Coronary Heart Disease in Women and underrepresented populations

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Disclosures

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CCMC Ethics credit is approved for this course. The CCMC Code of Professional Conduct will be referenced in this presentation. View the CCMC Code of Professional Conduct here.

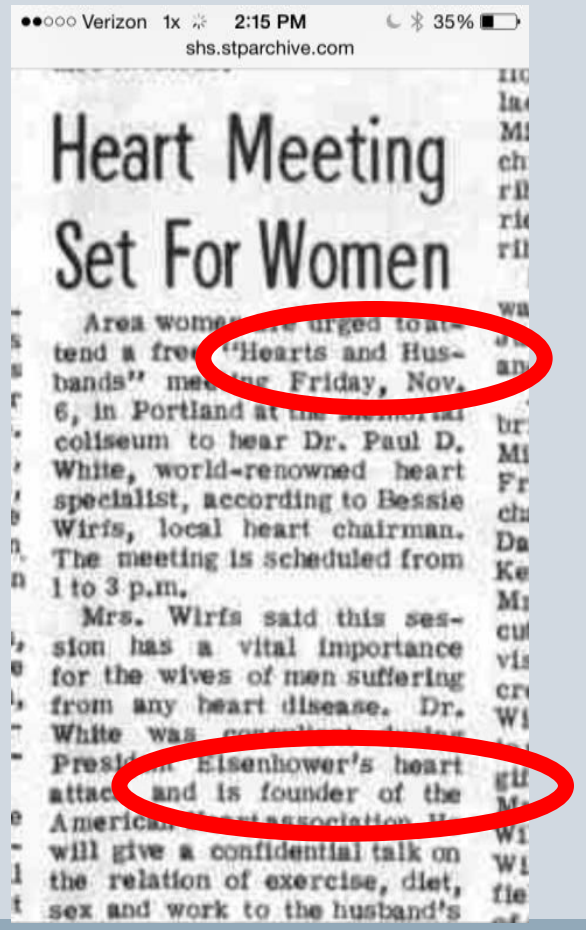
1964 – AHA held the first conference on women and heart disease

Featuring Paul Dudley White

" Hearts and Husbands"

It was basically about How to Care for Your Man

- **"This session has vital importance for the *wives of men suffering from any heart disease*"**



2016 –AHA releases the first scientific statement on myocardial infarction in women

AHA Scientific Statement

Acute Myocardial Infarction in Women

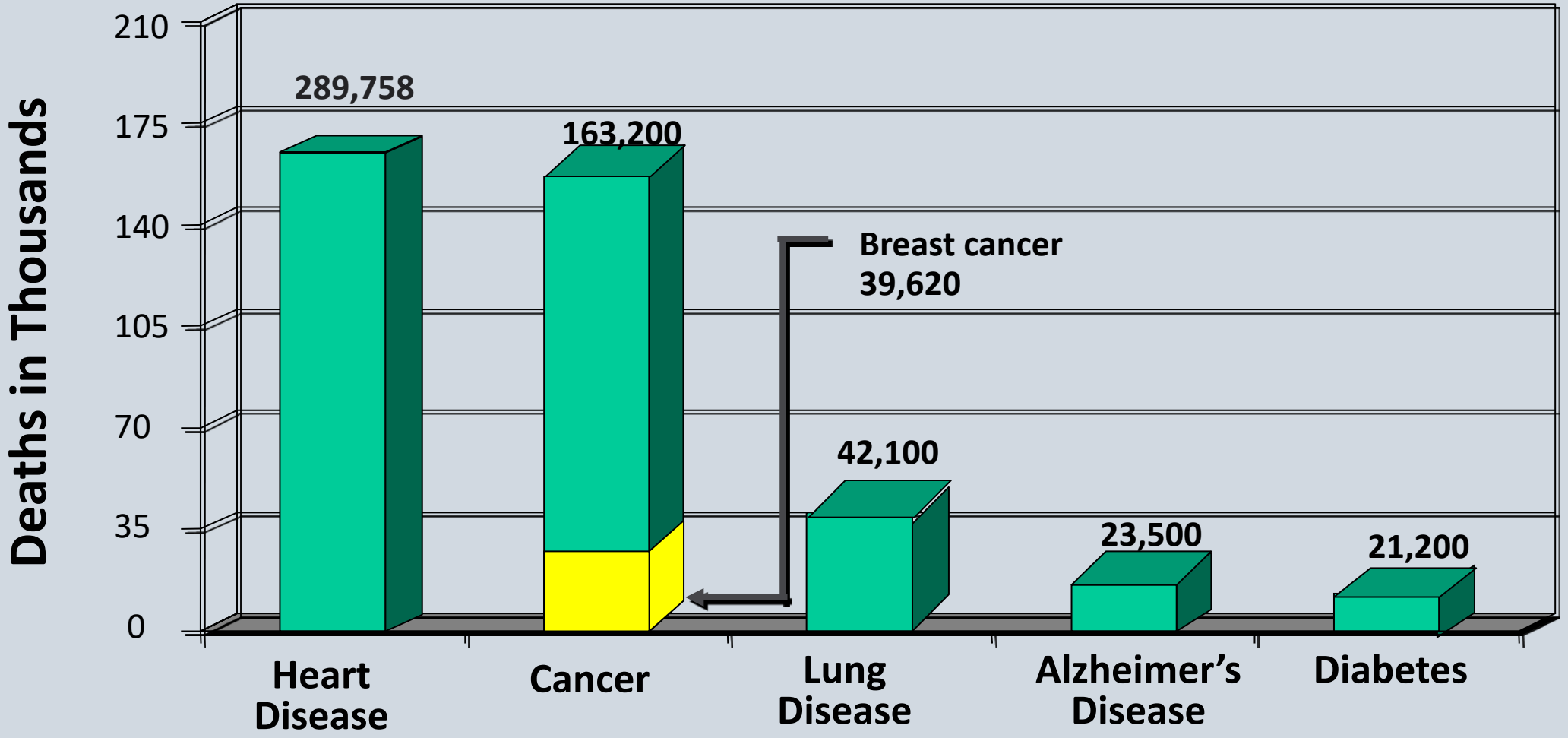
A Scientific Statement From the American Heart Association

Laxmi S. Mehta, MD, FAHA, Chair; Theresa M. Beckie, PhD, FAHA, Co-Chair; Holli A. DeVon, PhD, RN, FAHA; Cindy L. Grines, MD; Harlan M. Krumholz, MD, SM, FAHA; Michelle N. Johnson, MD, MPH; Kathryn J. Lindley, MD; Viola Vaccarino, MD, PhD, FAHA; Tracy Y. Wang, MD, MHS, MSc, FAHA; Karol E. Watson, MD, PhD; Nanette K. Wenger, MD, FAHA; on behalf of the American Heart Association Cardiovascular Disease in Women and Special Populations Committee of the Council on Clinical Cardiology, Council on Epidemiology and Prevention, Council on Cardiovascular and Stroke Nursing, and Council on Quality of Care and Outcomes Research

Abstract*—**Cardiovascular disease is the leading cause of mortality in American women. Since 1984, the annual cardiovascular disease mortality rate has remained greater for women than men; however, over the last decade, there have been marked reductions in cardiovascular disease mortality in women. The dramatic decline in mortality rates for women is attributed partly to an increase in awareness, a greater focus on women and cardiovascular disease risk, and the increased application of evidence-based treatments for established coronary heart disease. This is the first scientific statement from the American Heart Association on acute myocardial infarction in women. Sex-specific differences exist in the presentation, pathophysiological mechanisms, and outcomes in patients with acute myocardial infarction. This statement provides a comprehensive review of the current evidence of the clinical presentation, pathophysiology, treatment, and outcomes of women with acute myocardial infarction. (Circulation*. 2016;133:916-947. DOI: 10.1161/CIR.0000000000000351.)**

Key Words: AHA Scientific Statements ■ cardiovascular diseases ■ coronary disease ■ myocardial infarction ■ women

Heart Disease is the #1 Cause of Death in Women

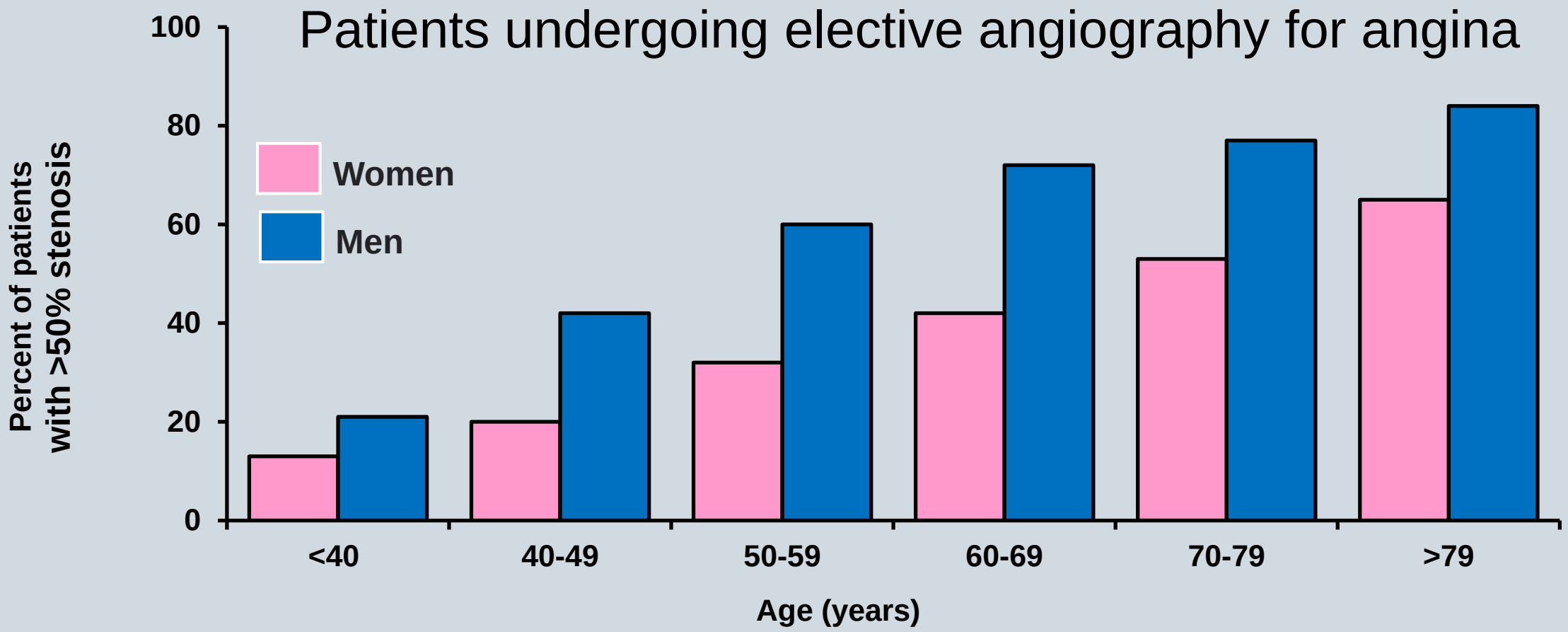


Center for Disease control and Prevention 2013 data

Heart Disease in Women

- **Ischemic heart disease in women**
  - biology, risk factors, response to therapy
- **Ischemic syndromes of particular importance to women**
  - MINOCA, Microvascular Dysfunction, SCAD
- **Heart failure syndromes of particular importance to women**
  - Takotsubo cardiomyopathy

