Cost/Effectiveness Analysis

Robert M. Kaplan

NIH RCT Summer Training Course

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Questions to be addressed today

- What is the meaning of life?
- How much health care and how many doctors do we need?
- What is disease?
- How can we best use our resources to improve public health?
- Hey-- we have a whole hour-- well almost

Challenge

- Suppose you could get rid of our health care system and design a new one.
- Your goal is to improve the health of the population.
- How would you go about it?

A COMPREHENSIVE FRAMEWORK FOR CARDIOVASCULAR HEALTH:
The progressive development of CVD (heart disease and stroke) and opportunities for CVH promotion and CVD prevention

The progressive development of CVD (heart disease and stroke)

UNFAVORABLE SOCIAL AND ENVIRONMENTAL CONDITIONS → **ADVERSE BEHAVIORAL PATTERNS** → **MAJOR RISK FACTORS** → **FIRST EVENT/ SUDDEN DEATH** → **DISABILITY/ RISK OF RECURRENCE** → **LATE DEATH** →

WHOLE POPULATION: *281,000,000*

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ESTABLISHED RISK FACTORS:

SMOKING *53,000,000*
HBP *50,000,000*
TC *41,000,000*
DM *10,000,000*

FIRST FATAL OR NON-FATAL EVENTS/YR:

STROKE *500,000*
MI *650,000* CHF ADM *550,000*

SURVIVORS >1 YR:

STROKE *375,000*
MI *450,000*
CHF ADM *450,000*

LATE DEATHS /YR

CVD *525,000*

POLICY AND ENVIRONMENTAL CHANGE | **BEHAVIOR CHANGE** | **RISK FACTOR DETECTION AND CONTROL** | **EMERGENCY CARE/ACUTE CASE MANAGEMENT** | **REHABILITATION/ LONG-TERM CARE** | **END-OF-LIFE CARE**

Prevention of risk factors in the first place - 0 | 0 | 1° | 2° | 3 °

Cardiovascular health promotion | Cardiovascular disease prevention | Palliation

INCREASE QUALITY AND YEARS OF HEALTHY LIFE

ELIMINATE HEALTH DISPARITIES

GOAL 1 → ***GOAL 2*** → ***GOAL 3*** → ***GOAL 4*** →

Opportunities for CVH promotion and CVD prevention

CDC

Question 1

What is the meaning of life?

Ziggy Theorem

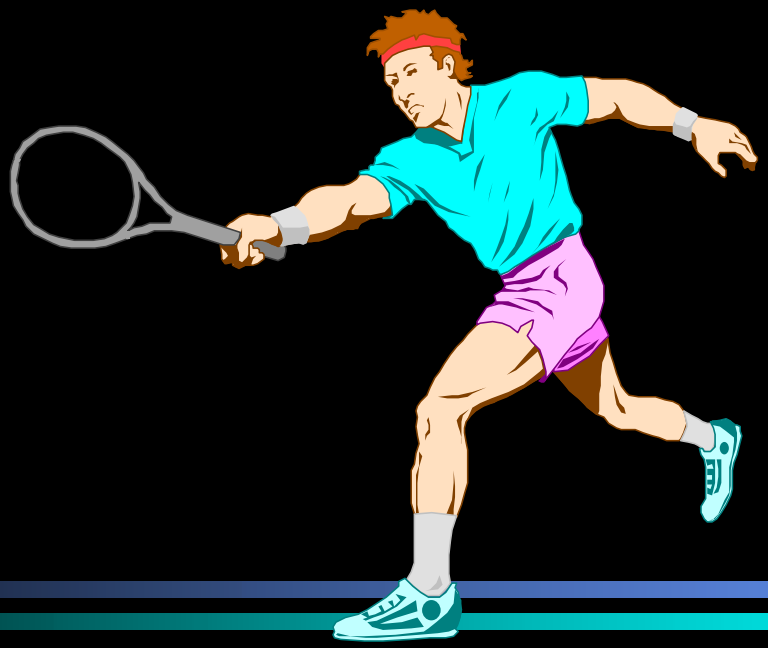
- What is the meaning of life?
- The meaning of life is -- “doing stuff”
- Extended life expectancy
- Quality of life during life prior to death
- Maximize the quality adjusted life expectancy (QALYs)

Survival Analysis

- Alive 1.0
- Dead 0.0

Problem with Survival Analysis

- Tennis player 1.0
- Man in coma 1.0



Purpose of Quality Adjusted Survival Analysis

- To summarize life expectancy with adjustments for quality of life

Quality-Adjusted Life Year

- Combines morbidity and mortality into a single index
- Represents life expectancy with adjustments for quality of life
- Is defined as a year of life free of all disabilities and symptoms

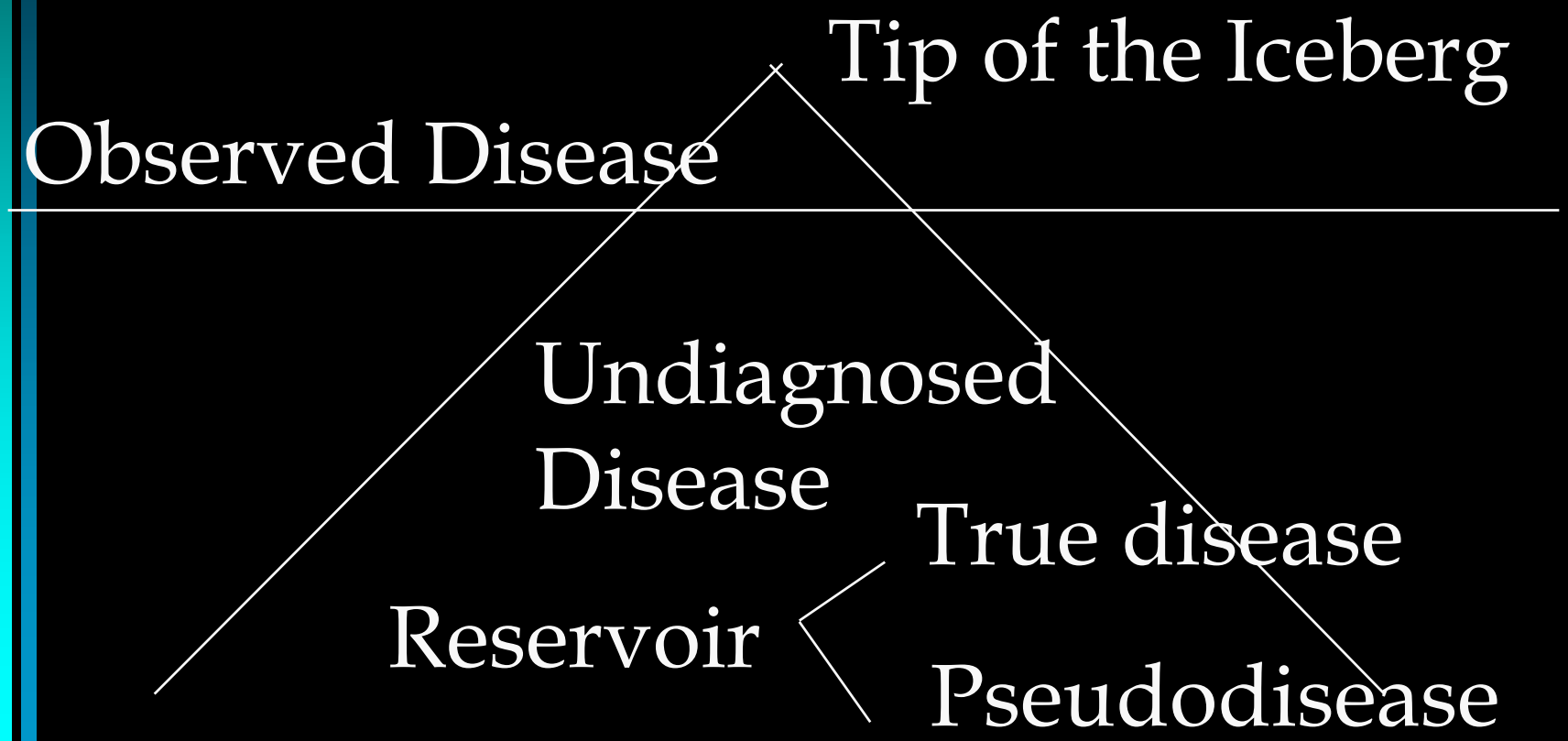
Theory: Disease Reservoir Hypothesis

- Disease is common, particularly in older adults
- If you look hard for disease, you will find it
- Much of the disease is actually “pseudodisease”, defined as detectable disease that, if left alone, would have no clinical significance

Common Perceptions of Chronic Disease

- Disease starts at diagnosis
- Disease is binary (you got it or you don't)
- All disease must be treated
- Untreated disease leads to likely death or disability
- Bad health outcomes usually result from failure to detect disease early

Disease prevalence, according to ACS, ATS, AHA, ADA...



Question 2

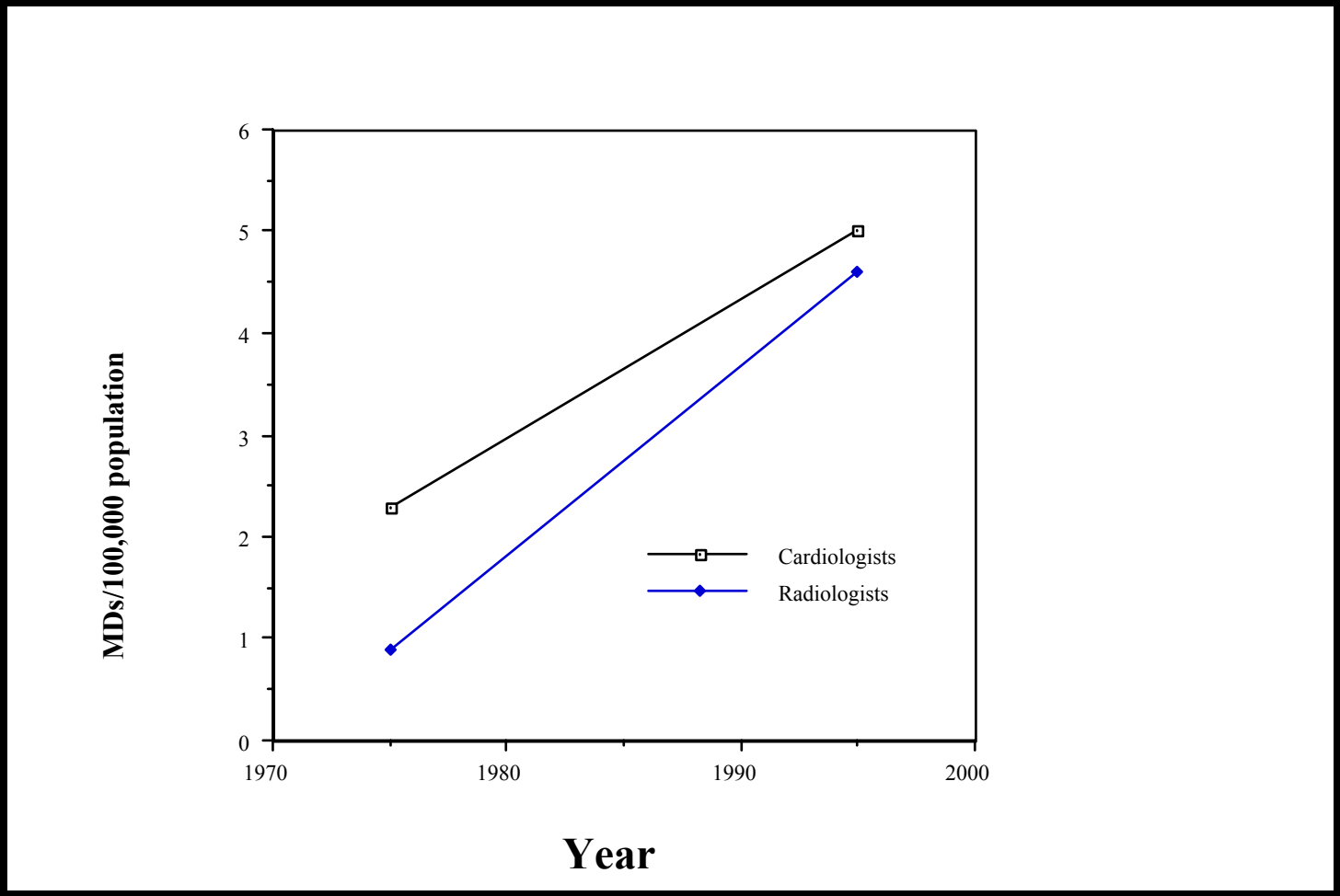
How much health care do we need?

How many doctors should we train?

Problems in contemporary health care

- Despite managed care, health care costs expected to increase significantly next year
- In past 2 decades, number of cardiologists has doubled and number radiologists has increased five fold
- Despite much greater growth in costs of health care in the USA, there is no evidence our health status has shown greater gains than other G7 countries.

Increase in cardiologists and radiologists per 100,000 in population between 1975 and 1995 (adapted from Fisher and Welsch, 1999)



With more doctors, we have discovered that more people are sick

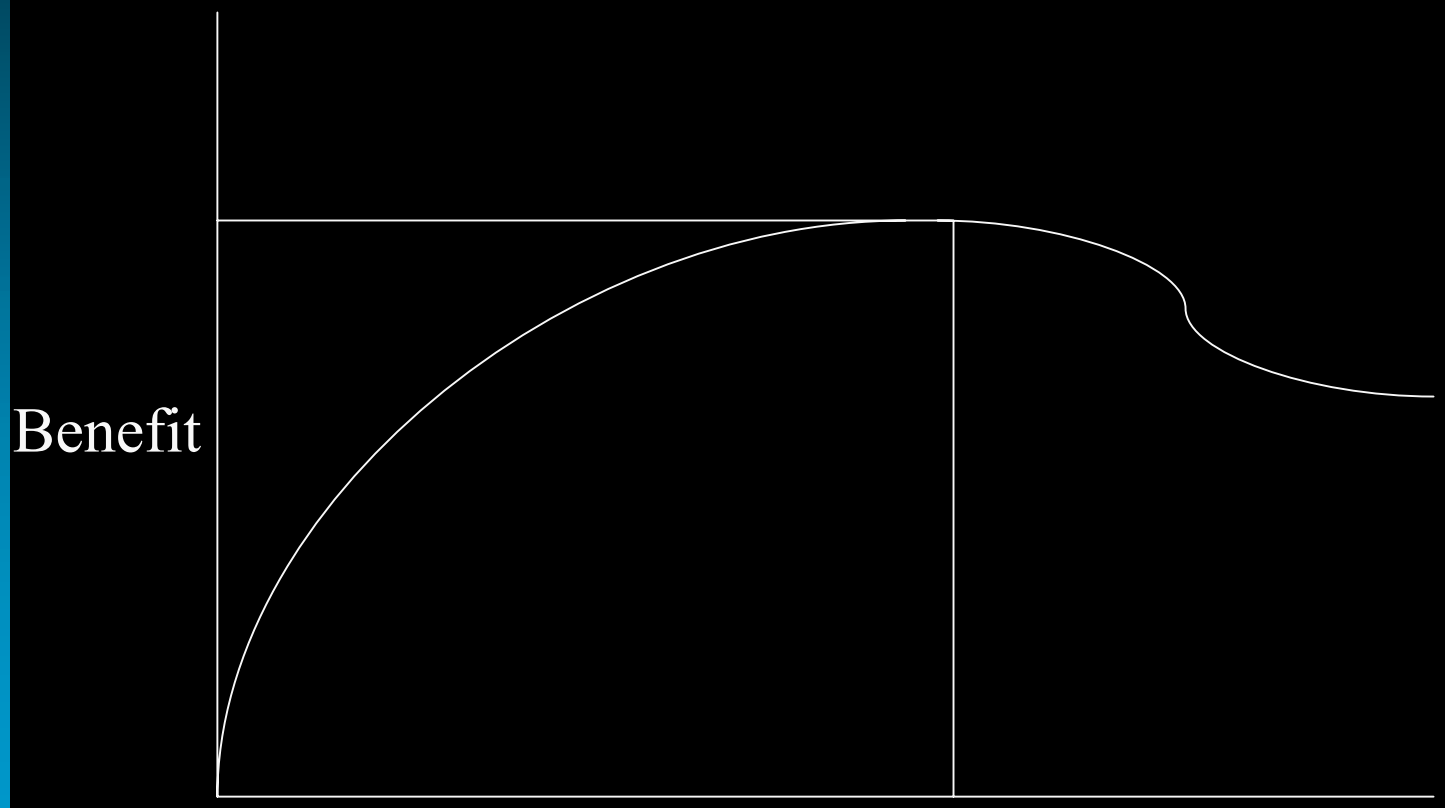
- New spiral CT scans can detect hepatic lesions of 2mm. In 1982, only 20mm lesions could be detected
- MRI can detect abnormalities of the knee in 25% of healthy young men.
- MRI can find lumbar disc bulge in 50% of adults, many who have no back pain
- Early experience with electron beam CT identifies nodules in an unexpectedly high number of cases

Rethinking the Assumptions

- Few people are well-- most of us are sick
- It is okay to be sick
- Better methods for diagnosing our illnesses may produce harm

The law of diminishing returns

(after Fisher & Welch, 1999)



Issue 2: There is variability in clinical judgment

- Reliability of diagnostic judgment
  - If a doctor tells you you have a disease, do you have it?
  - If a doctor does not find a disease, are you well?

