

# Cardiovascular Aging: Clinical Implications

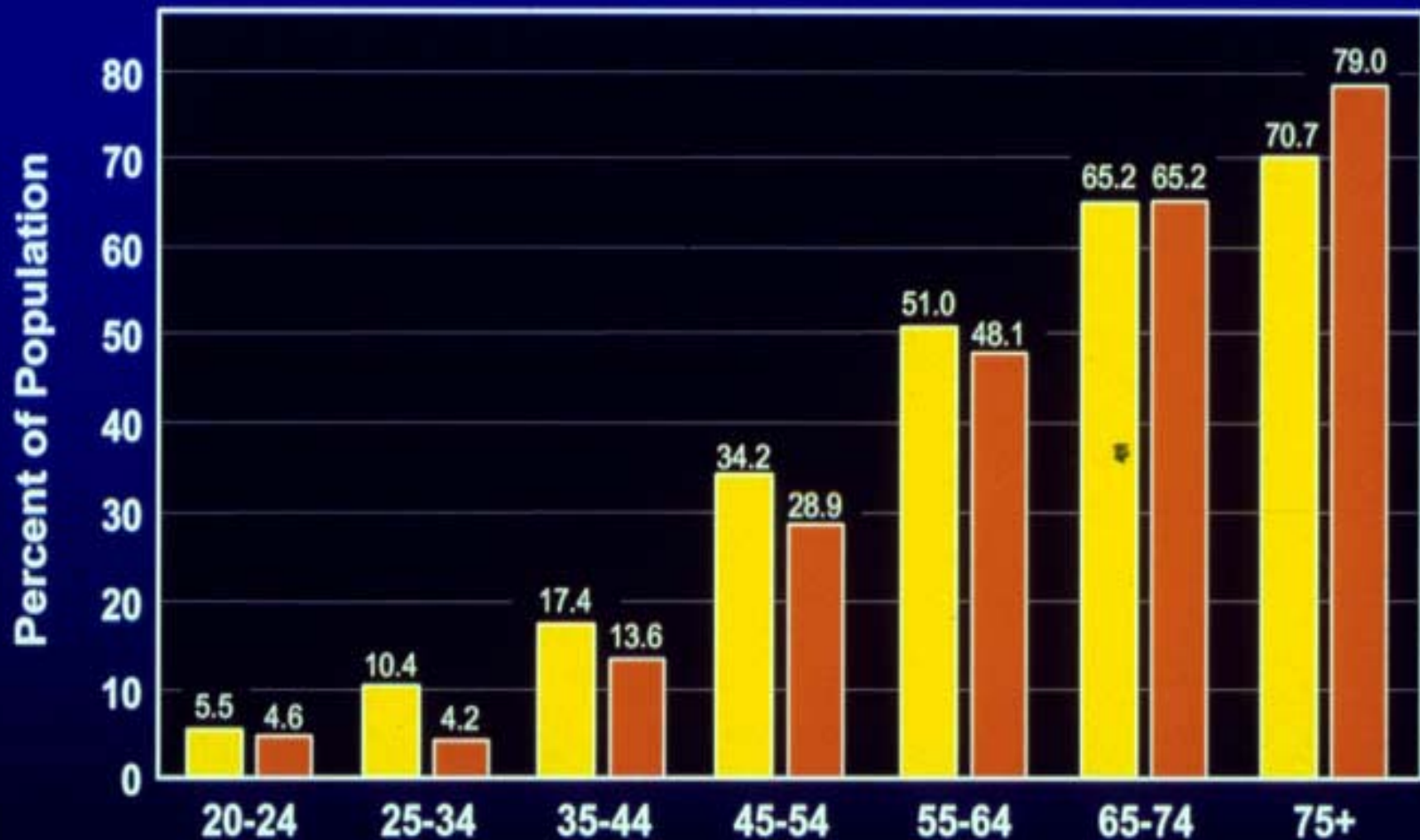
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# Estimated Prevalence of Cardiovascular Diseases in Americans Age 20 and Older by Age and Sex United States: 1988-94



Source: NHANES III (1988-94) CDC/NCHS and the American Heart Association

# Admissions for Cardiovascular Disease

## Number of Admissions (in thousands)

	<b>Total</b>	<b>Age <math>\geq</math> 65</b>	<b>Age <math>\geq</math> 75</b>
<b>Acute MI</b>	783	500 (63.9%)	284 (36.3%)
<b>Coronary disease</b>	1412	790 (55.9%)	378 (26.8%)
<b>Arrhythmias</b>	670	464 (69.3%)	288 (43.0%)
<b>Heart failure</b>	978	773 (79.0%)	529 (54.1%)
<b>Cerebrovascular disease</b>	1010	746 (73.9%)	493 (48.8%)

Source: National Hospital Discharge Survey, 1998.

# Hospital Mortality for Cardiovascular Causes

	<b>Total deaths (in thousands)</b>	<b>Age <math>\geq</math> 65</b>
<b>Acute MI</b>	78	68 (87.2%)
<b>Arrhythmias</b>	17	12 (70.6%)
<b>Heart failure</b>	42	37 (88.1%)
<b>Cerebrovascular disease</b>	65	49 (75.4%)

Source: National Hospital Discharge Survey, 1998.

# Major Cardiovascular Procedures by Age

Number of Procedures (in thousands)

	<b>Total</b>	<b>Age <math>\geq</math> 65</b>	<b>Age <math>\geq</math> 75</b>
<b>Cardiac catheterization</b>	1202	597 (49.7%)	243 (20.2%)
<b>PCI/stent</b>	926	456 (49.2%)	180 (19.4%)
<b>Coronary bypass</b>	553	304 (55.0%)	117 (21.2%)
<b>Pacemaker implant</b>	364	309 (84.9%)	211 (58.0%)

Source: National Hospital Discharge Survey, 1998.

# Reasons for Increasing Prevalence of Cardiovascular Disease with Age

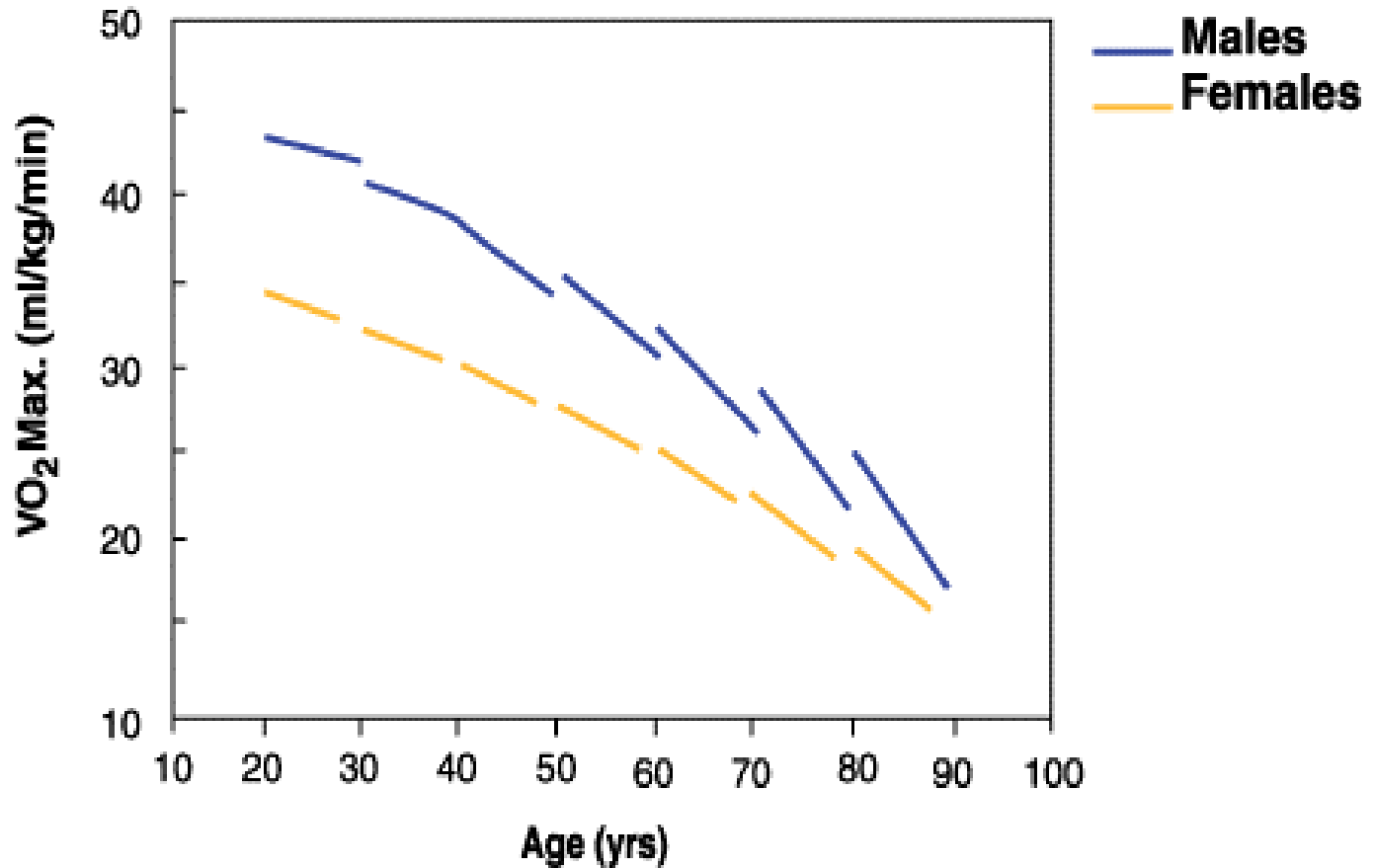
- Normative cardiovascular aging
- Cumulative effects of cardiovascular risk factors
- Improved survival of middle-aged patients with cardiovascular disease

# Principal Effects of Aging on Cardiovascular Structure and Function

- Increased vascular stiffness
- Increased myocardial stiffness
- Decreased  $\beta$ -adrenergic responsiveness
- Impaired mitochondrial ATP production
- Decreased baroreceptor responsiveness
- Impaired sinus node function
- Impaired endothelial function

**Net effect:** marked reduction in CV reserve

# *Age and $VO_2$ max in Healthy Subjects*



*Source: Circulation 2000;102(Suppl II):II-602*

# Effects of Aging on Other Organ Systems

## ☐ Kidneys

- Reduced GFR (8 cc/min/decade)
- Impaired Na/H<sub>2</sub>O excretion
- Impaired electrolyte homeostasis

