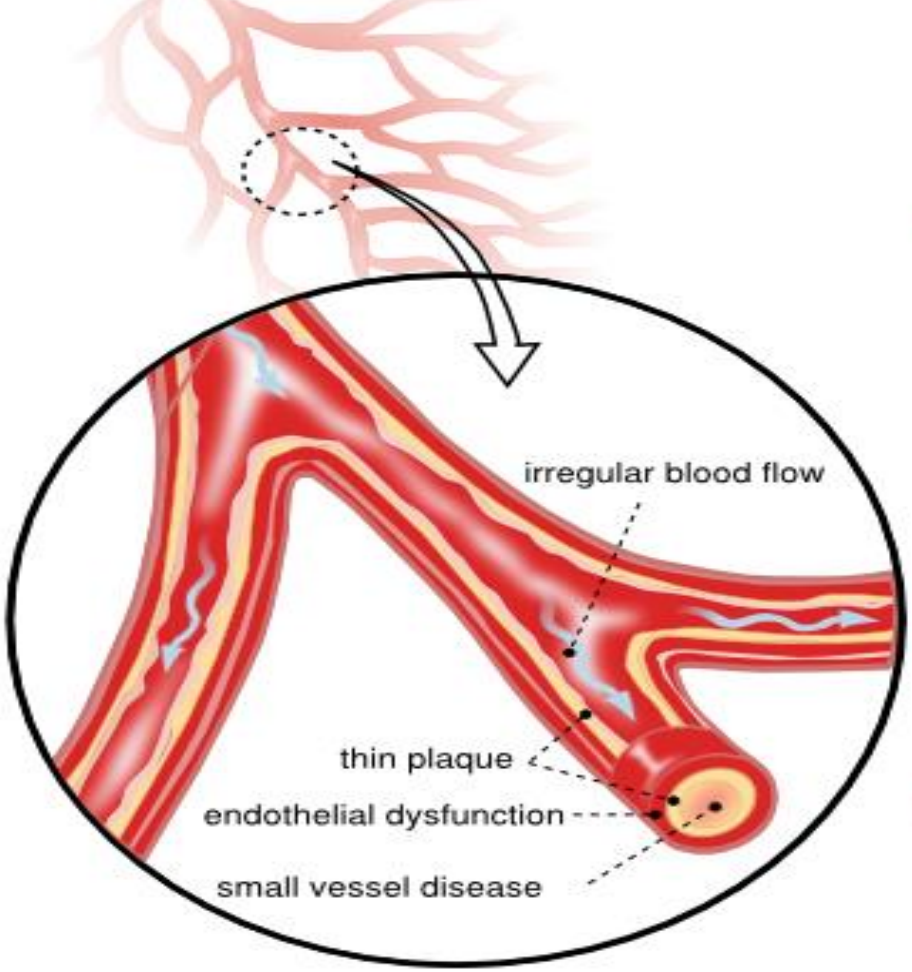
Barriers to Lowering Heart Disease Risk

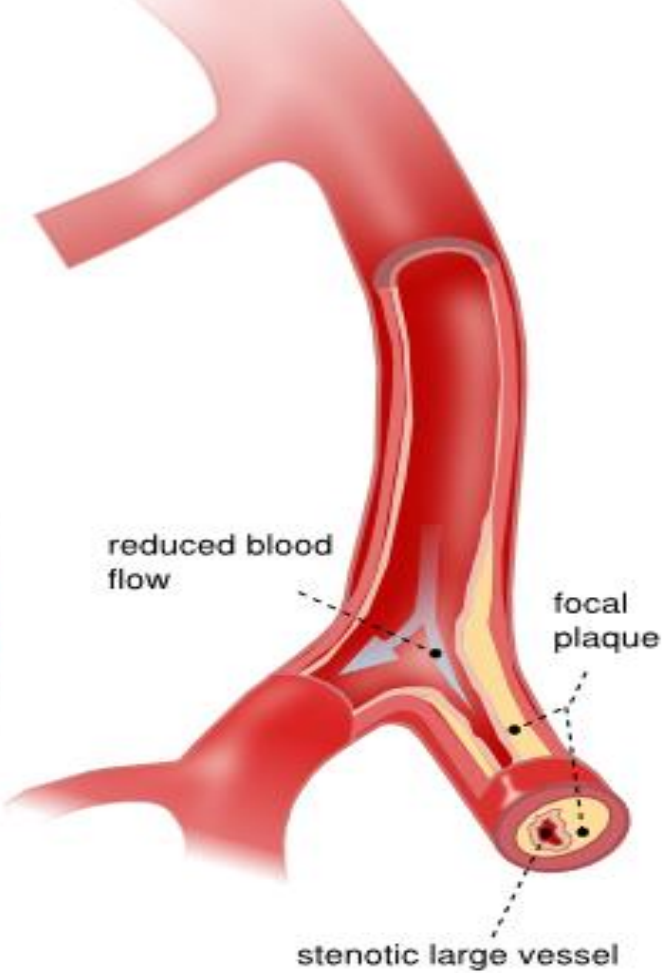
- Caregiver obligations
- Confused by media
- God/higher power determines my health
- Not confident I can, don't know how to change, too complicated, fear change
- Financial/insurance barriers
- I am not at risk for heart disease
- I don't WANT to change
- Stress
- No support from health care provider or family

MAYO CLINIC

Mosca et al: Circ Cardiovasc Qual Outcomes, 2010
AHA Survey


RESEARCHERS HAVE PROVEN THAT WORK-ING WITH EVIL OR STUPID PEOPLE CAUSES HEART DISEASE.





♀ Microvascular coronary disease in women

♂ Focal coronary disease in men

“Run for it…It’s a heart attack!!”

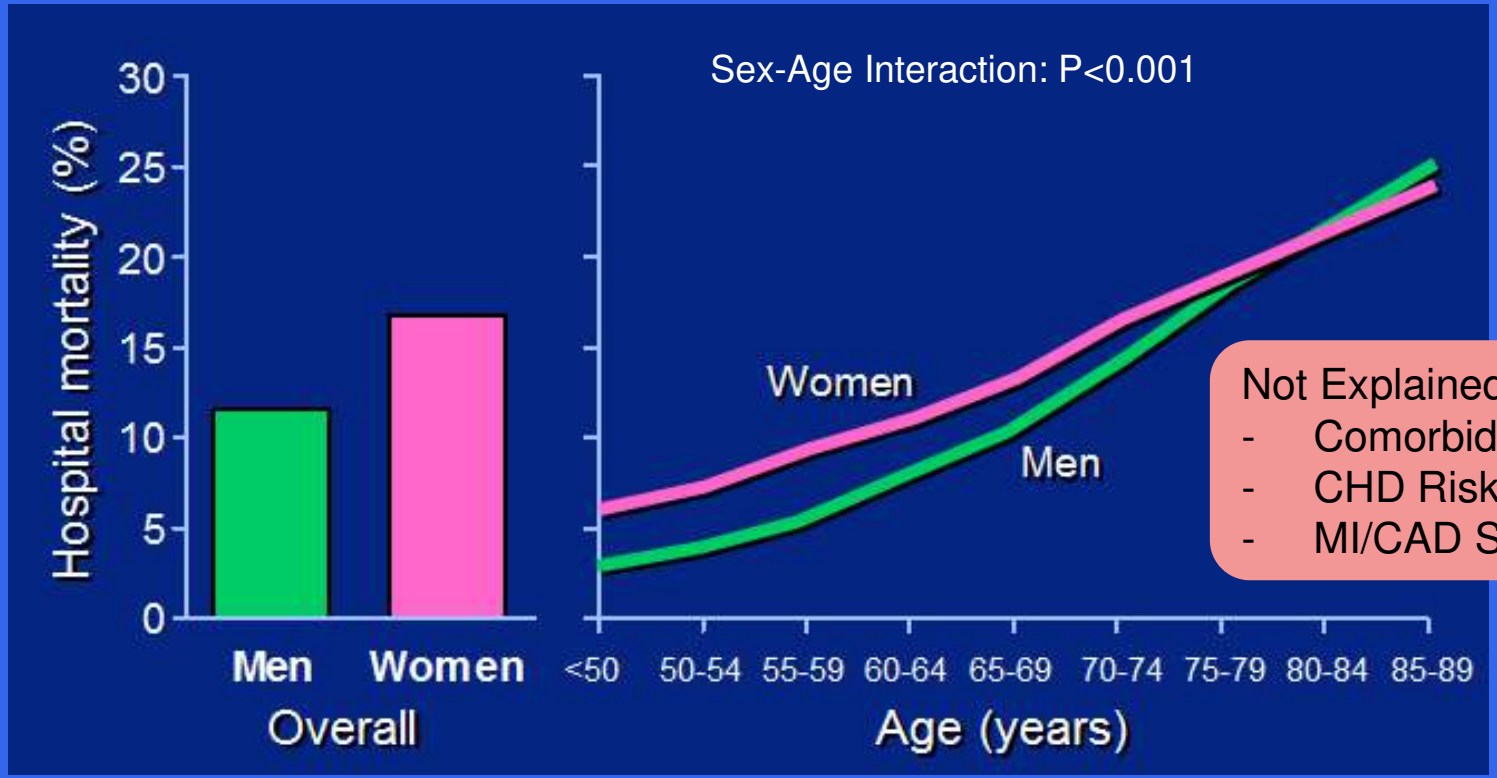
Prevention Alert!