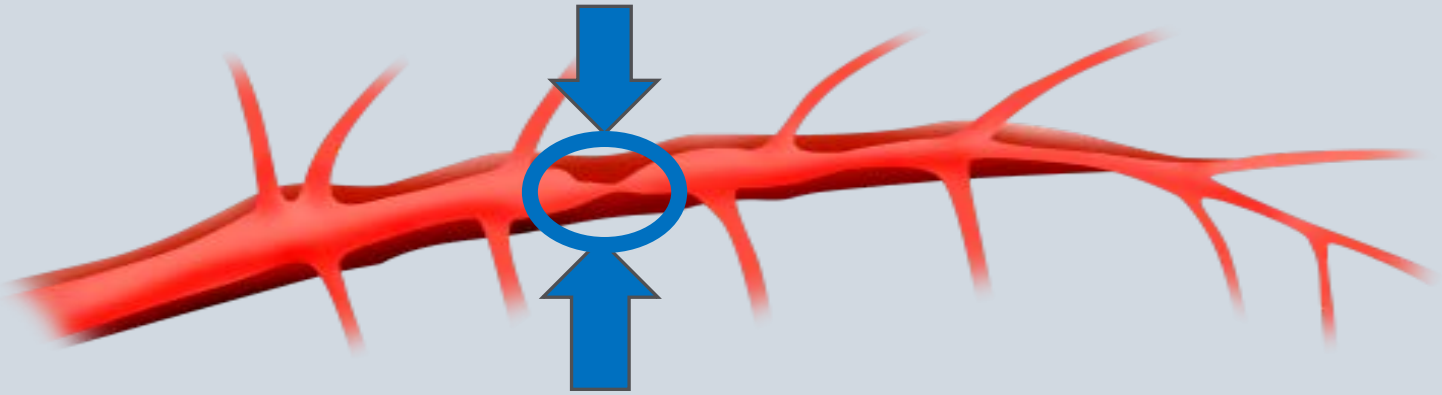
Women have less obstructive CAD



ACC-National Cardiovascular Data Registry™. *J Am Coll Cardiol.* 2006

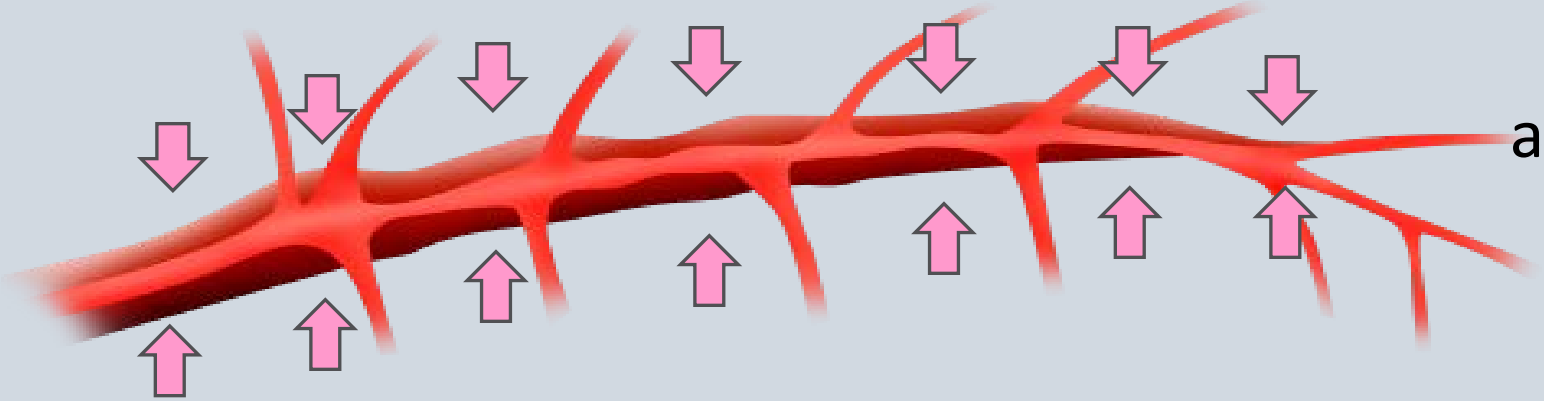
CAD develops differently in women

MEN



Focal Stenosis

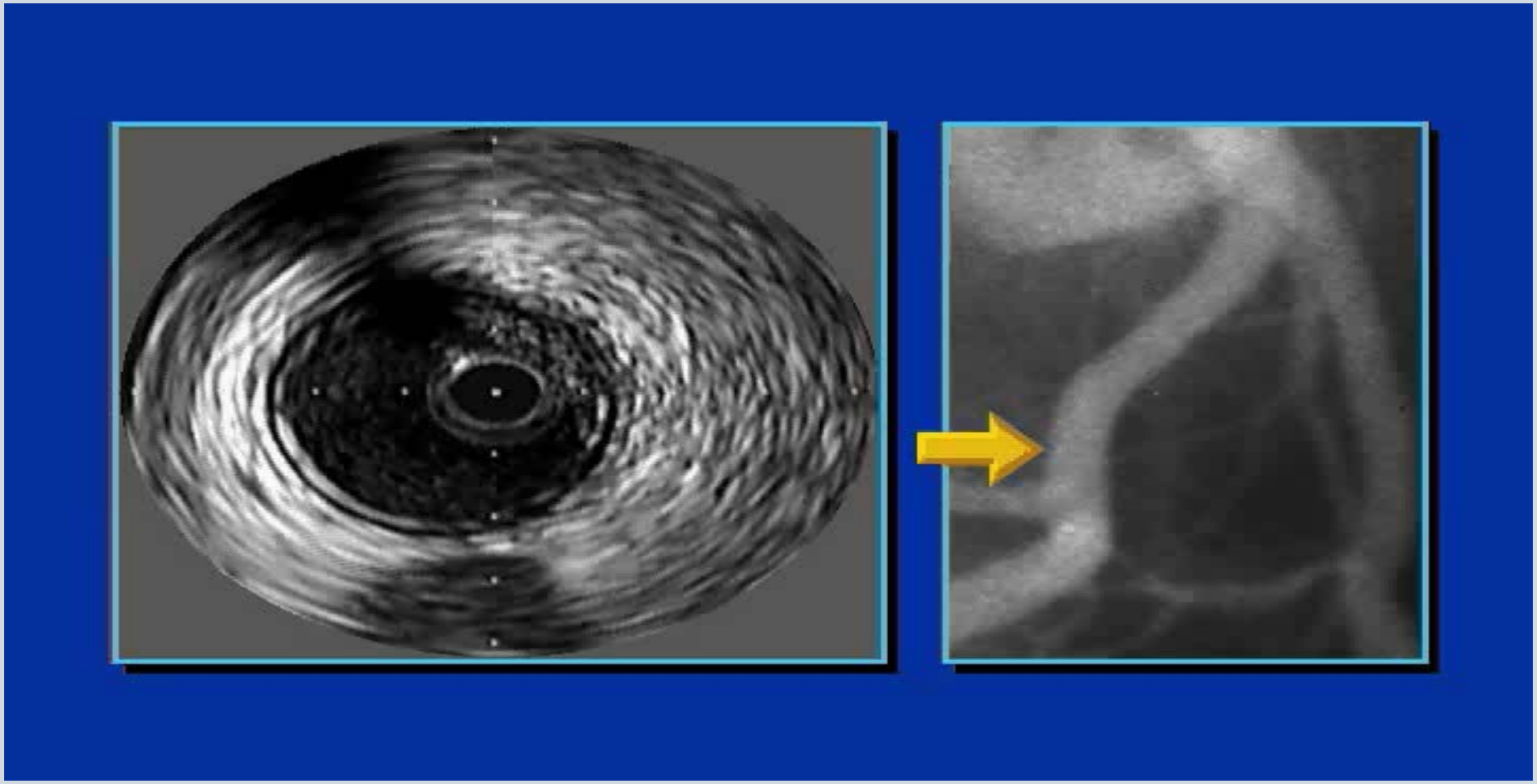
WOMEN



Diffuse atherosclerosis

Moghavi et. al. Circulation. 2003; 108: 1664-1672

A large amount of atherosclerosis can hide



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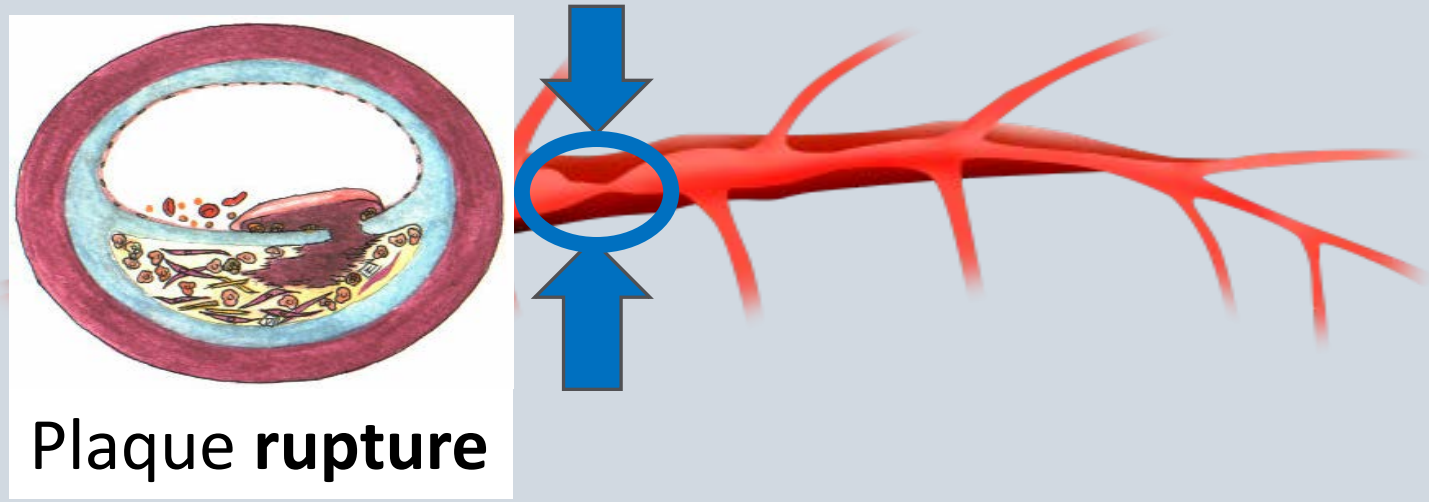
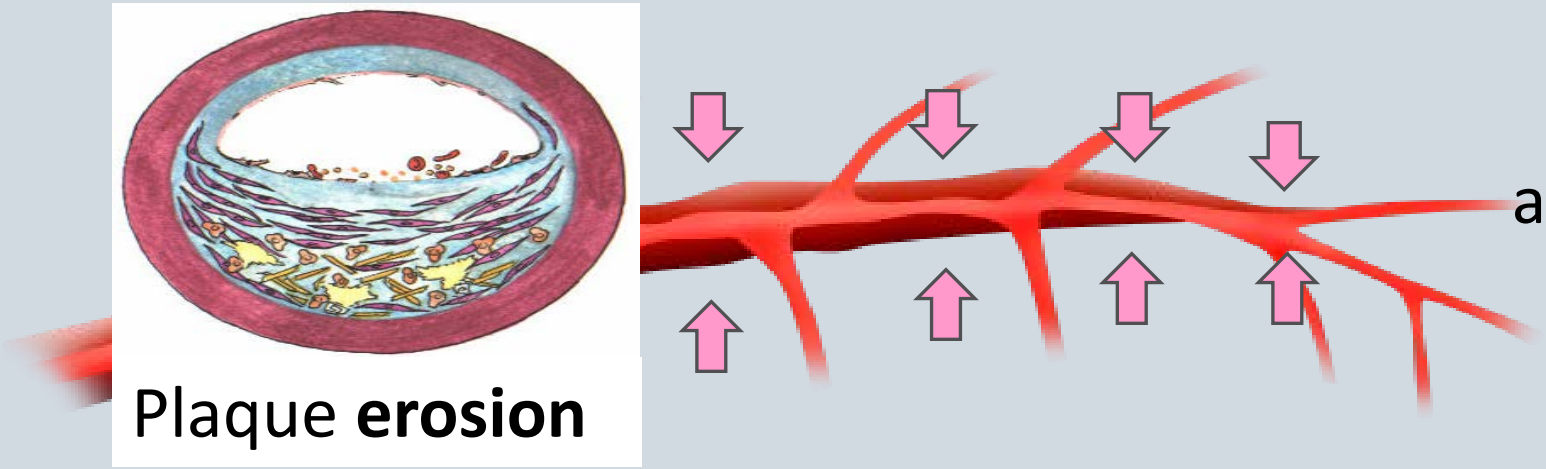


Plaque **rupture**

Focal Stenosis

WOMEN



Plaque **erosion**

Diffuse atherosclerosis

Moghavi et. al. Circulation. 2003; 108: 1664-1672

Men have “classic” symptoms

Women have “atypical” symptoms

Chest pain or discomfort

Unusual upper body discomfort

Light-headedness or sudden dizziness

Shortness of breath

Nausea

Diaphoresis

Unusual or unexplained fatigue

Risk Factors for Heart Disease

- Smoking
- Diabetes
- Hypercholesterolemia
- Hypertension
- Obesity/Overweight
- Physical inactivity
- Family history
- Age

Risk Factors of particular importance to women

- Auto-immune disease
- Breast cancer treatments
- SAD Risk factors (Stress, Anxiety and Depression)
- Pregnancy Complications
  - Pre-term delivery
  - Pregnancy induced hypertension
  - Gestational diabetes

Reproductive Hormone transition times are high risk for women's CV systems

- Puberty
  - Boys grow taller and thinner; girls grow taller and heavier
- Pregnancy
  - A "stress test" for the cardiovascular system
- Menopause
  - The menopause "bump"

Pregnancy – a Stress Test for the heart

Preeclampsia with preterm delivery

- 8 x ↑ risk of future death CVD
- 5 x↑ risk of future stroke

Preeclampsia with full term delivery

- 3 x ↑ risk of future death CVD

Gestational diabetes

- ~30 % ↑ risk of future death CVD
- 20-60% will develop type 2 DM within 5-16 yrs

C. Valdiviezo et al Clin. Cardiol. 35, 3, 160–165 (2012)

Menopause

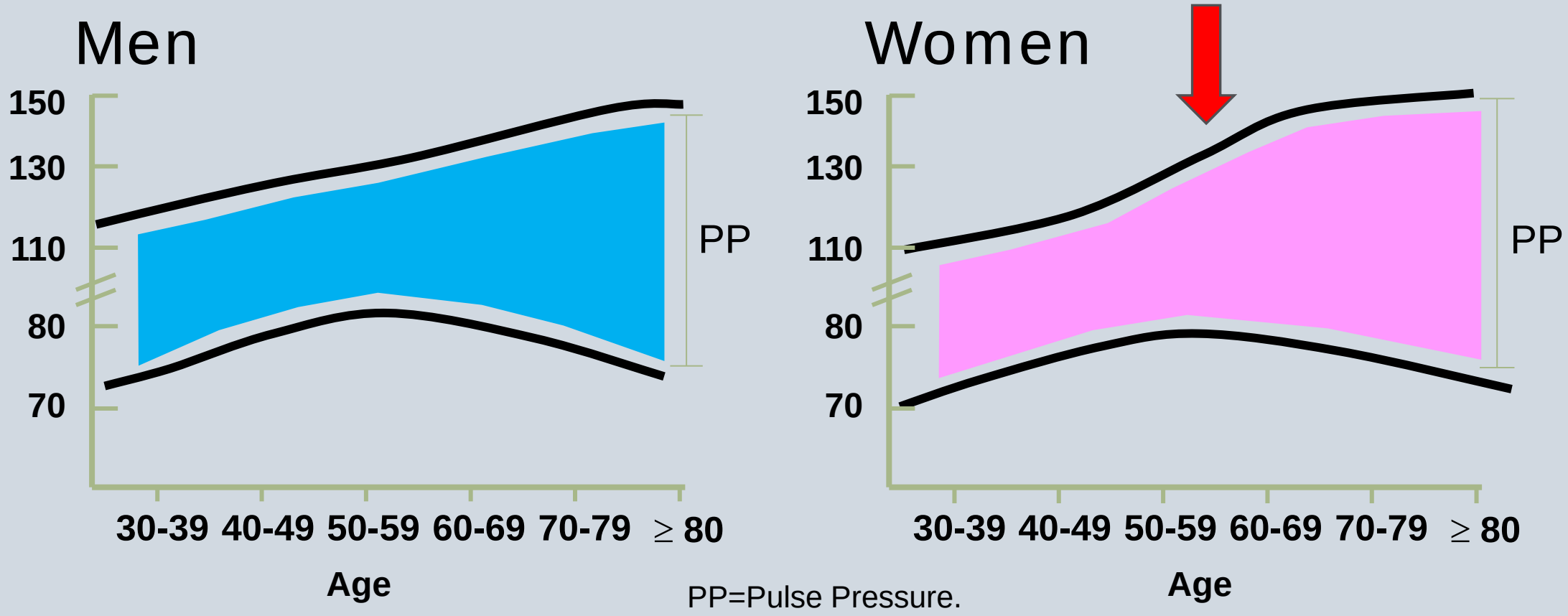
Loss of estrogen puts women at higher risk for developing CVD

Before the onset of menopause, women have ~1/5 the rate of heart disease as men

10 years after menopause, rate of MI equals that of men

The Menopause Bump

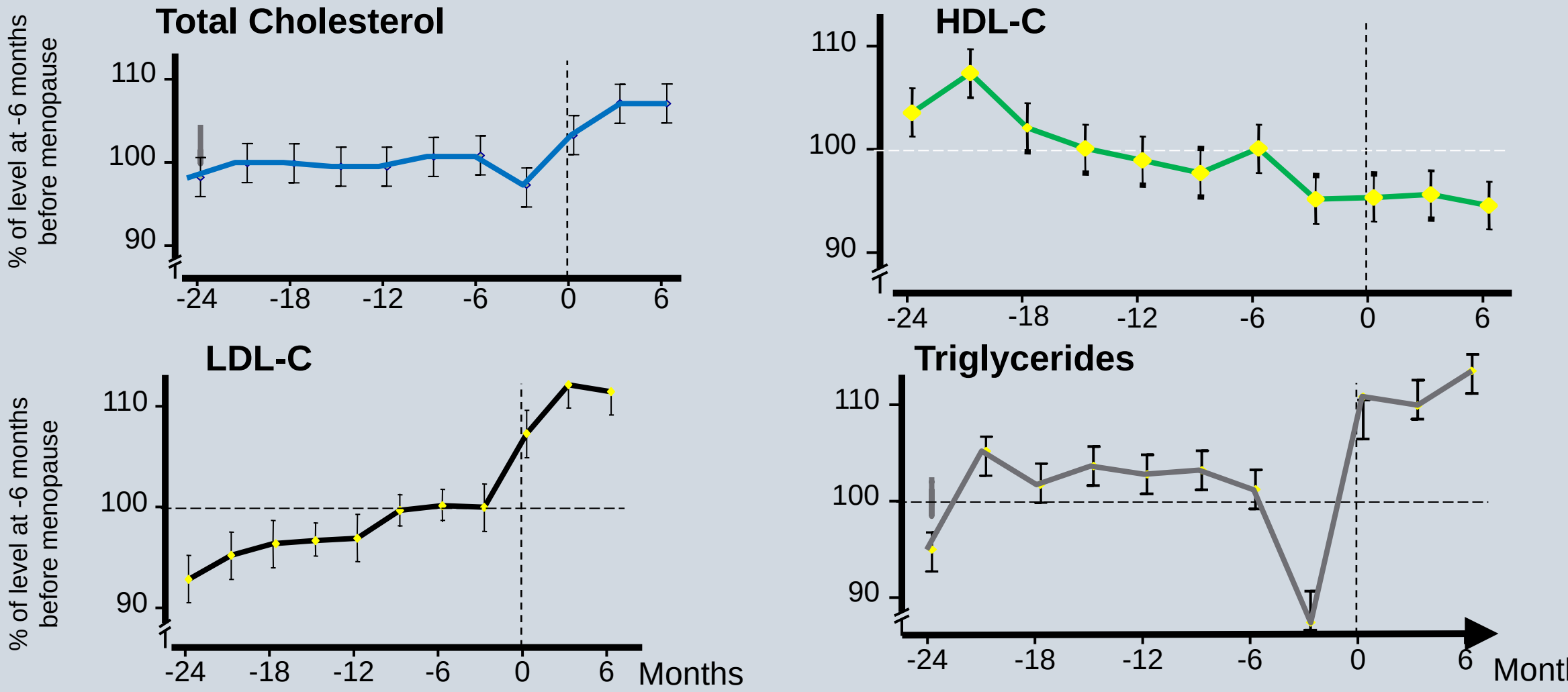
Blood Pressure Levels by Age



PP=Pulse Pressure.

Adapted from : Third National Health and Nutrition. Examination Survey, *Hypertension* 1995;25:305-13

Lipid Changes Peri-Menopause



Jensen J et al. *Maturitas* 1990;12:321-31.

Pre and post menopause changes

Cross-sectional study of 3,636 women

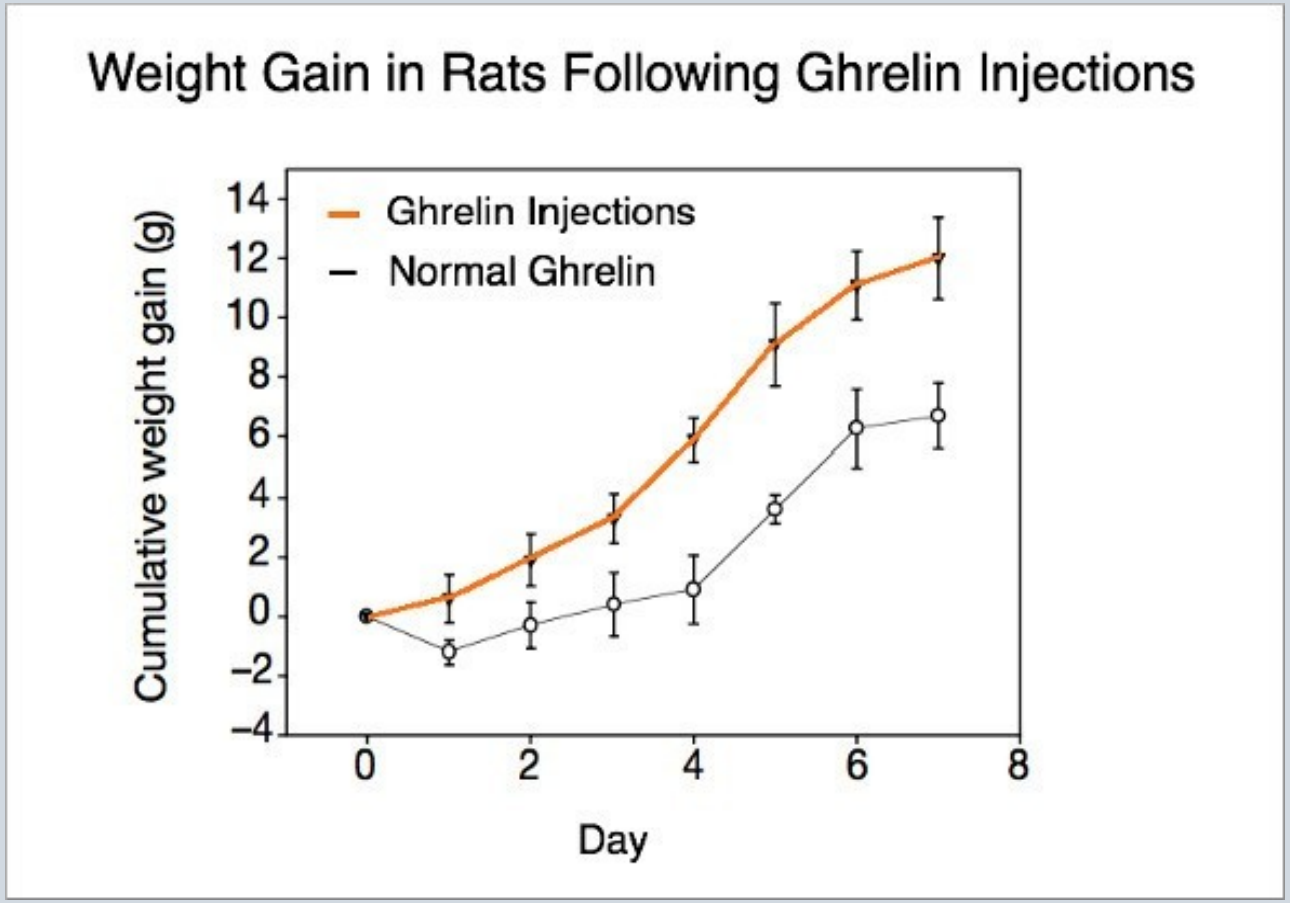
(40–59 years old)

Variable	PRE	POST	p
AGE	49.7	55.2	0.001
Activity (METS)	5502	2458	NS
BMI	26.9	28.1	0.001
% BF	34.1	36.2	0.001
HTN (%)	55.2%	60.4%	0.01
LDL-c	121.6	132.2	0.001
HDL-c	63.7	62.5	NS
TG	100.8	113.0	0.001
Glucose	92.0	95.8	0.001