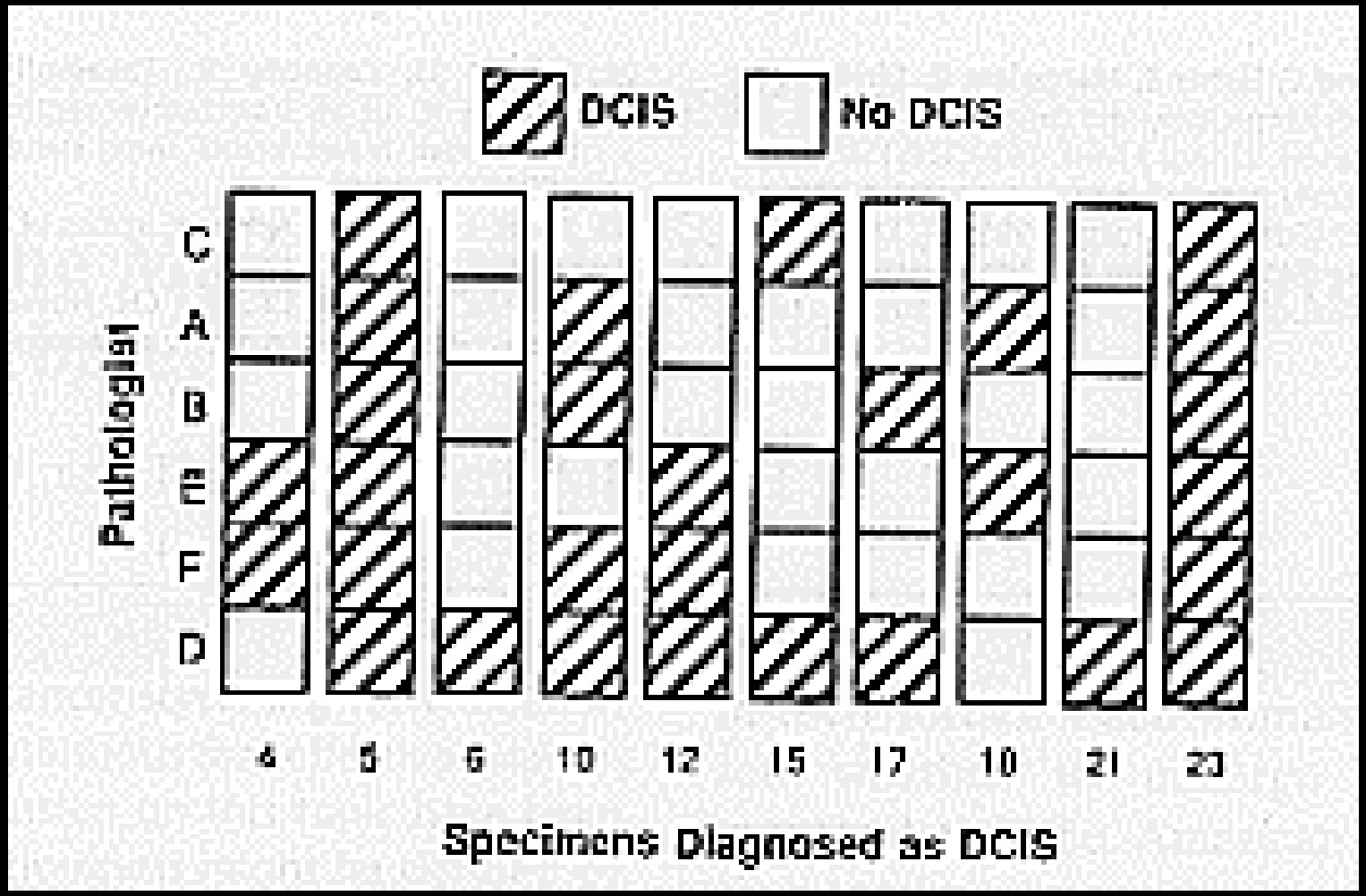
Are There Problems With MD Judgment?

- MD decisions are highly variable
  - they disagree with their peers who have reviewed the same patient
  - they disagree with themselves when presented with the same patient records at two points in time.

Angiography Examples

- Four cardiologists given high-quality angiograms and asked to say if stenosis in the proximal or distal left anterior descending artery is >50%.
  - The cardiologists disagreed on 60% of the cases (Zir et al. Circulation, 1976,53,627)
  - Cardiologists looking at the same angiograms at two points in time disagree with themselves 8%to 37% of the time (Detre et al Circulation 1975, 52, 979)

Interobserver Agreement Among 6 Pathologists on DCIS for 10 Case (Schnitt et al, 1992)

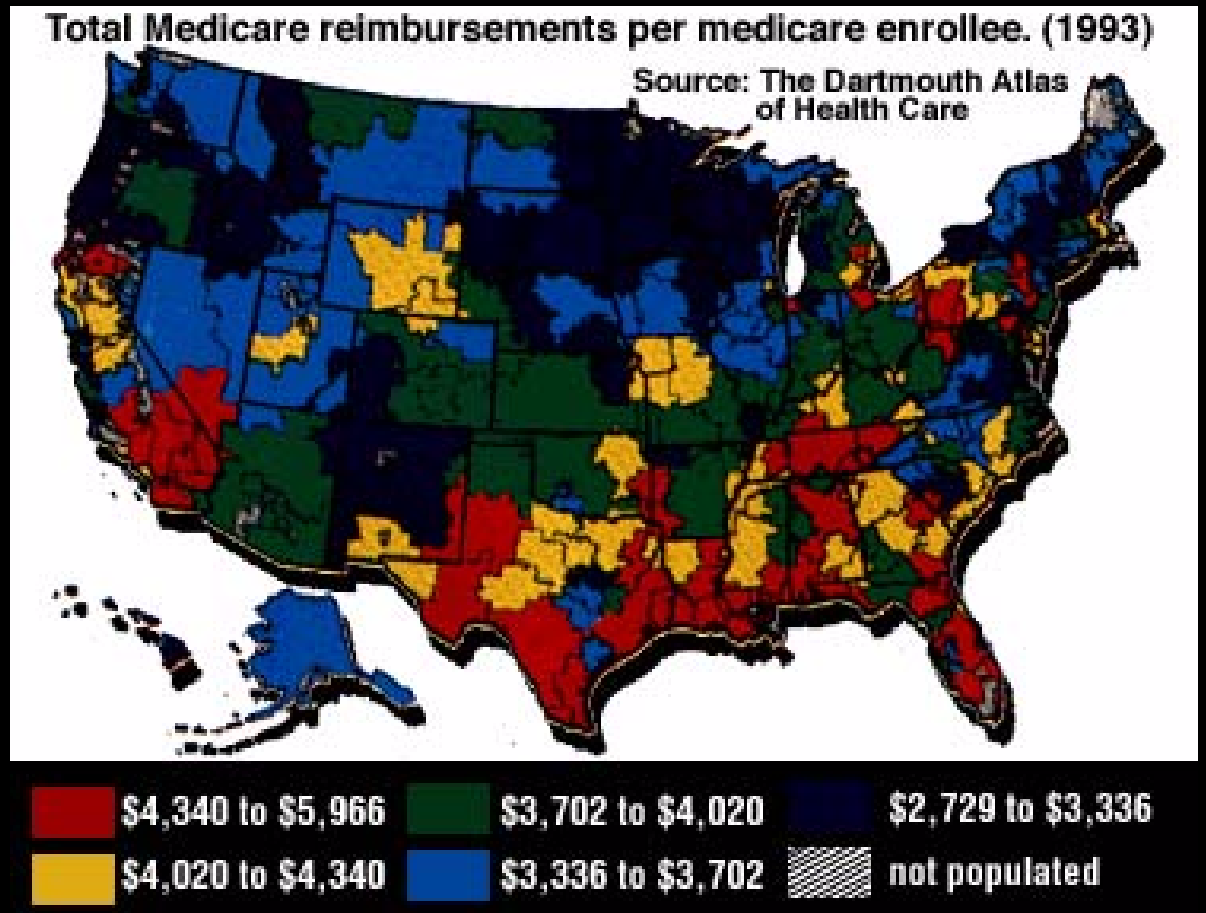


Why does this matter?

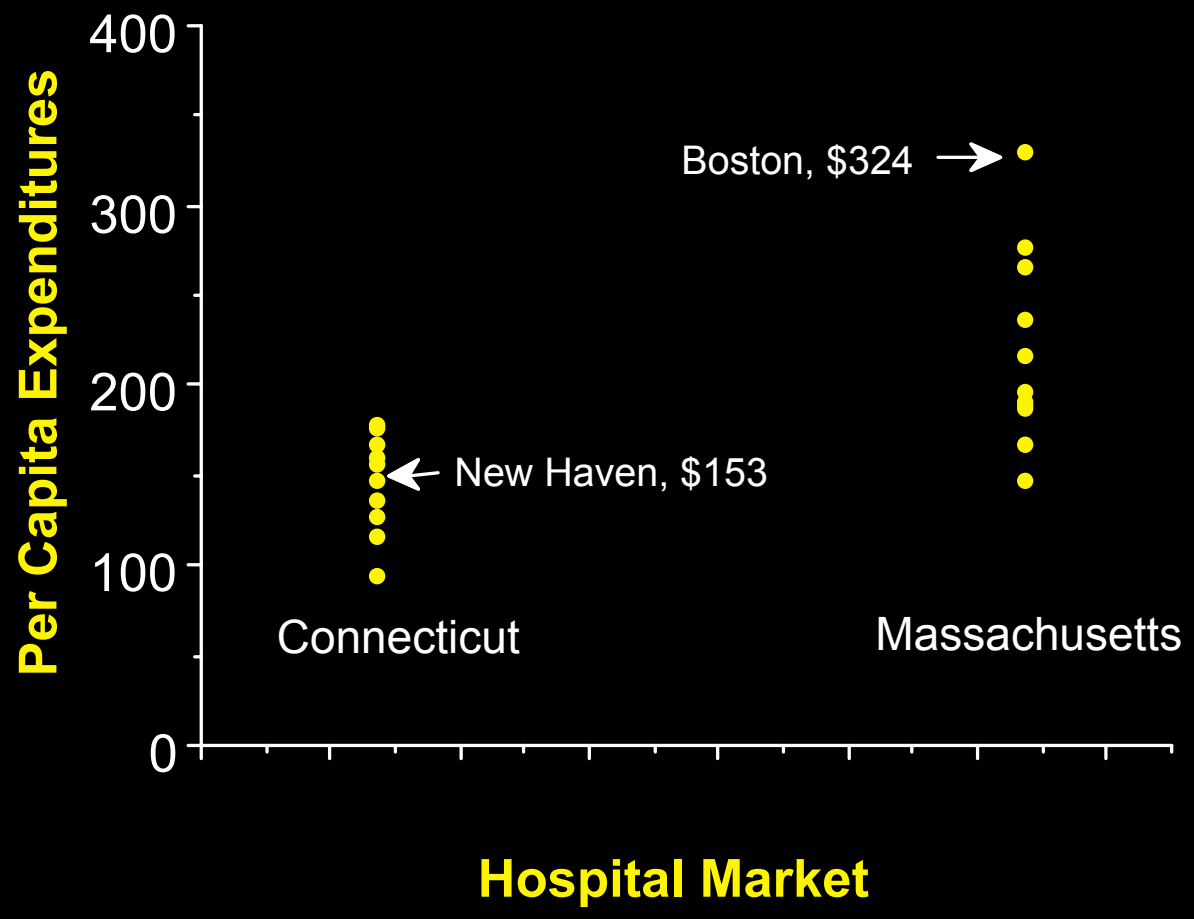
Diagnosis rate can vary, despite constant prevalence of disease

Medicare Expense Variations

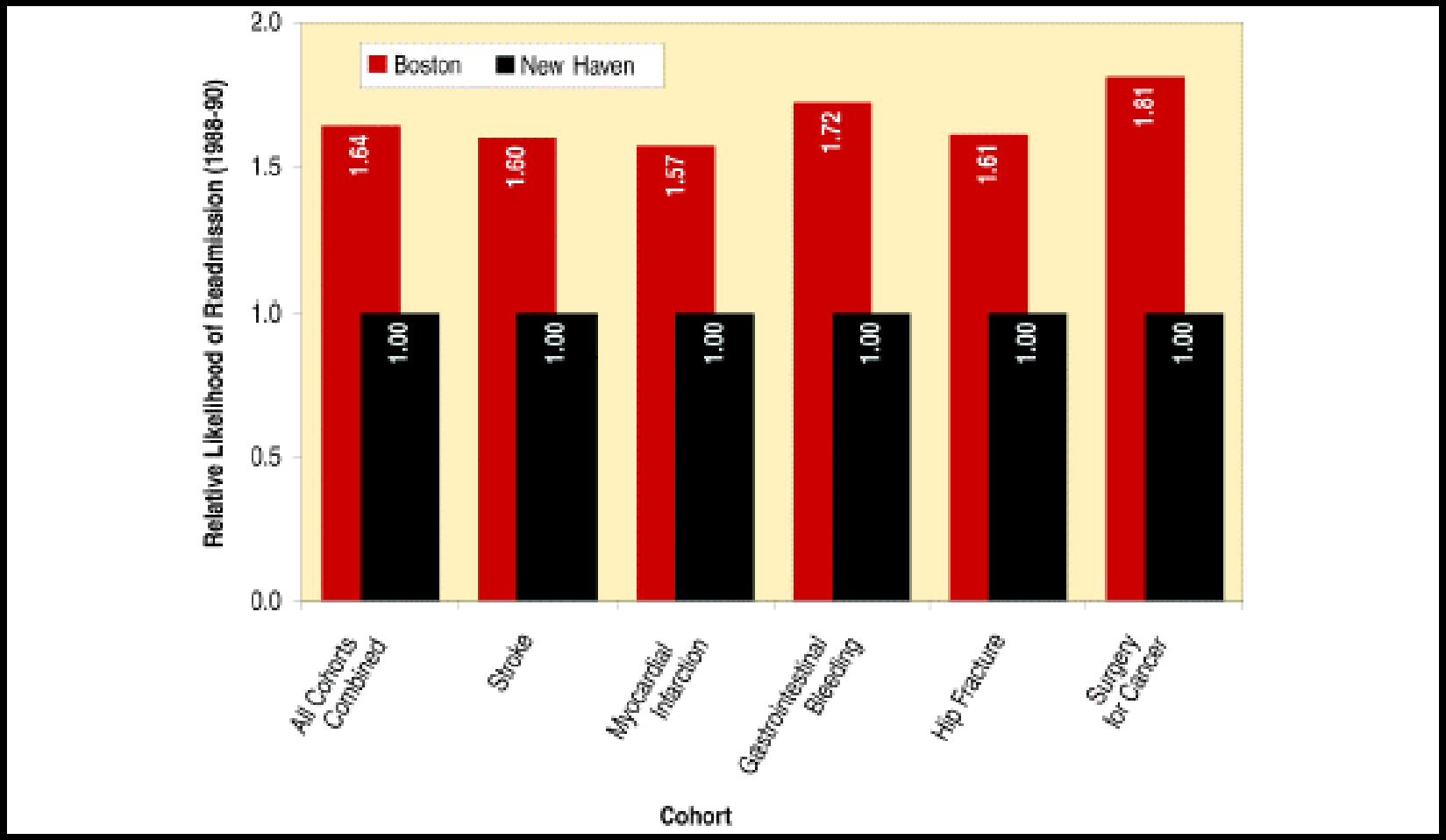
Medicare reimbursements for all services



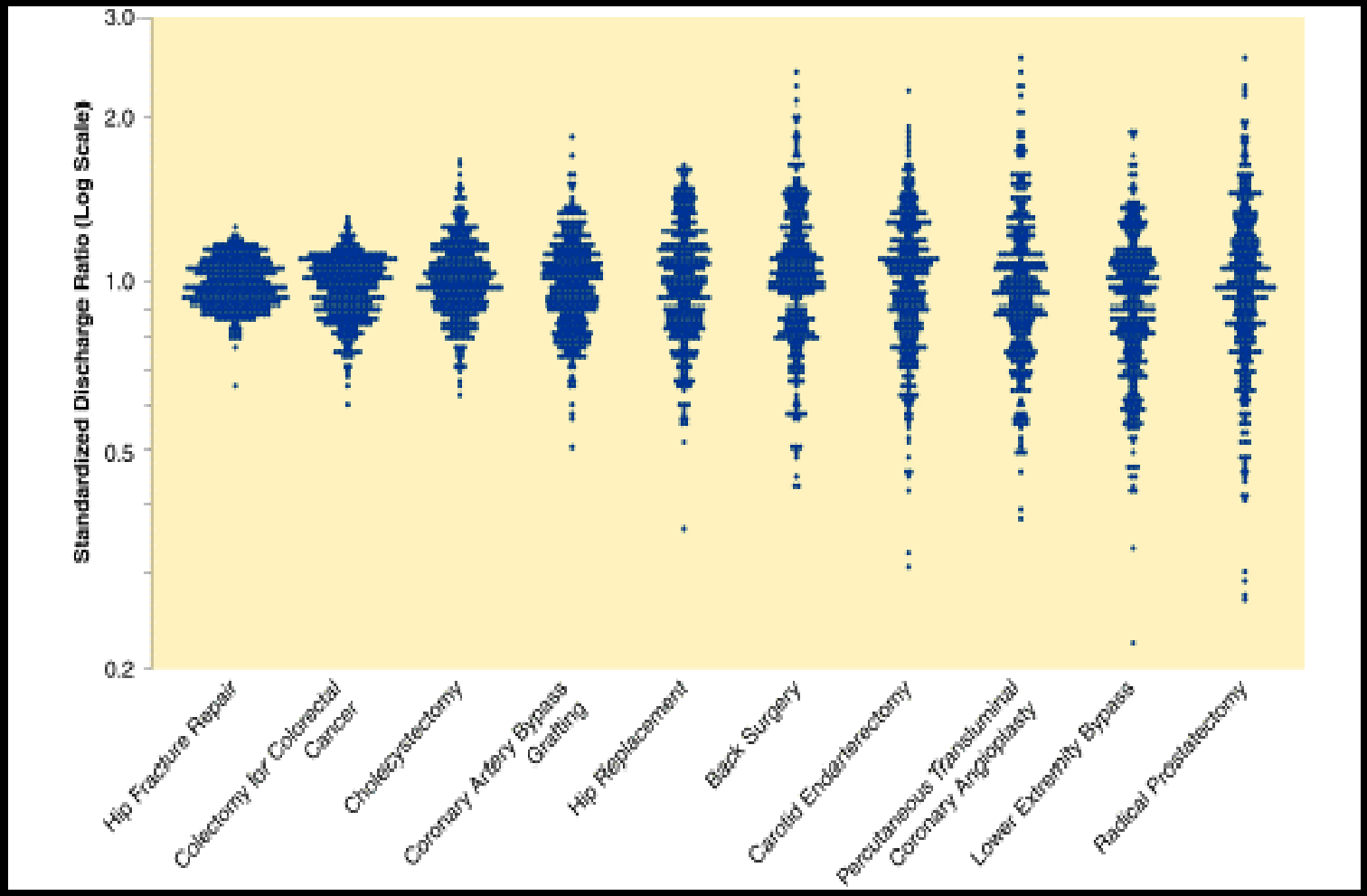
Hospital Expenditures in Connecticut and Massachusetts, 1975 (Wennberg, 1990)



