

Evidence-Based Guidelines for Cardiovascular Disease Prevention in Women

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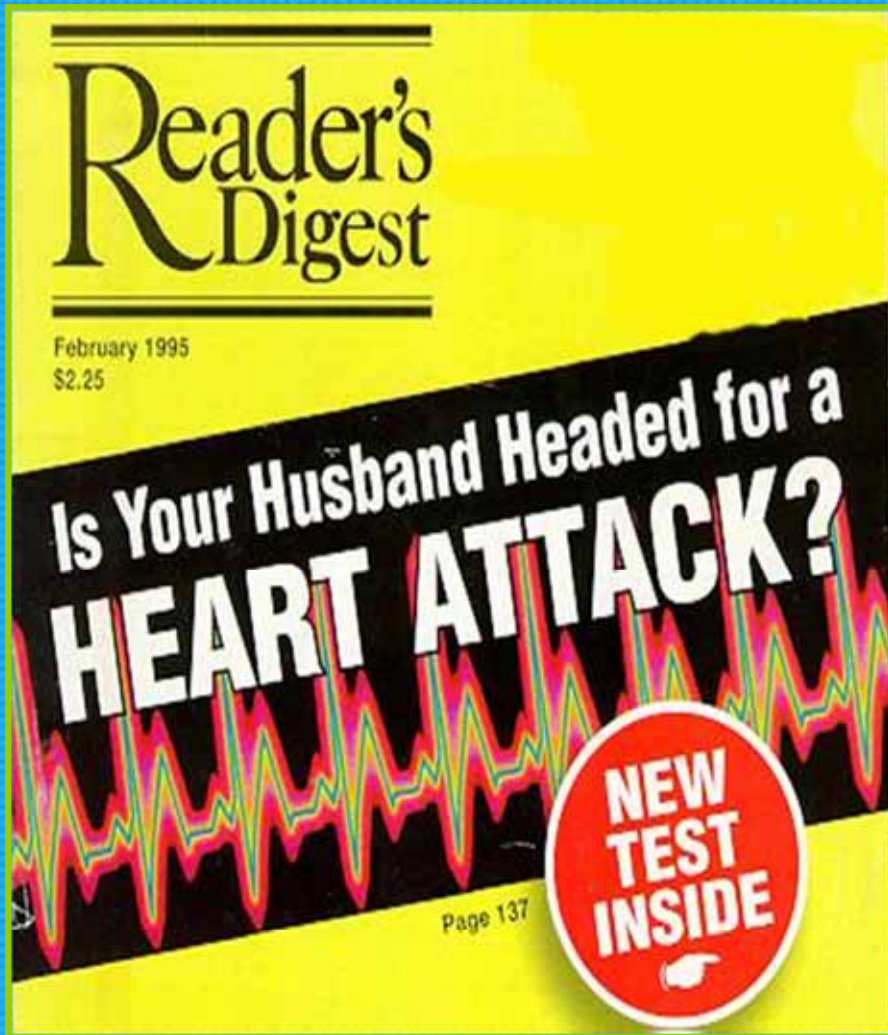
Interventional Cardiologist

&

Cardiac CT Angiography Specialist

Objectives

- **To present strategies to assess and stratify women into high risk, at risk, and optimal risk categories for cardiovascular disease**
- **To summarize lifestyle approaches to the prevention of cardiovascular disease in women**

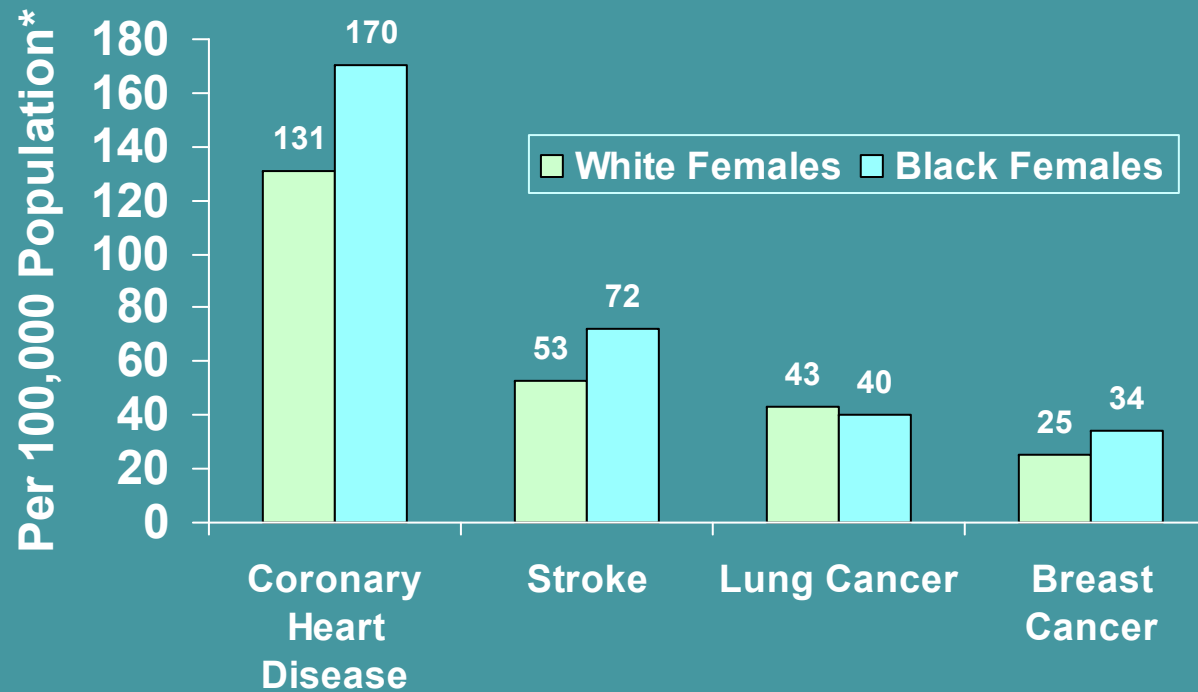


Objectives

- **To review evidence-based approaches to cardiovascular disease prevention for patients with hypertension, lipid abnormalities, and diabetes**
- **To review an evidence-based approach to pharmacological risk intervention for women at risk for cardiovascular events**

Death Rates for White and Black Females by Disease

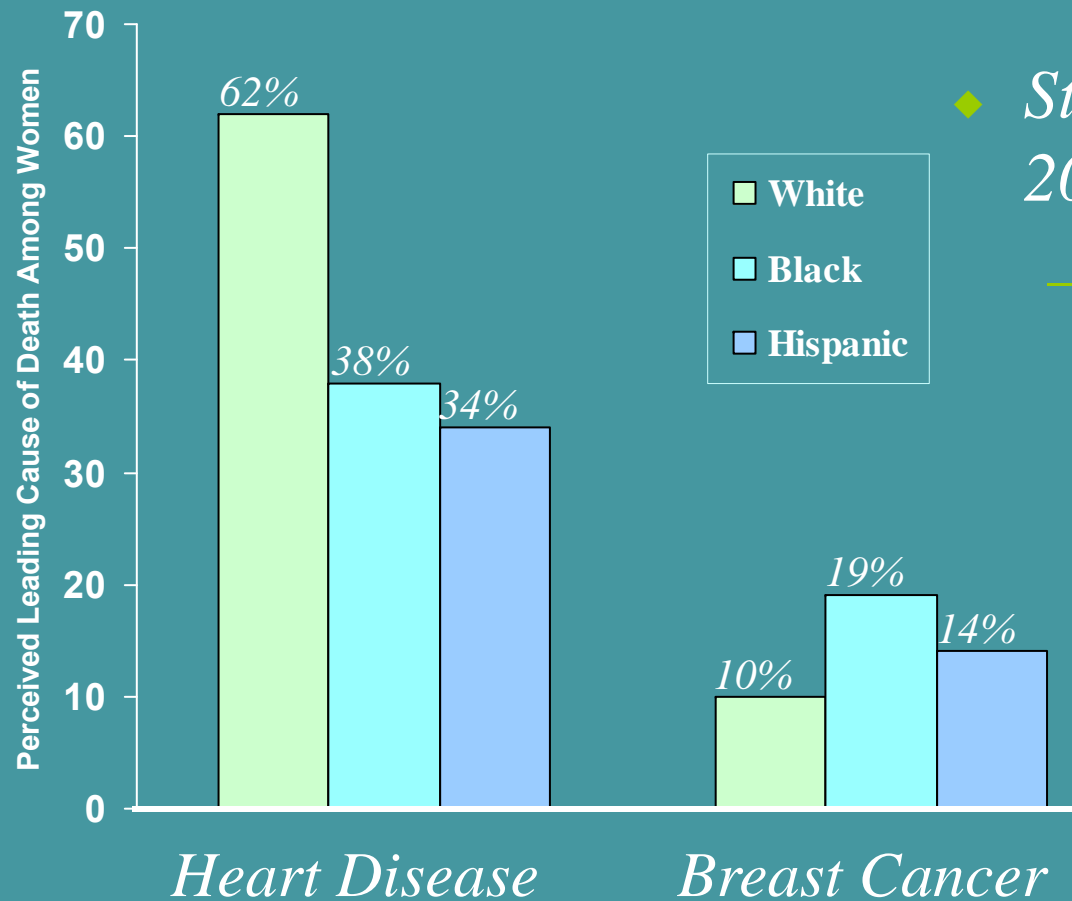
Age-Adjusted Death Rates, United States: 2002



**Numbers have been rounded.*

*American Heart Association. Heart Disease and Stroke Statistics—2005 Update.
Dallas, Tex: American Heart Association; 2005.*

Awareness of Leading Cause of Death in Women 2005



◆ *State of the Heart Report 2006:*

— *“Good news: death rates are down and awareness is up, but there are still gaps in care”*

• *Dr. Alice Jacobs, Past AHA President*

Objectives

- **To summarize commonly used therapies that should not be initiated for the prevention or treatment of heart disease, because they lack benefit, or because risks outweigh benefits**

Update on Gender-Specific Cardiovascular Research 2006

**Lessons from the Women's Ischemic
Syndrome Evaluation Trial (WISE)**

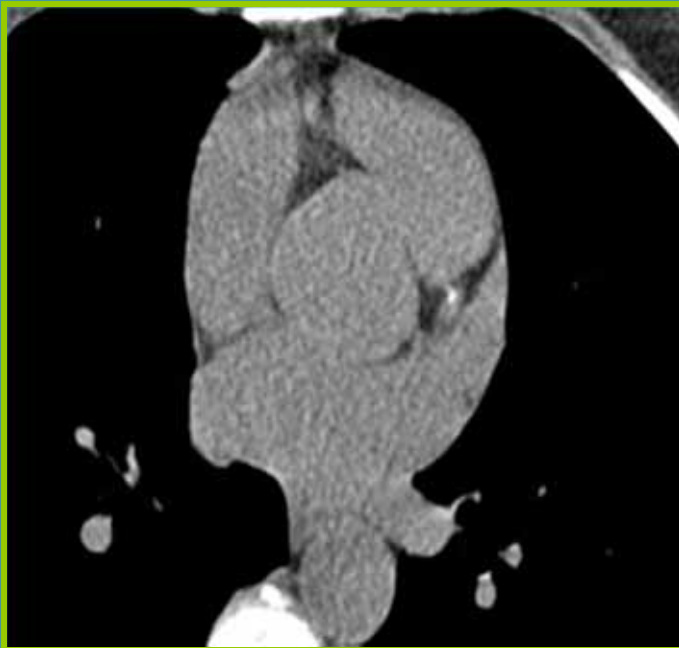


Decisive Findings From the WISE Study

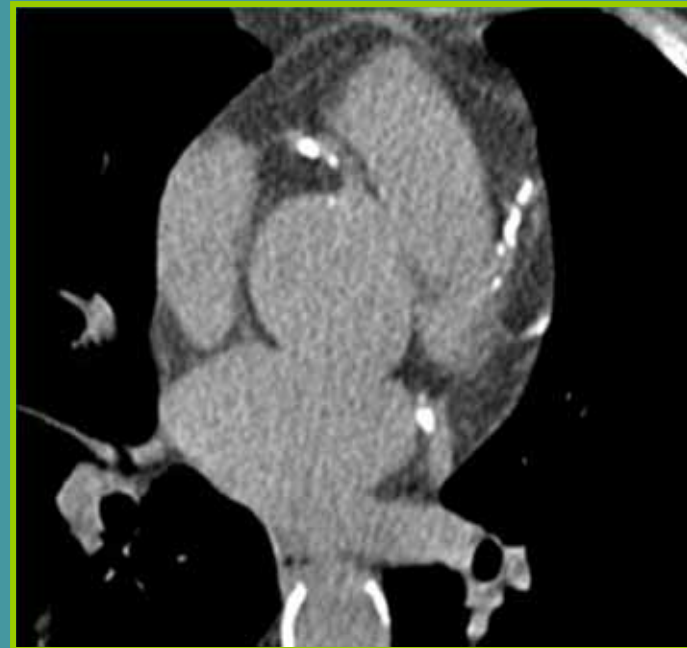
- **Approximately 50% of women referred for evaluation of ischemia do not have obstructive coronary disease**
 - Prognosis for these women is intermediate for future adverse cardiac events and persistent symptoms
- **Practitioners should no longer ignore nonobstructive coronary angiograms in women**
- **Practitioners should not call evidence of clear ischemia in this setting, such as a positive troponin or an abnormal stress perfusion test, a false positive**

