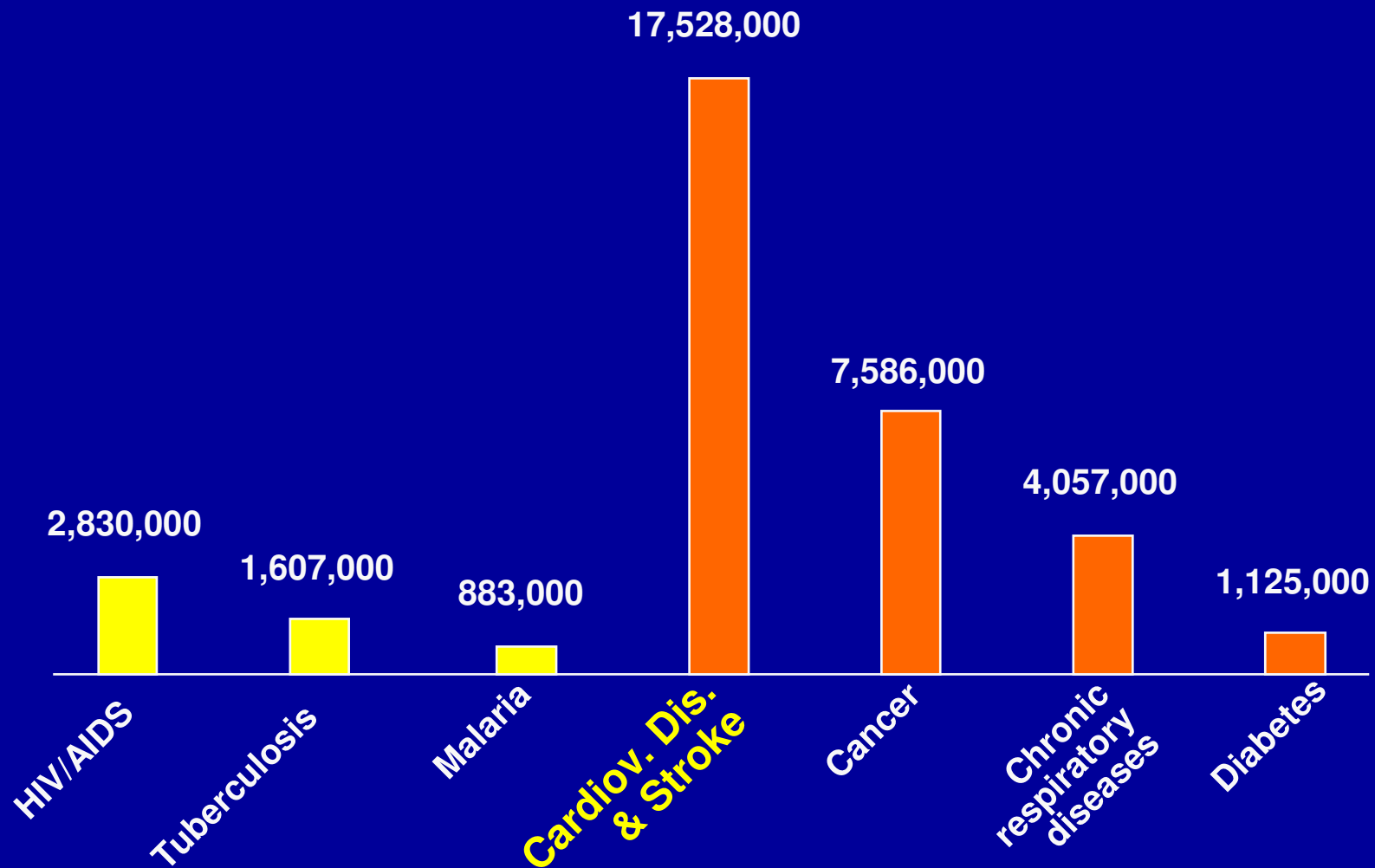


MY FUTURE
ACADEMIC CARDIOVASCULAR MEDICINE - 2007

-) Clinical Opportunities**
-) Research: Challenges & Opportunities**
-) A Personal Search and Approach**
-) “ Clinician /Academician ”**
-) “ Researcher ”**
-) “ Educator ”**

1a) PROJECTED GLOBAL DEATHS BY CAUSE, ALL AGES, 2005

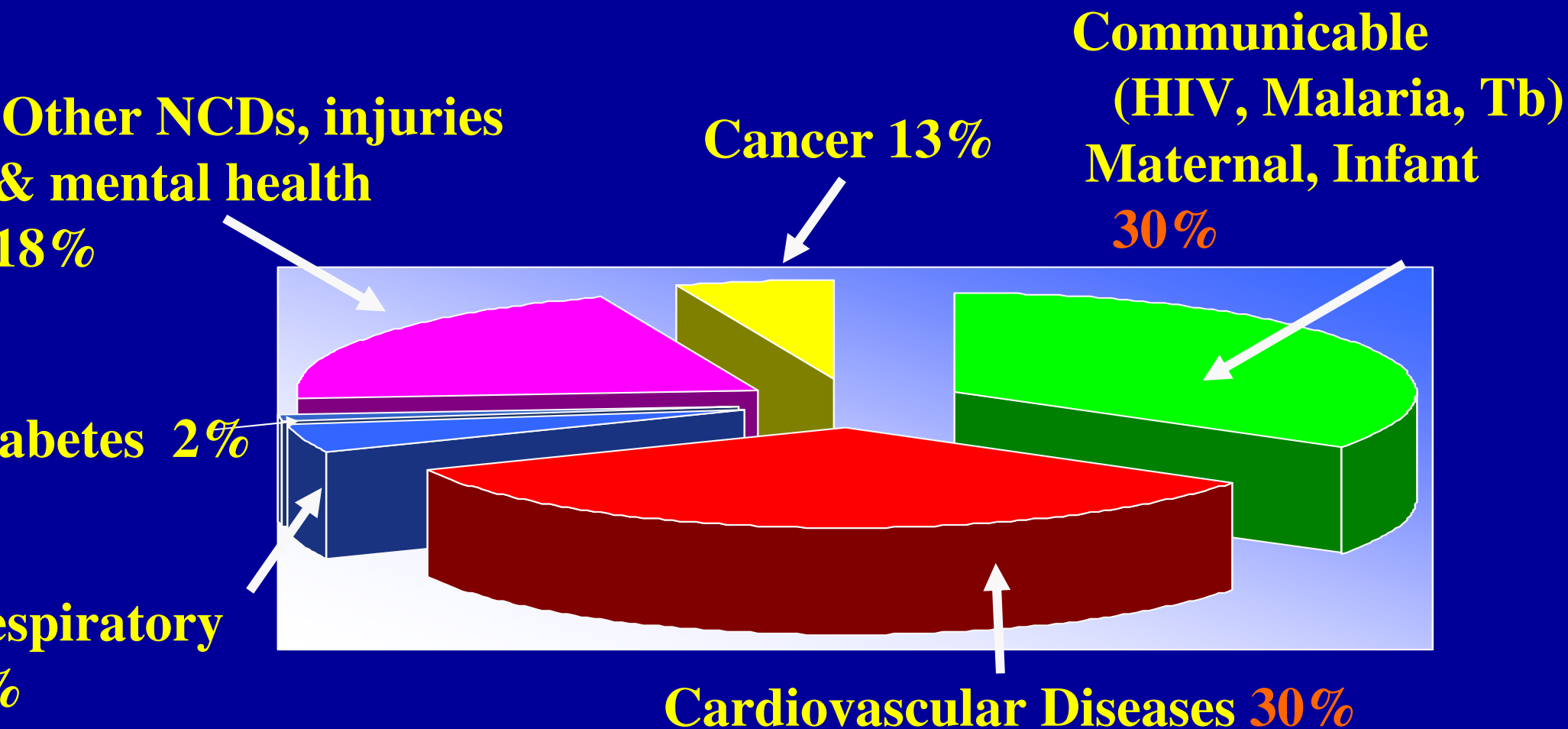


Total Deaths: 80% in Low and Middle Income Countries

Cluster V, Voûte J. Lancet 2005; 366:1512

Modified from WHO 2005 - Chronic Diseases and Health Promotion

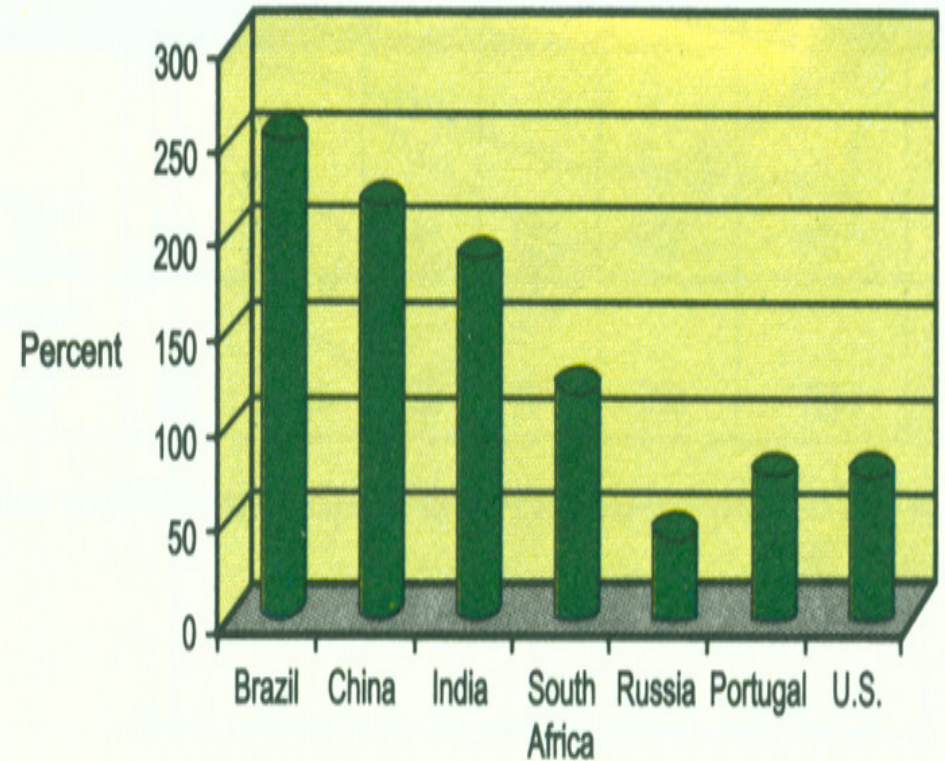
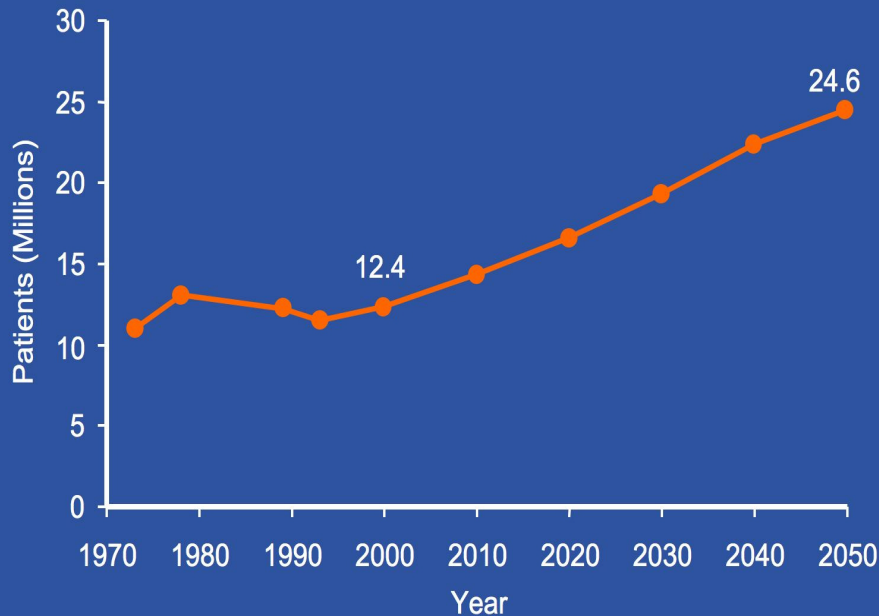
b) Which Conditions Should be Given Priority in Low Income Countries?