PLOS ONE 11(4): e0154511. https://doi.org/10.1371/journal.pone.0154511

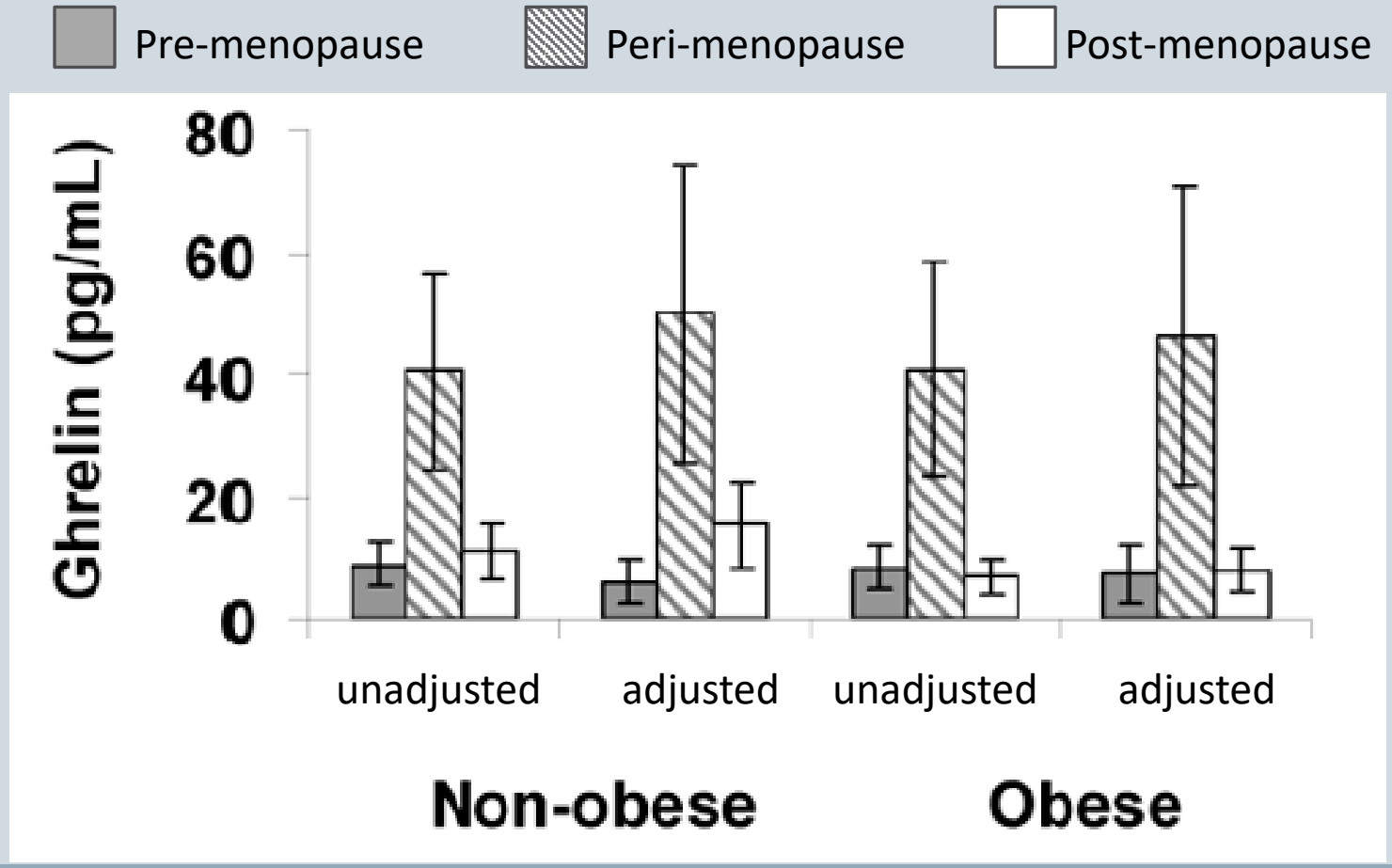
Ghrelin

Ghrelin (discovered in 1999) is a hormone that stimulates appetite



Wren et. al. Diabetes 2001 Nov; 50(11): 2540-2547.

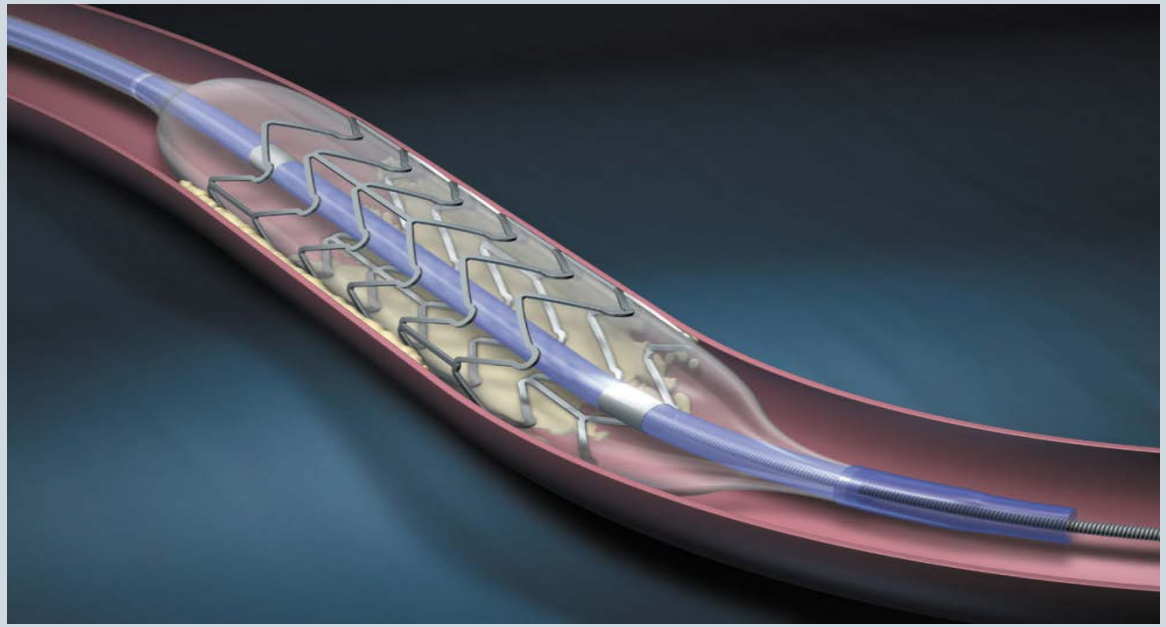
Ghrelin levels increase in peri-menopause



Sowers et. al. *Maturitas*. 2008 February 20; 59(2): 149–157.

Therapeutic Approaches in IHD

Invasive Management

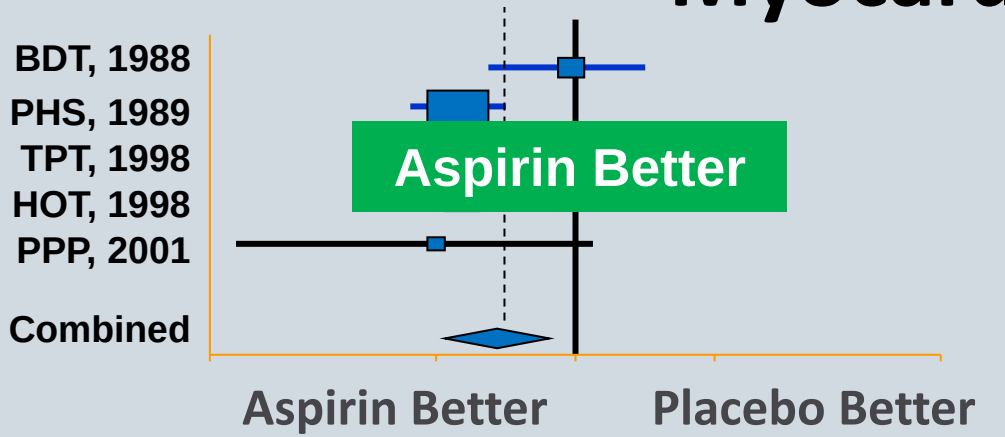


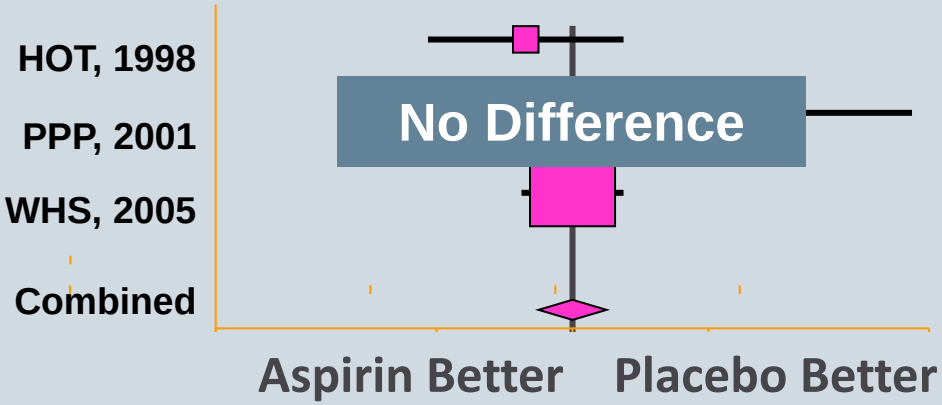
vs.

Medical Management

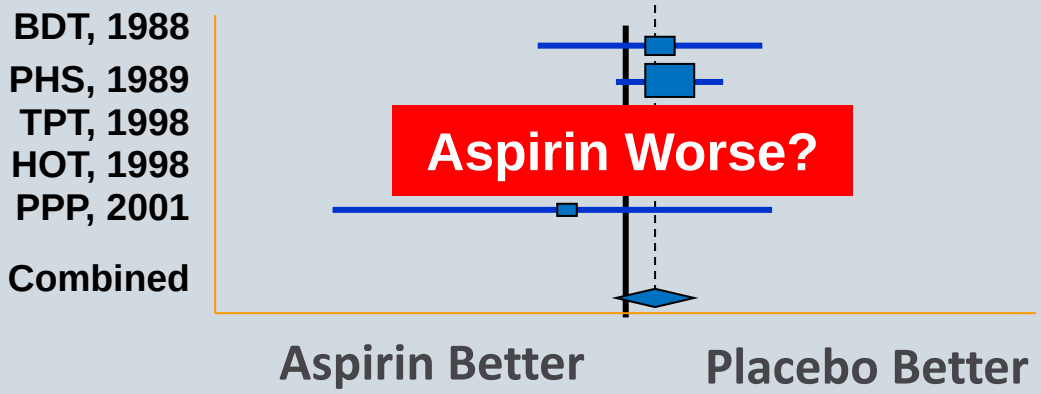
Aspirin Effects by sex

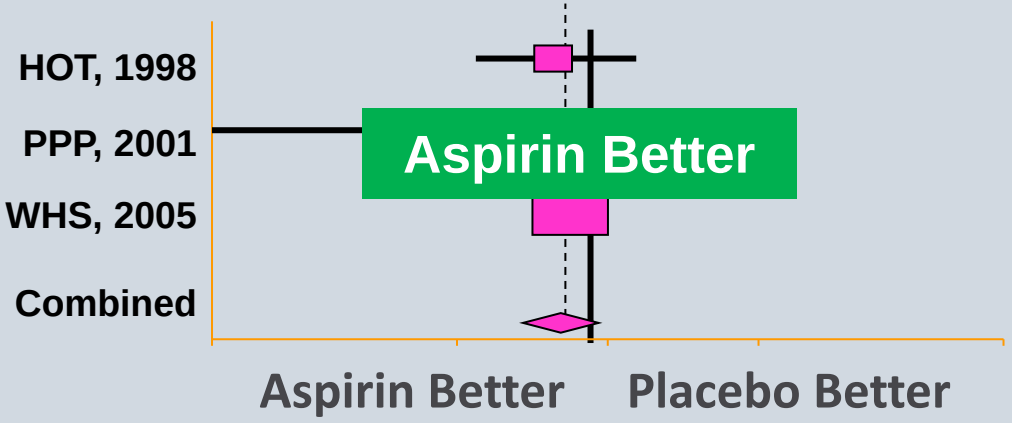
Myocardial Infarction





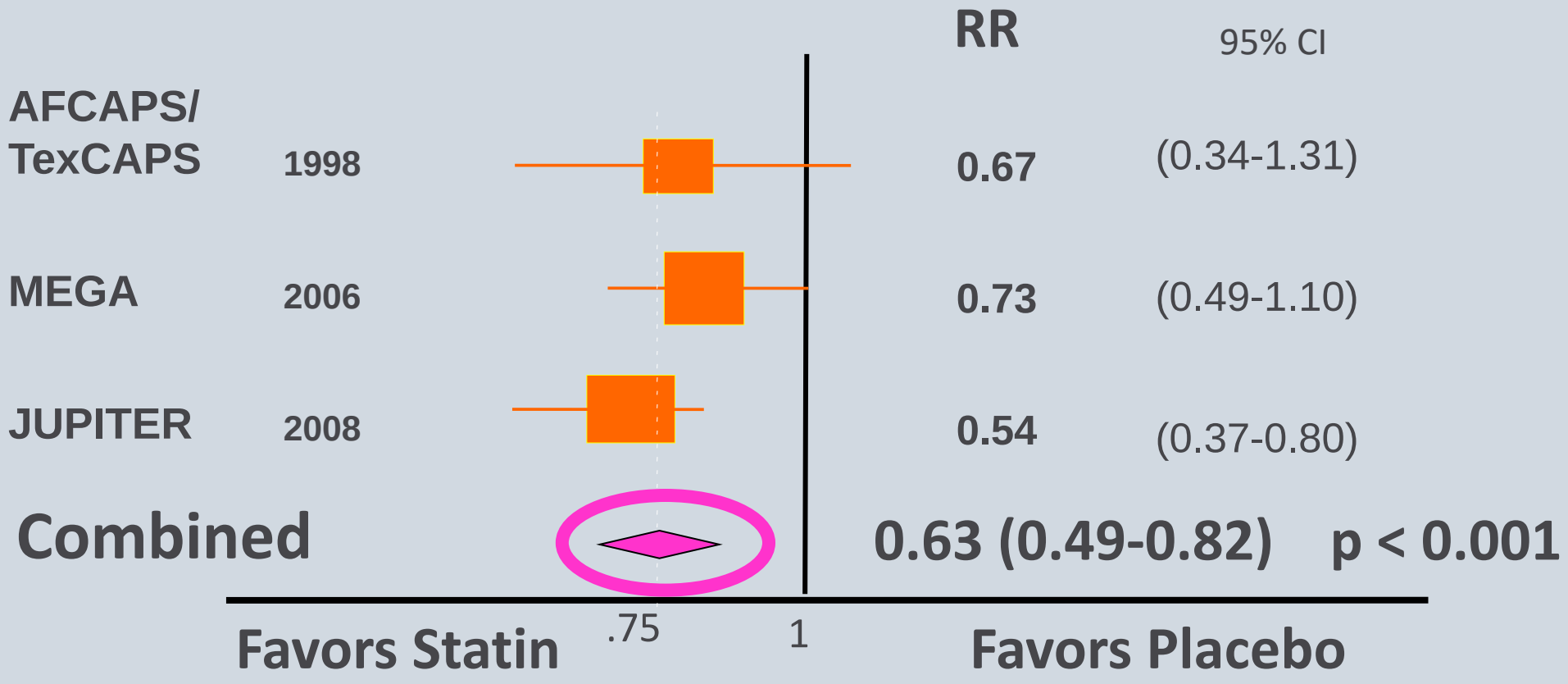
Stroke





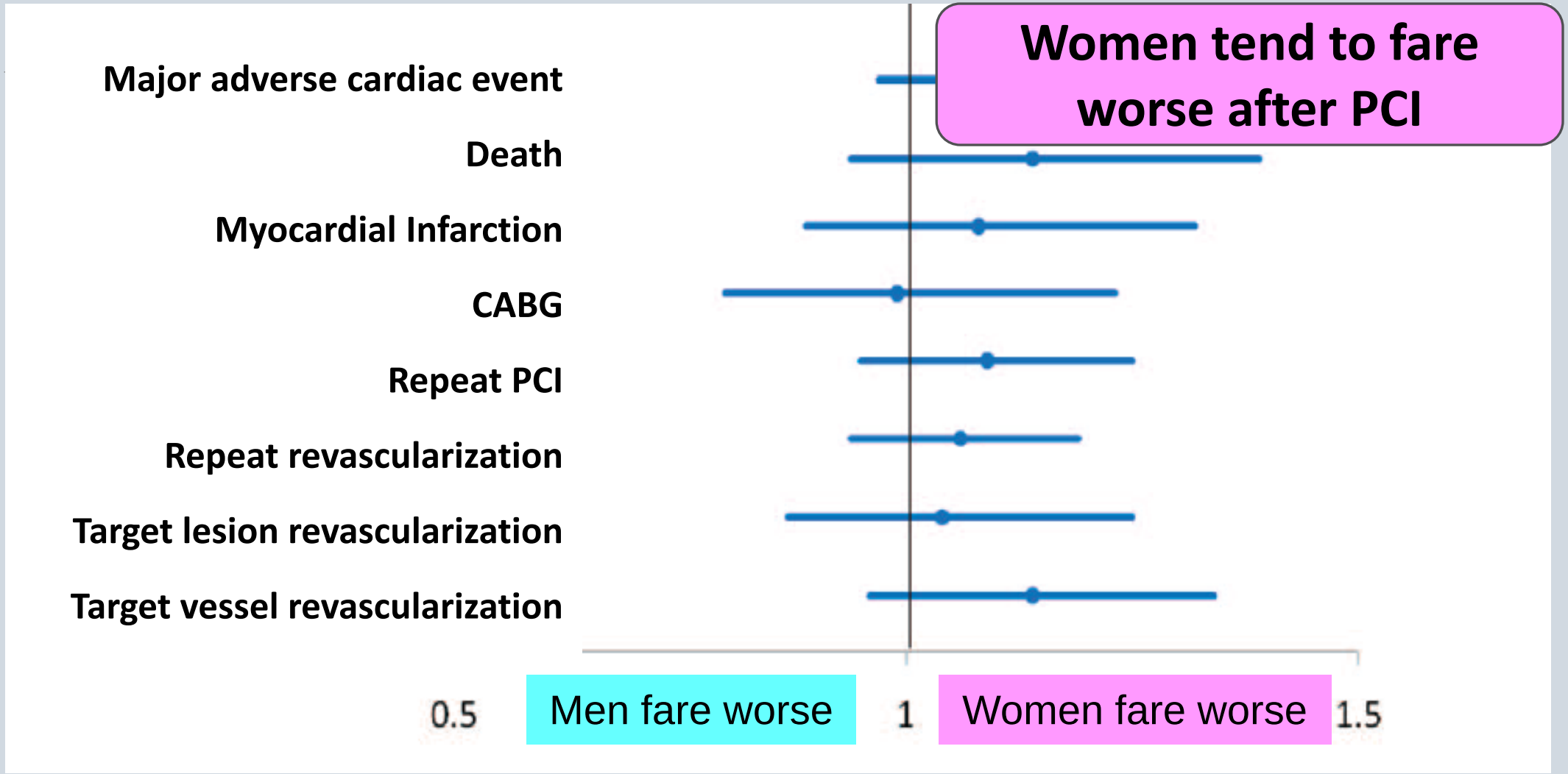
Ridker, P. et al., *N Engl J Med* 2005; 352:1293-204.

