Emerging Cardiac Issues for Women

RI Women's Health Council, October 15, 2015

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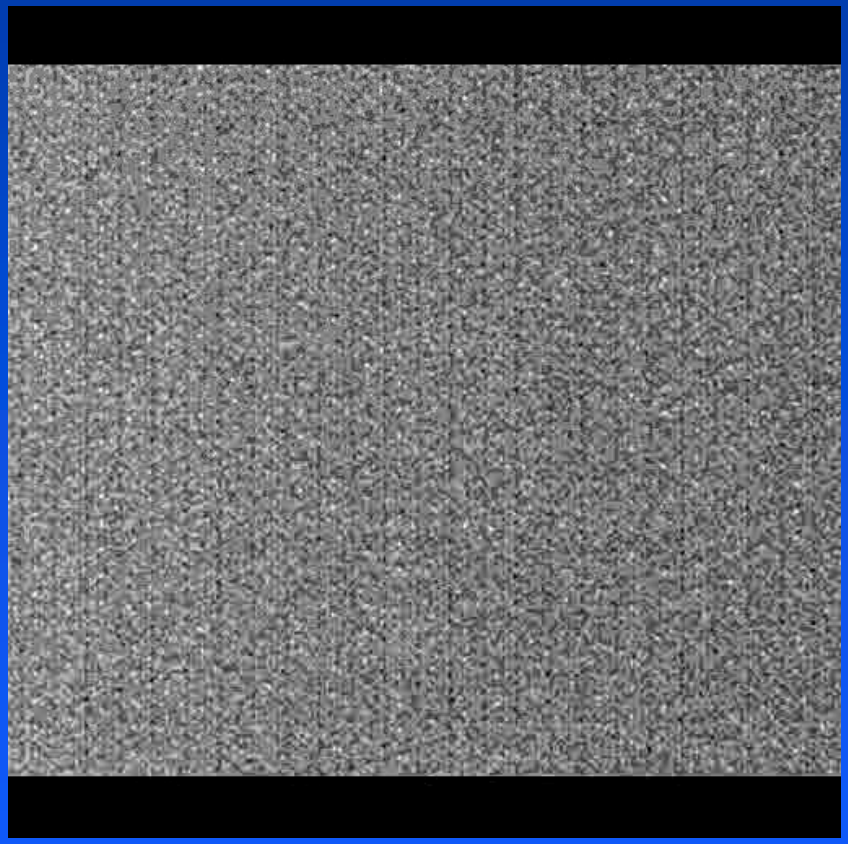
Disclosures: GE

Case: 45yow with ACS

- PMHx: choly, G2P2
  Meds: Vitamin E
- SHx: divorced, secretary, quit tobacco 10yrs
- FHx: father MI age 54
- PE: 5'2", 160lbs, 148/94, 90
- Labs: chol 220, HDL 35

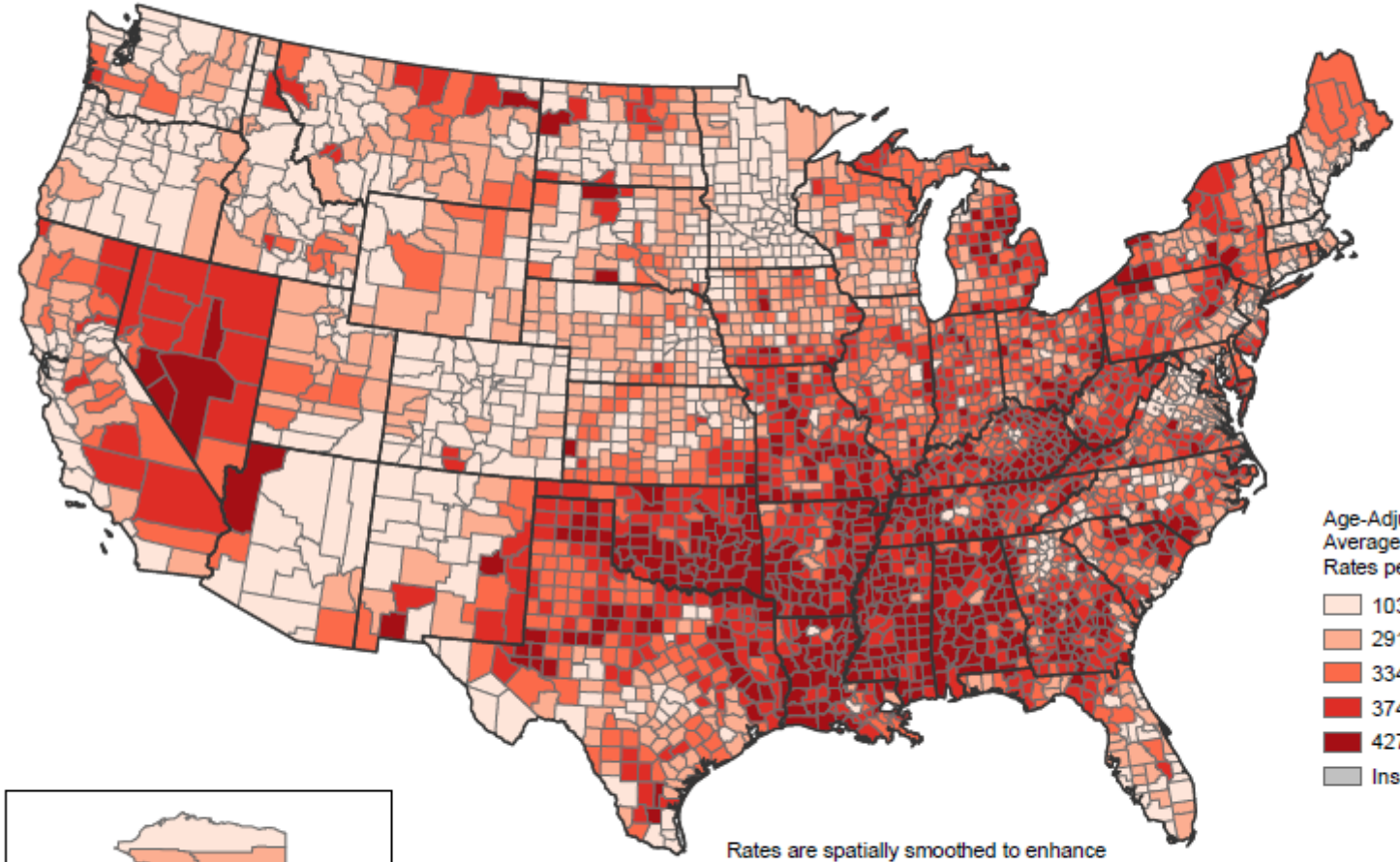
WHY ME?



Cardiovascular Disease in Women:

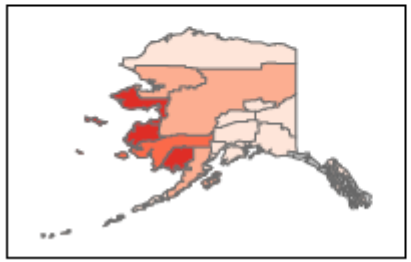
- Emerging Trends
  - Outcomes cardiac and vascular events
- Guidelines for women
  - Unique risk factors
- Coronary artery disease
  - Pregnancy and pathobiology
- Valvular Disease
  - AVR vs TAVR

Heart Disease Death Rates, 2011-2013
Adults, Ages 35+, by County



Age-Adjusted
Average Annual
Rates per 100,000

- 103.6 - 291.0
- 291.1 - 334.6
- 334.7 - 373.9
- 374.0 - 427.5
- 427.6 - 1094.1
- Insufficient Data

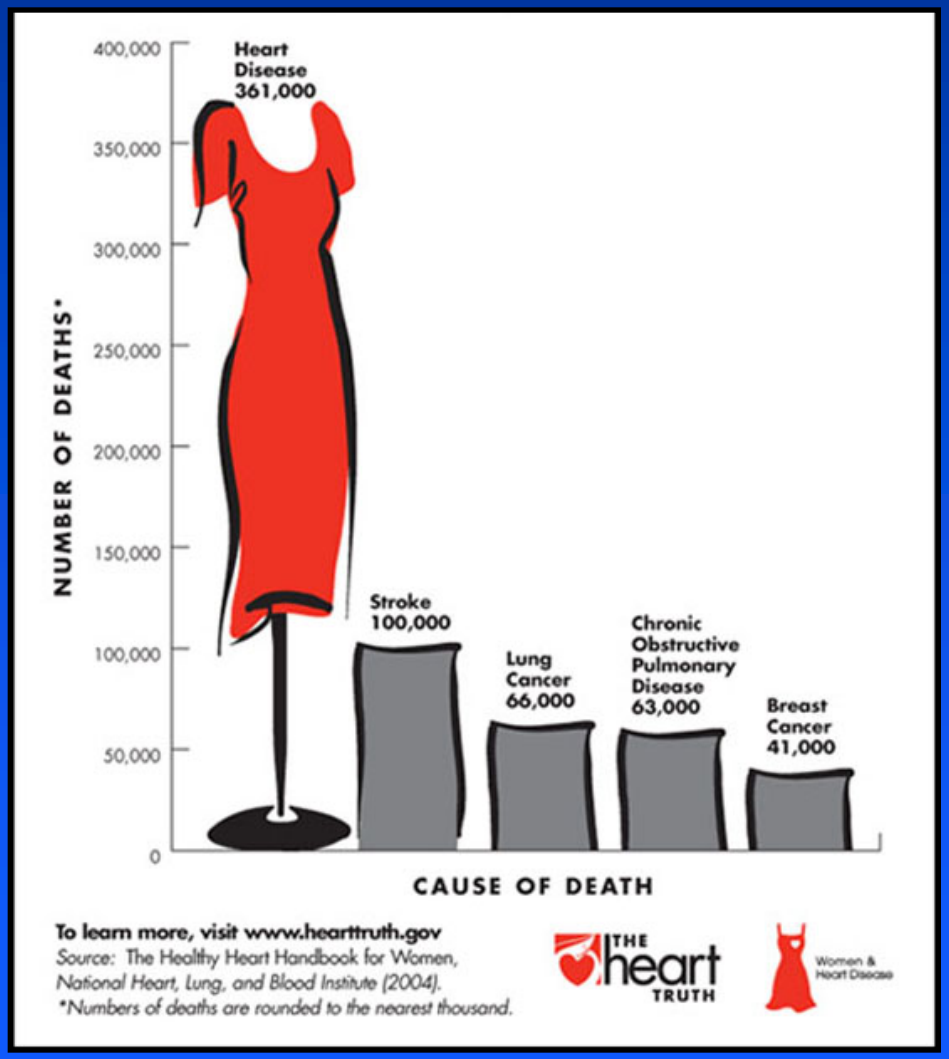


Rates are spatially smoothed to enhance the stability of rates in counties with small populations.

Data Source:
National Vital Statistics System
National Center for Health Statistics

CDC

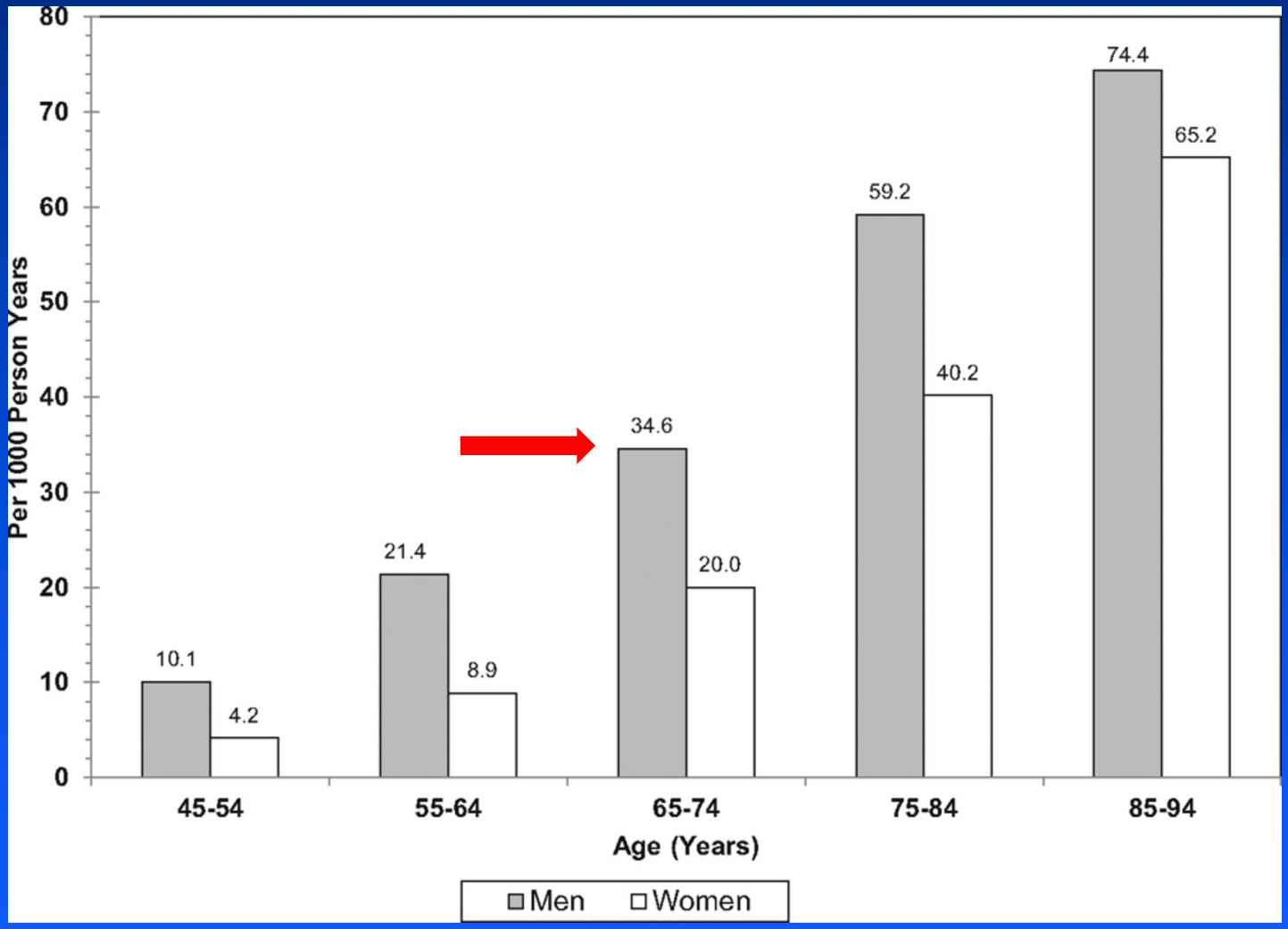
CVD is the leading killer of women



Cardiovascular vs Coronary Risk

- In middle age:
  - Men have greater risk of CAD events
  - Women have greater risk of CVA and CHF than CAD events
  - 55,000 more women than men have CVA
- Important for risk models
  - Short term (10 year)
  - Longer term (30 year)