Make The Call Don't Miss a Beat

- Only **53%** of women would call 911 if **they** were experiencing the symptoms of a heart attack
- However, **79%** said they would call 911 if **someone else** was having a heart attack
- 46% of women would do something **other than call 911** if they had chest pain —such as take an aspirin, go to the hospital, or call the doctor

DHHS Office on Women's Health, 2011

Higher Mortality in Young Women With MI



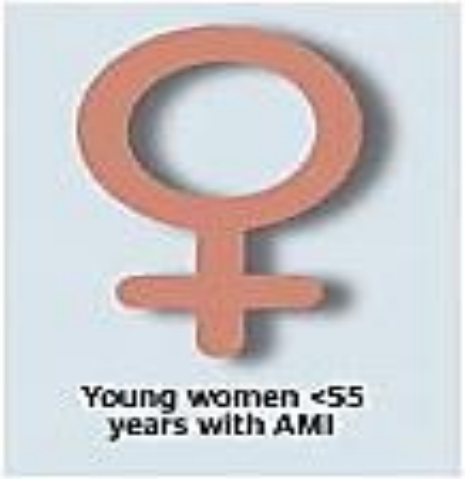
Not Explained by:
- Comorbidities
- CHD Risk Factors
- MI/CAD Severity

NRMI 1994-1998 N=384,878

Vaccarino e., N Engl J Med 1999; Vaccarino ,Arch Int Med 2009; Izadnegahdar , J Wom Health 2014

AMI Trends for Young Women & Men

2001-2010 [230,684 hospitalizations (total 1,129,949)]

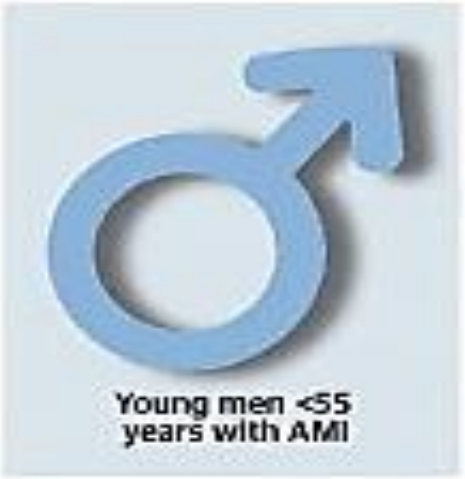


> Comorbidities

< AMI Hospitalization Rate

> Length-of-Stay

> In-hospital Mortality



AMI hospitalization rates in the young have not declined. Sex differences persist.

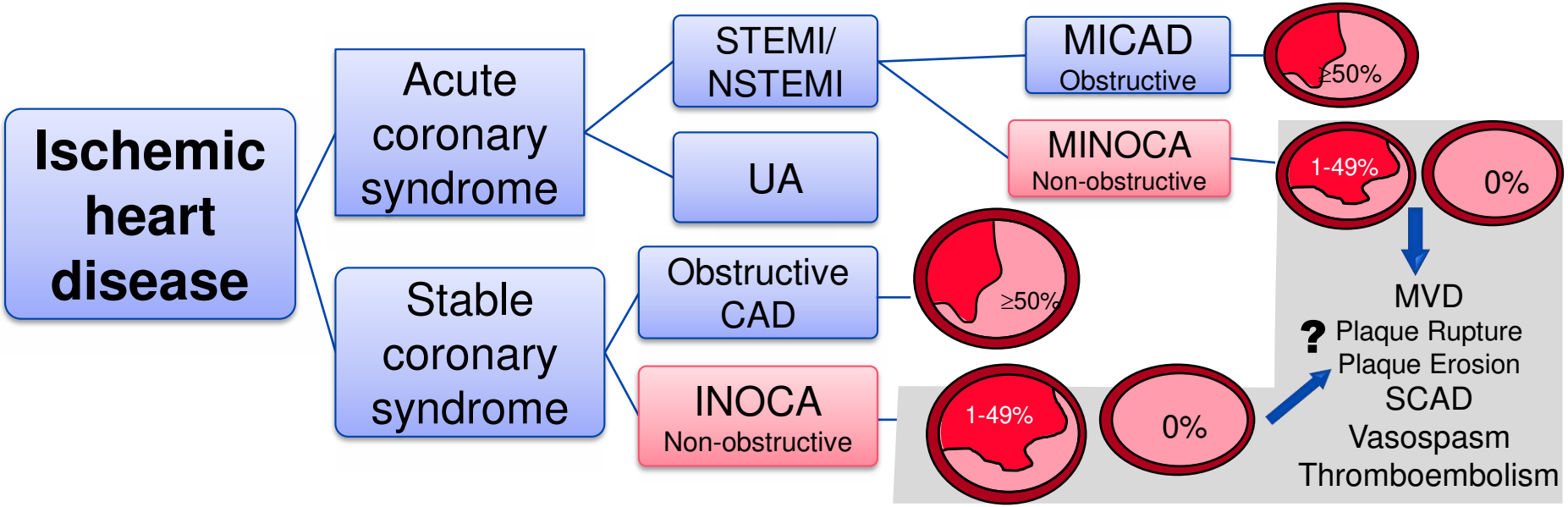
Gupta A et al. J Am Coll Cardiol 2014; 64:337–345

ACS in Young Women: Different disease??

Potential Explanations

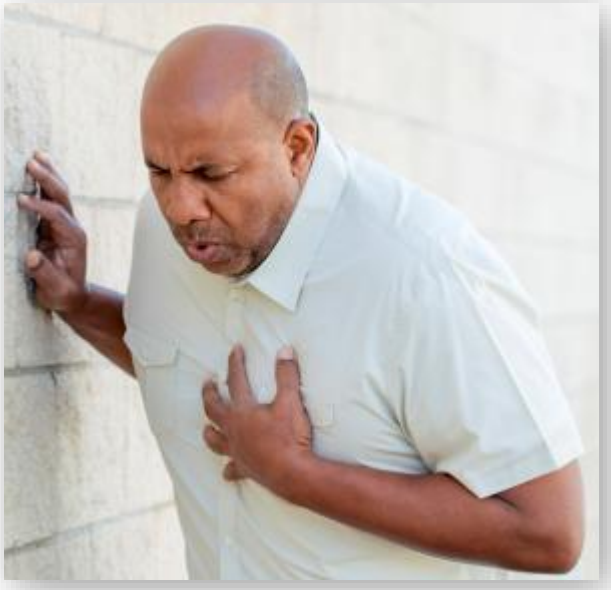
- ? Vasospasm (migraines, Raynaud's)
- ? Thrombosis (hormones)
- ? Hormones, pregnancy
- ? Genetics, epigenetics
- ? Inflammation (autoimmune Dz burden)
- ? Psychosocial burdens
- ? SCAD, connective tissue disorders

Ischemic Heart Disease Phenotypes



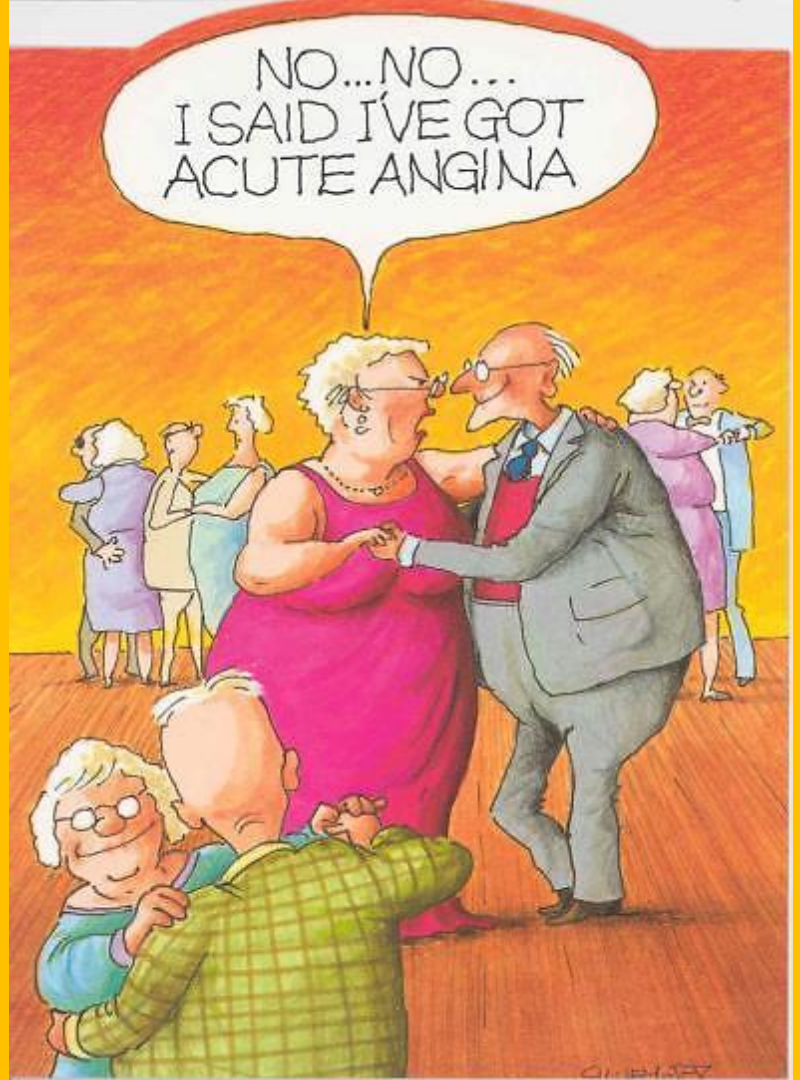
GENESIS-PRAXY: Raparelli et al: Can J Cardiol, 2018

Symptom Triggers May Be Different in Women



Emotional stress is more frequently a trigger for women than men

Sex AND gender differences: **pathophysiology, prevention, acute care, attitudes, all** contribute to young women's elevated AMI mortality



