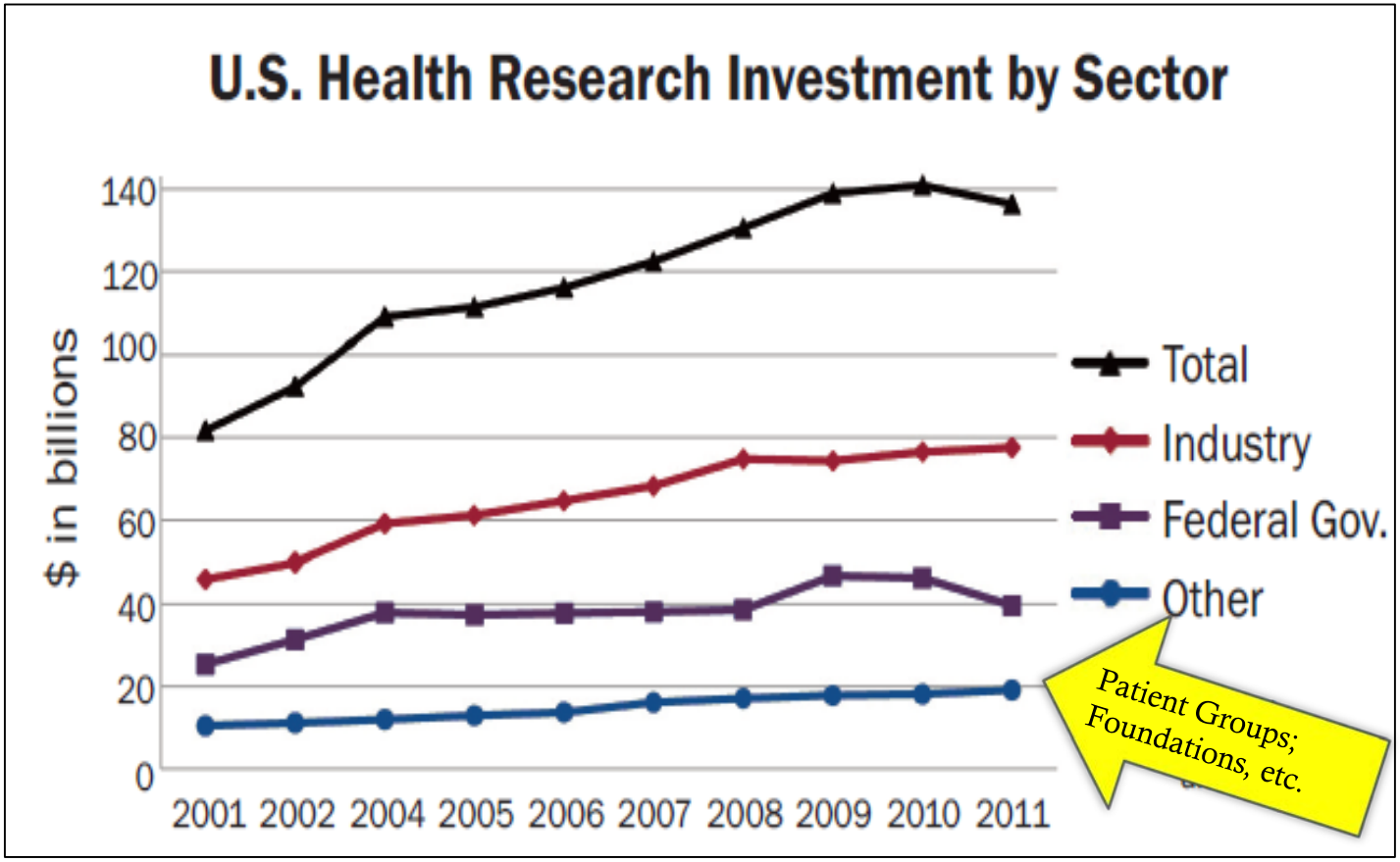
Panel: Assessing the Value of Biomedical Research from public and patient perspectives

NIH SMRB Meeting: October 24, 2013

Elaine K. Gallin, Ph.D.

QE Philanthropic Advisors

U.S. Health Research Investment



For more information, see http://www.researchamerica.org/research_investment.

Philanthropic Funding the Health Research Continuum

HHMI, Burroughs Wellcome, Keck

Robert Wood Johnson. Kaiser, Community HealthFoundations

Doris Duke

Voluntary Health Associations

Cystic Fibrosis Foundation, Multiple Myeloma Foundation, Juvenile Diabetes Research Foundation, American Heart Association, American Cancer Society, Susan G. Komen, etc

Philanthropic Sector: Assessment and Impact Evaluation

- **Approaches and emphasis on assessment and impact evaluation vary considerably.**
- **Organizations focused on product development often use milestones to track progress and evaluate their investments.**
- **In contrast, assessing career development programs, is more difficult -- career paths don't follow rigid milestones, researchers receive support from a variety of funders and career times can be long.**

SMRB Question 1: What NIH goals matter most to you?

- **Advancing knowledge whose application can improve health**
- **Applying that knowledge to improve health**

Other critically important and closely related goals:

- **Developing and supporting an outstanding biomedical research workforce**
- **Contributing to U.S. competitiveness & economic growth**
- **Fostering scientific and health literacy**

SMRB Questions 2 & 3: Communicating NIH's Value

Articulating compelling examples is a powerful approach.

- **Examples of health improvements**
  - **ARTs to treat AIDS**
  - **Gleevac to treat CML**
  - **Robotics to replace limbs**
  - **HPV vaccine and its promise to eliminate cervical cancer risk for most women**

- **Examples of basic research achievements**
  - **Genome Project**
  - **Stem cell technology**
  - **Imaging technology**
  - **3-D printing of human tissues**

SMRB Question 4: Measures of Health

- **Multiple measures should be collected including measures that can be related to economic impact.**
- **Measures should link new knowledge to specific health interventions and their impacts.**
  - **Improved survival- transformation of acute diseases to chronic diseases**
  - **Vaccines (and other preventions)**
  - **Evidence-based medicine and health care delivery advances that result in 'more health for the money'**

Challenge: The full impact of NIH's health contributions can be limited by external factors (example: HPV vaccine)

A Suggestion

Aggregating data from different funding sectors is difficult.

To promote data harmonization and analysis and to foster collaboration among all funding sectors, NIH should rapidly share the new approaches and tools it develops.

RESEARCH!AMERICA

AN ALLIANCE FOR DISCOVERIES IN HEALTH®

Perspectives of an NIH Advocate

Mary Woolley, President, Research!America

Oct. 24, 2013
Bethesda, MD

NIH Scientific Management Review Board

Making the Case for NIH: The Good News

- NIH has a clear and compelling mission, i.e. funding research to improve health
- The American public is positive about research, including basic research
- Scientific opportunity has never been greater

Advocacy does make a difference: NIH has fared better than many other interests in recessionary times.