Lab) Predicted Increased Prevalence of CVD Mortality

Scope of the Problem

Prevalence of U.S. Heart Disease



CVD deaths for the year 2040 over the year 2000

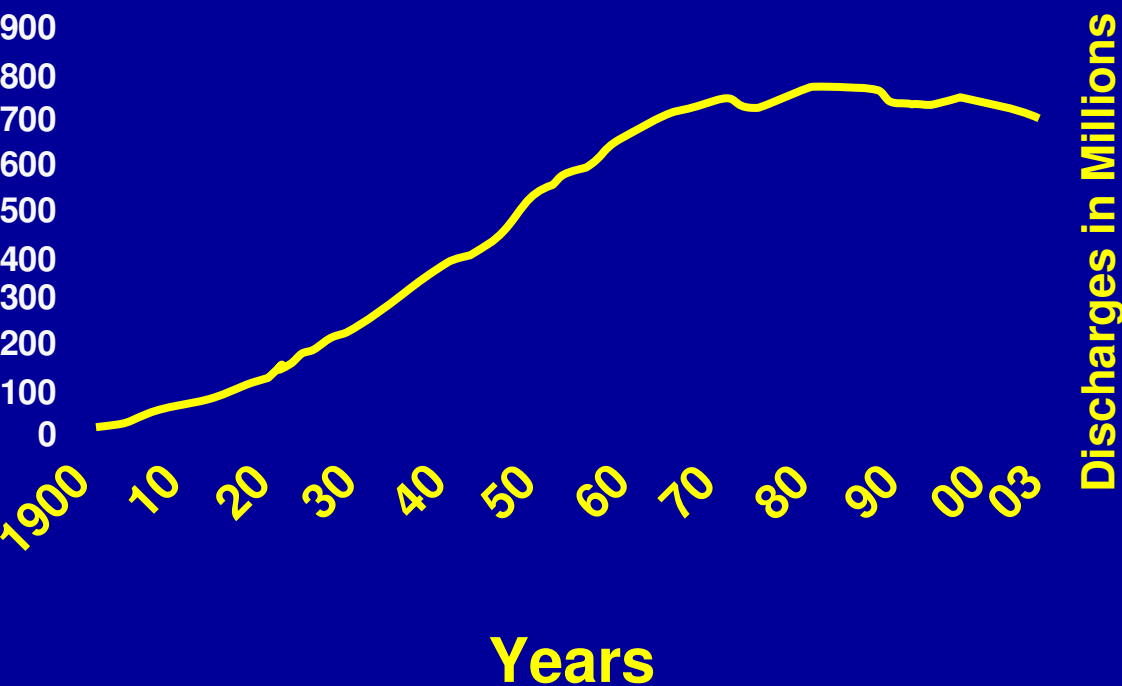
Foot DK et al JACC 2000;35:1067

Leeder, S et. al. Columbia University, Press. 2004.

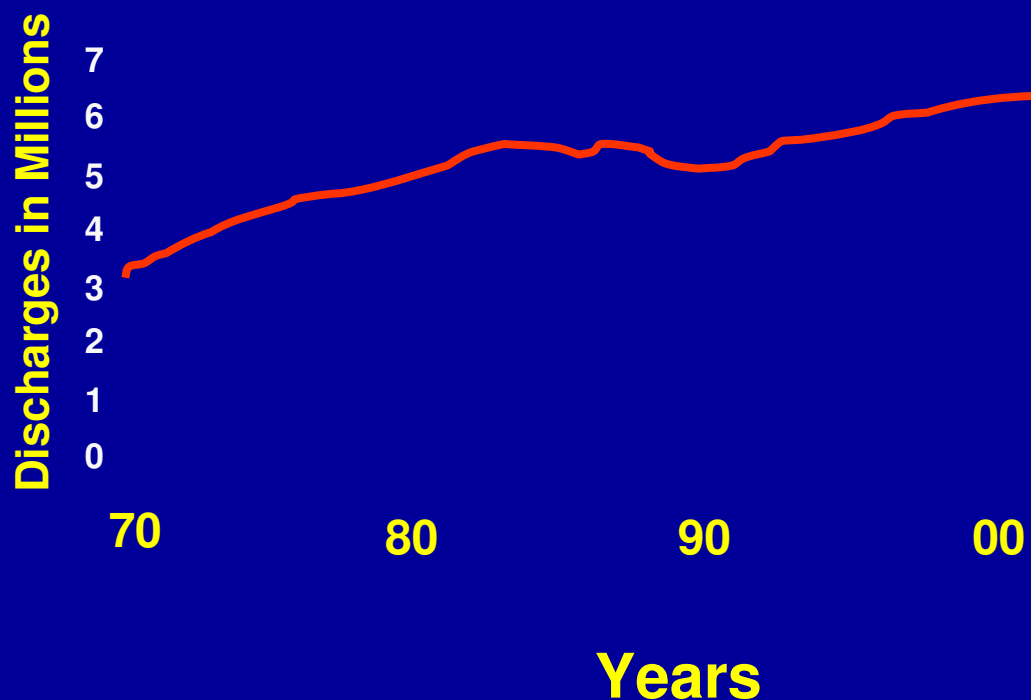
a) United States, Cardiovascular Deaths & Hospitalization

LITTLE CHANGE

POSTPONED (PREVENTION ?, BETTER Rx ?)

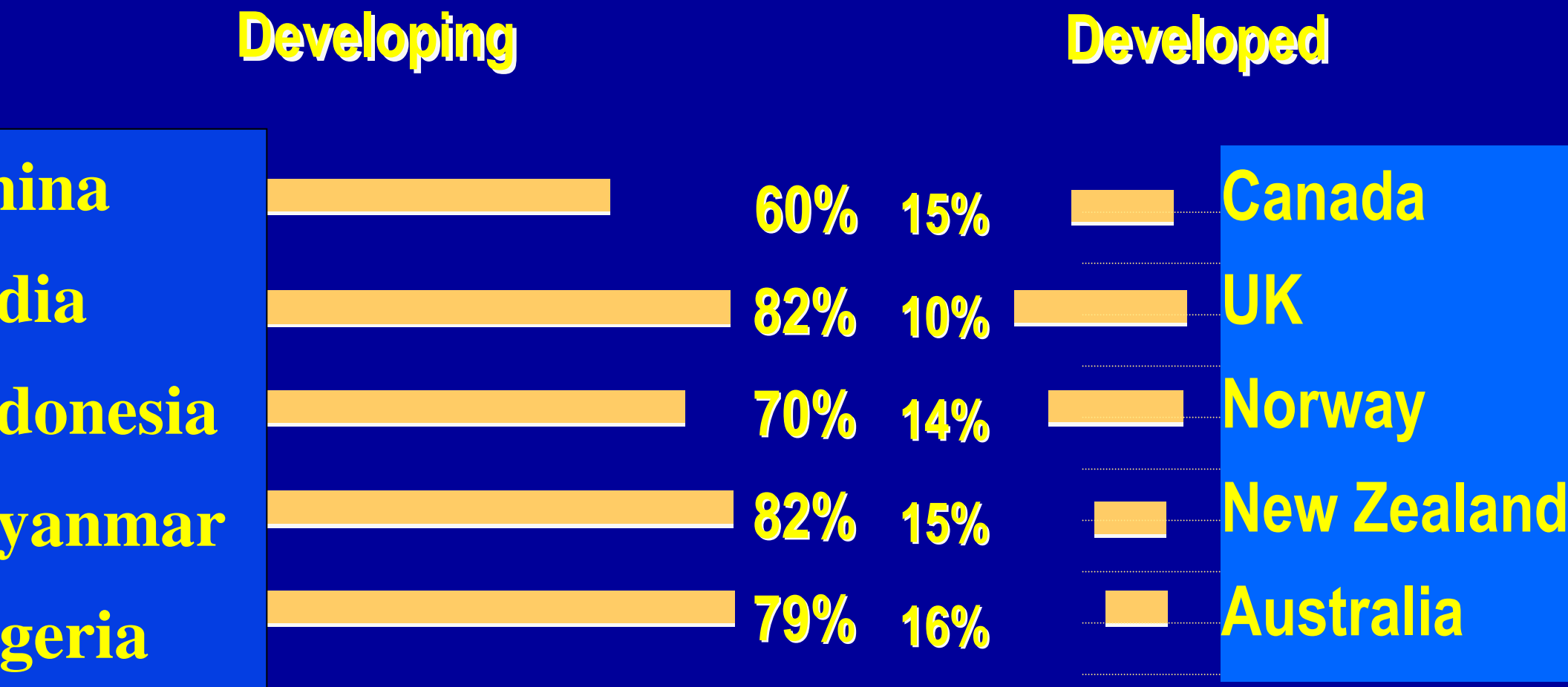


INCREASED (BETTER Rx)

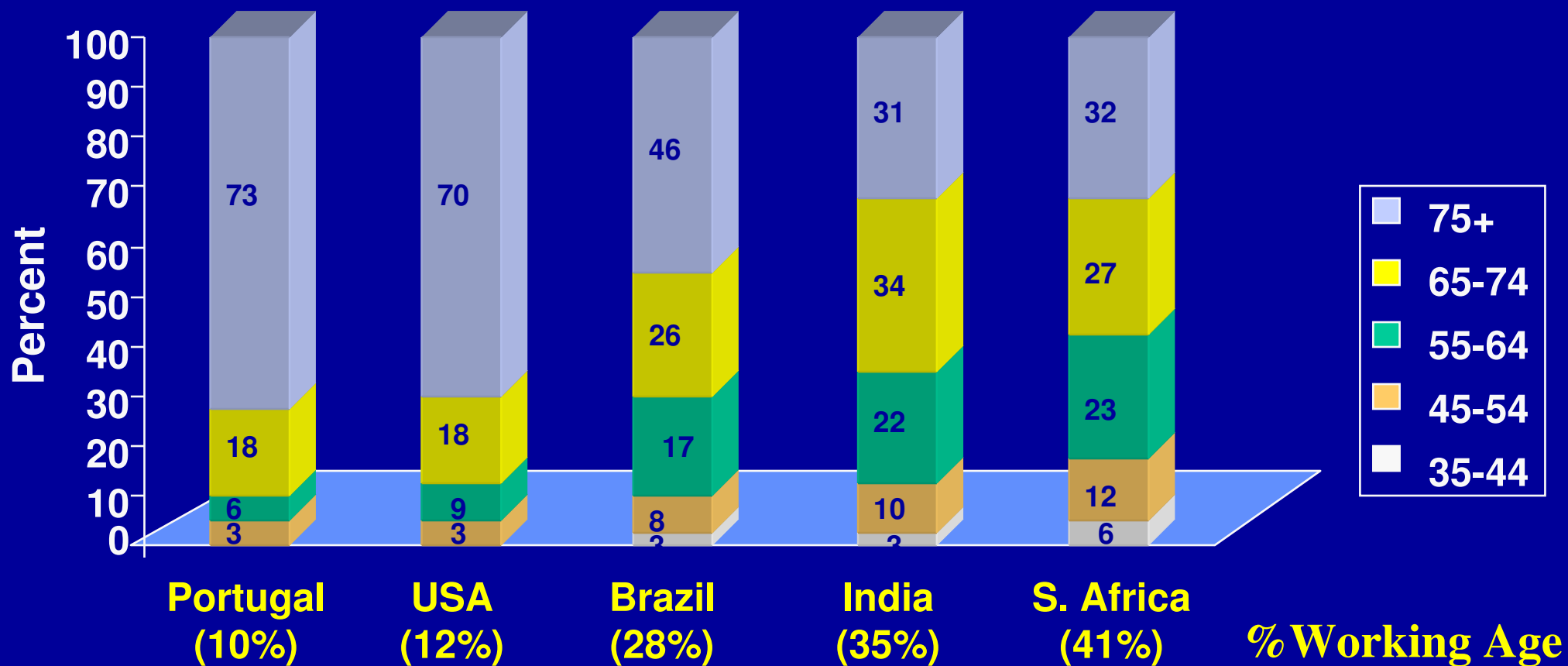


DC / NCHS / NHLBI Circ. 2006; 113:85 – ECONOMIC BURDEN - \$368 Bill

b) Out of Pocket Expenditure on Health



PROJECTED CVD MORTALITY FROM 2000 to 2030 – AGE, COUNTRY



Leeder, The Earth Institute, Columbia Univ, New York, 2004
 Fuster et al., Circ 2007 (In Press)