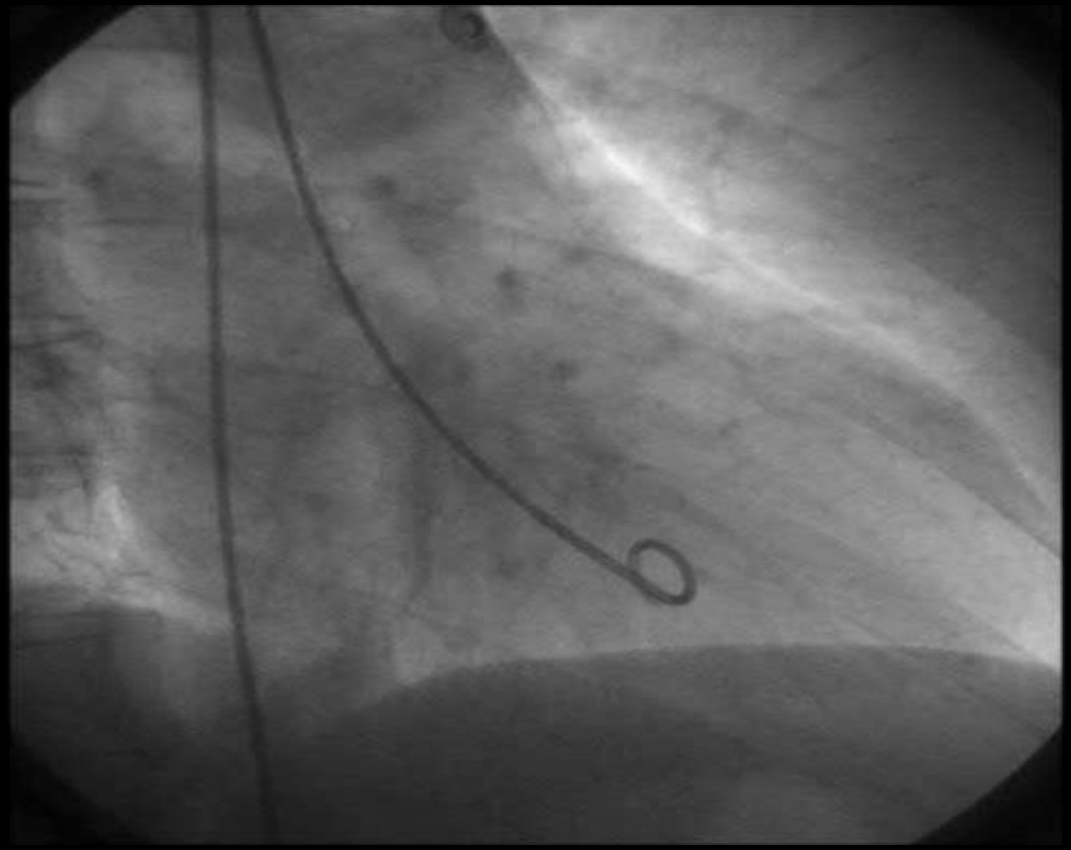
70 y/o Woman: Chest Pain for <2 Hrs.

PMH

- HTN
- Dyslipidemia
- Migraines
- Multiple negative cardiac evaluations for CP

- Learned of husband's death <1 hr before Sx
- ECG: mild ST elevation V1-V3

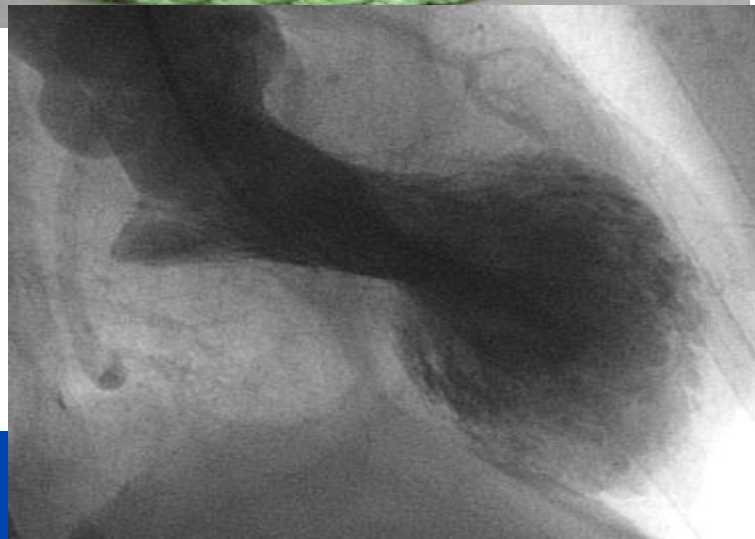
Normal coronaries: LV gram



Peak troponin 0.6 ng/ml

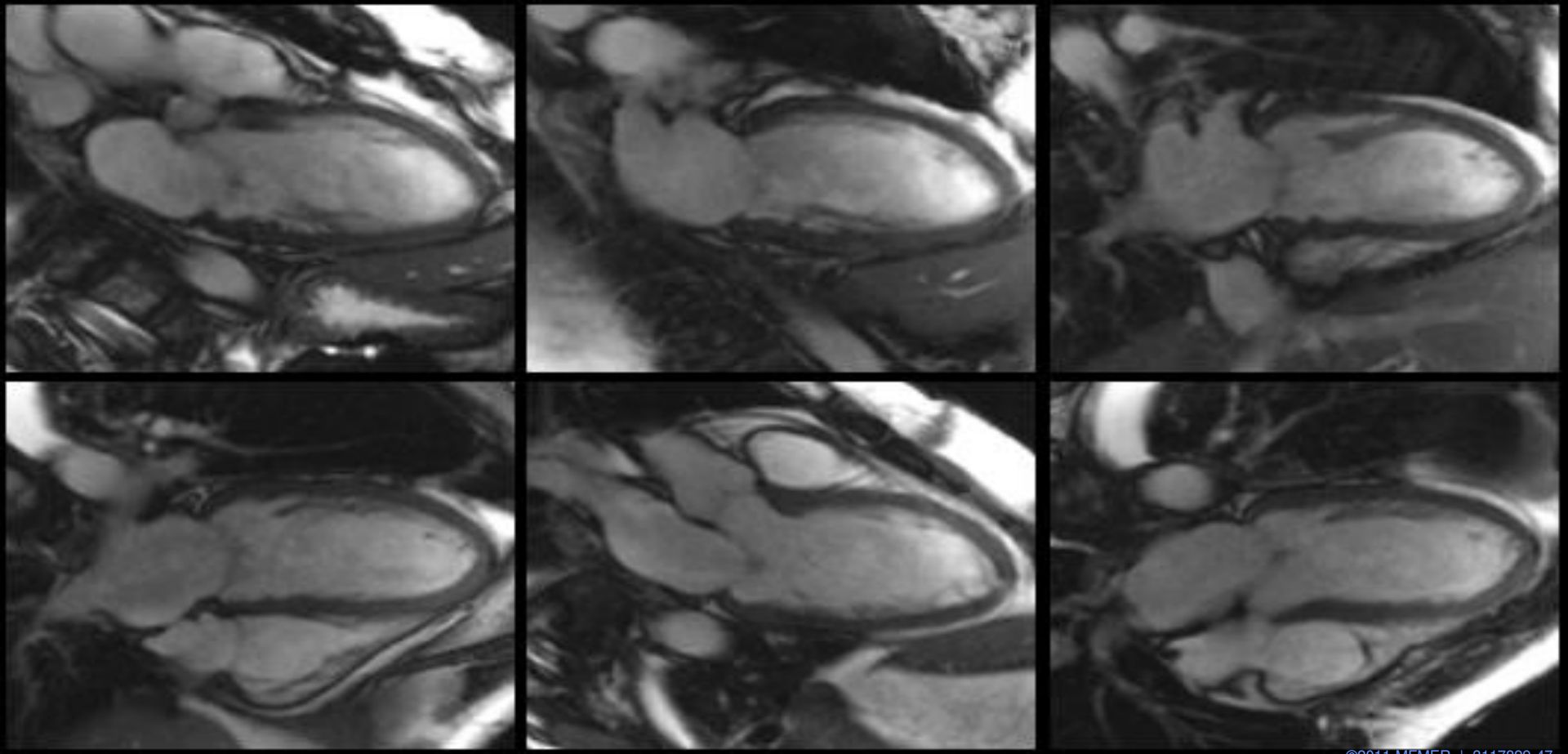
Tako-tsubo = Octopus Trap

- Transient, reversible LV dysfunction
- First described in Japan 1990
- ~2% of ACS presentations
- LV mid & apical hypo/akinesis with hyperdynamic base
- Variants: mid-ventricular, LVOT obstruction
- 30% RV involvement



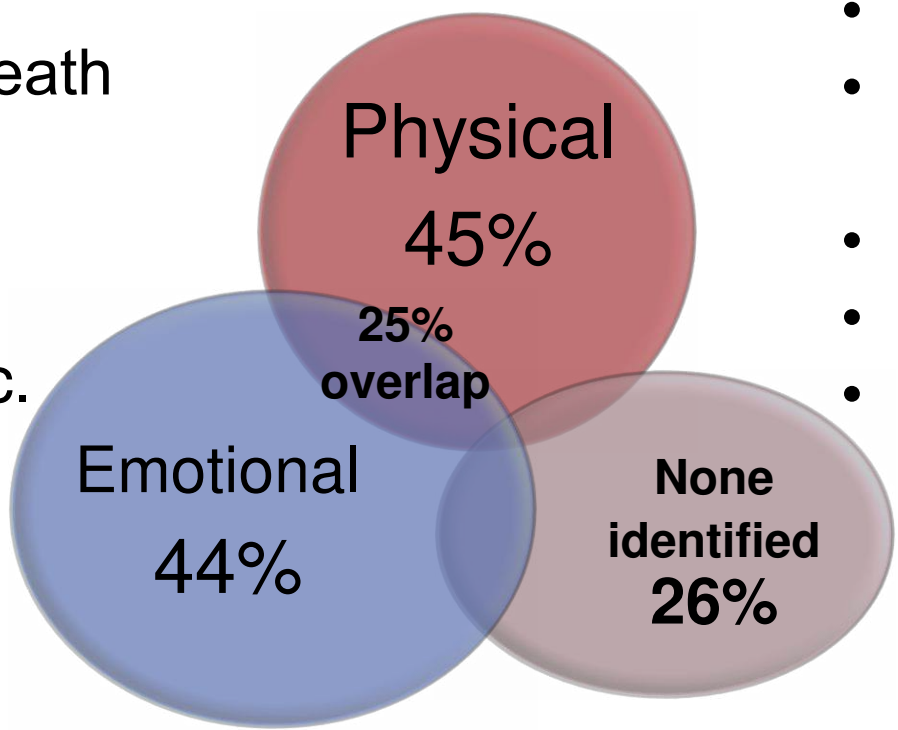
MAYO CLINIC
Sato.et al. Clinical Aspect of Myocardial Injury:1990;
Dote K, et al. Am J Cardiol.1991

Stress Cardiomyopathy



Clinical Presentation: Stressors

- Relative's illness, death
- Arguments
- Family problem
- Tax preparation
- Public speaking, etc.