## ☐ Lungs

- Reduced vital capacity
- Increased V/Q mismatching

## ☐ Nervous system

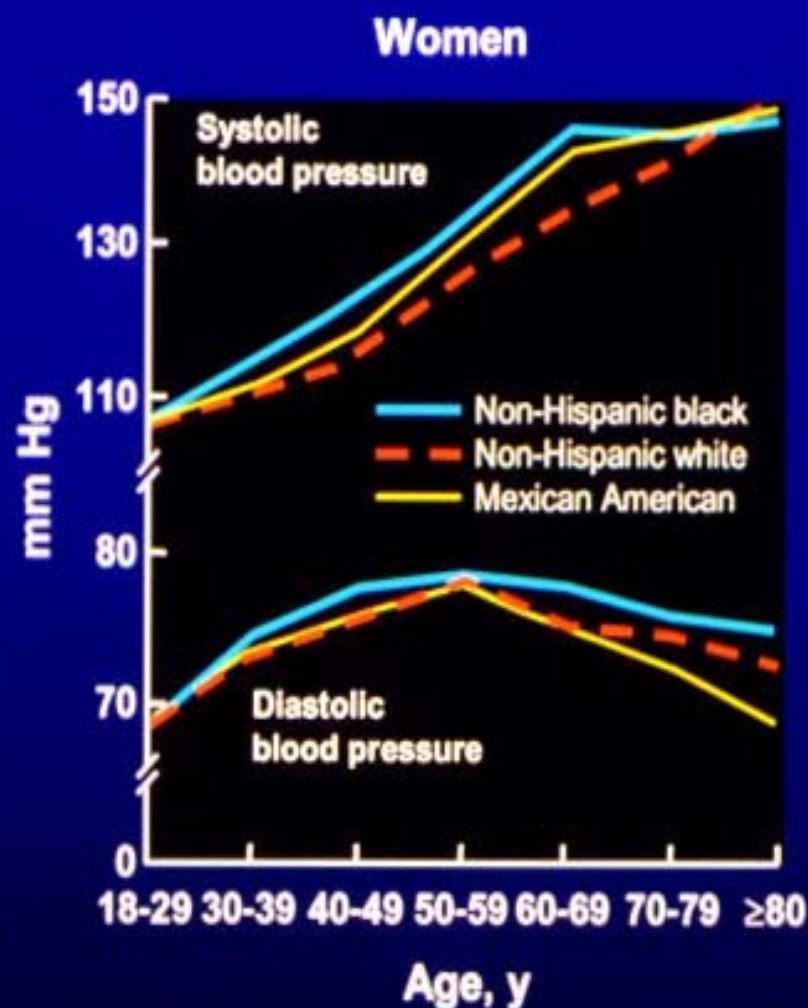
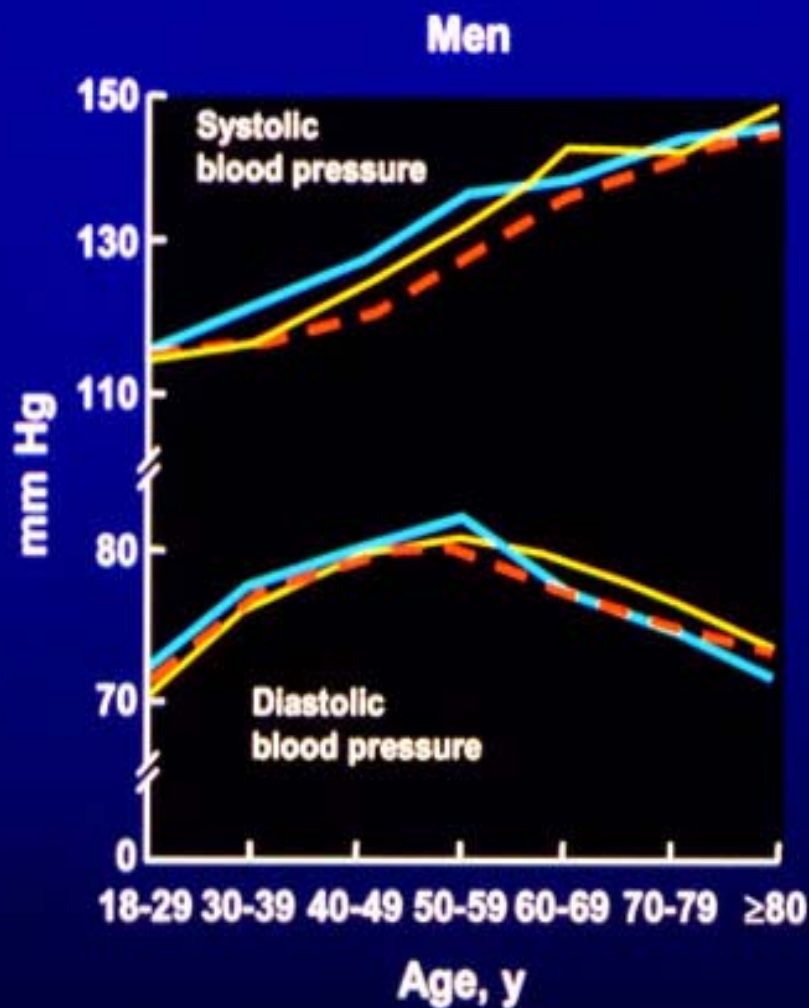
- Diminished reflex responsiveness
- Reduced CNS autoregulatory capacity
- Impaired thirst mechanism

# Risk Factors for Cardiovascular Disease

- Increasing age
- Family history
- High blood pressure
- High cholesterol
- Diabetes
- Smoking
- Obesity
- Physical inactivity

# Blood Pressure Ranges

Normal	$< 120/80$ mmHg
Pre-hypertension	120-139/80-89 mmHg
Stage 1	140-159/90-99 mmHg
Stage 2	$\geq 160/\geq 100$ mmHg



**Mean systolic and diastolic blood pressures in the United States by age, gender, and race**

*Source: National Health and Nutrition Examination Survey*

# Hypertension as a Risk Factor

- Systolic blood pressure is a potent risk factor for fatal and non-fatal cardiovascular events (incl. stroke) in persons over 65 years of age.
- The importance of elevated diastolic blood pressure as a risk factor declines with age.
- Widened pulse pressure, a marker of vascular aging, is also associated with increased cardiovascular risk in the elderly.

# Trials of Antihypertensive Treatment in the Elderly

Trial	N	Age	Risk Reduction (%)			
			CVA	CAD	CHF	All CVD
Australian	582	60-69	33%	18%	NR	31%
EWPHE	840	> 60	36%	20%	22%	29%
Coope	884	60-79	42%	-3%	32%	24%
STOP-HTN	1627	70-84	47%	13%	51%	40%
MRC	4396	65-74	25%	19%	NR	17%
HDFP	2374	60-69	44%	15%	NR	16%
SHEP	4736	≥ 60	33%	27%	55%	32%
Syst-Eur	4695	≥ 60	42%	26%	36%	31%
STONE	1632	60-79	57%	6%	68%	60%
Syst-China	2394	≥ 60	38%	33%	38%	37%

# Treatment of Hypertension in the Elderly

- Lifestyle modifications
  - Weight loss (if applicable)
  - Salt restriction
  - Regular exercise
  - Avoidance of excess alcohol
  - Smoking cessation
- Medications
  - Diuretics
  - Beta blockers
  - Calcium channel blockers
  - ACE inhibitors
  - Angiotensin receptor blockers

# Cholesterol

## Total cholesterol

<b>Desirable</b>	<b>&lt; 200 mg/dl</b>
<b>Borderline high</b>	<b>200-239 mg/dl</b>
<b>High</b>	<b>≥ 240 mg/dl</b>

## LDL cholesterol

<b>Optimal</b>	<b>&lt; 100 mg/dl</b>
<b>Near optimal</b>	<b>100-129 mg/dl</b>
<b>Borderline high</b>	<b>130-159 mg/dl</b>
<b>High</b>	<b>160-189 mg/dl</b>
<b>Very high</b>	<b>≥ 190 mg/dl</b>

## HDL cholesterol

<b>Low</b>	<b>&lt; 40 mg/dl</b>
<b>High</b>	<b>≥ 60 mg/dl</b>

# Cholesterol Levels in Men and Women in the U.S.

Age	Total, mg/dl		LDL, mg/dl		HDL, mg/dl	
	Men	Women	Men	Women	Men	Women
20-34	189	185	120	110	47	56
35-44	207	195	134	117	46	54
45-54	218	217	138	132	47	57
55-64	221	237	142	145	46	56
65-74	218	234	141	147	45	56
≥ 75	205	230	132	147	45	57

Source: National Health and Nutrition Examination Survey (NHANES)

# Lipids as a Risk Factor

- Strength of association between lipids and cardiovascular disease declines with age
- Preponderance of evidence indicates that LDL and HDL levels predict CV risk at least up to age 80
- Although relative risk declines with age, the population attributable risk of dyslipidemias for the development of coronary artery disease may be higher in the elderly



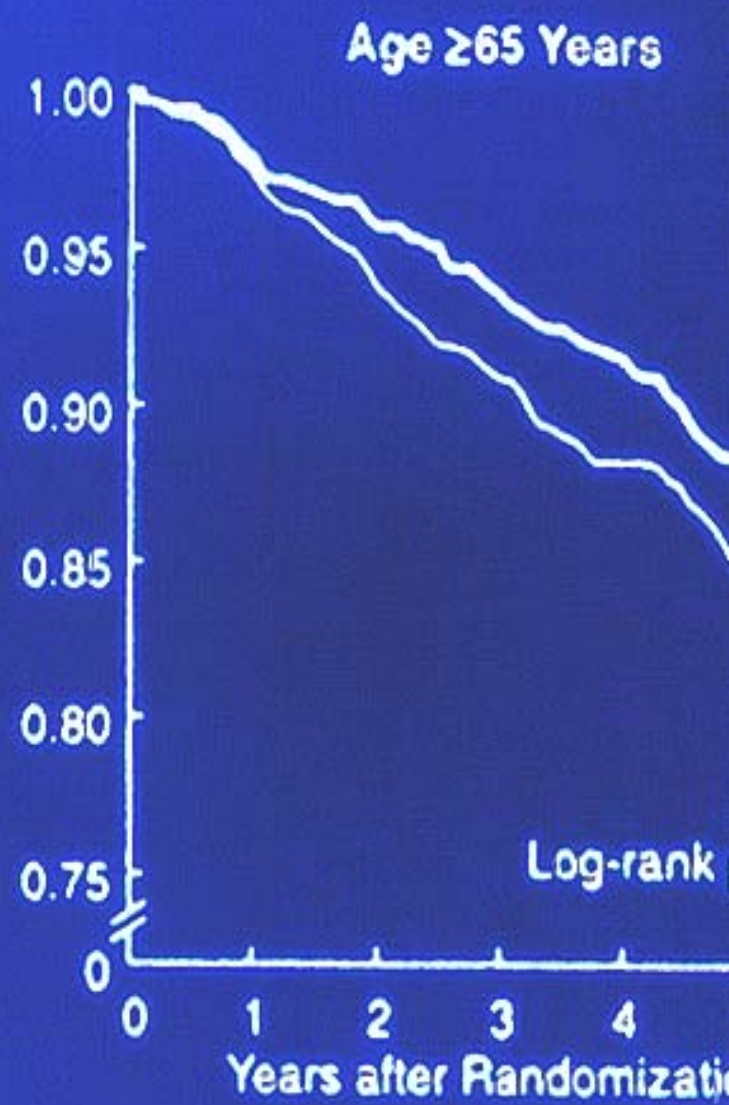
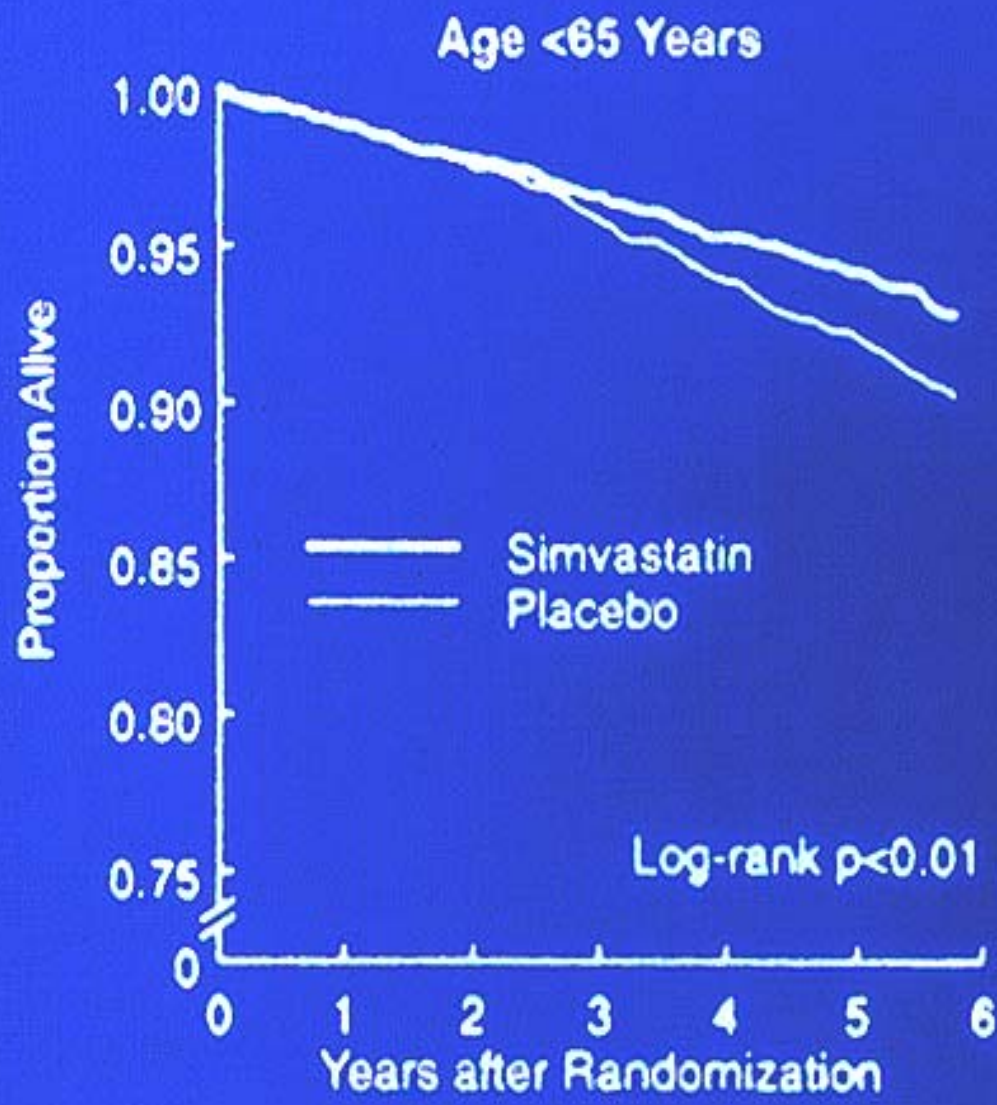


FIG 3. Kaplan-Meier survival curves for all-cause mortality in patients  $\geq 65$  and  $< 65$  years of age.