Interdisciplinary Background: Future Focus



Mechanical Era. Cardiac Surgery



Minimally Invasive Era. Catheter-based



Biological Era. Promoting Health

Yesterday

Primary Cardiac Care

Acute Cardiac Care

Cardiac Surgery

Today

Specialist

Interventionalist

EPS

Tomorrow

Bioimaging

Genetic Screening,

Outcomes / Economics

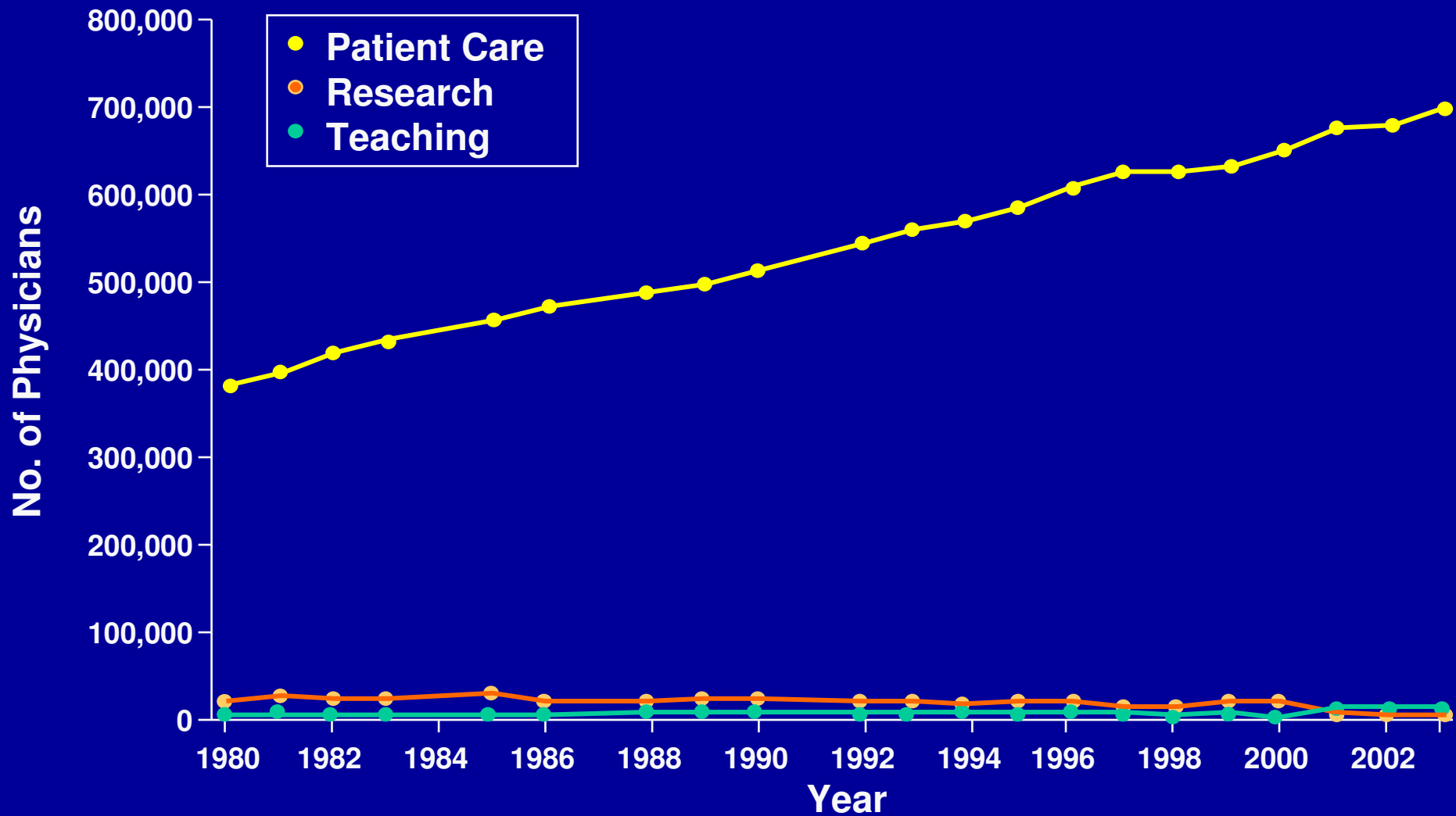
CARDIOVASCULAR “DEMAND CATALYSTS”

- 1) **Aging** population with more chronic cardiac patients.
- 2) The “epidemics” of **obesity and type 2 diabetes**.
- 3) The decline of **managed care’s gatekeeper model**.
- 4) Better informed **public**, clinical trials and expectations.
- 5) **Technological** and procedural **innovations**.
- 6) More widespread use of cardiovascular **screening tests**.
- 7) Increasing **awareness among women**.
- 8) **Crisis by no increase in female cardiologists & IMGs**

Modified from WB Fye. Circ **2004**; 109:813

PHYSICIAN WORKFORCE IN THE UNITED STATES, 1980-2003

MAJOR PROFESSIONAL ACTIVITY



J Levy, LE Rosenberg. JAMA 2005; 294:1343 (Source: AMA)

MY FUTURE

ACADEMIC CARDIOVASCULAR MEDICINE - 2007

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- 2) Research: Challenges & Opportunities**
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- 5) “ Researcher ”**
- 6) “ Educator ”**






1) “EXCEPTIONAL RETURNS THE ECONOMIC VALUE OF AMERICA’S INVESTMENT IN MEDICAL RESEARCH”

Six research papers authored by **nine** of America’s most **distinguished economists** - working independently of each other

The report documents that “**extended healthy lives**” of Americans, in great part **due to advances in medical research** (\$45 billion annually), **generates dramatic returns** (\$ trillions annually)

“If you think research is expensive, try disease”
(Mary Lasker, 1901-1994)

2) Physician-scientists are catalysts of translational research.

| | | |
|---|--|---|
| <p>Alfred Nobel (1833-96)</p> |  | <p>Establish "a fund, the interest on which shall be annually distributed in the form of prizes to those who, during the preceding year, shall have conferred the greatest benefit on mankind." <i>Key clause in will signed 1 year before his death from cardiovascular disease.</i></p> |
| <p>•Willem Einthoven (Nobel 1924) Goal: Perfect the EKG</p> |  | <p>capillary electrometer string galvanometer LBBB in same patient 30 years apart "May I be permitted to communicate something about the string galvanometer, its latest improvements and its use in electrocardiography." <i>Nobel speech Dec 11, 1925</i></p> |
| <p>•Werner Forssmann •André Courmand •Dickenson Richards (Nobel 1956) Goal: heart catheterization</p> |  | <p>"In cases of shock... it may be desirable to deliver medications directly to the heart... I considered a new method to approach the heart in a less dangerous fashion, namely the catheterization of the right heart from the venous system. Experiments on a cadaver were productive. I was able to catheterize any vein in the anticubital fossa and ... reach the right ventricle.... I next undertook experiments on a living subject, namely on myself."...<i>Forssmann</i></p> |
| <p>•Michael Brown •Joseph Goldstein (Nobel 1985) Goal: Identify Cholesterol disorders in atherosclerosis</p> |  | <p>"It is far too easy to learn one technique and then to repeat the same experiment over and over. In this fashion one can write many papers, receive large research grants, and remain solidly rooted in the middle of a scientific field. But the true innovator has the confidence to drop one set of experimental crutches and leap to another when he or she must move forward."...<i>Brown</i></p> |
| <p>•Sir James Black (Nobel 1988) Goal: β-blockers to treat ischemic heart disease</p> |  | <p><chem>CC(C)NCC(O)c1ccc2ccccc12</chem> Pronethalol- first β-blocker</p> |
| <p>•Robert Furchgott •Louis Ignarro •Ferid Murad (Nobel 1998) Goal: Identify endothelial-derived relaxing factor (NO)</p> |  | <p>Salvador Moncada "Keep Ithaca always in your mind. Arriving there is what you're destined for. But don't hurry the journey at all. Better if it lasts for years, so you're old by the time you reach the island, Wealthy with all you've gained on the way, Not expecting Ithaca to make you rich. Ithaca gave you the marvelous journey. Without her you wouldn't have set out." ...<i>CP Kavafy (Ithaca)</i></p> |

3) FROM GENES TO HEALTH AND HEALTH TO GENES ^{1,2,3}

1

TRANSLATIONAL

GENES ↔ CELL ↔ TISSUE ↔ PHYSIOL. ↔ PHENOTYPE ↔ POPUL. ↔ HEALTH

TRAINING / MENTORS

ENABLING APPROACHES

Imaging: Non Inv. Molec.

Clinical Proteomics

Inform. / Science / Techn.

Behav. Instrum./ Technol.

Clinical Trials Infrastr.

4

SPECIFIC AIMS

Genetics /Proteomics /Embryogenes

Regenerative Biol./ Replac.Therapy

Immunobiol./ Inflammation / Thromb

Public Health / Genom.Proteo.

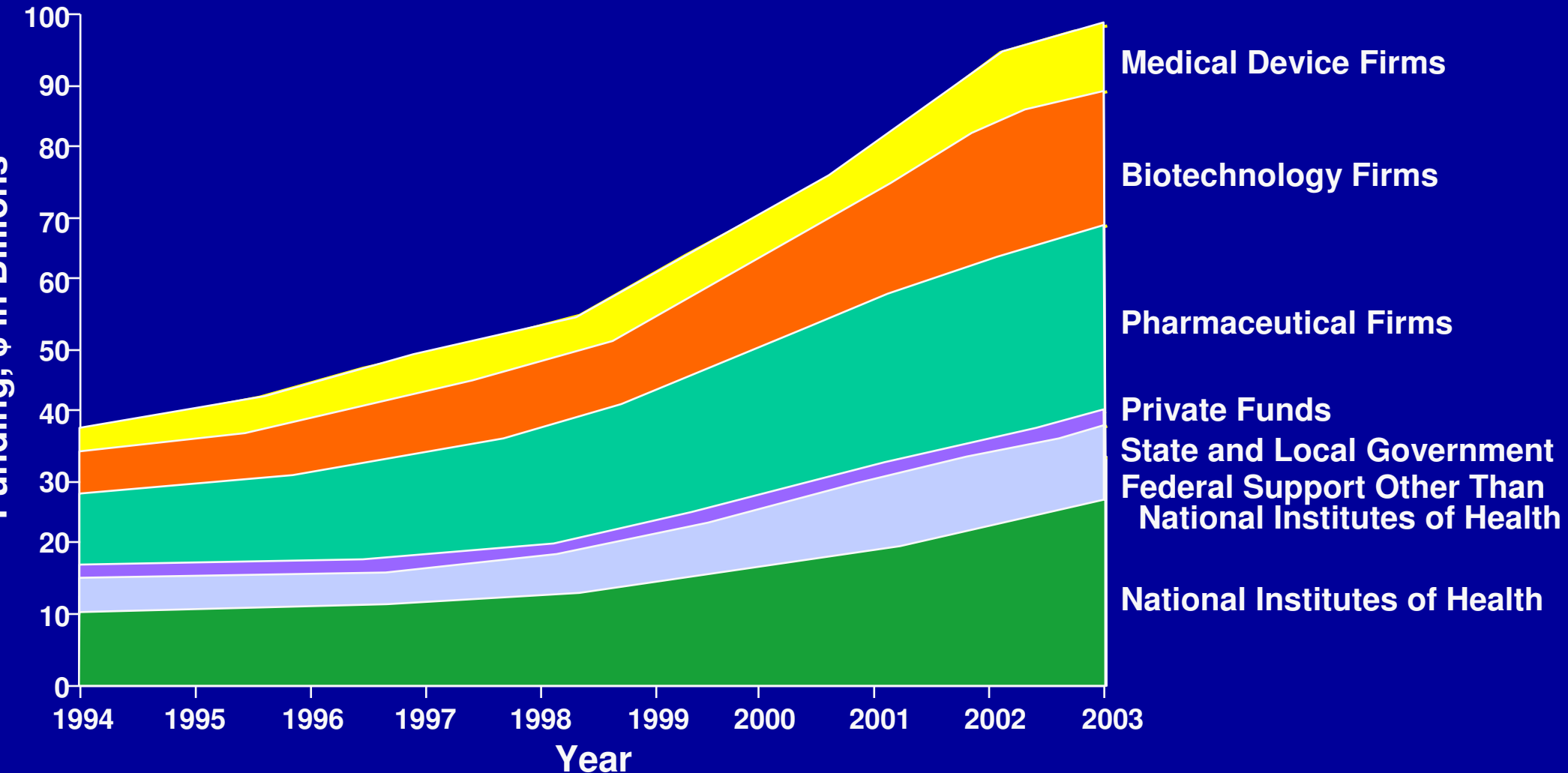
¹NHLBI SPARK I 1998-2002

Circ 1999; 99:1132 & 2064 - Defined Circ 2002;106:162 – Update

²NHLBI SPARK II 2003-2007 - Prospective (Jan 20, 2003)