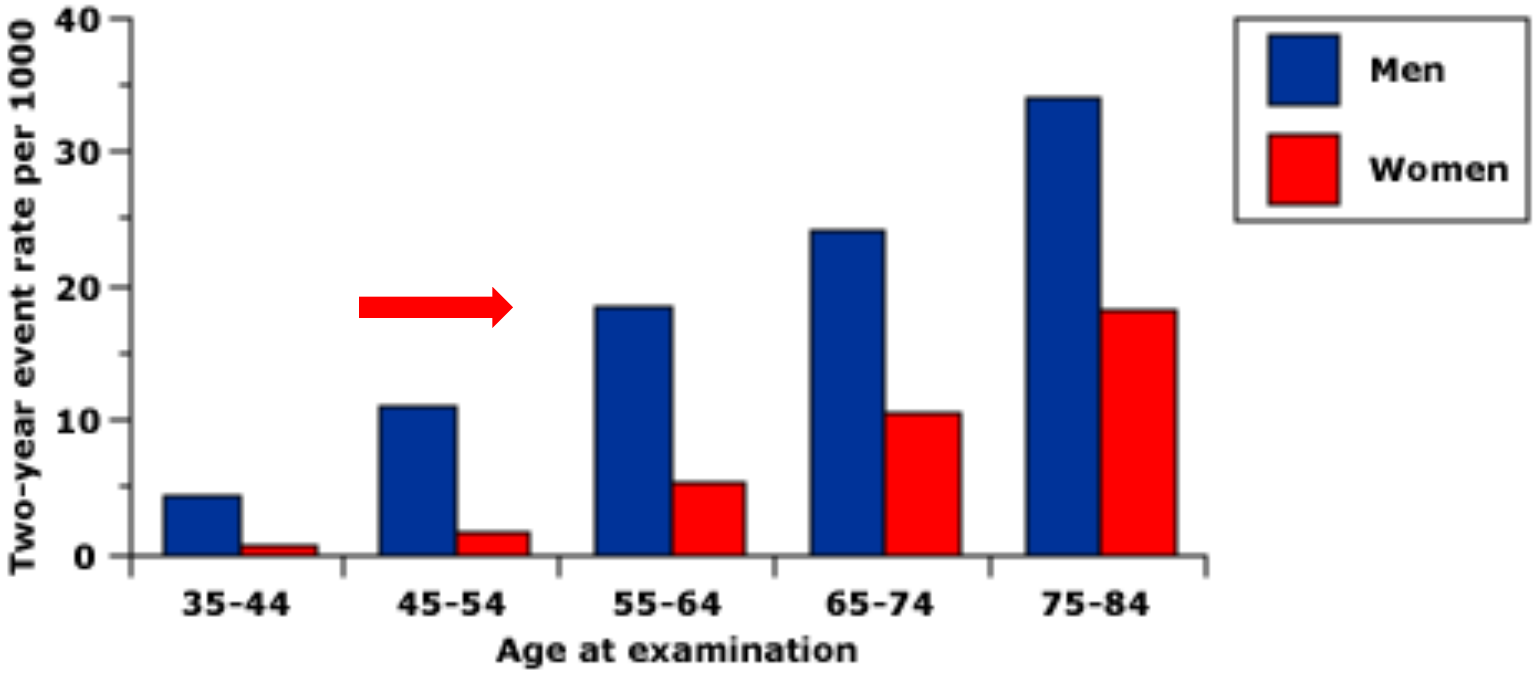
Incidence of cardiovascular disease* by age and sex (FHS, 1980–2003).
*Coronary heart disease, heart failure, stroke, or intermittent claudication.



Go A et al. Circulation 2013;127:e6-e245

American Heart Association
Learn and Live

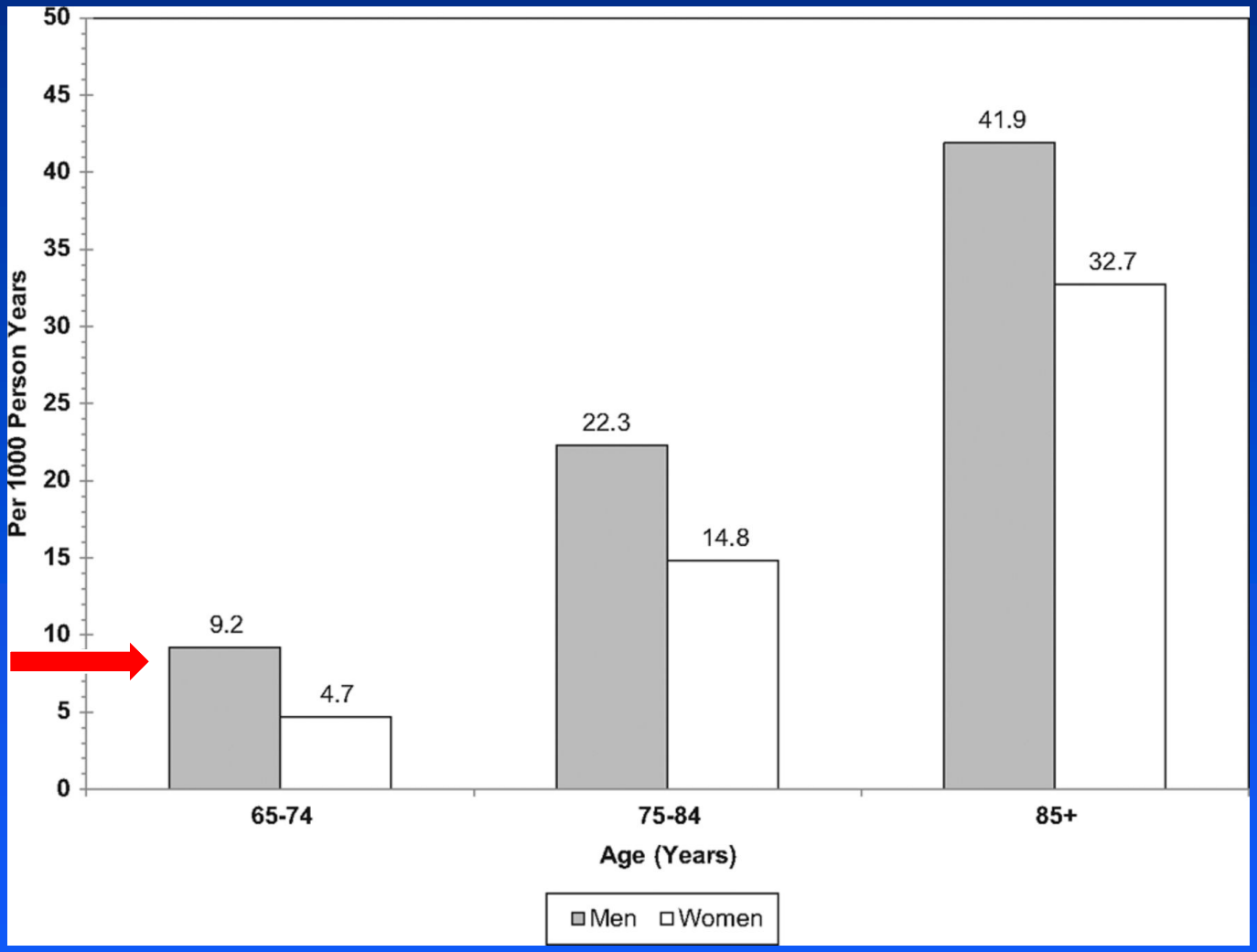
Incidence of myocardial infarction in men and women



Incidence of myocardial infarction by age and sex in a 26-year follow-up in the Framingham study. The incidence increases with age in both sexes, but occurs later (primarily after menopause) in women.

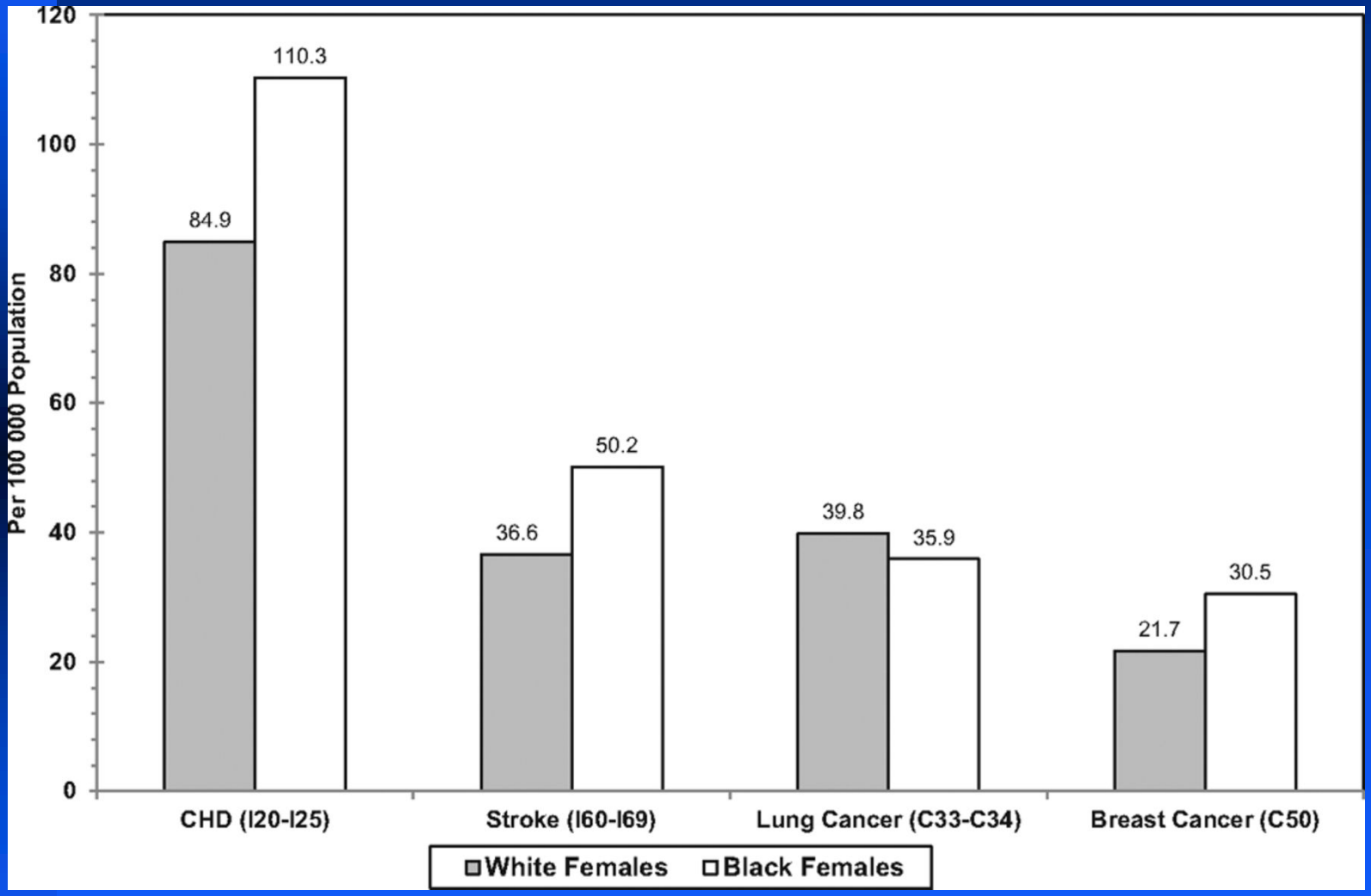
Data from: Lerner DJ, Kannel WB. Am Heart J 1986; 111:383.

Incidence of heart failure (based on physician review of medical records and strict diagnostic criteria) by age and sex (FHS 1980–2003).



Go A et al. Circulation 2013;127:e6-e245

Age-adjusted death rates for coronary heart disease (CHD), stroke, lung and breast cancer for white and black females (US: 2009).



Go A et al. Circulation 2013;127:e6-e245

American Heart Association
Learn and Live

Editorial

Heart Disease Prevention in Young Women

Sounding an Alarm

Elizabeth G. Nabel, MD

We have come a long way in the past 50 years toward reducing death and disability from cardiovascular diseases (CVDs). And yet, as articulated by Wilmot et al in this edition of *Circulation*,[1] we still have a long way to go, especially for young women and some racial/ethnic groups. These new findings highlight the value of looking "behind the curtain" at health data, in particular, teasing apart age- and sex-related outcomes.