Electron-Beam Computed Tomography

EBCT Scans

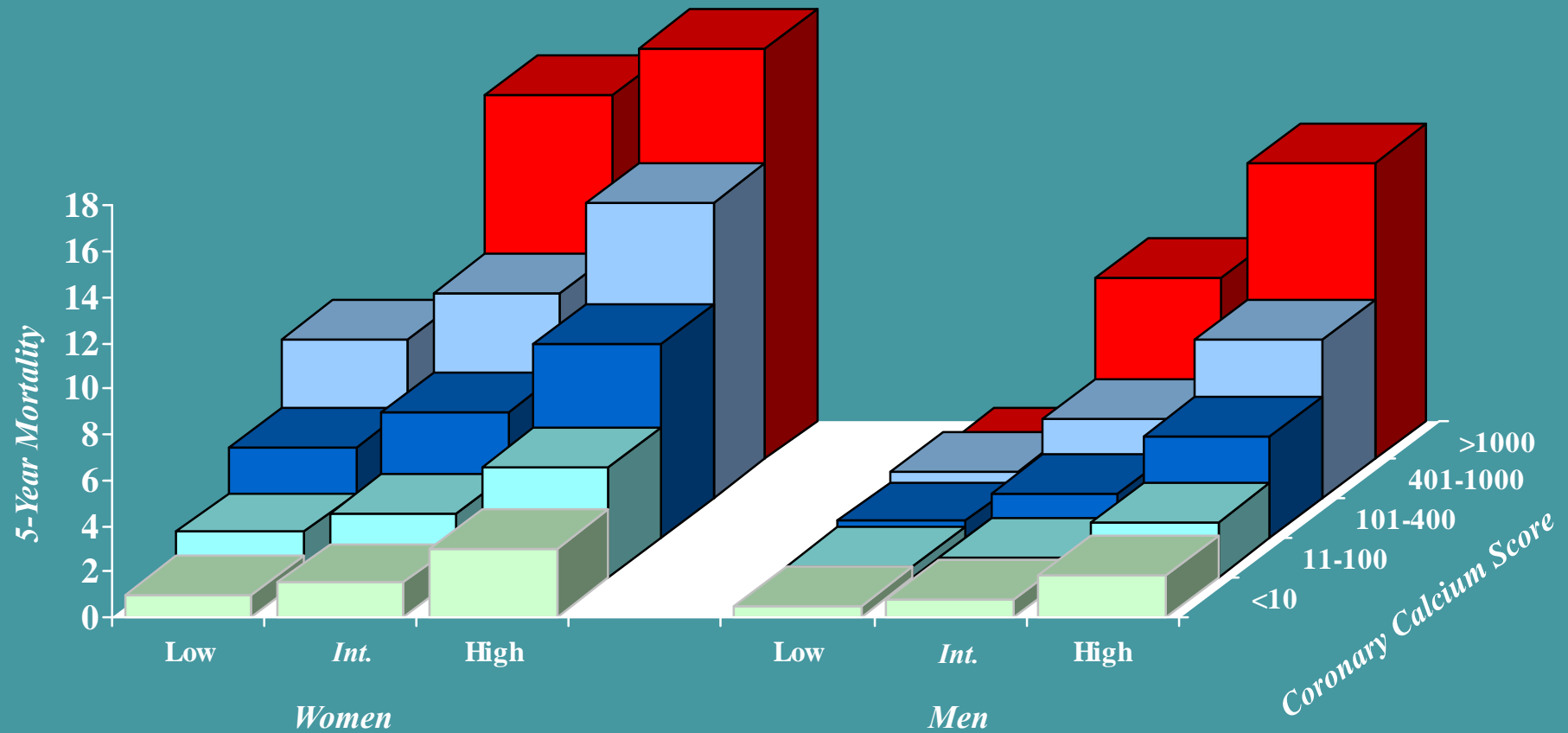


Minimal coronary calcification (total coronary calcium score [CCS] = 5) in the proximal LAD of 59-year-old woman.



Severe coronary calcification involving all 3 major coronary arteries (total CCS = 1612); heavy calcification is also seen in the wall of the descending aorta.

Predicted Mortality in Women and Men by FRS* by CAC Scores



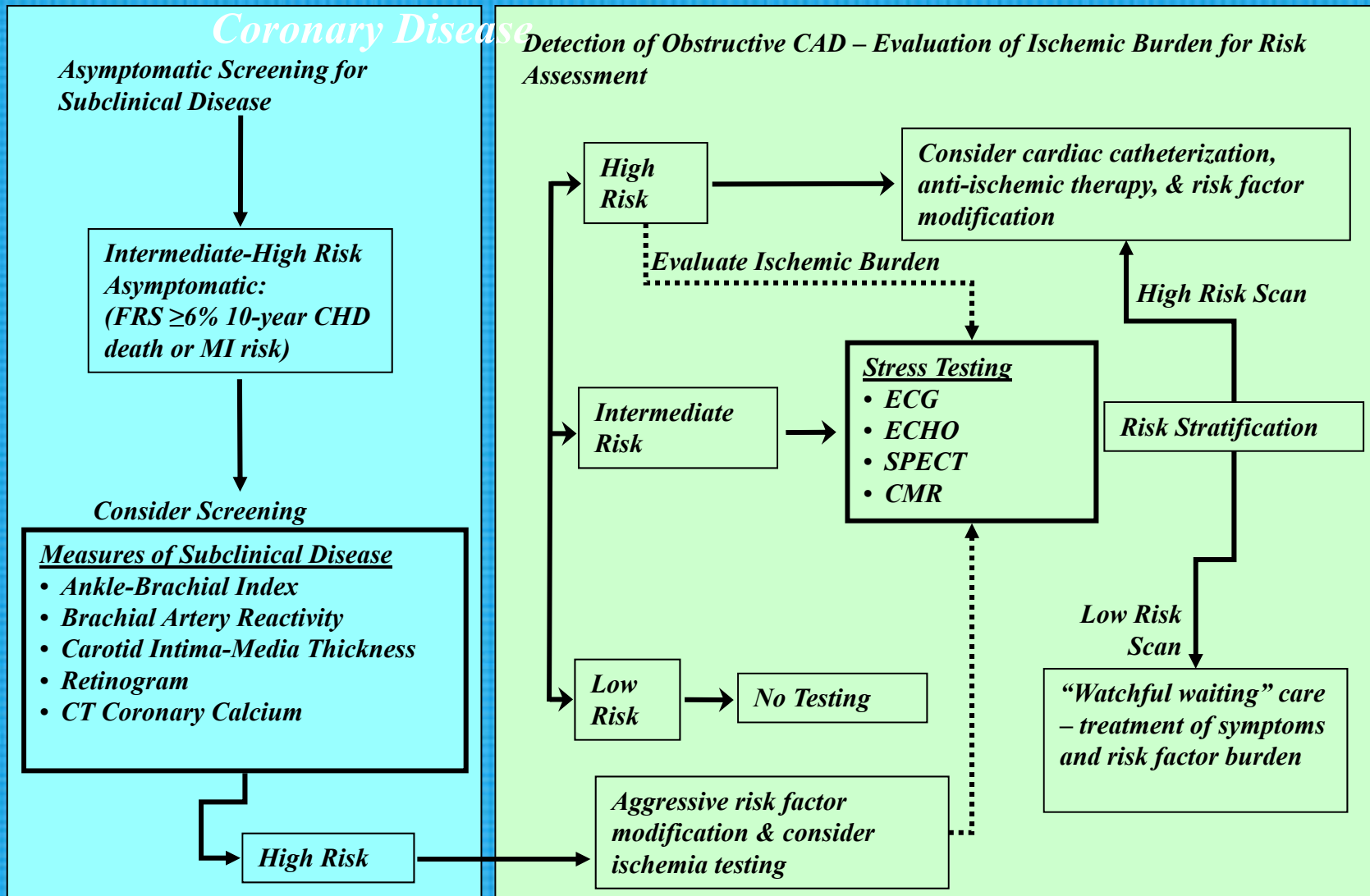
5-Year Predicted Mortality

1. *FRS = Framingham Risk Score.

1. Raggi et al. *J Womens Health (Larchmt)*. 2004;13:273-282.

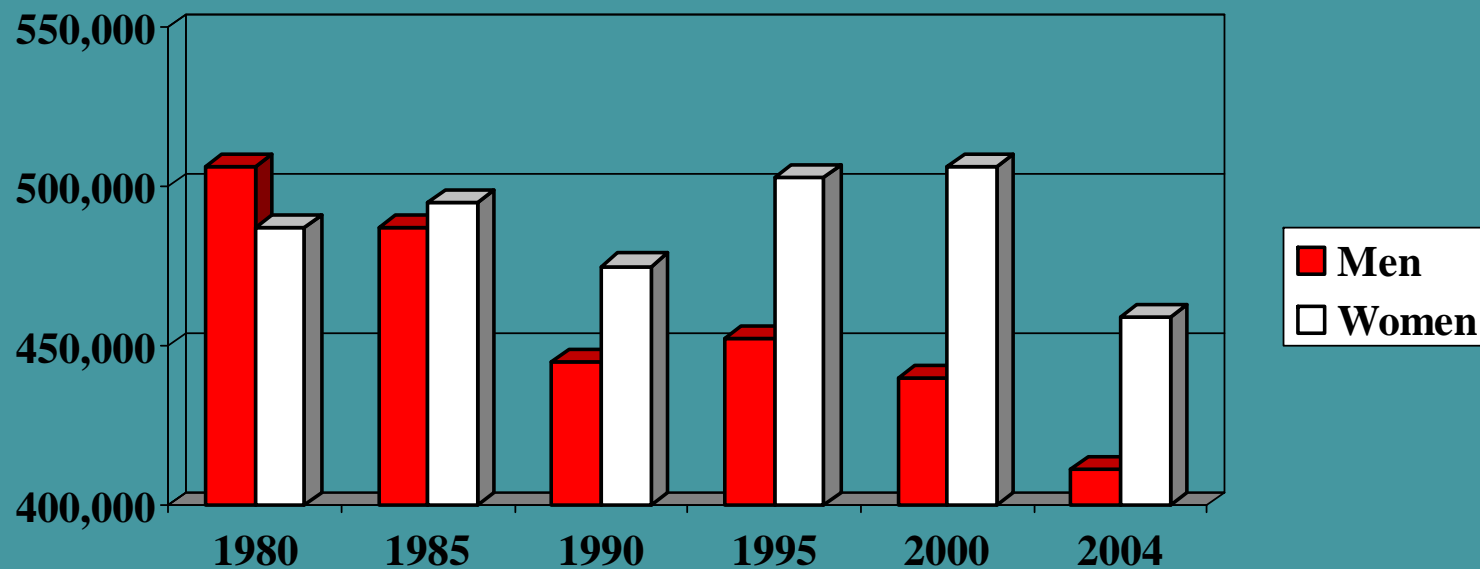
Proposed Paradigm for CAD Testing in Asymptomatic and Symptomatic Women

Includes Detection of Subclinical and Obstructive



Adapted from Shaw et al. *J Am Coll Cardiol.* 2006;47:4S-20S.