³NHLBI – Site Visit - March 17,2006

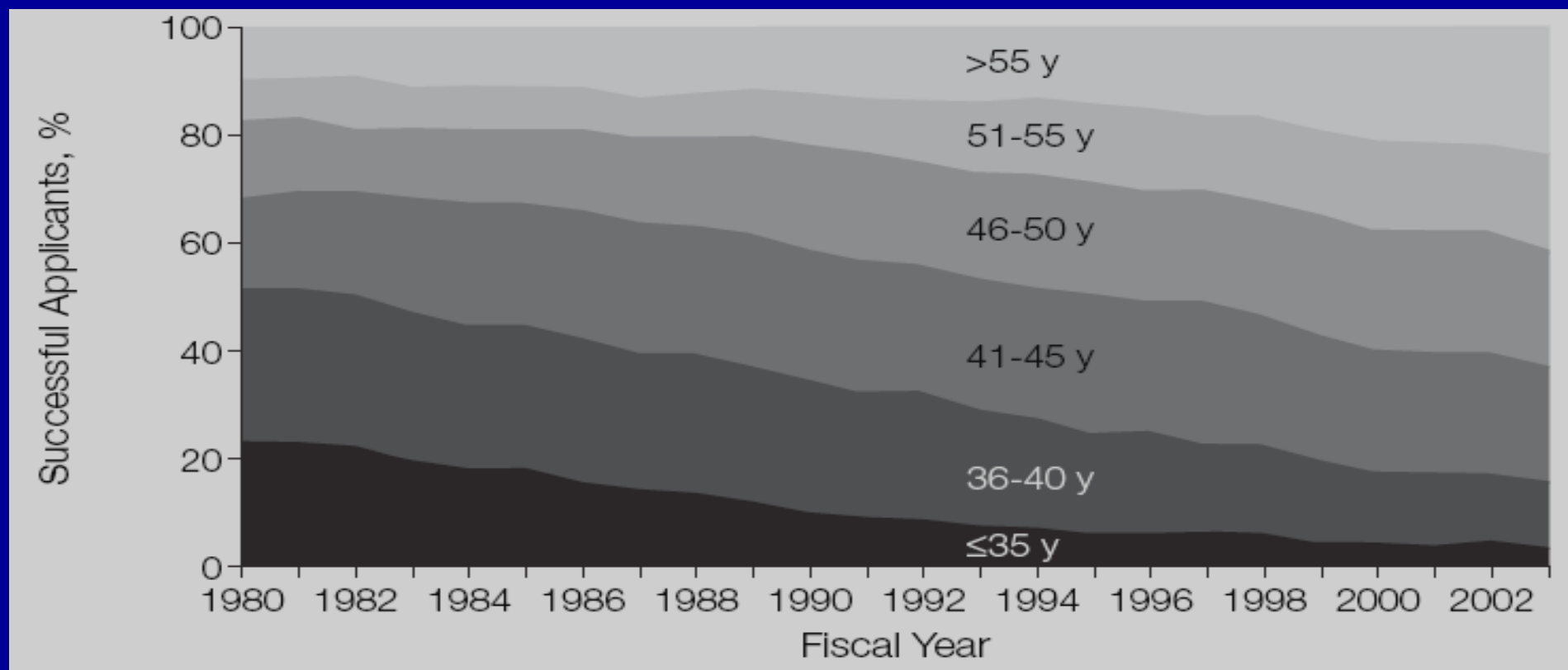
FUNDING FOR BIOMEDICAL RESEARCH BY SOURCE, 1994-2003



Moses et al., JAMA 2005; 294:1333

1. CHANGES IN US BIOMEDICAL RESEARCH OVER THE PAST 25 YR

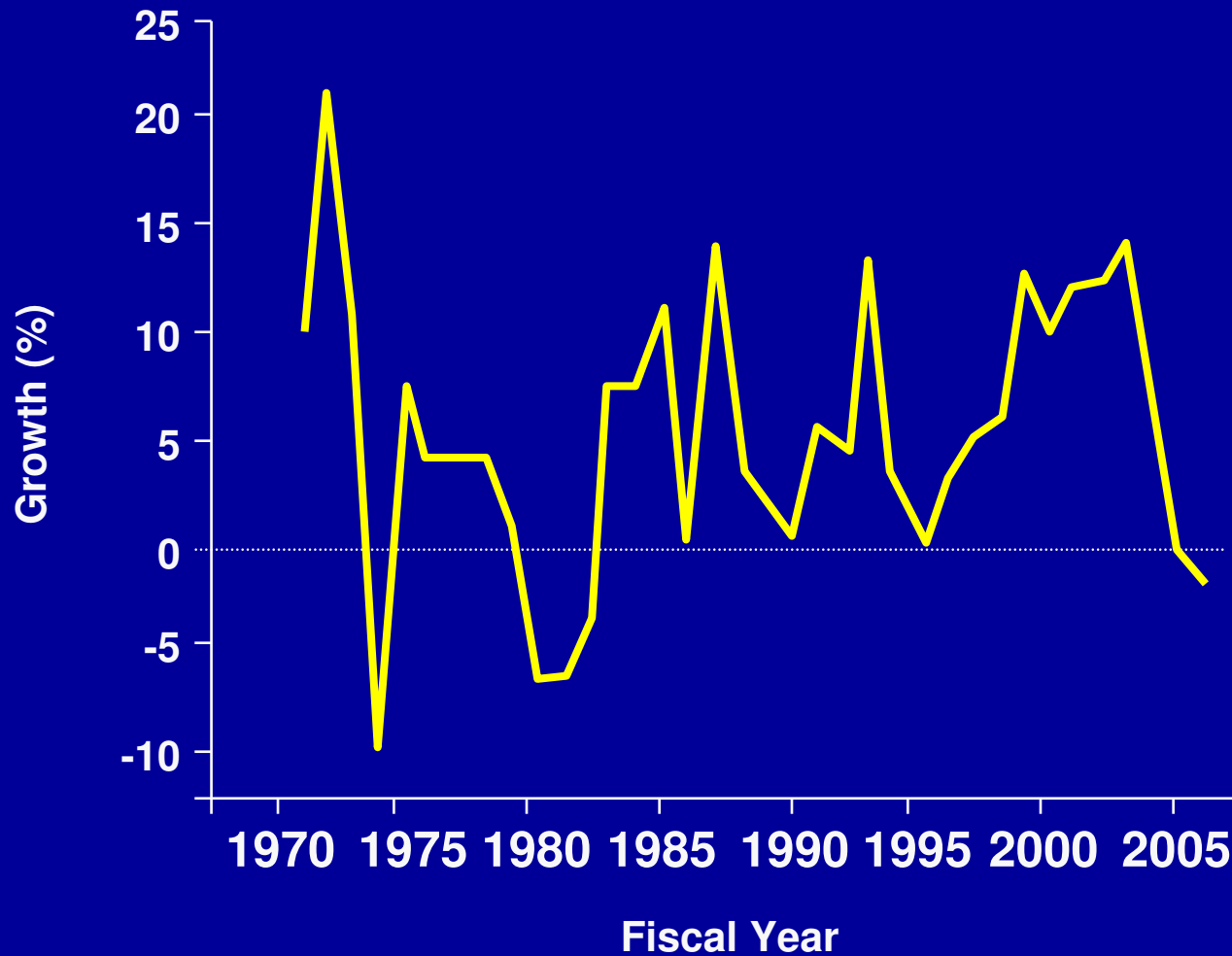
Distribution of Successful R01, R23, R29, or R37 Applicants by Age



R. Cech, *JAMA* 2005;294:1390.

U Levy, LE Rosenberg. *JAMA* 2005;294:1343 – >50 yrs: MD, PhD

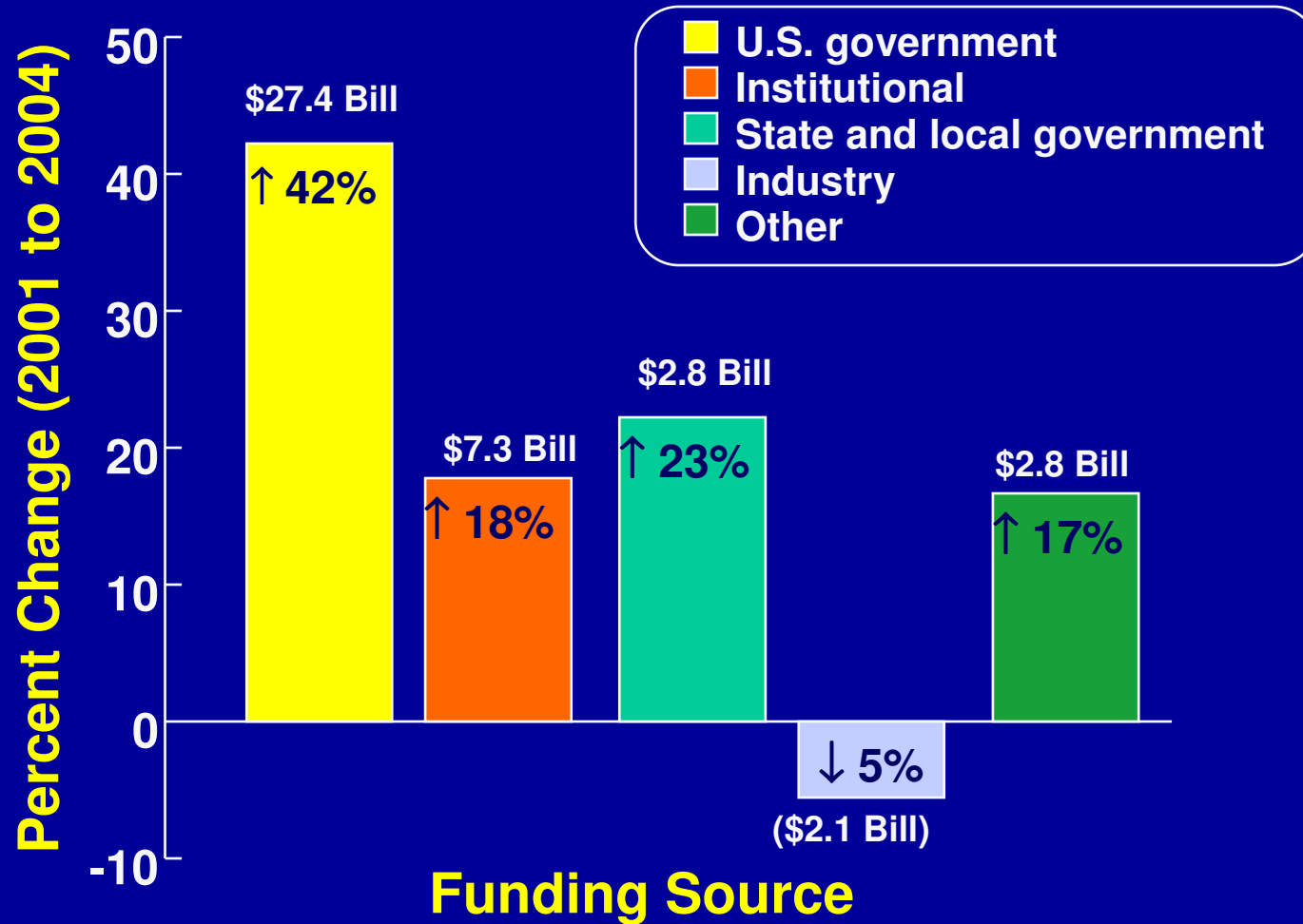
FLUCTUATIONS - ANNUALIZED NIH BUDGET, 1971 - 2005



It would be preferable for academic medical centers to cease relying so heavily on the NIH for research funding.