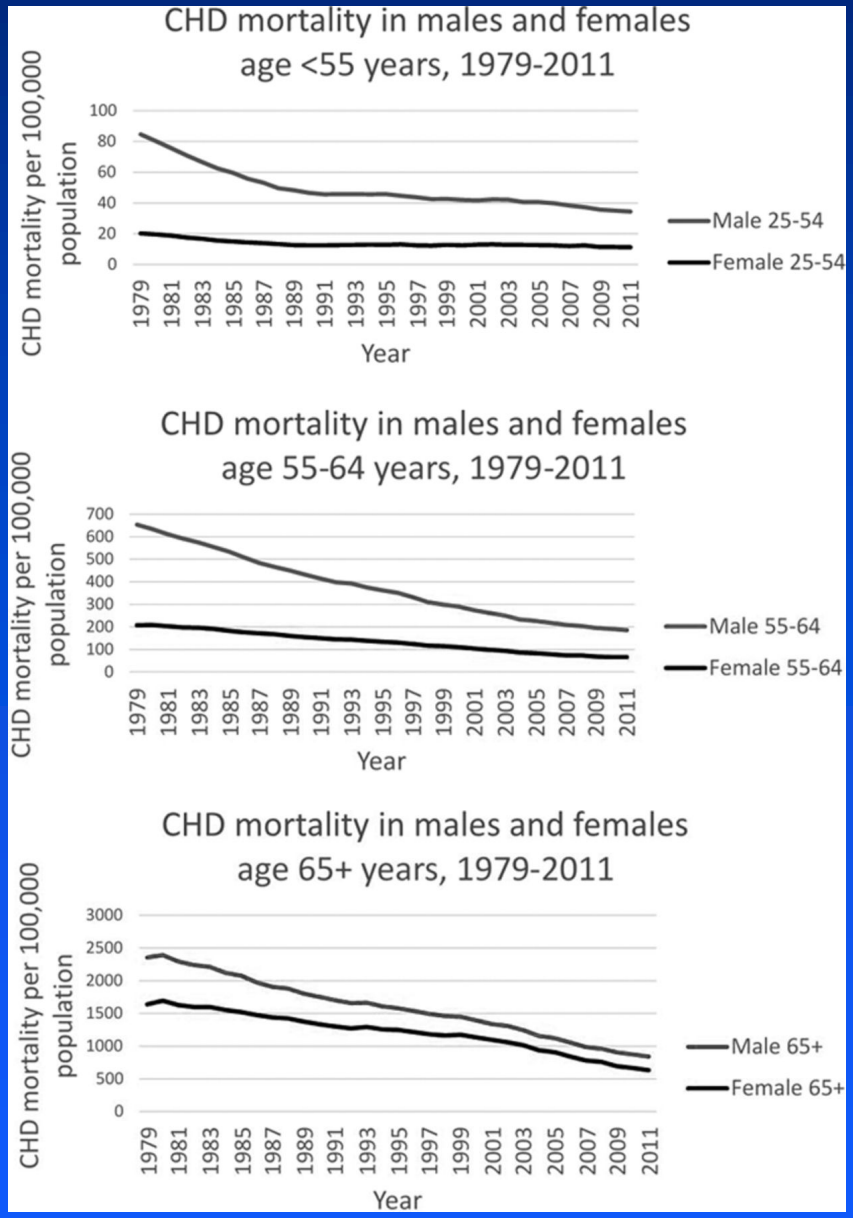
Article see p 997

Wilmot et al now build on our understanding of CVD mortality by highlighting recent trends in subpopulations, including young women, and those trends are troubling. These

did women in comparison within age groups <65 years. For example, women <55 years had the lowest decline in CHD mortality. Furthermore, when stratified by race, whites exhibited greater rates of decline than blacks. One bright note in the new data is that the disparity in CHD mortality between men and women in the earlier decades, before 2002, has narrowed in the most recent decade, because young women and men showed a similar declining trend, despite a low estimated annual percentage change.

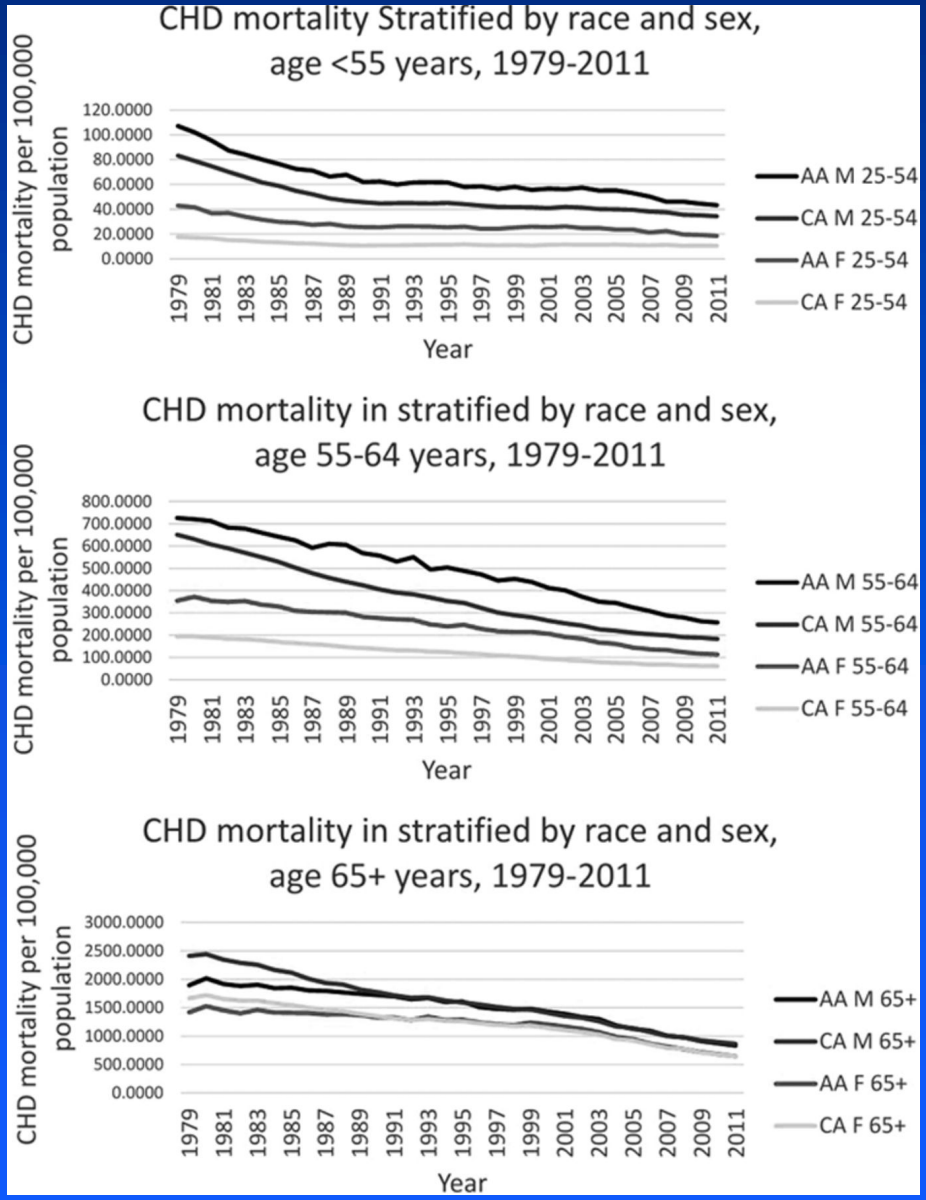
How Did We Get to Our Current Situation and Where Do We Need to Go Next?

Trends in age-specific coronary heart disease mortality rates



Kobina A. Wilmot et al. Circulation. 2015;132:997-1002

Trends in coronary heart disease (CHD) mortality rates.



Kobina A. Wilmot et al. Circulation. 2015;132:997-1002

Cardiovascular Disease Mortality Trends by Gender and Age

Table 2. CHD Mortality Rates and EAPC per Decade Among US Adults ≥25 Years, 1979 to 2011

	1979–1989			1990–1999			2000–2011		
	Mean Rate per 100 000	EAPC	95% CI	Mean Rate per 100 000	EAPC	95% CI	Mean Rate per 100 000	EAPC	95% CI
Age <55 y									
Men	64.2	–5.5	–6.4 to –4.6	45.4	–1.2	–2.3 to –0.2	39.1	–1.8	–2.8 to –0.7
Women	16.1	–4.6	–5.5 to –3.7	12.6	0.1	–1.7 to 1.9	12.3	–1.0	–3.1 to 1.0
Age 55–64 y									
Men	540.7	–3.7	–4.1 to –3.2	366.7	–4.0	–5.0 to –2.9	232.3	–3.9	–4.8 to –3.0
Women	187.6	–2.5	–3.6 to –1.4	135.3	–3.3	–4.4 to –2.1	85.3	–4.5	–5.9 to –3.2
Age ≥65 y									
Men	2113.3	–2.6	–4.0 to –1.3	1589.8	–2.1	–3.0 to –1.3	1121.2	–4.4	–5.5 to –3.4
Women	1539.3	–1.7	–3.3 to – 0.2	1242.9	–1.6	–2.7 to 0.4	898.0	–5.0	–6.3 to –3.7

CHD indicates coronary heart disease; CI, confidence interval; and EAPC, estimated annual percentage change.

Wilmot KA. Circ 2015;132:997.

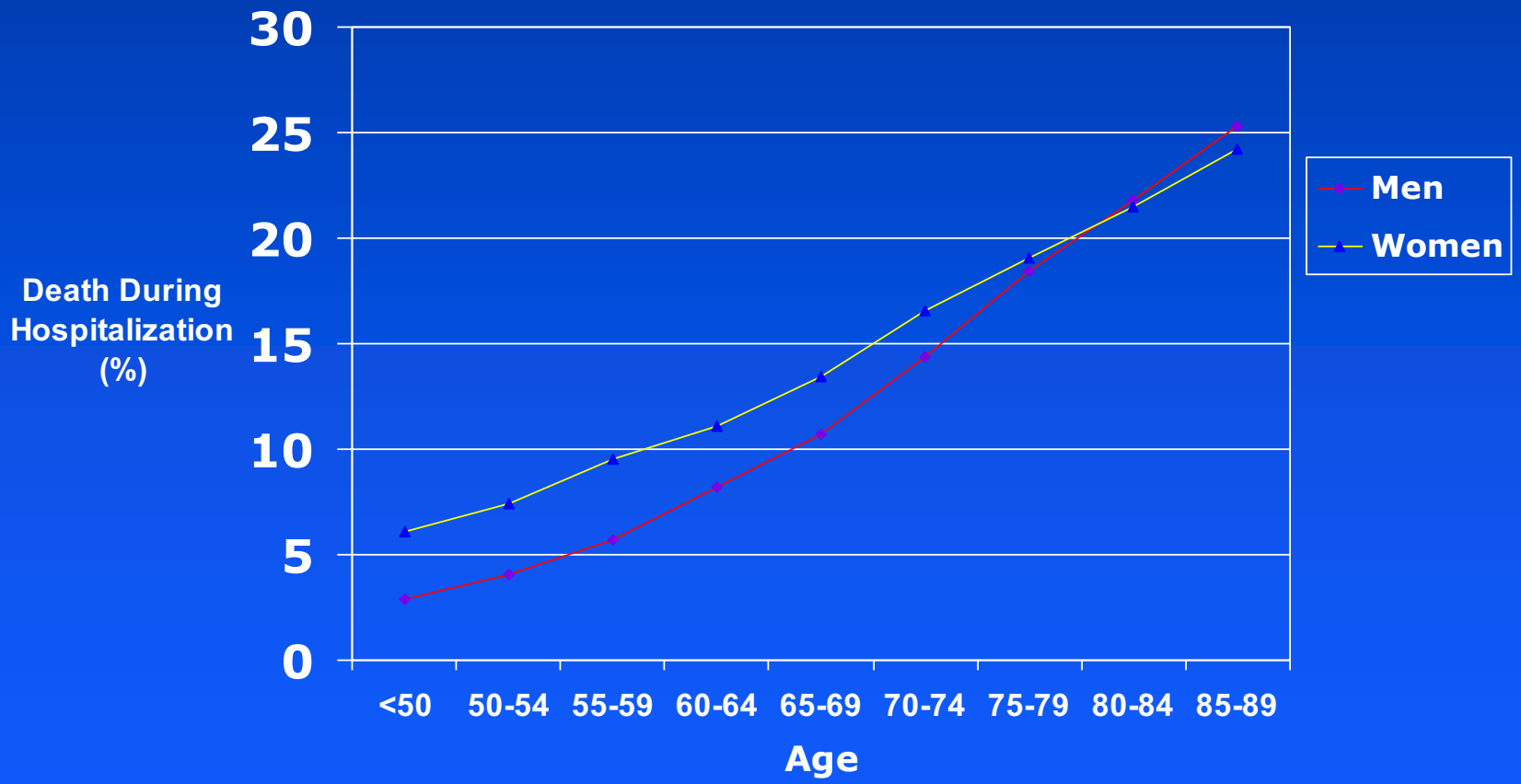
Trends

- CVD mortality has declined by 50% in both men and women BUT
- Actual increase in mortality in younger women
  - Ford ES JACC 2007;50:2128