- Surgery
- COPD exacerbation
- Pneumonia
- Fracture
- DSE

Scantlebury et al. Am J Card 2013

Stress Cardiomyopathy Patients/Diagnosis

- M:F ratio~ 1:9, Post menopausal, (Mean age 70.2 yrs)
- Preceding stressful situation (physical or emotional)
- WMA's with mild, non-obstructive coronary disease
- New ECG abnormalities and *modest* elevation in troponin
- **Recurrence rate** ~10% at 4-5 years; Excess mortality persists
- Treat comorbidities; **manage HTN, stress**

Prevention Alert!

** CVA, drug abuse, anxiety & mood disorders, malignancy, liver Dx, sepsis, smoking, alcohol abuse, hyperlipidemia*

Scantlebury. Am J Card 2013; Scantlebury Circ J, 2014; Bybee et al , AJC 2004; Zorzi, EHJ: ACC, 2015; El-Sayed et al. Am J Card 2013; *Deshmukh et al. AHJ 2012

Cardiac Rehabilitation Referral and Participation

Prevention Alert!

- Cardiac rehabilitation (CR): essential component of comprehensive care after AMI
- Class I recommendation after MI
- CR has failed to reach >80% of eligible women for decades
- Young & female-risk factor for no CR
- Lack of referral is largest impediment


Reunion Dinner,
bad, CA


249


111
154
301
307

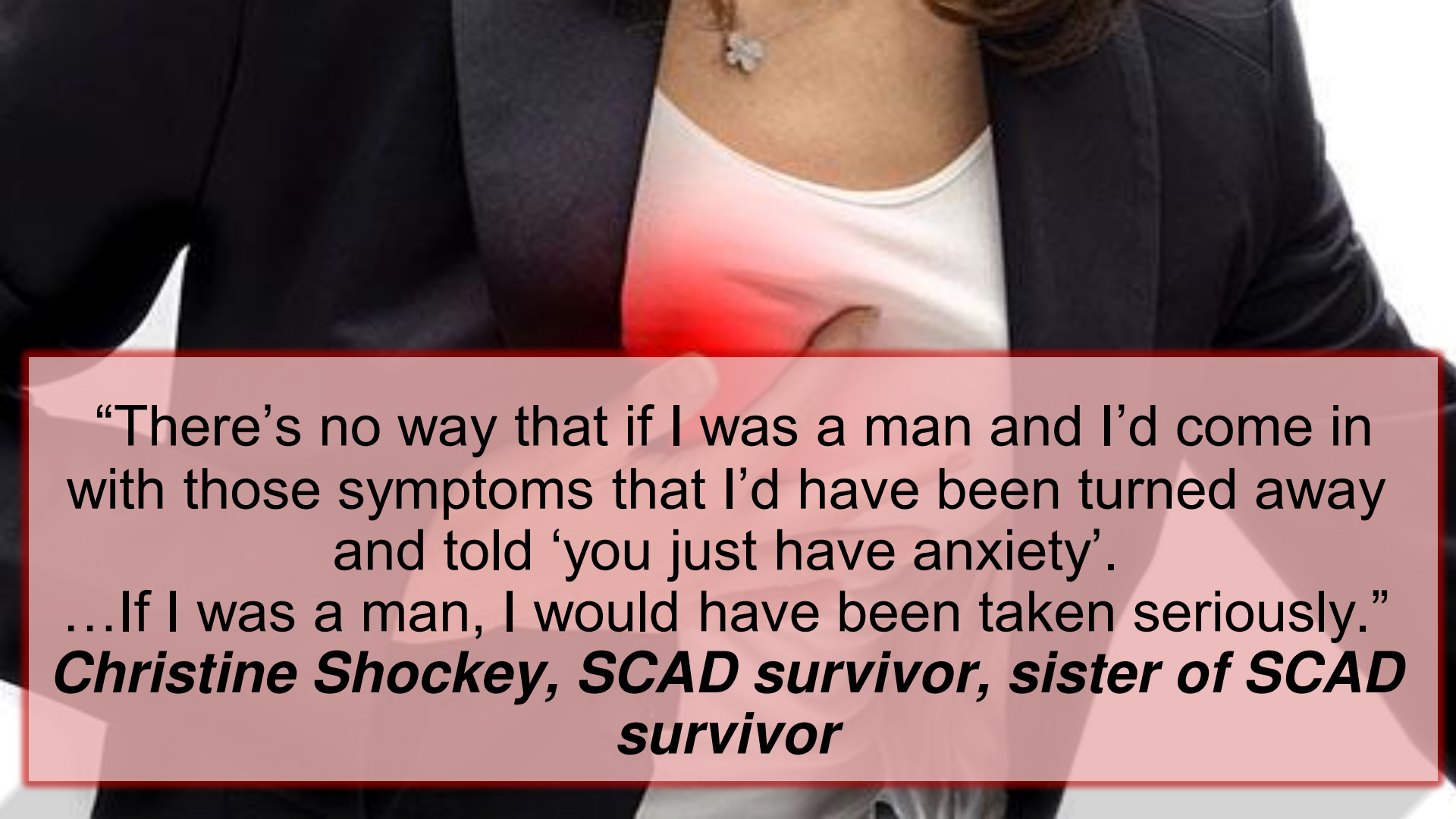

700

A Tale of 2 Sisters: 43 y/o Attorney, 2 days CP

- Emergency Department eval:
  - Hx preeclampsia, gestational diabetes X 2, & anxiety.
  - No other CVD risk factors
  - Sister had MI 10 days prior **(SCAD!!)**
  - ↑Troponin
  - Dismissed **(!)**
- Outpatient stress treadmill = negative
- Continued severe pain, shortness of breath
  - Rx: gabapentin (Day 3)

43 y/o Attorney: 2 Days - Severe Chest Pain

- Another 48 hrs of 9/10 chest, L arm pain (Day 5)
  - Internist: Rechecked the troponin, ↑ further
  - ECG =“ST elevation”
  - Echo=wall motion abnormality
  - Diagnosis=“myopericarditis”.
  - Cath scheduled for ***next day*** **(!)**
- Day 6-Angio: LAD SCAD, TIMI-0, Ejection fraction: 40%
  - Stent X 2
  - Subsequent Dx FMD



"There's no way that if I was a man and I'd come in with those symptoms that I'd have been turned away and told 'you just have anxiety'.
…If I was a man, I would have been taken seriously."
Christine Shockey, SCAD survivor, sister of SCAD survivor


SCAD
IS BAD
SCAD
IS BAD
SCAD
IS BAD

E-patients:
Equipped, Enabled, Empowered, Engaged

- Patients discuss the latest treatments, trials
- Peer-to-peer healthcare
- Eager “rare disease” community

MAYO CLINIC

WOMENHEART

RE: Spontaneous Coronary Artery Dissection

Dear Dr. Hayes,

I am writing to follow-up on our conversation at the Science & Leadership Symposium regarding a potential research opportunity for women diagnosed with spontaneous coronary artery dissection (SCAD).

The attached document provides a summary of the information I've collected from the WomenHeart "Inspire" online community. As of today, 86 User IDs represent women who have been told they had a spontaneous dissection of an artery. The material is segmented by "cause unknown" and "postpartum." Fifty-eight women (67%) are "cause unknown." Twenty-eight women (33%) are postpartum. Each category is arranged by age at time of SCAD.

Among the issues the women hope a research effort would address are SCAD's relationship to:

- Hormone fluctuations (occurrence with pregnancy vs. menstrual period vs. ovulation vs. menopause)
- History of birth control pill use
- Connective tissue disorders
- Congenital heart defects
- Vasospasm/Prinzmetals
- Migraines
- Heredity
- Thyroid conditions
- LAD vs. RCA
- Extreme exertion (exercise or labor)
- Choice of treatment (medication only vs. stents vs. bypass surgery)

Naturally, our overriding concerns are whether we will suffer another SCAD (two women in the data claim they have); and, have we (will we) pass on the potential for SCAD to our children.

"If this small universe from the online community provides a starting point, maybe a mechanism could be set up for cardiologists nationwide to report SCAD for inclusion in ongoing research."

Sincerely,

Katherine K. Leon
WomenHeart Champion, 2009

SCAD Research Population…

2young4this

Shazz

QueenE

Saintster

Sunshyne

Texheart

Dee81

Mommyto2many

Brknhrtgirl

Sunshine10

Niffy

Heartsyl

Rnow52

Asurvivor

Heartmother

THE WALL STREET JOURNAL

TUESDAY, AUGUST 30, 2011 - VOL. CCLVIII NO. 51

HEART BEAT | AUGUST 30, 2011

When Patients Band Together

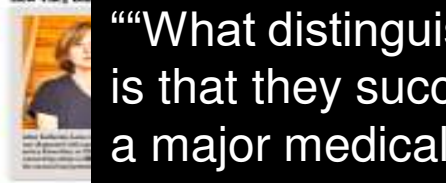
Using Social Networks To Spur Research for Rare Diseases; Mayo Clinic Signs C

By RON WINSLOW

When Katherine Leon began feeling crushing chest pain six weeks after the birth of her second child, doctors were perplexed about what was causing her symptoms.

Ms. Leon was then 38 years old and healthy, and doctors didn't believe she was having a heart attack. She saw her physician and made two visits to the emergency room. Finally, doctors decided to perform an X-ray angiogram to check for arterial blockages. What they found was so serious, she was whisked to the operating room within 30 minutes for bypass surgery.