Cardiovascular Disease Mortality: U.S. Males and Females 1980-2004



Source: Adapted from Rosamond 2008

In perspective:

- **1 in 2 women will die of heart disease.**
- **1 in 25 women will die of breast cancer.**

Coronary Heart Disease in Women

- Presentation and differences from men
- 2/3 of women who die suddenly have **no** previously recognized symptoms.
- Women are more prone to non-cardiac chest pain.....
- In fact they may experience little or no squeezing chest pain in the center of the chest, lightheadedness, fainting, or shortness of breath with an MI (as seen on “ER”).

Nationally:

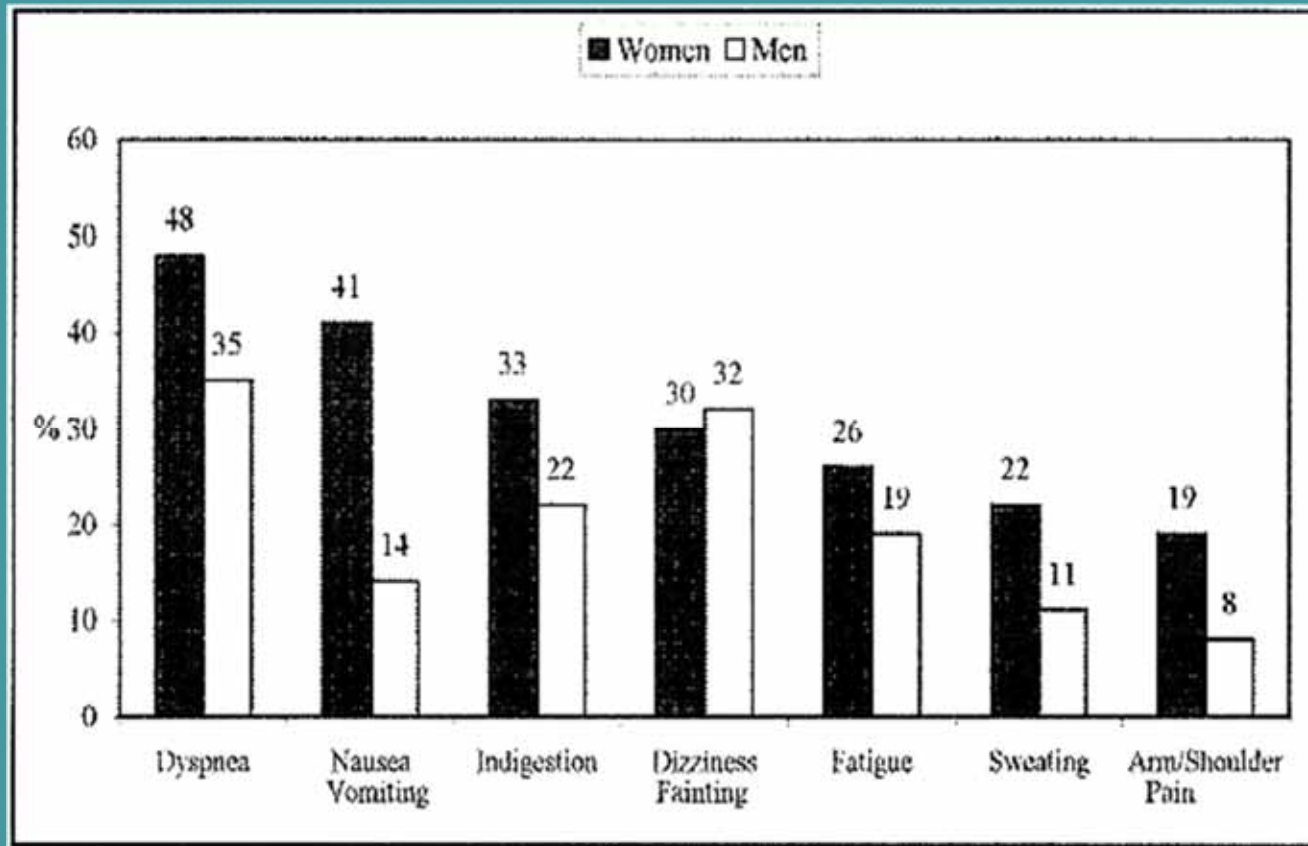
The Problem – AWARENESS

- Perception
- 67% knowledgeable that chest pain can be heart disease
- <10% knowledgeable that SOB, nausea, indigestion can be heart disease
- Reality
- chest pain is the presenting symptom in <50% of women
- Almost half of MIs in women present with SOB, nausea, indigestion, fatigue and shoulder pain

Causes of Confusion:

- **Women may experience more dizziness, nausea, indigestion, and *fatigue* than men.**
- **Women are more likely to have *neck, arms, back and shoulder pain*.**

Evidence based information about symptoms suggests a gender focus



*Women have
More
atypical
Symptoms of*

Not so straightforward

- Because of these *atypical symptoms*, women seek medical care *later* than men and are more likely to be misdiagnosed.
- Women presenting with MI and CAD are more likely to be older, have a history of DM, HTN, Hyperlipids, CHF, and unstable angina than male counterparts.

(J Am Coll Cardiol 1997;29)

- Because of these *comorbid conditions*, there

Misperceptions and Missed Opportunities Leading to Access Inequity

- **Women were less likely to have an EKG or be admitted to the telemetry floors.**
- **Women are under-diagnosed and can therefore get a false sense of security.**
- **Less aspirin, beta-blockers, statins, antiarrhythmic treatment, cardiac cath, PTCA, CABG**
- **Women were less likely to enroll in cardiac rehabilitation after an MI or bypass surgery.**

CHD Mortality in Younger Women

Women under 65 suffer the highest relative sex-specific CHD mortality

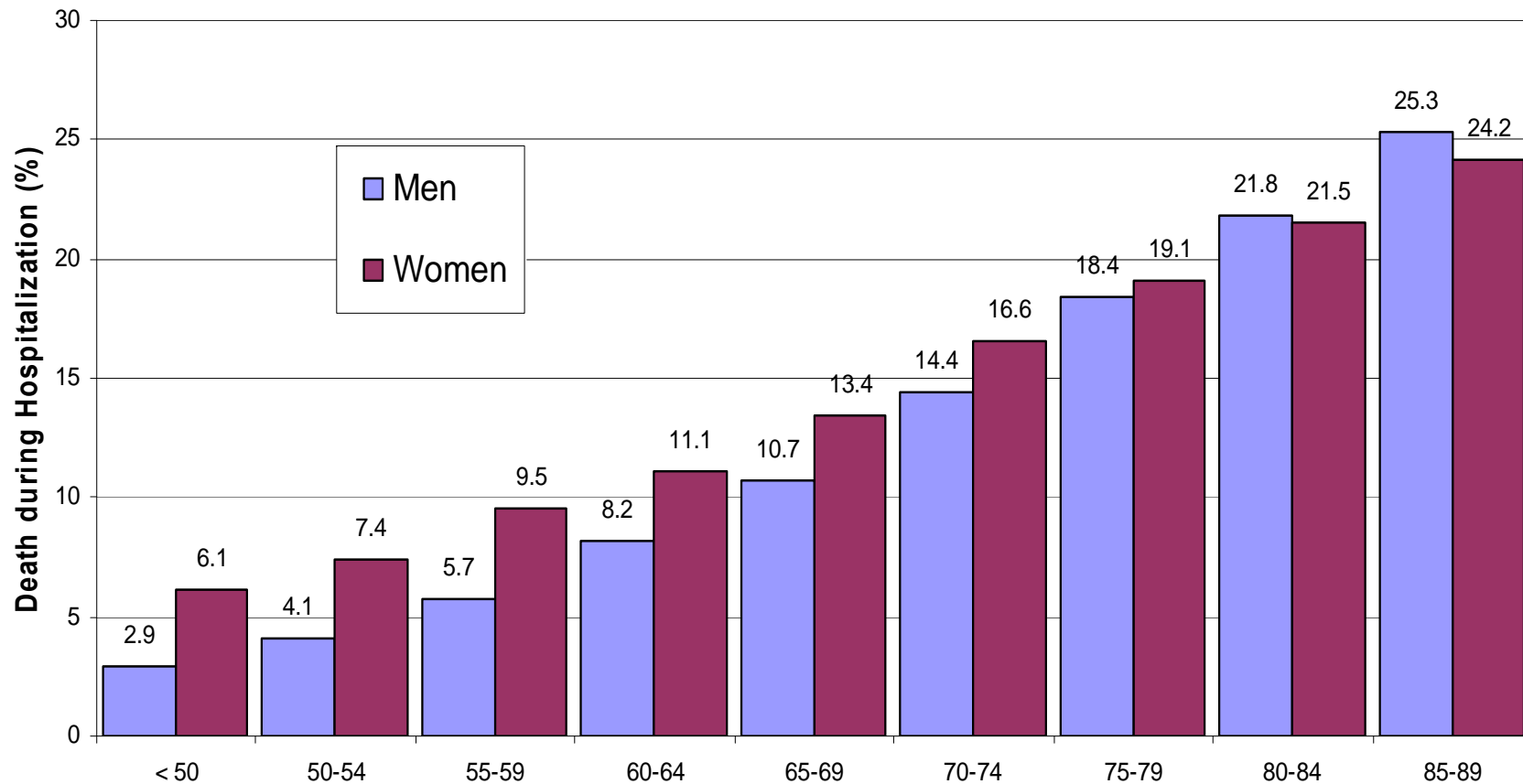


Figure 1. Rates of death during hospitalization for Myocardial Infarction among women and men, according to age. The interaction between sex and age was significant ($P < 0.001$).

The Need for **Prevention** in Women

- 9,000 US women younger than 45 sustain a heart attack each year.
- “Thus the priority for coronary prevention is substantial for women of all ages.”
- Mortality associated with acute MI among women younger than 65 y/o is almost **twice as high among men.**

Women vs. Men:

- Mortality from CABG-particularly among younger women-is **double** that among men.
- **More women** than men die 1 year after an MI.
- **CHD is Largely Preventable**
- We need to address risk factors **earlier** and more aggressively, thereby reducing women's cardiovascular risk.