# UK Heart Protection Study

- ❑ 20,536 patients, age 40-80
- ❑ High risk due to:
  - Angina or prior myocardial infarction
  - Prior stroke
  - Significant peripheral arterial disease
  - Diabetes mellitus
  - Hypertension
- ❑ Randomized to simvastatin 40 mg or placebo
- ❑ Followup 5 – 5 ½ years

# UK Heart Prevention Study

## Results

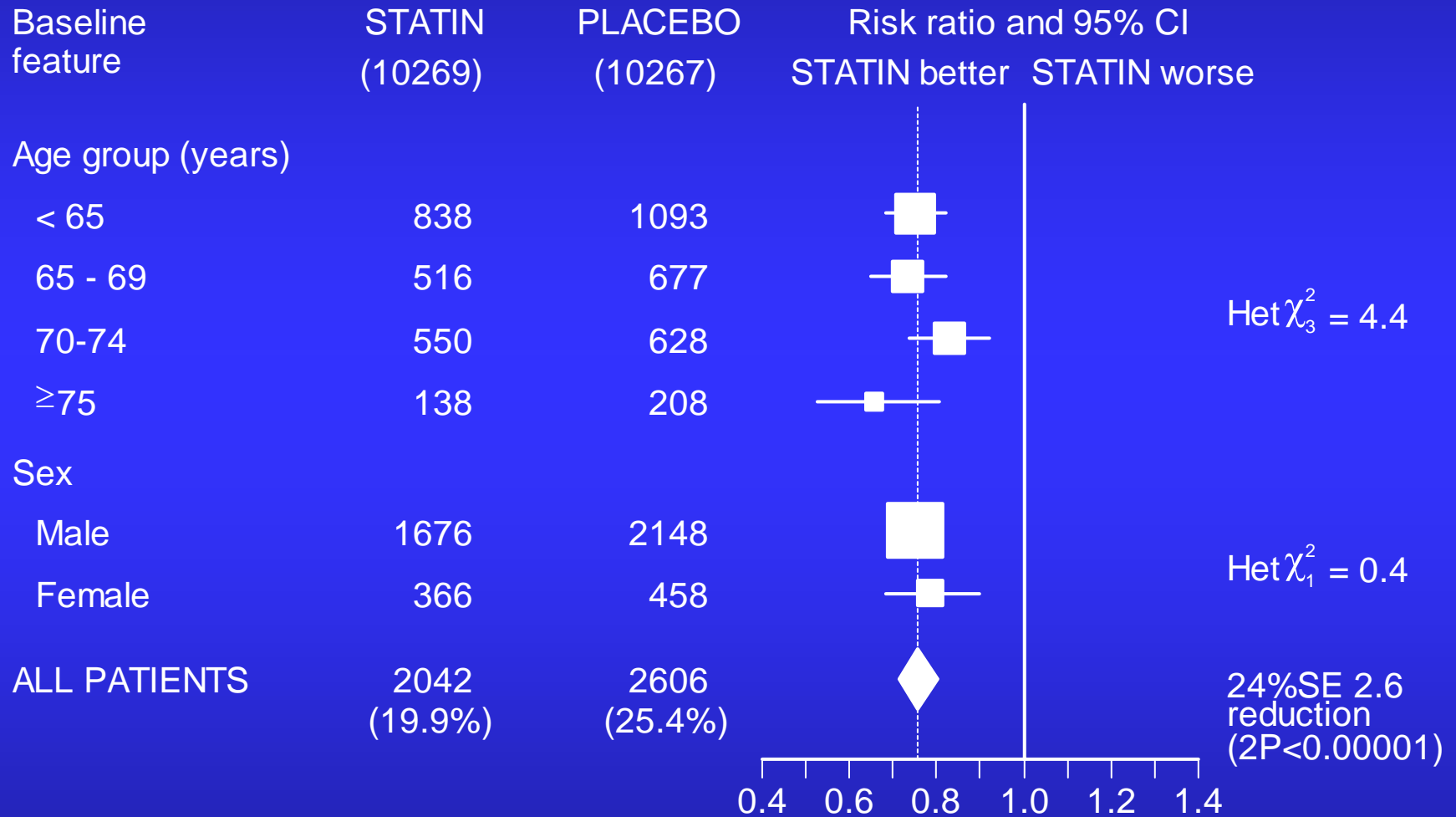
- ❑ 24% reduction in major vascular events (MI, CVA, revascularization procedures, death)
- ❑ 28% reduction in MIs and CVAs in diabetics
- ❑ 17% reduction in CV mortality (791 vs. 943)
- ❑ 12% reduction in all-cause mortality

# UK Heart Protection Study

## Results (continued)

- ❑ Benefits evident in all subgroups
  - Age  $\geq 75$  years
  - Women
  - Total chol  $< 200$ , LDL  $\leq 115$  mg/dl
- ❑ Excellent safety profile
  - Adverse events similar to placebo