Loscalzo. NEJM 2006; 354:1665

INDUSTRY SHRINKS ACADEMIC SUPPORT

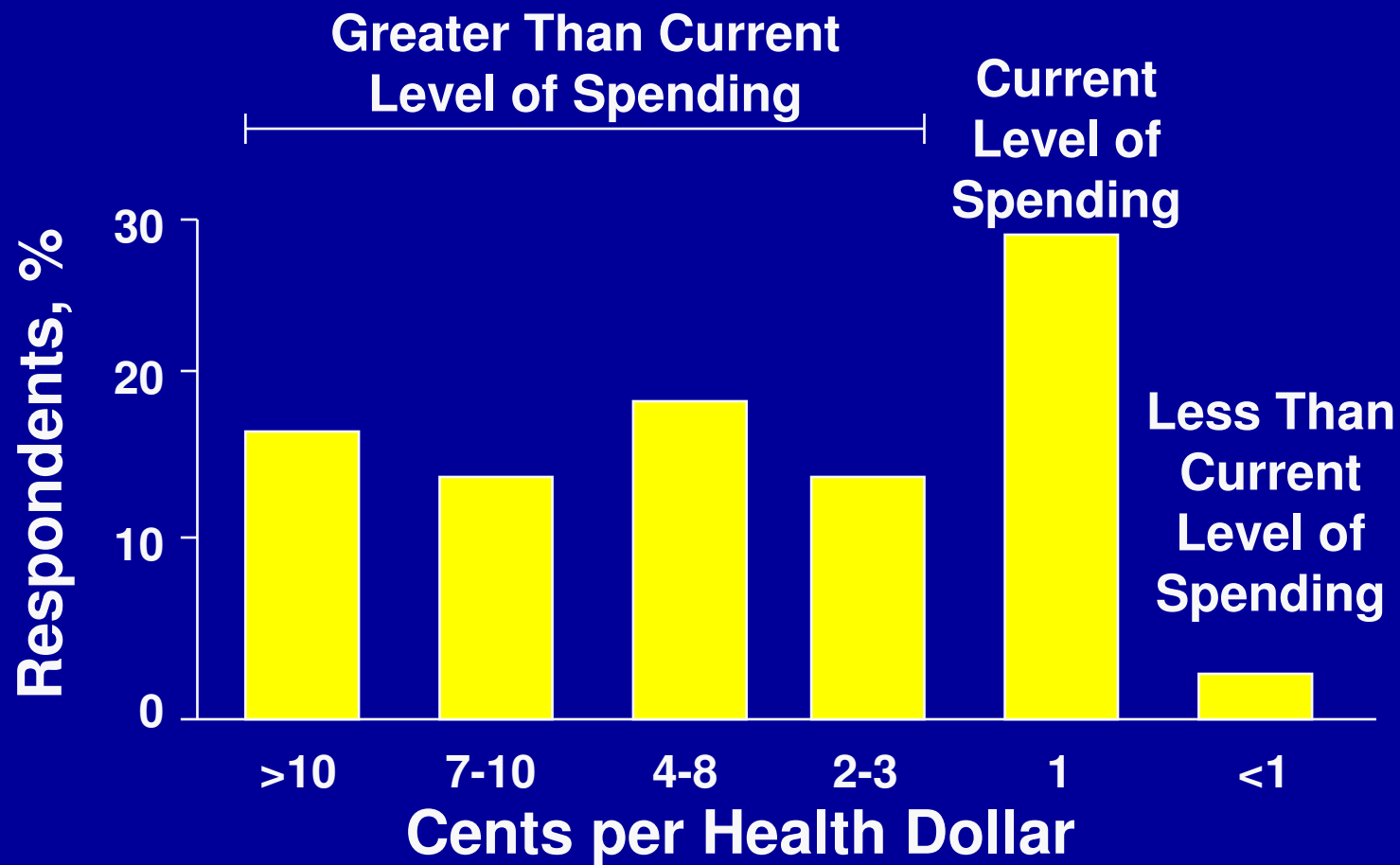


THE BIOMEDICAL RESEARCH BOTTLENECK



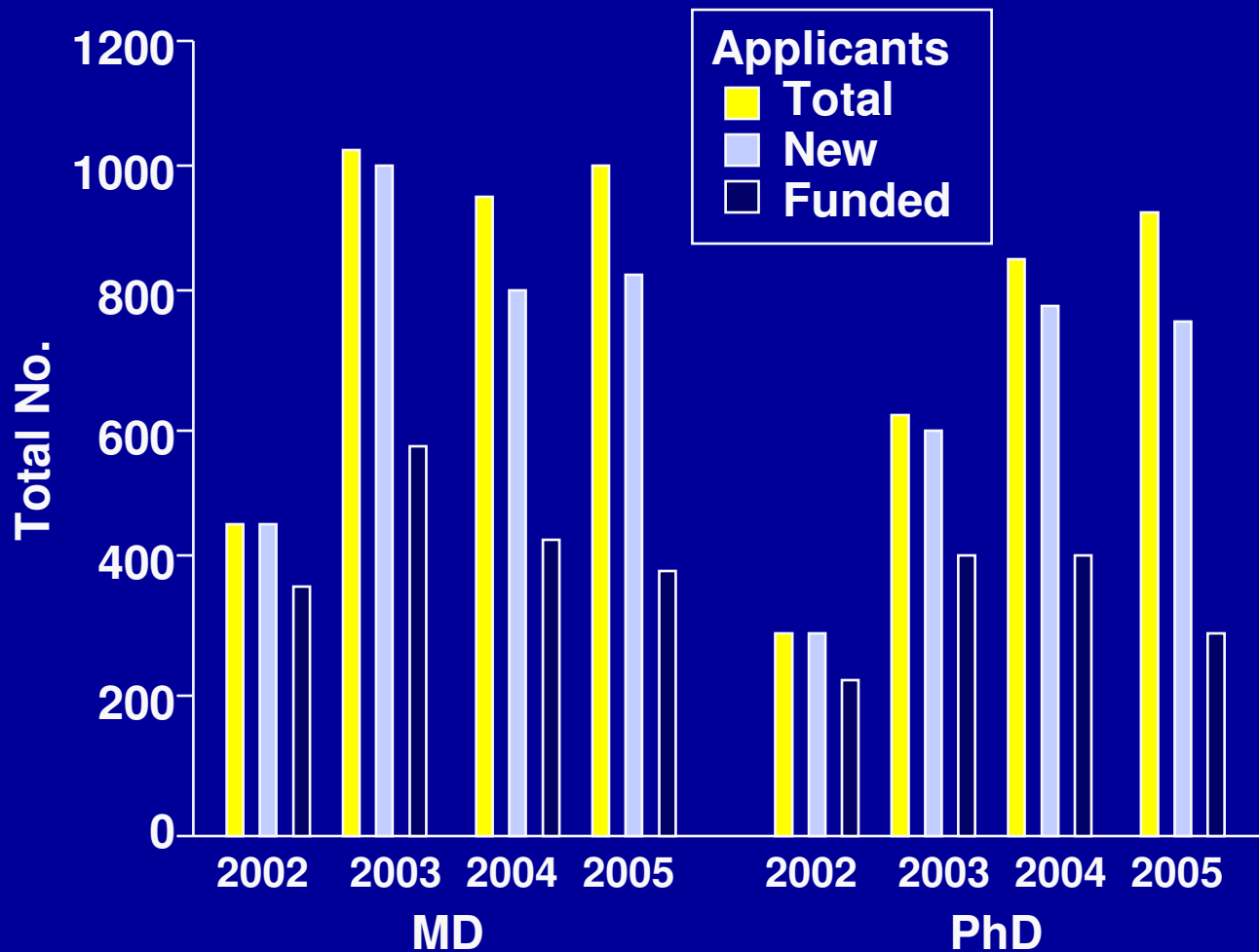
T. R. Cech et al., Science 2001; 293,573

2. PERCENTAGE OF AMERICANS WANTING MORE MONEY SPENT ON PUBLIC HEALTH RESEARCH - SURVEYS OF 8 STATES (N=6400)



Woolley, SM Propst. JAMA 2005; 204:1380 (Harris Polls)

NIH LOAN REPAYMENT PROGRAM (LRP) ACTIVITY 2002-2005 - INCENTIVE (CLINICALLY ORIENTED RESEARCH)



J Levy, LE Rosenberg. JAMA 2005; 294:1343 (Source: NIH)

Notes From the Director National Heart, Lung, and Blood Institute Fostering New Investigators

1. **Increased Pay Line**
2. **Full Award Duration**
3. **Expedited Review**
4. **Other Approaches**
 - a) **Increase the yield of K Awards**
 - b) **Comprehensive network** that includes significant mentoring and career development components, laboratory and project management training and grant writing experiences.
 - c) **“Mentoring bank”**

NHLBI - SOURCES OF SUPPORT INFORMATION

National Institutes of Health; National Heart, Lung, and Blood Institute (NIH/NHLBI)

<http://www.nih.gov>

<http://www.nhlbi.nih.gov>

Award Program Announcements — “K Kiosk”

<http://grants2.nih.gov/training/careerdevelopmentawards.htm>

The Original How to Write a Research Grant Application

<http://www.nhlbi.nih.gov/nen/grants/write/index.htm>

Advisor, Teacher, Role Model, Friend: On Being a Mentor to Students in Science and Engineering. National Academy Press

<http://www.nap.edu/readingroom/books/mentor/>

<http://books.nap.edu/catalog/5789.html>

W Balke. JACC 2005; 46(Suppl A):8A

***OTHER BRIDGING FUNDING OPPORTUNITIES
FOR YOUNG INVESTIGATORS***

American Heart Association

<http://www.americanheart.org>

American College of Cardiology

<http://www.acc.org>

GSK

<http://www.cvfoundation.org>

OTHER BRIDGING FUNDING OPPORTUNITIES -YOUNG INVESTIGATORS

HA National Scientist Development Grant

HA Fellow To Faculty Transition Award

CCF/Merk Fellowship in Cardiovascular Disease. The Metabolic Syndrome

CCF/GE Healthcare Cardiovascular Career Development Awards in Cardiovascular Imaging

CCF/Pfizer Career Development Award in Clinical Cardiovascular Medicine

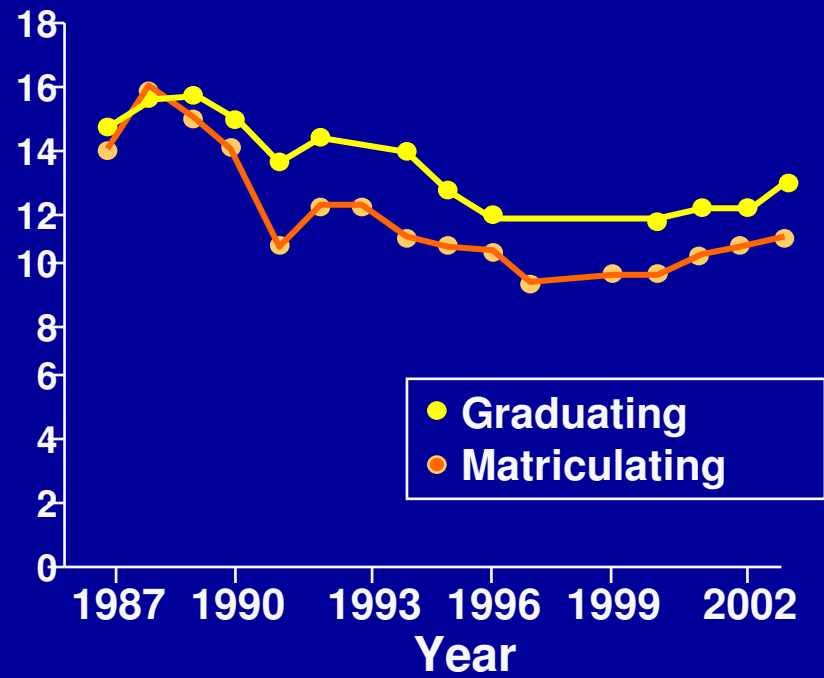
CCF/ Guidant Foundation Fellowship and Career Development Award in Women's Cardiovascular Health