Acute MI Mortality by Age and Sex

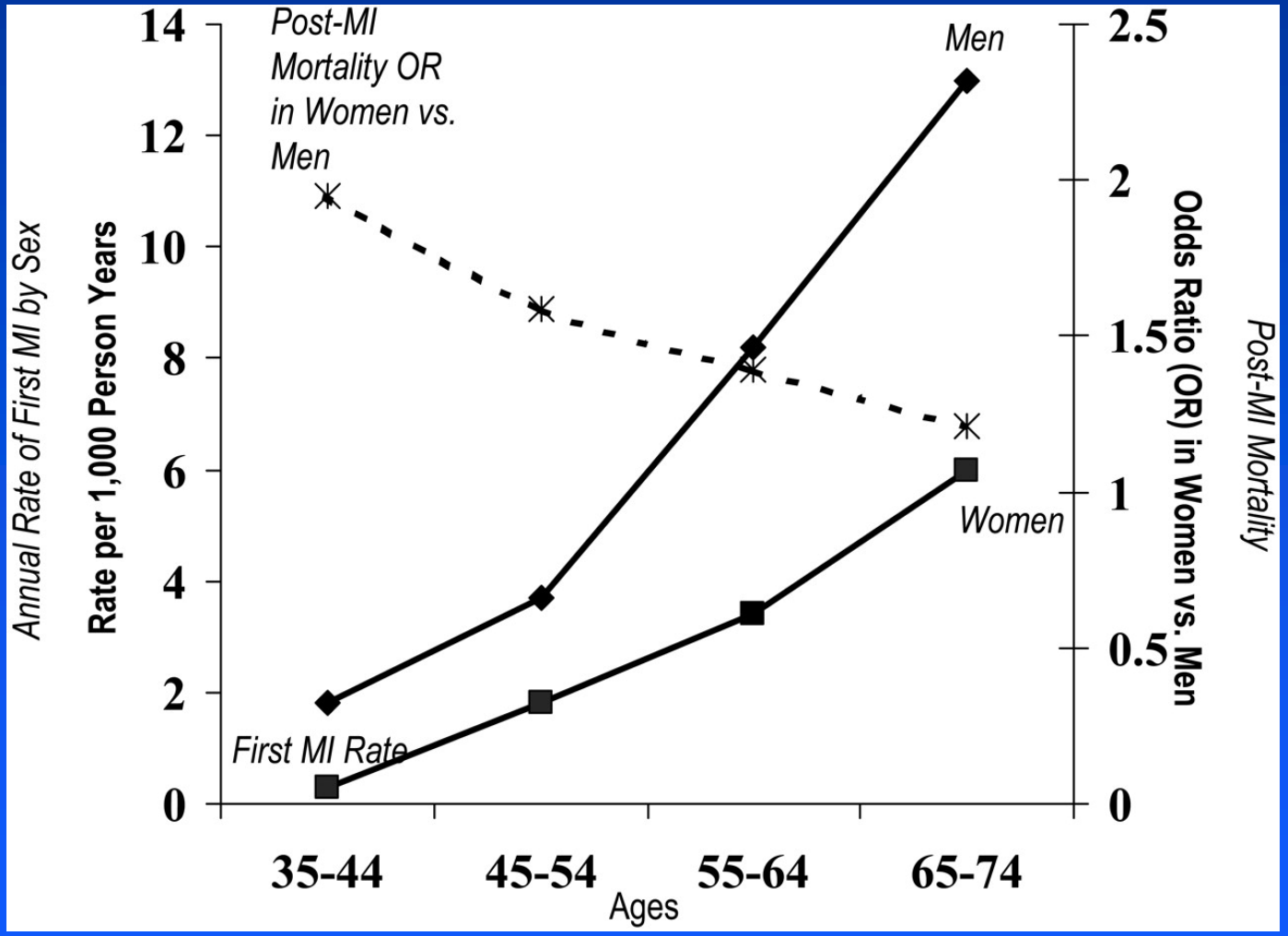
- Biological Factors
- Differences in social and economic supports
- Variation in compliance with medications
- Depression
- Inability to stop smoking

Acute MI Mortality: Age and Sex



Adapted from Vaccarino 1999

Relative Risk of Death Highest at Youngest Age



Bairey Merz, C. N. et al. J Am Coll Cardiol 2006;47:S21-29S

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PRACTICE GUIDELINE

Effectiveness-Based Guidelines for the Prevention of Cardiovascular Disease in Women—2011 Update

A Guideline From the American Heart Association

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Effectiveness (benefits and risks) vs efficacy (benefits) of prevention interventions

High risk

At risk

Ideal risk

Table 2. Classification of CVD Risk in Women

Risk Status	Criteria
High risk (≥1 high-risk states)	Clinically manifest CHD
	Clinically manifest cerebrovascular disease
	Clinically manifest peripheral arterial disease
	Abdominal aortic aneurysm
	End-stage or chronic kidney disease
	Diabetes mellitus
	10-y Predicted CVD risk ≥10%
At risk (≥1 major risk factor[s])	Cigarette smoking
	SBP ≥120 mm Hg, DBP ≥80 mm Hg, or treated hypertension
	Total cholesterol ≥200 mg/dL, HDL-C <50 mg/dL, or treated for dyslipidemia
	Obesity, particularly central adiposity
	Poor diet
	Physical inactivity
	Family history of premature CVD occurring in first-degree relatives in men <55 y of age or in women <65 y of age
	Metabolic syndrome
	Evidence of advanced subclinical atherosclerosis (e.g., coronary calcification, carotid plaque, or thickened IMT)
	Poor exercise capacity on treadmill test and/or abnormal heart rate recovery after stopping exercise
	Systemic autoimmune collagen-vascular disease (e.g., lupus or rheumatoid arthritis)
	History of preeclampsia, gestational diabetes, or pregnancy-induced hypertension
Ideal cardiovascular health (all of these)	Total cholesterol <200 mg/dL (untreated)
	BP <120/<80 mm Hg (untreated)
	Fasting blood glucose <100 mg/dL (untreated)
	Body mass index <25 kg/m^2
	Abstinence from smoking
	Physical activity at goal for adults >20 y of age: ≥150 min/wk moderate intensity, ≥75 min/wk vigorous intensity, or combination
	Healthy (DASH-like) diet (see Appendix)

CVD indicates cardiovascular disease; CHD, coronary heart disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C; high-density lipoprotein cholesterol; IMT, intima-media thickness; BP, blood pressure; and DASH, Dietary Approaches to Stop Hypertension.

Mosca JACC 2011

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Mosca JACC 2011

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Mosca JACC 2011

WHI: validation of risk stratification in 161,808 women age 50-79, 8yrs

Groups	MI/cad death	+ CVA
11% high risk	12.5%	19%
72% at risk	3.1%	5.5%
4% optimal risk	1.1%	2.2%
13% no CRF	1.3%	2.6%

- Hsia J Circ CV Qual Outcomes 2010;3(2):128

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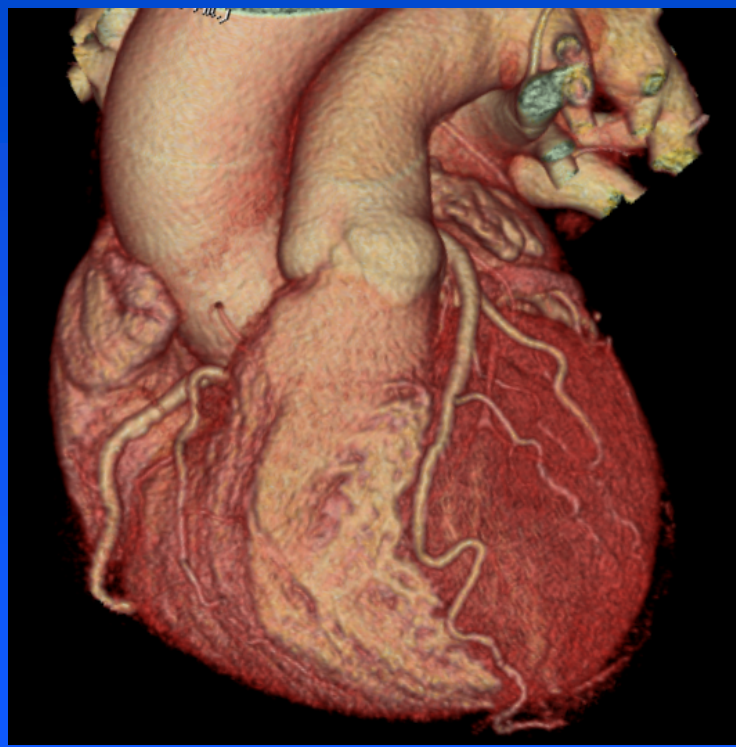
Evaluation of Women

Risk Factors

- Age
- Family history
- Personal history of CVD
- Peripheral vascular disease
- Tobacco*
- Hypertension*
- Lipids*
- Diabetes Mellitus*



NCEP, ACC, AHA guidelines

Smokers present two decades earlier:
Age of First MI

Women:

Nonsmokers age 79

Smokers age 60

Men:

Nonsmokers age 71

Smokers age 64

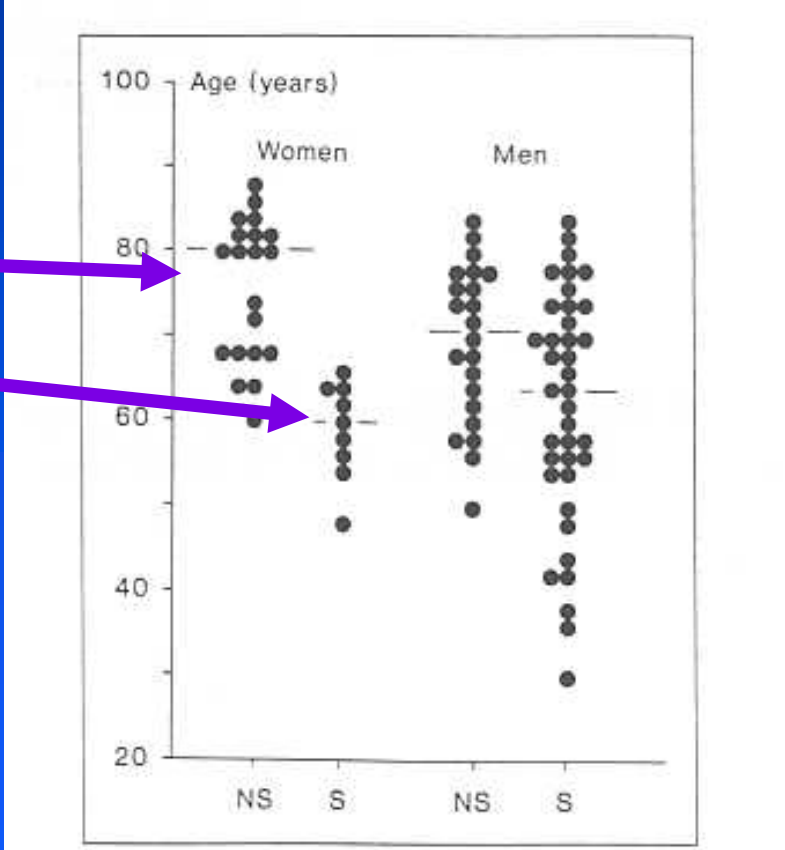


FIGURE 2. Age at time of first acute myocardial infarction for male and female nonsmokers (NS) and smokers (S). *Bars* denote median values.

Prescott, BMJ 1998

Tobacco in Women

- 20% of women in U.S. smoke
  - Worse for lower SEC, education
- Cessation rates have declined more slowly in women c/w men
- 50% of MI in middle aged women are attributable to smoking
  - Worse in premenopausal women
- 1 to 4 cigarettes/day = 2.5 x risk

NEJM 1995; 332: 1758-1766
Cleve Clin J Med 1998; 65: 464-469 Go Circ 2013

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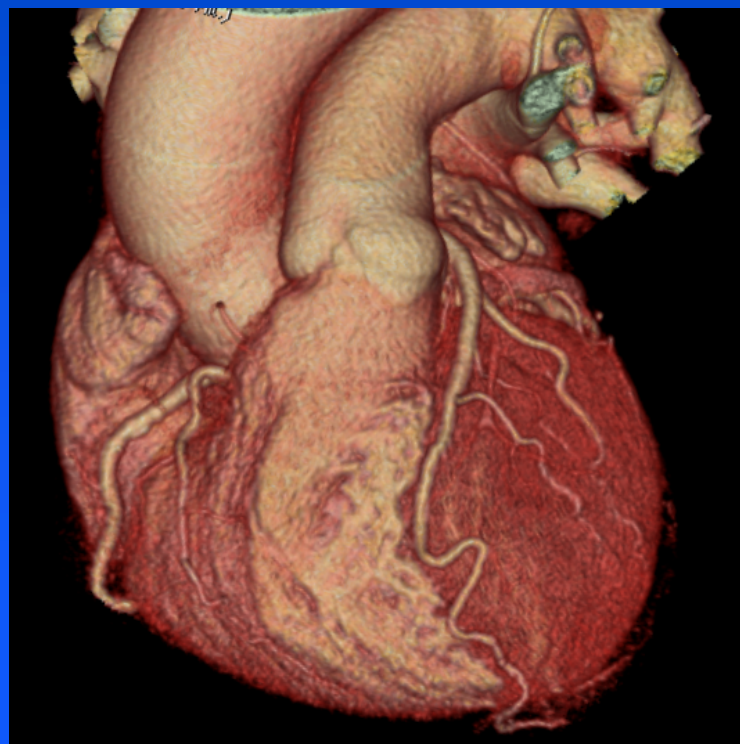
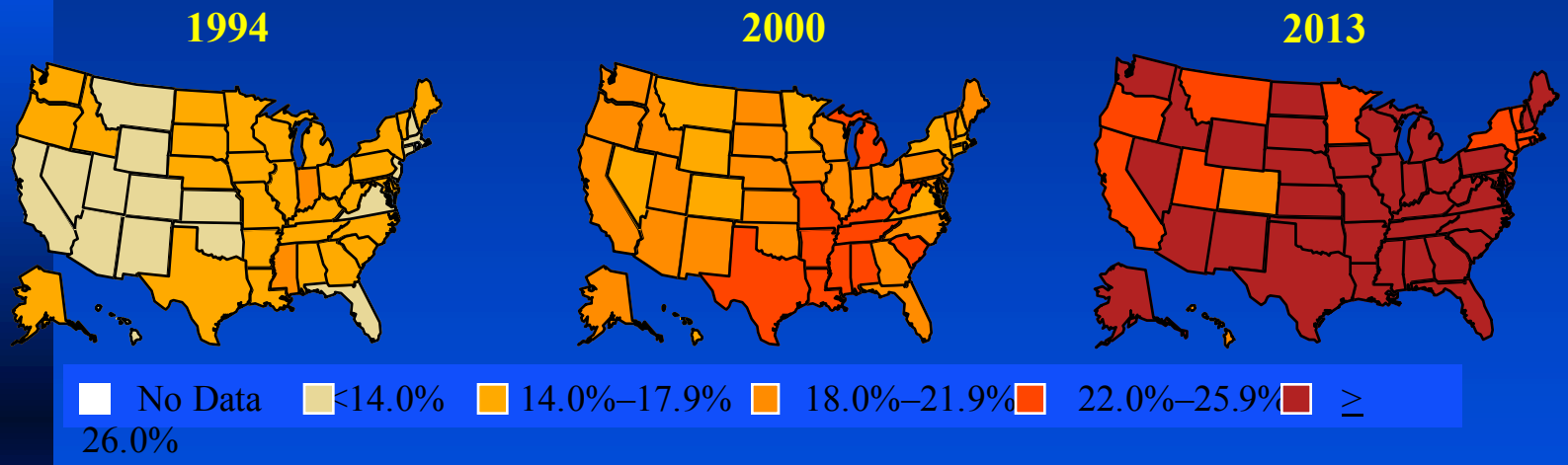