# SIMVASTATIN: VASCULAR EVENT by AGE & SEX



# Treatment of Dyslipidemias in the Elderly

## NCEP: ATP-III

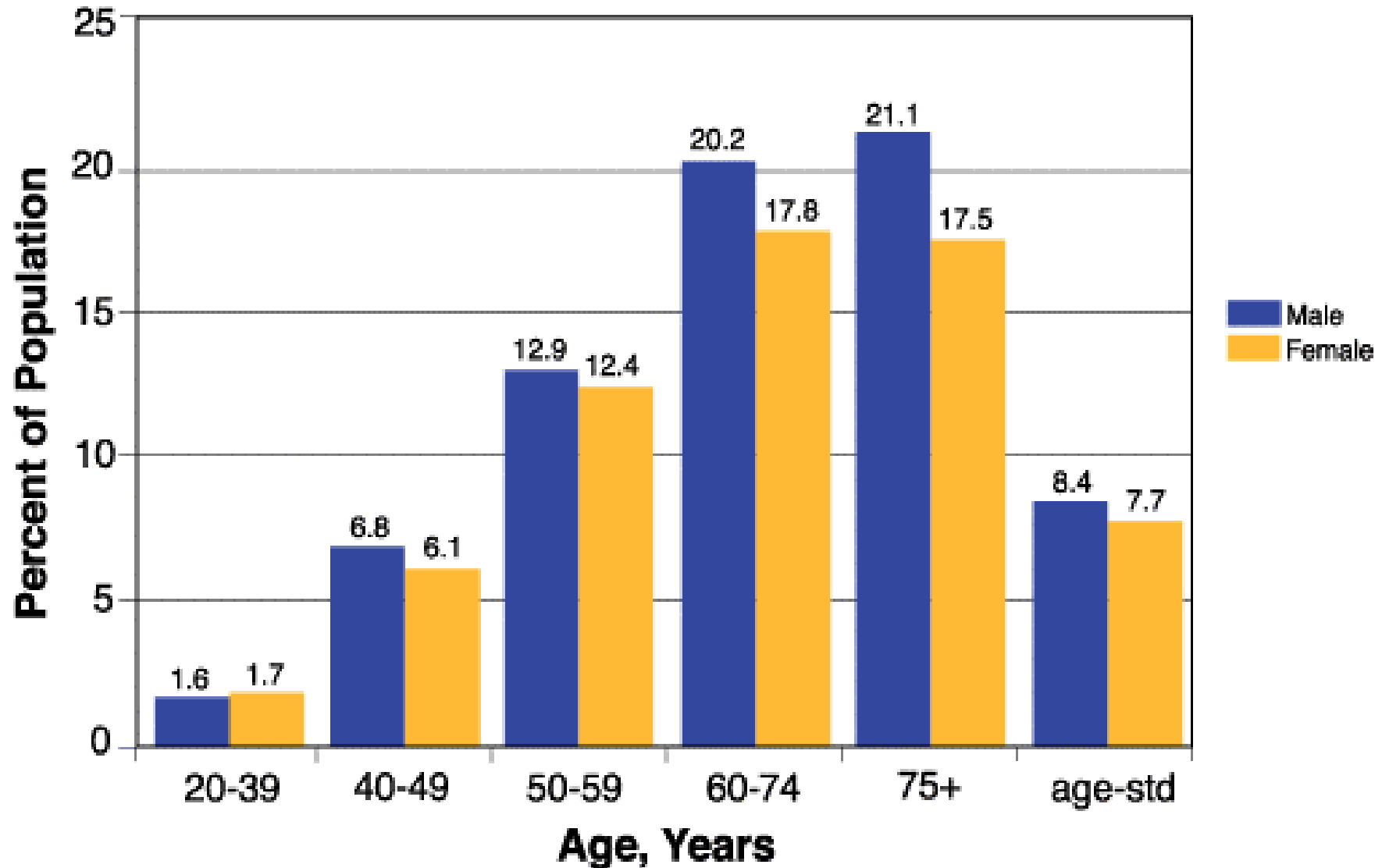
### □ Primary prevention

- Therapeutic lifestyle changes
- Drug therapy in high risk patients

### □ Secondary prevention

- Similar to younger patients
- Target LDL-C < 100 mg/dl

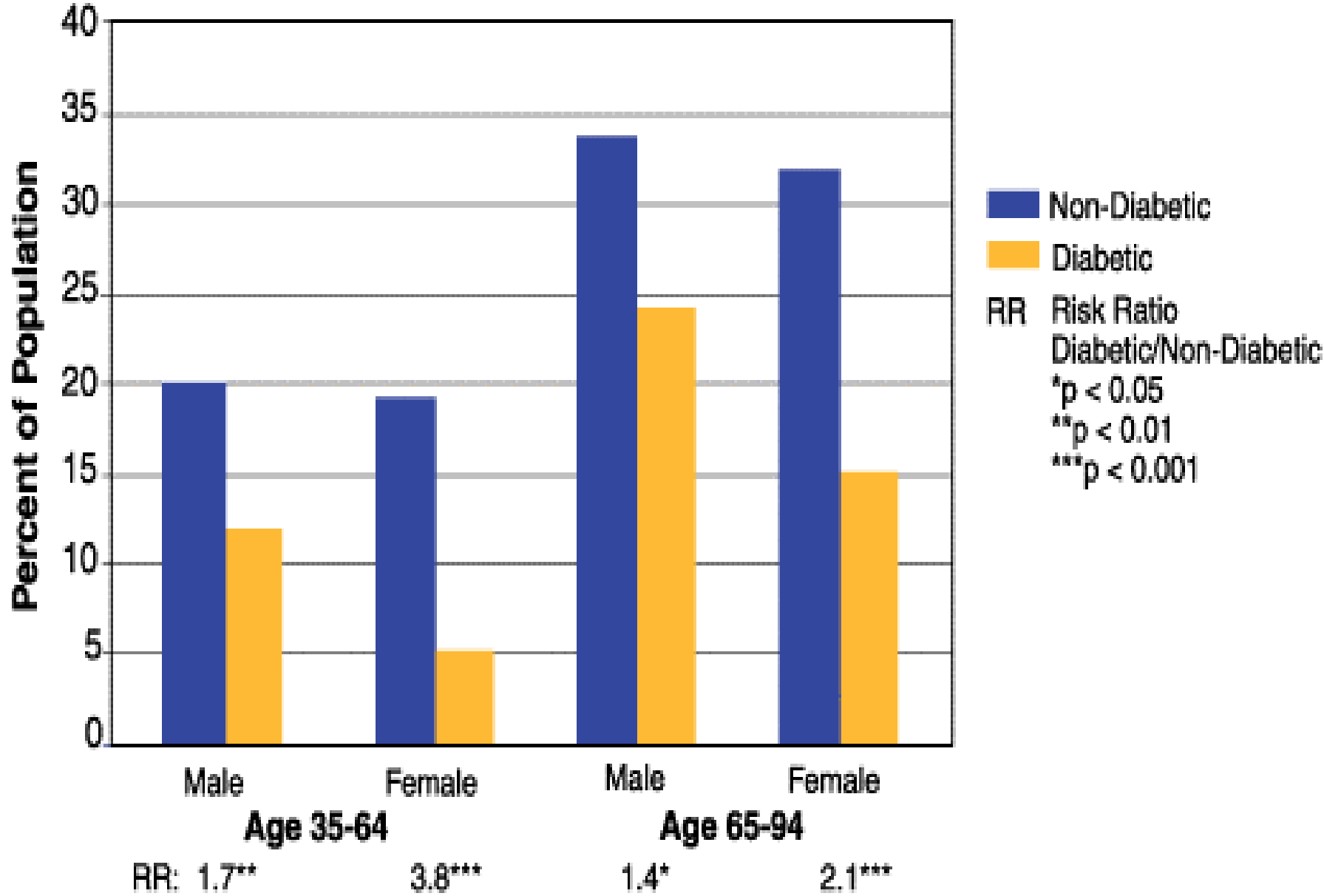
# Prevalence of Diabetes in the U.S. Population



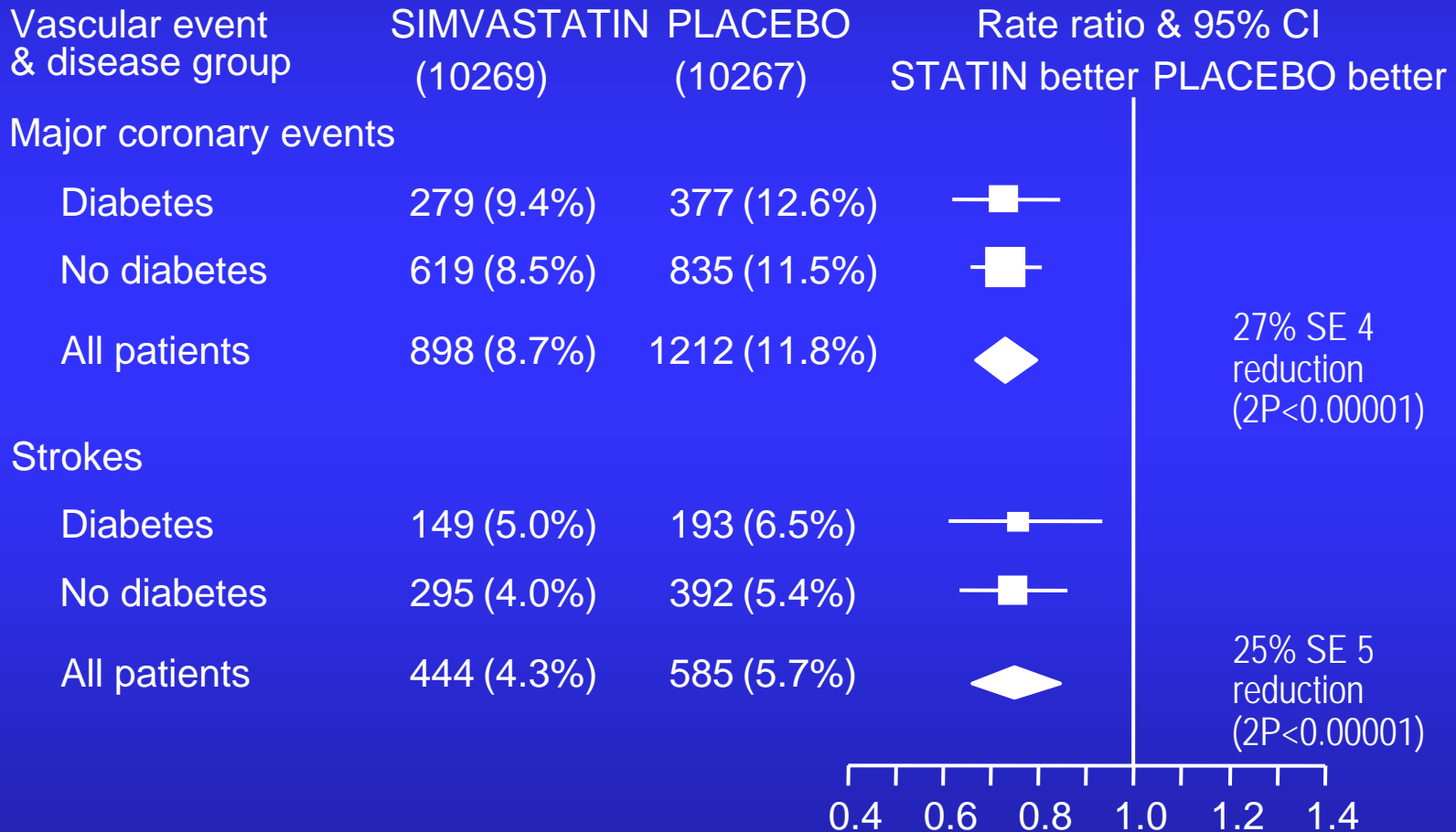
Source: National Health and Nutrition Examination Survey III

# Age-Adjusted Incidence Rates for Coronary Heart Disease Based on Diabetic Status

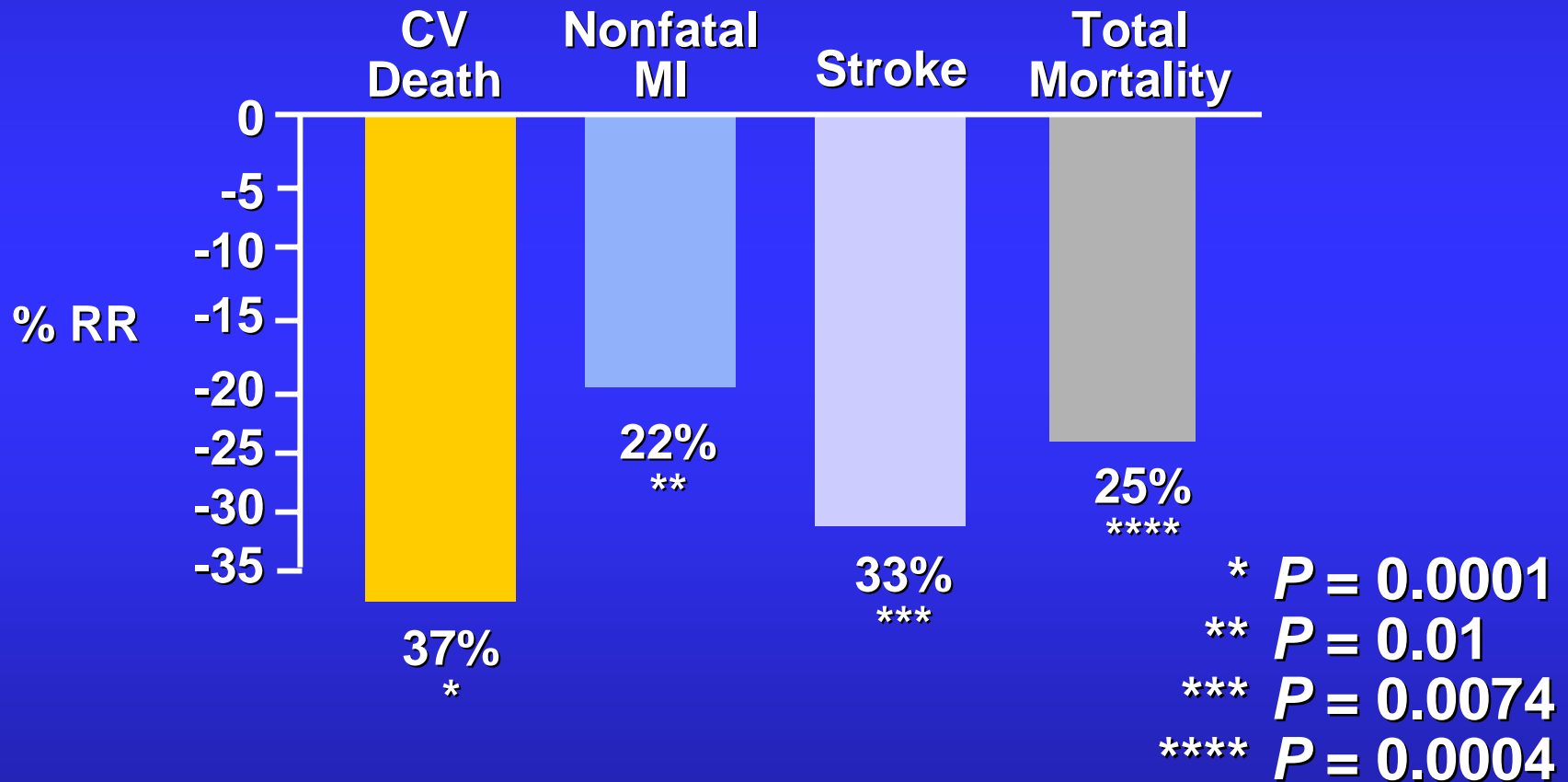
Framingham Study, 30-Year Follow-Up.



# SIMVASTATIN: MAJOR CORONARY EVENTS and STROKE by prior DIABETES



# MICRO-HOPE: Effects of Ramipril on Primary Endpoints and Total Mortality



*Lancet 2000;355:253-9.*

# Smoking Status of Adults: 1998

Age, yrs	Never	Former	Current	Advised To Quit
< 55	40.4%	22.7%	36.9%	71.7%
55-64	31.5%	37.8%	30.7%	72.4%
65-74	41.5%	43.4%	15.1%	72.7%
75-84	49.5%	41.4%	9.1%	66.3%
≥ 85	64.8%	30.7%	4.5%	56.1%

Source: MMWR 2000;49:797-801

# Risk of Continued Smoking: The CASS Registry

Age, years	Relative Risk for Death*	Relative Risk for Death or MI*
55-59	1.5	1.5
60-64	2.0	1.4
65-69	1.4	1.5
≥ 70	3.3	2.9