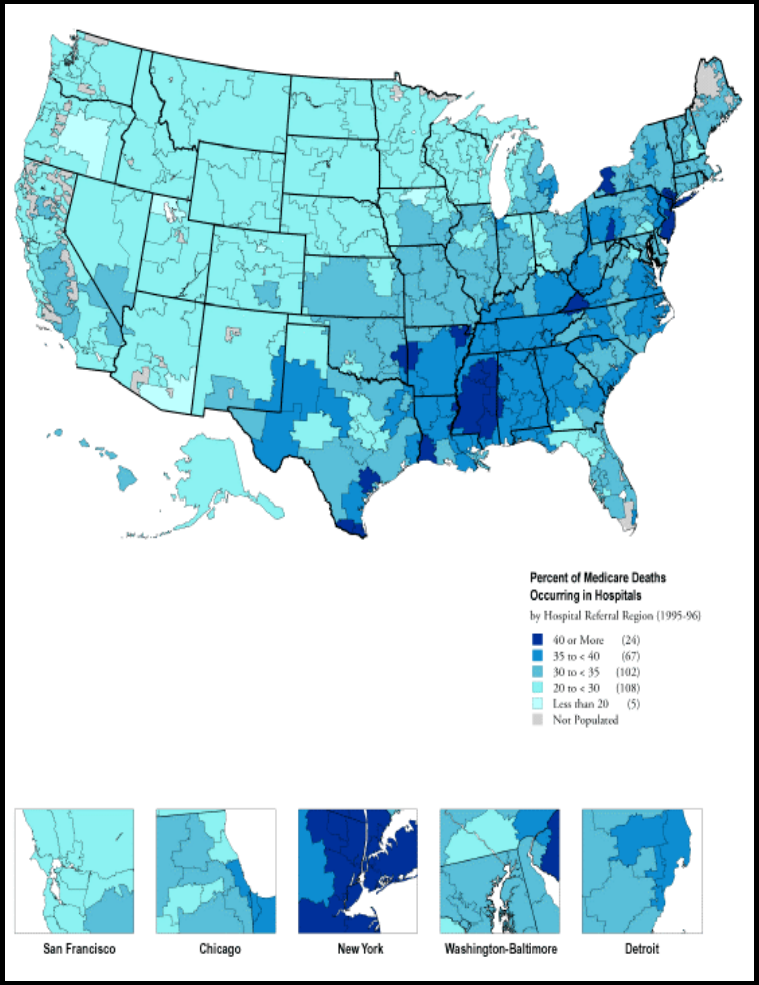
The Boston New Haven Difference Continues Through 2000



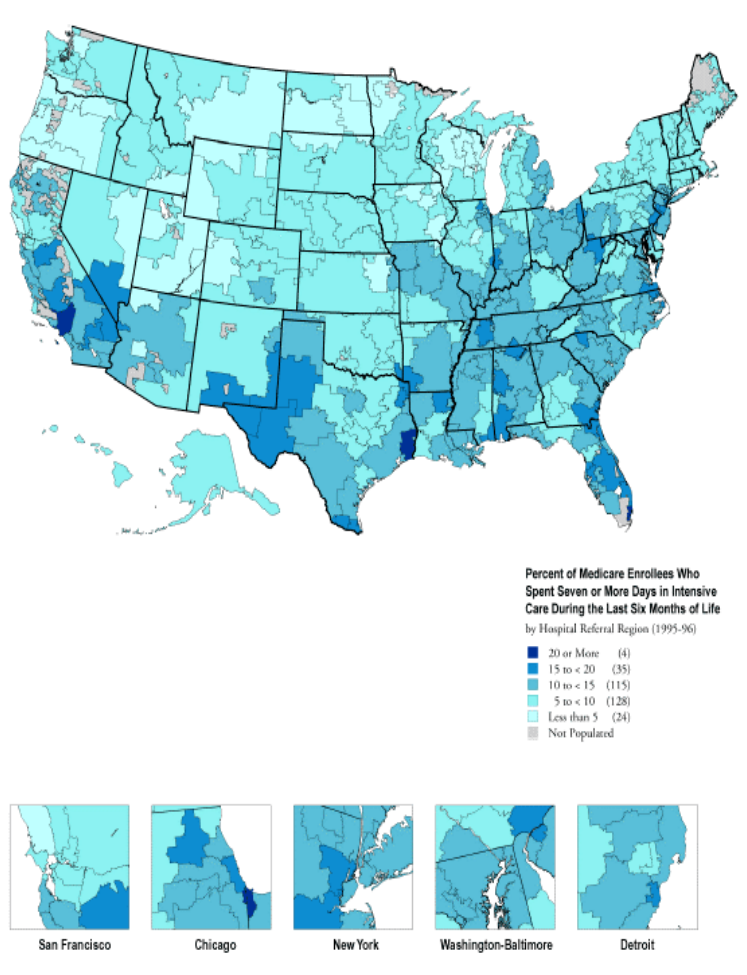
Quantitative Measures of Variability of Ten Common Surgical Procedures by Hospital Referral Region (1995-96)



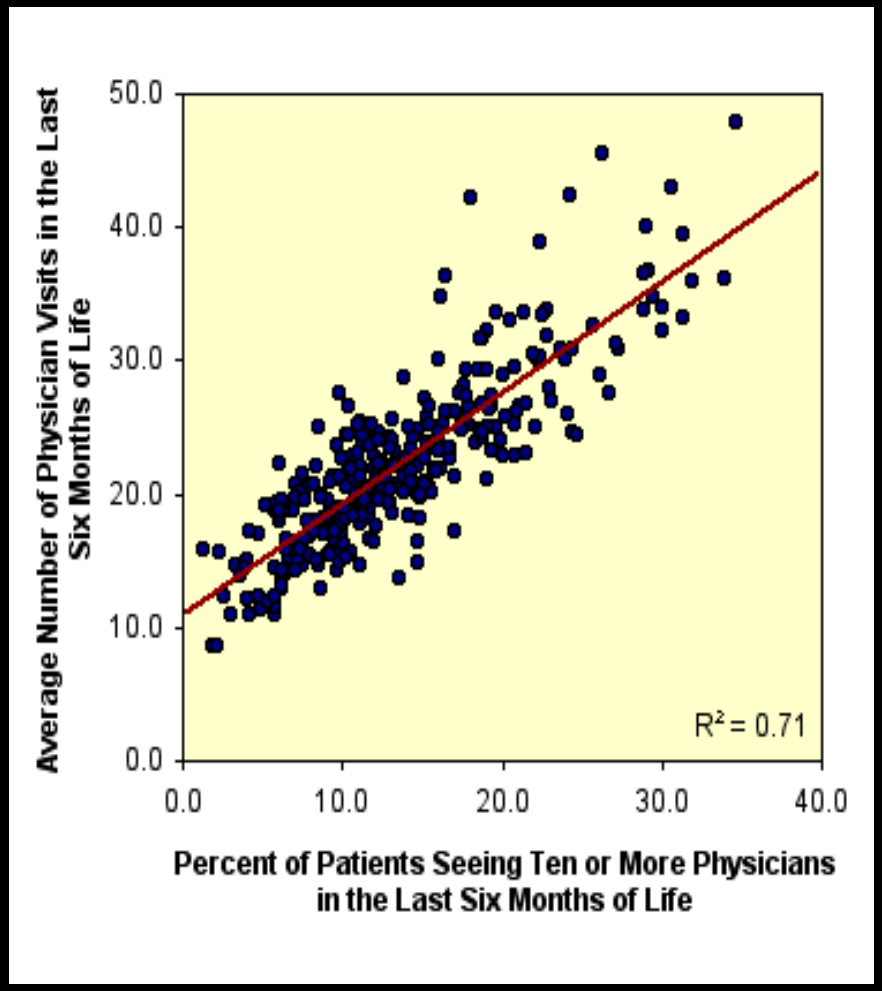
Percent of Medicare Deaths Occurring in Hospitals: 1995-1996

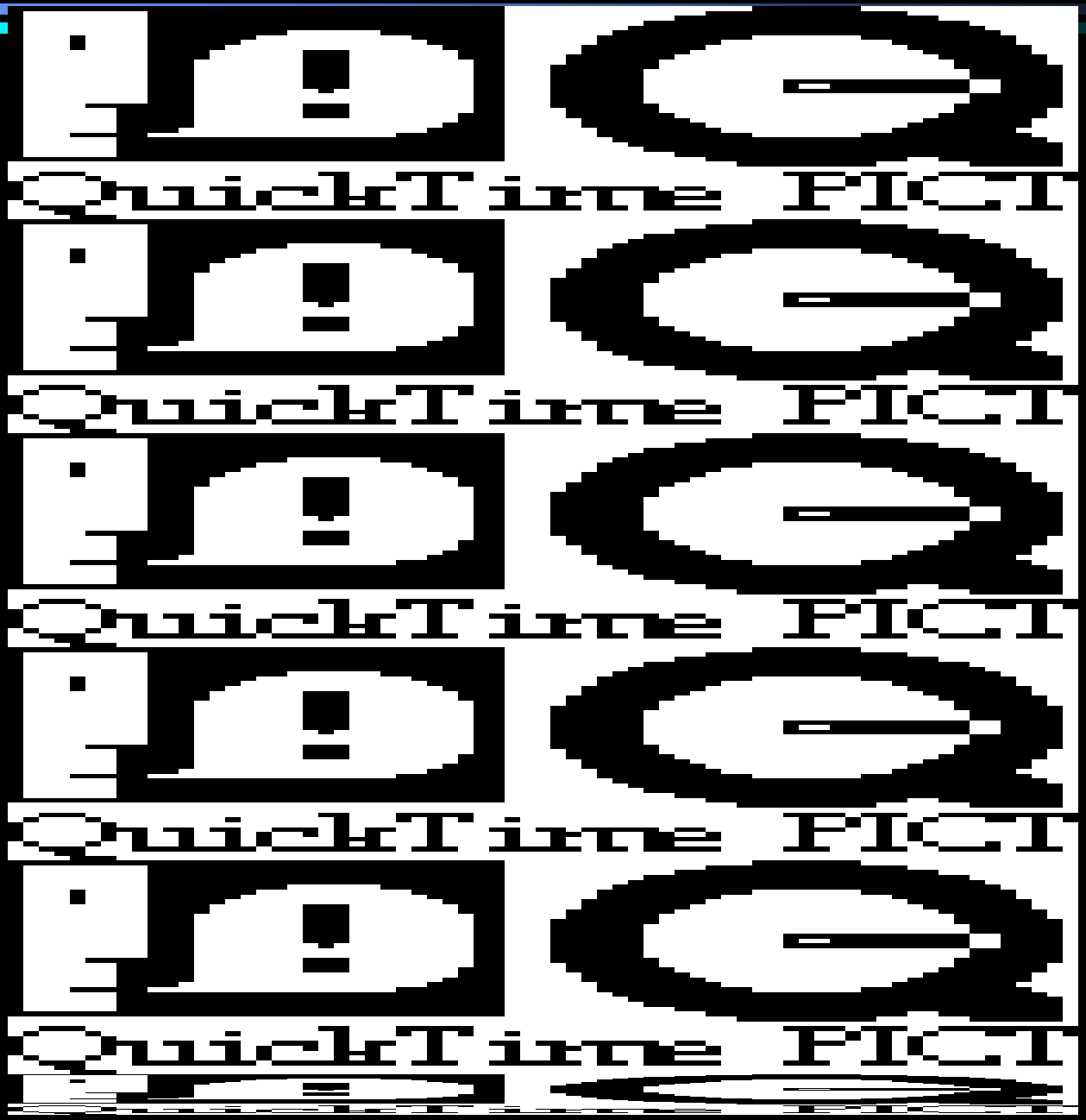


Percent Seven or more days in ICU during last 6 months of life: 1995-1996



Percent Seeing 10 or More Doctors During Last 6 Months of Life: 1995-1996

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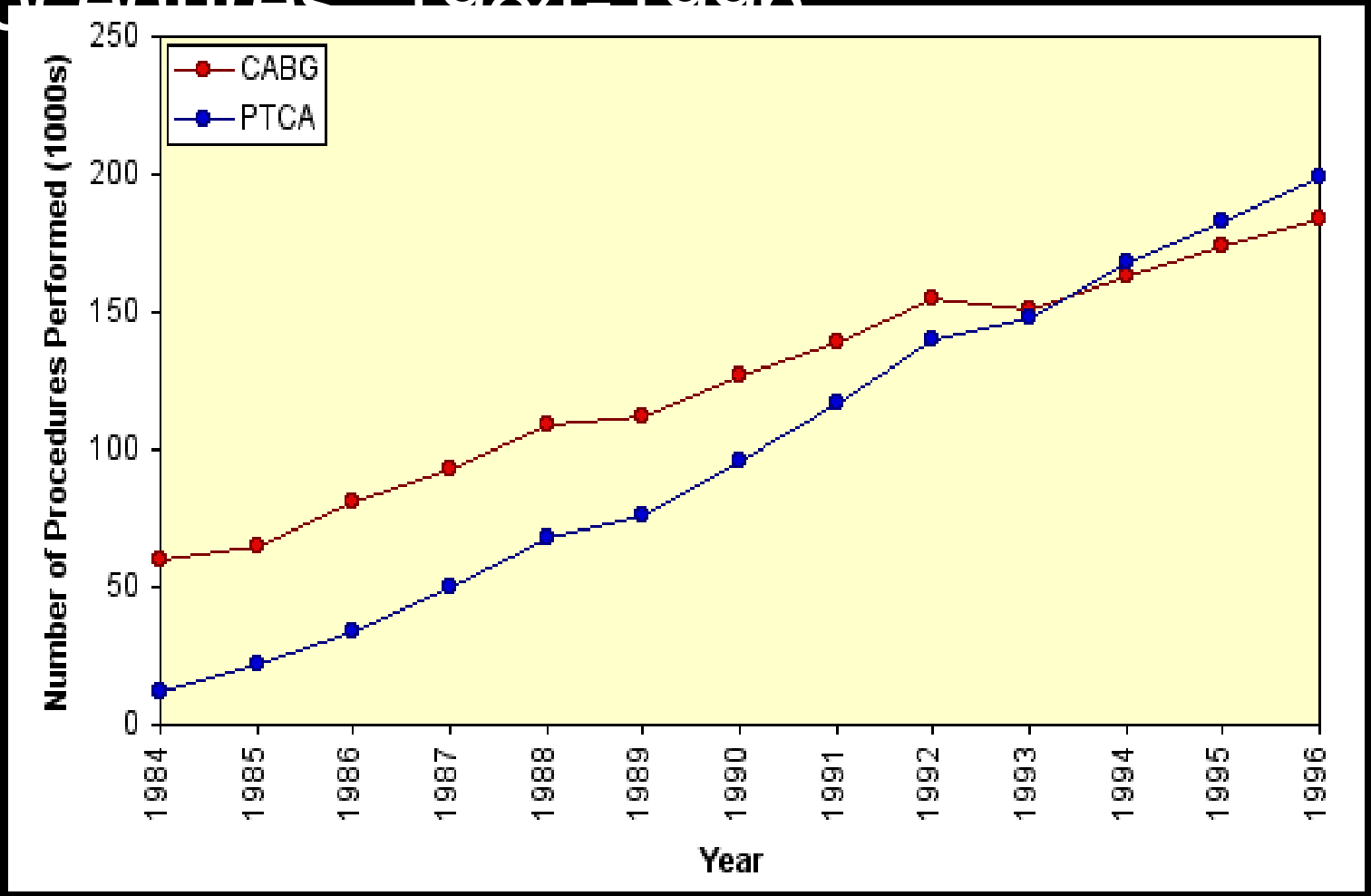
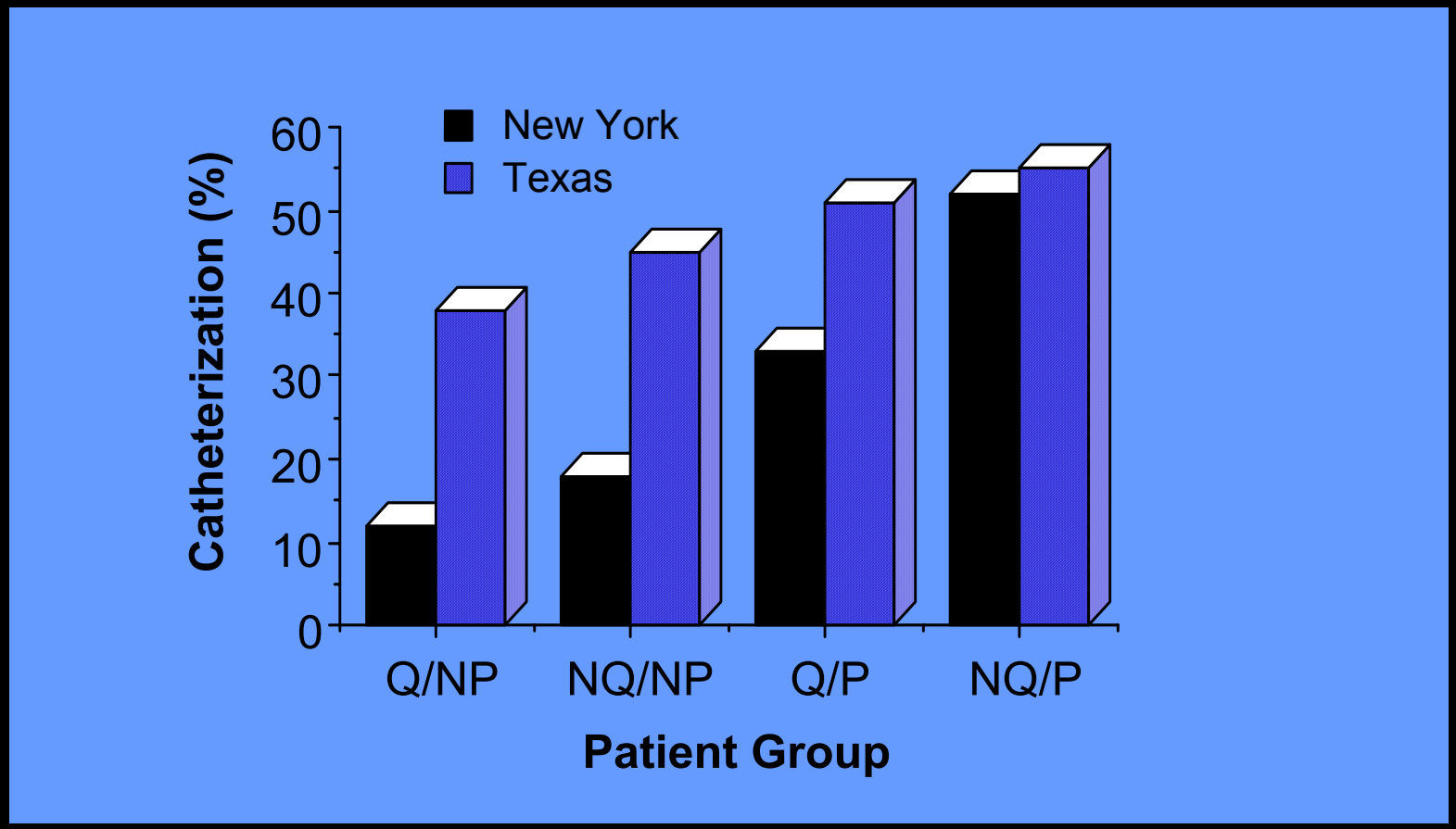
Growth of invasive cardiac procedures: 1984-1996