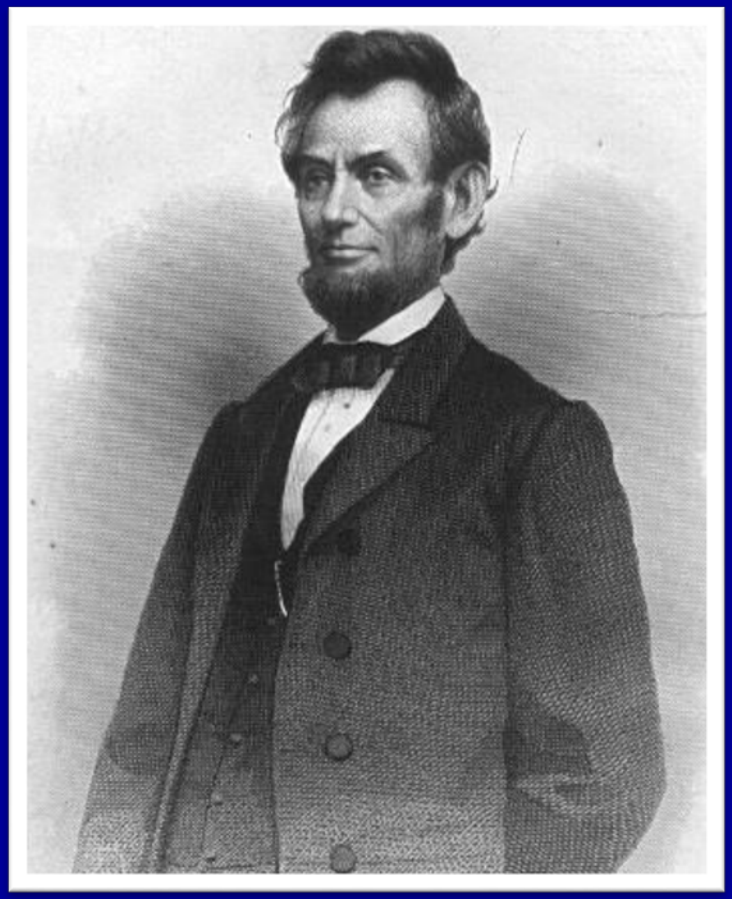
RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

Making the Case for NIH: Challenges

- Perceived lack of accountability; not enough palpable "progress"; people don't see solutions and results
- Other stakeholders in the research-for-health ecosystem don't always feel valued or heard
- Science and scientists are largely "invisible"
- Economic impact analyses are unconvincing
- ACA conversation consumes health mindshare, crowding out research for health
- Most health care providers — the most trusted sources for research information — do not talk about research

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

Public Support Matters



"…public sentiment is everything. With public sentiment, nothing can fail; without it nothing can succeed."

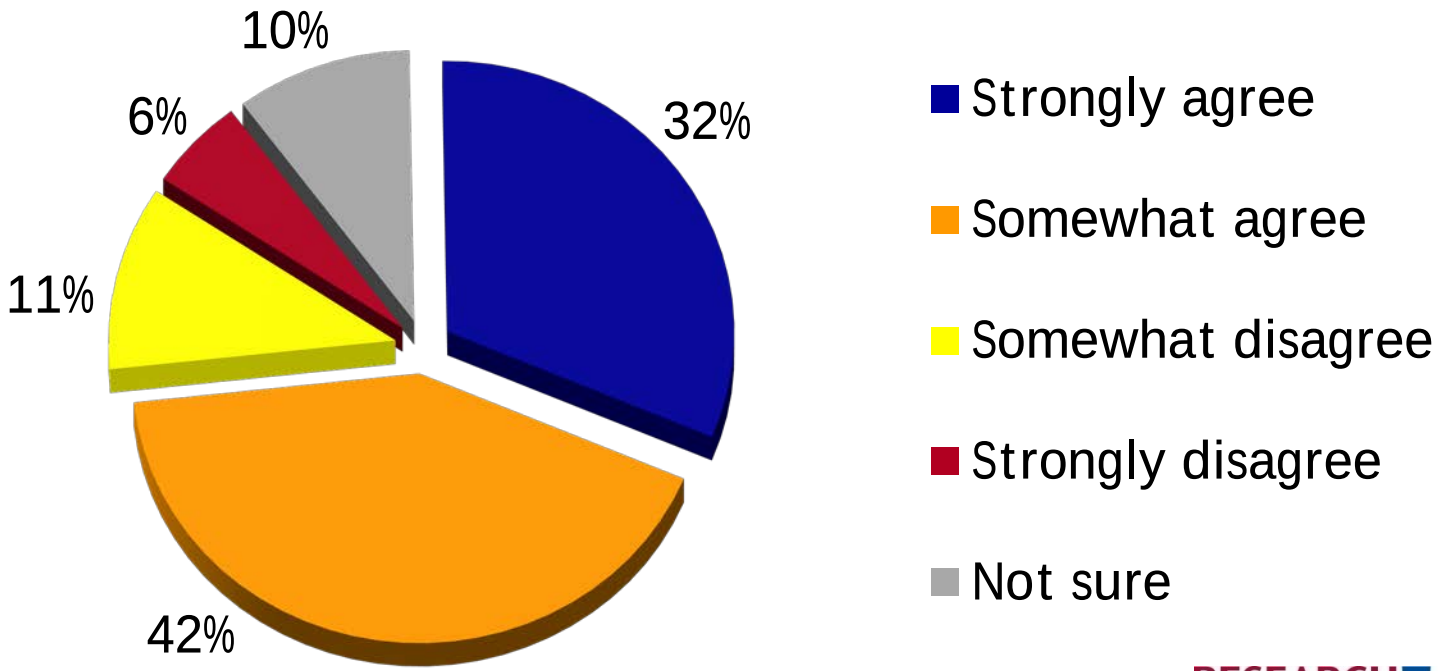
Abraham Lincoln

Research!America Polling

- Commissioning public opinion polls on research issues for 21 years:
  - National Polls
  - State-Based Polls
  - Issue-Specific Polls
- Telephone (random-digit dialing) polls are conducted with a sample size of 800-1000 adults (age 18+) and a maximum theoretical sampling error of +/- 3.5%. Data are demographically representative of adult U.S. residents (state or national).
- Online polls are conducted with a sample size of 1000-2000 adults and sampling error of +/-3.1%. The data are weighted in two stages to ensure accurate representation of the U.S. adult population.

Most Agree that Basic Research is Necessary

Do you agree or disagree with the following statement? “Even if it brings no immediate benefits, basic scientific research that advances the frontiers of knowledge is necessary and should be supported by the federal government.”