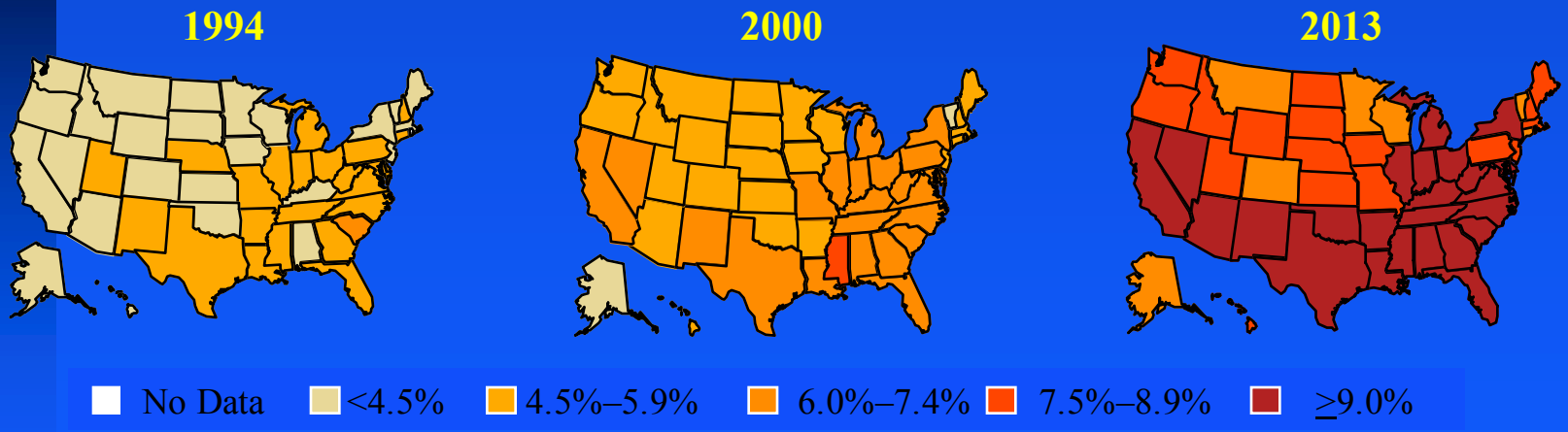
NCEP, ACC, AHA guidelines

Age-adjusted Prevalence of Obesity and Diagnosed Diabetes Among US Adults

Obesity (BMI ≥30 kg/m^2)



Diabetes



CDC's Division of Diabetes Translation. National Diabetes Surveillance System available at http://www.cdc.gov/diabetes/statistics

Diabetes in Women

- American women with Diabetes, increasing
  - HALF Preventable w/ diet/exercise
- 60-80% of mortality due to CVD
  - 68% *do not* consider CVD a possible complication
- Women 50% excess relative risk of CVD death
  - 450,000 pts Australia, (Huxley abstract 2005)
- Diabetes eliminates the female advantage

CDC, ADA, HHS

Evaluation of Women

Emerging Risk Factors

- Obesity and Sedentary lifestyle
- Psychosocial
- Pregnancy complications

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	Systemic autoimmune collagen-vascular disease (e.g., lupus or rheumatoid arthritis)
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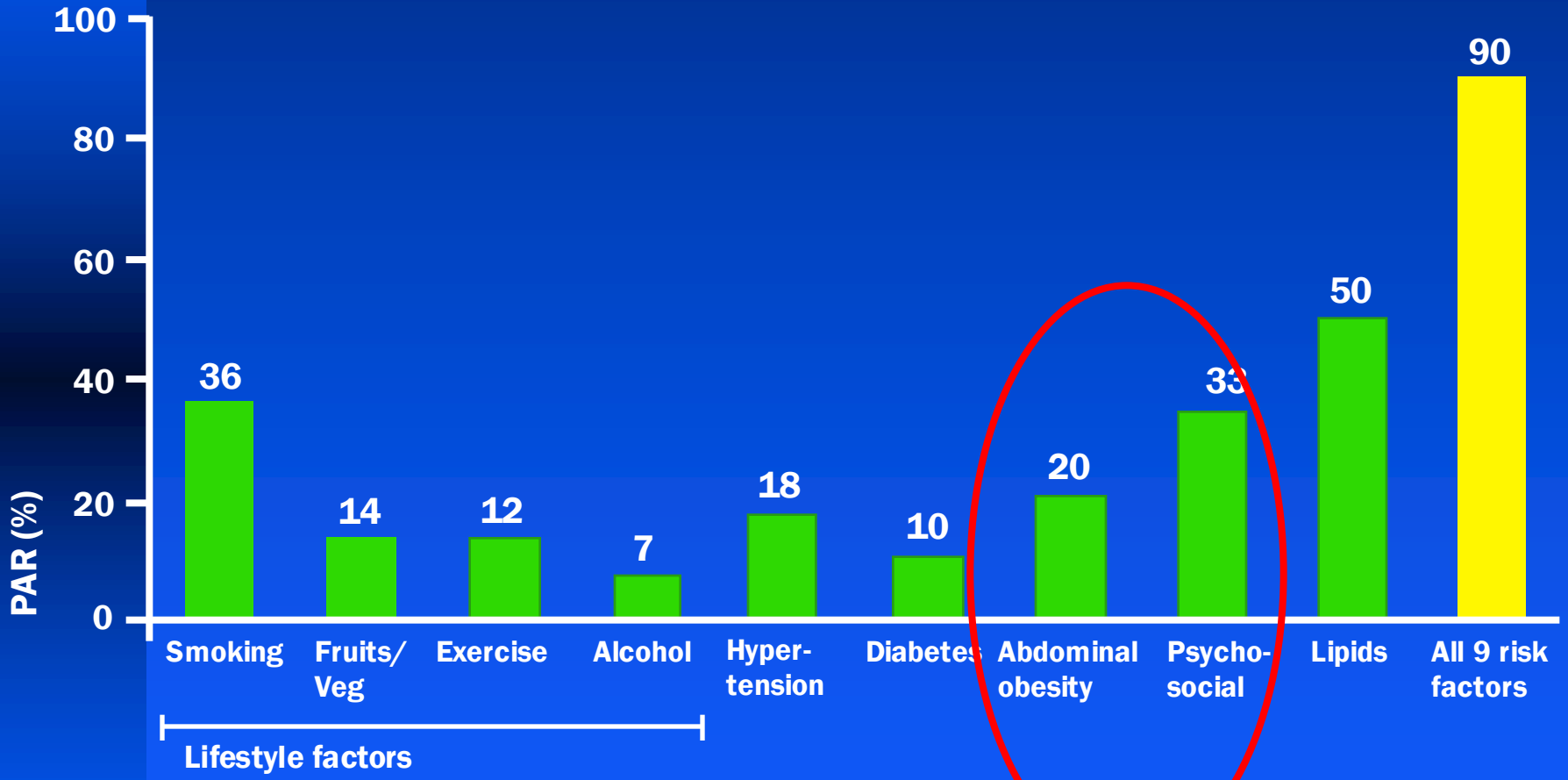
Mosca JACC 2011

Attributable Risk Factors for a First Myocardial Infarction

INTERHEART Study



n=15,152 patients and 14,820 controls in 52 countries

MI=Myocardial infarction, PAR=Population attributable risk (adjusted for all risk factors)

Source: Yusuf S et al. *Lancet*. 2004;364:937-952

Obesity in Women

- AHA/NIH
  - Overwt BMI 25-29
  - Obesity BMI >30
- Central obesity
- Women increase weight 5-10 lbs every 10 yrs
- 1 kg increment in BMI = 12% incrd risk

Framingham, CDC, AHA data

Definition of Metabolic Syndrome

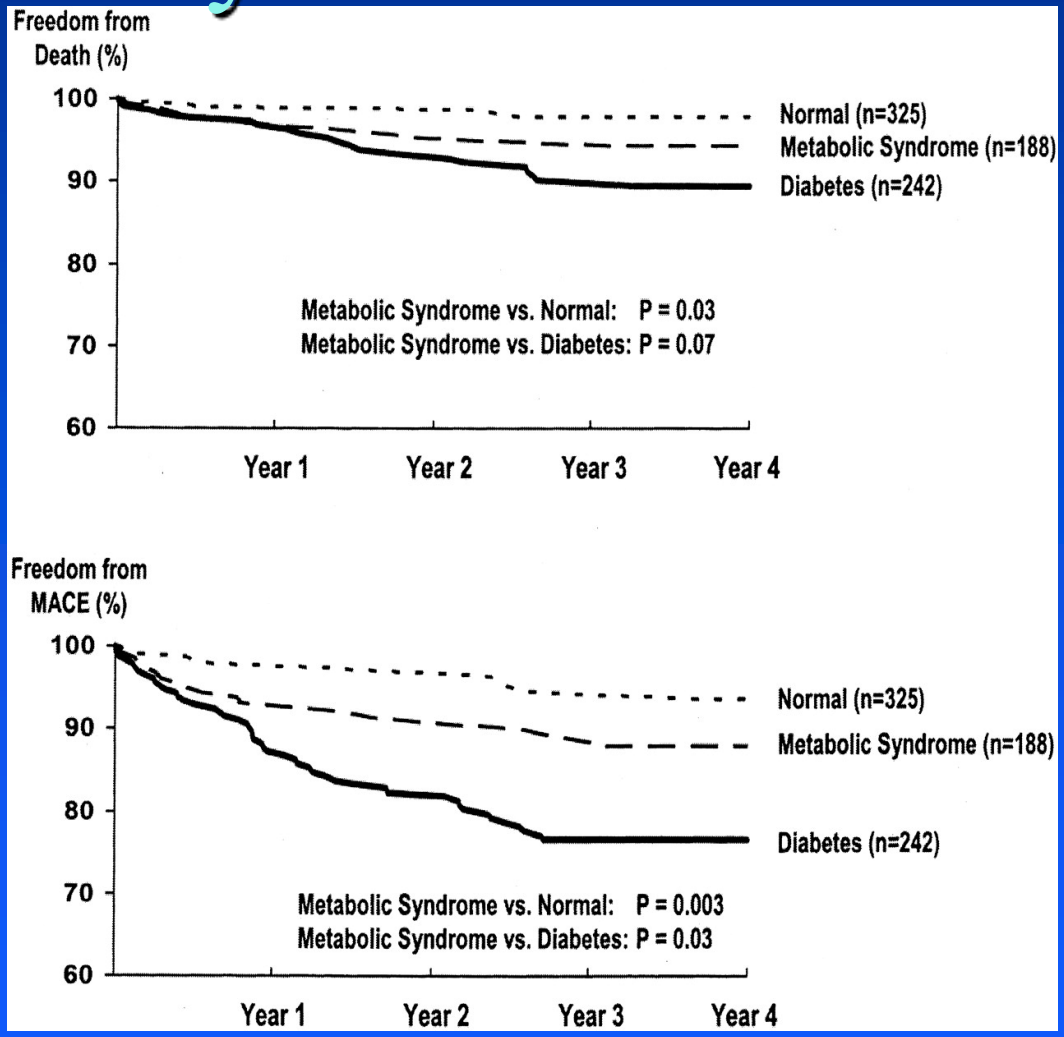
Three of Five Criteria:

- Abd obesity - waist circumference > 35 in.
- High triglycerides ≥ 150mg/dL
- Low HDL cholesterol < 50mg/dL
- Fasting glucose ≥ 100mg/dL
- Elevated BP ≥ 130/85mm Hg

***Greater loss of physical functioning contributes to greater wt gain, insulin resistance and HTN**

Grundy SM et al. AHA/NHLBI. Circ 2005 and Shaw et al. JACC 2006

Diabetes and Metabolic Syndrome in Women



Shaw, L. J. et al. J Am Coll Cardiol 2006;47:S4-20S

Psychosocial Stress

- Women with no history of CHD:
  - Depression is an independent predictor of death
    - Nurses Health Study Arch 2004;164:289
- Women with CHD:
  - marital stress was associated with 3-fold increased risk of recurrent CHD events
  - Living alone and work stress did not significantly increase recurrent CHD events
    - Orth-Gomer K. JAMA 2000; 283:3008-3014.