Women and Heart Disease

Risk Factors

JNC 7 RECOGNIZES THE FOLLOWING AS CARDIOVASCULAR (CV) RISK FACTORS

- Hypertension
- Dyslipidemia
- Cigarette smoking
- Obesity (BMI ≥ 30 kg/m²)
- Physical inactivity
- Diabetes mellitus
- Microalbuminuria (or estimated GFR* < 60 mL/min)
- Age (> 55 years for men, > 65 years for women)
- Family history of premature CVD (men < 55 years or women < 65 years)

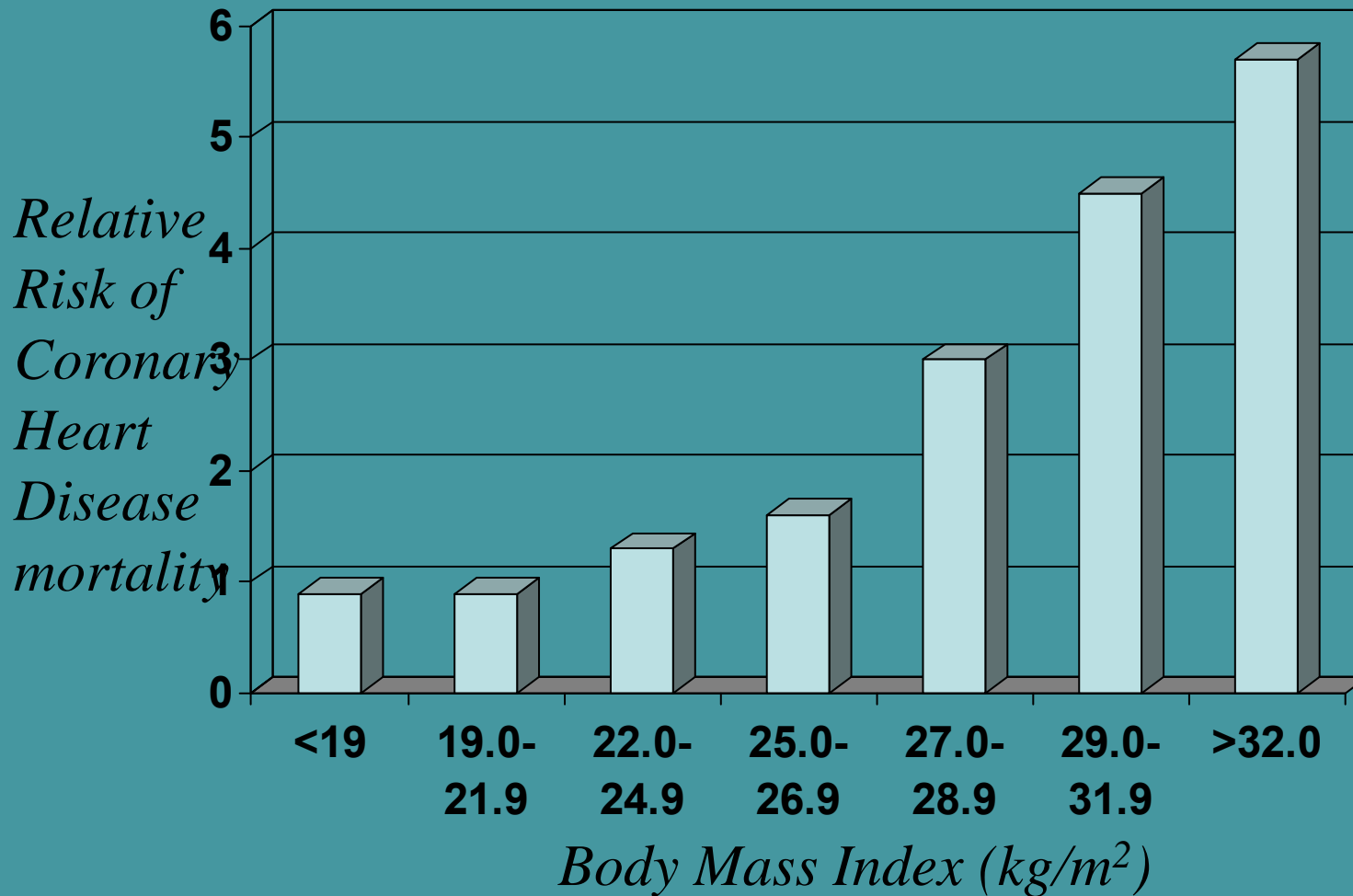
*GFR = glomerular filtration rate.

JNC 7, *JAMA*, 2003.

American Heart Association, *Heart Disease and Stroke Statistics—2003 Update*, 2002.

Obesity and Coronary Heart Disease Mortality

Nurses' Health Study: Women who never smoked



P < 0.001 for trend

Manson JR, et al. N Engl J Med. 1995;333:677-685.

Hypertension

- **65% of all hypertension remains either undetected or inadequately treated.**
- **People who are normotensive at 55 have a 90% lifetime risk of developing HTN.**
- **Prevalence increases with age and women live longer- hypertension is more common in females.**
- **HTN is more common with OCP and obesity.**

Risk Factors: Diabetes

- Diabetes increases the risk of **CHD 3-7 X's in women** versus 2-3 X's in men.
- **Diabetic** women who smoke have a 84% higher risk of developing stroke than nonsmokers.
- 2 of 3 people with diabetes die from CHD or stroke.

Non-modifiable Risk Factors

- **Age > 55**
 - CAD rates are 2-3x's higher in postmenopausal women
- **Family history**
 - CHD in primary 1st degree relative male<55 or female<65

The #1 Preventable Risk- Smoking



- **A. 50% of heart attacks among women are due to smoking. Smokers tend to have their first heart attack 10 years earlier than nonsmokers.**
- **B. If you smoke, you are 4-6x's more likely to suffer a heart attack and increase your risk of a stroke.**
- **C. Women who smoke and take OCP's increase their risk of heart disease 30x's.**

2. Obesity

- A. 1/3 of adult women are obese and its *increasing***
- B. Active women have a 50% risk reduction in developing heart disease.**

Lifestyle Modification for HTN

Modification	Recommendation	Expected systolic reduction
Weight reduction	Goal of BMI 18-25 Waist <35inches	5-20 mm Hg per 10kg wt loss
DASH	Fruits, veges, low-fat dairy products, less fat	8-14 mm Hg
Sodium restriction	<2.4 g every day	2-8 mm Hg
Physical activity	30 mins of aerobic 4x's a week	4-9 mm Hg
Reduced EtOH (1/2 for women)	2-12 oz beer, 1 10oz wine, 3 oz 80proof whiskey in men	2-4 mm Hg

Exercise

- 30-45 mins of walking 5x's/week **reduces risk of MI in females 50%.**
- **Helps control BP, increases HDL, decreases body fat, DM risk, possibly prostate, breast and uterine cancers.**

Glycemic control In Diabetes

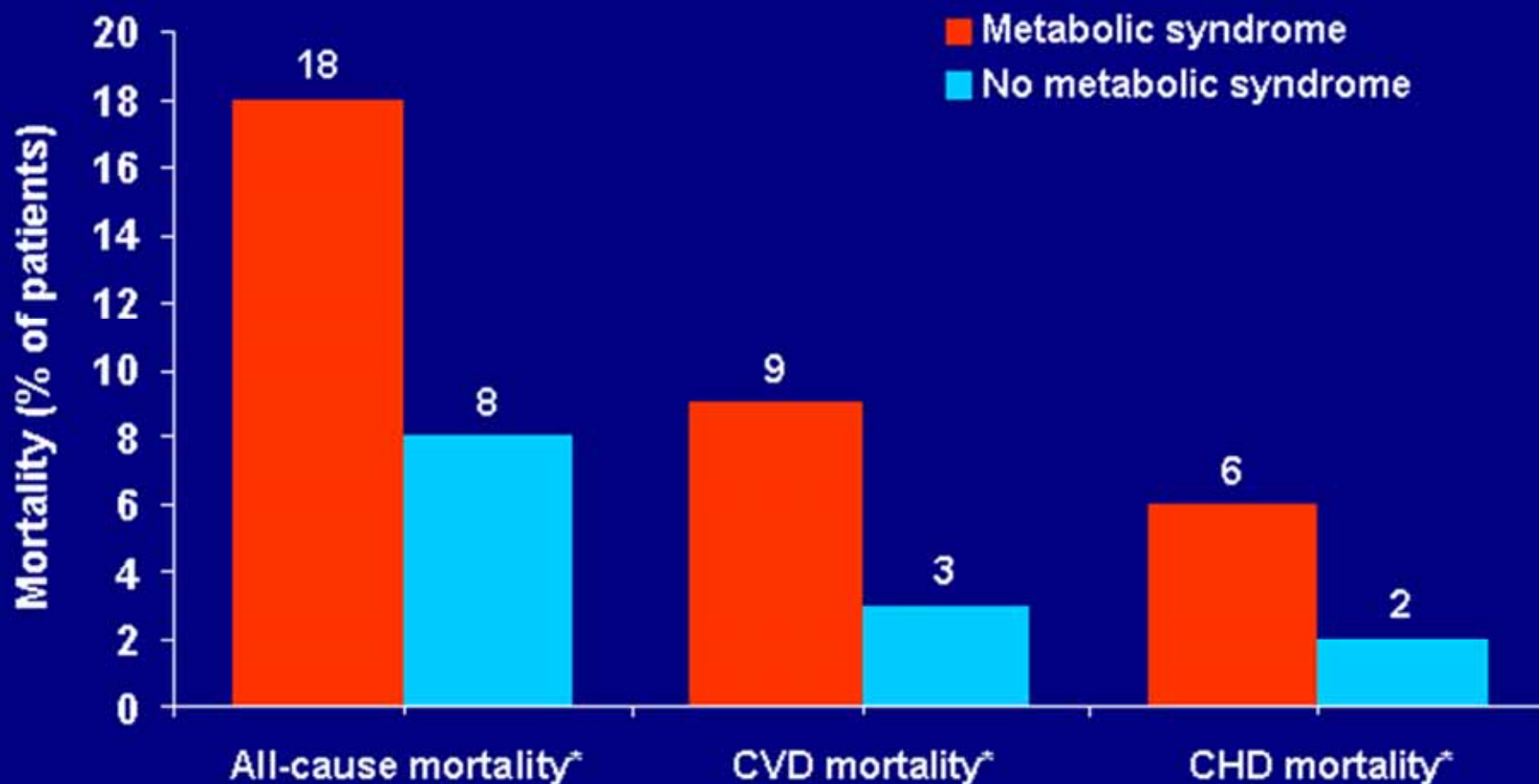
- Treatment of hyperglycemia has been shown to reduce or delay complications of diabetes such as retinopathy, neuropathy, and nephropathy
- keep HBA1C \leq 6.5%
- FPG <100
- 2 hour 75g GTT-Impaired glucose tolerance- 140-199.

Metabolic Syndrome

RISK FACTOR	DEFINING LEVEL
Abdominal Obesity	Waist Circumference
Men	>40 inches
Women	>35 inches
TG's	≥ 150
HDL	
Men	<40
Women	<50
BP	$\geq 130/85$
Fasting Glucose	≥ 100 mg/dl



Mortality Associated With Metabolic Syndrome



*Adjusted for known CHD risk factors.

EDUCATE!!!

- **Women's main source of information on heart disease:**
 - Magazines 45%
 - TV 34%
 - Newspaper 27%
 - MD's 24%
- **Only 38% of pts in a recent survey said they discussed CHD prevention with their MD's.**

Keys to reducing mortality from CHD:

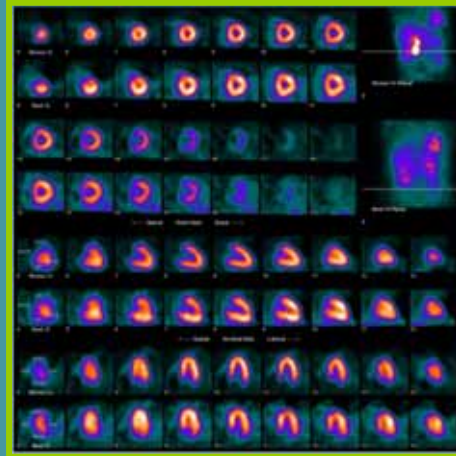
***Women and Heart Disease:
Keys to Improving Outcomes***

- **Early recognition of symptoms**
- **Accurate diagnosis of CAD**
- **Treatment**