Meta-analysis of Primary Prevention Statin Trials in Women

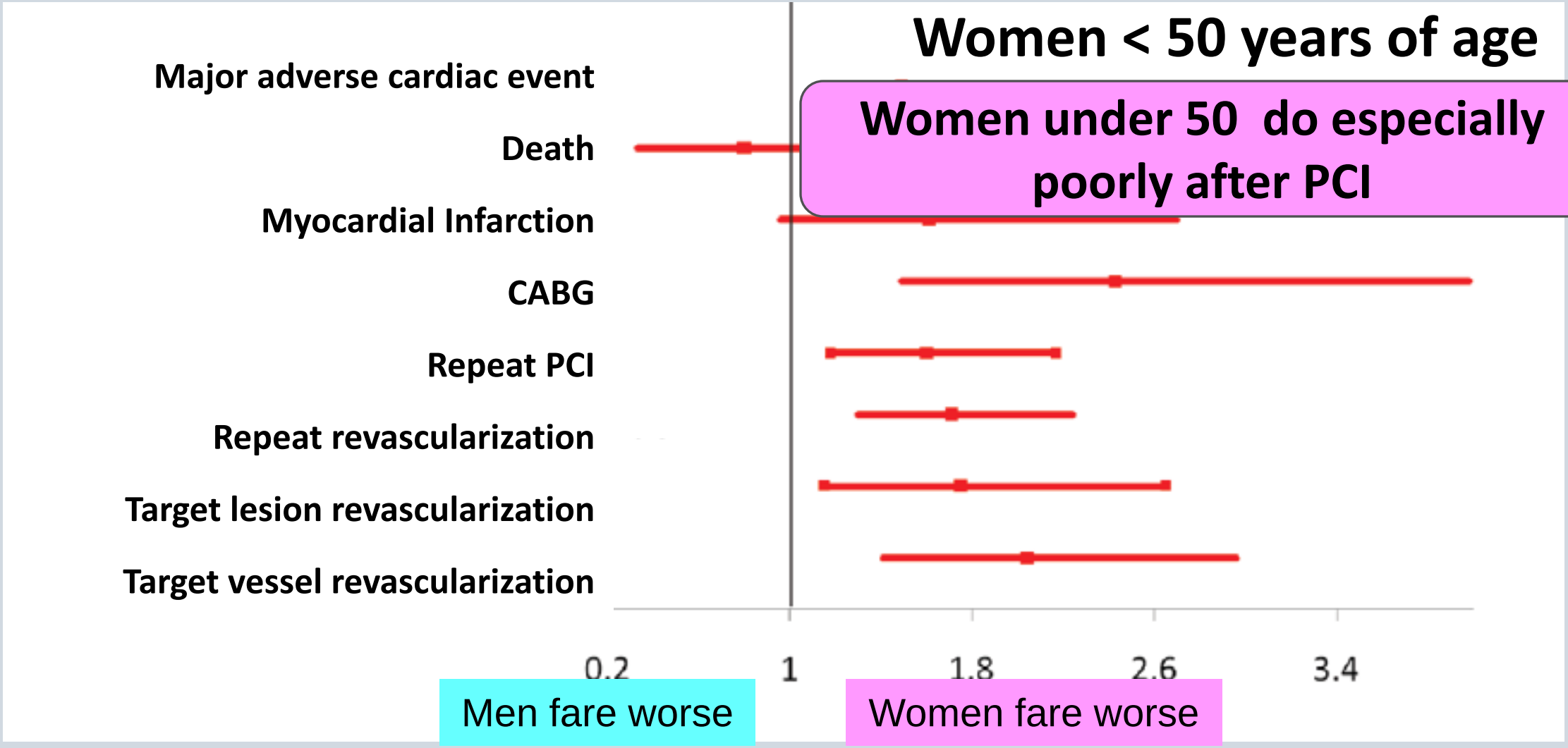


Mora S et al Circulation 2010; 1069

Women have poorer outcomes post PCI



Young women have especially poor outcomes



Heart Disease in Women

- **Ischemic heart disease in women**
  - biology, risk factors, response to therapy
- **Ischemic syndromes of particular importance to women**
  - MINOCA, Microvascular Dysfunction, SCAD
- **Heart failure syndromes of particular importance to women**
  - Takotsubo, peripartum cardiomyopathy HFpEF
- **The link between breast cancer and heart disease**

What is MINOCA?

Table 1. Definition of MINOCA

1. Acute myocardial infarction (AMI) criteria[5]

Clinical evidence of AMI including any of the following:

- Symptoms – chest pain criteria
- ECG – new changes including ST segments, LBBB, pathological Q waves
- Myocardial perfusion imaging – new loss of viable myocardium
- Left ventricular functional imaging – new regional wall motion abnormality

2. Non-obstructive coronary arteries[6]

No stenosis ≥50% on coronary angiography

3. No clinically overt cause for AMI presentation

LBBB = left bundle branch block; MINOCA = MI with non-obstructive coronary arteries.

European Cardiology Review , 2015; 10 (2):79–82

Clinical Presentation

55-year old female presented with sudden onset of central chest pain for 2 hours.

Troponin T (Reference Range <29ng/L)

Initial: 99 ng/L

6 Hours: 301 ng/L

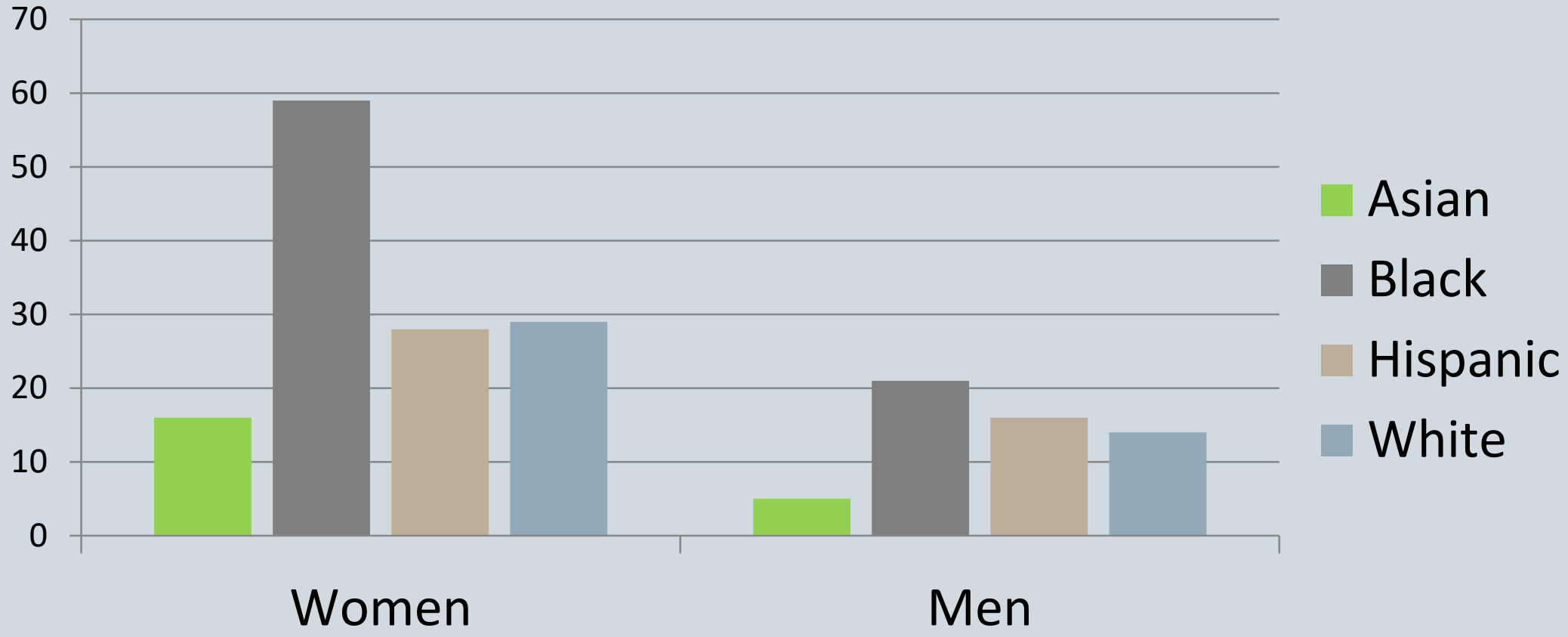
ECG

ST elevation in V3-

1. Acute Myocardial Infarction

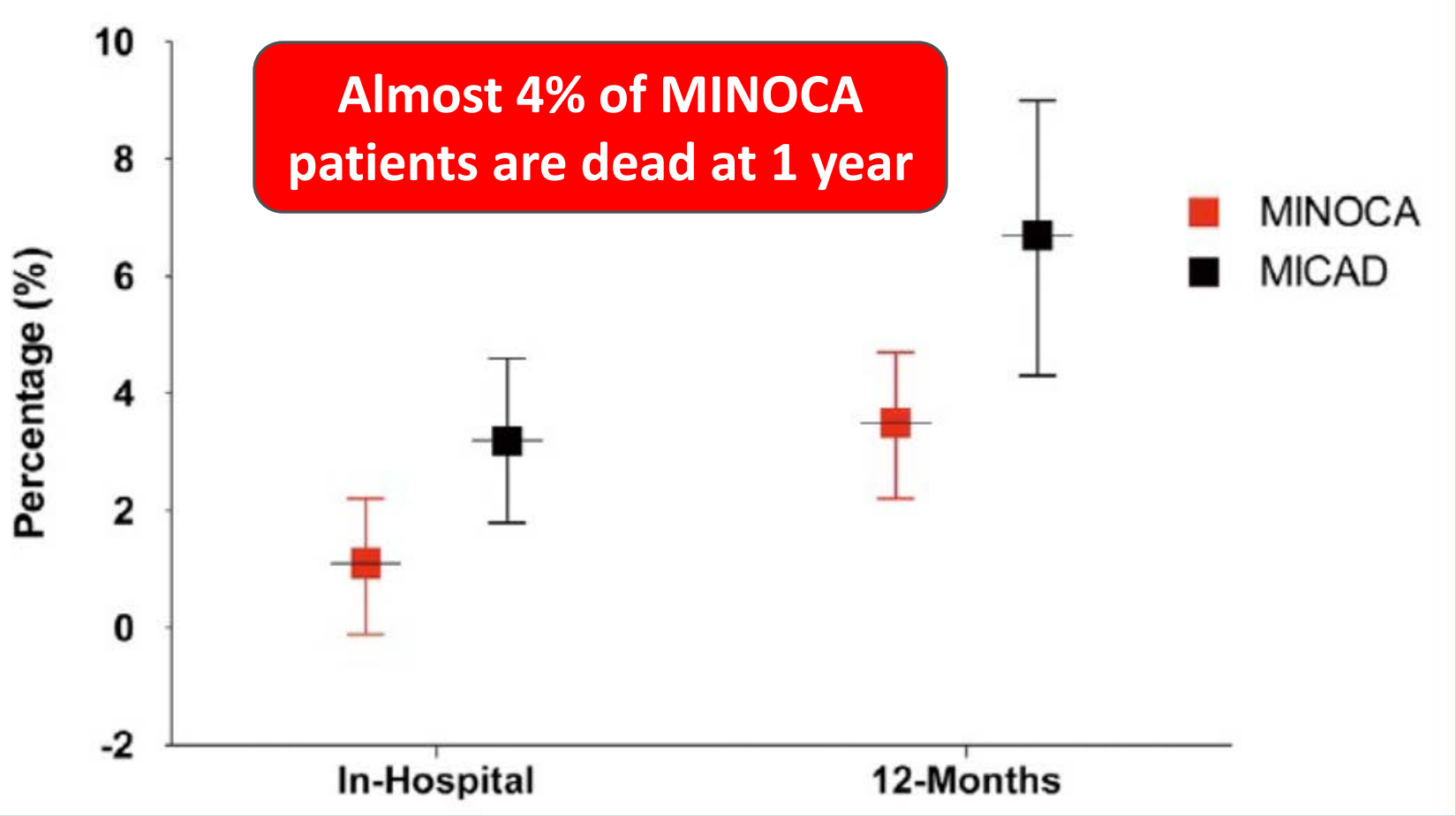
MINOCA

Women are more likely to have MINOCA



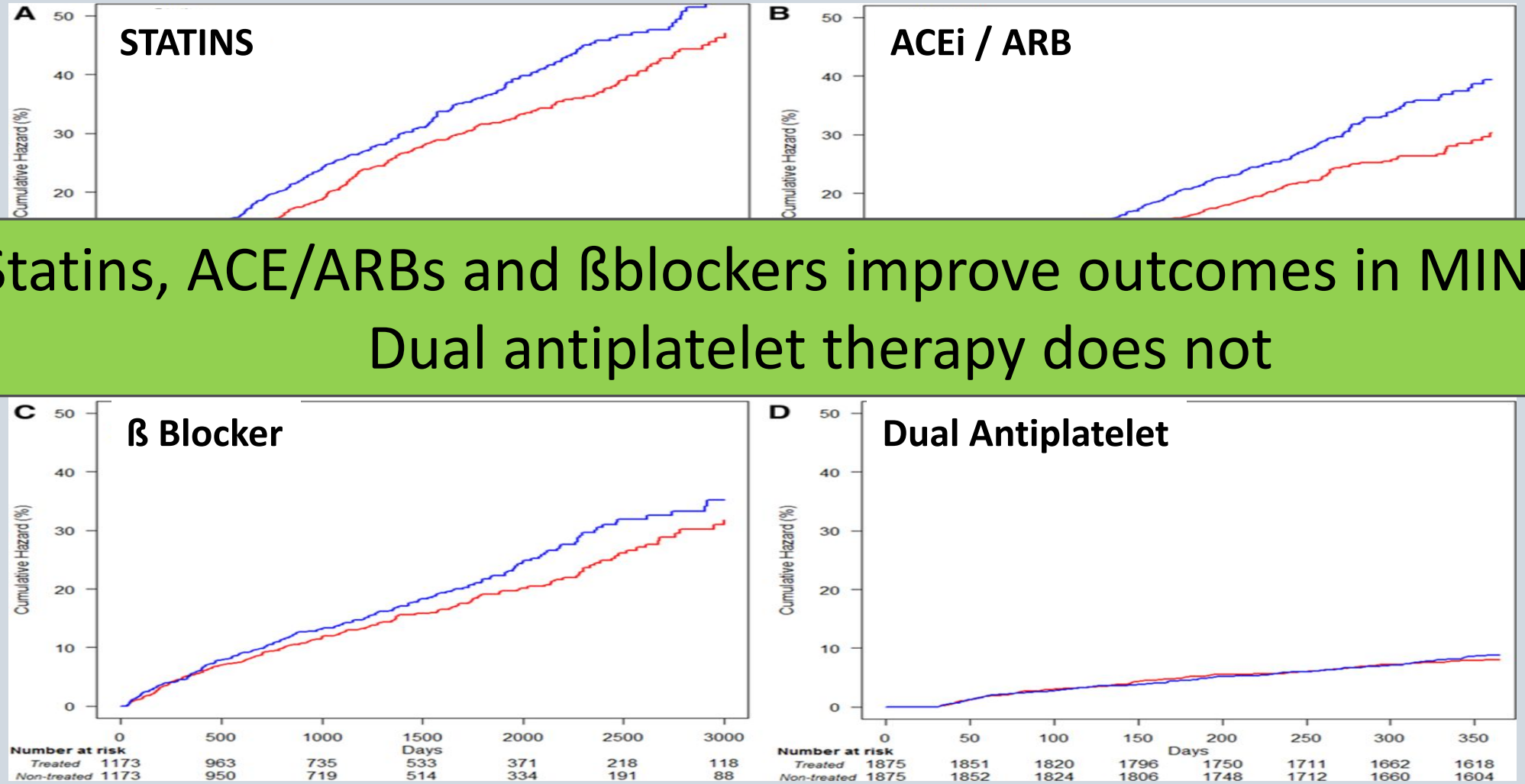
Chokshi et. al. Clin Cardiol 33:8 495-501:861 2015