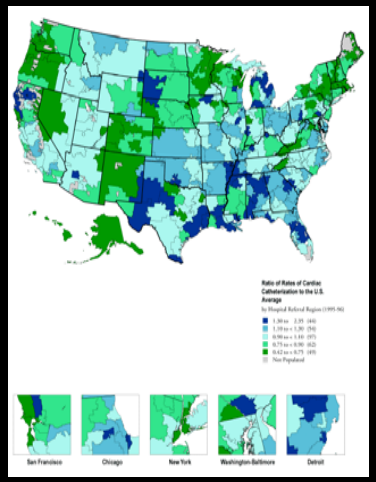


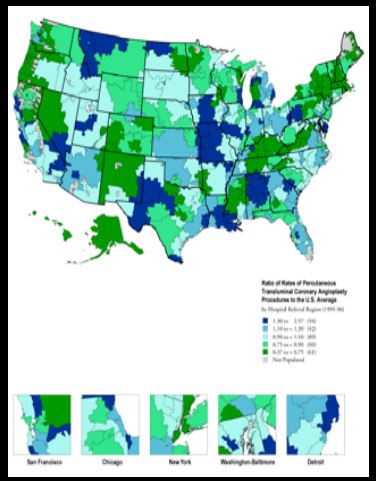
Catheterization rates in New York and Texas (Guadagnoli et al, 1995)



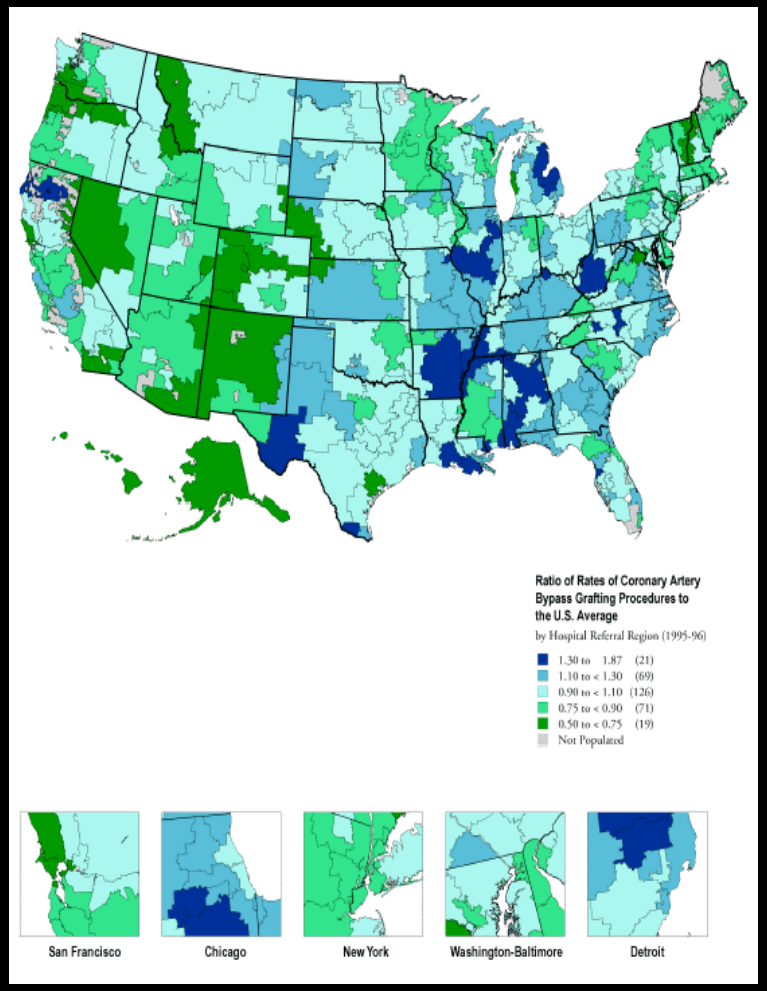
Diagnostic intensity is a source of variation in invasive care

- The more you look the more you find
- Top is rates of catheterization, 1995-1996
- Bottom, rates of PTCA, 1995-1996

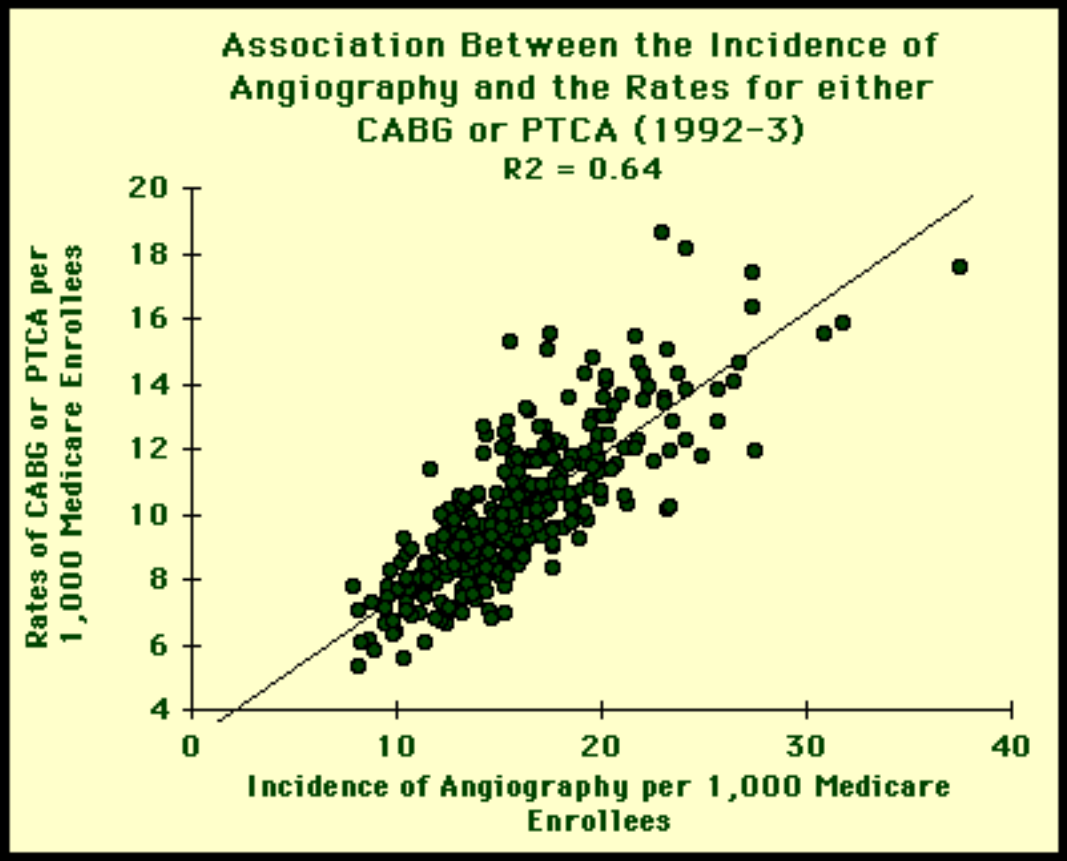




CABG map of the US (From 1999 Dartmouth Atlas)

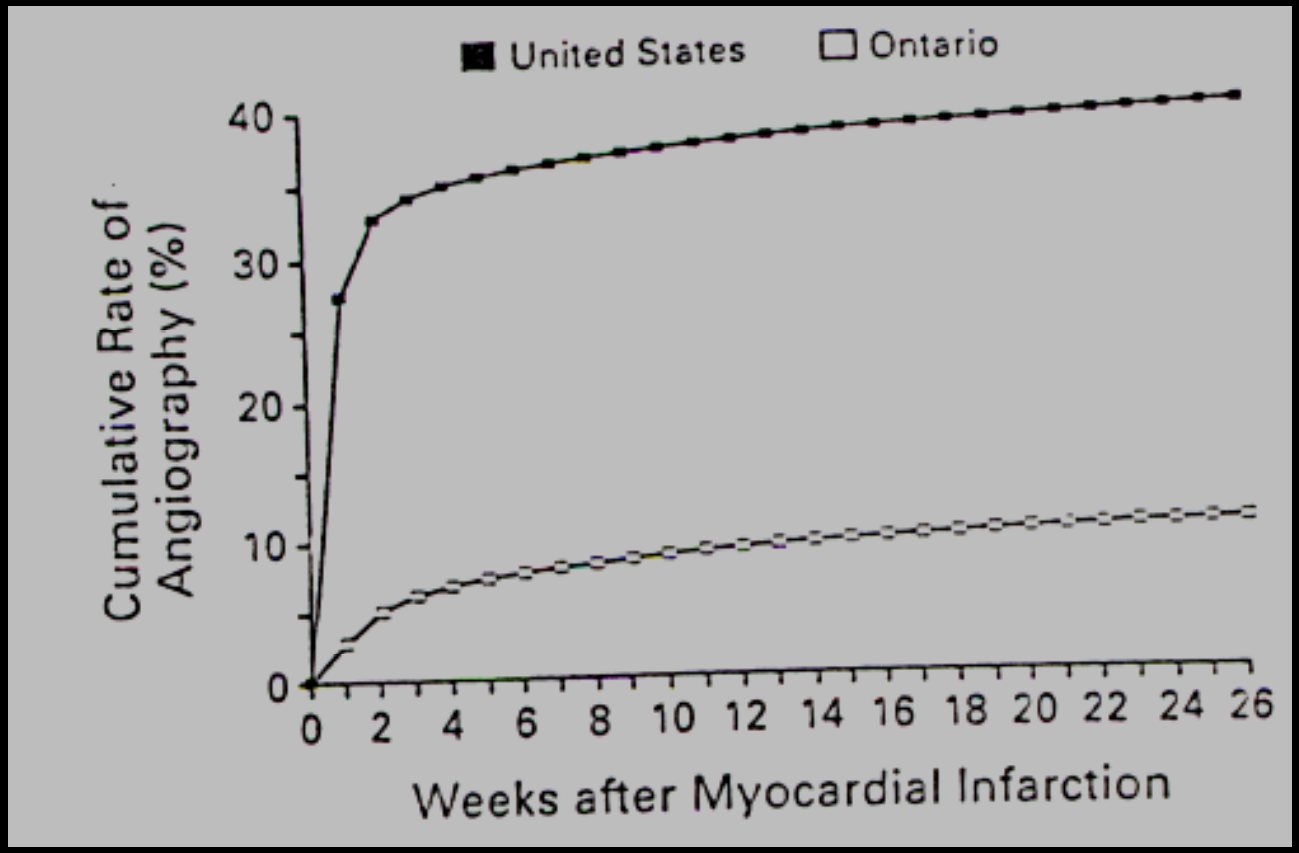


Relationship between angiography and procedures

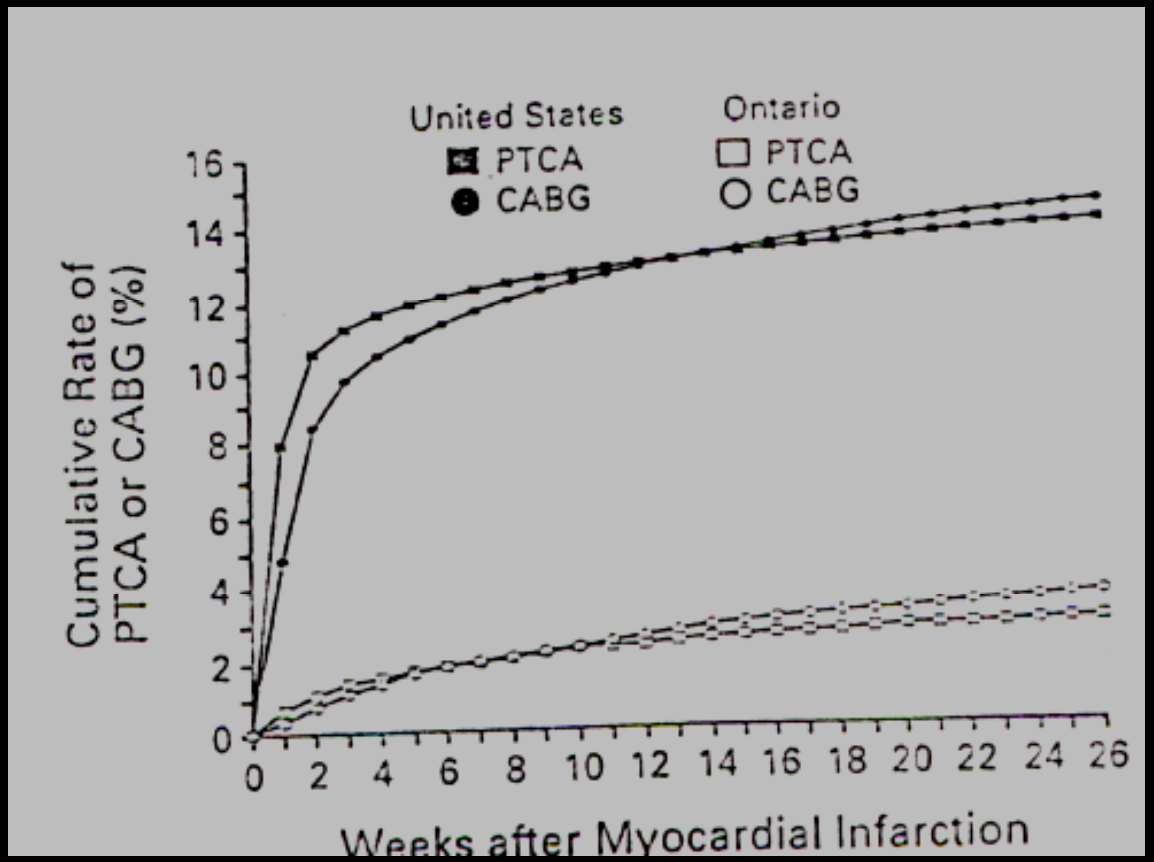


There appears to be no correlation between procedures and disease prevalence

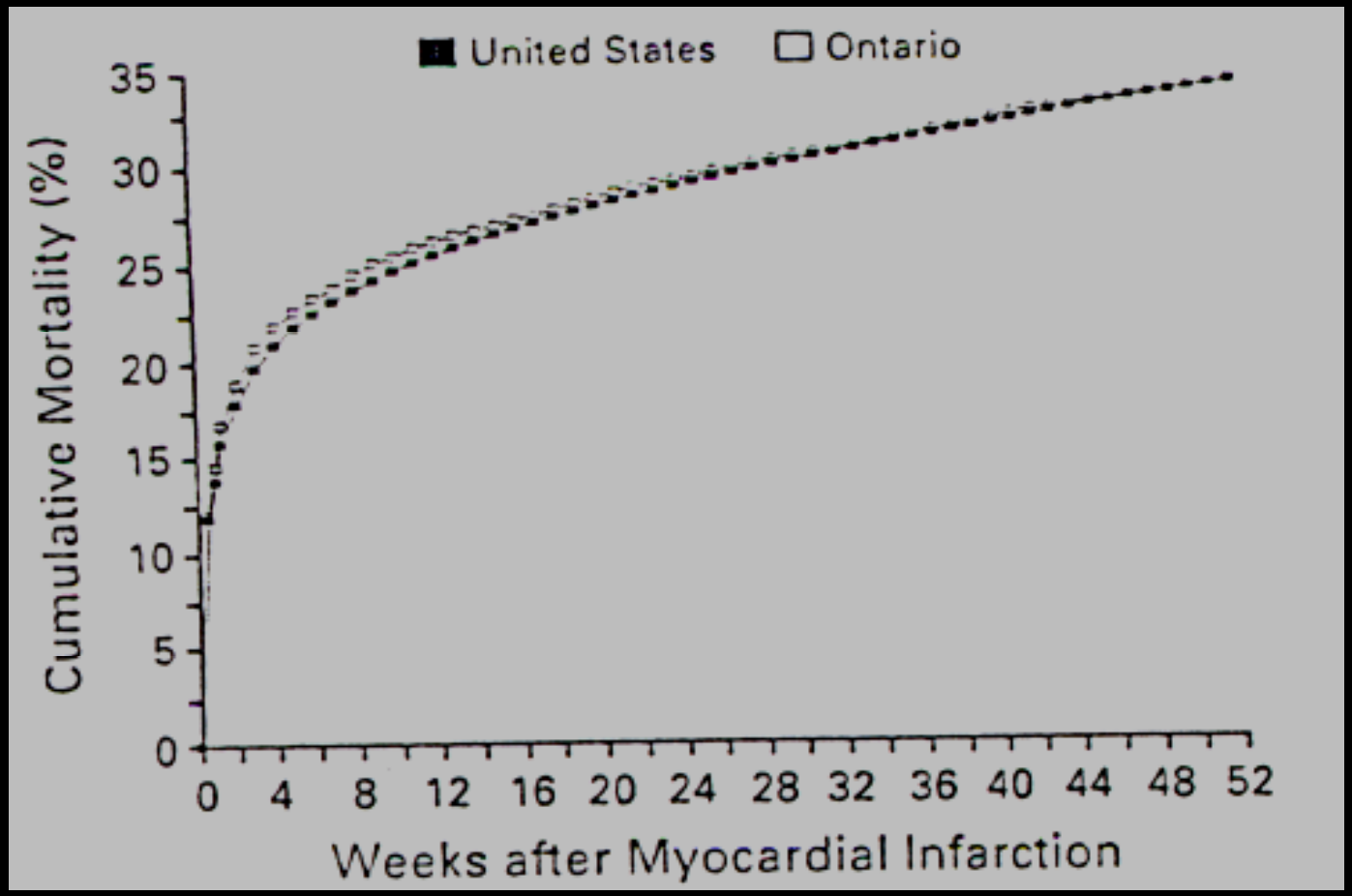
Angiography US Vs. Canada



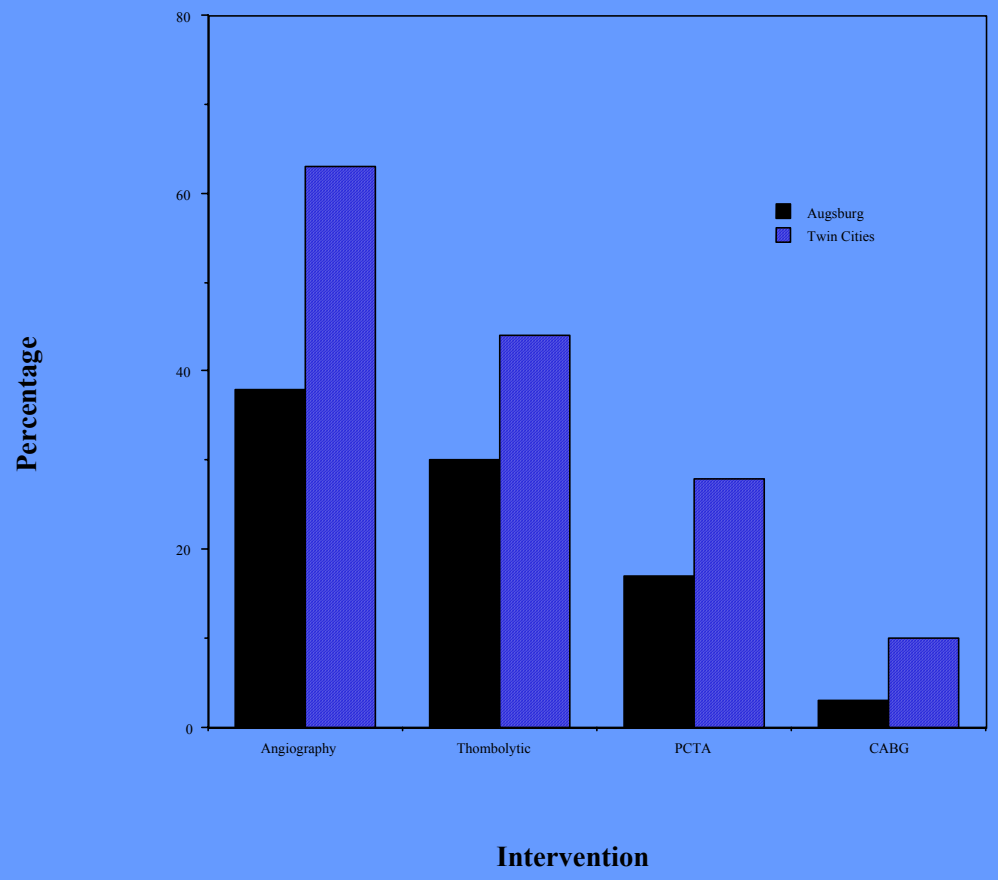
Procedures US Vs Canada



Mortality US Vs Canada



Minnesota vs Southern Germany (Shahar, Lewis, Keil, McGovern, et al, 1996)