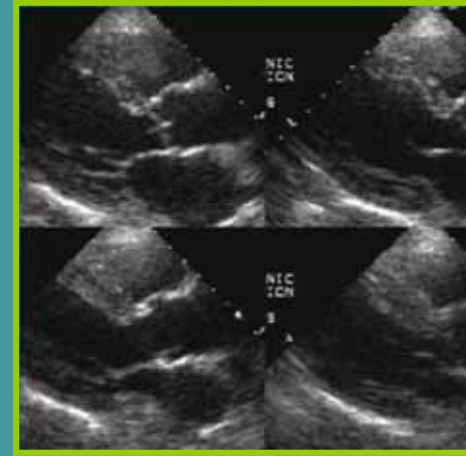
Some Noninvasive Testing Options



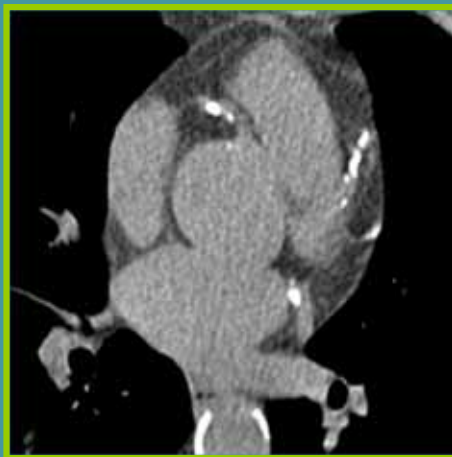
Stress ECG



Stress MPI/PET



Stress ECHO

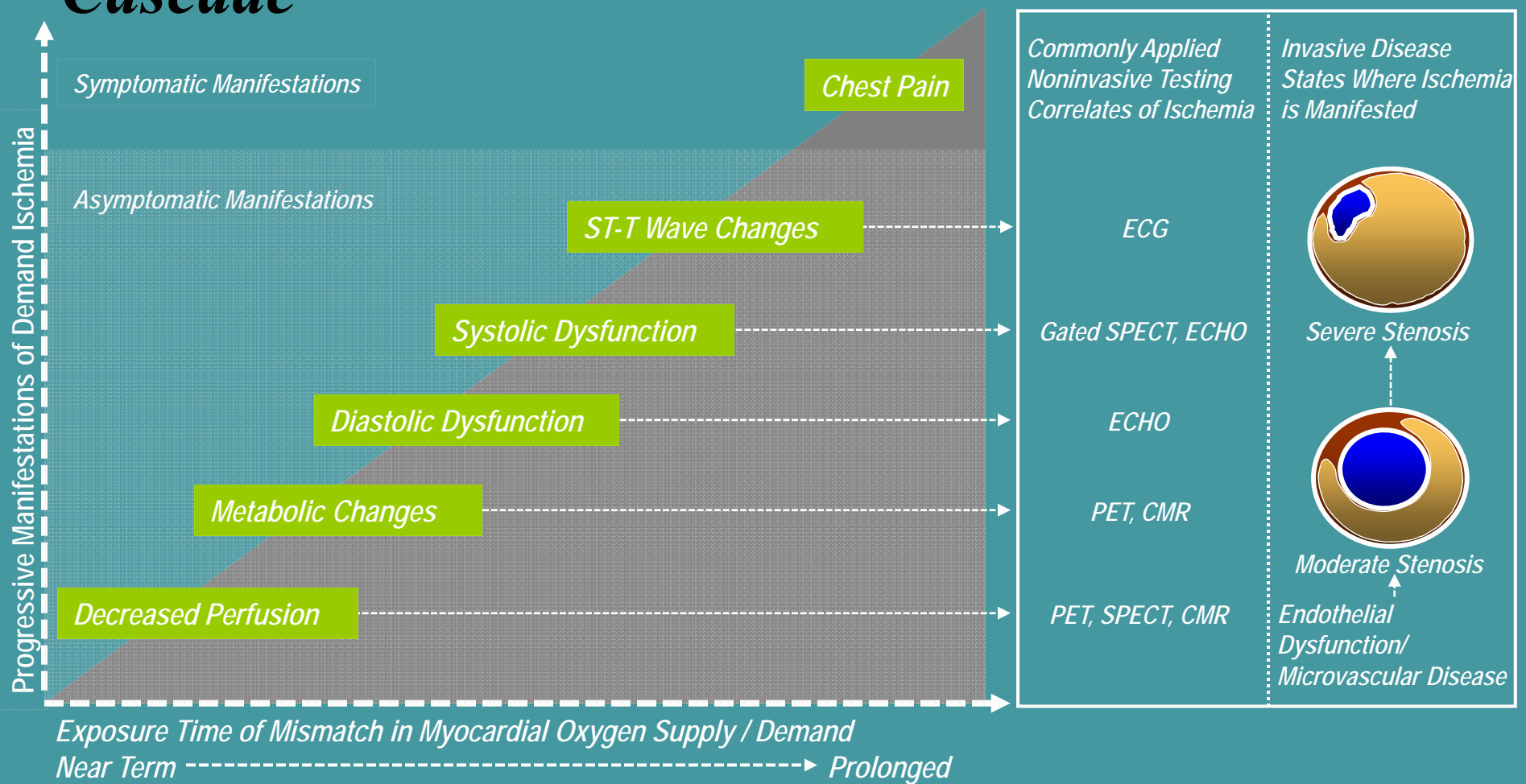


EBCT/CTA



MRI

Progressive Manifestations of Myocardial Ischemia as Illustrated by the Ischemic Cascade



ECG = electrocardiogram; SPECT = single-photon emission computed tomography; PET = positron-emission tomography; ECHO = echocardiogram; CMR = cardiovascular magnetic resonance imaging.

Adapted from Mieres et al. Am Fam Physician. 2006. In press.

ECG Testing in Women: Sensitivity and Specificity of ≥ 1 mm ST Segment Depression

Comparison of AHRQ Results to Prior Studies in Women*						
	Ex ECG		ECHO		SPECT	
	Sn	Sp	Sn	Sp	Sn	Sp
Fleischmann 1998	-	-	85%	77%	87%	64%
Kwok 1999	61%	70%	86%	79%	78%	64%
Grady (AHRQ) 2003			81%	73%	77%	69%

Sn = Diagnostic sensitivity (true positive / CAD)

Sp = Diagnostic specificity (true negative / no CAD)

*AHRQ = Agency for Healthcare Research and Quality.

Fleischmann et al. *JAMA* 1998;280:913-920.

Kwok et al. *Am J Cardiol.* 1999;83:660-666.

Grady et al. AHRQ Publication No. 03-E037. May 2003. Available at:

<http://www.ahrq.gov/downloads/pub/evidence/pdf/chdwomtop/chdwmtop.pdf>.

Diagnostic Accuracy of Exercise ECG Testing in Women

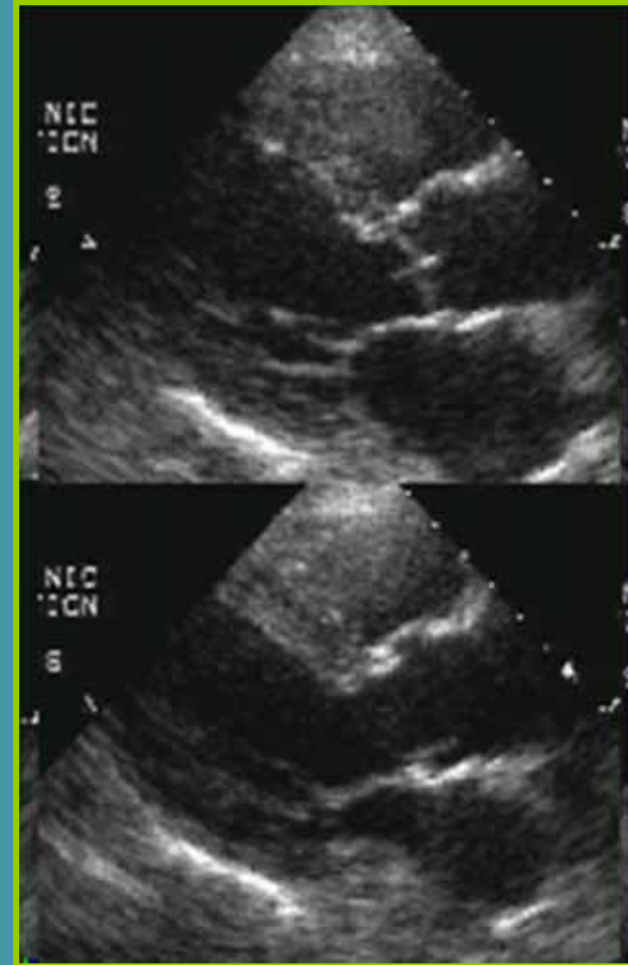
- **Altered prevalence of disease^{1,2}**
- **Reduced predictive accuracy in younger women²**
- **Potential factors affecting diagnostic accuracy¹:**
 - Hormonal influences
 - Reduced functional capacity
 - Resting ST-T wave abnormalities
 - Comorbidities

1. Isaac D, et al. *Can J Cardiol.* 2001;17(suppl D):38D-48D.

2. Shaw LJ, et al. In: Charney P, ed. *Coronary Artery Disease in Women: What All Physicians Need to Know.* Philadelphia, Pa: American College of Physicians. 1999:327-350.

Stress ECHO

- ◆ *Ultrasound performed both at rest and during peak stress*
- ◆ *Exercise or other stress*
- ◆ *Ischemia defined by development of wall-motion abnormalities*



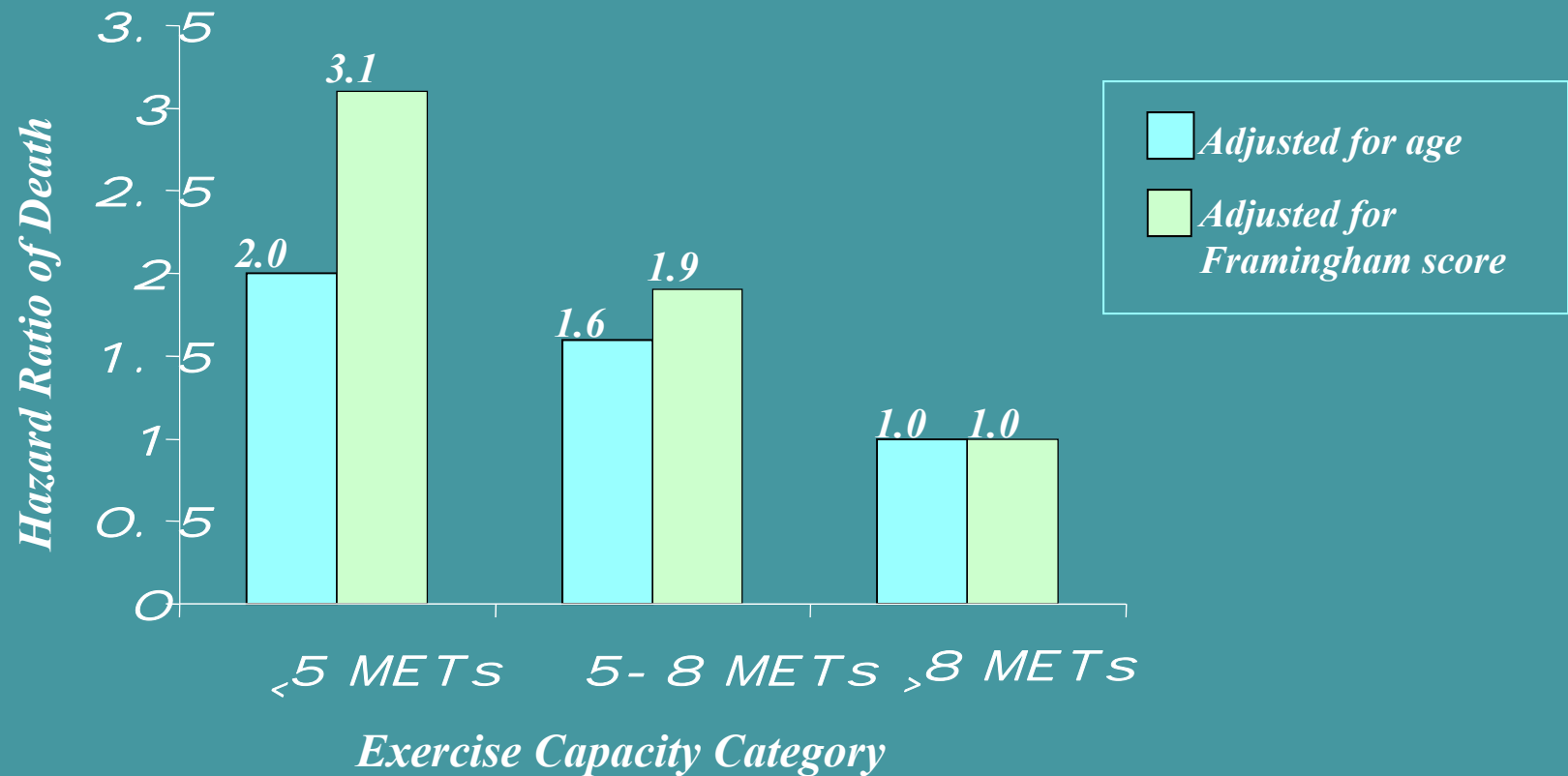
CVD in Women – *under-diagnosed, under-treated and under-researched*