Mortality is high in patients with MINOCA



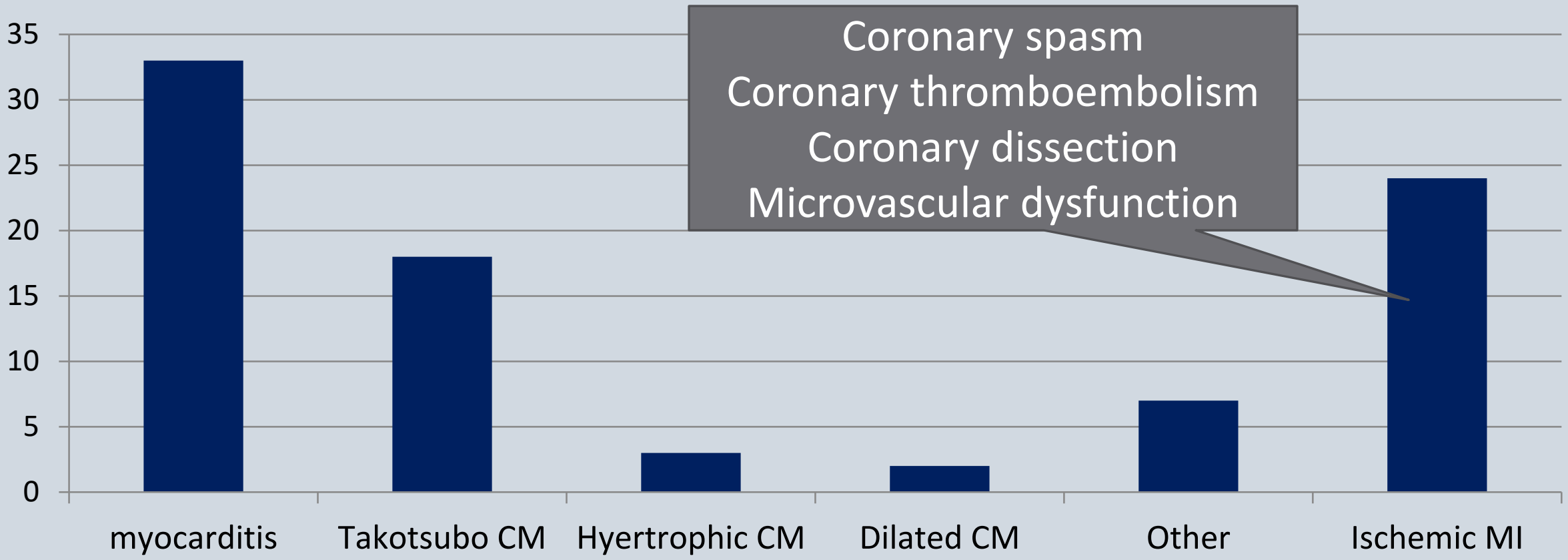
Pasupathy et. al. Circulation 131:861 2015

Treatment of MINOCA



Bertil Lindahl et al. Circulation. 2017;135:1481-1489

MINOCA – Cardiac MR Diagnoses



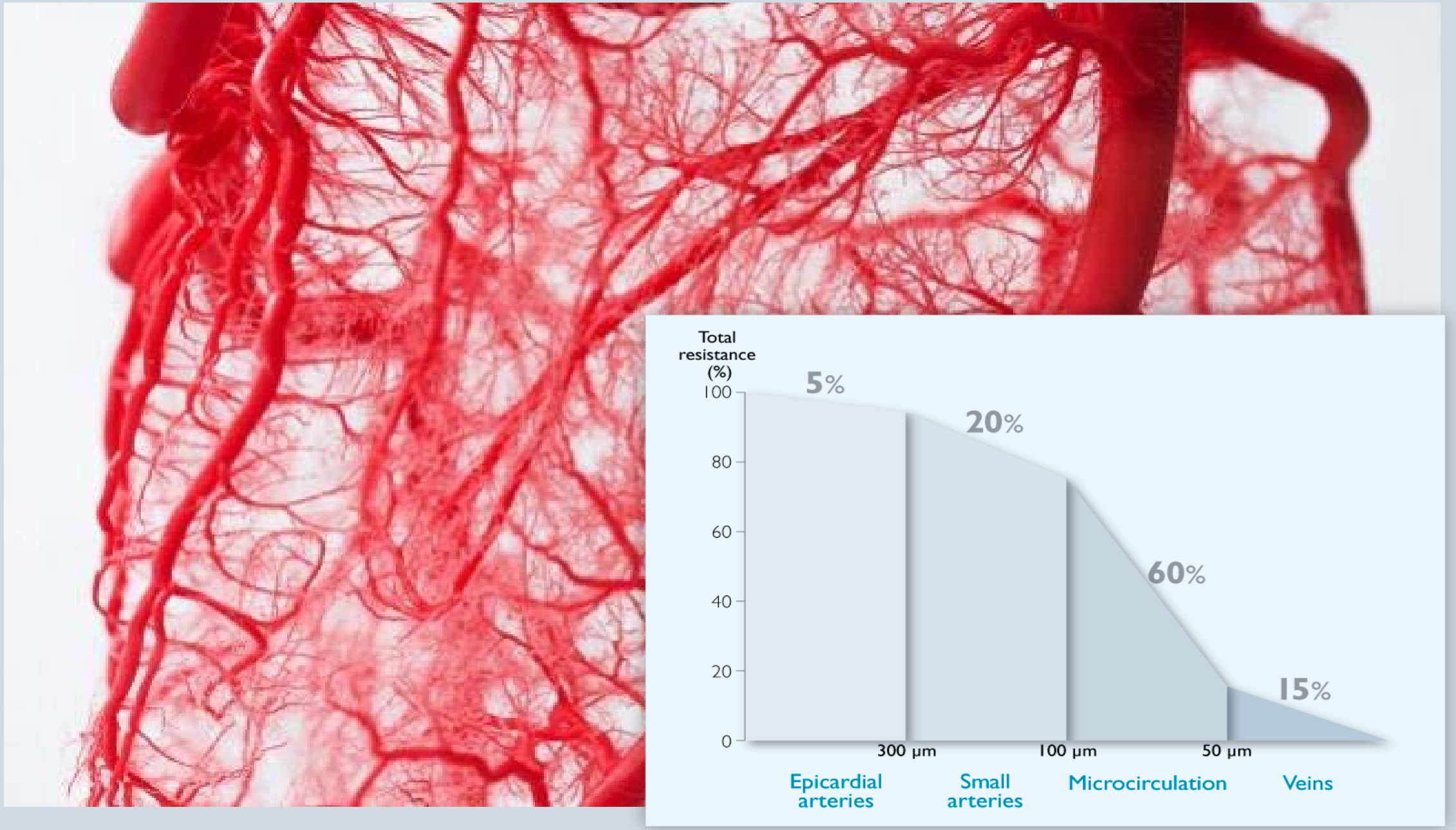
Pasupathy et. al. Circulation 131:861 2015

The microvasculature is important

Epicardial coronary arteries (>500 µm) are where we focus most of our attention

Microvessels (<500 µm) are much more abundant and carry most of myocardial blood flow

Image from Prof. P Camici



Chilian WM. *J Nucl Cardiol*. 2001;8:599.

Microvascular disease (MVD)

Microvascular dysfunction (MVD) can cause ischemic heart disease

Microvascular dysfunction (MVD) is more common in women

MVD may be influenced by hormonal fluctuations and by cardiac risk factors (especially diabetes)

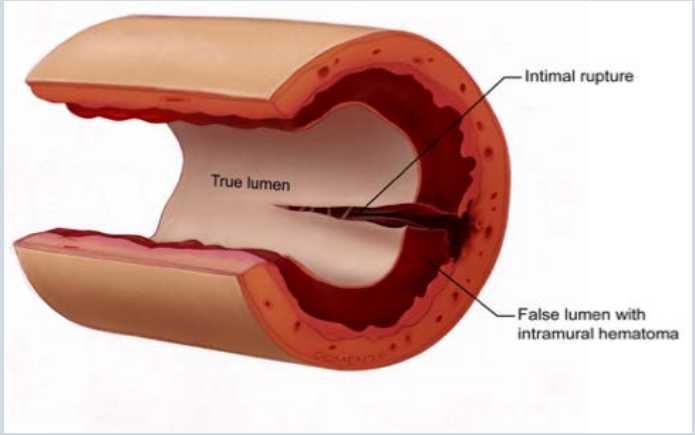
The microcirculation has the greatest impact on coronary blood flow

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

Significant association with fibromuscular dysplasia

- -? Generalized vasculopathy

The Canadian SCAD (CanSCAD) a prospective, observational study

750 SCAD patients from Canada (20 centers) and the US (2 centers)

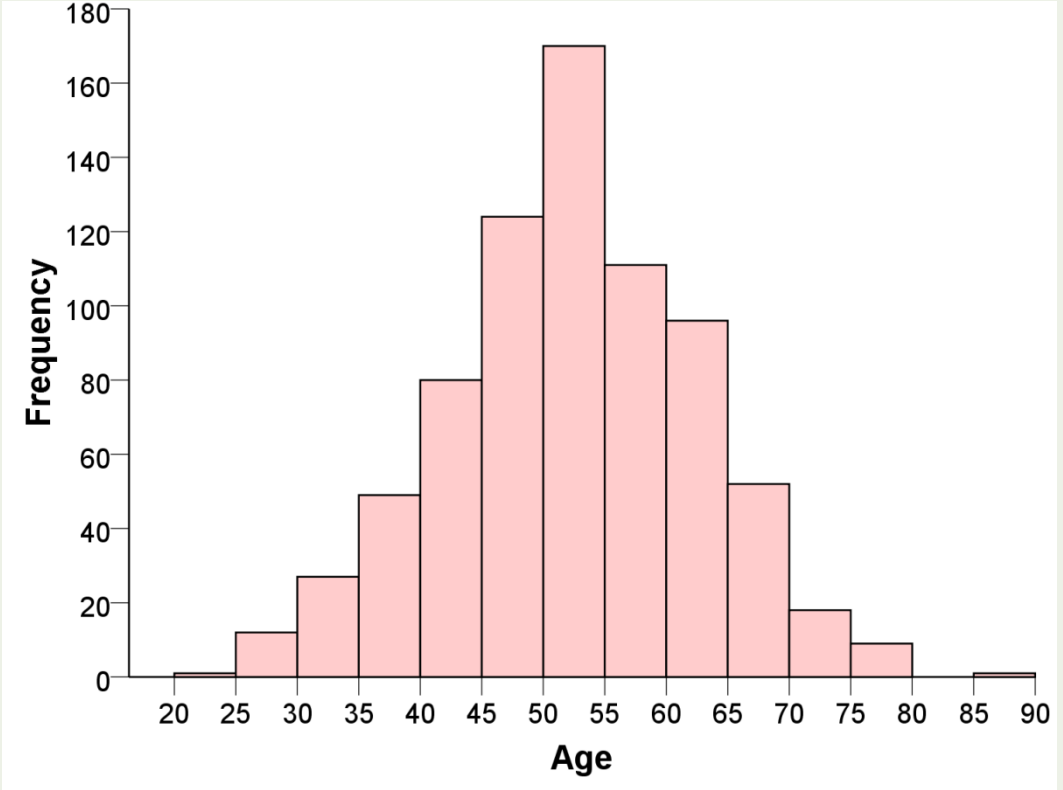
Average age was 51.8 years

89% were female

55% were postmenopausal

Only 4.5% were peripartum

33.9% had NO cardiac risk factors



The Canadian SCAD (CanSCAD) study through 2018

50.3% reported high or severe levels of emotional stress

28.9% reported unusually intense physical stress

9.8% reported Isometric stress >50 lb. weight lifting

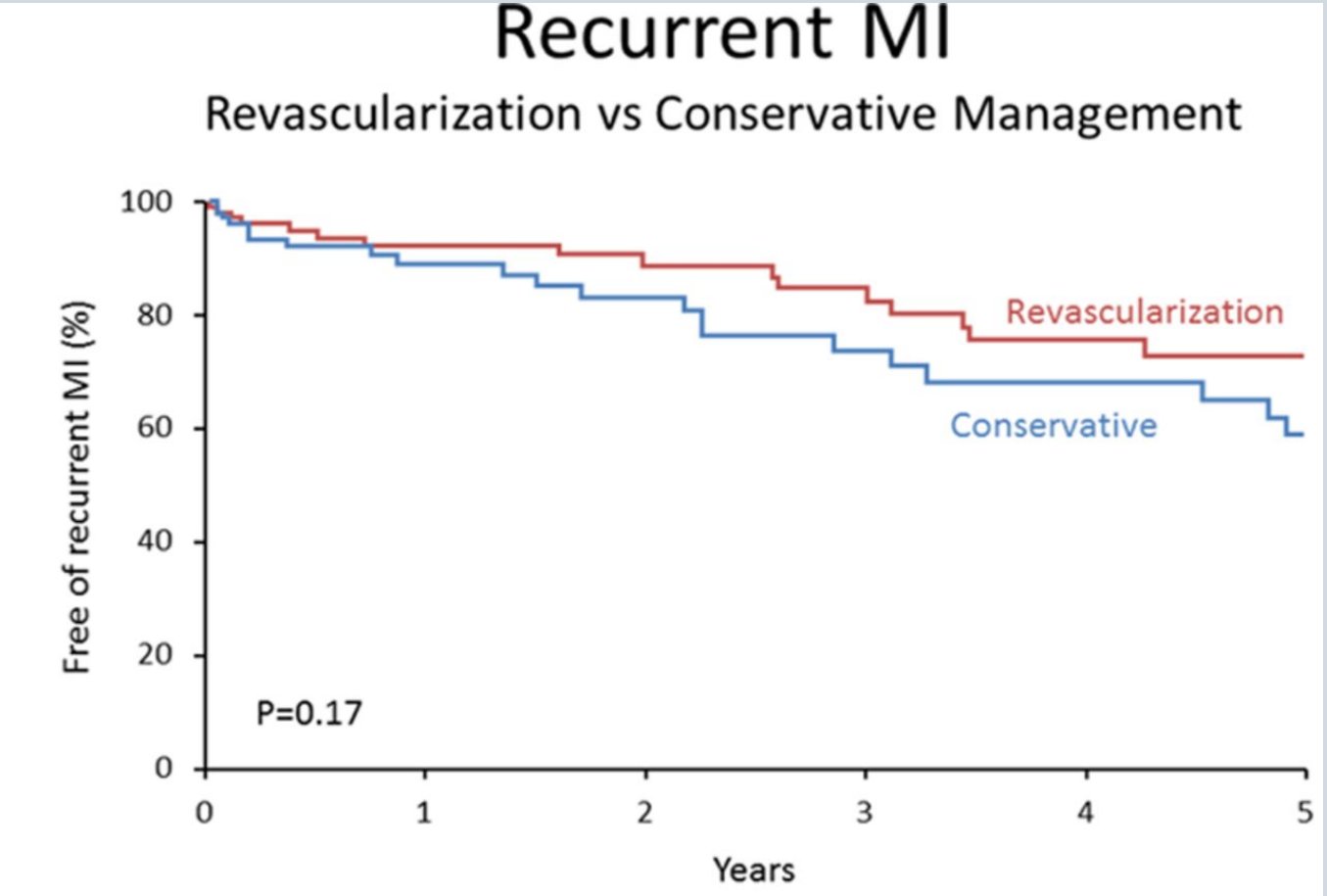
32.5% had a history of migraines

31.1% had ***fibromuscular dysplasia***

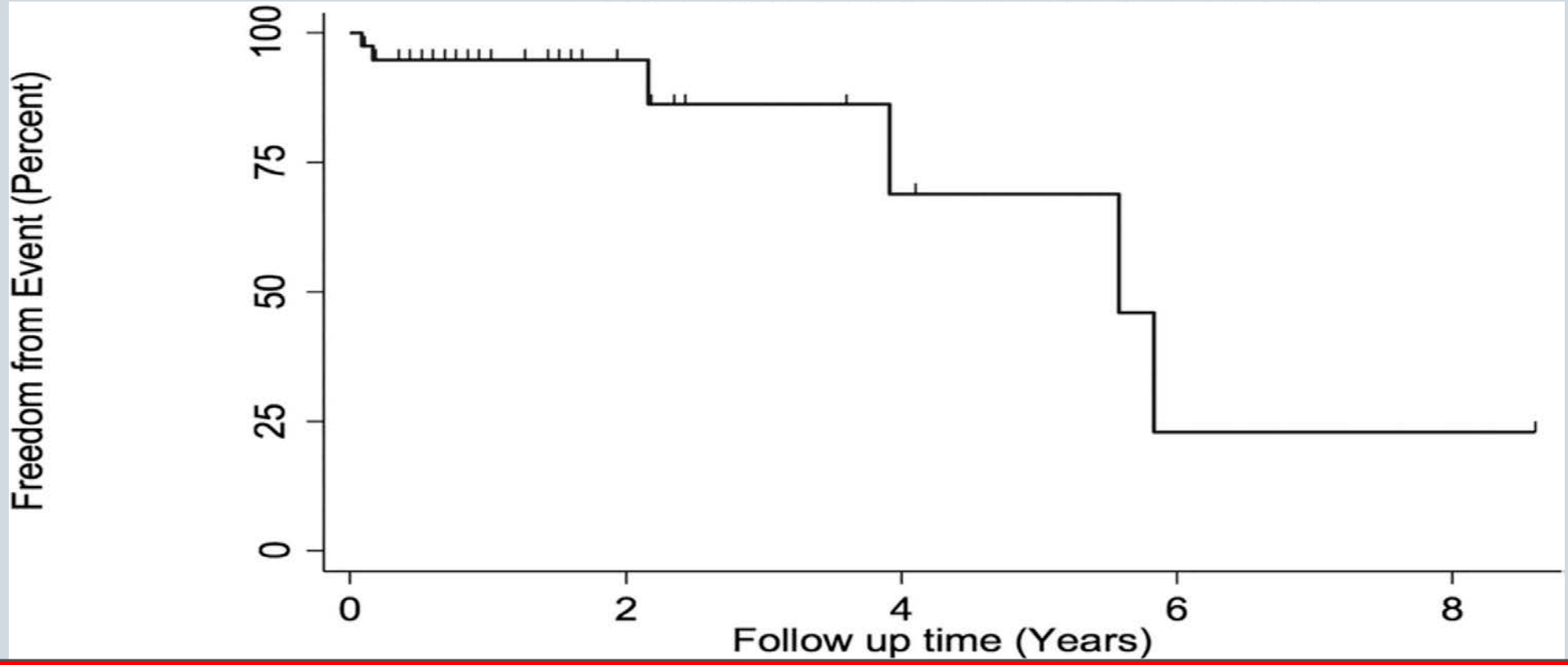
- 27.7 % renal arteries
- 21.0 % femoral and/or iliac
- 29.5 % cerebrovascular
- 7.1% had cerebral aneurysms

Presented at the European Society of Cardiology conference in Munich, Germany August 2018