Other Foundations: Sarnoff, Doris Duke, Robert Wood Johnson, Glaxo Smith Kline, Schearing-Plough

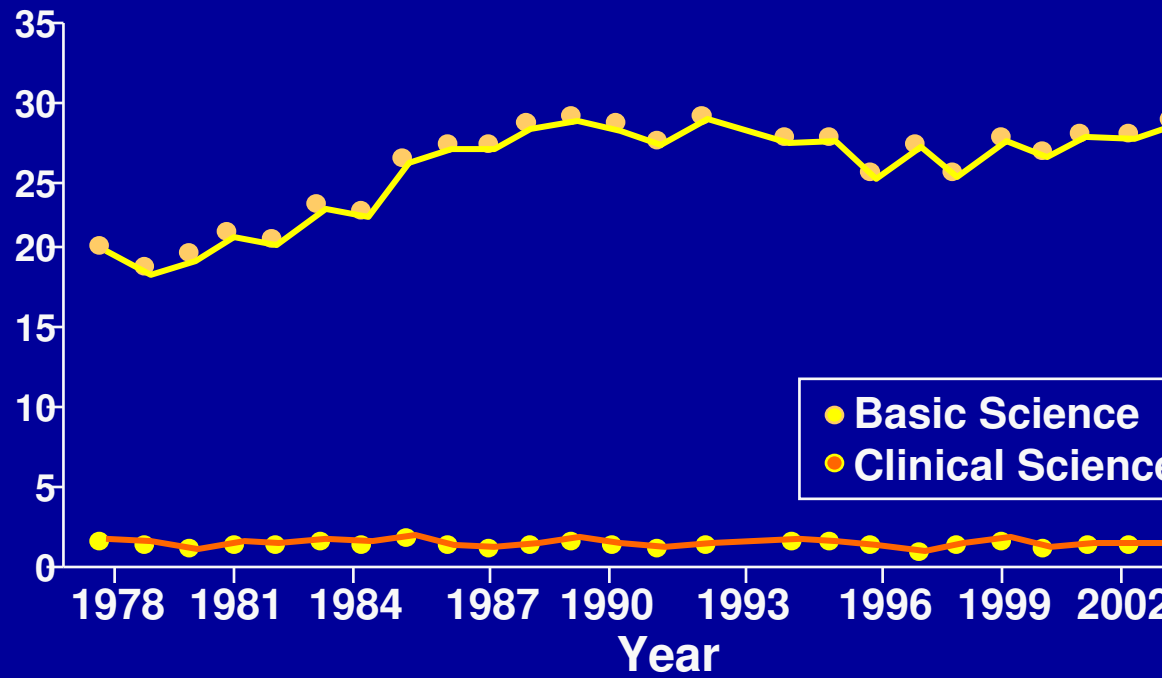
O Bonow. JACC 2005; 46:(Suppl A):15A

3. MEDICAL STUDENT INTEREST IN RESEARCH

Exclusive or Significant Interest in Research

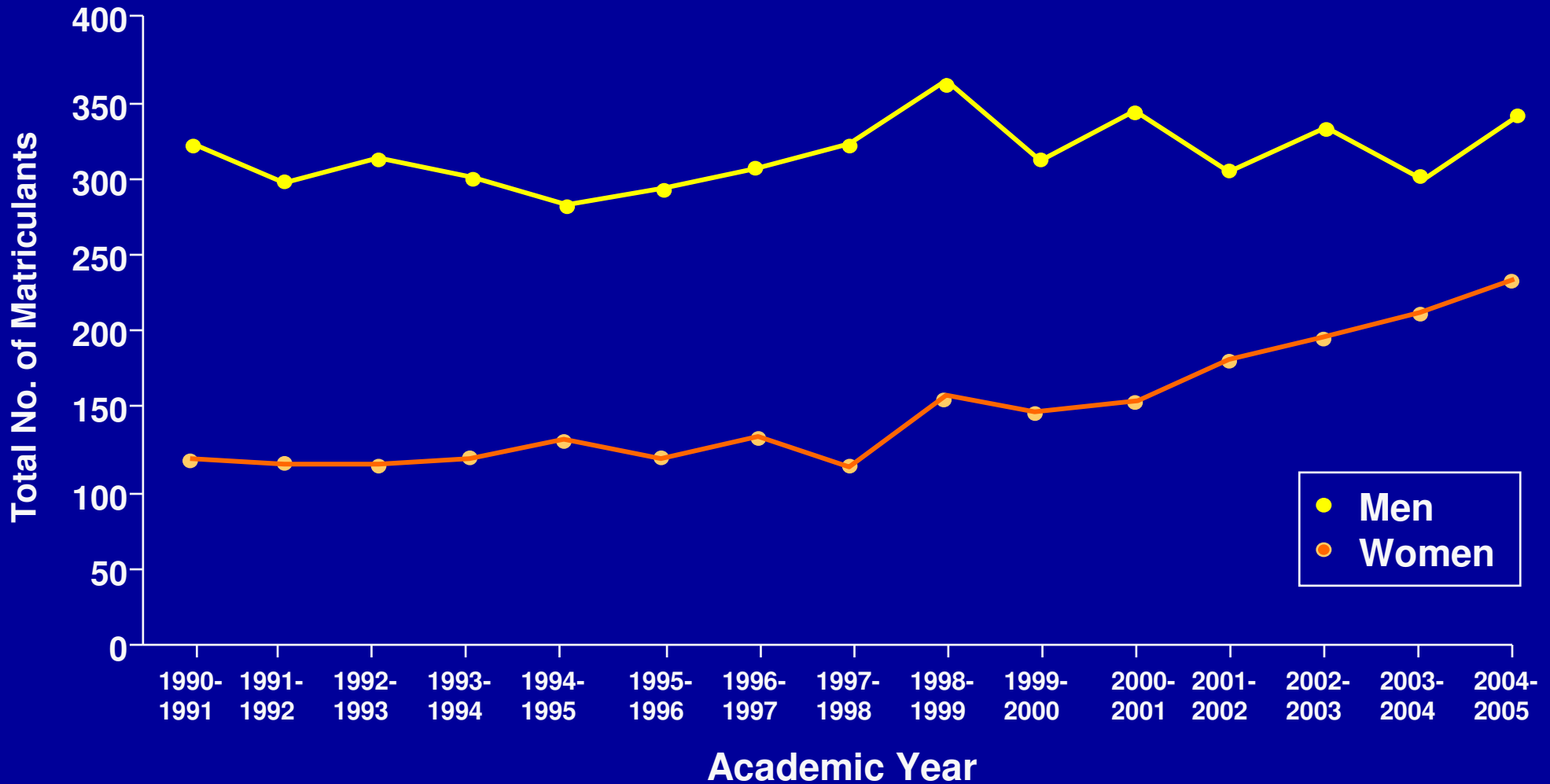


Interest in Teaching or Research (Graduates)



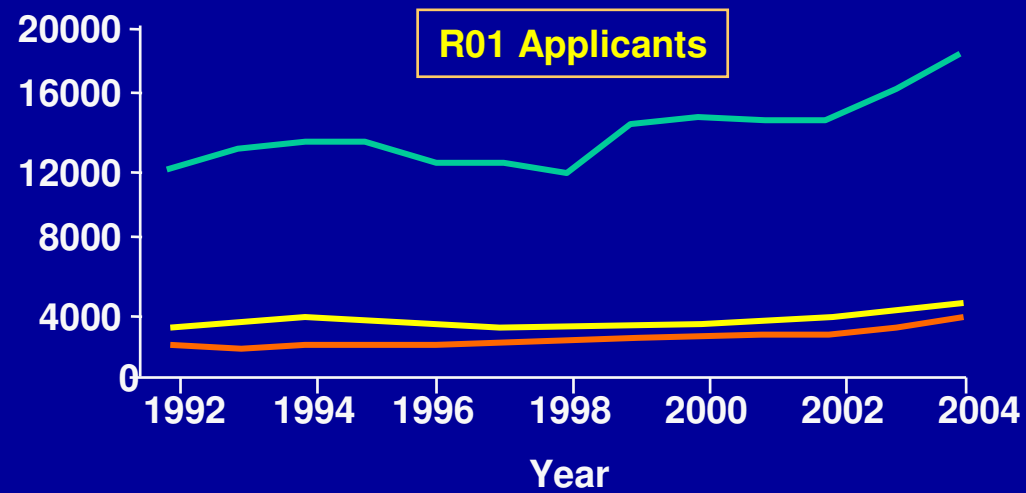
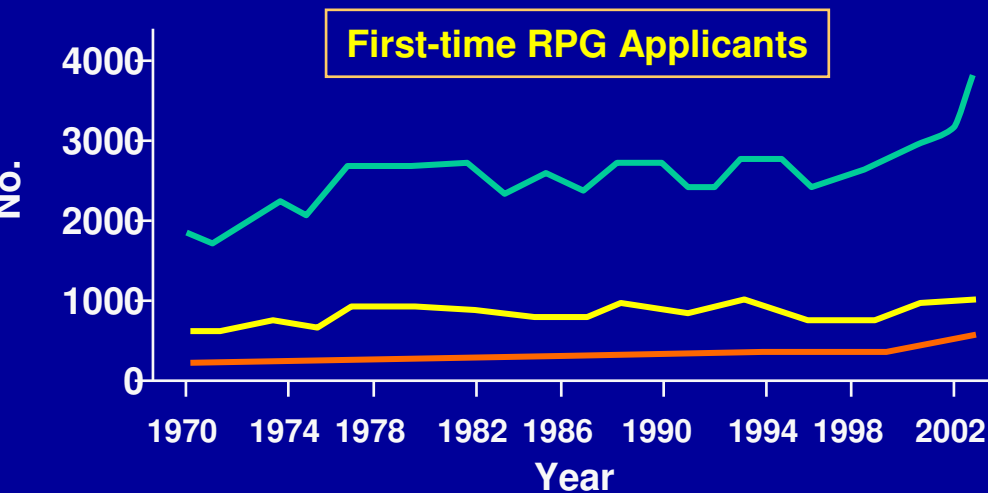
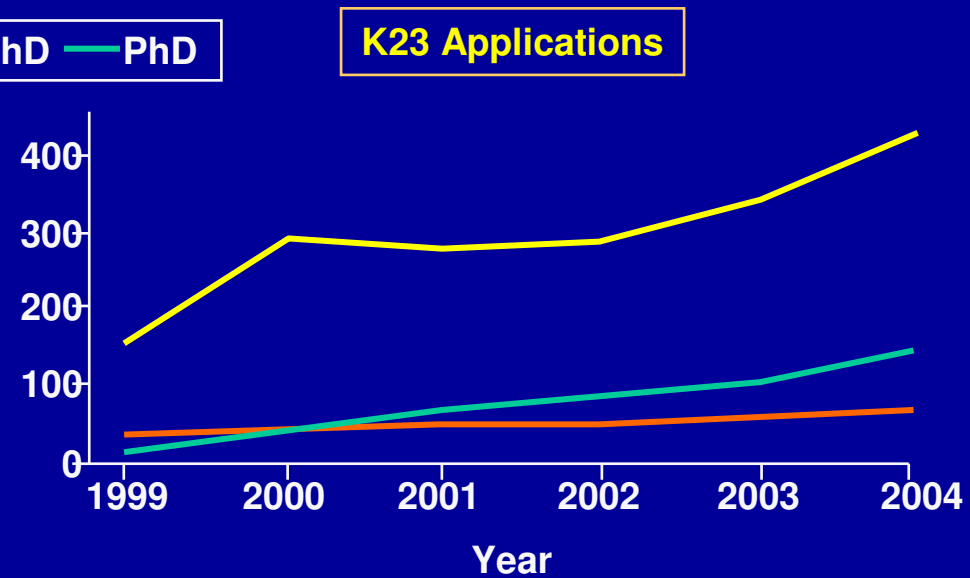
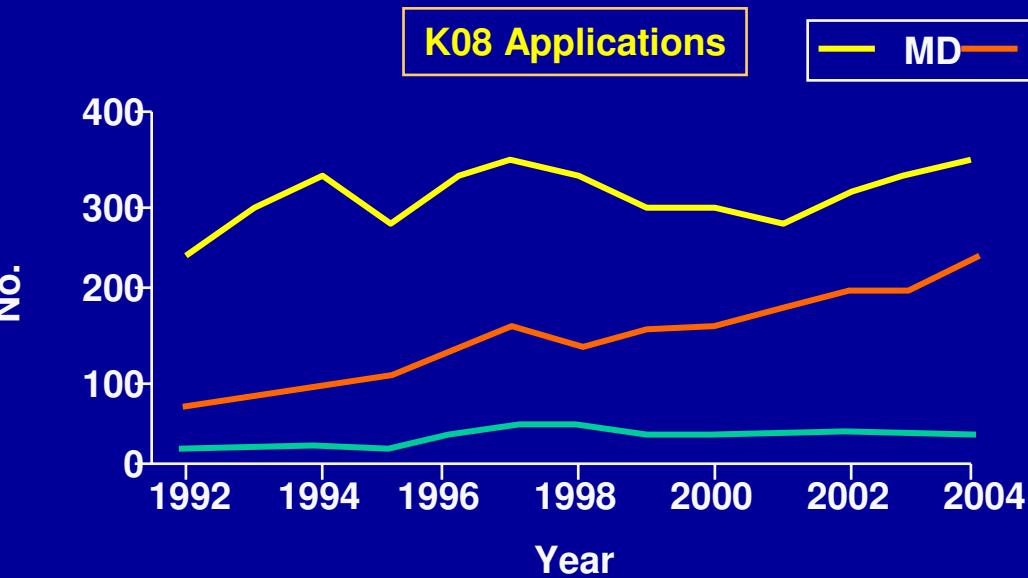
J Levy, LE Rosenberg. JAMA 2005; 294:1343
(Source: AAMC Questionnaire)