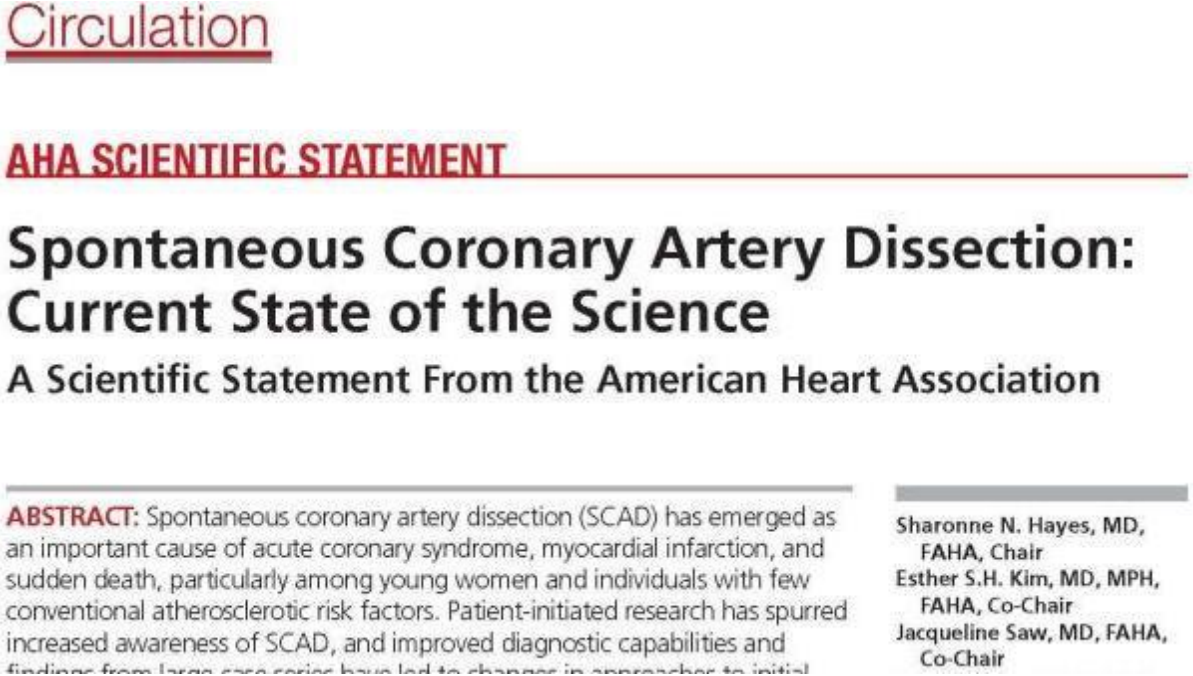
The diagnosis: Ms. Leon had spontaneous coronary artery dissection, or SCAD, a mysterious condition in which the internal layer of an artery separates from the outer wall, creating a fissure where blood clots can form and potentially block blood flow. SCAD is so rare that little research has been done into what causes it, who is at risk and what treatments are most effective. It mainly affects women and can be fatal.



more about SCAD.

Tuesday, results of a pilot study conducted by researchers at the Mayo Clinic are being published online by the journal Mayo Clinic Proceedings. The study, which involved 12 SCAD patients from the message board, found that it is feasible to collect data and medical records from patients with different doctors and from far-flung locales. The study

""What distinguishes this group of patients, however, is that they succeeded in persuading researchers at a major medical center to launch a research program to learn more about SCAD"



Circulation

AHA SCIENTIFIC STATEMENT

Spontaneous Coronary Artery Dissection: Current State of the Science

A Scientific Statement From the American Heart Association

ABSTRACT: Spontaneous coronary artery dissection (SCAD) has emerged as an important cause of acute coronary syndrome, myocardial infarction, and sudden death, particularly among young women and individuals with few conventional atherosclerotic risk factors. Patient-initiated research has spurred increased awareness of SCAD, and improved diagnostic capabilities and findings from large case series have led to changes in approaches to initial

Sharonne N. Hayes, MD, FAHA, Chair
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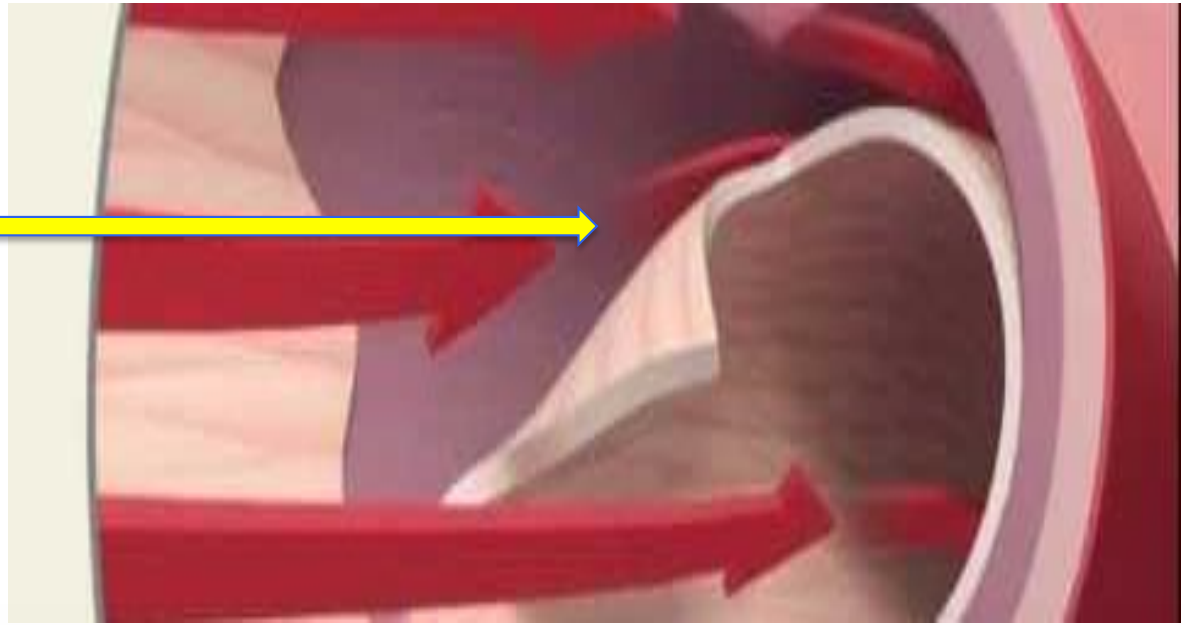
SCAD Defined

+/-
Intimal
Tear



+/- Vaso
vasorum
rupture

Spontaneous~Non-traumatic~Non-iatrogenic
Non-atherosclerotic

SCAD 2019-What We Know Now

- **NOT atherosclerosis!**
  - Average age 42-52 yrs
  - ~90% women, ~5-15% of women peripartum
  - CVD risk factors absent
- **NOT "rare"! (we were missing it…)**
  - 1-4% of MI patients overall
  - #1 cause pregnancy-related MI
  - #1 cause MI women <40 yrs

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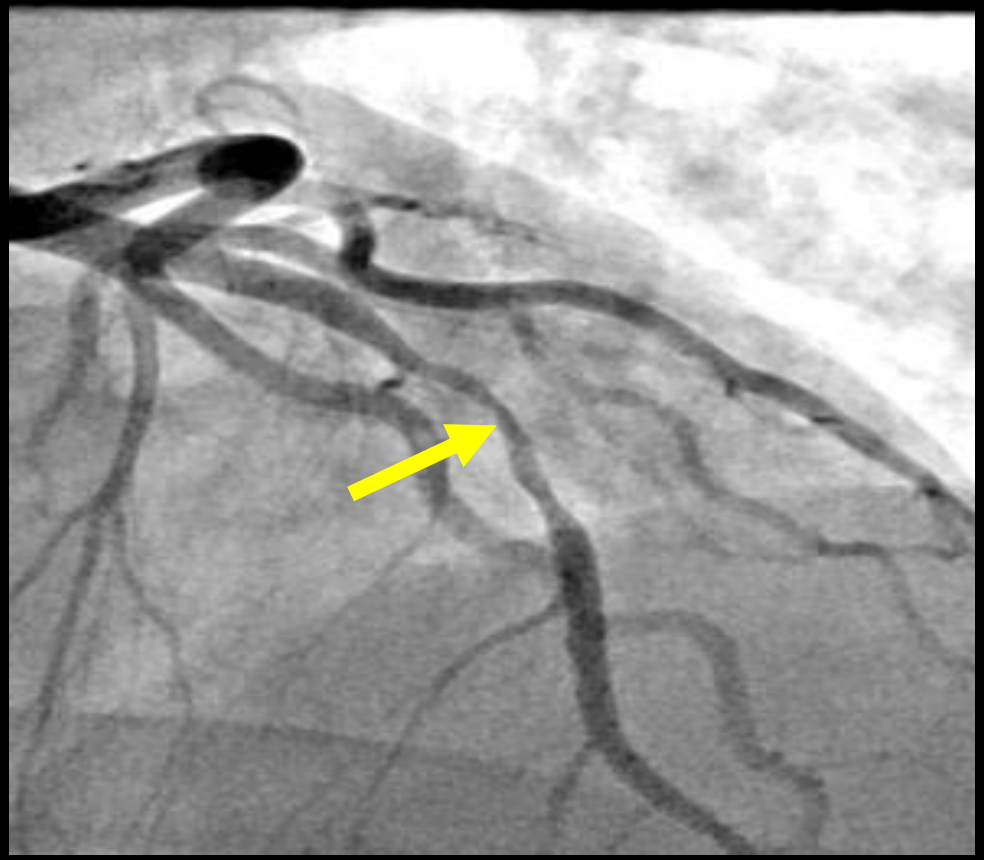
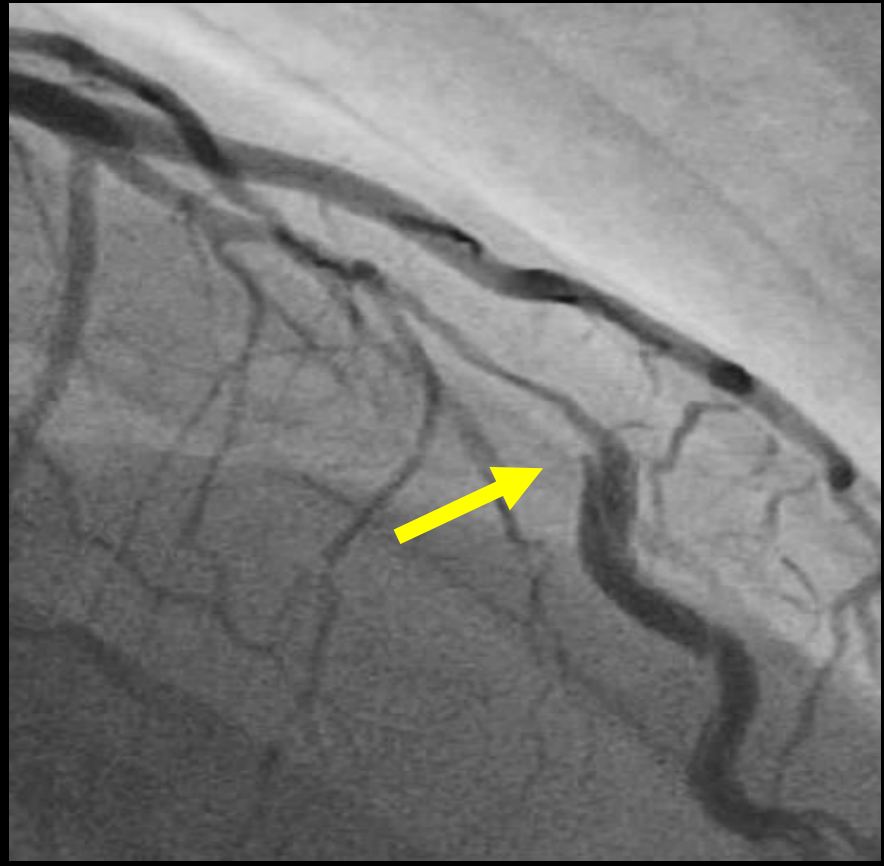
Tweet et al, Circulation 2012; Saw, Circ Cardiovasc Interv. 2012
Nishiguchi Eur Heart J. 2013 (Japan) Elkayam U. Circulation. 2014