Minnesota vs So. Germany Outcomes- Survival Odds Ratios

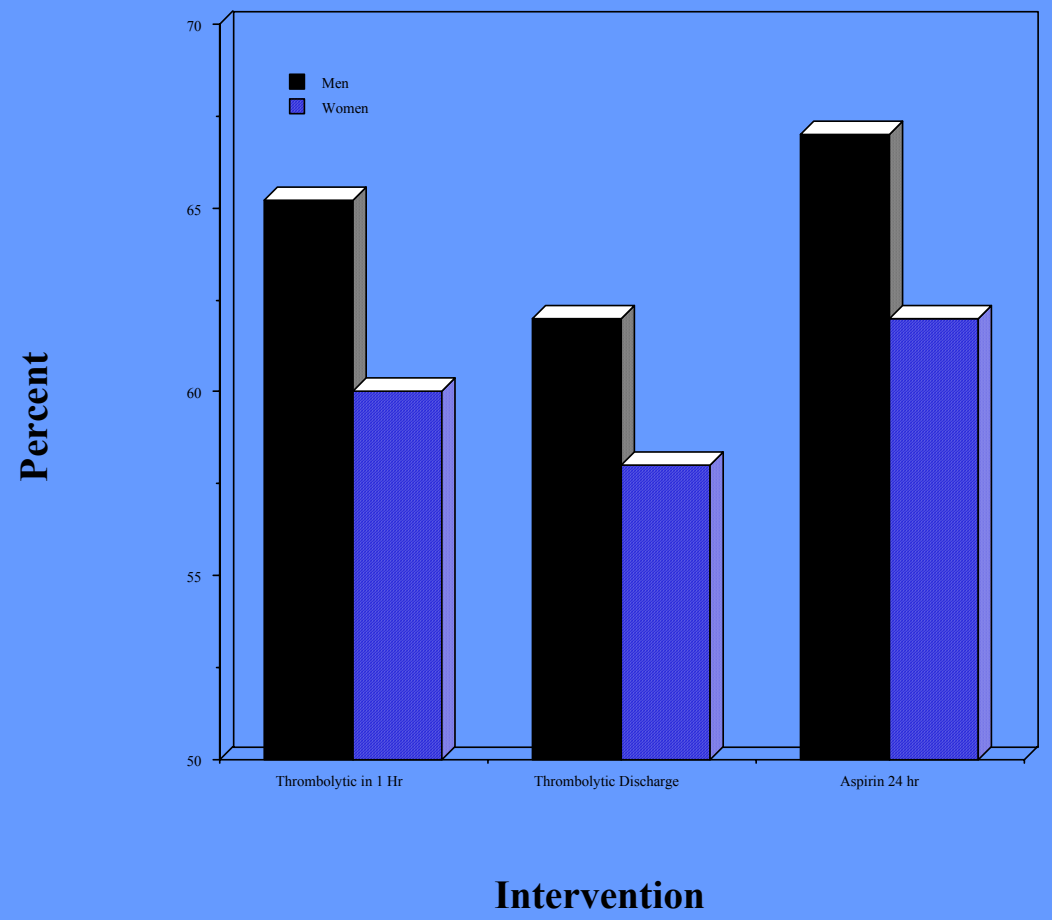
- 28 day mortality

  1.0

- 1-year mortality

  1.1

Gender Treatment Bias Gan et al NEJM 2000, 343, 8-15



Gan et al

30 Day male/female mortality ratio

- 1.02 (.99- 104)

If there is a reservoir...

- The better the technology for looking, the more you will find.

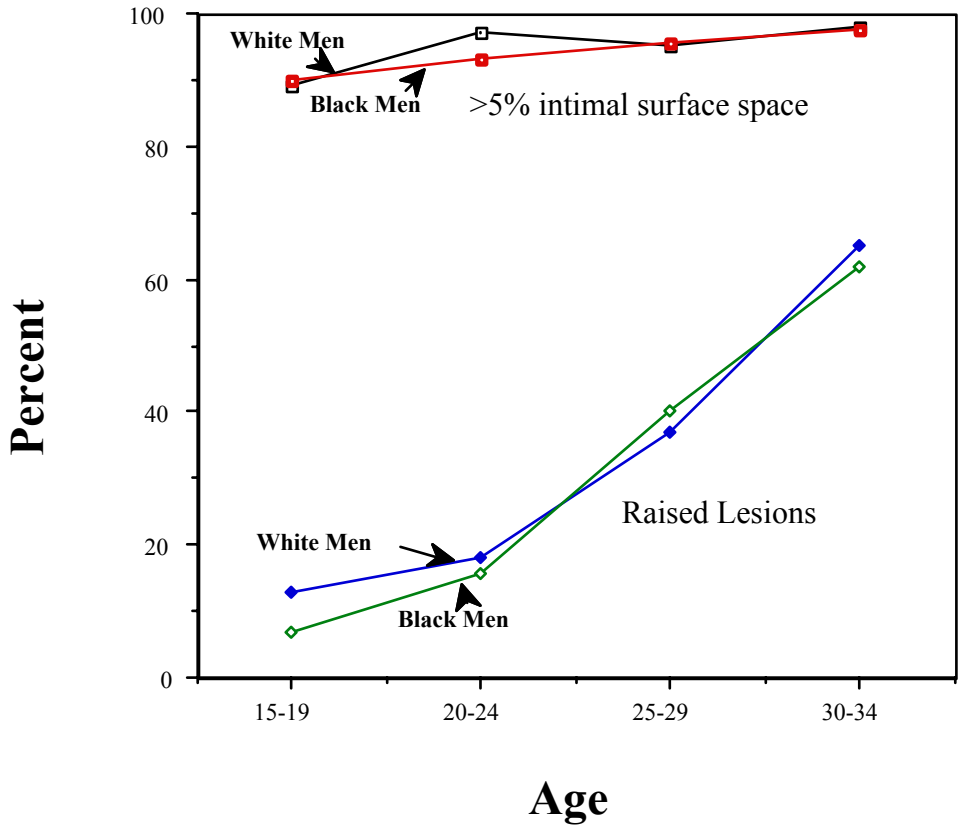
How many people have cancer?

Site	Deaths	Autopsy
Breast	3%	39%
Prostate	3%	46%
Thyroid	0.1%	100%

Prevalence of DCIS by number of slides per breast

Reference	Slides	% DCIS
Bartow et al, 1987	9	0
Kramer et al, 1973	40	4.3
Neilsen et al, 1984	95	14.3
Neilson et al, 1987	275	39

Abdominal aortic lesions >5% intimal surface and raised lesions for black and white males (adapted from Strong et al, 1999)



Coronary atherosclerosis in male trauma victims

(Joseph et al, 1993)

Study	N	Mean Age	Incidence
Enos et al 1955 (Korean)	300	22.1	77.3
Virmani et al, 1987 (Korean)	94	20.5	56.0
McNamara et al, 1971 (Vietnam)	105	22.1	45.0
Joseph et al, 1993	95	25.6	75.8

G. Howard, 1999

- “Some of us are walking around with holes in our heads…”

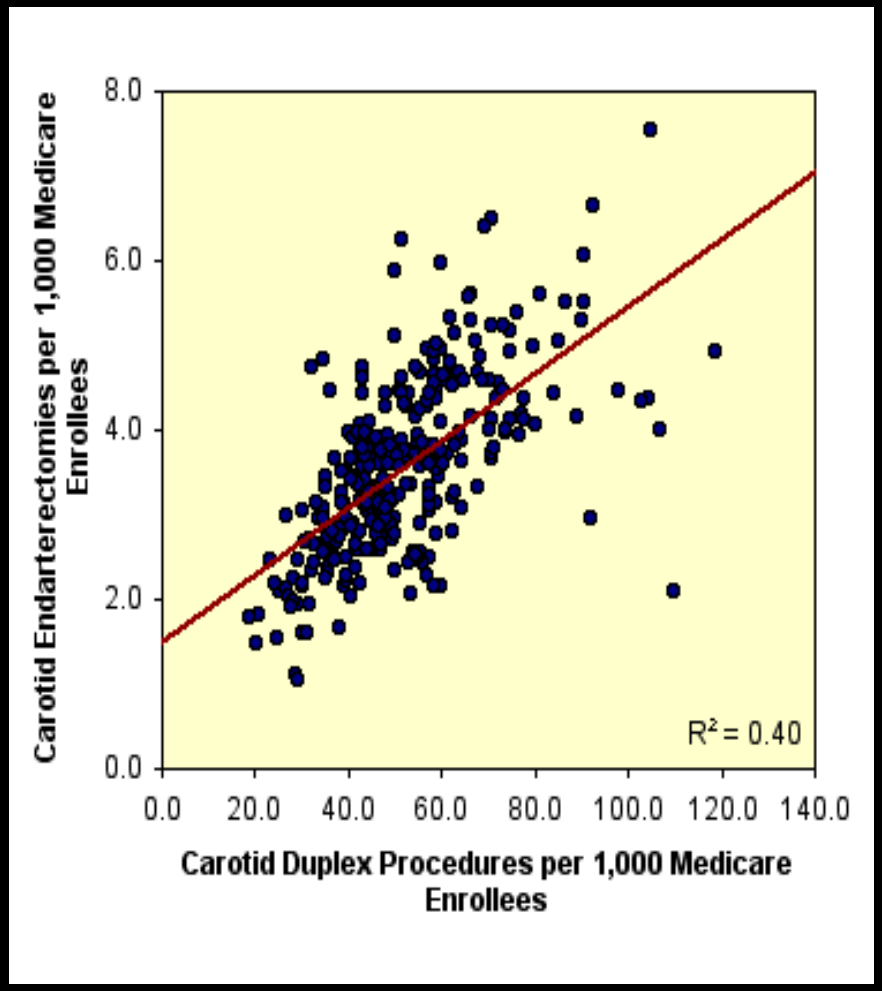
Lacunar infarcts in elderly
(Longstreth et al, 1998)

- In Cardiovascular Health Study 3,660 participants >65 years underwent cranial MRI
- Lacunes defines as subcortical areas consistent with infarcts 3 to 20 mm

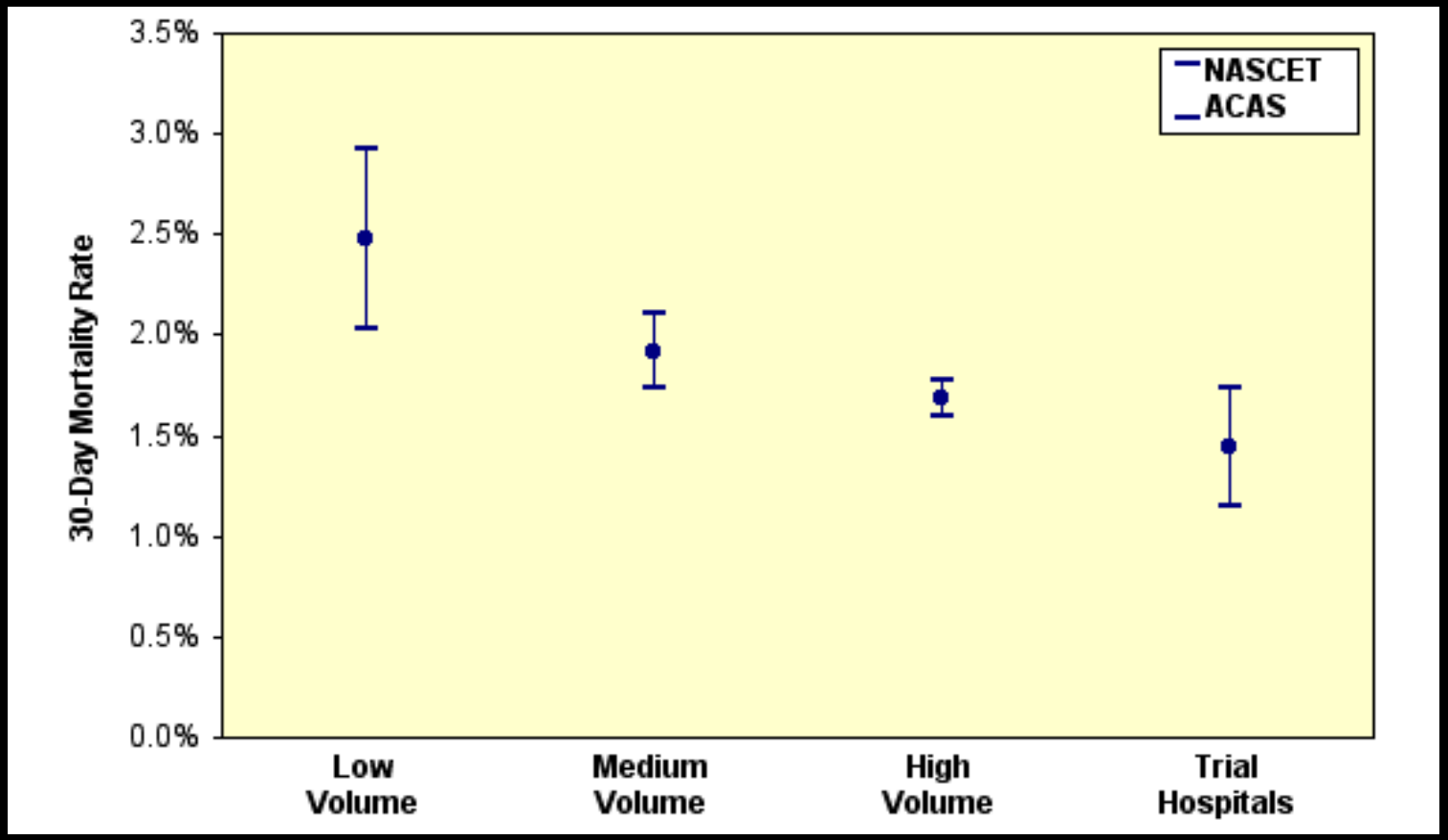
Lacunar infarcts in elderly-- Among 3,660 (Longstreth et al, 1998)

- 2529 (69%) infarct free
- 1270 lacunes in 841 participants (23%)
- Most of these 841 subjects had lacunes that were single (66%) and silent (89%)

Relationship between carotid duplex testing and endarterectomies (From 1999 Dartmouth Atlas)