NUMBERS OF MATRICULATING MD-PhD STUDENTS IN THE UNITED STATES, 1990-2004



J Levy, LE Rosenberg. JAMA 2005; 294:1343 (Source: AAMC)

APPLICATION TRENDS FOR NIH GRANTS



MY FUTURE
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SUPPLEMENT TO
JACC

JOURNAL *of the* AMERICAN COLLEGE *of* CARDIOLOGY

OCTOBER 4, 2005
VOLUME 46, No. 7
(SUPPLEMENT A)

Co-sponsored by the
American College of
Cardiology and the Council
on Clinical Cardiology
of the American Heart
Association in cooperation
with the National Heart,
Lung, and Blood Institute

May 14–15, 2004 and
December 3–4, 2004
Bethesda, MD

How to Become a Cardiovascular Investigator: A Symposium

Directed by Valentin Fuster, MD, PhD, FACC
Co-directed by Robert O. Bonow, MD, FACC



ELSEVIER

1. A Personal Search and Three Step Approach

WHAT I AM GOOD AT → MOVE ON → ENJOY / SUCCEED

The Three Commandments of Success

A) MENTOR: OUTSTANDING AND COMMITED

"The scientific chiefs will be rated on mentorship of juniors as well as research productivity"

B) INFORMATION & PURSUE IN DEPTH

"The harder I work, the luckier I get"

"Luck favors only the prepared mind"

"Take time to think"

C) FOCUS, FOCUS, FOCUS

"Ideally a high-risk and a low-risk project"

2. CHARACTERISTICS CREATIVITY OR INNOVATION

- P**assion “Talent”
- R**isk “Unknown”
- O**rganization “Physician Scientist”
- L**iberal “Unbiased, Humble”
- I**dealistic “Dream, no false expectations”
- F**riendly “Family team”
- I**ntense work “8 to 5?, No weekends?”
- C**onsistent “Accept Fluctuations”

Genetic and Acquired

V Fuster, Nature Cardiovascular 2007 (In Press)

3. CARDIOVASCULAR RESEARCH SOURCES OF SATISFACTION

- Chance to do good**
- Intellectually challenging**
- Thrill of discovery**
- Colleagues-laboratory, institutional, world-wide**
- Attend conferences, Give lectures**
- Consulting to industry and government**

**JL Breslow - In: How to Become A Cardiovascular Investigator
(Bethesda Sept 2001 - NHLBI/AHA/ACC - V Fuster, RO Bonow)**

MY FUTURE

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RESEARCHER vs CLINICIAN / ACADEMICIAN ¹

Professional Clinical Investigator: 80% in clinical trials, outcomes research or epidemiology. Advanced training (e.g., MD, MPH, etc.)

Clinical Investigator:¹ In patient care as a **team player** with professional clinical investigator. **No special training**

Physician Scientist: 80% laboratory research in the interface with the clinic. **Advanced research training (MD or MD/PhD)** are the most threatened in major medical centers.

Translational Scientist:¹ Clinically oriented research (from molecules to outcomes) as a **team player**. **Advanced research training (PhD)**.

Organizational Challenges



Altshuler, JS et. al. *Nature* 2004;429:479.

MY FUTURE

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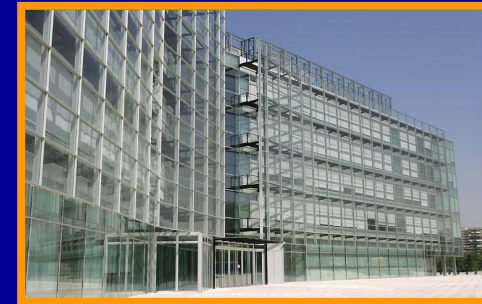
1. EDUCATIONAL GUIDE

- 1. The Choice of Research Projects(s)**
- 2. Writing a Paper(s)**
- 3. General Literature Update**
- 4. I am really a Doctor ?**

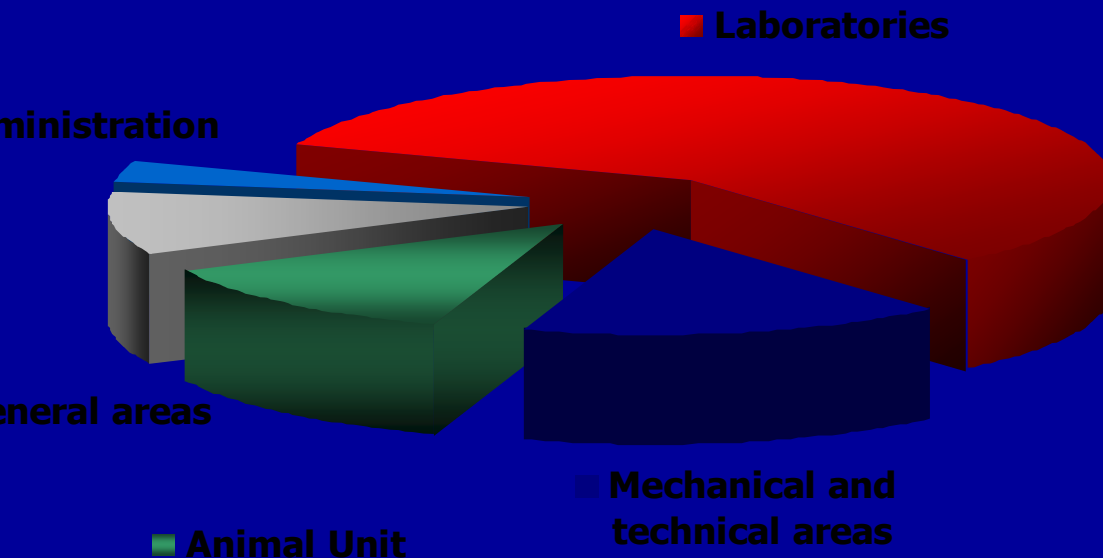
2) The CNIC Building

23000 m² for research

Capacity for
300 scientists
+ 100 other staff



€ 60 million



2007-2008 – Imaging
Ciclotron

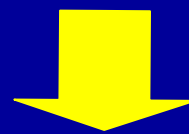
2007-2008 – Pigs

Zebra Fish

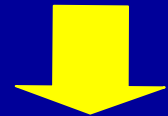
Innovative Model of Funding: 7 Years



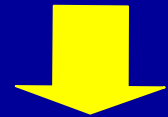
38%



Ministerio de Sanidad y Consumo



Instituto de Salud Carlos III



62%



Mission & Vision

1. To promote Excellence in Cardiovascular Research

Basic and Clinical

2. Identify and Inspire

Tomorrow's Scientists

THE CNIC SHOULD PRODUCE A GENUINE IMPROVEMENT

IN SPANISH RESEARCH

AND IN CARDIOVASCULAR HEALTH IN SPAIN AND WORLDWIDE

Mission & Vision

Training program for young people - “CNIC Joven”



Aim

To bring biomedical research closer to young people and create a reservoir of future top researchers in the cardiovascular area

- ✓ Programme ACERCATE: Senior High-school students
- ✓ Programme CICERONE: UNIVERSITY students
- ✓ Programme INVESMIR: PHYSICIANS in specialist training
- ✓ Programme CARDIOJOVEN: Young CARDIOLOGISTS
- ✓ Programme PREDOCTORAL Biomedical Scientist – Thesis
- ✓ Programme POSTDOCTORAL Biomedical PhD – 2 or 3 years
INTERNATIONAL



July 2006

2)

CONGRESS

July 2007

July 2007













EDUCATIONAL GUIDE

- 1. The Choice of Research Projects(s)**
- 2. Writing a Paper(s)**
- 3. General Literature Update**
- 4. I am really a Doctor ?**

THE CHOICE OF RESEARCH PROJECTS

Two Projects

- Going on (less risky)
- Not going on (risky, hobby)

Infrastructure

- Mentor general and specific (anywhere)
- Literature

Feasible

- Time to devote
- Funding
- Role in the team

Action

EDUCATIONAL GUIDE

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WRITING A PAPER

Project (s)

- Almost done

Literature, Mentor (Infrastructure)

Feasible

- Time to devote
- Role in the team

Action

- Start on “white paper” - Turn title to discussion
- Time: one month to write
one week to review
two weeks to re-write

Publication

- At two years
- Then sequence of papers

EDUCATIONAL GUIDE

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GENERAL LITERATURE UPDATE

Journals

Nature

Nature Medicine

Science

JCI

New England J Medicine

JAMA

Lancet

Annals of Internal Medicine

Circulation

Circulation Research

JACC

Nature Cardiovascular

Heart

European Heart Journal

Action

Six hours per month

Screening, reading and filing

EDUCATIONAL GUIDE

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FACTORS THAT DETERMINE PLACEBO OR CONTEXT EFFECTS (BASED ON 25 TRIALS)

Treatment characteristics

(eg, color, size, shape of drug)

Patient's characteristics

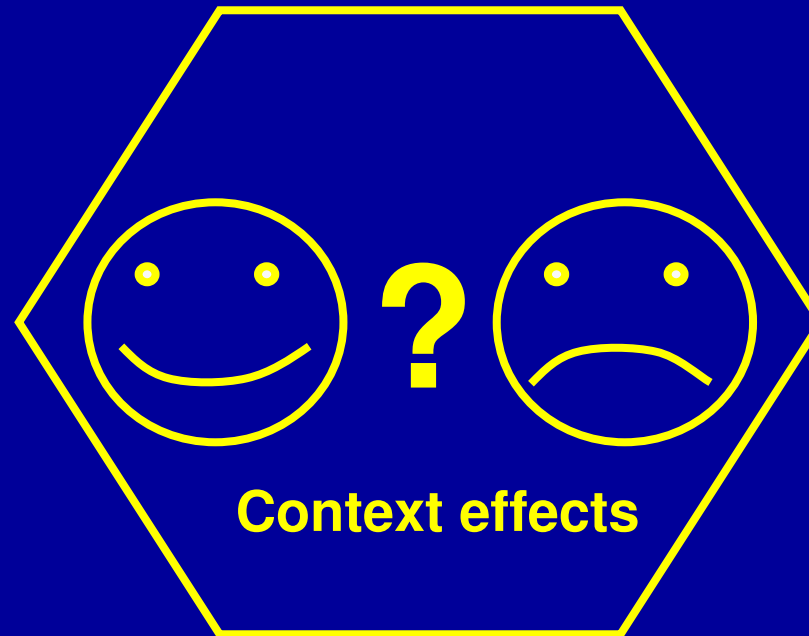
(eg, treatment and illness beliefs, anxiety, adherence)

Patient-practitioner relationship

(eg, suggestion, reassurance, compassion)

Health-care setting

(eg, home or hospital, room layout)



Practitioners' characteristics

(eg, status, sex, treatment, and illness beliefs)