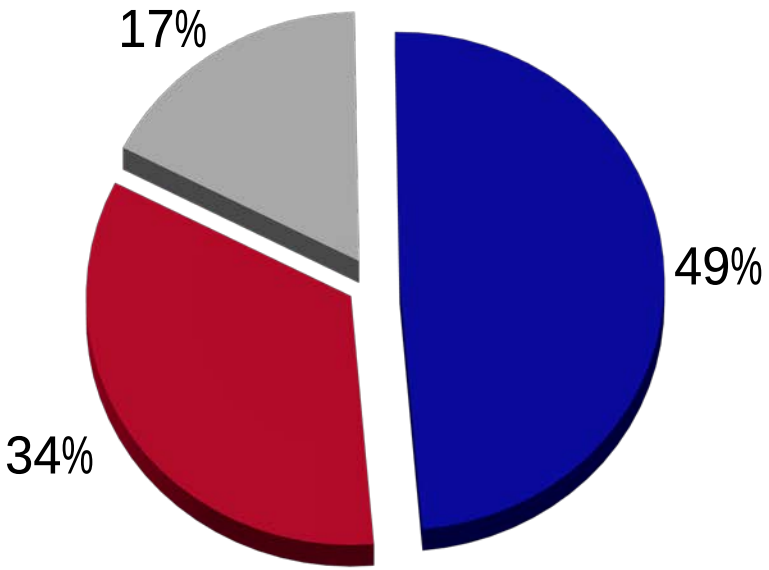
Zogby Analytics

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in December 2012.

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

49% of Americans Say U.S. Should Not Scale Back Medical Research

The planned across-the-board budget cuts mean that, next year, the federal government would fund approximately 2,300 fewer medical research grants across the country. Which comes closer to your views on this reduction in medical research grants?



- Our nation should not scale back medical research.
- It is OK to scale back medical research as part of deficit reduction.
- Not sure

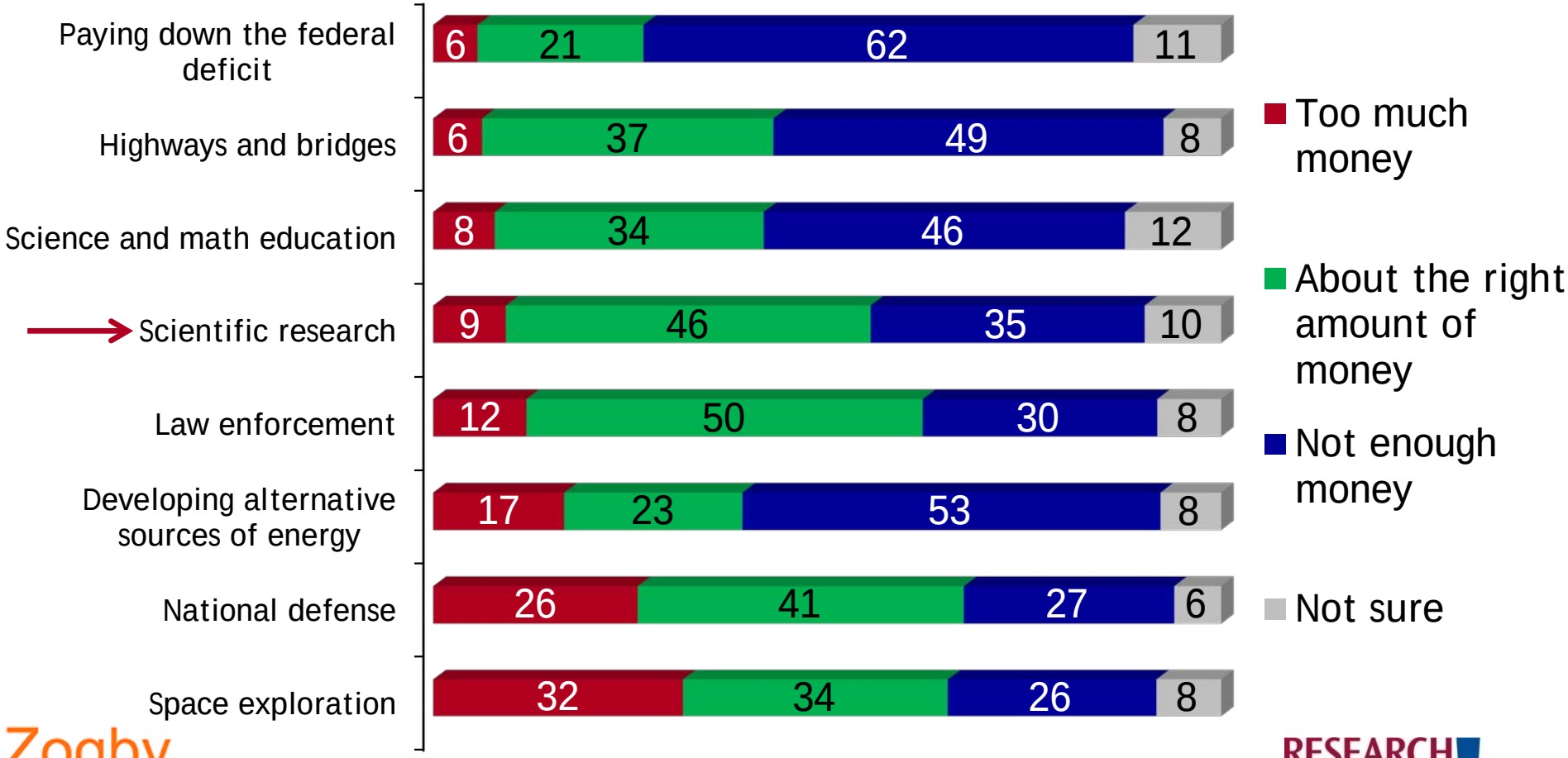
Zogby Analytics

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

Source: A Research!America poll of likely voters conducted in partnership with Zogby Analytics, with support from United for Medical Research, in September 2012.