Gender Differences

- **Presentation**
- **Investigation**
- **Treatment**
- **Prognosis**

Exercise Capacity and Mortality Risk in Women

Hazard Ratios of All-Cause Death Adjusted for Age and Framingham Risk Scores for Each Exercise Capacity Category



Adapted from Gulati et al. Circulation. 2003;108:1554-1559

Risk Factors

- Age
 - *Smoking
 - *Diabetes Mellitus
 - *Hypertension (LVH)
 - *Hyperlipidaemia (especially HDL, TG in women)
 - Family History of CHD
 - Homocysteine
 - *CRP
-
- Menopause
 - Sedentary Lifestyle

Biggest Risk factor is the misconception that CHD is a "Man's Disease"

AHA and ACC – guidelines for gender specific risk assessment
- guidelines for primary and secondary prevention

ESC

BCS- guidelines in progress

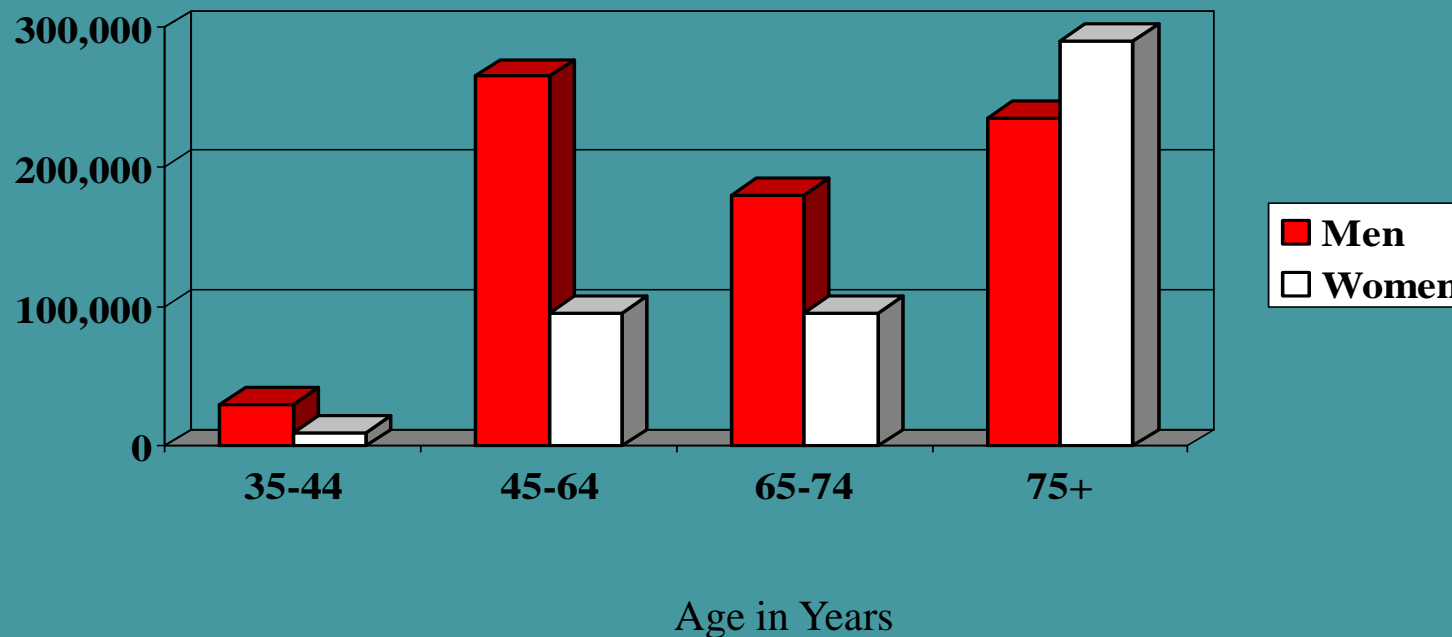
3-Year Survival by Gender, Diabetic Status, and Extent of Myocardial Ischemia

	<i>No Ischemia</i>	<i>1-Vessel Ischemia</i>	<i>≥2-Vessel Ischemia</i>
<i>Diabetic Men</i>	86.3%	77%	79%
<i>Nondiabetic Men</i>	93.8%	88%	85%
<i>Diabetic Women</i>	96.5%	72.5%*	60%*
<i>Nondiabetic Women</i>	95.5%	85%	77.5%

* $P < 0.05\%$.

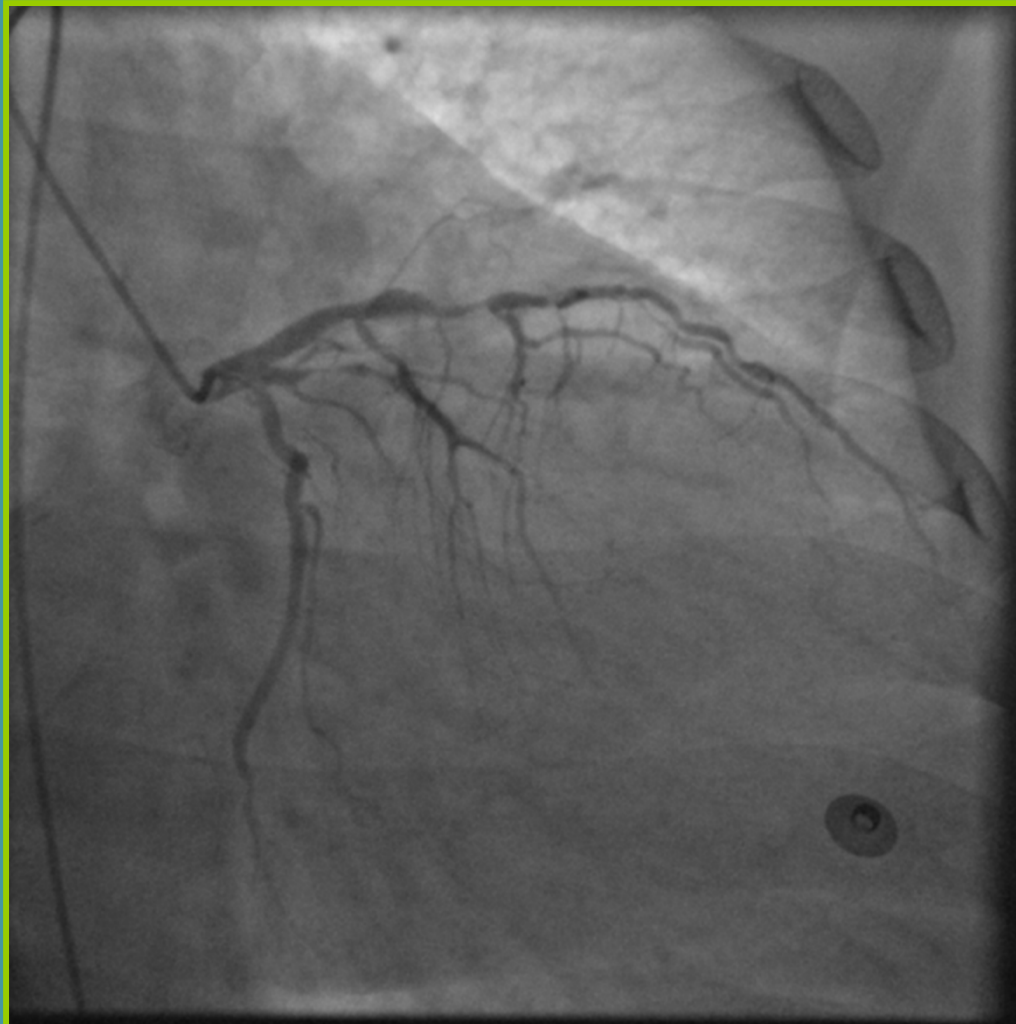
Giri et al. Circulation. 2002;105:32-40.

Annual Numbers of U.S. Adults Diagnosed with Myocardial Infarction and Fatal CHD by Age and Sex Categories: 1987-2004



Source: Adapted from Rosamond 2008

Cardiac Catheterization

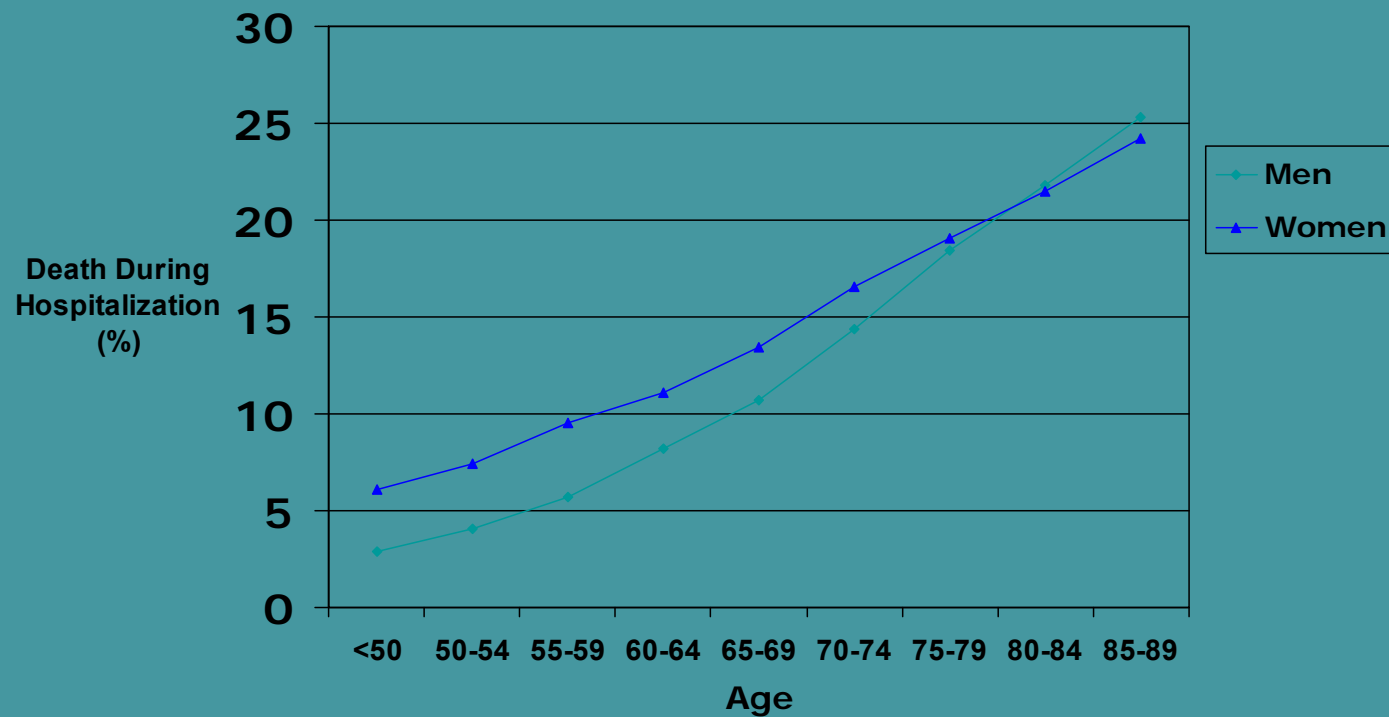


Women Received Less Interventions to Prevent and Treat Heart Disease

- **Less cholesterol screening**
- **Less lipid-lowering therapies**
- **Less use of heparin, beta-blockers and aspirin during myocardial infarction**
- **Less antiplatelet therapy for secondary prevention**
- **Fewer referrals to cardiac rehabilitation**
- **Fewer implantable cardioverter-defibrillators compared to men with the same recognized indications**

Sources: Chandra 1998, Nohria 1998, Scott 2004, O'Meara 2004, Hendrix 2005, Chou 2007, Hernandez 2007, Cho 2008

Acute MI Mortality by Age and Sex



Source: Adapted from Vaccarino 1999

Evidence-based Guidelines for Cardiovascular Disease Prevention in Women: 2007 Update

Mosca L, et al. Circulation 2007; 115:1481-501.