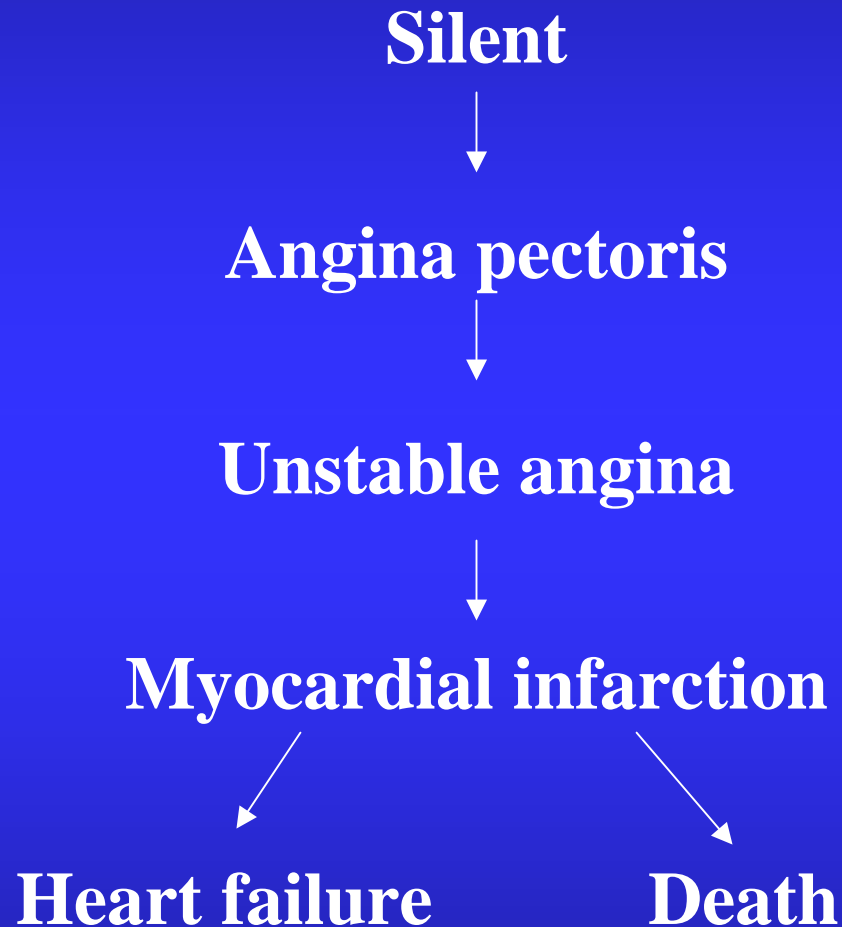
\* Compared to persons who stopped smoking, 6 year follow-up

*NEJM 1988;319:1365-9*

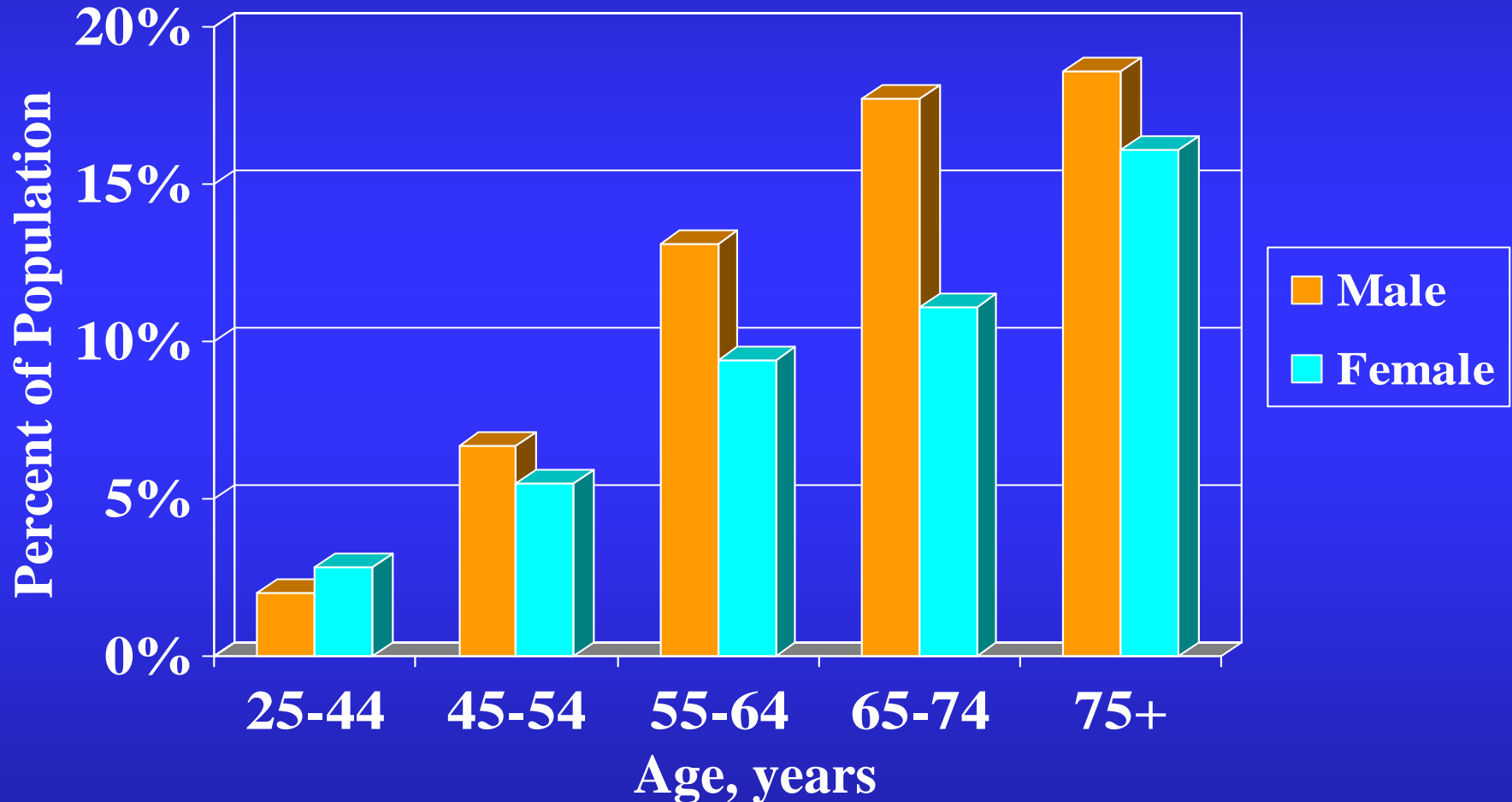
# Coronary Artery Disease (CAD)

- Most common cause of death in U.S. in both men and women
- Narrowing of coronary arteries due to buildup of cholesterol plaque
- Arteries may be narrowed up to 75% without causing symptoms

# Spectrum of CAD



# Prevalence of Coronary Heart Disease by Age and Sex in the U.S. from 1988-94

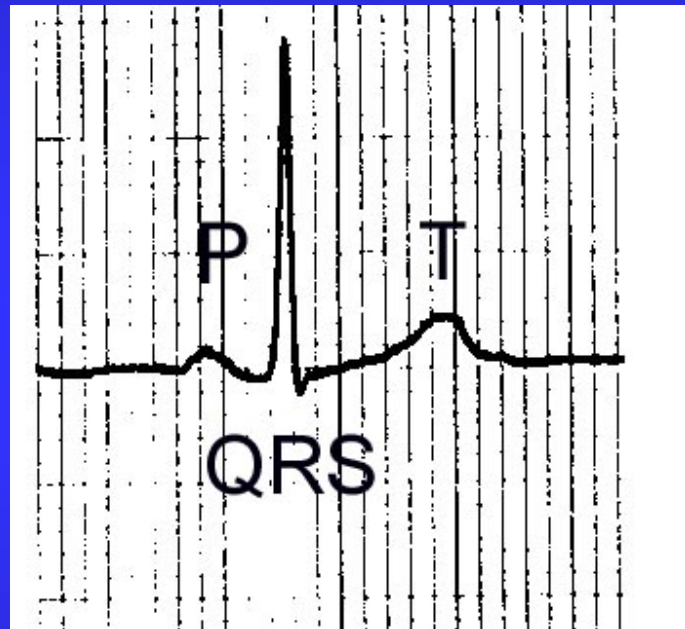


*Source: National Health and Nutrition Examination Survey*

# Diagnosis of CAD

- Symptoms
- Electrocardiogram (ECG)
- Stress test
- Cardiac catheterization

# ECG Waveforms



# Normal 12-lead ECG



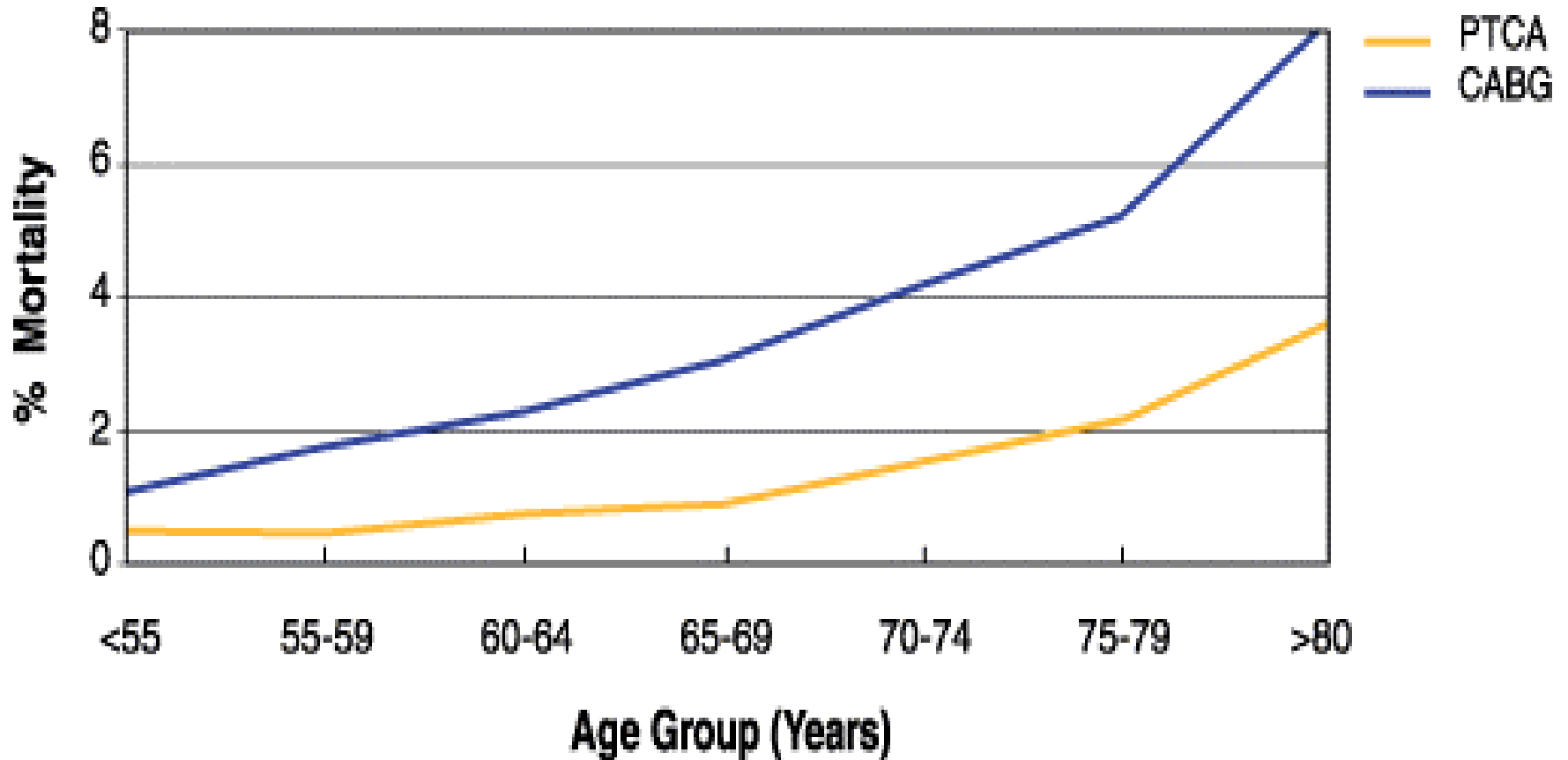
# Angina Pectoris

- Chest tightness, pressure, heaviness
- Brought on by exertion, emotional stress
- May radiate to arm, throat, jaw
- May be associated with SOB, weakness
- Relieved by rest, nitroglycerin

# Treatment of Coronary Artery Disease

- Lifestyle modifications
- Treatment of risk factors
- Medications
  - Aspirin/Clopidogrel
  - Nitrates
  - Beta blockers
  - Calcium channel blockers
  - ACE-inhibitors/ARBs
  - Statins
- Revascularization
  - PTCA/stenting
  - Coronary bypass surgery (CABG)

# *Mortality Following PTCA and CABG*



# Case 1: Prolonged chest pain

An 82 y.o. man with hypertension, elevated cholesterol, PUD, mild CRI, and stable exertional angina presents to the ED with a 2 hr h/o moderate chest pain radiating to the shoulders and upper arms and associated with SOB, weakness, and pallor. He took 3 “nitros” at home without relief. HR 90, regular. BP 160/80 mmHg. RR 22/min. Heart: RRR, normal tones, no murmurs. Lungs: bibasilar moist crackles.