AIMS 2007: QUALITY AND/OR QUANTITY OF LIFE

DIAGNOSTIC CRITERIA

| Criteria | Examples | Requirements |
|----------------------------|--|---------------------|
| Functional capacity | Class III | Talking |
| Physiology | R cardiac failure atrial fibrillation | Teaching |
| Anatomy | Sev MS, mil AI | Time |
| Etiology | Rheum Heart Dis | Thinking |

MANAGEMENT CRITERIA

| | |
|--------------------------|-----------------|
| Diagnosis | T.T.T.T. |
| Natural history | Trials |
| Unnatural history | Trials |

ETIOLOGIC AND ANATOMIC-PHYSIOLOGIC CLUE

- 1. Hypertensive heart disease**
- 2. Diseases of the aorta**
- 3. Pulmonary hypertension**
- 4. Rhythm and conduct. abnormalities**
- 5. Coronary artery disease**
- 6. Acquired valvular heart disease**
- 7. Congenital heart disease**
- 8. Infective endocarditis**
- 9. Cardiac tumors**
- 10. Myocardial disease**
- 11. Pericardial disease**
- 12. Trauma**
- 13. Hyper- and hypokinetic states**
- 14. Drug side effects**

ETIOLOGIC AND ANATOMIC-PHYSIOLOGIC CLUES

1. Systemic Hypertension

Asynchronous palpation of radial-femoral pulses

Left ventricular hypertrophy (LHV): Palpation, S₄, ECG

Left ventricular diastolic dysfunction: dyspnea with good EF (echo)

Left ventricular failure: Contributor (age, CAD cardiomyopathy)

• O₂ consumption: afterload, heart rate, contractility, preload

Coronary disease:

• Risk factor: Atherosclerosis (diastolic hypertension), post-MI

• ↑ Angina pectoris: O₂ consumption

Potassium depletion: Very common

• If chronic, ECG more reliable than serum K level

• Orange juice, 8 oz; tomato juice, 8 oz; banana

(13 meq)

(14 meq)

(16 meq)

1. Hypertensive heart disease
2. **Diseases of the aorta**
3. Pulmonary hypertension
4. Rhythm and conduct. abnormalities
5. Coronary artery disease
6. Acquired valvular heart disease
7. Congenital heart disease
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| Natural history | Trials |
| Unnatural history | Trials |

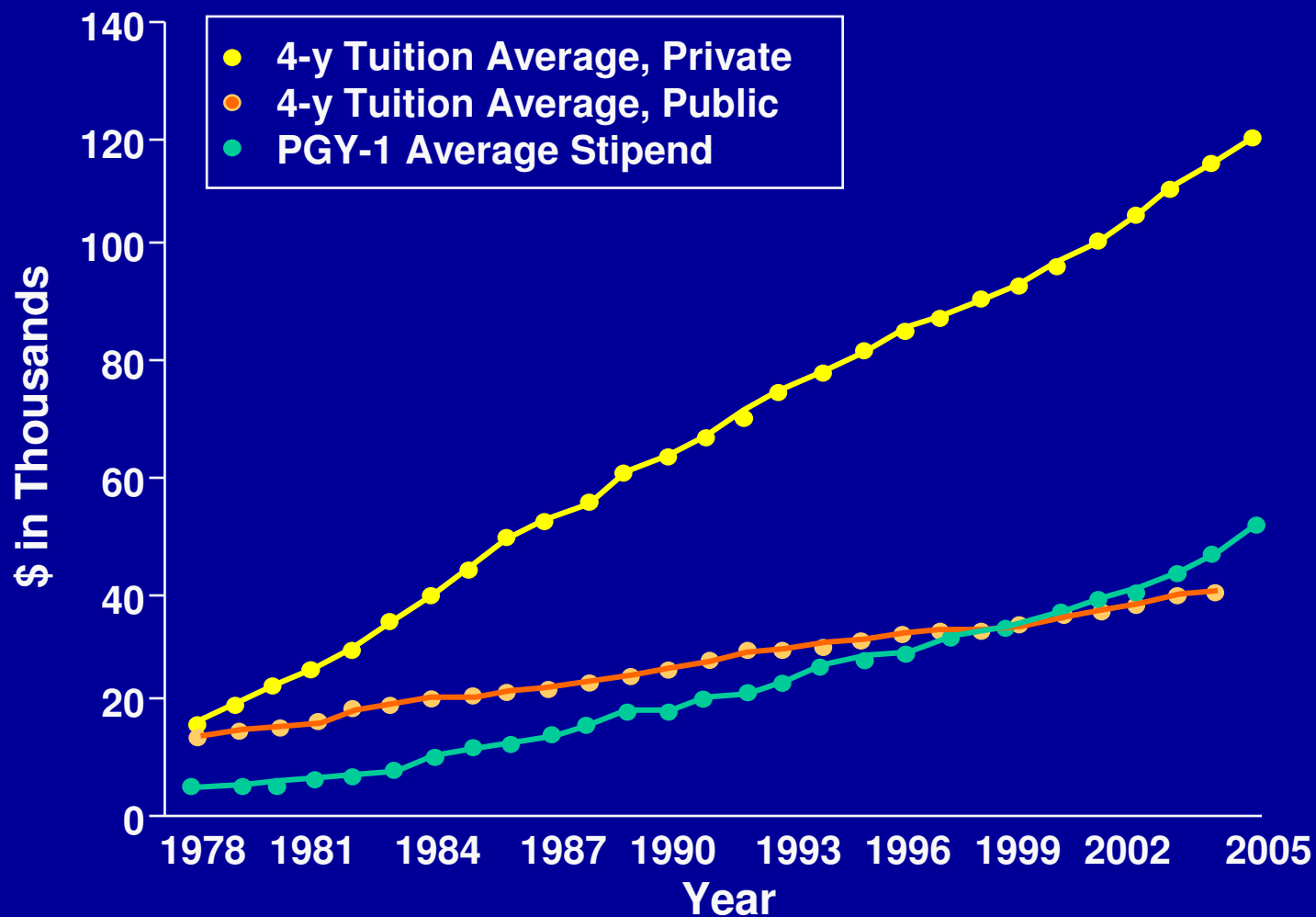
GENERAL PREVENTION GUIDELINES FOR CANCER, CVD AND DIABETES IN ADULTS

| TEST | AGE 20 | 30 | 40 | 50+ |
|---|--------|--------|--|--|
| BMI | | | | Each regular health care visit |
| Blood Pressure | | | | Each regular health care visit (or at least once every 2 years if BP < 120/80 mm Hg) |
| Lipid Profile | | | | Every 5 years |
| Blood Glucose test | | | | Every 3 years |
| Clinical Breast Exam (CBE) and Mammography | | | CBE every 3 yrs | Yearly CBE and Mammography |
| Pap test | | Yearly | Every 1-3 years; depends on type of test and past results. | |
| Colorectal Screening | | | | Frequency depends on test preferred |
| Prostate specific antigen test and/digital rectal exam | | | | Offer yearly, assist informed decisions |

***MY FUTURE
ACADEMIC CARDIOVASCULAR MEDICINE -2007***

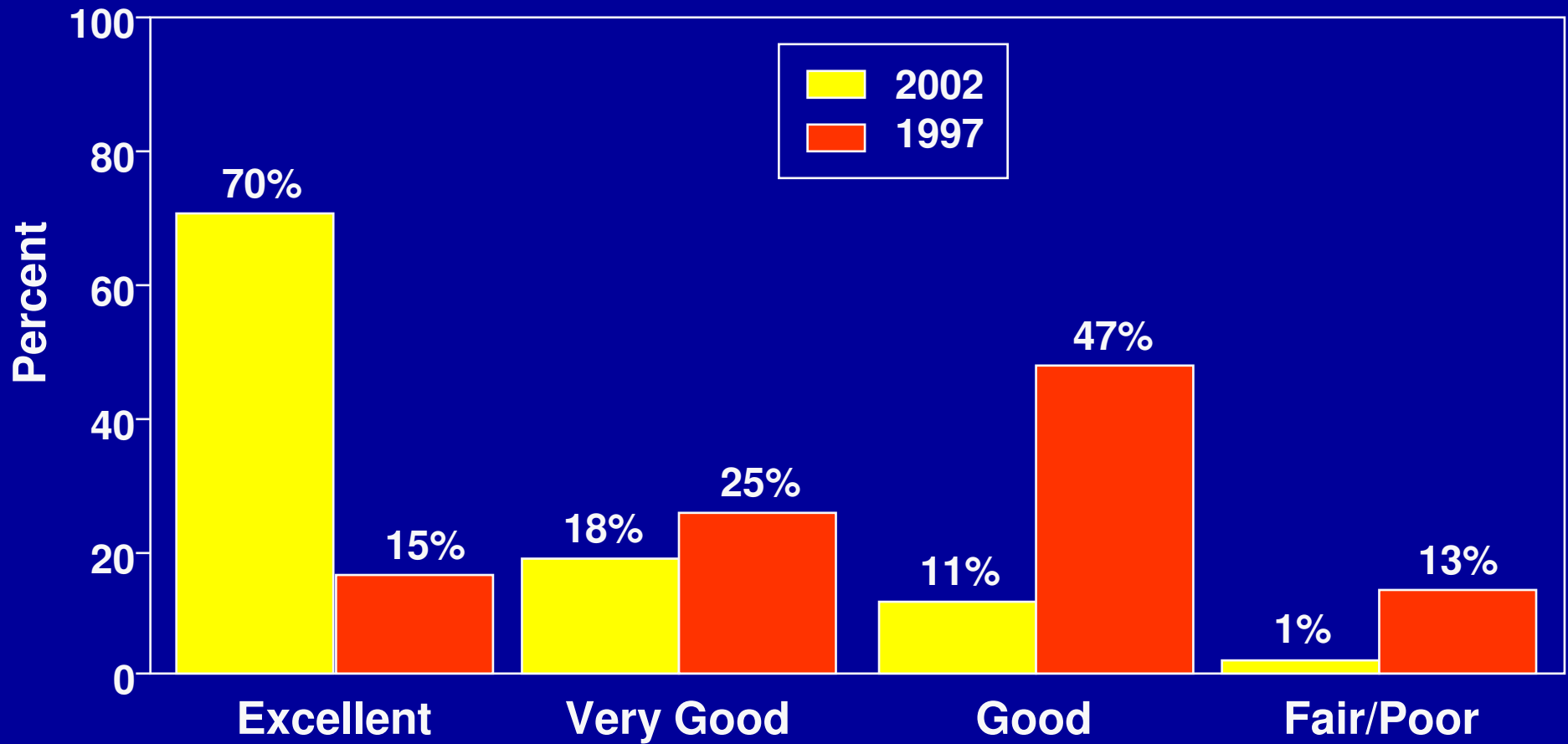
-) Clinical Opportunities**
-) Research: Challenges & Opportunities**
-) A Personal Search and Approach**
-) “ Clinician /Academician ”**
-) “ Researcher ”**
-) “ Educator ”**

2b) AVERAGE 4-YEAR MEDICAL SCHOOL TUITION COSTS COMPARE WITH AVERAGE POSTGRADUATE YEAR 1 (PGY-1) WAGES 1977-2004 - DISINCENTIVE



J Levy, LE Rosenberg. JAMA 2005; 294:1343 (Source: AAMC)

ASSESSMENT OF CURRENT JOB MARKET FOR CARDIOLOGY SENIOR FELLOWS (2002 vs 1997)



3b) CAMPAIGN TO REVITALIZE ACADEMIC MEDICINE GOALS OF THE PROJECT

How should academic medicine look in the **21st century**?

How can we increase the impact of academic medicine on the rest of **medicine and on health and healthcare**?

How should academic medicine be positioned **internationally** within medicine and also in the wider intellectual arena?

How can recruitment to and **job satisfaction** of those working in academic medicine be increased?

Tugwell - Heart **2004**; 90:833
BMJ **2004** - Lancet 2004

CNIC - Mision & Vision

Cardiovascular

**Heart
Failure**

**Hyper
tension**

CAD

**Arrhyth-
mias**

**Structural
Heart
Disease**

Cardiovascular Developmental Biology

Regenerative Cardiology

Vascular Biology and Inflammation

• Cardiovascular Epidemiology and Population Genetics

Atherothrombosis and Imaging

Translation

Intramural & Extramural