Few Likely Voters Think Gov't Spends too Much on Research

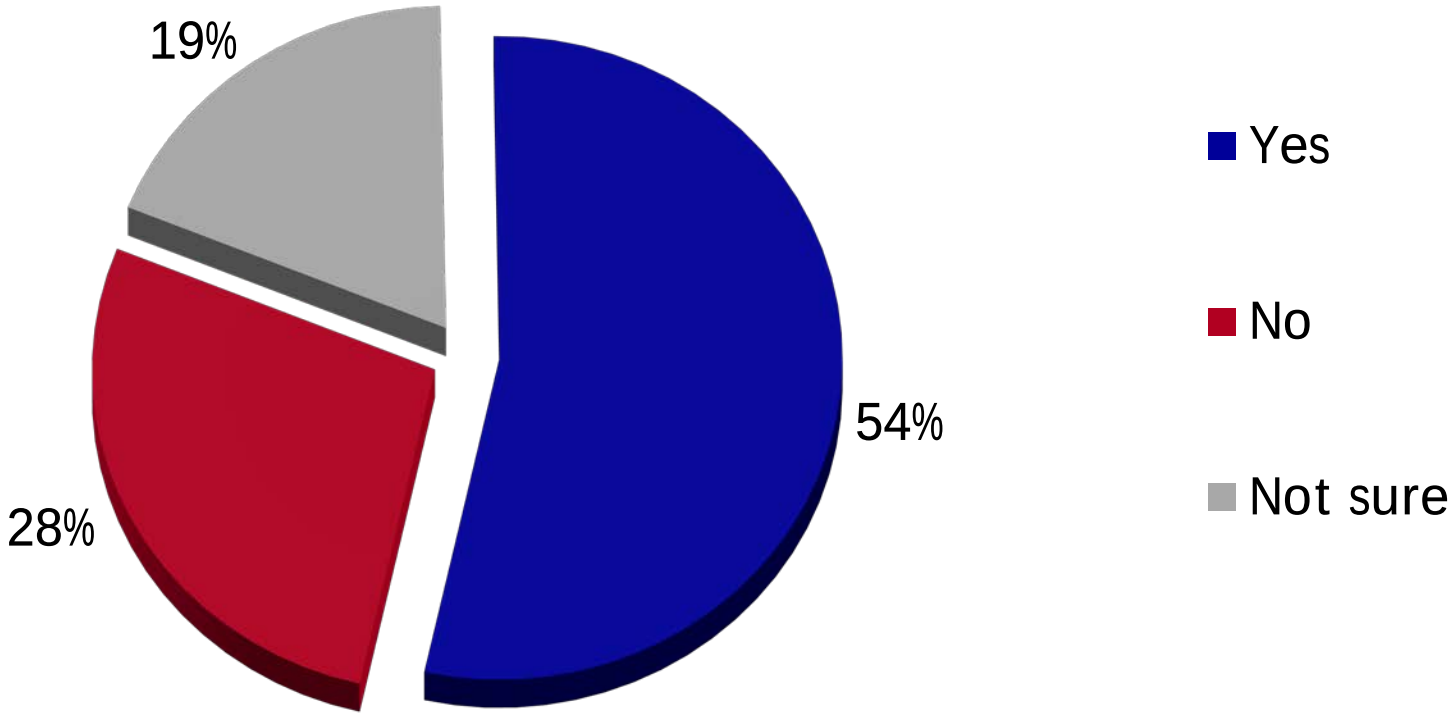
For each of the problems listed, is the government spending …



Source: A Research!America poll of likely voters conducted in partnership with Zogby Analytics in March 2012.

More than Half of Americans Willing to Pay Tax for Research

Would you be willing to pay $1 per week more in taxes if you were certain that all of the money would be spent on additional medical research?



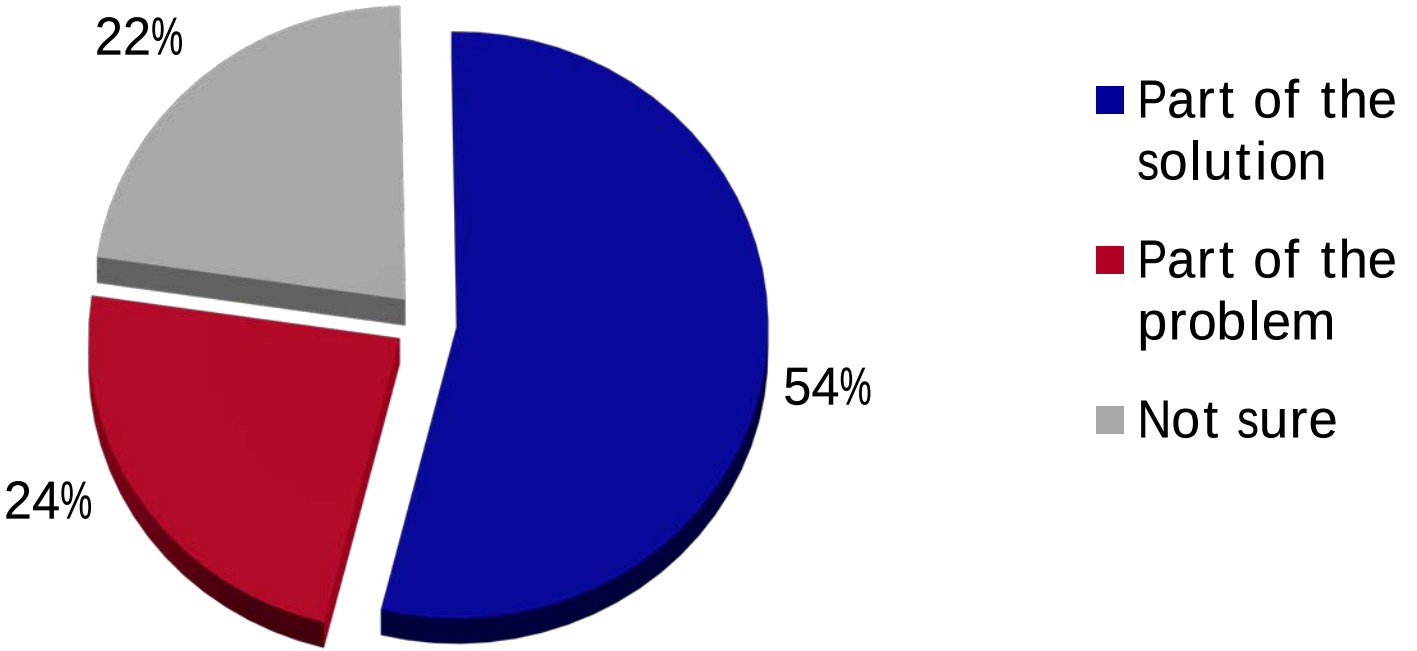
Zogby Analytics

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in December 2012.

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

Research is Part of the Solution to Rising Health Care Costs

When it comes to rising health care costs, would you say research to improve health is part of the problem or part of the solution?