SCAD 2019-**We've Been Missing It**

- **Not "benign"**
  - STEMI~50%, Vfib~15%, Multivessel 25%
  - Traditional ACS treatments often cause harm
  - Recurrence rates ~ 20+% over time
- **Different associated factors**: pregnancy, FMD, arterial tortuosity, stress, exercise, migraines
- **Making the diagnosis** affects management!

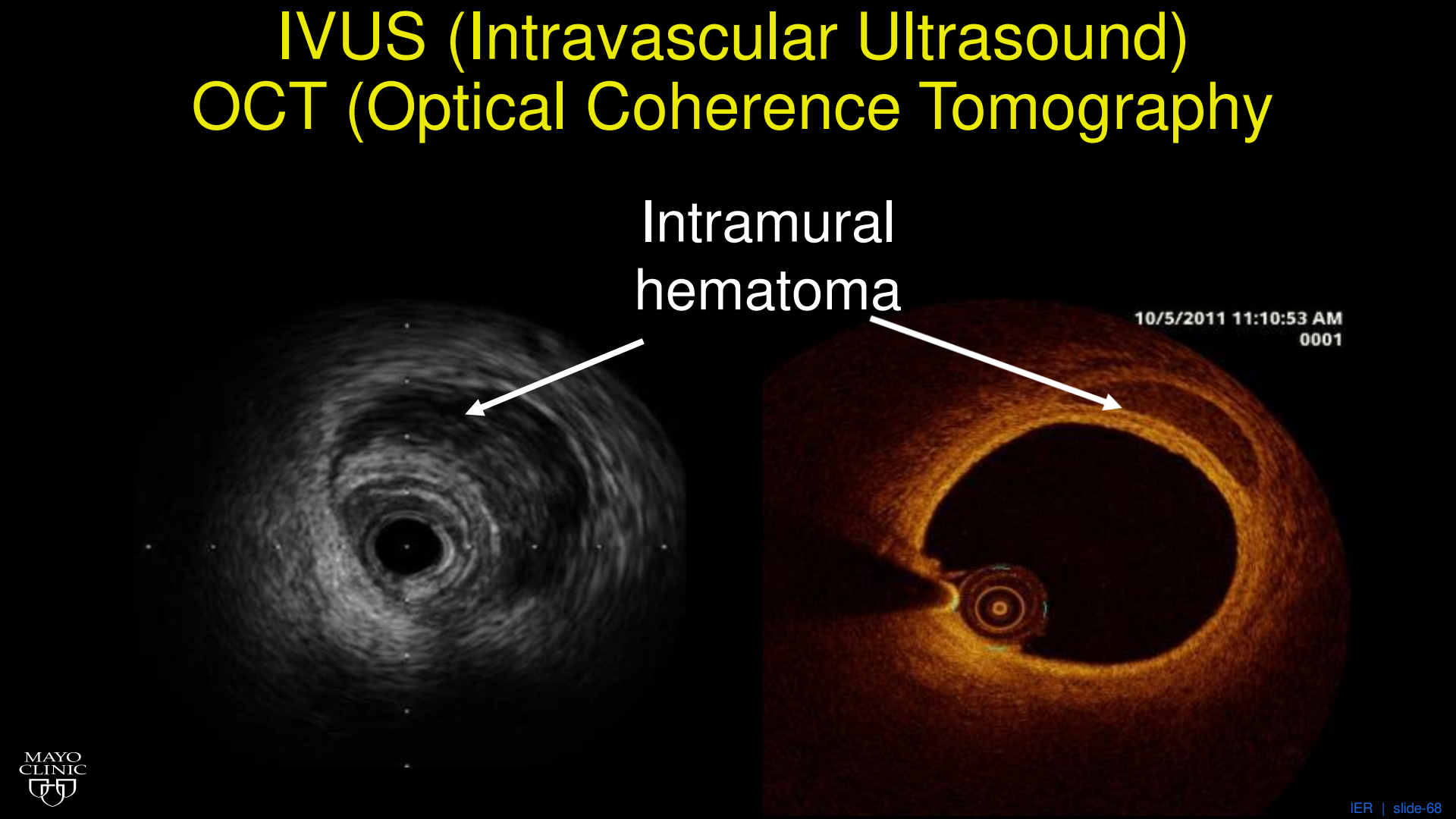
Tweet et al, Circulation 2012; Saw, Circ Cardiovasc Interv. 2012
Nishiguchi Eur Heart J. 2013 (Japan) Elkayam U. Circulation. 2014