SCAD should be treated conservatively



Long term outcomes of SCAD are poor



Long term outcomes are poor in SCAD with high recurrent CV event rates

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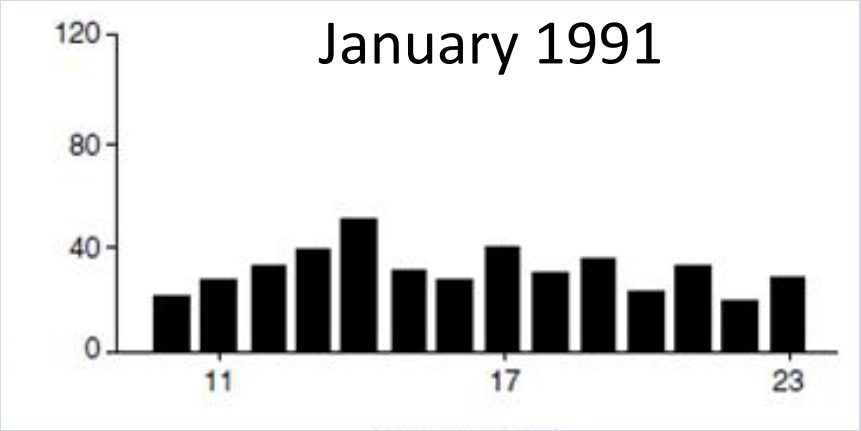
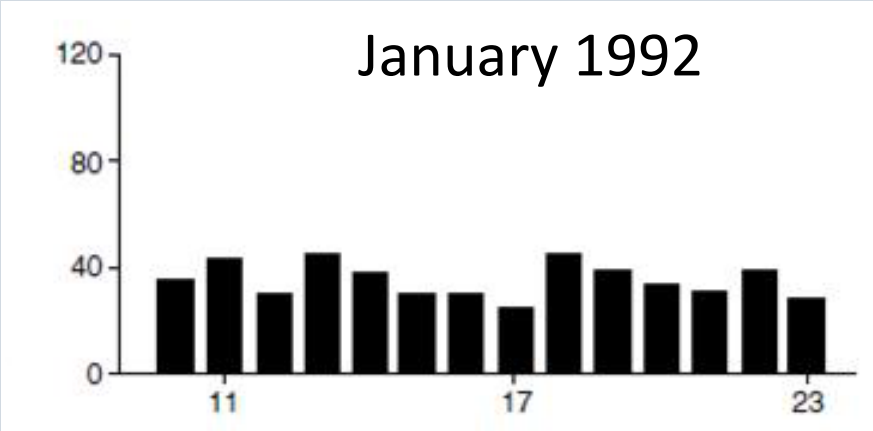
- **The link between breast cancer and heart disease**

Takotsubo: Stress and the heart

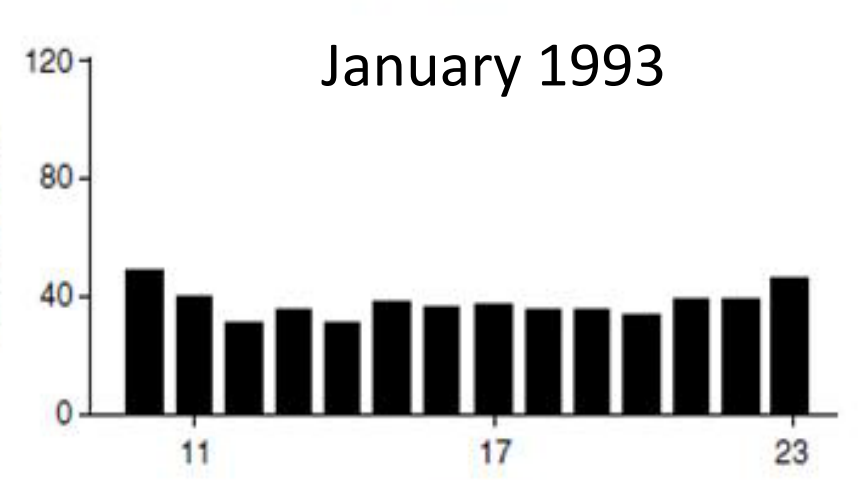
Northridge earthquake and Cardiac Deaths

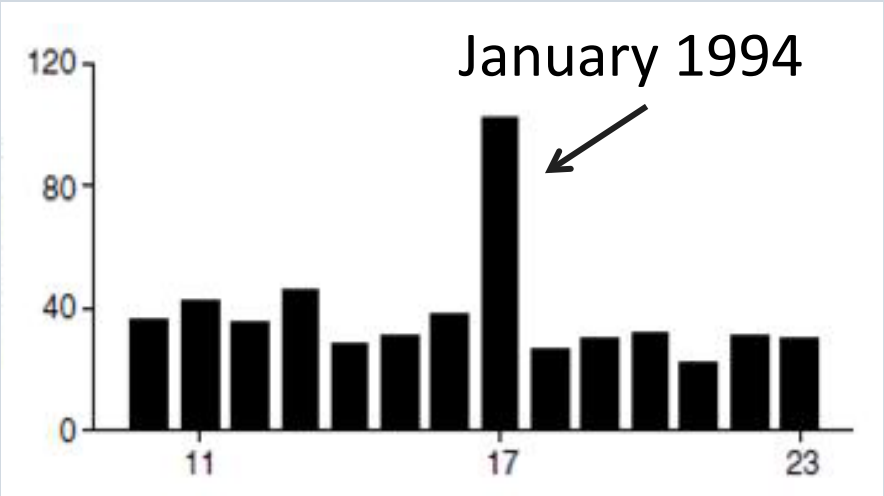
Number of Cardiac Deaths





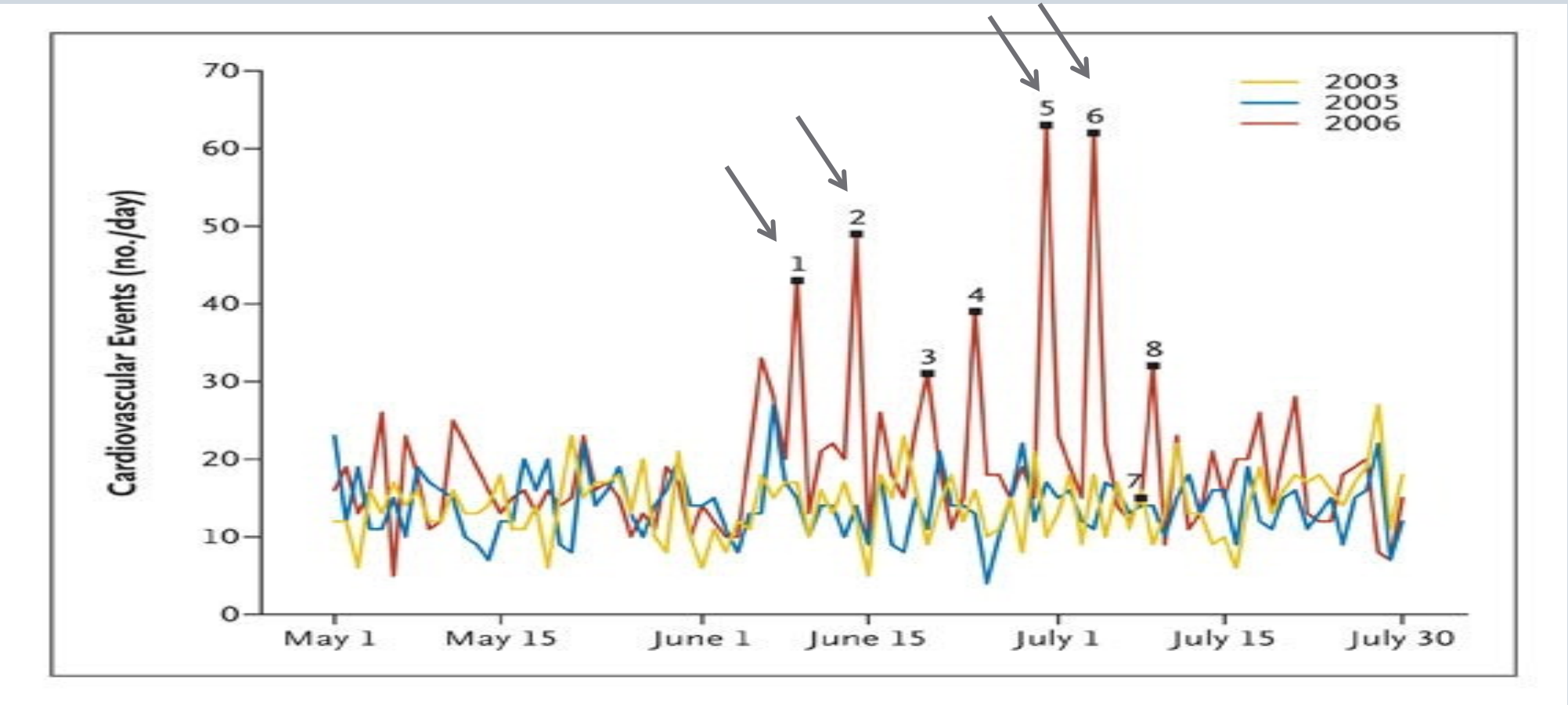
Number of Cardiac Deaths





Leor J et. al. New England Journal of Medicine Feb 15' 334(7); 413-9

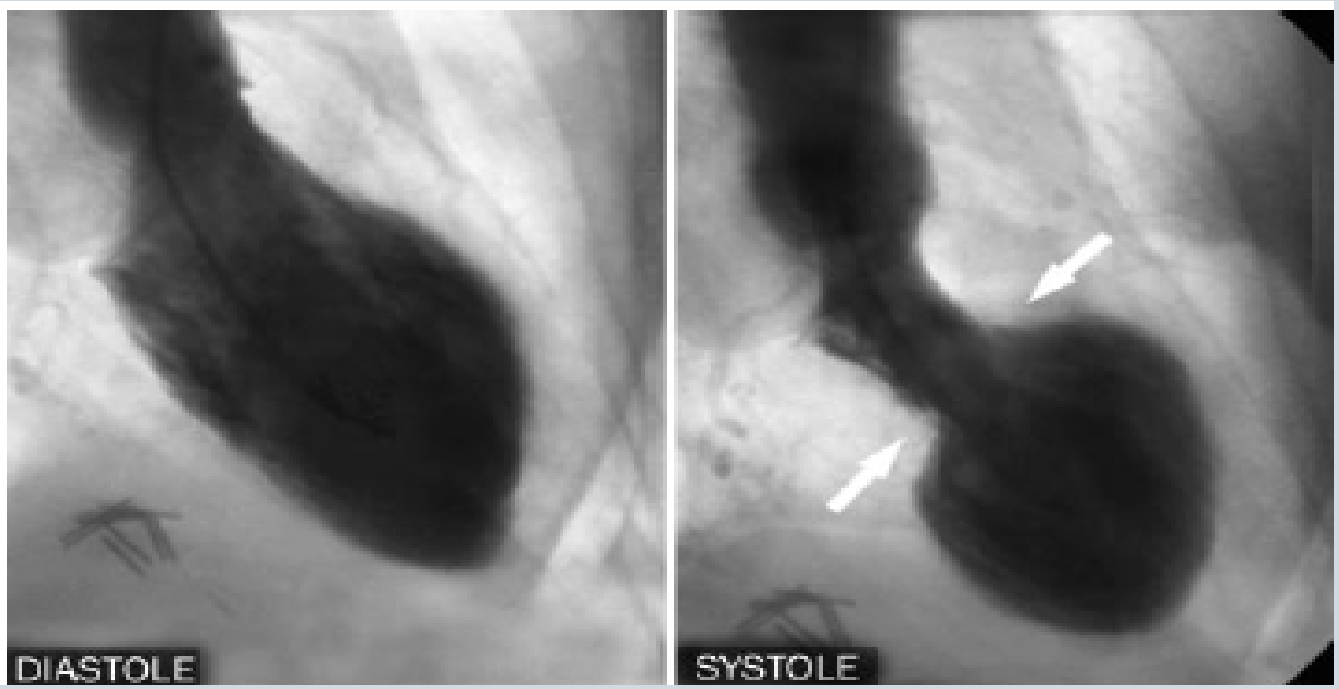
Cardiac Deaths and World Cup soccer in Germany



Wilbert-Lampen U et al. N Engl J Med 2008;358:475-483.

“Stress” is an Important Cardiovascular Risk Factor in women

TAKOTSUBO CARDIOMYOPATHY

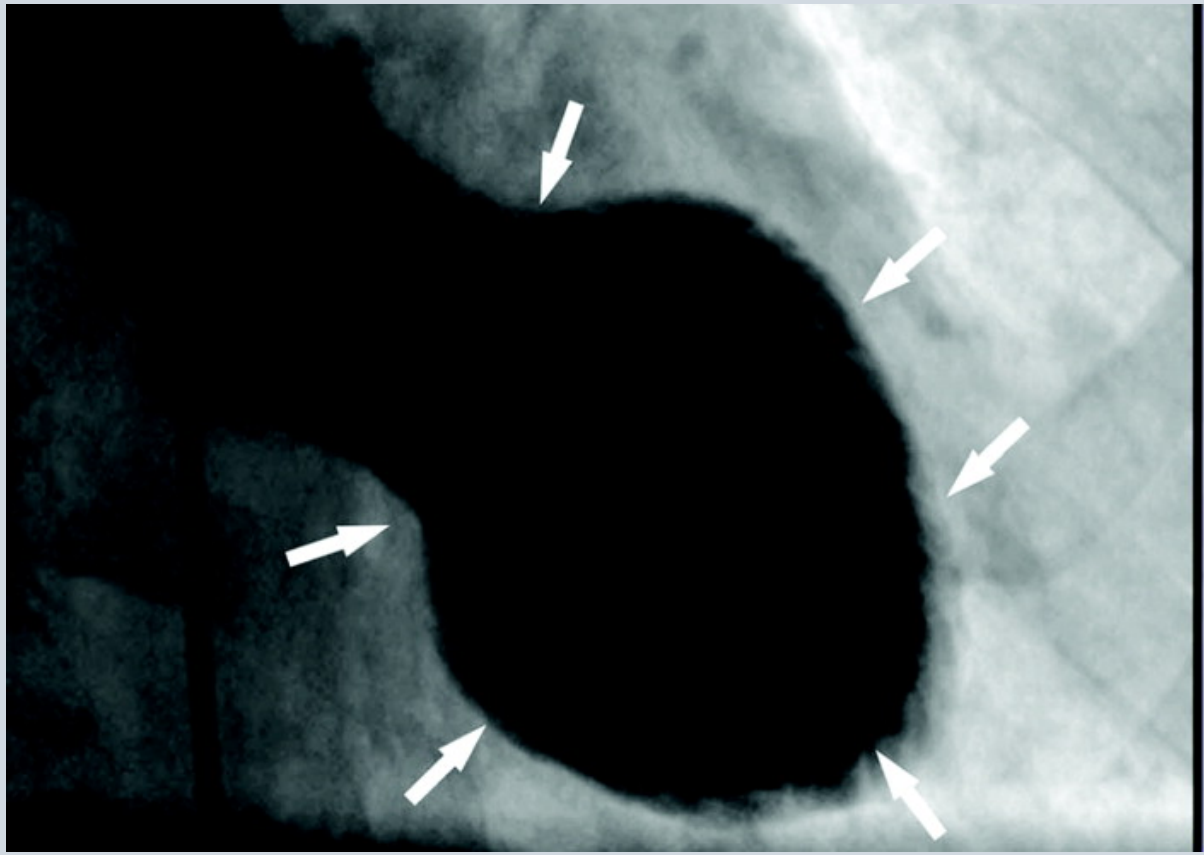


- Non-atherosclerotic form of acute myocardial infarction
- Cardiomyopathy with apical sparing (resembling a “takotsubo”)
- Preceding emotional stressor (*“lifetime crisis”)* or physical trigger
- 90% post-menopausal females

Sharkey et al. *Circulation* 2005. Chou and Shaw. *Can J Cardiol* 2014.

Takotsubo

- Broken Heart Syndrome
- Stress Cardiomyopathy

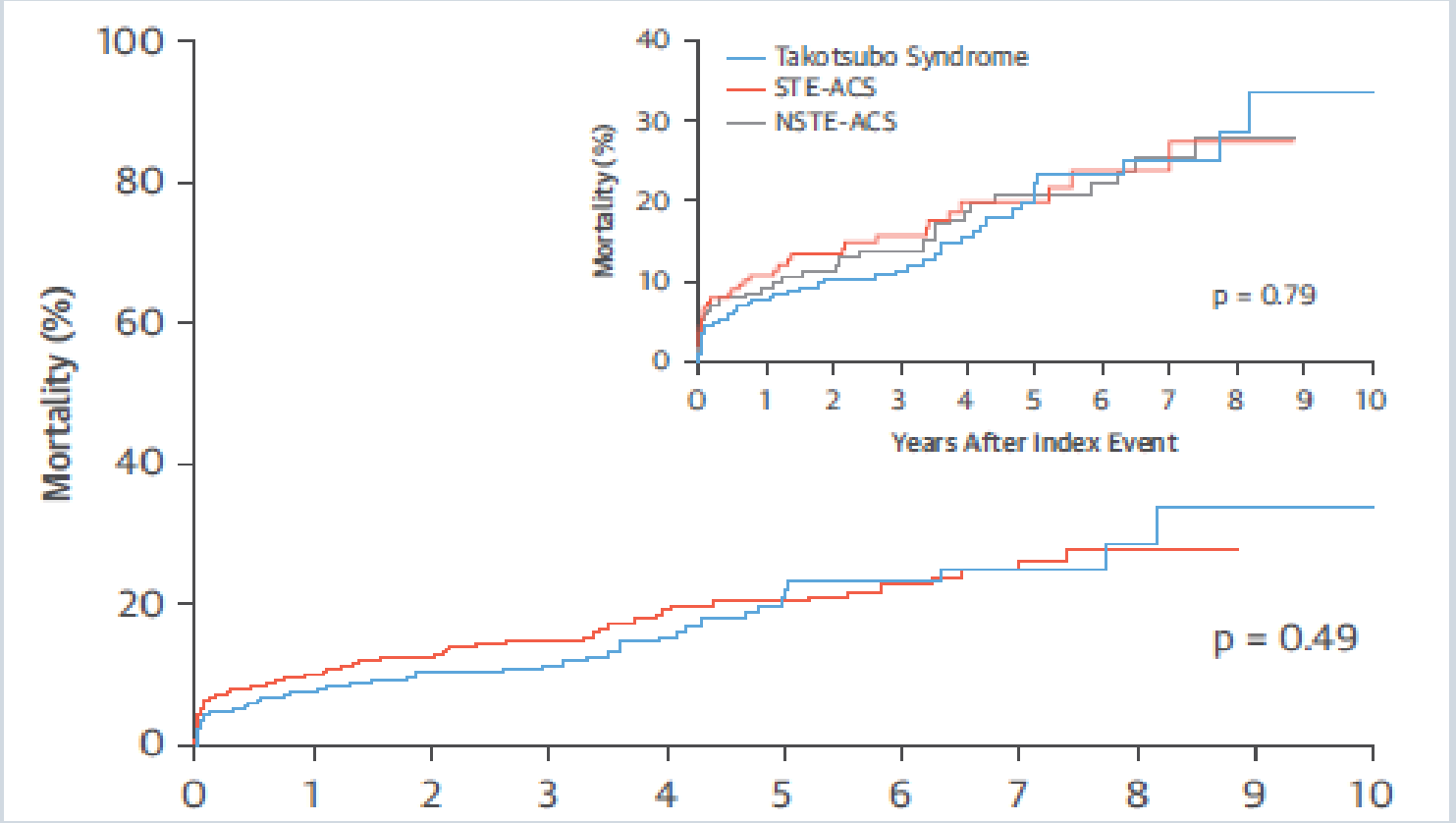


Japanese octopus trap

Scott W. Sharkey et al. Circulation. 2011;124:e460-e462

Takotsubo outcomes similar to ACS outcomes

- 1,613 patients enrolled in the International Takotsubo Registry.
- 90% women
- Takotsubo patients had similar long-term mortality to ACS patients