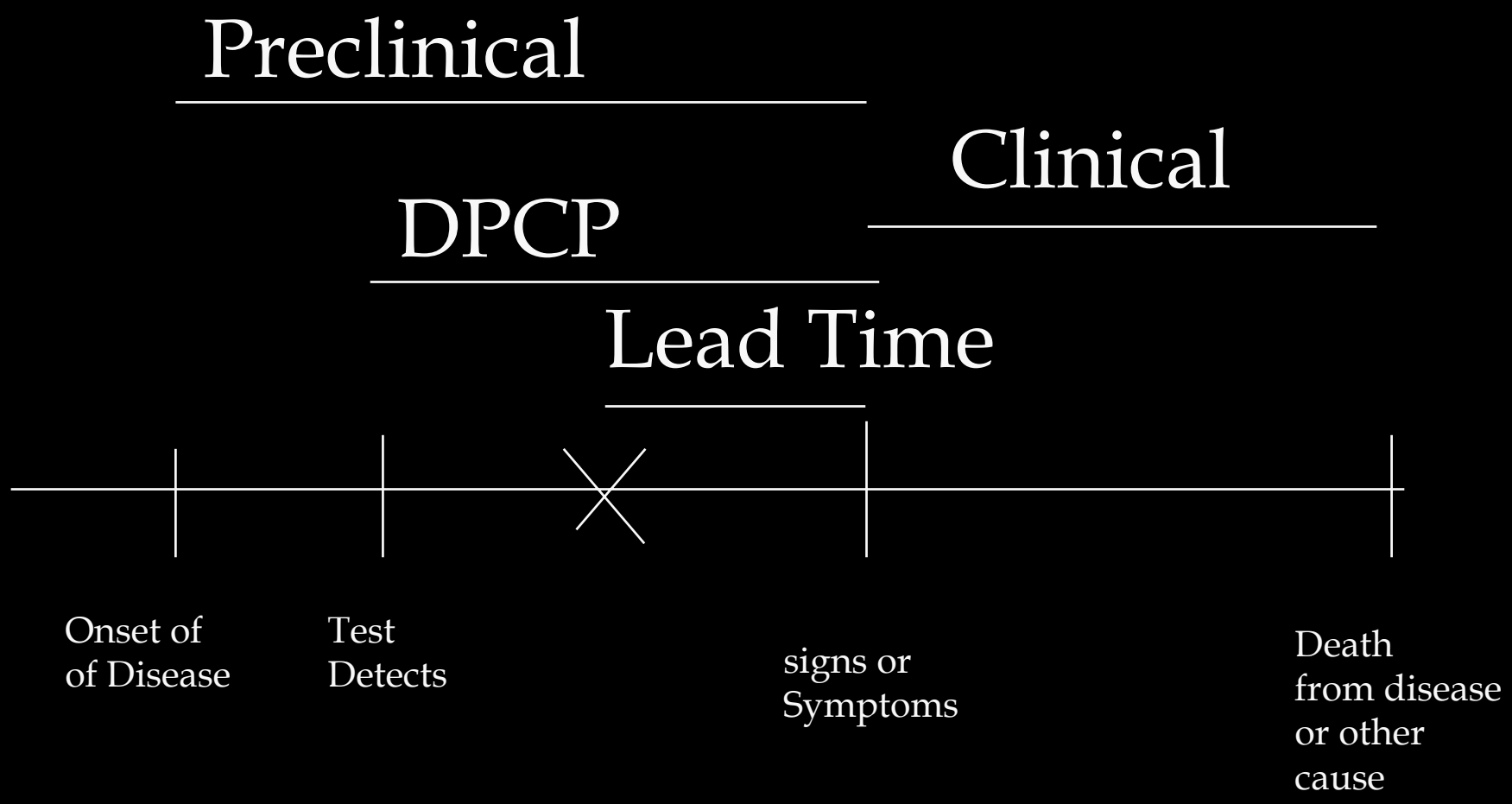
There is a relationship between volume and outcome for most surgical procedures (From 1999 Dartmouth Atlas)



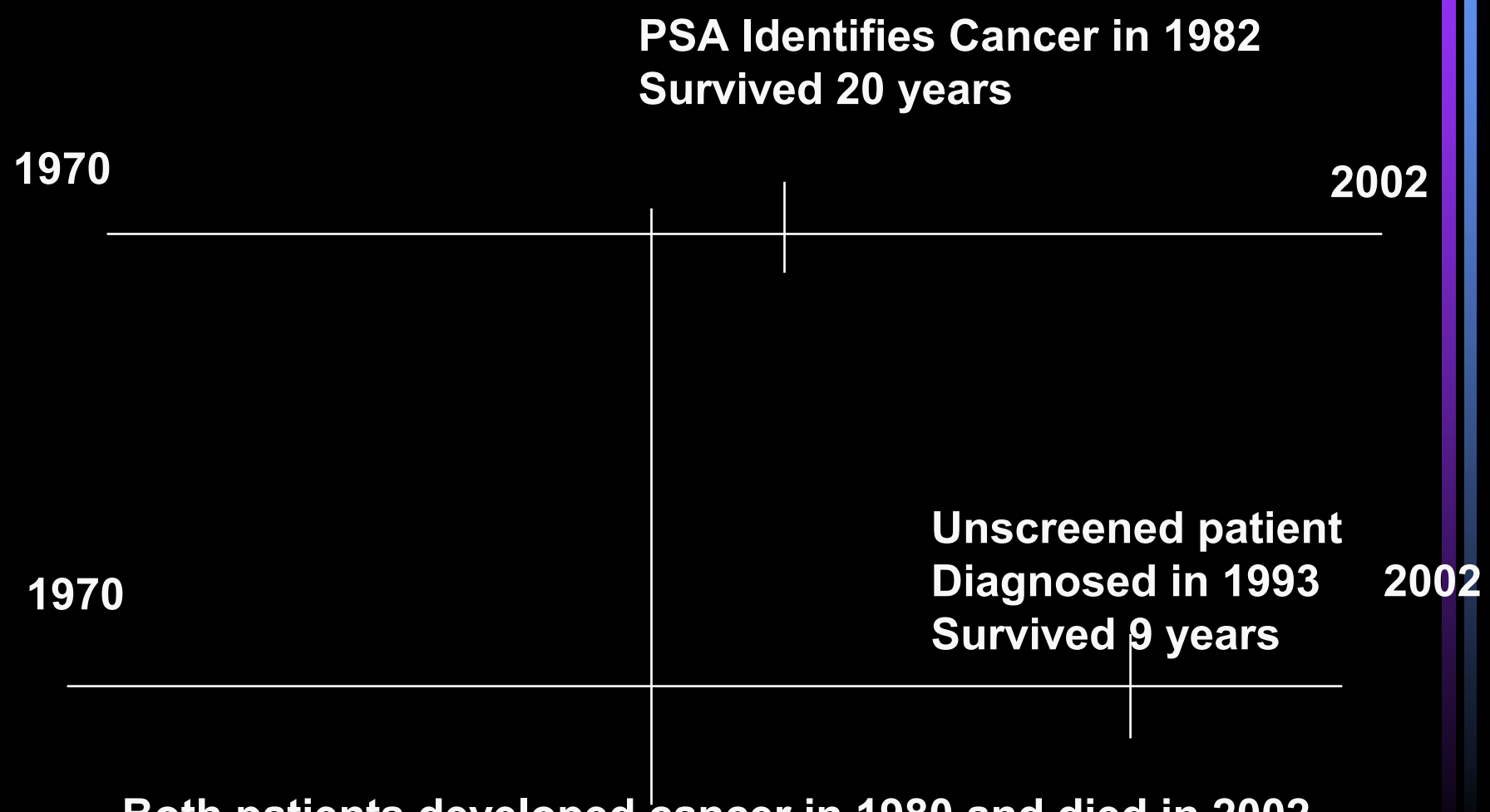
Question 3: What is disease?

- Natural history of disease
- What happens if a condition is left untreated?

Natural History of Disease

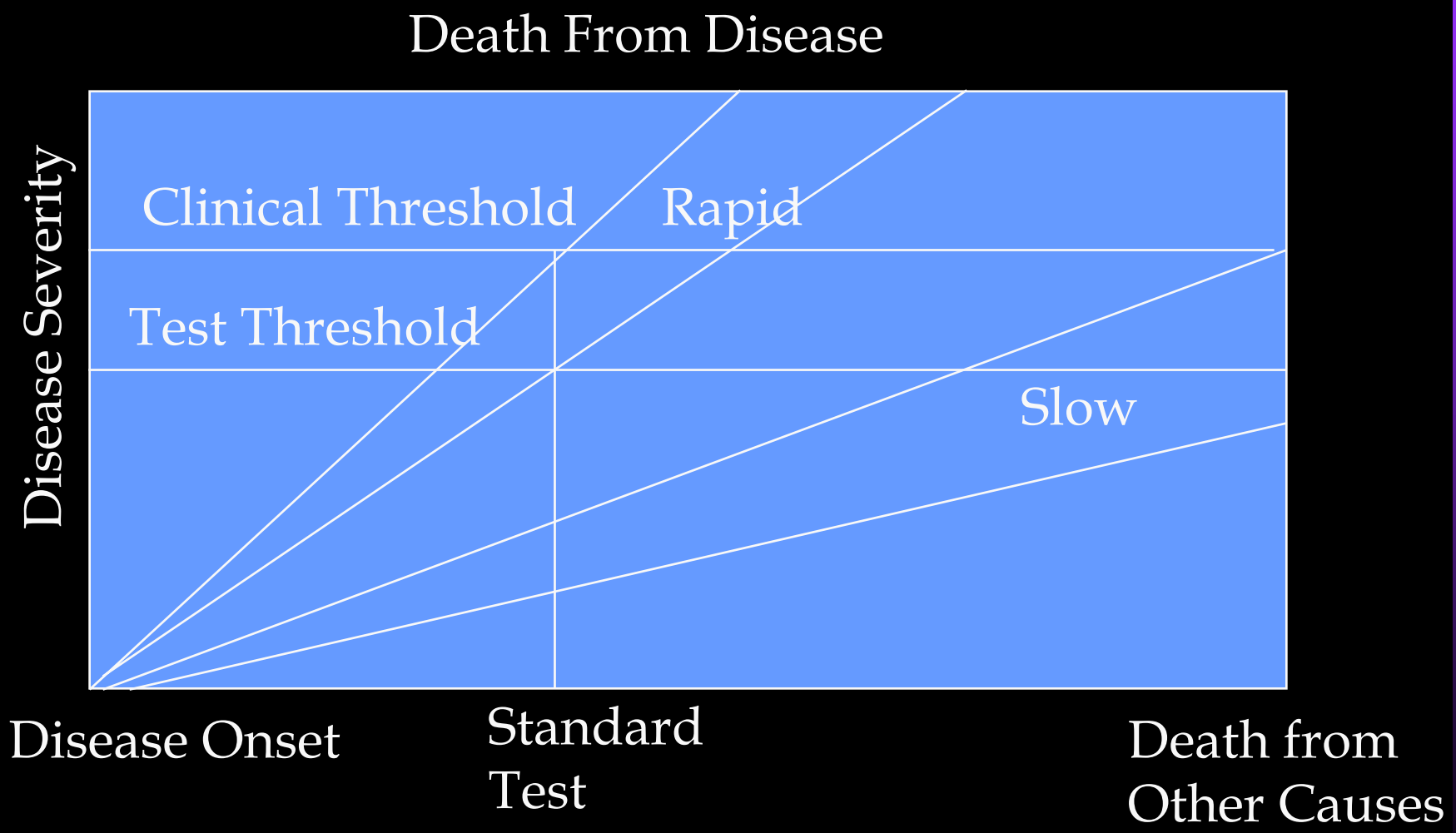


Lead Time Bias

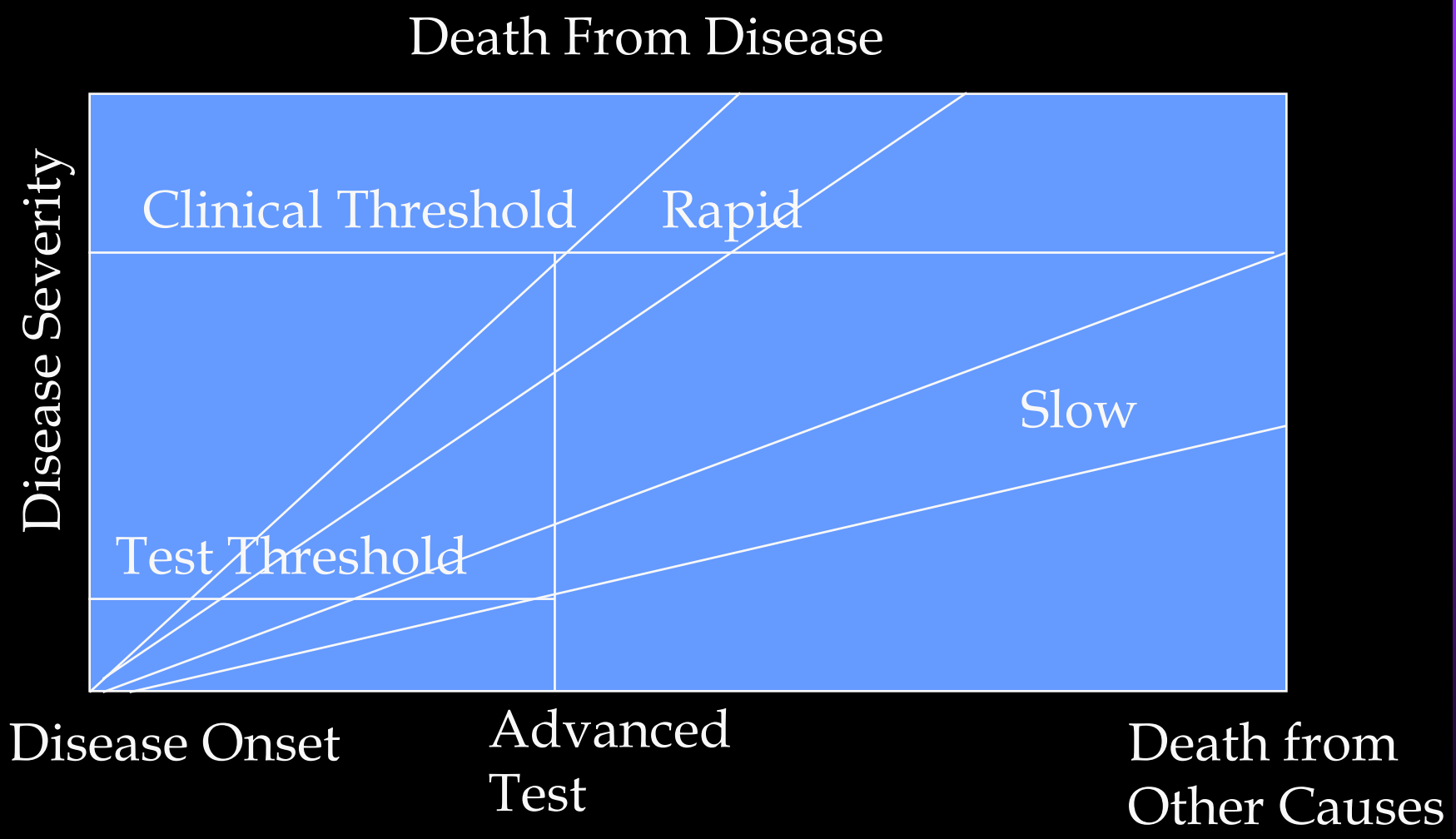


Both patients developed cancer in 1980 and died in 2002

Length Bias: Standard Test (Black & Welch, 1993)



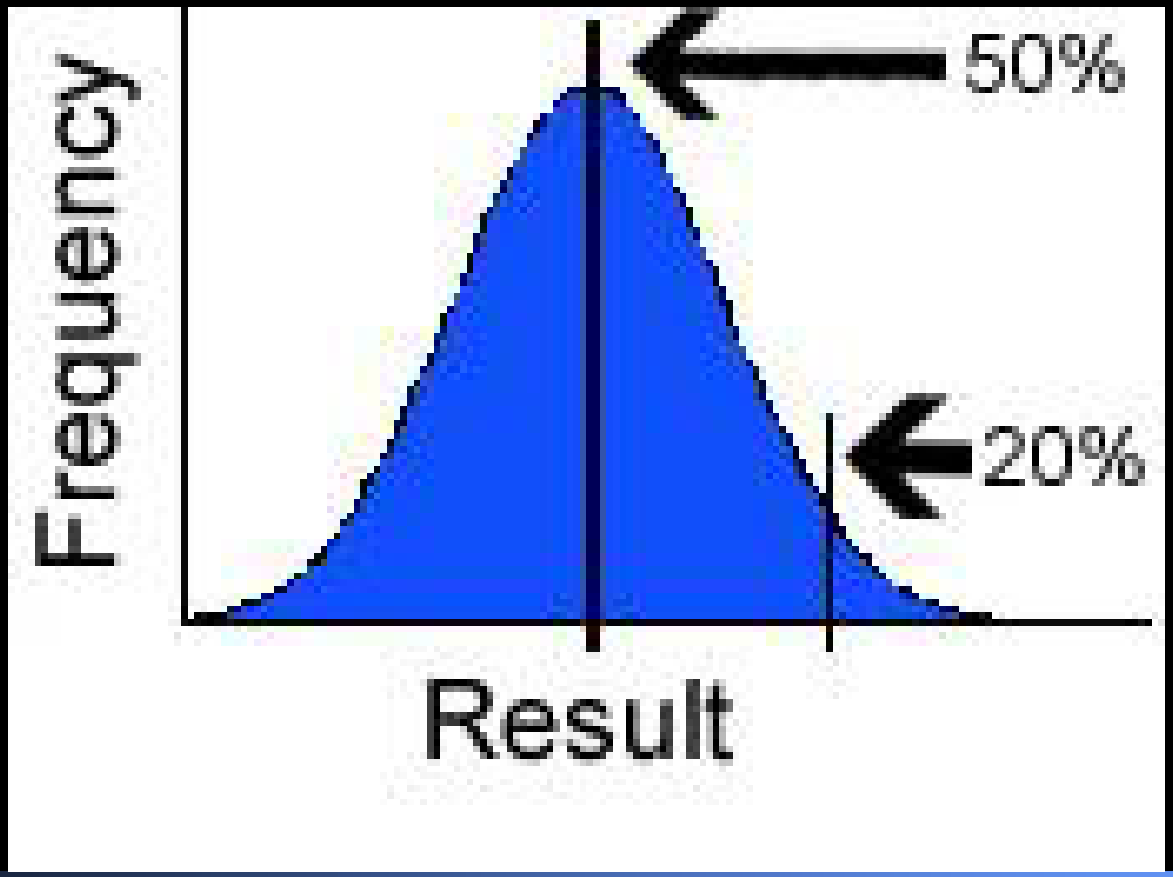
Length Bias: Advanced Test (Black and Welch, 1993