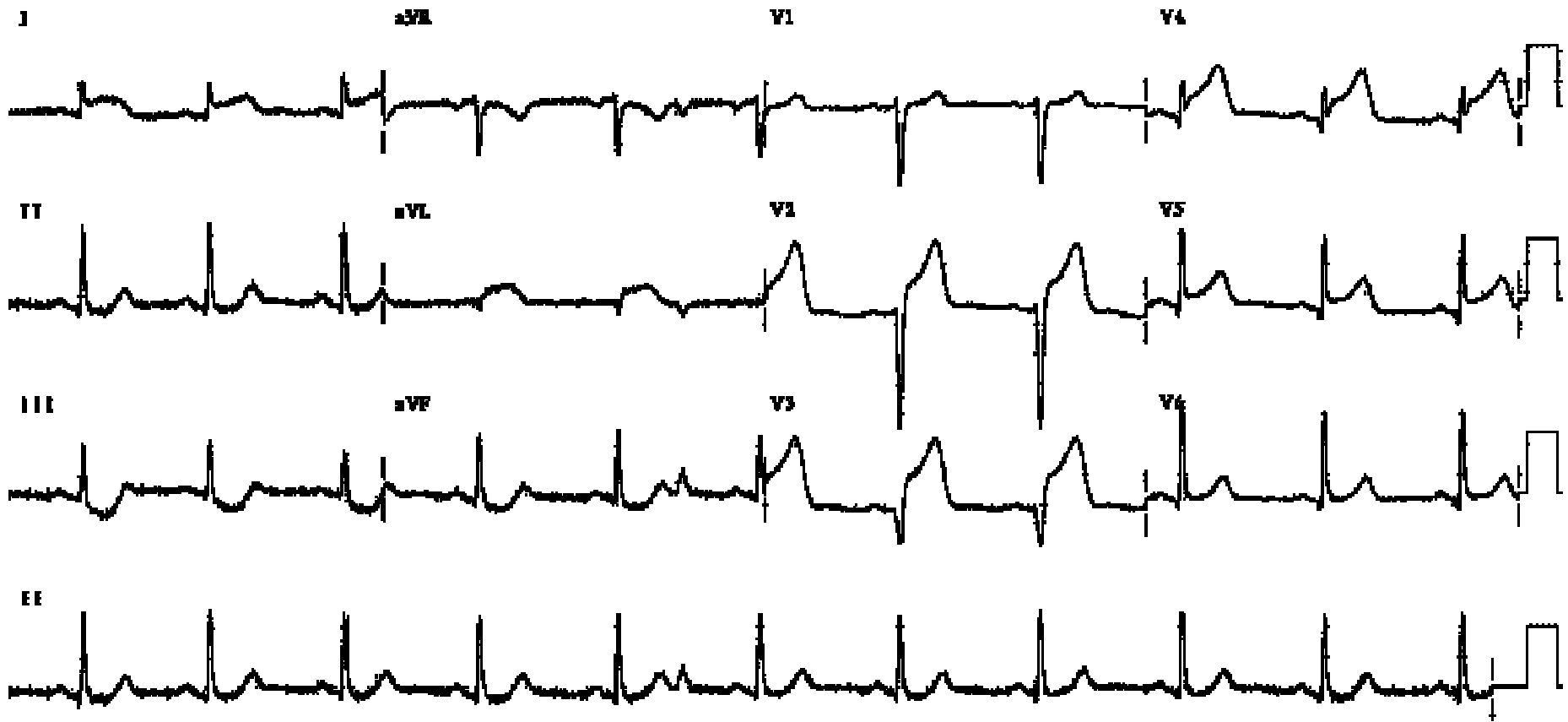
*What is the cause of this patient's symptoms?*

*How should he be treated?*

# Acute Myocardial Infarction

- Death of heart muscle due to plaque rupture with sudden occlusion of artery by blood clot
- More severe and prolonged symptoms
- High risk of death in early hours
- Requires emergency hospitalization

# Acute Anterolateral MI



LOC 00000-0000 Speed: 25 mm/sec Limb: 10 mm/mV Chest: 10 mm/mV

50% 0.15-150 Hz

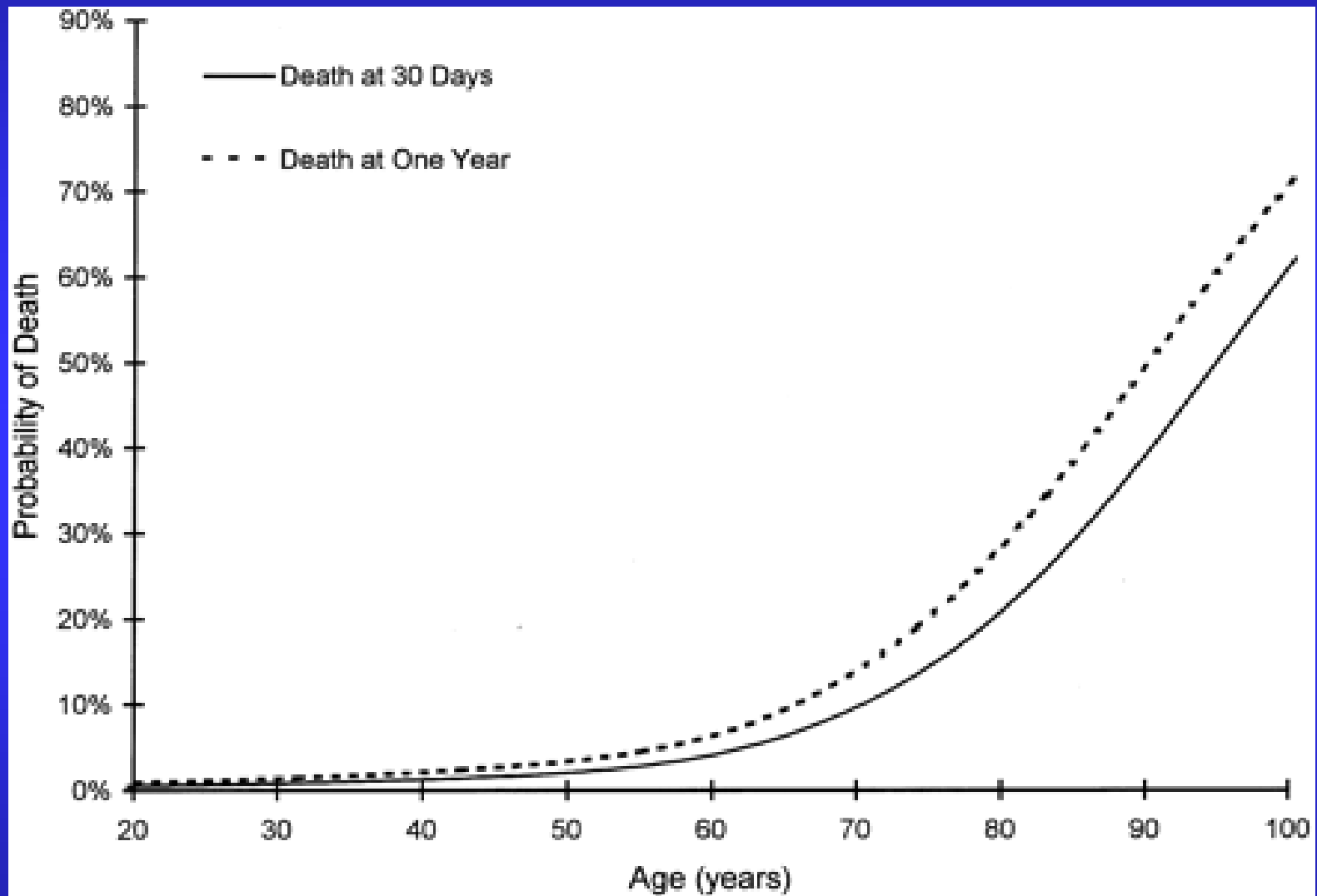
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# Epidemiology of Acute MI in the United States

<b>Age, years</b>	<b>% of Population</b>	<b>No. of MIs (in 1000s)</b>	<b>% of MIs</b>	<b>% of MI Deaths</b>
<b>15-64</b>	<b>66.3%</b>	<b>320</b>	<b>38.6%</b>	<b>&lt; 20%</b>
<b>≥ 65</b>	<b>12.6%</b>	<b>509</b>	<b>61.4%</b>	<b>&gt; 80%</b>
<b>≥ 75</b>	<b>6.1%</b>	<b>305</b>	<b>36.8%</b>	<b>~ 60%</b>

*Source: 1999 National Hospital Discharge Survey*

# Prognosis after Acute MI by Age



*Source: Circulation 1996;94:1826-33*

# Treatment of Acute MI

- Reperfusion therapy
  - Thrombolysis
  - PTCA/stenting
- Aspirin / anti-thrombotic therapy
- Beta blockers
- ACE inhibitors

# Heart Valves

- Ensure proper direction of blood flow through the heart
- Right side: tricuspid, pulmonic
- Left side: mitral, aortic
- Valve disorders
  - Stenosis (narrowing)
  - Regurgitation (leakage)

# Diagnosis of Valve Disorders

- Symptoms: fatigue, chest pain, dizziness, heart failure
- Signs: heart murmur, heart failure
- Echocardiogram
- Cardiac catheterization

# Aortic Stenosis

- Prevalence: 15% of persons  $\geq 75$  years
- Second most common reason for heart surgery
- Symptoms: angina, shortness of breath, dizziness, syncope
- Diagnosis: physical exam, echocardiogram
- Treatment: aortic valve replacement
- Prognosis: favorable with surgery

# Mitral Regurgitation

- Prevalence: 30% of persons  $\geq 75$  years
- Symptoms: shortness of breath, ankle swelling
- Diagnosis: physical exam, echocardiogram
- Treatment: medications, surgery
- Prognosis: variable; depends on severity, etiology, other factors (e.g. LV function)

# Heart Failure

- Inability of the heart to pump a sufficient supply of blood to meet the body's needs
- Quintessential disorder of cardiovascular aging

## Case 2: Exertional shortness of breath

An 83 y.o. woman with hypertension, o/w healthy, c/o increasing SOB with walking. 2 yrs ago she could walk to the store (3 blks) without difficulty, but now she has to stop to “catch my breath”. She also reports difficulty climbing stairs. She denies CP or SOB at rest, but tires more easily. She smoked 1 PPD for 30 yrs but quit 20 yrs ago. Her husband died 1½ yrs ago from cancer; since then she “hasn’t felt like doing anything”.