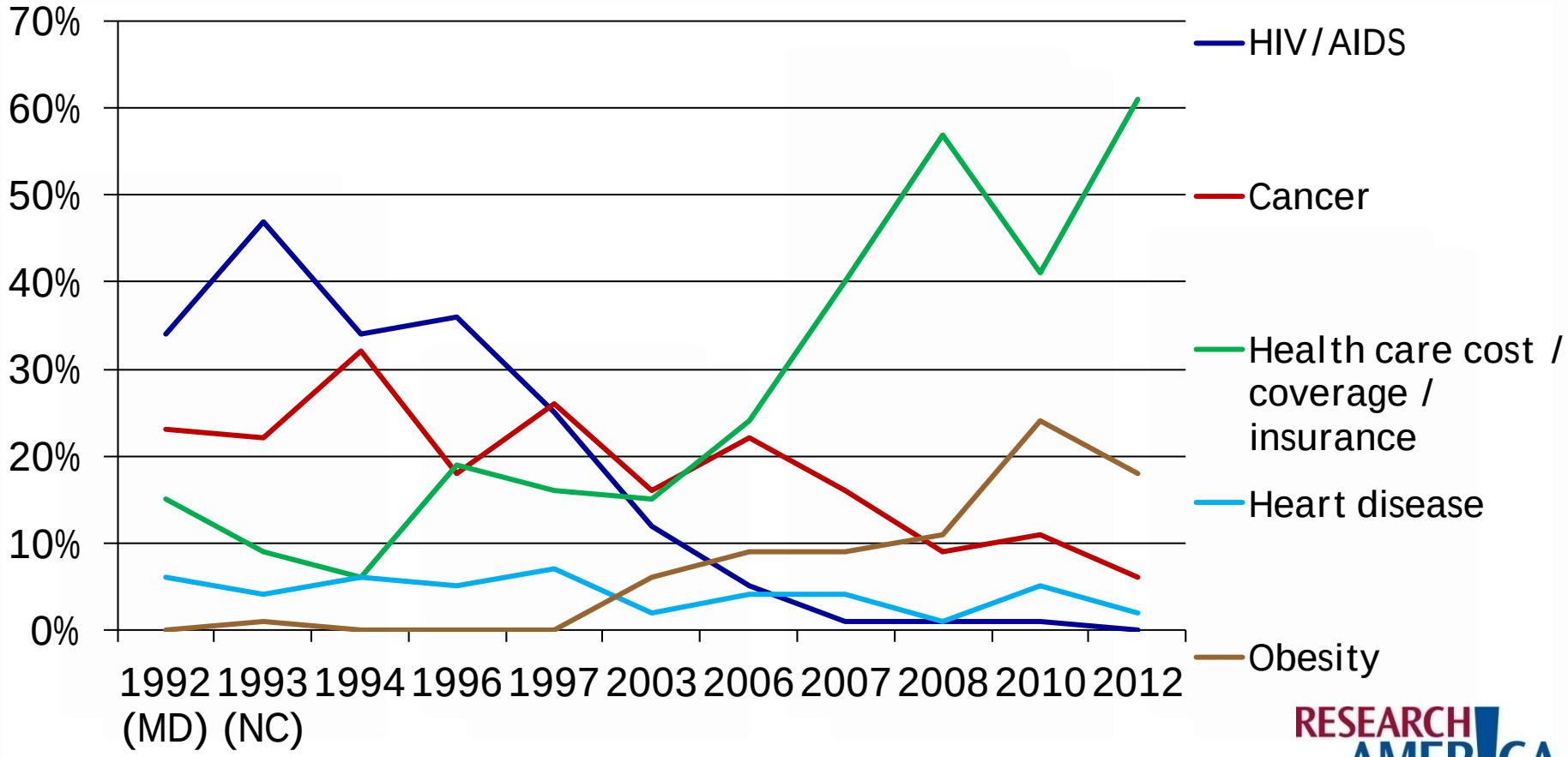


Source: National Public Opinion Poll, October 2011, Zogby Analytics for Research!America

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

Opinions on America's Most Important Health Issue

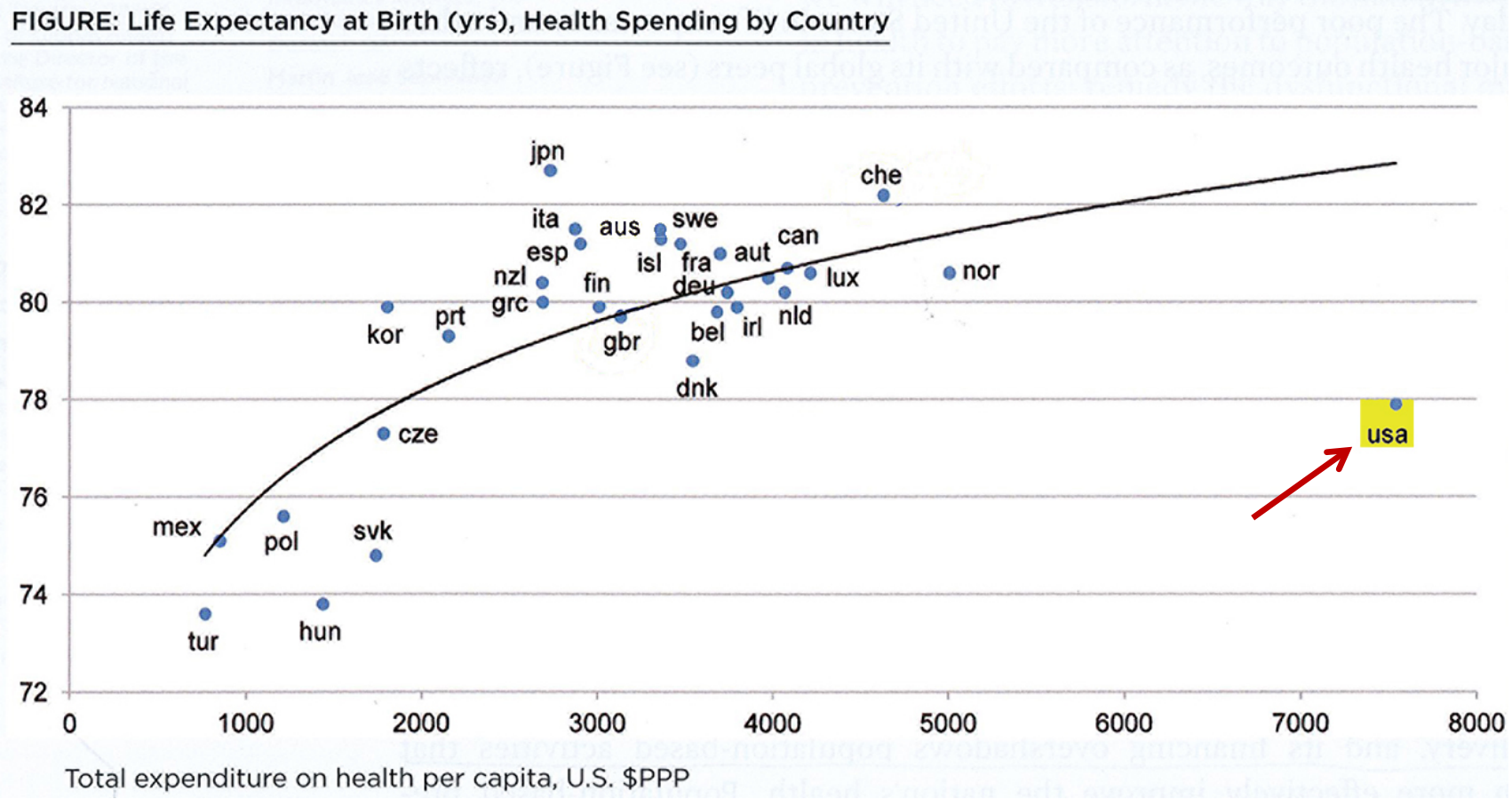
What would you say is the single most important health issue facing people in the U.S. today? (first volunteered responses)