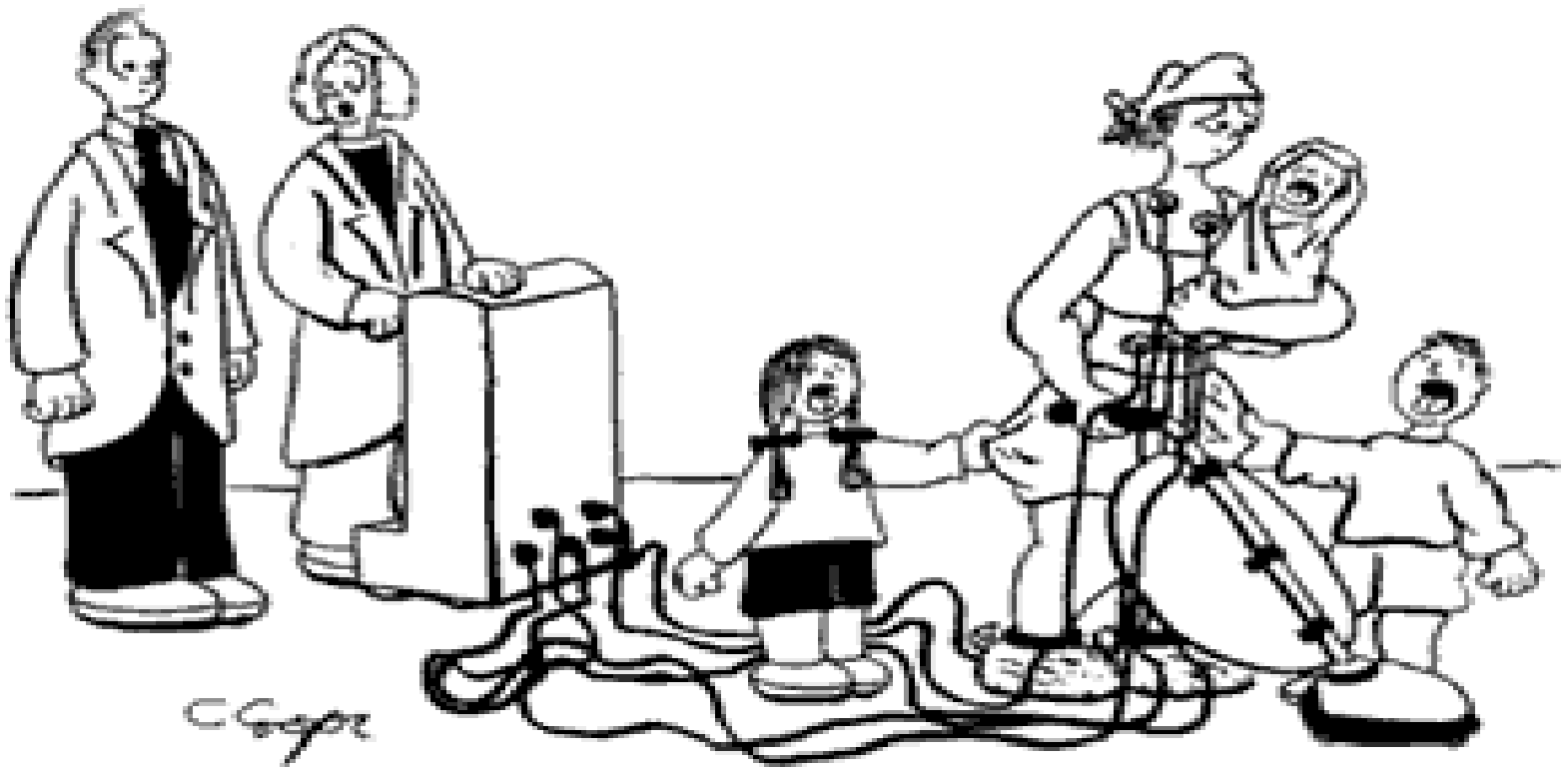


J Am Coll Cardiol 2018;72:874–82

Urinary stress hormone levels Women vs. Men

Variable*	Female n=348	Male n=306	P Value
Smoking Status, % Never / former / current smoker	59/34/7	38/49/13	<0.001
Diastolic Blood Pressure, mmHg	67.4 ± 9.62	73.5 ± 9.52	0.00001
Blood pressure medications, %	49	39	0.0134
BMI, kg/m2	29.6 ± 5.9	28.0 ± 4.5	0.0014
HDL cholesterol, mg/dl	56.6 ± 15.80	46.3 ± 14.45	<0.0001
Urinary Catecholamines			
NE, (ln ng/ creatinine mg/dl)	29.1(23.1-40.6)	24.2(17.9-32.0)	<0.0001
EPI, (ln ng/ creatinine mg/dl)	2.3(1.4-3.0)	2.4 (1.5-3.3)	0.4200
DA, (ln ng/ creatinine mg/dl)	242.9[19]	198.4(158.5-250.5)	<0.0001

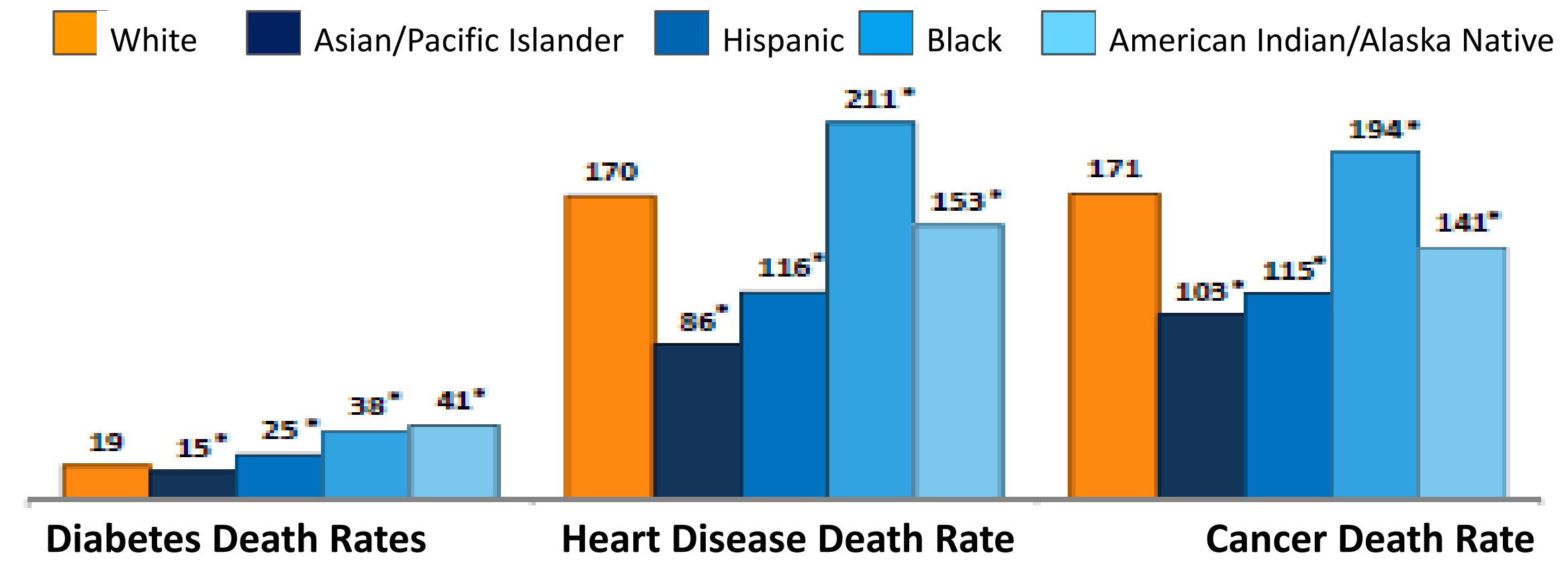
Zipursky, Horwich, Calfon Press…Watson, et. al. In submission



"We wanted to make the stress test as realistic as possible."

Underrepresented Minorities

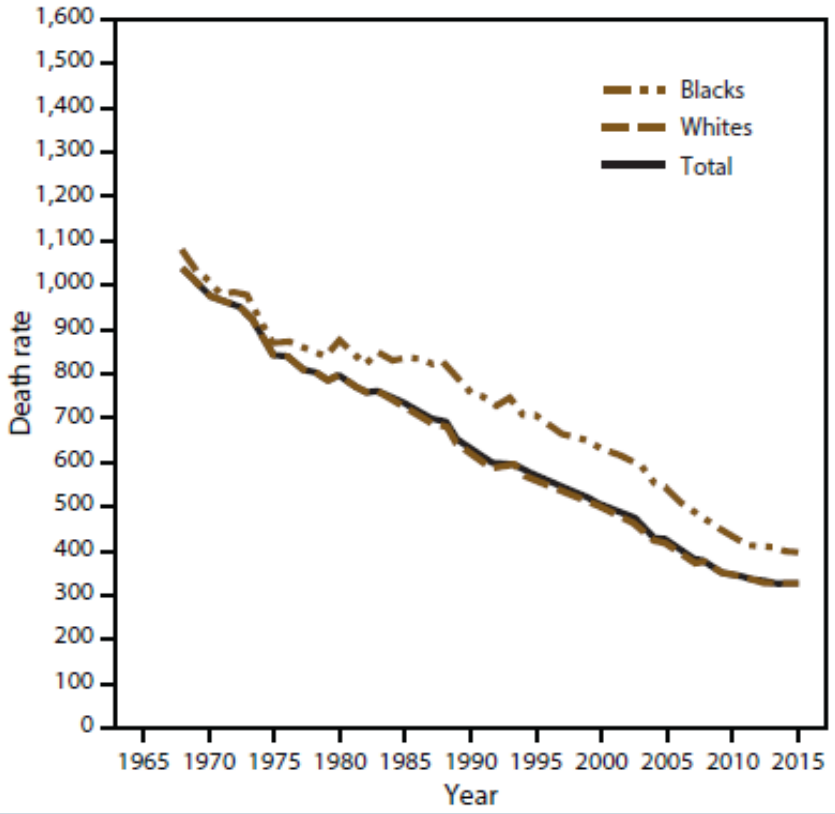
Death rates by race-ethnicity



Centers for Disease Control and Prevention, National Center for Health Statistics. WONDER Online Database 2014

Disparities in heart disease death rates

FIGURE 1. Heart disease death rates* and annual percentage changes among adults aged ≥35 years, by race — United States, 1968–2015



Black have higher heart disease death rates than white.

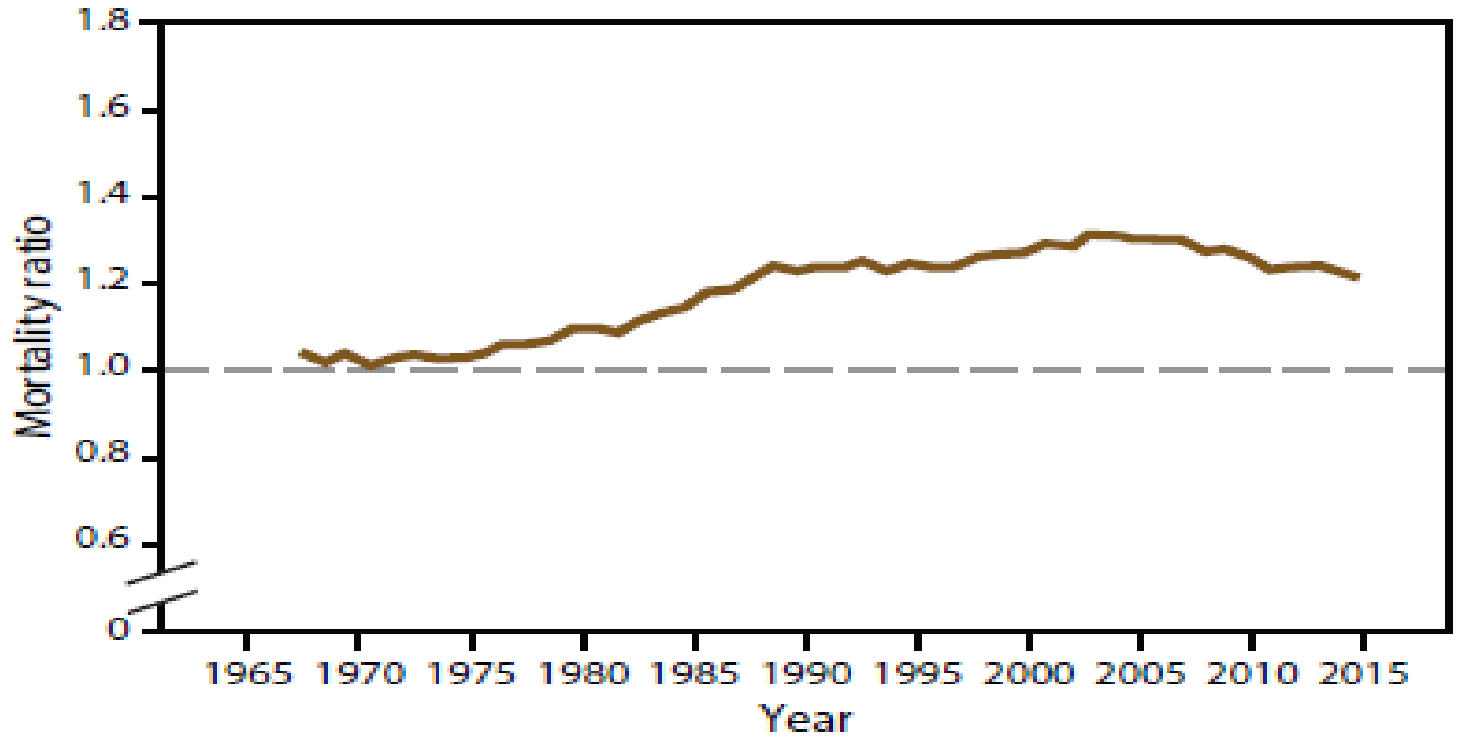
This has been true since 1970

The gap is not closing

MMWR March 30, 2018 vol 67; No. 5. US Department of Health and Human Services/Centers for Disease Control and Prevention

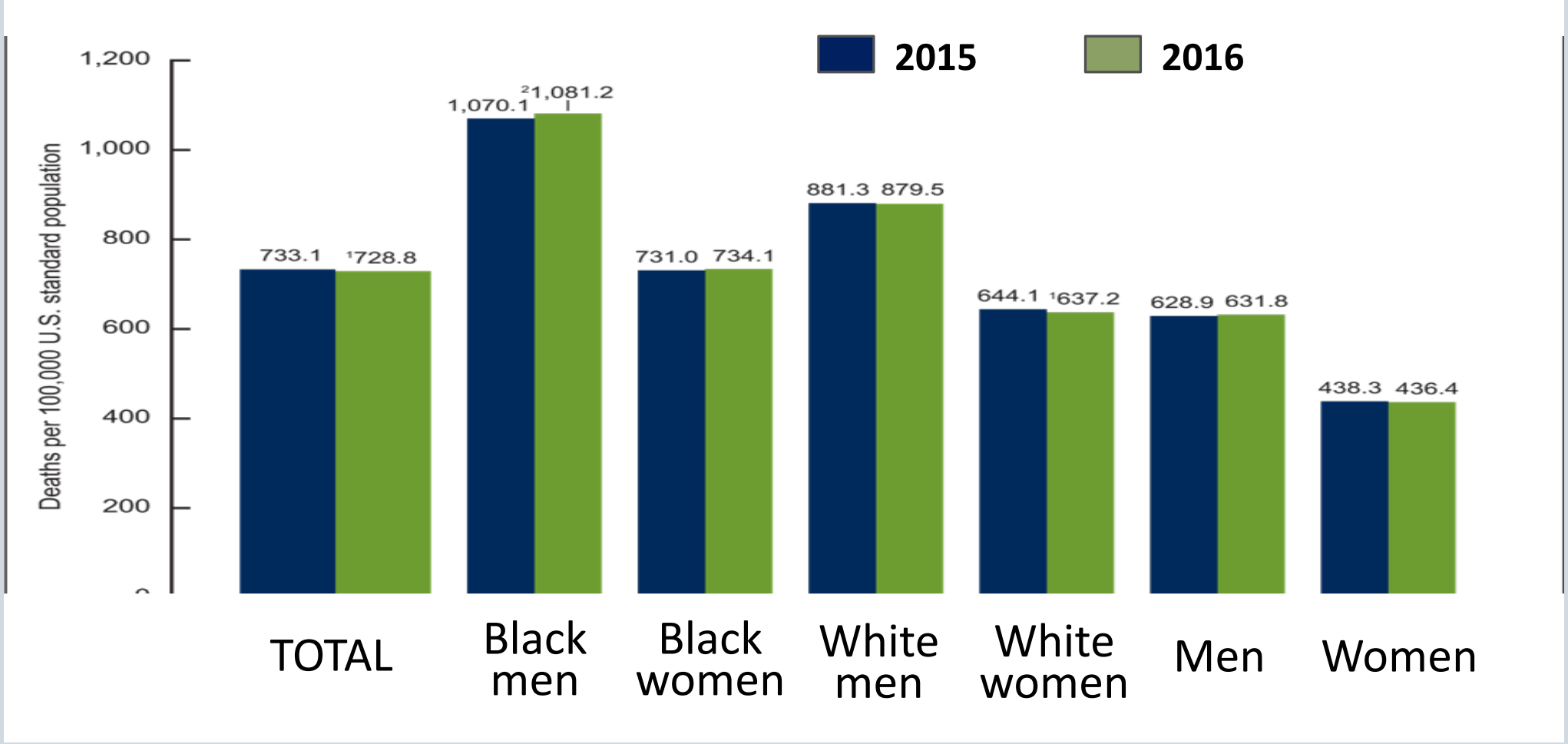
Disparities in heart disease death rates