<http://www.circ.ahajournals.org>

Cardiovascular Disease Prevention in Women: Current Guidelines

- **A five-step approach**
 - Assess and stratify women into high risk, at risk, and optimal risk categories
 - Lifestyle approaches recommended for all women
 - Other cardiovascular disease interventions: treatment of HTN, DM, lipid abnormalities
 - Highest priority is for interventions in high risk patients
 - Avoid initiating therapies that have been shown to lack benefit, or where risks outweigh benefits

Risk Stratification:

- **High Risk**
 - Diabetes mellitus
 - Documented atherosclerotic disease
 - Established coronary heart disease
 - Peripheral arterial disease
 - Cerebrovascular disease
 - Abdominal aortic aneurysm
 - Includes many patients with chronic kidney disease, especially ESRD 10-year Framingham global risk > 20%, or high risk based on another population-adapted global risk assessment tool

Risk Stratification:

- **At Risk:**
 - ≥ 1 major risk factors for CVD, including:
 - Cigarette smoking
 - Hypertension
 - Dyslipidemia
 - Family history of premature CVD (CVD at < 55 years in a male relative, or < 65 years in a female relative)
 - Obesity, especially central obesity
 - Physical inactivity
 - Poor diet
 - Metabolic syndrome
 - Evidence of subclinical coronary artery disease (eg coronary calcification), or poor exercise capacity on treadmill test or abnormal heart rate recovery after stopping exercise

Definition of Metabolic Syndrome in Women

- **Abdominal obesity - waist circumference \geq 35 in.**
- **High triglycerides \geq 150mg/dL**
- **Low HDL cholesterol $<$ 50mg/dL**
- **Elevated BP \geq 130/85mm Hg**
- **Fasting glucose \geq 100mg/dL**

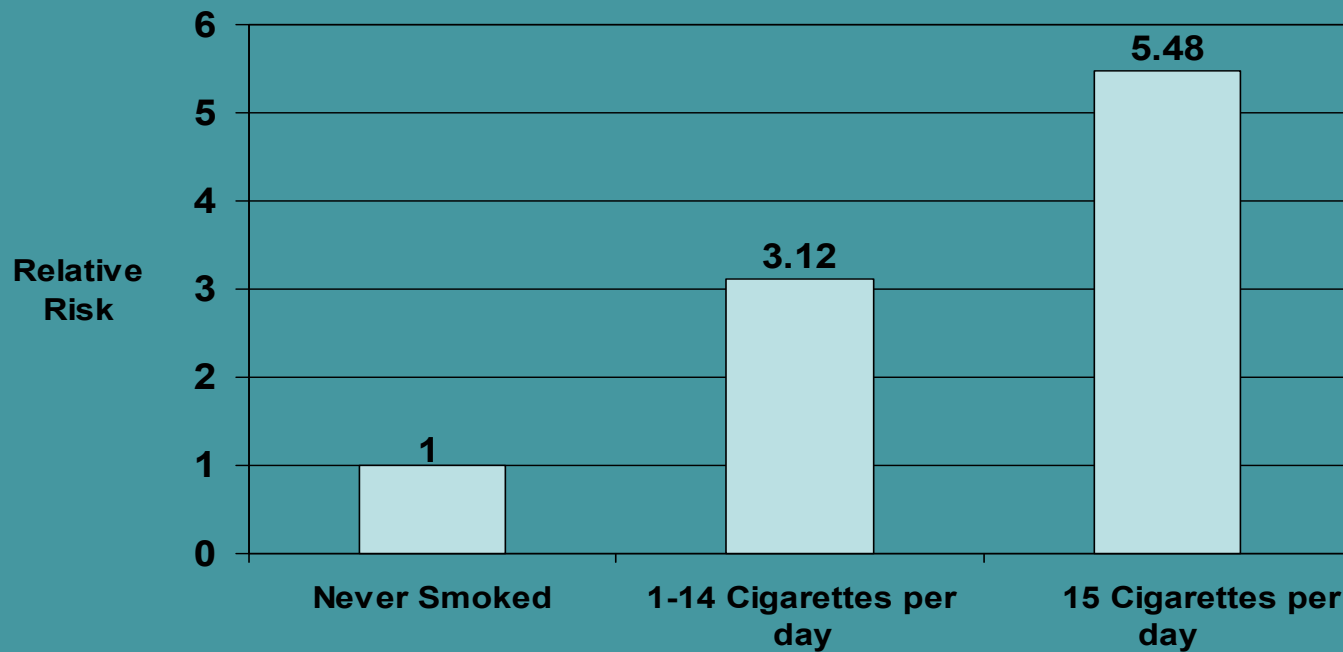
Risk Stratification:

- **Optimal risk:**
 - No risk factors
 - Healthy lifestyle
 - Framingham global risk < 10%

Lifestyle Interventions

- **Smoking cessation**
- **Physical activity**
- **Heart healthy diet**
- **Weight reduction/maintenance**

Relative Risk of Coronary Events for Smokers Compared to Non-Smokers

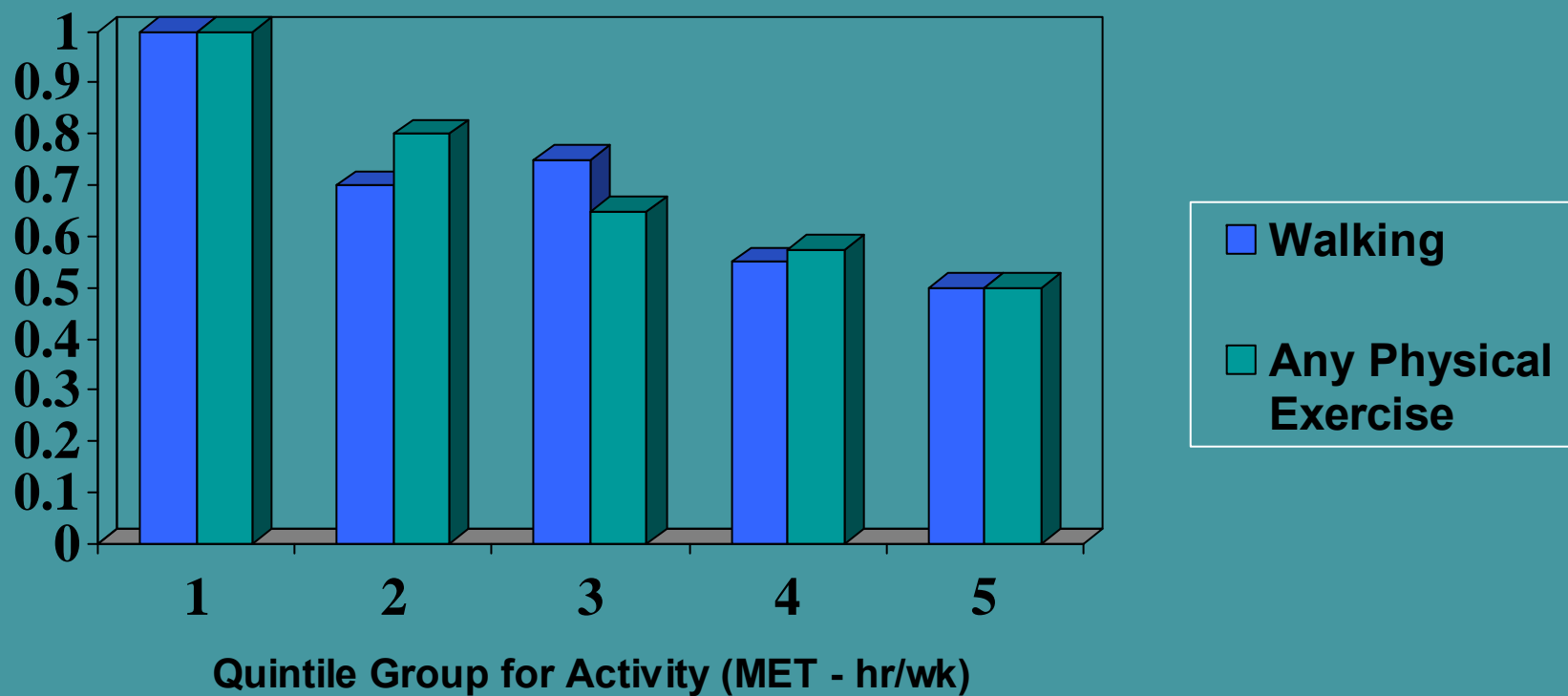


Source: Adapted from Stampfer 2000

Smoking

- **All women should be consistently encouraged to stop smoking and avoid environmental tobacco**
 - The same treatments benefit both women and men
 - Women face different barriers to quitting
 - Concomitant depression
 - Concerns about weight gain
- **Provide counseling, nicotine replacement, and other pharmacotherapy as indicated in conjunction with a behavioral program or other formal smoking cessation program**

Risk Reduction for CHD Associated with Exercise in Women

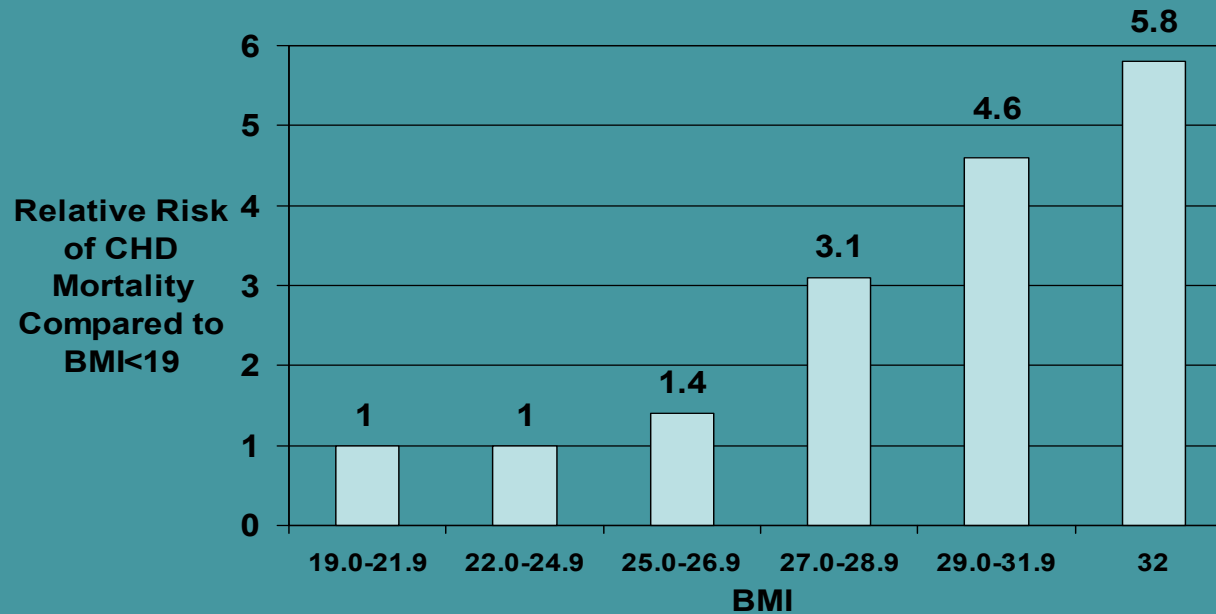


Source: Manson 1999

Physical Activity

- **Consistently encourage women to accumulate a minimum of 30 minutes of moderate intensity physical activity on most, or preferably all, days of the week**
- **Women who need to lose weight or sustain weight loss should accumulate a minimum of 60-90 minutes of moderate-intensity physical activity on most, and preferably all, days of the week**