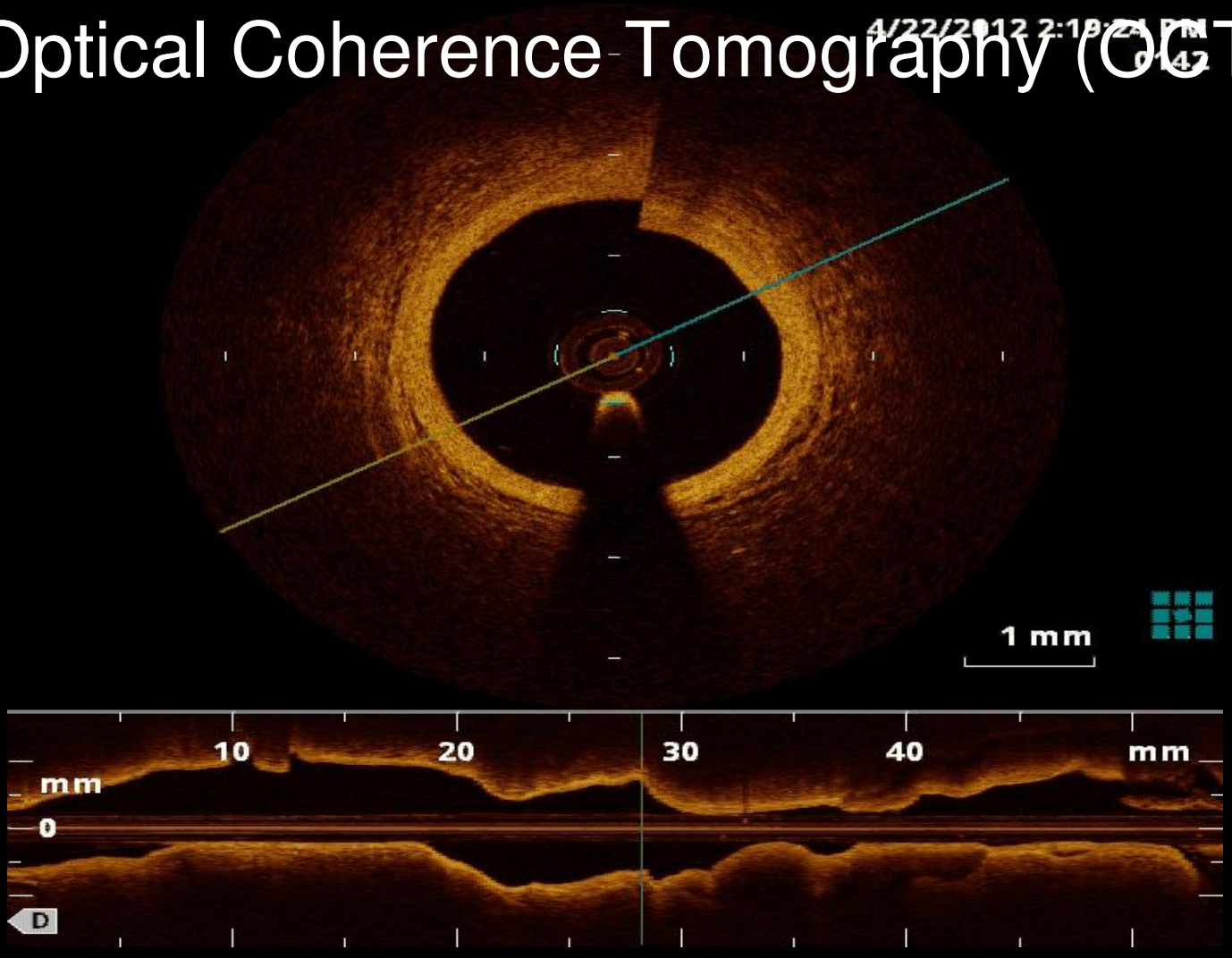


Medial Hematoma vs. Intimal Tear

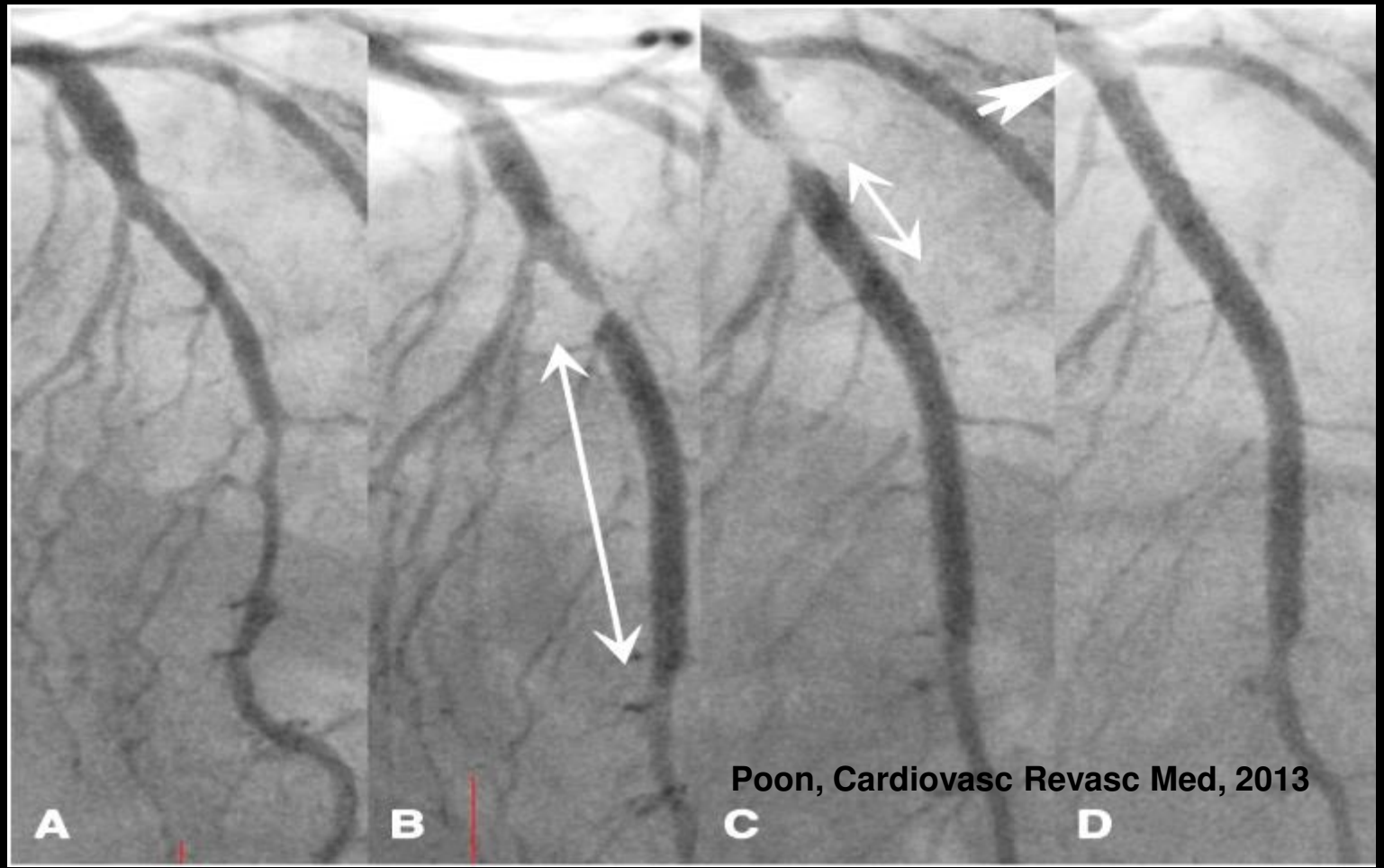
IVUS (Intravascular Ultrasound)
OCT (Optical Coherence Tomography



Optical Coherence Tomography (OCT)



Dissection Propagation with PCI



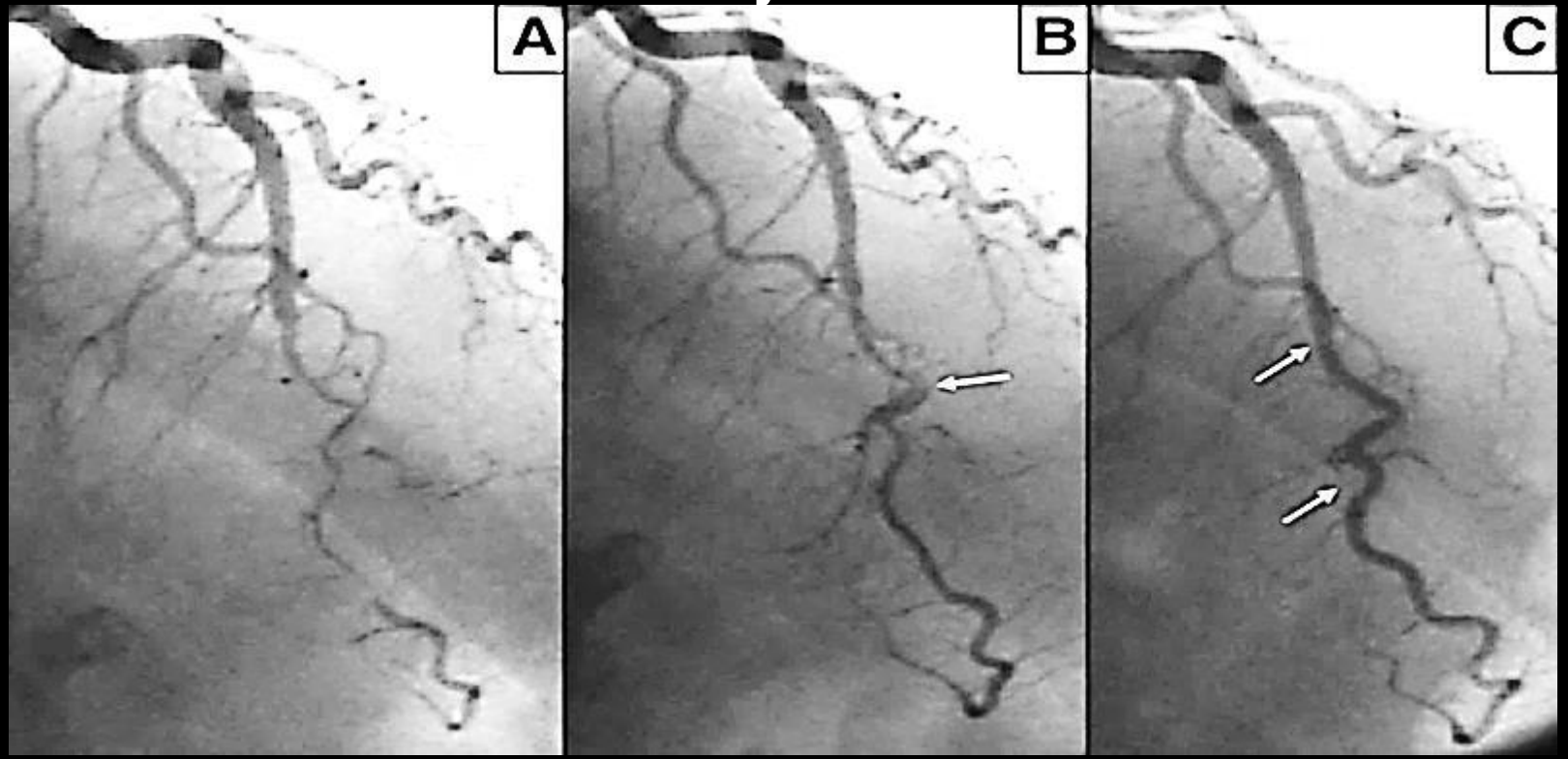
Acute Outcomes & Recurrence

- **Survival** excellent- 93-95% @ 10 yrs
- **Recurrent SCAD:**
  - Incidence: 2-3%/year
  - **Typically occurs in different vessel**
  - >3-4 recurrences reported (rare)
- **PCI/CAB: no protection from recurrent SCAD**
- **Dissection healing** without intervention, **60%-100%**

Tweet , Circulation 2012; Tweet Circ CV Interv 2014; Lettieri, AJC 2015; Saw, Circ CV Interv 2014; Eleid, Circ CV Interv. 2014; Alfonso F, JACC CV Interv. 2012