Source: Public Opinion Polls, 1992-2010

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

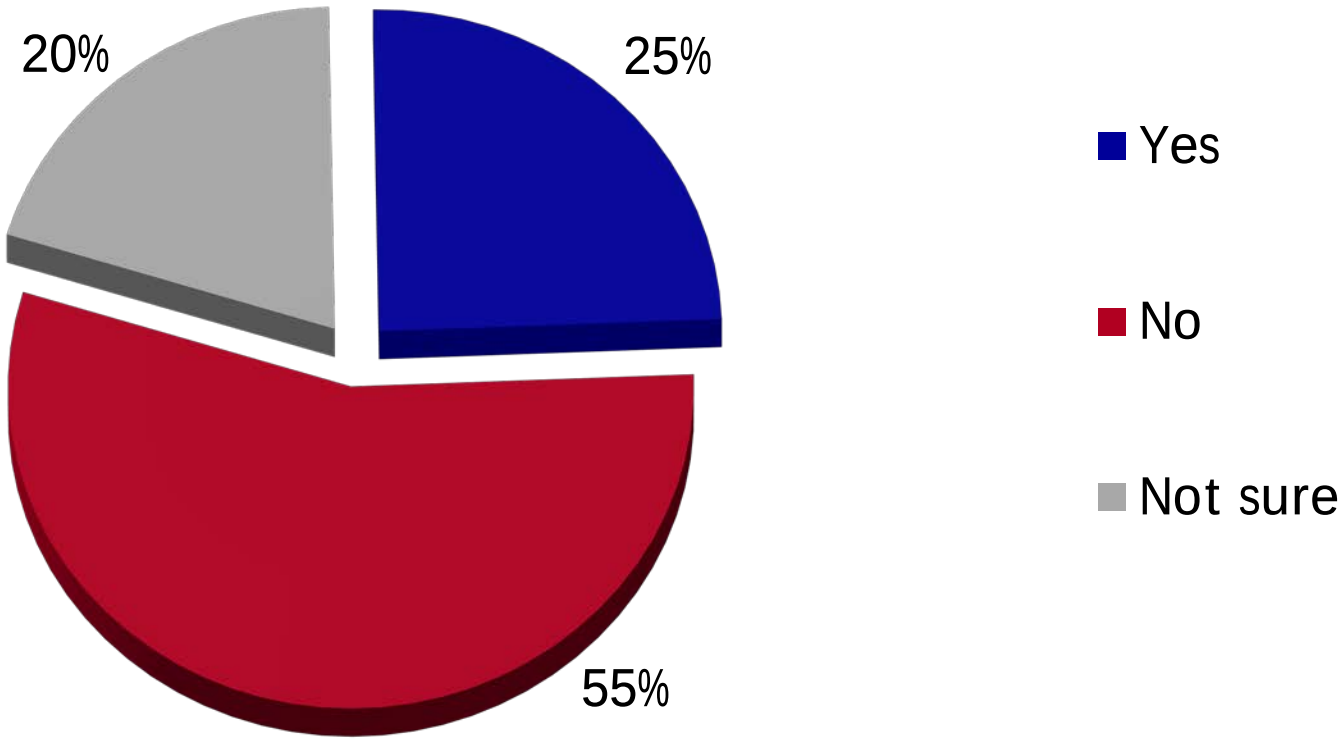
U.S. Spends Big on Health but Ranks Low in Return on Investment



Source: Organisation for Economic Co-operation and Development; Institute of Medicine

Majority: Medical Research is Not Making Sufficient Progress

Do you believe that we are making enough progress in medical research in the U.S.?



Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in December 2012.

Skepticism about Economic Impact

What science is really worth

Spending on science is one of the best ways to generate jobs and economic growth, say research advocates. But as **Colin Macilwain** reports, the evidence behind such claims is patchy.

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

Source: Nature 465, June 9, 2010

Skepticism about Economic Impact

Does R&D Drive Economic Growth?

The Mythology of Innovation

October 29, 2012 | Roger Pielke Jr

It is a claim that you hear often in discussions of the role of research and development in the economy: "Federal investments in R&D have fueled half of the nation's economic growth since World War II." This particular claim appeared in a recent *Washington Post* op-ed co-authored by a member of the US Congress and the chief executive of the American Association for the Advancement of Science. It would be remarkable if true. Unfortunately, it is not.

Source: The Breakthrough Institute (thebreakthrough.org)

Skepticism about Economic Impact

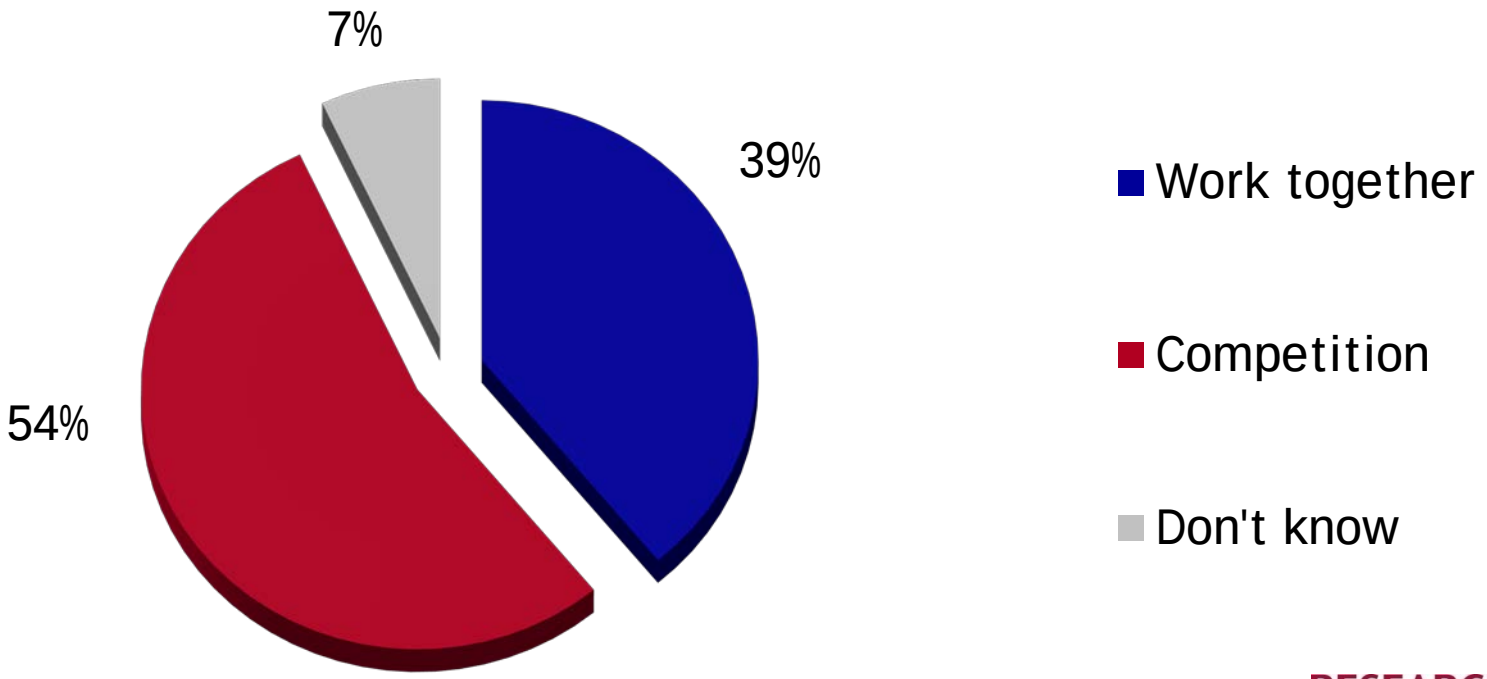
The main reason that countries are slow to realize the benefits of their research is because there have been few economic analyses of the knowledge economy. Better economic models are needed to understand the impact of investments.