Body Weight and CHD Mortality Among Women



P for trend < 0.001

Source: Adapted from Manson 1995

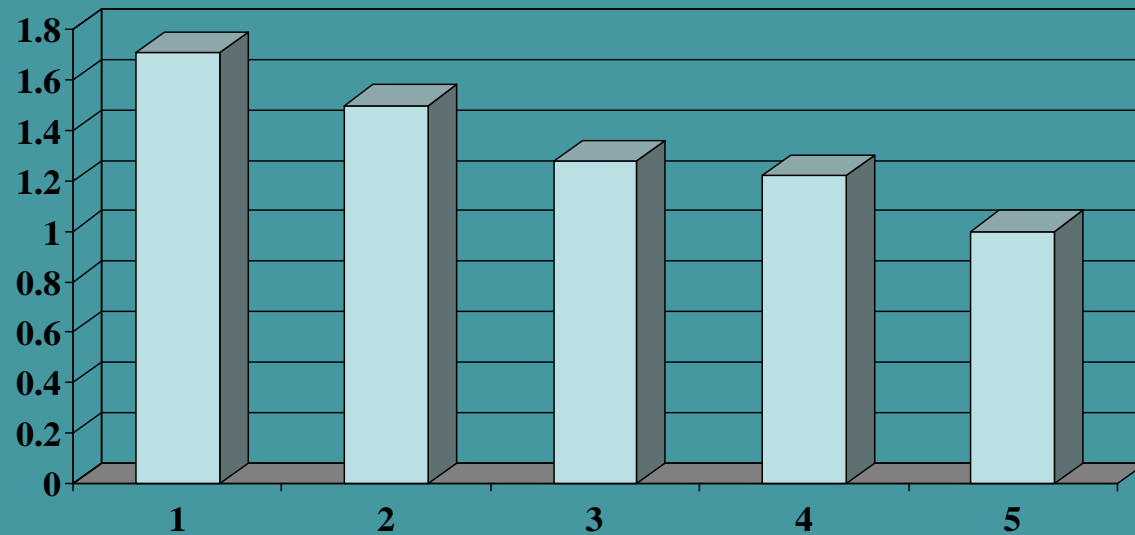
Weight Maintenance/Reduction Goals

- **Women should maintain or lose weight through an appropriate balance of physical activity, calorie intake, and formal behavioral programs when indicated to maintain:**
 - BMI between 18.5 and 24.9 kg/m²
 - Waist circumference \leq 35 inches

Low Risk Diet is Associated with Lower Risk of Myocardial Infarction in Women

Relative Risk of MI*

P < .05 for quintiles 3-5 compared to 1-2



*Adjusted for other cardiovascular risk factors

Diet Score by Quintile (1= least vegetables, fruit, whole grains, fish, legumes)

Source: Akesson 2007

Diet

- **Consistently encourage healthy eating patterns**
 - Healthy food selections:
 - Fruits and vegetables
 - Whole grains, high fiber
 - Fish, especially oily fish, at least twice per week
 - No more than one drink of alcohol per day
 - Less than 2.3 grams of sodium per day
 - Saturated fats < 10% of calories, < 300mg cholesterol
 - Limit trans fatty acid intake (main dietary sources are baked goods and fried foods made with partially hydrogenated vegetable oil)

Major Risk Factor Interventions

- **Blood Pressure**
- **Lipids**
- **Diabetes**

Hypertension

- Encourage an optimal blood pressure of $< 120/80$ mm Hg through lifestyle approaches
- Pharmacologic therapy is indicated when blood pressure is $\geq 140/90$ mm Hg or an even lower blood pressure in the setting of diabetes or target-organ damage ($\geq 130/80$ mm Hg)
- Thiazide diuretics should be part of the drug regimen for most patients unless contraindicated, or unless compelling indications exist for other agents
- For high risk women, initial treatment should be with a beta-blocker or angiotensin converting enzyme inhibitor or angiotensin receptor blocker

Lifestyle Approaches to Hypertension in Women

- **Maintain ideal body weight**
 - Weight loss of as little as 10 lbs reduces blood pressure
- **DASH eating plan**
 - Even without weight loss, a diet rich in fruits, vegetables, and low fat dairy products can reduce blood pressure
- **Sodium restriction to 2300 mg/d**
 - Further restriction to 1500 mg/d may be beneficial, especially in African American patients
- **Increase physical activity**
- **Limit alcohol to one drink per day**
 - Alcohol raises blood pressure
 - One drink = 12 oz beer, 5 oz wine, or 1.5 oz liquor

Lipids

- **Optimal levels of lipids and lipoproteins in women are as follows (these should be encouraged in all women with lifestyle approaches):**
 - LDL < 100mg/dL
 - HDL > 50m/dL
 - Triglycerides < 150mg/d
 - Non-HDL (total cholesterol minus HDL) < 130mg/d

Lipids

- **In high-risk women or when LDL is elevated:**
 - Saturated fat < 7% of calories
 - Cholesterol < 200mg/day
 - Reduce trans-fatty acids
 - Major dietary sources are foods baked and fried with partially hydrogenated vegetable oil

Lipids

- **Treat high risk women aggressively with pharmacotherapy**
 - LDL-lowering pharmacotherapy (preferably a statin) should be initiated *simultaneously* with lifestyle modification for women with LDL>100mg/dl

Very High Risk Women

- **Recent heart attack or known CAD, along with one or more of the following:**
 - Multiple major risk factors, particularly in diabetics
 - Severe or poorly controlled risk factors (i.e., continued smoking)
 - Multiple risk factors of the metabolic syndrome, especially TG \geq 200 mg/dL AND HDL < 40 mg/dL
- **LDL goal of < 100mg/dL**
- **Consider statin, even if LDL < 100mg/dL**
- **Optional LDL goal of < 70mg/dL per ATP III 2004 update**

High Risk Women

- **$\geq 20\%$ 10-year risk of CHD**
- **CHD, large vessel atherosclerotic disease, DM**
- **Goal LDL < 100mg/dL, consider statin even if LDL < 100 mg/dL**

At-Risk Women: Multiple or Severe Risk Factors, 10-20% 10-Year CHD Risk

- **Initiate drug therapy if LDL \geq 130 mg/dL after lifestyle therapy**
- **Goal LDL < 100 mg/dL, consider drug therapy if LDL \geq 100 mg/dL**

At-Risk Women: Multiple Risk Factors, 10-Year CHD Risk < 10%

- **Initiate drug therapy if LDL \geq 160 mg/dL after lifestyle therapy**

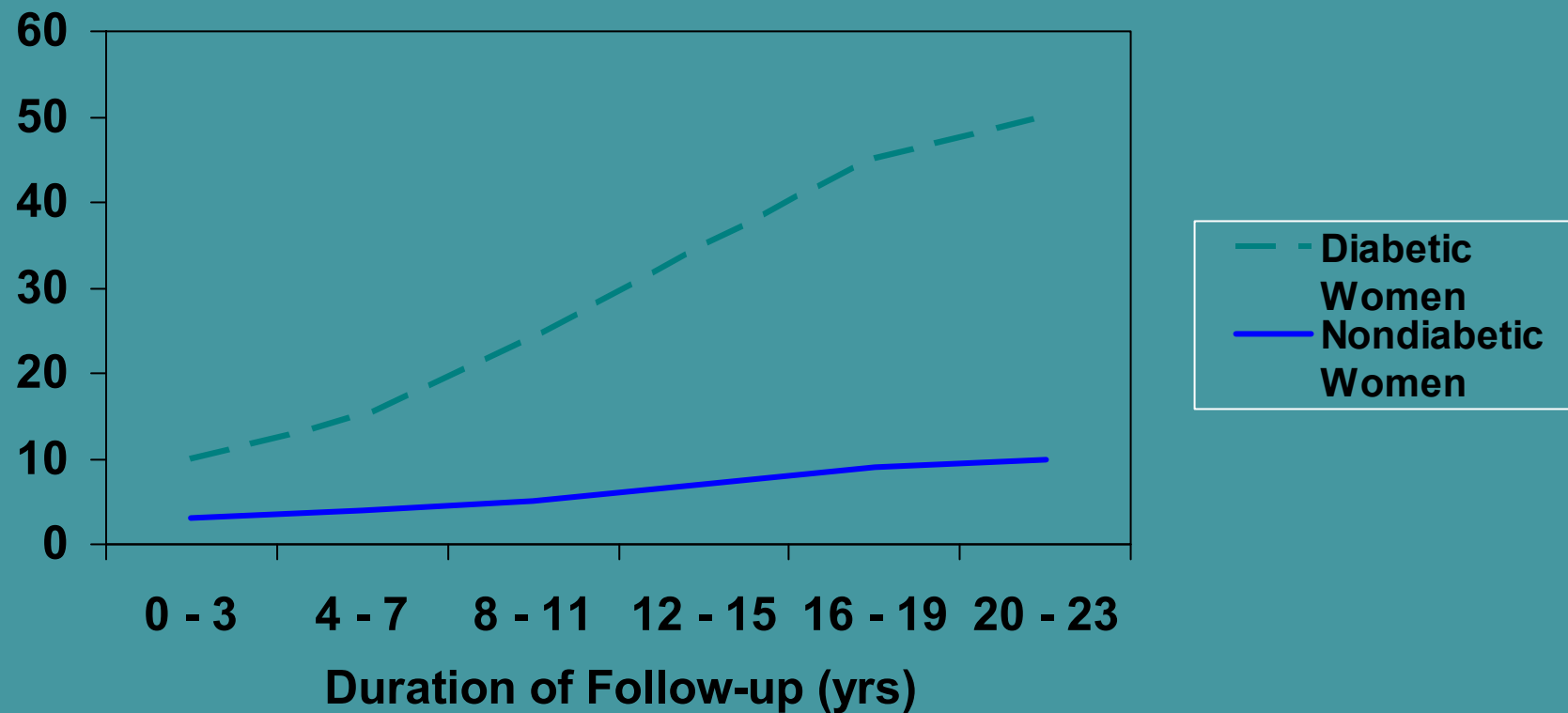
At-Risk Women: No Other Risk Factors, 10-Year CHD Risk < 10%

- **Initiate drug therapy if LDL \geq 190 mg/dL after lifestyle therapy**
- **Drug therapy optional for LDL 160-189 mg/dL after lifestyle therapy**

Diabetes

- **Recommendation: Lifestyle and pharmacotherapy should be used as indicated in women with diabetes to achieve a HbA1C < 7%, if this can be accomplished without significant hypoglycemia**

Coronary Disease Mortality and Diabetes in Women



Source: Krolewski 1991

Preventive Drug Interventions for Women with CHD

- **Aspirin**
- **Beta-blockers**
- **Angiotensin converting enzyme inhibitors**
- **Angiotensin receptor blockers**

Menopausal Hormone Therapy, SERMs and CVD: Summary of Major Randomized Trials

- **Use of estrogen plus progestin associated with a small but significant risk of CHD and stroke**
- **Use of estrogen without progestin associated with a small but significant risk of stroke**
- **Use of all hormone preparations should be limited to short term menopausal symptom relief**
- **Use of a selective estrogen receptor modulator (raloxifene) does not affect risk of CHD or stroke, but associated with an increased risk of fatal stroke**

Source: Hulley 1998, Rossouw 2002, Anderson 2004, Barrett-Connor 2006

Interventions that are not useful/effective and may be harmful for the prevention of heart disease

- **Hormone therapy and selective estrogen-receptor modulators (SERMs) should not be used for the primary or secondary prevention of CVD**

Interventions that are not useful/effective and may be harmful for the prevention of heart disease

- **Antioxidant supplements and folic acid supplements**
 - No cardiovascular benefit in randomized trials of primary and secondary prevention

Prevention of Cardiovascular Disease in Women

- **Stratify women into high, at risk, and optimal risk categories**
- **Encourage lifestyle approaches**
- **Treat hypertension, lipid abnormalities, and diabetes**
- **Implement pharmacologic interventions for women at high and intermediate risk, pharmacologic interventions may be appropriate for some lower risk women**
- **Avoid initiating therapies without benefit, or where risks outweigh benefits**