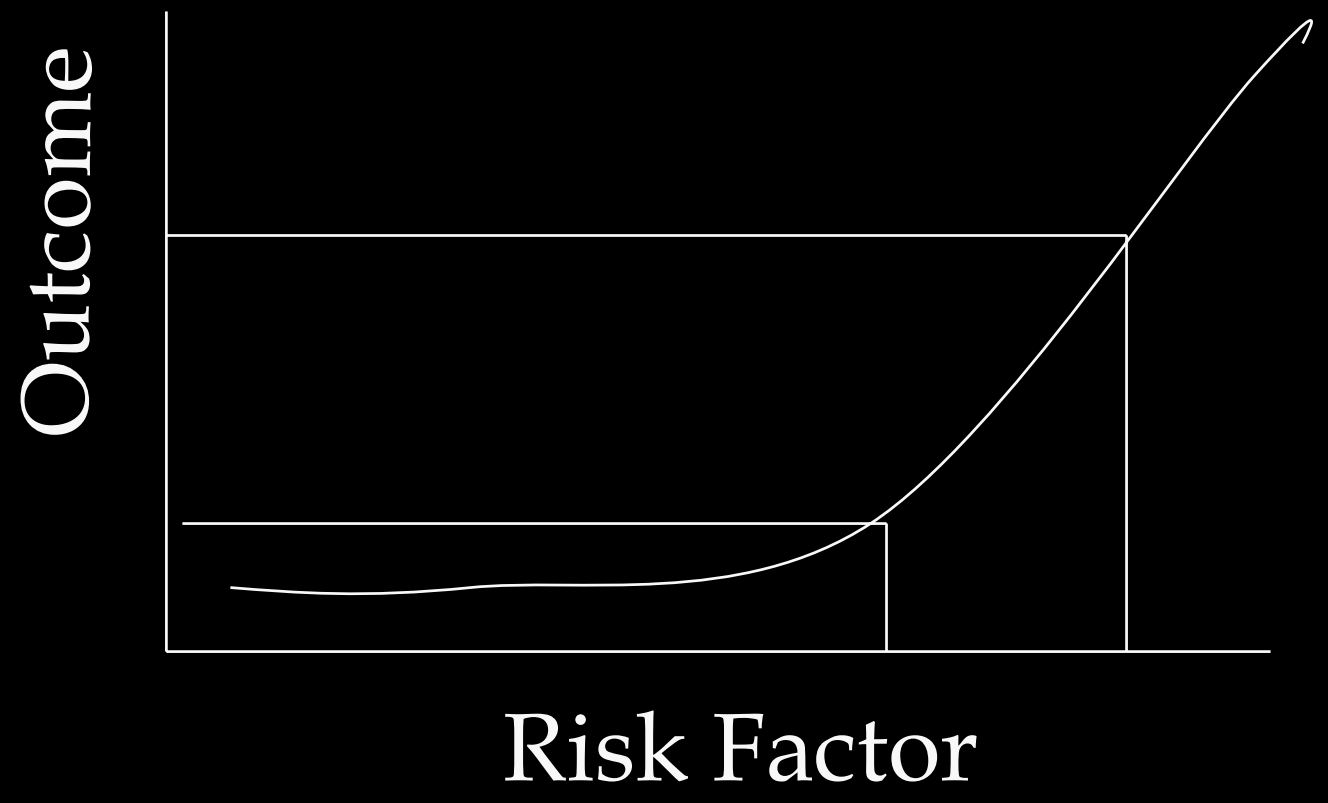
Discussion Examples

- Type 2 Diabetes Mellitus
- Asthma
- Depression
- High cholesterol
- Obesity

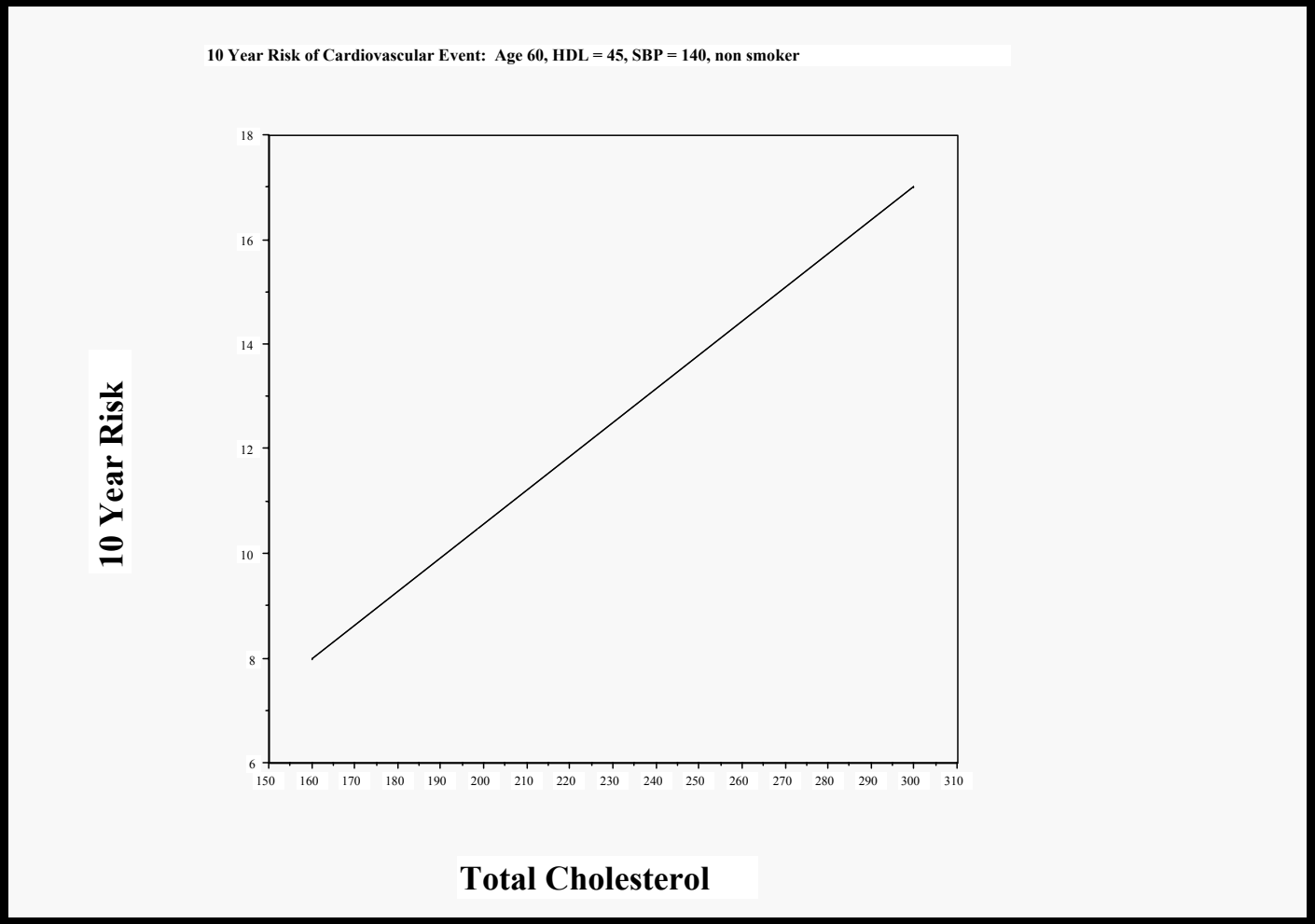
Percent of US Population with Total Cholesterol over 240mg/dl and 200mg/dl



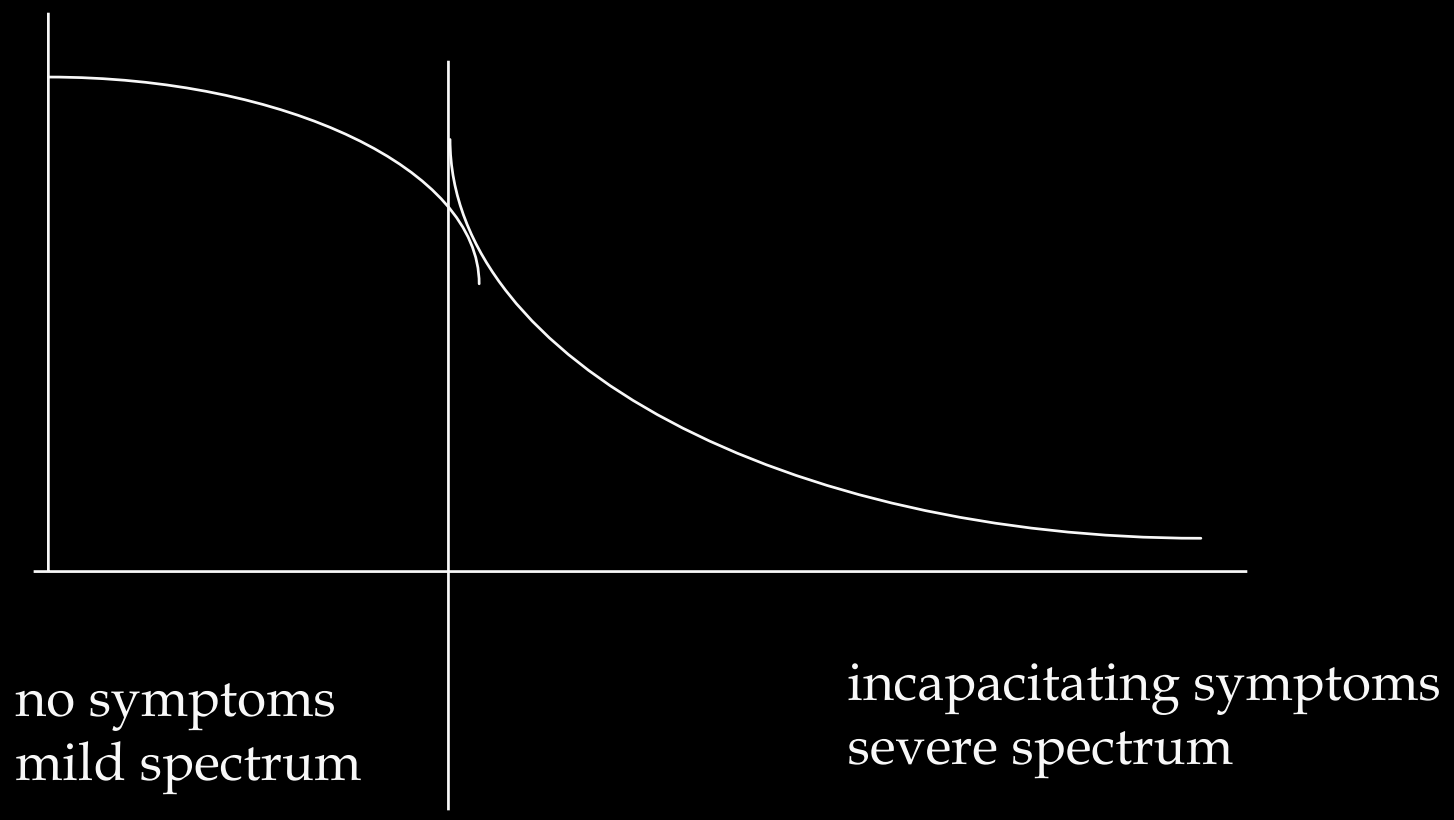
Where does disease begin?



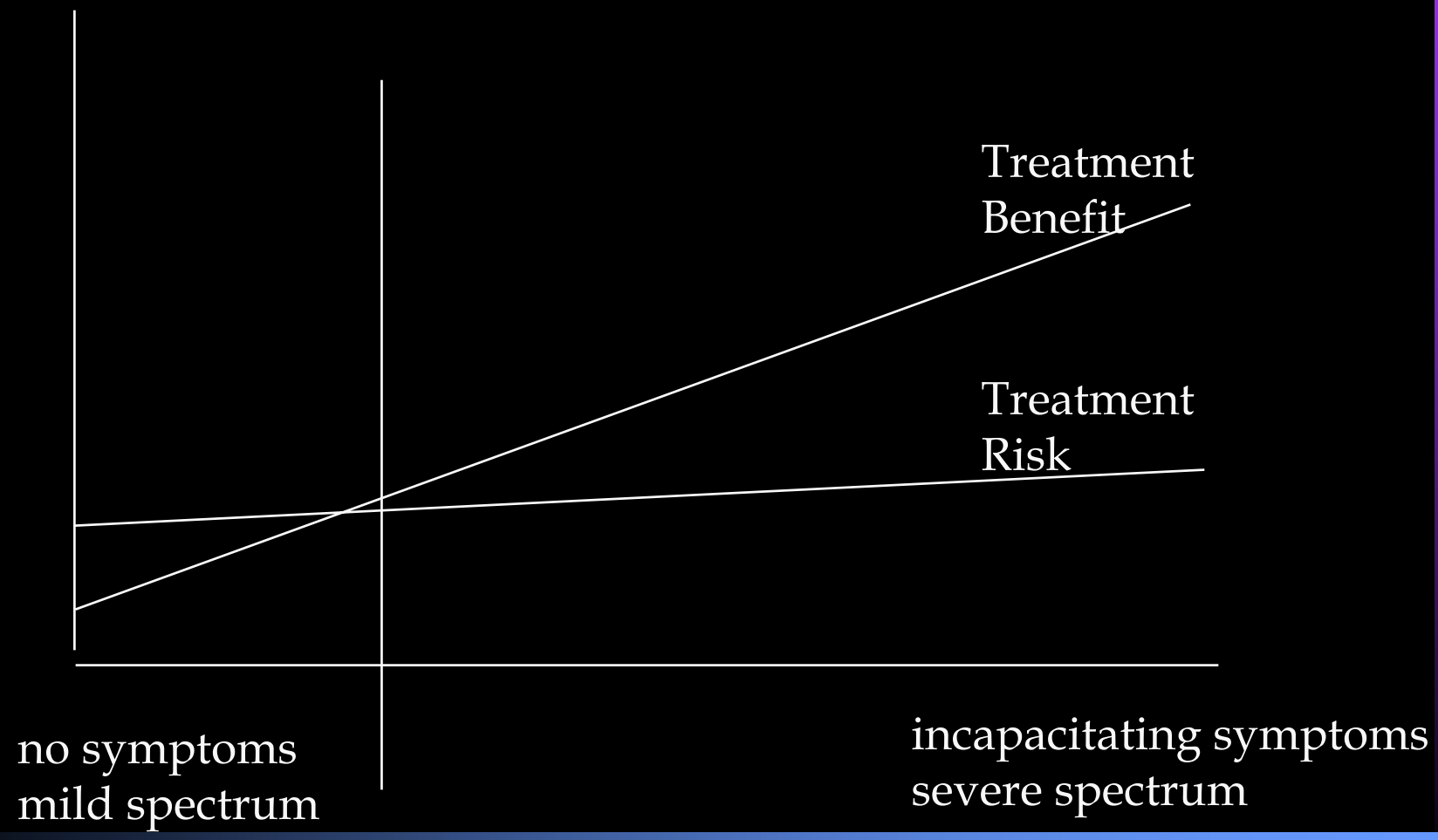
Argument in favor of population screening



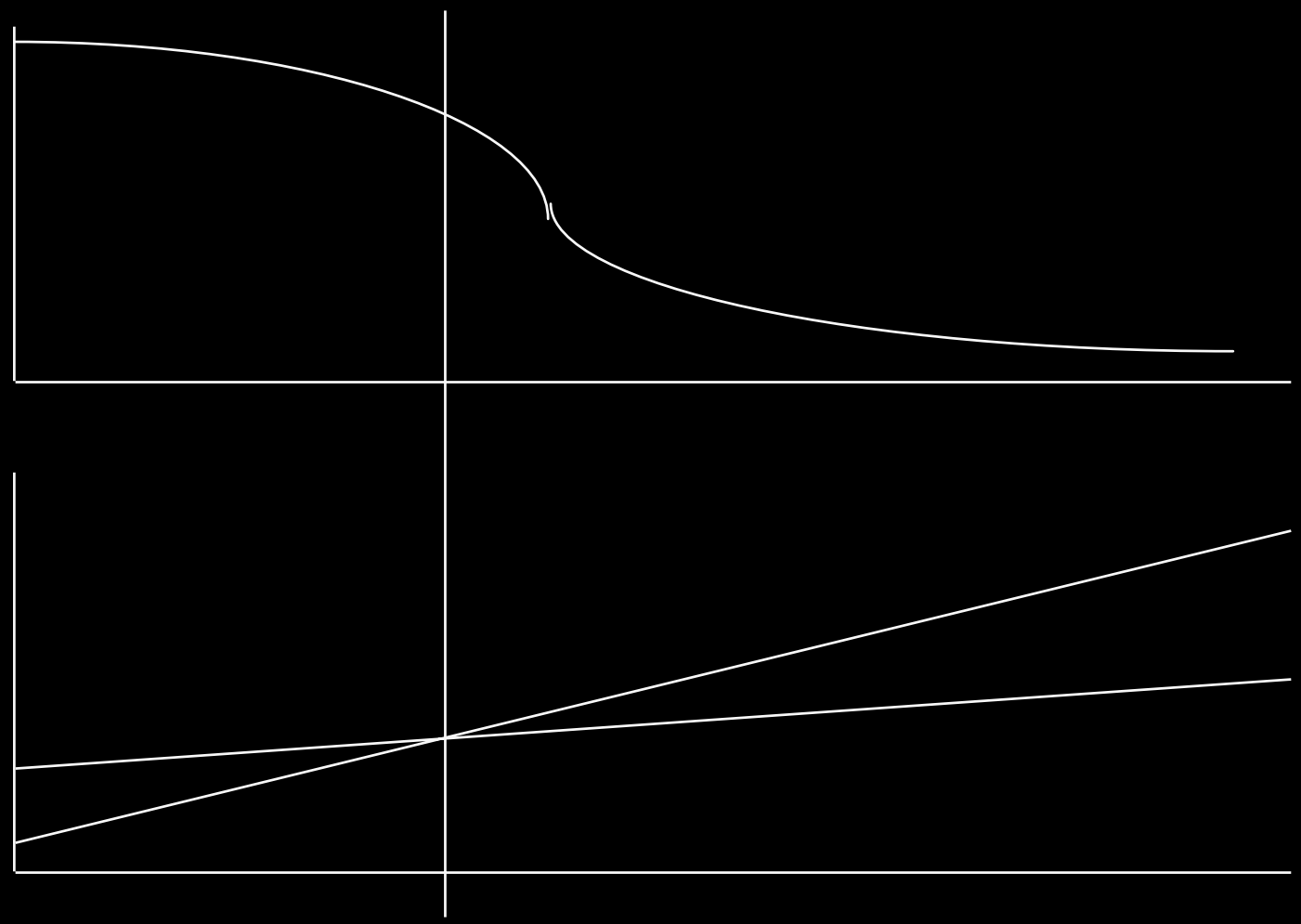
Number of people affected by mild and severe spectrum disease (Fisher & Welsch, 1997)



For mild spectrum disease, treatment harm may exceed benefit (Fisher & Welsch, 1997)



Increased diagnostic capacity shifts spectrum of detected disease left, benefit declines because treatment risk declines more slowly than treatment benefit



Changes in Diagnostic Thresholds

- Change in total cholesterol from 240 mg/dl to 200 mg/dl
- 40,6000,000 to 100,870,000 become eligible for therapy (about 60 million people)
- BMI of 25 for obesity
- 43,600,000 to 106,940,000 become obese (63 million people)

Drug costs

- It is not unusual for low-income patients without drug coverage to have to choose between food, rent, and expensive medication for chronic conditions like hypertension or diabetes.
- Spending on prescription drugs has increased much more than spending on other health care services,
- Drug costs increased twice as fast as the total national health spending between 1992 and 1997.

Changing Diagnostic Threshold for High Cholesterol from 240mg/dl to 200mg/dl: Assumptions

Drug	Lipitor 40 mg
Cost 30 pills	93.92
Compliance	0.5
Years of Use	20
Expected Diagnosis rate	0.33

Cost Implications of Changing Diagnostic Threshold From 240mg/dl to 200mg/dl

Lifetime costs/patient	22540.8
Number of Potential Cases	60000000
Market Increase (.33 of Patients)	19800000
Sales Increase	4.46308E+11

Reasons for increased drug costs(Conway et al 2002)

- spending growth in a few heavily advertised categories; newer, more expensive patented drugs that tend to rapidly dominate
- an increase of elderly individuals with treatable chronic conditions;
- direct marketing by pharmaceutical companies to consumers; development of new, expensive drugs for conditions that were previously not treatable.