Complications of Pregnancy predict higher risk of CVD

- Preeclampsia 6-8% of pregnancy
  - More common due to obesity and older age
  - 4x increased risk of HTN
  - 2x increased risk of iHD, CVA, DVT
- Stillbirths 2.5x increased risk of MI
- Miscarriage 40% increased risk of MI
  - recurrent (>3) had 5x increased risk of MI
  - No association with CVA

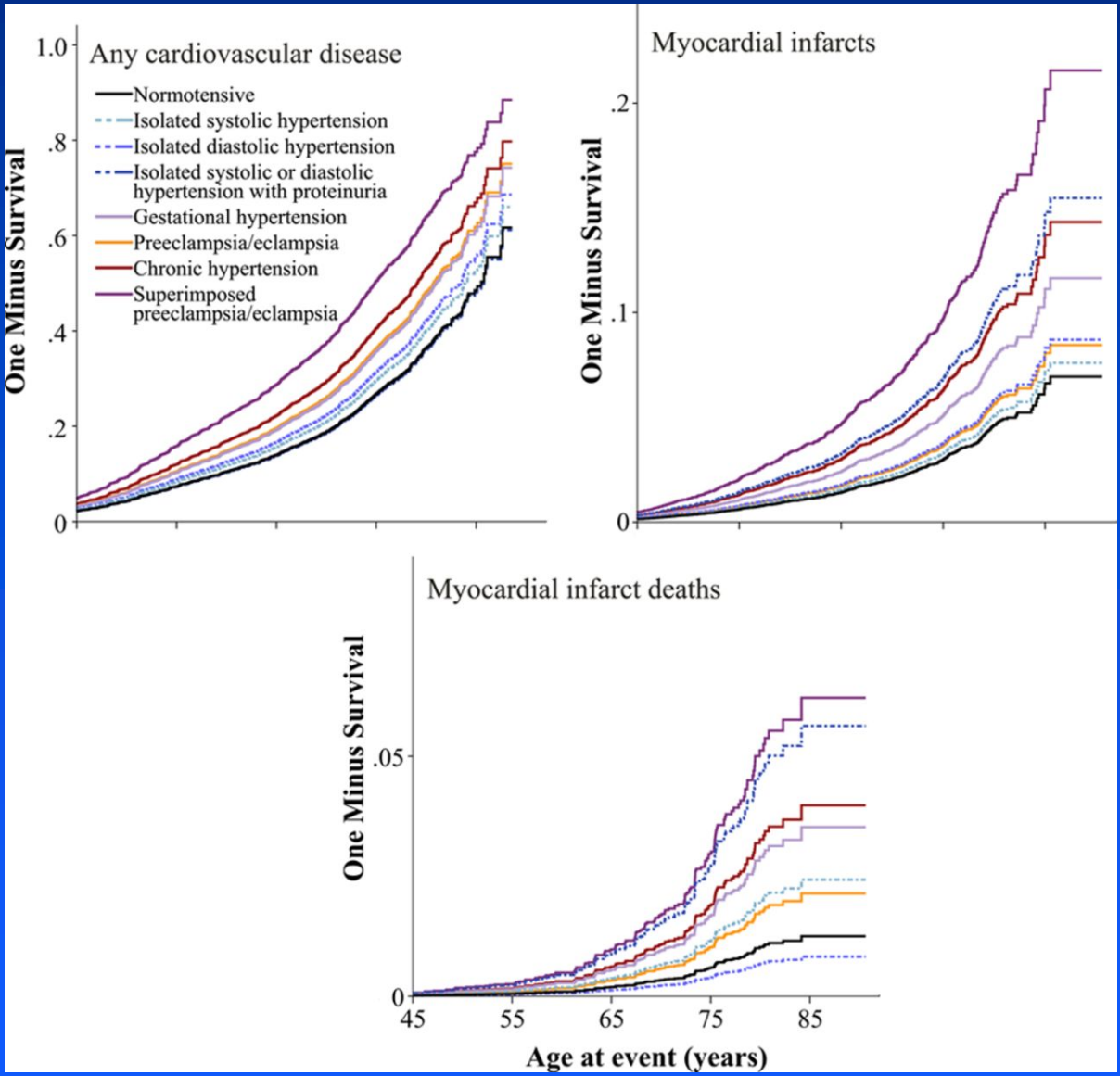
Bellamy BMJ 2007, NHLBI workshop 2010, Kharazmi Heart 2011

Any elevated BP in Pregnancy predicts higher risk of CVD

- Prospective Finish cohort 10,314 women
- 40 years of followup and able to adjust for confounding risk factors
- Increased risk of ischemic HD, MI, MI death, heart failure, stroke. HR=1.4-3.0

Männistö T et al. Circulation 2013;127:681-690

1-survival curves for total cardiovascular disease, myocardial infarcts, and myocardial infarct deaths with hypertension during pregnancy.



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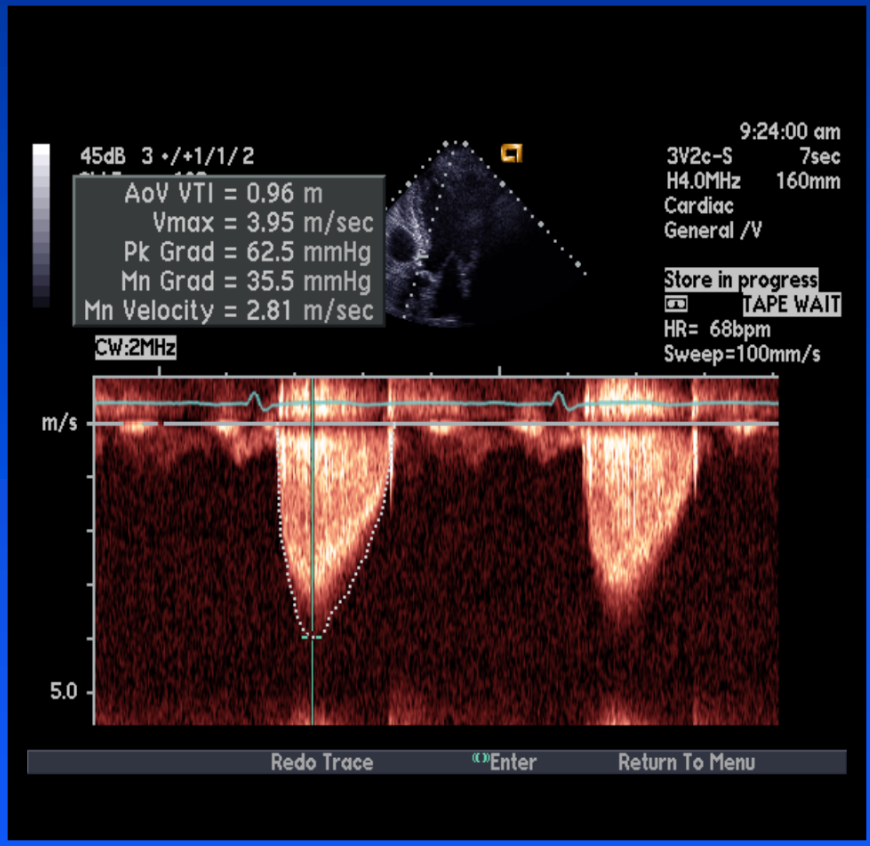
Aortic Stenosis and women

- Prevalence with age
  - Age 75 = 1%,
  - Age 86 = 6%
- By gender.
  - Women= 8.8%
  - Men =3.6%
- Cardiac remodeling and fibrosis differs
  - Men: Collagen and matrix metalloproteinase expression

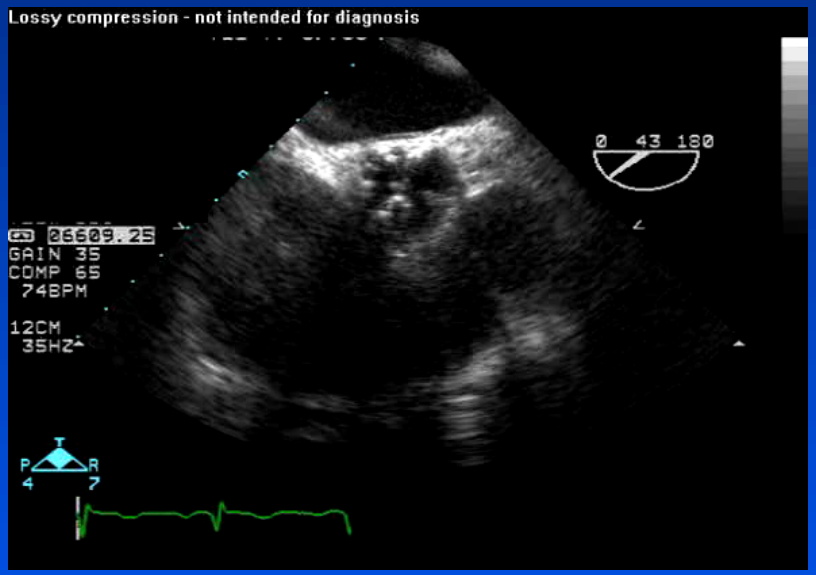


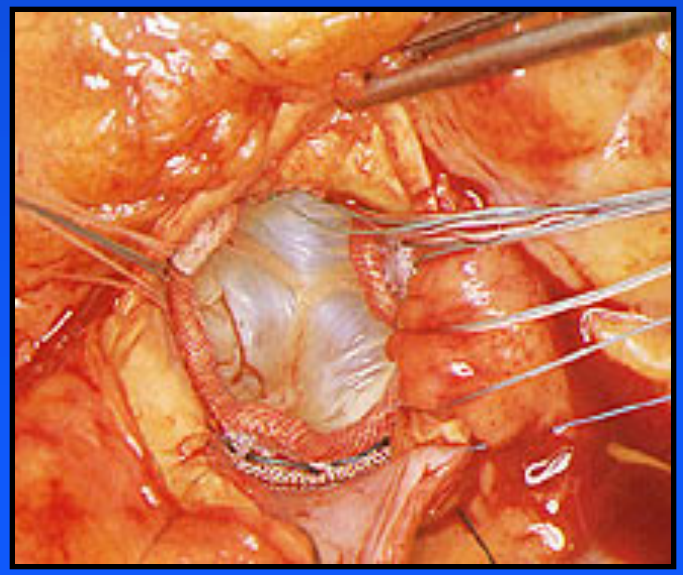
AJC ’96, JACC ’93

Women and Aortic Valve Replacement

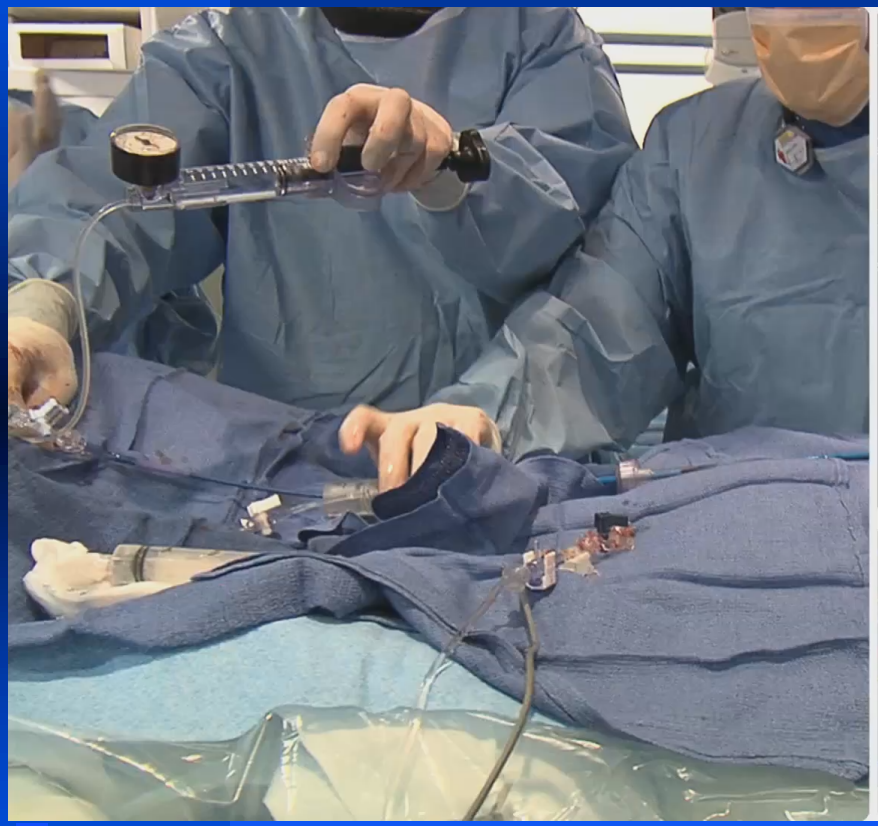
Patient-prosthesis mismatch

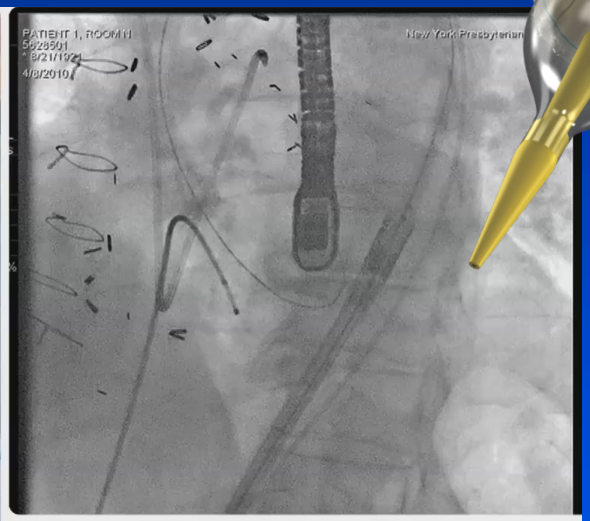
- Smaller annulus/ prosthesis
- Higher transvalvular grad
- Increased periop and longterm morbidity & mortality