Cunningham, P. Nature. 2013. 502:433-434

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

Competition or Cooperation in Medical Research?

Do you think the different types of institutions conducting medical research in this country, such as government, universities, and private industry, work together to develop new treatments and cures, or do you think they are in competition?

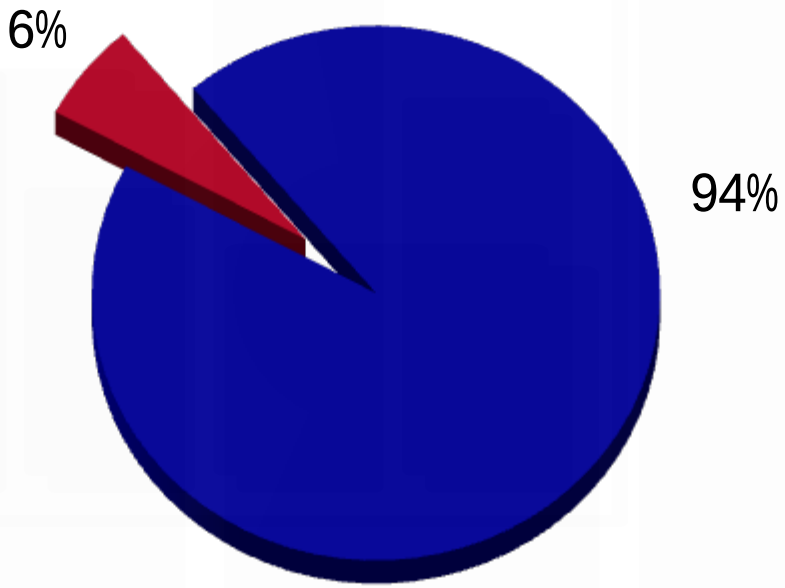


Source: National Poll, November 2008
Charlton Research Company for Research!America

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

Research Institutions Should Work Together

Do you think the institutions conducting medical and health research in this country, such as government, universities, and private industry, should work together to develop new treatments and cures, or not?

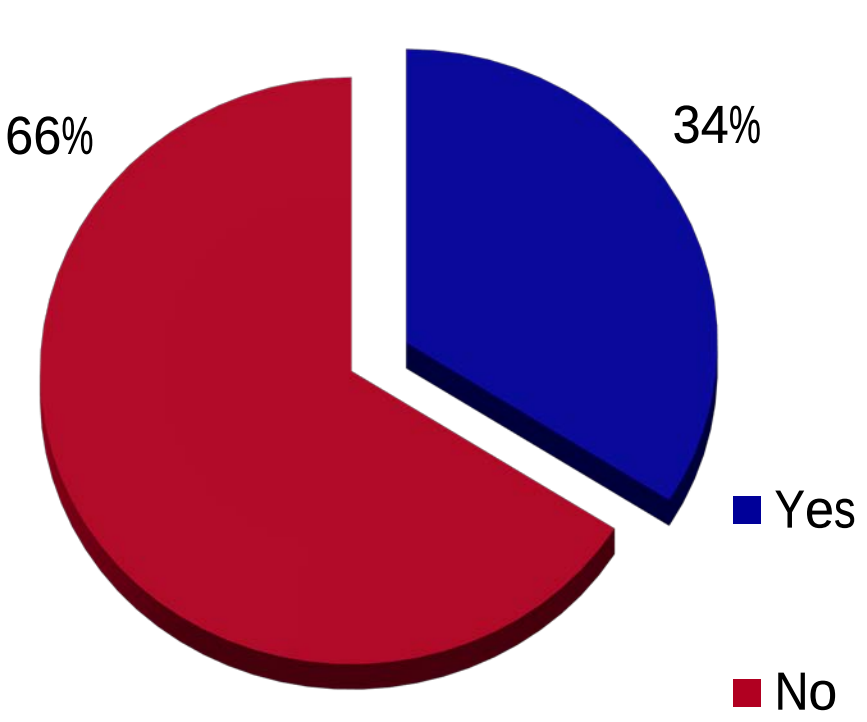


Source: Research Enterprise Poll, February 2010
Charlton Research Company for Research!America

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

Most Americans Can't Name a Living Scientist

Can you name a living scientist? (first volunteered responses)