Top Selling Pharmaceutical Lines 2002 (based on data in Rosenthal et al, NEJM, 2002, 346(7), 503.

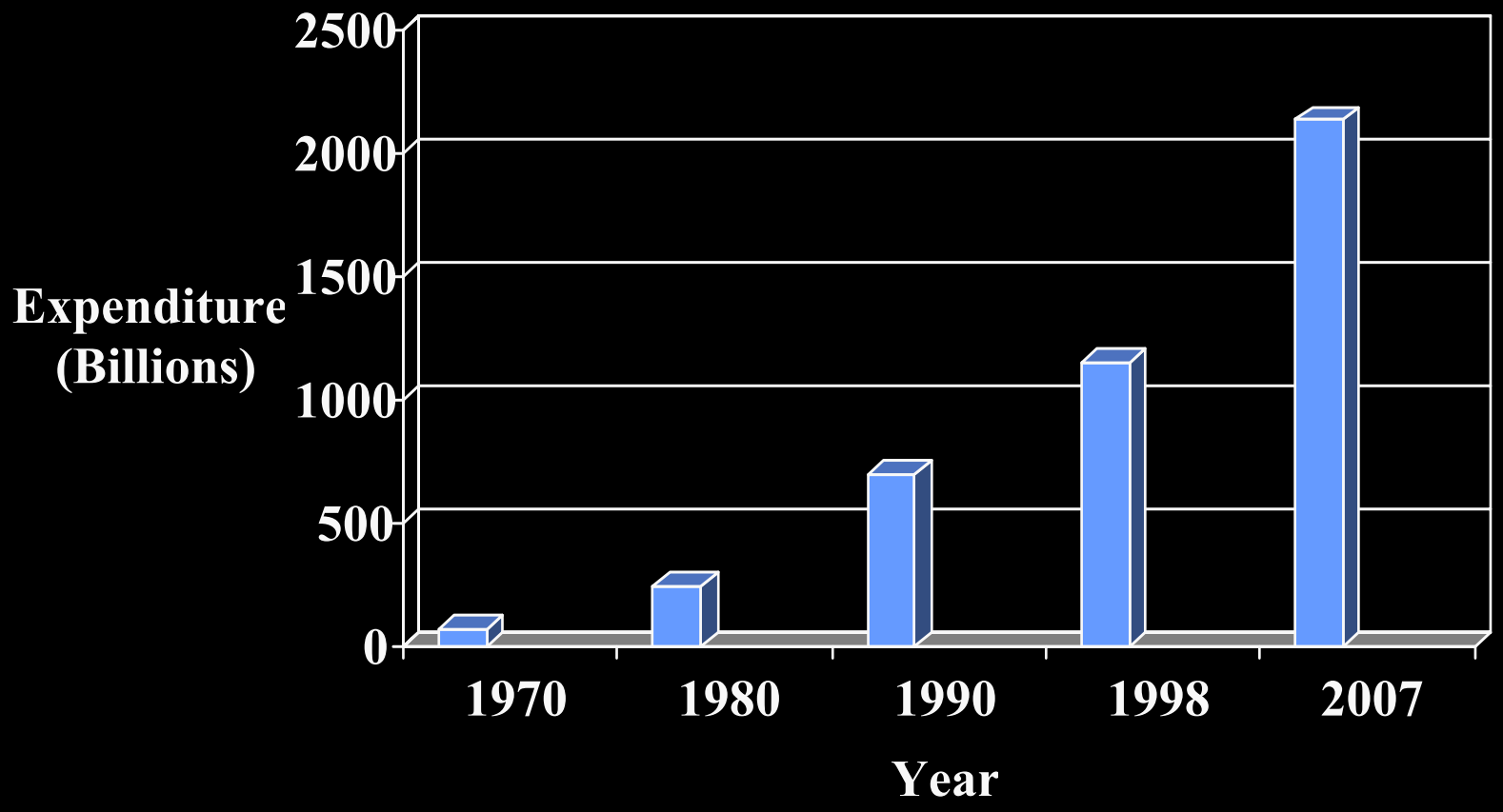
Product	Advertising	Sales
Antidepressants	32	6,843
Antihistamines	226	3,879
Lipidemics	92	6,045
Nasal Sprays	114	990
Proton Pump Inh	80	5,731

In millions of US dollars

Question 4

How can we best use our resources to improve public health?

Actual and Expected National Expenditures on Healthcare in the USA (Inglehart, NEJM, 1999)



Level of Economic Analysis

- Macro level--informs policy
- Micro level-informs clinical decisions

Example Macro Problem

- Oregon - late 1980s
- Medcaid costs were increasing 25% per year
- Medicaid coped with the problem by changing eligibility threshold
- Number of people covered reduced to 200,000 among 600,000 eligible
- Proposed rationing services rather than people
- Goal was to increase number covered

Macro Level Decision

- Fixed level of resources
- Potentially infinite demand
- Need to make effective/efficient use of resources
- Set priorities-make choices

Micro Level Decision

- I am 82 years old
- I feel good and my memory is fine
- My doctor says I have >85% stenosis of my carotid arteries
- She wants to operate ASAP
- She says I may die from the surgery
- She also thinks I may die of a stroke
- What should I do?

Quality-Adjusted Life Year

- Combines morbidity and mortality into a single index
- Represents life expectancy with adjustments for quality of life
- Is defined as a year of life free of all disabilities and symptoms

Differences Between CBA,CEA, and CUA

Type	Resources Measured in	Outcomes Measured in
Cost/Benefit	$s	$s
Cost/Effectiveness	$s	Clinical measure (ie mmHg
Cost/Utility	$s	QALYs

C/E Ratio

CEA evaluates a given health intervention through the use of a cost-effectiveness ratio. In this ratio, all health effects of the intervention (relative to a stated alternative) are captured in the denominator, and changes in resource use (relative to the alternative) are captured in the numerator and valued in monetary terms.

From Gold et al, 1996

Cost/Utility of Secondary Prevention

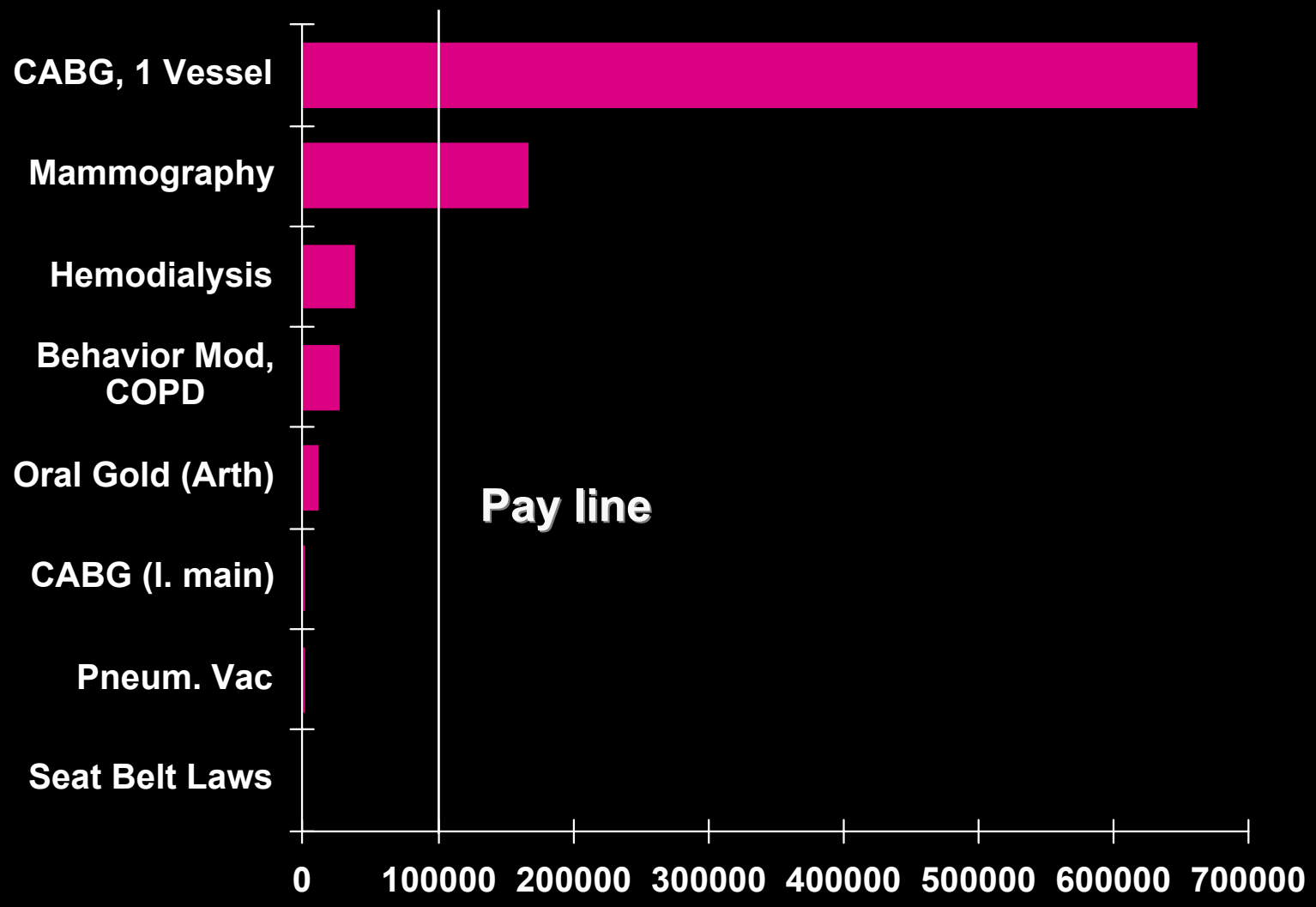
Topic	Reference	Compared to	Cost/QALY
SECONDARY PREVENTION PROGRAMS			
Mammography Women age 40-49	Eddy, 1989	No Mammography	$240,000
Mammography Women age 40-49	Salzmann et al, 1998	No Mammography	$105,000
Surgery for Prostate Cancer	Flemming et at, 1993	Watchful waiting	Dominated--to treatment benefit
PSA screening men age 60 and age 70	Krahn et al, 1994	No screening	Dominated-screening causes reductions in QALYs
Cholesterol Screening and treatment with Lovastatin 20 mg/day, for men with cholesterol >300mg/dl	Goldman et al, 1991	No screening and treatment	$71,000-$135,000
Cholesterol Screening and treatment with Lovastatin 20 mg/day, for men with cholesterol >250-299 mg/dl	Goldman et al, 1991	No screening and treatment	$105,000-$270,000

Cost-Utility of Primary Prevention

Tobacco taxation, $2.00/pack	Kaplan et al, 1995	No change in tax	<$0
Tobacco Restriction policy for minors	US Food and Drug Administration, 1996, Graham et al, 1998	No restrictions	<$1,000
Smoking Cessation Counseling	Cromwell et al, 1997	No counseling	$1,915
Regular jogging beginning age 35	Hatziandreu et al, 1988	No change in activity	$11,313
Daytime use of running lights in automobiles	Williams and Lanchaster, 1995	No use of lights	<$0
Law requiring lap and should belts in automobiles, assumes only 50% compliance	Graham et al, 1997	No restraints	<$0

Cost/QALY for Selected Interventions

From Kaplan, 1993), p 127



Opportunity Costs; Life years/$1 million, IOM 1999

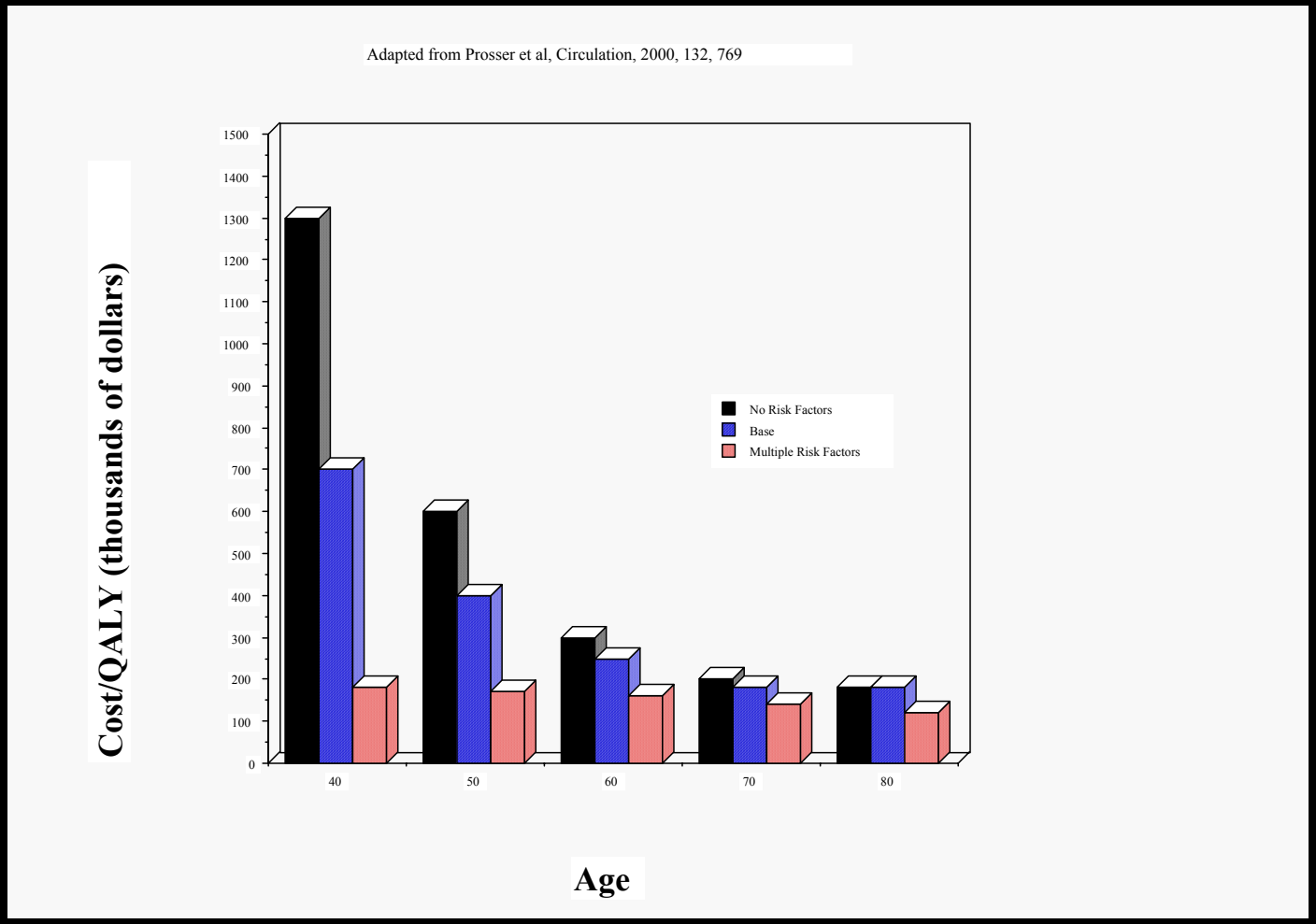
- Influenza vaccine, persons 65+ 7,750
- Smoking cessation 217
- Lovastatin 20 mg men total chol 300 42
- Captopril for hypertension 8
- Pap smear every 3 years 36
- Pap smear every year <.5

Misconceptions about Cost/utility analysis

- CUA is usually used to justify cutting budgets
- CUA will damage patients
- CUA is about saving money

- CUA is neutral with regard to budget.
- Use of CUA should result in improved population health
- CUA is about saving lives

CEA for pravastatin for men the LDL cholesterol >160 by age



Opportunity Costs; Life years/$1 million, IOM 1999

• Influenza vaccine, persons 65+	7,750
• Smoking cessation	217
• Lovastatin 20 mg men total chol 300	42
• Captopril for hypertension	8
• Pap smear every 3 years	36
• Pap smear every year	<.5

A COMPREHENSIVE FRAMEWORK FOR CARDIOVASCULAR HEALTH:
The progressive development of CVD (heart disease and stroke) and opportunities for CVH promotion and CVD prevention

The progressive development of CVD (heart disease and stroke)

UNFAVORABLE SOCIAL AND ENVIRONMENTAL CONDITIONS → **ADVERSE BEHAVIORAL PATTERNS** → **MAJOR RISK FACTORS** → **FIRST EVENT/ SUDDEN DEATH** → **DISABILITY/ RISK OF RECURRENCE** → **LATE DEATH** →

WHOLE POPULATION: *281,000,000*

WHOLE POPULATION: *281,000,000*

ESTABLISHED RISK FACTORS:

SMOKING *53,000,000*
HBP *50,000,000*
TC *41,000,000*
DM *10,000,000*

FIRST FATAL OR NON-FATAL EVENTS/YR:

STROKE *500,000*
MI *650,000* CHF ADM *550,000*

SURVIVORS >1 YR:

STROKE *375,000*
MI *450,000*
CHF ADM *450,000*

LATE DEATHS /YR

CVD *525,000*

POLICY AND ENVIRONMENTAL CHANGE | **BEHAVIOR CHANGE** | **RISK FACTOR DETECTION AND CONTROL** | **EMERGENCY CARE/ACUTE CASE MANAGEMENT** | **REHABILITATION/ LONG-TERM CARE** | **END-OF-LIFE CARE**

Prevention of risk factors in the first place - 0 | 0 | 1° | 2° | 3 °

Cardiovascular health promotion | Cardiovascular disease prevention | Palliation

INCREASE QUALITY AND YEARS OF HEALTHY LIFE

ELIMINATE HEALTH DISPARITIES

GOAL 1 → ***GOAL 2*** → ***GOAL 3*** → ***GOAL 4*** →

Opportunities for CVH promotion and CVD prevention

CDC

Rethinking some basic assumptions

- Medicine is about diagnosis and treatment
- Outcomes in preventive medicine require early detection and treatment of disease
- Disease is binary
- Some people are healthy

- Medicine is about making decisions
- Early detection may not necessarily enhance outcomes and can cause harm
- Disease is a process
- We are all sick

What does this all mean?

- There is uncertainty surrounding many medical decisions
- Changes in the definition of illness can have major impacts on cost
- The effects of changes in illness thresholds upon population health has rarely been evaluated
- We need to develop tools for a “shared decision” paradigm