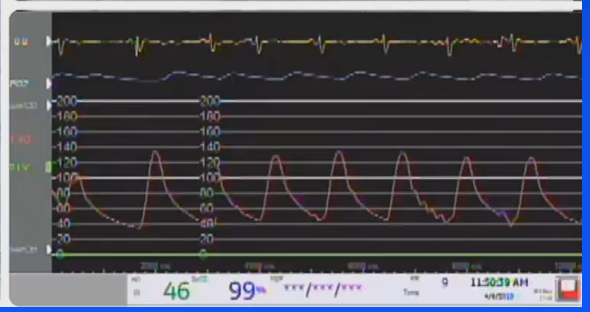


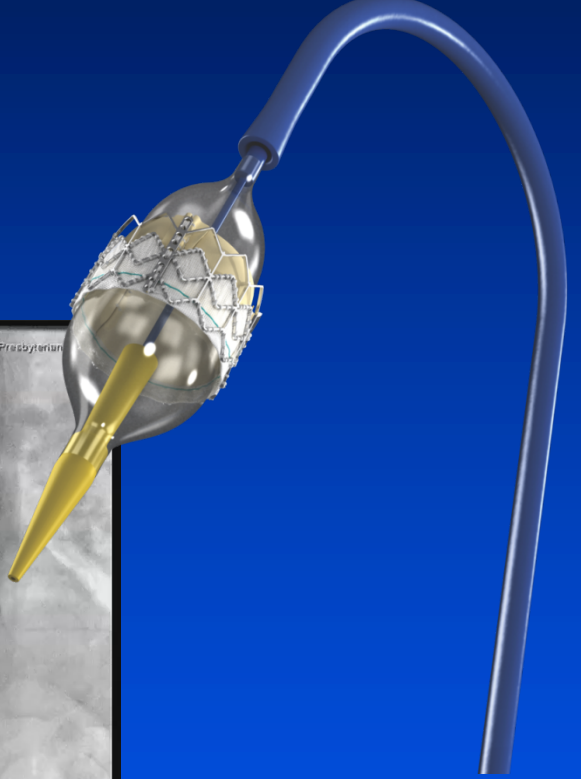


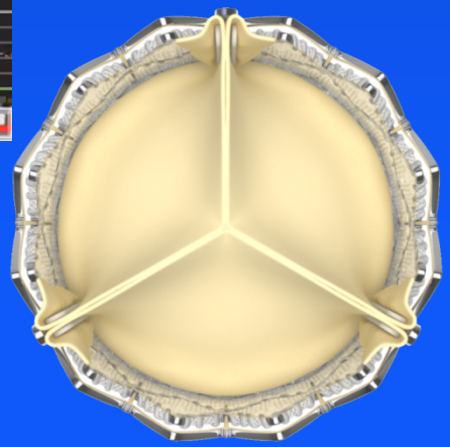
Percutaneous valve











TAVR vs sAVR in Women

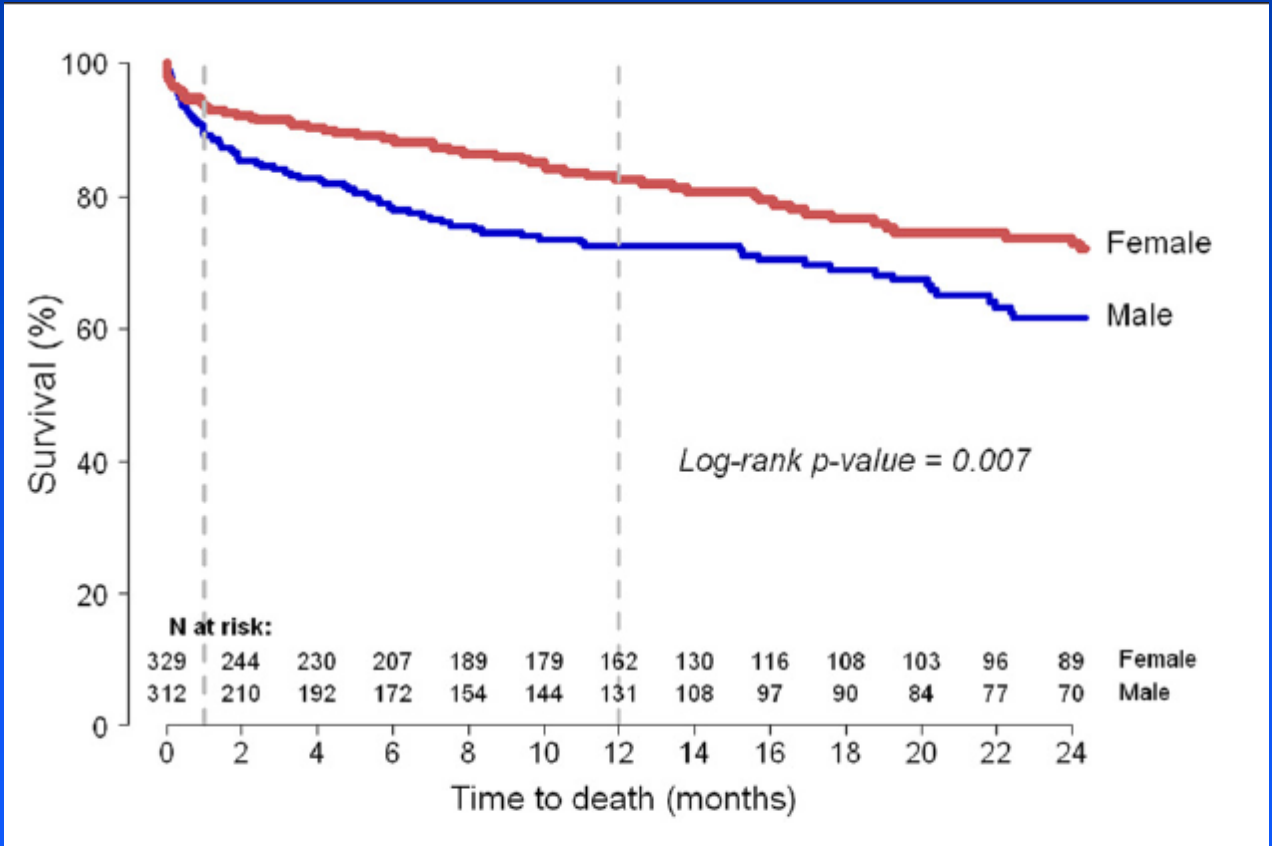
- Partner A: women with better unadj outcomes
- 2000 registry pts, female sex was indep pred:
  - sAVR: 30d mortality adj OR 2.34
  - TAVR: mjr vascular complications
- Case-controlled study Italian NIH
  - 388 women propensity matched of 5,231 patients
- Similar mortality differing complications
  - Vascular: 9.3% vs 0.5%
  - Stroke: 7.7% vs 2.5%
    - Onorati JTCS 2013, Onorati F ATS 2013;96:1336

TAVR: Men vs Women

- 2 Canadian centers, N= 641, 51% women
  - TA: 52% women, 38% men
  - Men more comorbidity
- Women increased complications:
  - Vascular: 12% vs 5%
  - Bleeding: 22% vs 16%
    - Humphries JACC 2012;60(10):882
- Women lower *adjusted* mortality
  - Similar to PARTNERS

TAVR: women with improved all cause mortality

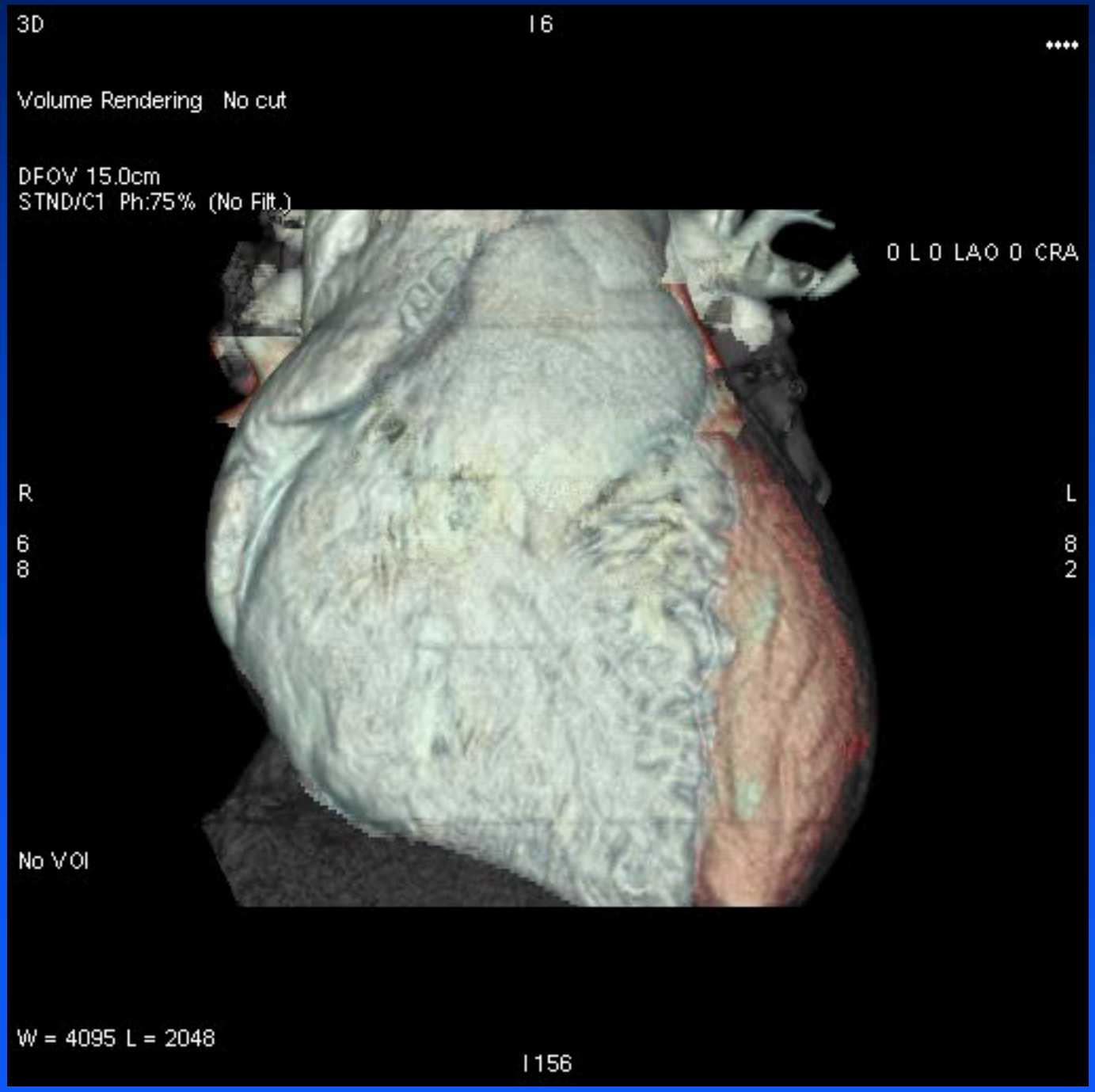
30 day adjusted OR 0.39 and 2 year 0.60 favored women



Humphries JACC 2012;60(10):882

Cardiovascular Disease in Women:

- Emerging Trends
  - Renew efforts in younger women
- Guidelines for women
  - Low, intermediate and high risk groups
- CAD: unique risk profile
  - Pregnancy complications confer increased risk
- Aortic stenosis and TAVR
  - Improved mortality but higher complications


3D
I 6
Volume Rendering No cut
DFOV 15.0cm
STND/C1 Ph:75% (No Filt.)
0 L 0 LAO 0 CRA
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8
8
2
No VOI
W = 4095 L = 2048
I 156

Case: 45yow with ACS

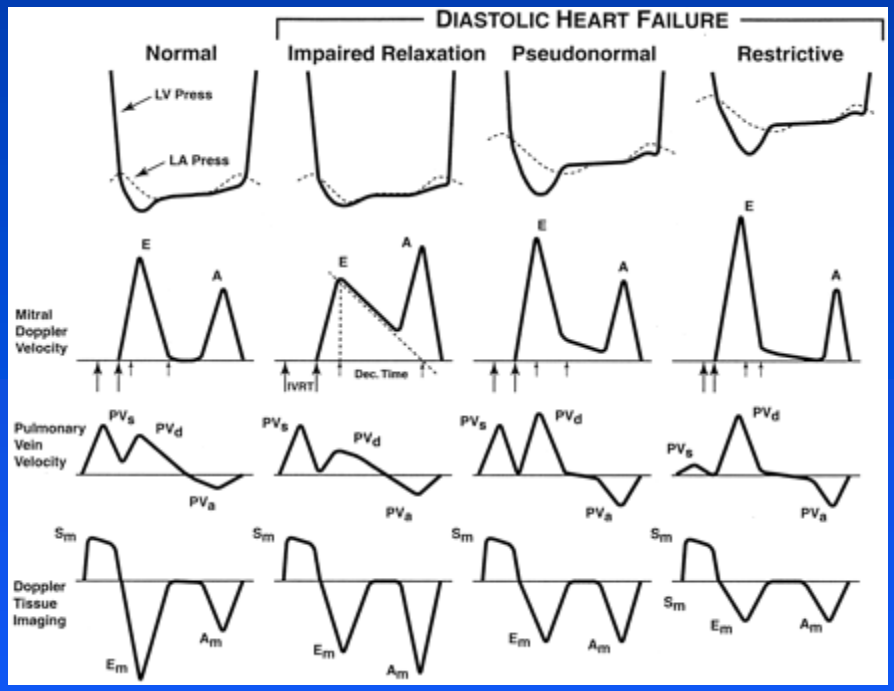
- PMHx: G2P2 → preeclampsia
- Meds: Vitamin E → Class III rec
- SHx: divorced, → Psychosocial stress
  quit tobacco 10yrs → Tobacco
- FHx: father MI age 54 → Family hx matters
- PE: 5'2", 160lbs, → Obese
  148/94, 90 → New HTN
- Labs: chol 220, HDL 35 → Low HDL

WHY NOT PREVENTED?

Thank you for your attention.