FIGURE 2. Black-white heart disease mortality ratios and annual percentage changes among adults aged ≥35 years — United States, 1968–2015



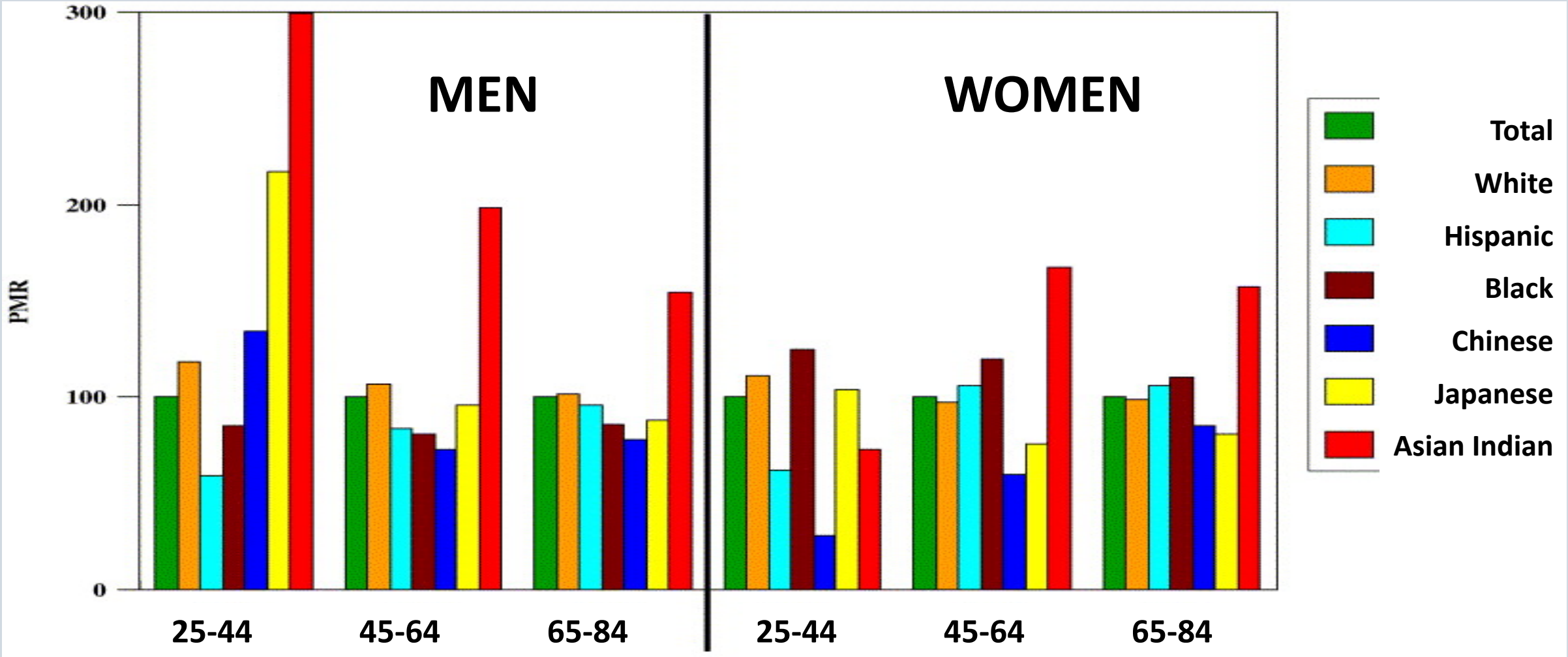
MMWR March 30, 2018 vol 67; No. 5. US Department of Health and Human Services/Centers for Disease Control and Prevention

Heart disease mortality is increasing in Black men



NCHS, National Vital Statistics System Mortality

CVD Mortality by Ethnic Group, in California



Palaniappan, et al. Annals of Epidemiology. 2004 August; 14(7): 495-506.

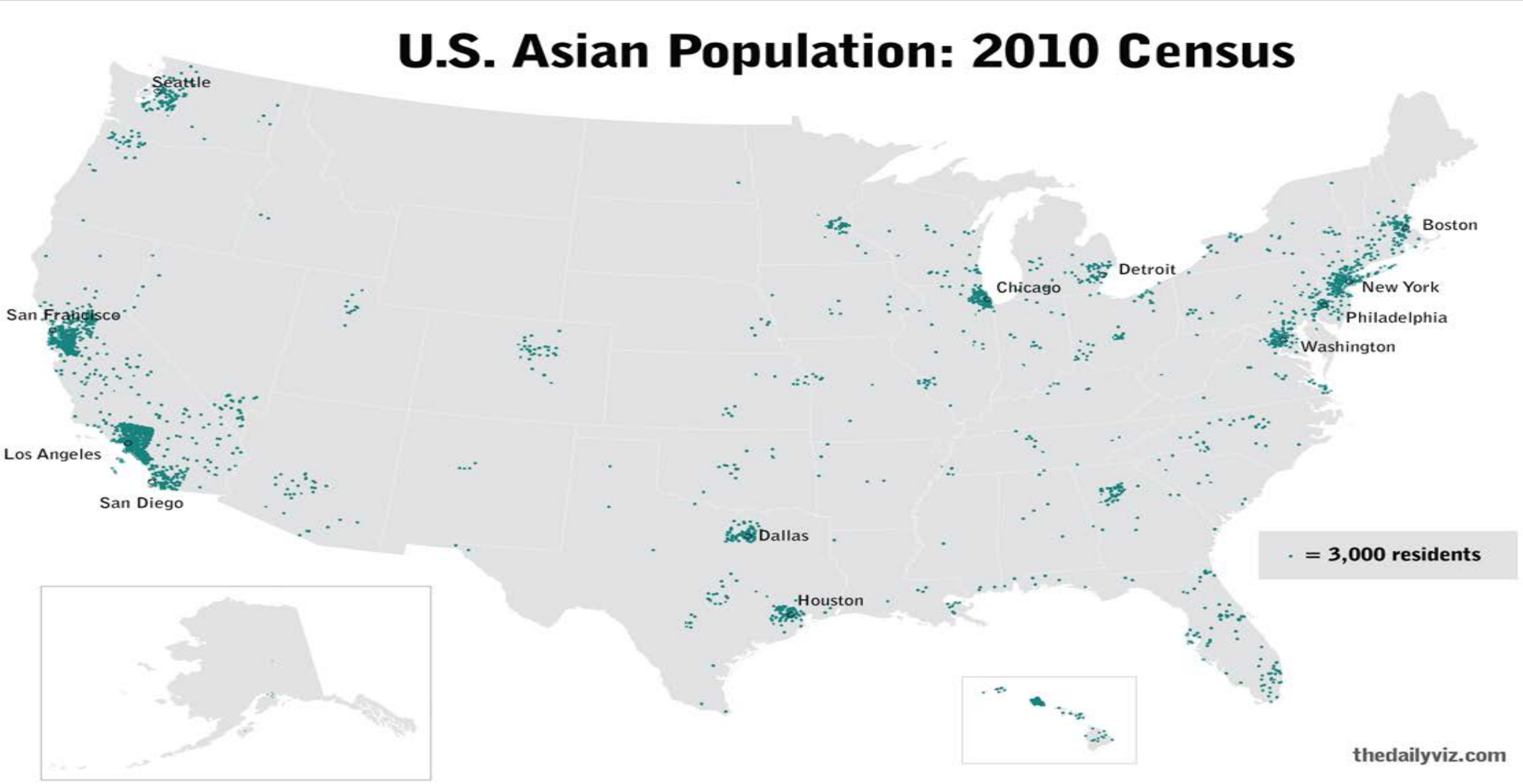
South Asians

South Asians

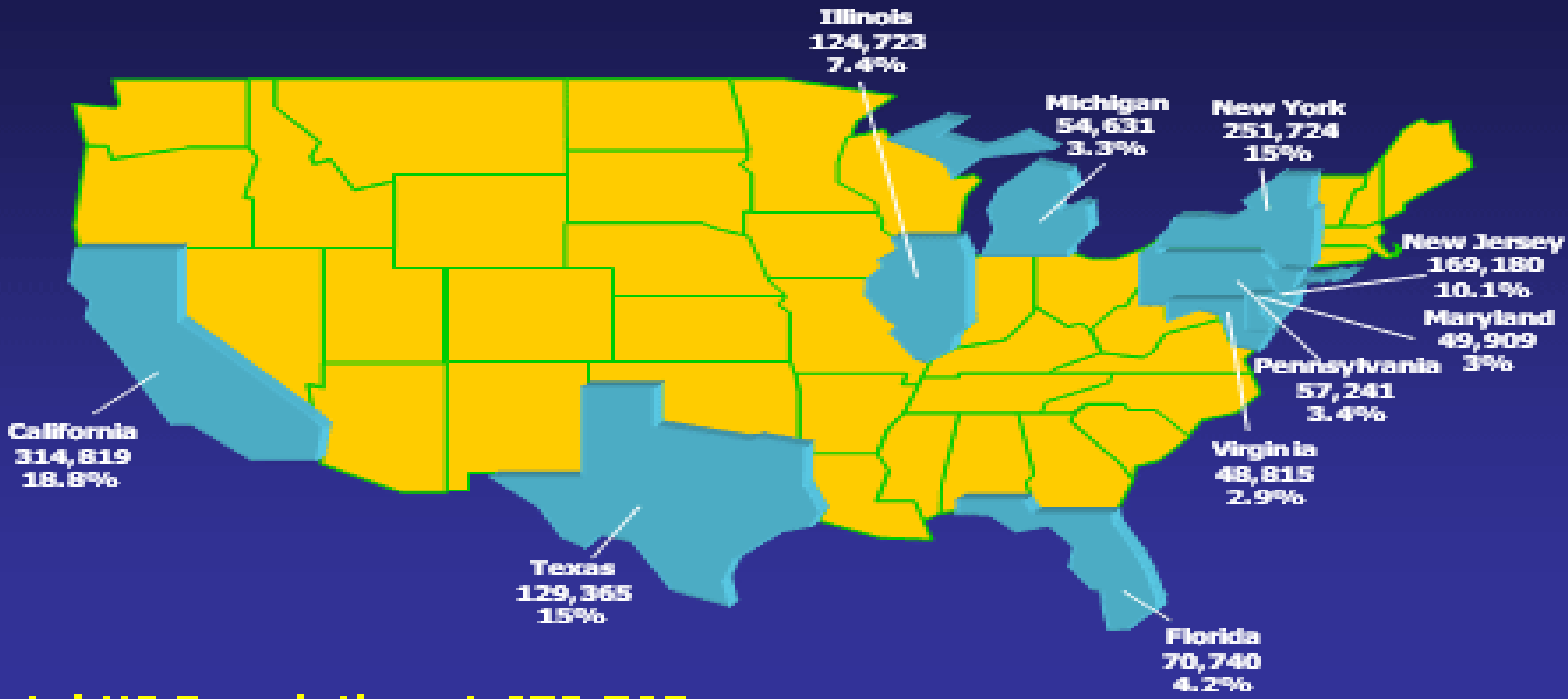
- Bangladesh, Bhutan, India, Nepal, Pakistan, Sri Lanka
- 1.6 billion individuals *(one-fifth of all humans!)*

Migration:

- 1890s-1920s: First wave, mainly from the Indian State of Punjab occurred
- 1960s: Second wave with passage of the 1965 immigration and nationality act (INA).
  - A total of 20,000 highly skilled professionals and 25,000 physicians emigrated from India to the US.
- 1980s: Third wave: Family reunification, allowing for parents and extended families of the settled professionals, to emigrate to the U.S.


U.S. Asian Population: 2010 Census
Seattle
San Francisco
Los Angeles
San Diego
Dallas
Houston
Chicago
Detroit
Boston
New York
Philadelphia
Washington
= 3,000 residents
thedailyviz.com

South Asians in the United States



Total US Population: 1,678,765

Image from: www.pamf.org/southasian/research/studies/EPCDSAI

South Asians in the U.S.

- Asian Americans 2010 Census
  - Chinese (3.79 million)
  - Filipino (3.41 million)
  - **Indian (3.18 million)**
  - Vietnamese (1.73 million)
  - Korean (1.7 million)
  - Japanese (1.3 million)
- 2010 U.S. Census: 3,863,963 South Asians
  - 6% are age 65 or older
- Largest numbers of South Asians are in New York, New Jersey, Michigan, Texas and Illinois

Cardiovascular Disease in South Asians

High rates of CAD for South Asians

- higher hospitalization and mortality rates from CAD
- Average 10 years earlier first event than other race/ethnicities

Heart Failure Younger age of onset

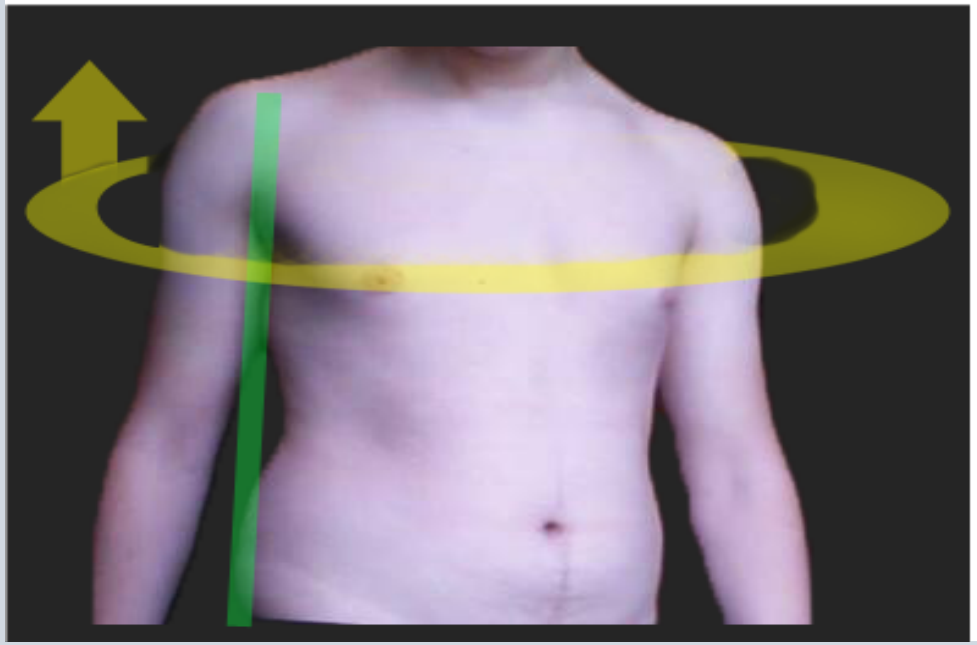
- Higher risk of ventricular arrhythmias and lower risk of AF
- More ischemic etiology responsible for HF

Risk Factors - Type 2 Diabetes Mellitus

- South Asians
  - Higher odds of diabetes compared to whites and Latinos
  - Not significantly different from African Americans and Chinese Americans
- Approximately 33% of participants have pre-DM, 25% DM
- South Asians develop DM 5–10 years earlier and at a lower BMI
- Migrant SAs more insulin-resistant than white Europeans across the life course and potentially experience β-cell exhaustion at a younger age

Traditional Risk Factors – Obesity

THE SKINNY-FAT PHENOTYPE



UNDERMUSCLED *in the shoulders, upper chest, arms, and upper back and back in general - what i call the* **"HALO"** *and* **"WINGS"** *- which makes for more of an "A" build rather than an "X" build, a very ectomorph build for muscle mass, but...*

FAT DEPOSITS *typically in the lower chest, love handles, and belly area*

HTTP://ANTHONYMYCHAL.COM

Emerging Risk Factors

Lipoprotein (a)

- LDL-like particle and the specific apolipoprotein(a) [apo(a)], covalently bound to the apoB of the LDL like particle
- Correlated with atherogenic activity and CVD outcomes with large genetic determination
- Multiple U.S. cohorts demonstrate elevated levels in South Asians when compared to white controls
- Correlation of Lp(a) has relationship to CAD severity in South Asians[23,24]

Circulation

AHA SCIENTIFIC STATEMENT

Atherosclerotic Cardiovascular Disease in South Asians in the United States: Epidemiology, Risk Factors, and Treatments

A Scientific Statement From the American Heart Association

ABSTRACT: South Asians (from Bangladesh, Bhutan, India, the Maldives, Nepal, Pakistan, and Sri Lanka) make up one quarter of the world's population and are one of the fastest-growing ethnic groups in the United States. Although native South Asians share genetic and cultural risk factors with South Asians abroad, South Asians in the United States can differ in socioeconomic status, education, healthcare behaviors, attitudes, and health insurance, which can affect their risk and the treatment and outcomes of atherosclerotic cardiovascular disease (ASCVD). South Asians have higher proportional mortality rates from ASCVD compared with other Asian groups and non-Hispanic whites, in contrast to the finding that Asian Americans (Asian Indian, Chinese, Filipino, Japanese, Korean, and Vietnamese) aggregated as a group are at lower risk of ASCVD, largely because of the lower risk observed in East Asian populations. Literature relevant to South Asian populations regarding demographics and risk factors, health behaviors, and interventions, including physical activity, diet, medications, and community strategies, is summarized. The evidence to date is that the biology of ASCVD is complex but is no different in South Asians than in any other racial/ethnic group. A majority of the risk in South Asians can be explained by the increased prevalence of known risk factors, especially those related to insulin resistance, and no unique risk factors in this population have been found. This scientific statement focuses on how ASCVD risk factors affect the South Asian population in order to make recommendations for clinical strategies to reduce disease and for directions for future research to reduce ASCVD in this population.

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Svati H. Shah, MD, FAHA
Karol E. Watson, MD, PhD, FAHA
On behalf of the American Heart Association Council on Epidemiology and Prevention; Cardiovascular Disease and Stroke in Women and Special Populations Committee of the Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Quality of Care and Outcomes Research; and Stroke Council

Conclusion

- Sex, race, and ethnicity matter in cardiovascular disease
- Heart disease is the No. 1 killer of women, and its signs and symptoms may differ from men.
- Many underrepresented populations are at higher risk for CHD
- Understanding the unique risk factors, pathophysiology, and response to therapy for patients at greatest risk will greatly improve cardiovascular outcomes

Why we need to prevent cardiovascular disease

If we keep on doing what we've always done...
we'll keep on getting what we've always gotten…