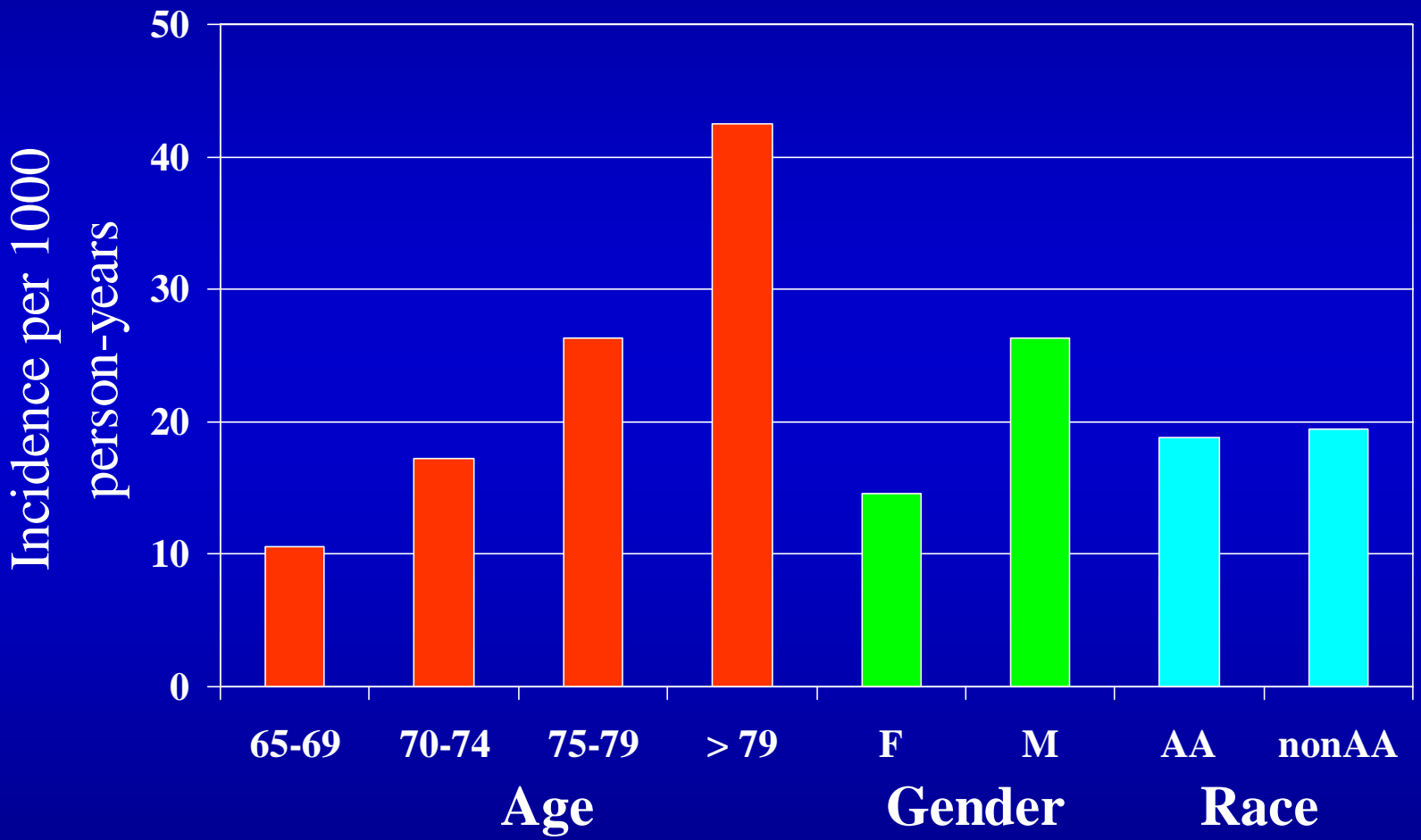
*What is the cause of this patient’s shortness of breath?*

Differential diagnosis: heart failure, angina, depression, deconditioning, COPD, anemia, thyroid disease, cancer?  
Or could it be “normal aging” (as the patient believes)?

# Epidemiology of Heart Failure in the United States

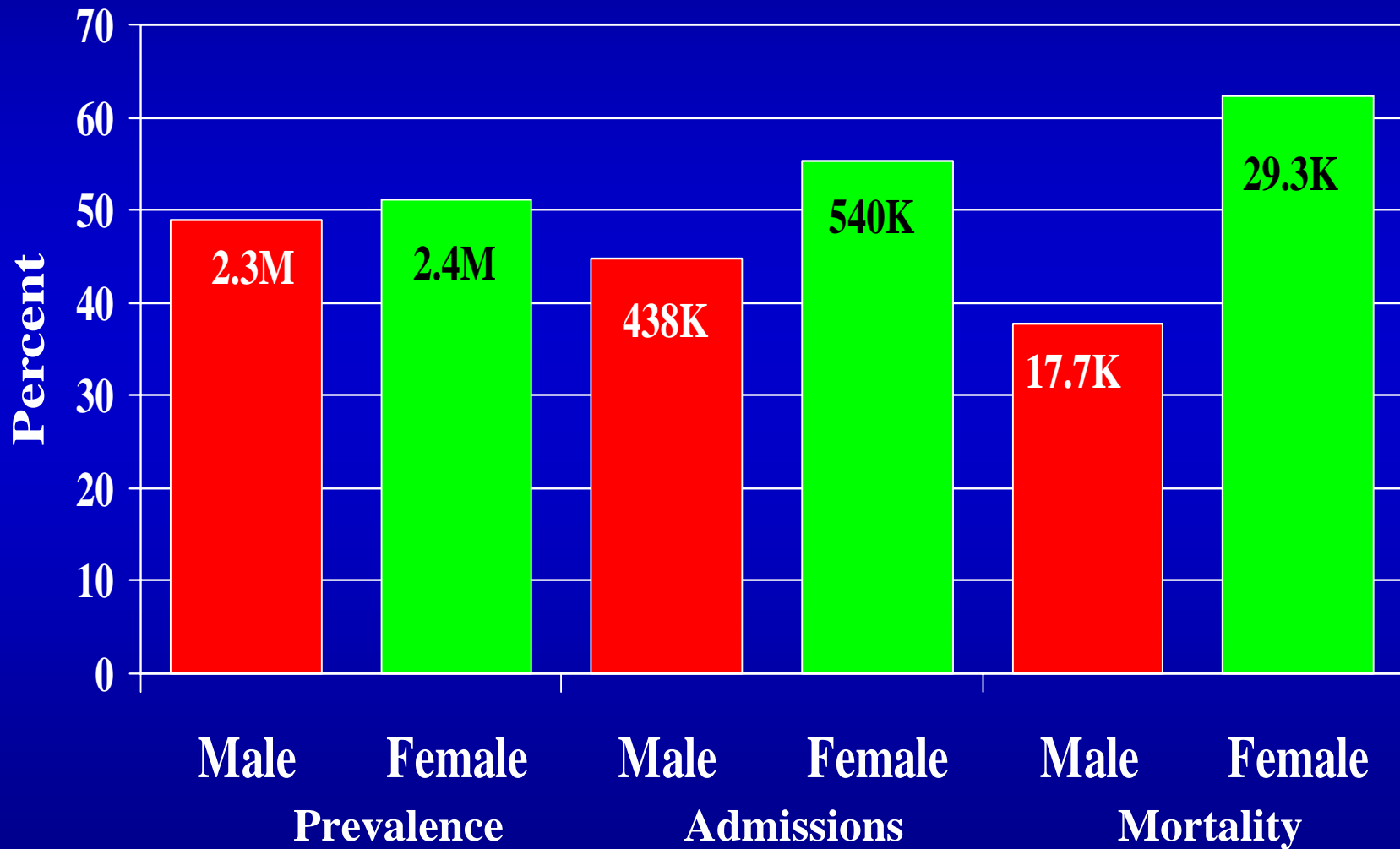
- ❑ Prevalence: 5.0 million (2.2%)
- ❑ Incidence: 550,000 new cases/year
- ❑ Hospitalizations: 999,000 in 2000
- ❑ Mortality: 47,000/220,000 per yr
- ❑ Cost: > \$25 billion annually
- ❑ Median age: 75 yrs
  - 78% of men  $\geq$  65 years
  - 85% of women  $\geq$  65 years
- ❑ Incidence and prevalence increasing

# Incidence of Heart Failure in the Elderly: The Cardiovascular Health Study

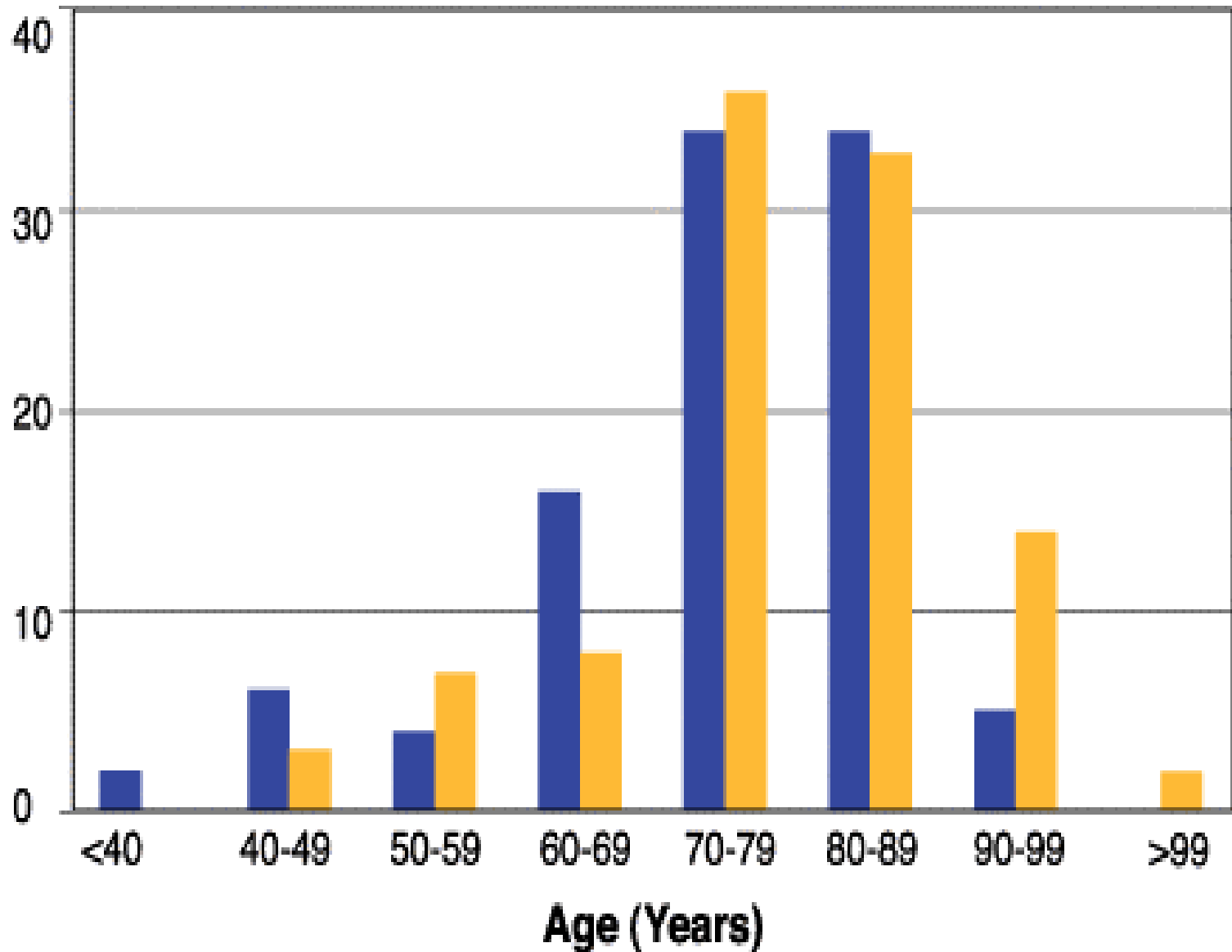


Gottdiener JS. JACC;35:1628.