Conservatively Managed SCAD

Baseline 4 Days 4 Mos



Eleid M F et al. Circ Cardiovasc Interv. 2014;7:656-662

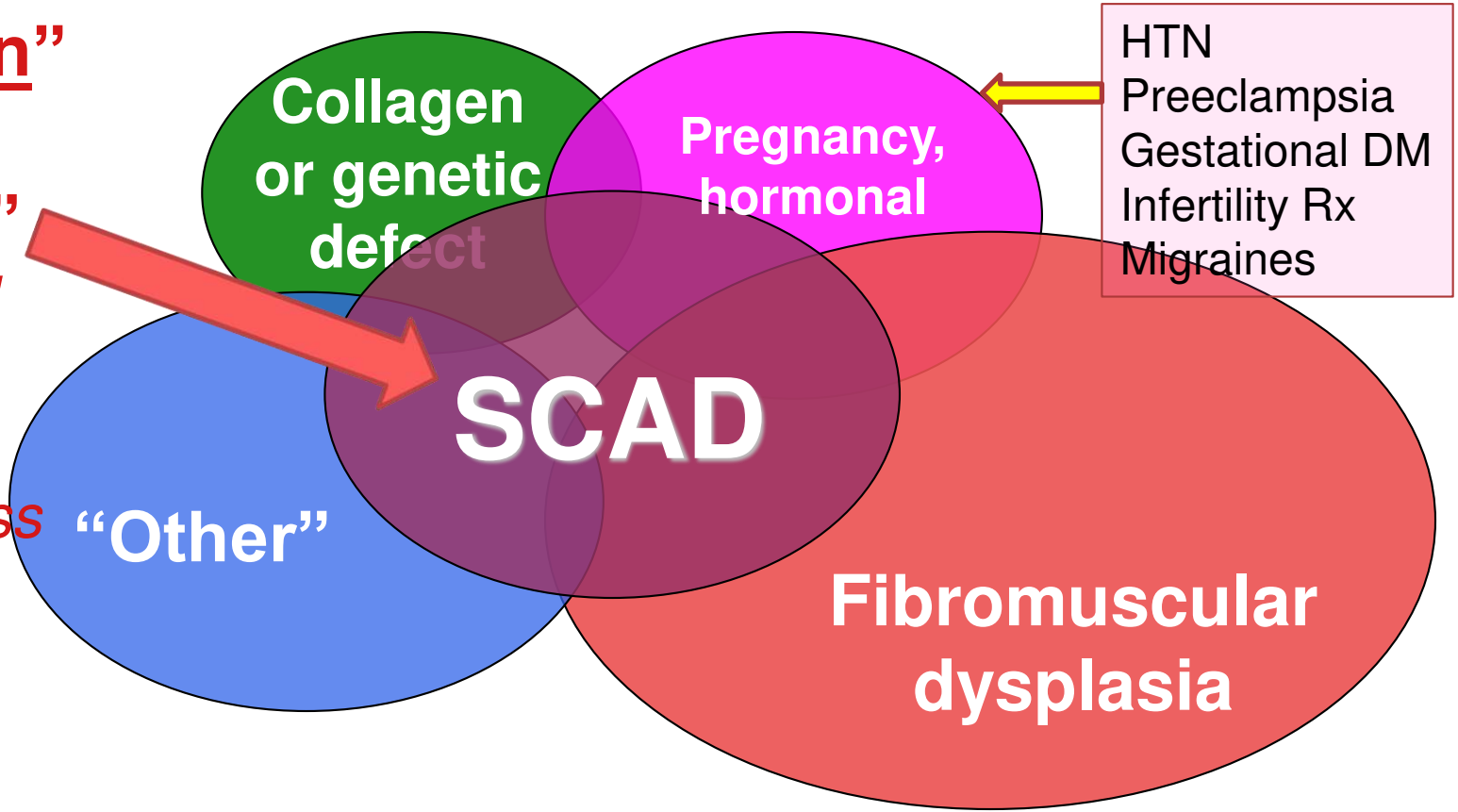
SCAD-Associated Conditions

"Condition"

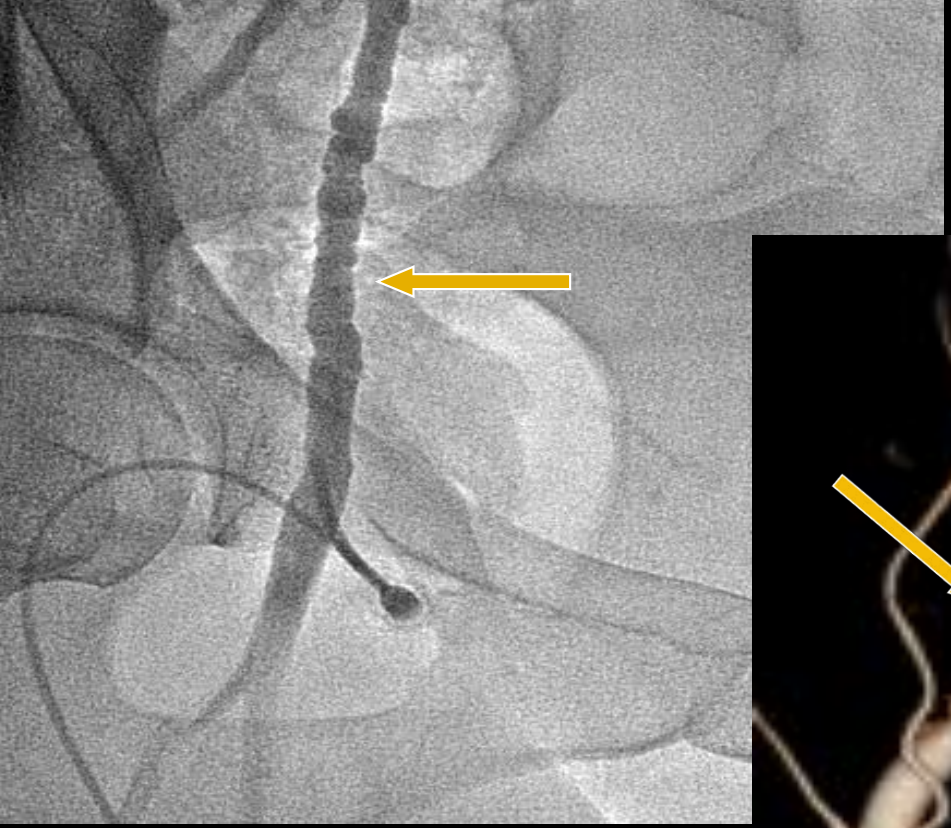
+

"Trigger"

Hormonal
Exertion
Emotion
Shear Stress
Other



HTN
Preeclampsia
Gestational DM
Infertility Rx
Migraines



Tweet, Circulation 2012
Tweet, Circ CV Interv 2014

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Early Therapy After SCAD?

Prevention Alert!

- ASA
  - vs DAPT? — Standard for ACS; MVO on MRI
  - vs NAPT? — Intramural hematoma frequent; Luminal thrombus rare
- **Beta-blocke**r (“*associated with”* lower recurrence-often poorly tolerated)
- **No statin** if normal lipids (no effect on recurrence)
- Other Rx per non-SCAD indication

Hayes et al, Circulation, 2018

Chest Pain After SCAD

- Common (30-70%) “Scary!” High rates of ED, inpatient CP evals
- CP ≠ ischemia. Chest wall pain, non-cardiac, restenosis, stent “issues”, new/recurrent SCAD…
- Menstrual cycle variations/angina is common
- “Second-look angiograms” in stable patients (no!)

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Hayes et al, Circulation, 2018; Tweet, JACC, 2017; 70:2308-9

Other SCAD Outcomes

- FMD, associated conditions, complications
- Uterine bleeding (DAPT, D/C OCPs)
- Migraine therapy issues
- Psychosocial burden
- “Losses” (e.g., health, reproductive options)
- Avoid pregnancy…↑recurrent SCAD risk even if 1st SCAD not P-SCAD
  - **Effective**, **nonhormonal** contraception (IUD OK, esp. if menorrhagia)

Long Term SCAD Management

- Physical activity guidelines- REHAB!-1-2 wks post SCAD is feasible, safe, and improves aerobic capacity, body composition, stress and depression
  - Avoid competitive, endurance, high intensity activity, extreme temps
  - Strength training (yes!): Lower resistance/higher reps
  - Limit lifting to what can be done w/o straining/Valsalva
- Vascular screening
- Medical Genetics referral
- Support for patient, family

Prevention Alert!

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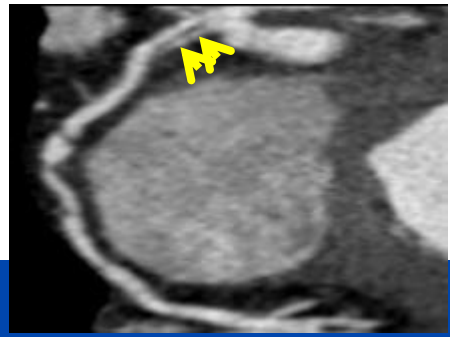
Silber: J Cardiopulm Rehabil Prev, 2015; Tweet, Circ 2012; Hayes, Circ. 2018

SCAD Conclusions

- Will see more SCAD (awareness, intravascular imaging)
- Index of suspicion essential (young, female, no CVD risks)
- **Correct diagnosis even more important because management different than ACS guidelines!!!**
- Strong association with systemic arteriopathies, esp. FMD
- Referrals welcome: Mayo Clinic Virtual and DNA SCAD Registries



Hayes et al, Circulation, 2018

www.mayo.edu/research/SCAD

WOMENHEART

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SCAD
SPONTANEOUS CORONARY ARTERY DISSECTION

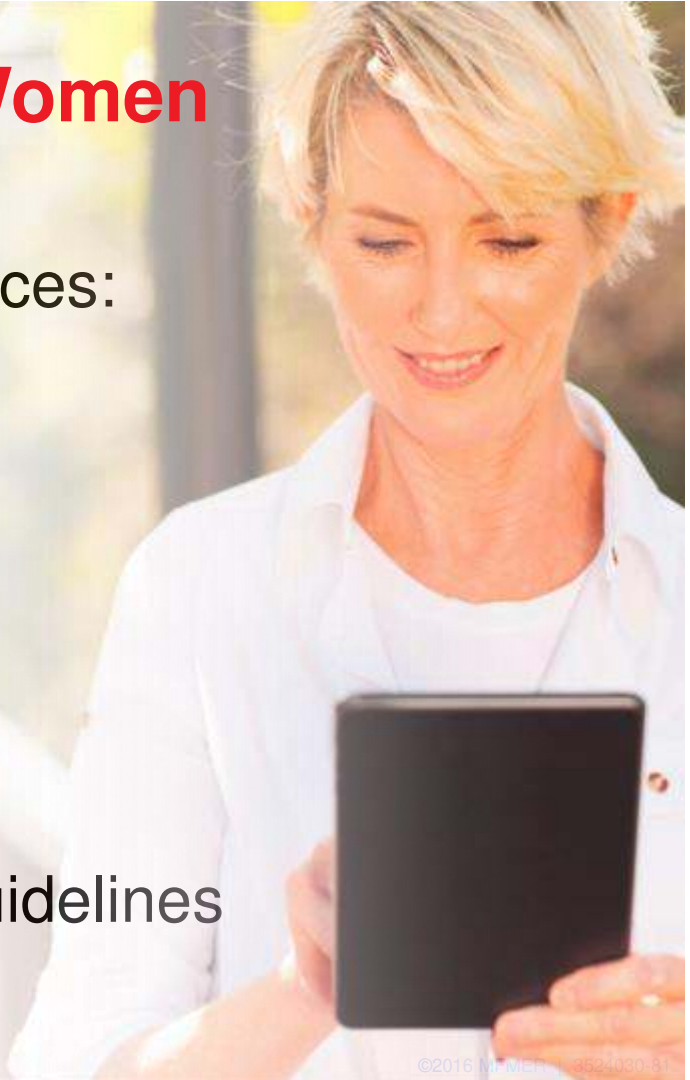
SCAD Research, Inc.

facebook

- SCAD at Mayo Clinic (Spontaneous Coronary Artery Dissection)
- "SCAD Survivors"

Reducing the Burden of CVD in Women

- Address, explore sex- & gender- differences: physiology, outcomes, disparities
- Support psychosocial needs
- Address knowledge, research gaps ($$)
- Mitigate provider bias (unconscious)
- Align policies, procedures
- Disseminate, employ best practices & guidelines



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