Women and Diastolic Dysfunction

- 40-50% of patients with CHF have nml LVEF
  - Vasan JACC '99
  - Grossman Circ '00
- Prevalence increases:
  - age
  - higher in women
- Etiology:
  - HTN/ LVH



Women and Diastolic Dysfunction

Hemodynamic Characteristics of Patient Groups

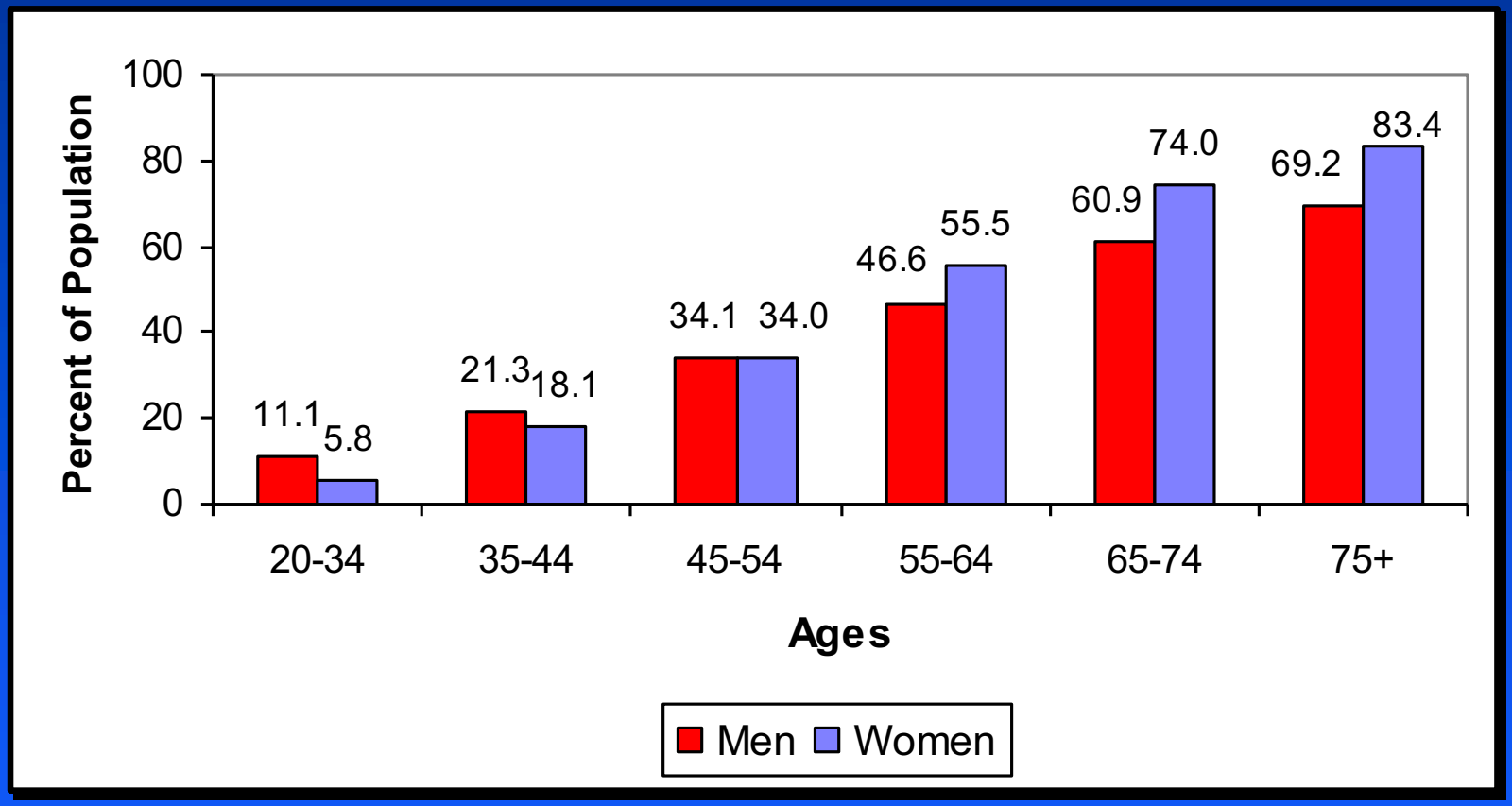
	CON-y (n=14)	CON-o (n=9)	CON-HTN (n=25)	HF-nlEF (n=10)	ANOVA *P*
Age, y	36±9.6	65±11.5*	68.8±7.9*	60.5±9.7*	<0.0001
Female sex, %	21	33	55	90	
Height, cm	171±9.2	163.4±9.3	165.6±8.0	162.5±9.3	0.13
Weight, kg	71.8±14.0	72.5±10.3	85.4±17.1†	79.9±11.2	0.03
Body surface area, m^2	1.81±0.18	1.83±0.2	2.00±0.22†	1.92±0.14	0.041
Diabetes mellitus, %	7	...	16	20	
Concurrent medications, %					
ACE/ARB	7	...	32	40	
Ca^+ channel blocker or β-blocker	50	33	60	70	
Diuretics	...	22	36	50	
Nitrates	21	33	...	10	
Heart rate, beats/min	79.2±11.9‡	80.3±23.3‡	62.6±8.7	82.5±14.1‡	0.0001
SBP, mm Hg	133.1±15.6	134.9±22.3	157.3±20.0§¶	167.2±20.5§¶	<0.0001
PP, mm Hg	52.9±12.1	59.7±16.2	76.5±13.6§¶	84.5±24.2§¶	<0.0001
Arterial resistance, dynes·s^{-1}·cm^{-5}	1456±513	1486±491	1880±450†	1872±441	0.024
EF, %	66.8±7.2	62.9±7.2	60.4±6.9	70.3±14.8‡	0.019
SV, mL	74.5±23.8	71.7±10.8	76.5±18.4	63.4±15.7	0.30
Wall thickness, cm	0.9±0.1	1.0±0.1	1.0±0.2	1.4±0.2*‡¶	<0.0001

Values are mean±SD unless otherwise indicated. CON-y indicates young (<50 years) normotensive controls; CON-o, age-matched (≥50 years) normotensive controls; CON-HTN, age-matched hypertensive controls; ACE/ARB, ACE inhibitors or angiotensin II receptor blockers; SBP, systolic blood pressure; PP, pulse pressure; EF, ejection fraction; and SV, stroke volume.

*$P \leq 0.0001$ vs CON-y; †$0.04 < P < 0.07$ vs CON-y; ‡$P < 0.05$ vs CON-HTN; §$P < 0.05$ vs CON-y; ¶$P < 0.05$ vs CON-o.

Kawaguchi M. Circ 2003.107:714

Hypertension is common



NHANES '99

Longer-term risk important for women

- 6329 pts age 20-79, NHNES '03-06
  - low 10 yr risk (<10%)
  - low lifetime (<39%) risk
  - High 10 yr risk (>10%) or DM
- More than half of adult Americans:
  - 10yr predicted risk of Coronary dz of <10%
  - BUT lifetime risk of cardiovascular dz >40%
    - Marma Ak. Circ CV Qual outcomes 2010;3:8-14

82% of adults are at low short term risk,
2/3 of this group are at high lifetime predicted risk for CV disease

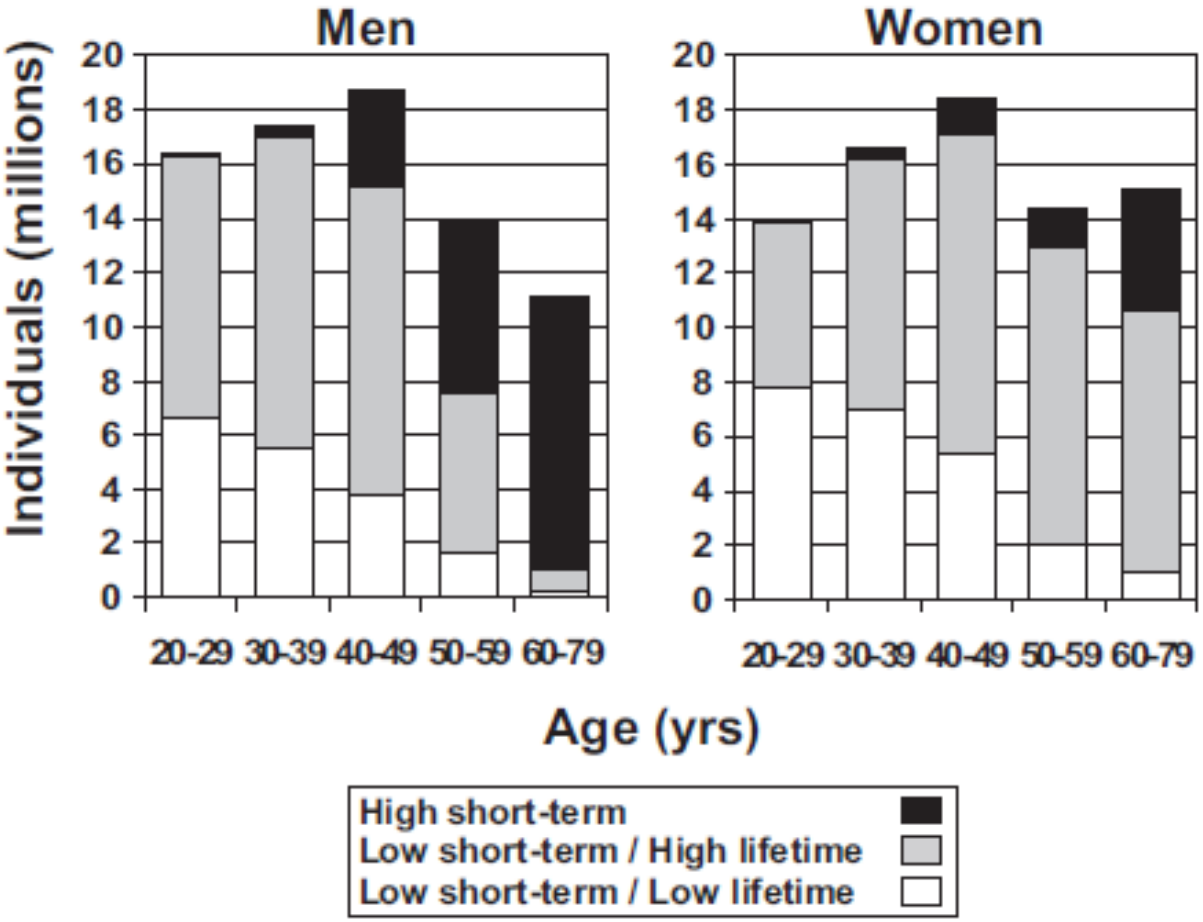
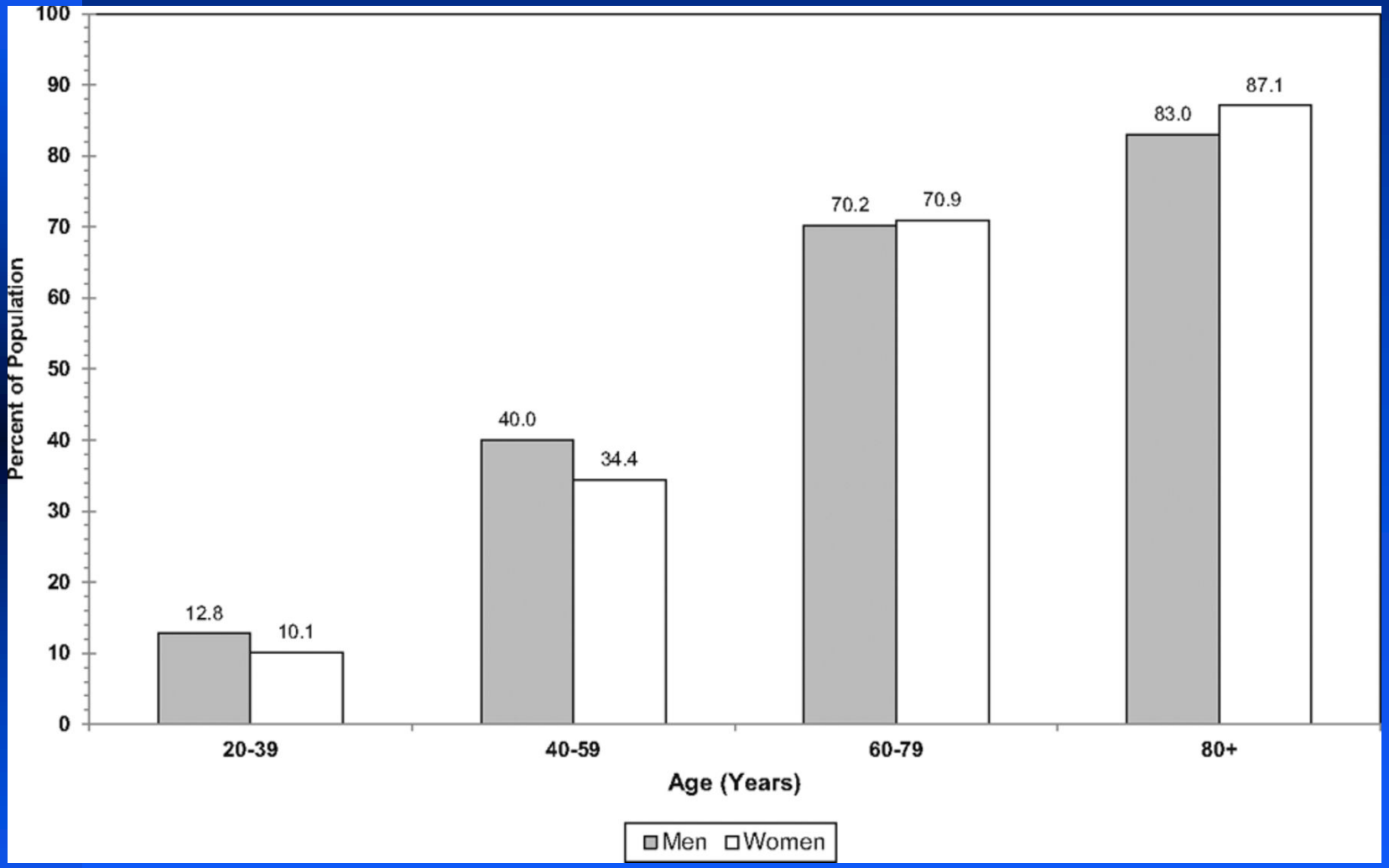


Figure 2. Sex- and age-specific population estimates of risk strata distribution among CVD-free, nonpregnant US adults ages 20 to 79 years. See Figure 1 for definitions.

Marma Ak. Circ CV Qual outcomes 2010;3:8-14

Prevalence of cardiovascular disease in adults ≥20 years by age and sex (National Health and Nutrition Examination Survey: 2007–2010).



Go A et al. Circulation 2013;127:e6-e245

American Heart Association
Learn and Live