# Heart Failure in the U.S.: Impact of Gender



# Numbers of Patients Hospitalized with Heart Failure



# Etiology of Heart Failure

- Coronary artery disease
- Hypertension
- Valvular heart disease
- Cardiomyopathy
  - Dilated
  - Hypertrophic
  - Restrictive
- Systolic vs. diastolic

# How is Heart Failure Diagnosed?

- Symptoms
- Physical examination
- Chest X-Ray
- Echocardiogram
- Cardiac catheterization

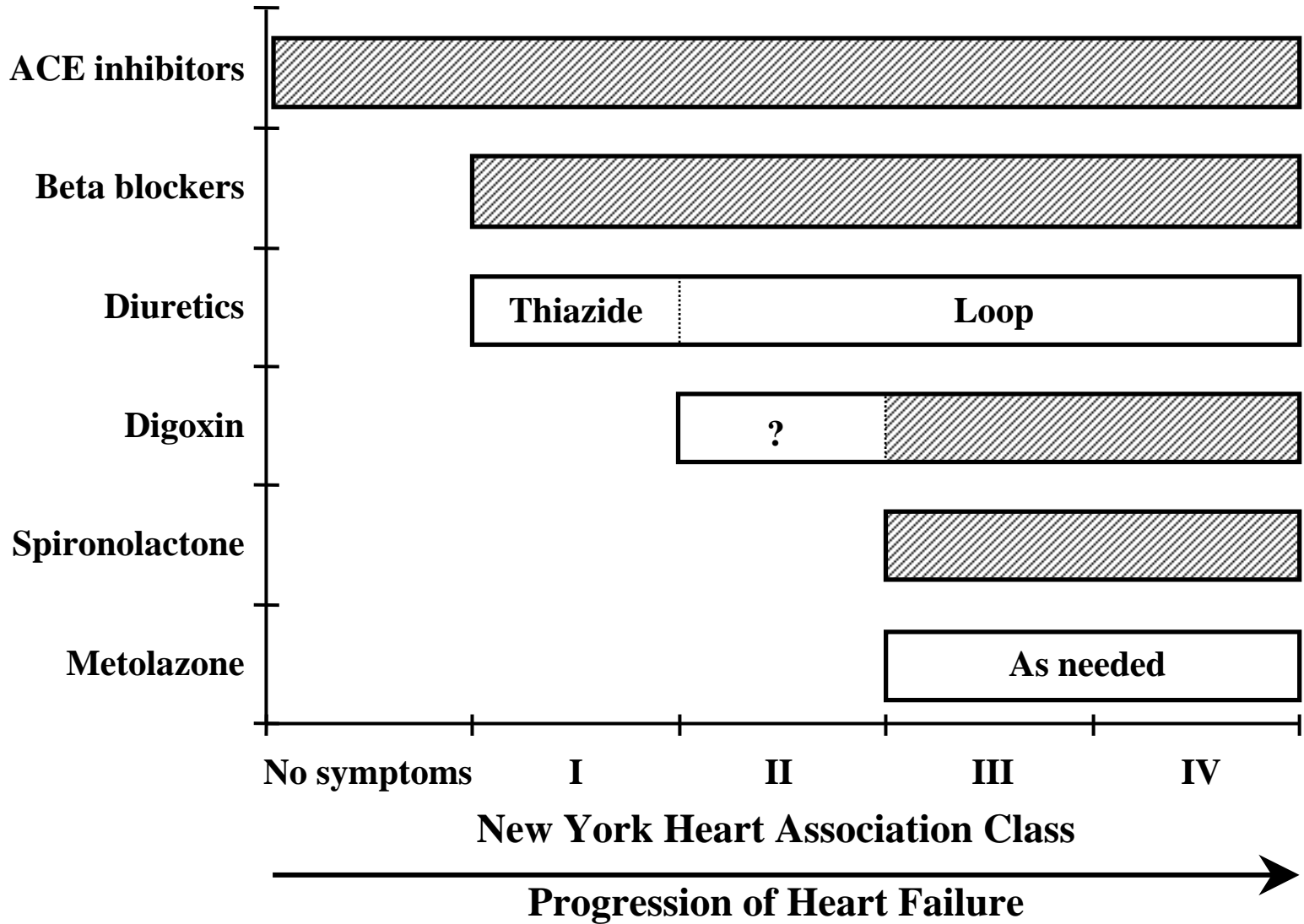
# What Are the Symptoms of Heart Failure?

- Exertional shortness of breath
- Decreased exercise tolerance
- Fatigue
- Orthopnea
- Paroxysmal nocturnal dyspnea (PND)
- Swelling of feet and ankles (edema)

# New York Heart Association Functional Classification

<b>Class</b>	<b>Description</b>
<b>I</b>	No limitations; symptoms only with strenuous activities
<b>II</b>	Mild limitations; symptoms with moderate activity, e.g. climbing several flights of stairs
<b>III</b>	Marked limitations; symptoms with common daily activities, e.g. walking less than 2 blocks
<b>IV</b>	Severe limitations; symptoms at rest or with minimal activity, e.g. going to the bathroom

# Pharmacotherapy of Systolic Heart Failure



# Management of Diastolic Heart Failure

- Optimize blood pressure control
- Treat ischemia (CAD)
- Medications
  - Diuretics
  - ACE inhibitors
  - Angiotensin receptor blockers
  - Beta blockers
  - Calcium channel blockers

# Readmission Rates for Heart Failure

				Readmission
Author	Year	Age	Time	Rate
Gooding	1985	$\geq 65$	6 mo	36%
Rich	1988	$\geq 70$	3 mo	29%
Vinson	1990	$\geq 70$	90 da	47%
Krumholz	1997	$\geq 65$	6 mo	44%
Philbin	1999	mean 76	6 mo	46%
Cowie	2002	mean 75	19 mo	59%
DiLenarda	2003	mean 74	6 mo	45%

# Why the Gap between RCTs and Clinical Practice?

- Underutilization of effective therapies
- Inadequate treatment of prevalent comorbidities
- Poor compliance with medications and diet
- Inadequate followup

**“At least 50% of HF admissions are preventable.”**

# Objectives of HF Disease Management

- ❑ Maximize physician/provider compliance with established practice guidelines
- ❑ Optimize management of comorbidities
- ❑ Enhance patient compliance and self-efficacy
- ❑ Identify barriers and intervene pro-actively
- ❑ Improve well-being and quality of life
- ❑ Reduce resource consumption and cost of care
- ❑ Increase functional survival

# HFDM Meta-analysis

- 18 RCTs from 8 countries (10 U.S.) involving 3304 in-patients with HF
- Mean age  $\geq 70$  yrs in 16/18 studies
- NYHA class, LVEF variable
- Mean follow-up 8 mo (range 3-12 mo)

JAMA 2004;291:1358-67

# HFDM Meta-analysis: Results

	Inter- vention	Control	RR	NNT	P
Readmissions	34.9%	43.2%	0.75	12	<.001
Death or readmission	44.1%	60.3%	0.73	6	0.02
All-cause mortality	14.2%	16.5%	0.87	43	0.06

JAMA 2004;291:1358-67

# HFDM Meta-analysis: Results

- 25.7% improvement in quality of life scores (p = 0.01; N = 6 studies)
- \$536 lower overall cost of care/pt among U.S. trials (95% CI \$115 to \$956, p = 0.03; N = 4 studies)
- \$359 lower overall cost of care/pt among non-U.S. trials (95% CI -\$45 to \$763, p = 0.10; N = 4 studies)

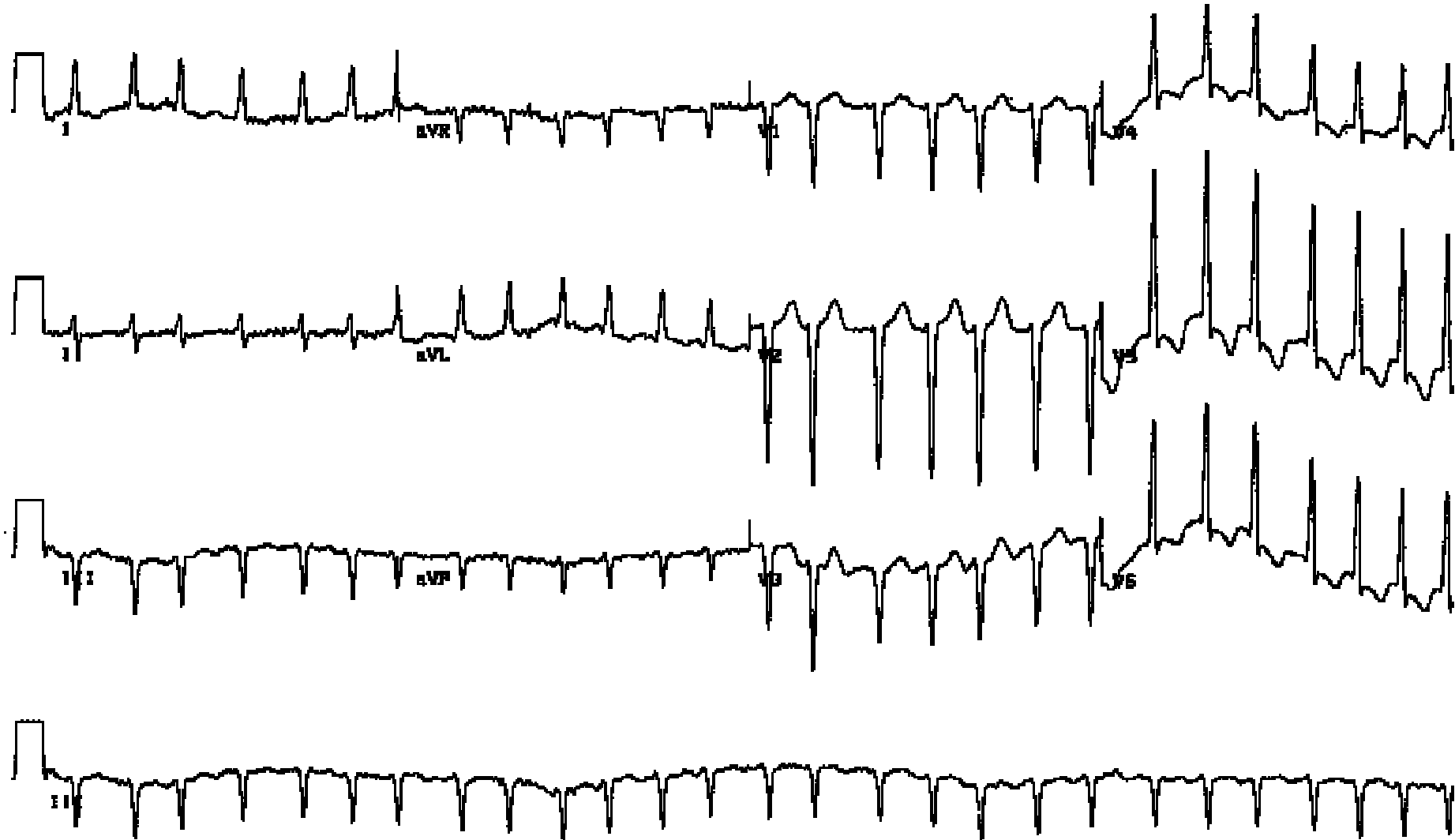
# Sick Sinus Syndrome

- Prevalence: increases progressively with age
- Etiology: degeneration of sinus node pacemaker cells
- Symptoms: dizziness, syncope, fatigue, effort intolerance, heart failure, angina
- Diagnosis: ECG -- brady and tachyarrhythmias
- Treatment: permanent pacemaker
- Complications: increased risk of stroke

# Atrial Fibrillation

- Chaotic beating of upper chambers (atria)
- Prevalence: > 10% after age 80
- Symptoms: palpitations, shortness of breath, angina
- Diagnosis: physical exam, ECG
- Complications: heart failure, stroke
- Prognosis: good with proper treatment

# Atrial Fibrillation with RVR



# Management of Atrial Fibrillation

- Rate control
  - Beta-blockers
  - Diltiazem, verapamil
  - Digoxin
  - AV node ablation
- Restoration and maintenance of sinus rhythm
  - Electrical cardioversion
  - Anti-arrhythmic agents
  - Surgery
- Anticoagulation
  - Warfarin (68% reduction in stroke)
  - Aspirin (22% reduction in stroke)

# Clinical Decision-Making: The Entropy of Aging

## Patient factors

- Lifestyle
- Goals/expectations
- Quantity vs. quality of life

## Clinician factors

- Avoidance of age bias
- Realistic appraisal

# Take Home Message #1

- Aging is associated with extensive changes throughout the cardiovascular system that markedly reduce cardiovascular reserve and predispose older adults to the development of cardiovascular disease.

# Take Home Message #2

- The prevalence of all major adult cardiovascular diseases increases with age due to the combined effects of cardiovascular aging and the cumulative effects of common cardiovascular risk factors.

# Take Home Message #3

- In general, cardiovascular therapies are at least as effective in the elderly as in younger patients, and age per se is rarely a contraindication to the use of established treatments. However, due to the marked heterogeneity of the elderly population, management of older patients must be individualized.

# Take Home Message #4

- Older patients with cardiovascular disease have a less favorable prognosis than younger patients, thus emphasizing the importance of preventive strategies, including aggressive management of major cardiac risk factors in persons of all ages.