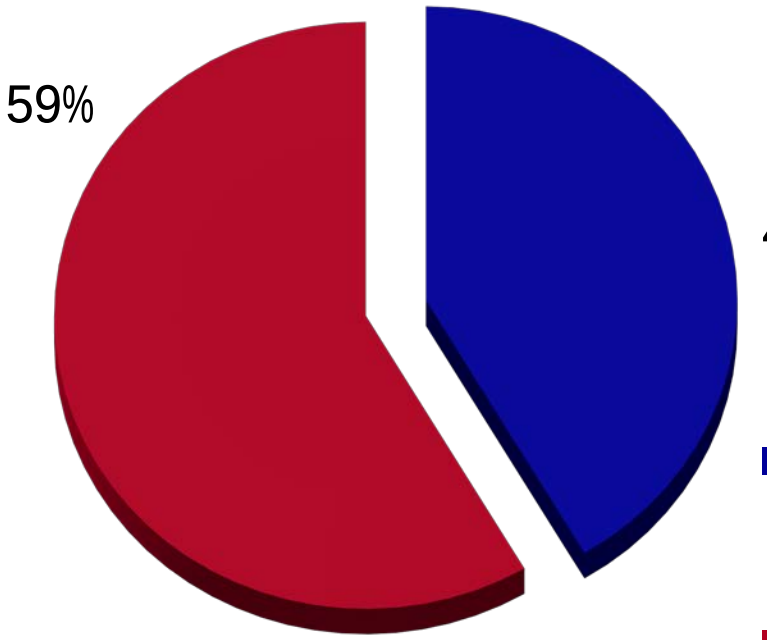
Stephen Hawking	15%
James Watson	1%
Jane Goodall	1%
Bill Nye	1%
Michio Kaku	1%
Neil Degrasse Tyson	1%
Other	14%

Source: *Your Congress – Your Health* Survey, March 2011
Charlton Research Company for Research!America

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

Most Americans Don't Know Where Research is Conducted

Can you name any institution, company or organization where medical and health research is conducted?



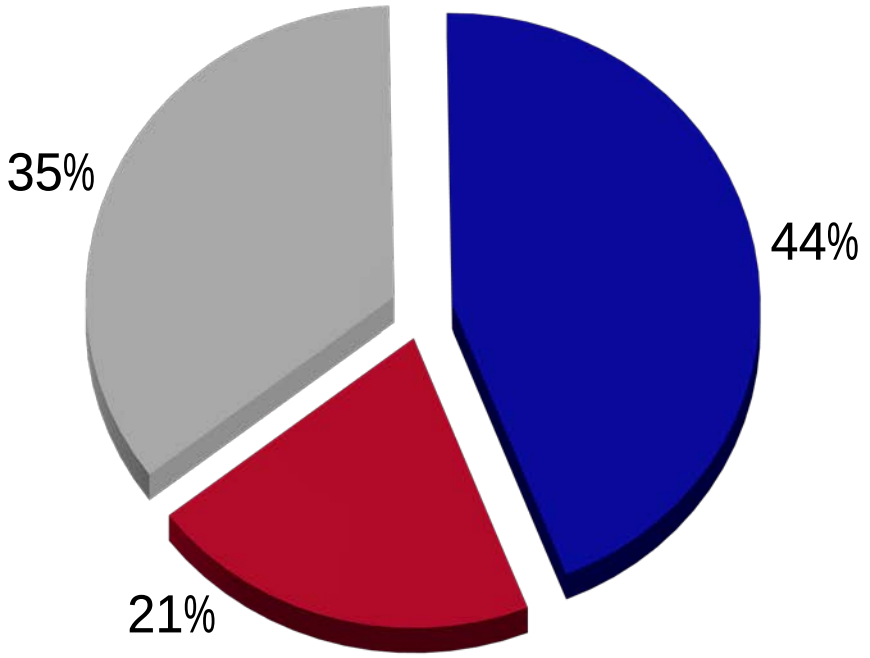
Mayo Clinic	10%
CDC	9%
NIH	7%
Johns Hopkins	6%
St. Jude	4%
Pfizer	3%
American Cancer Society	3%
Merck	2%
Duke Univ./Med. Ctr.	1%
OR Heath & Sci. Univ.	1%
UCSF	1%
Other	52%

Source: Your Candidates-Your Health Public Opinion Poll, October 2011, Zogby Analytics for Research!America

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

Less Than Half Know Medical Research Takes Place in Every State

To the best of your knowledge, would you say that medical research takes place in every state in the U.S.?



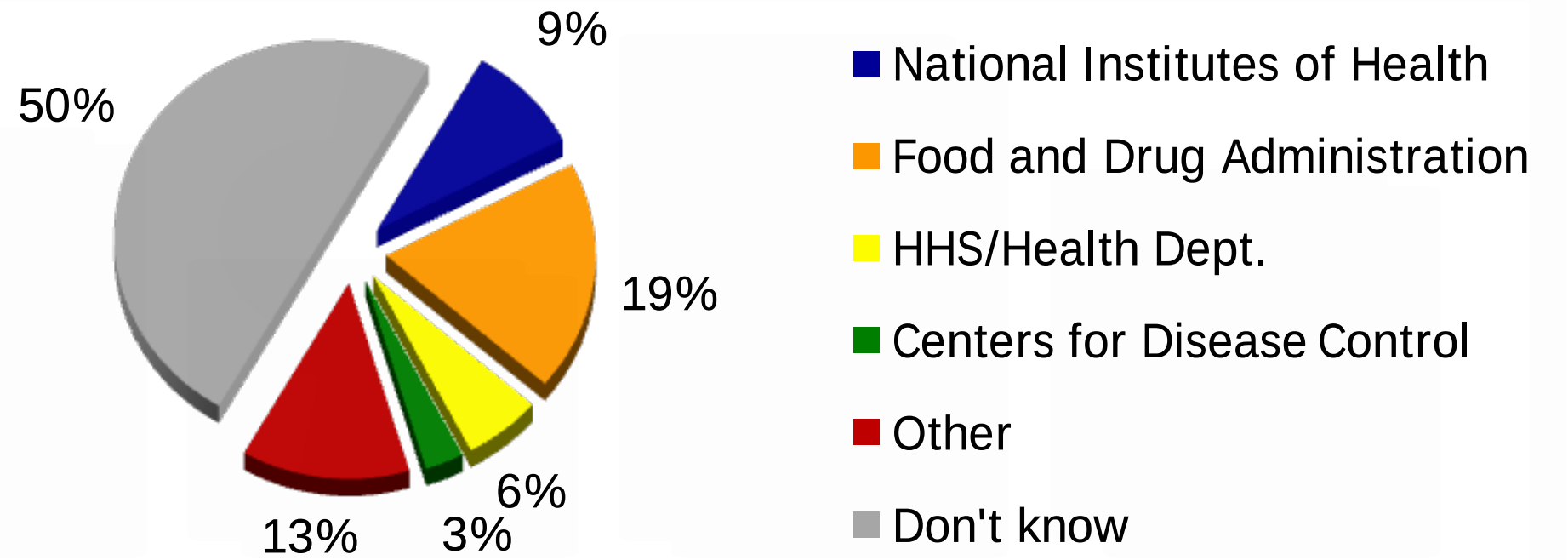
Zogby Analytics

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

Source: A Research!America poll of likely voters conducted in partnership with Zogby Analytics, with support from United for Medical Research, in September 2012.

Few Americans Recognize the National Institutes of Health

What is the name of the government agency that funds most of the medical research paid for by taxpayers in this country? (first volunteered responses)

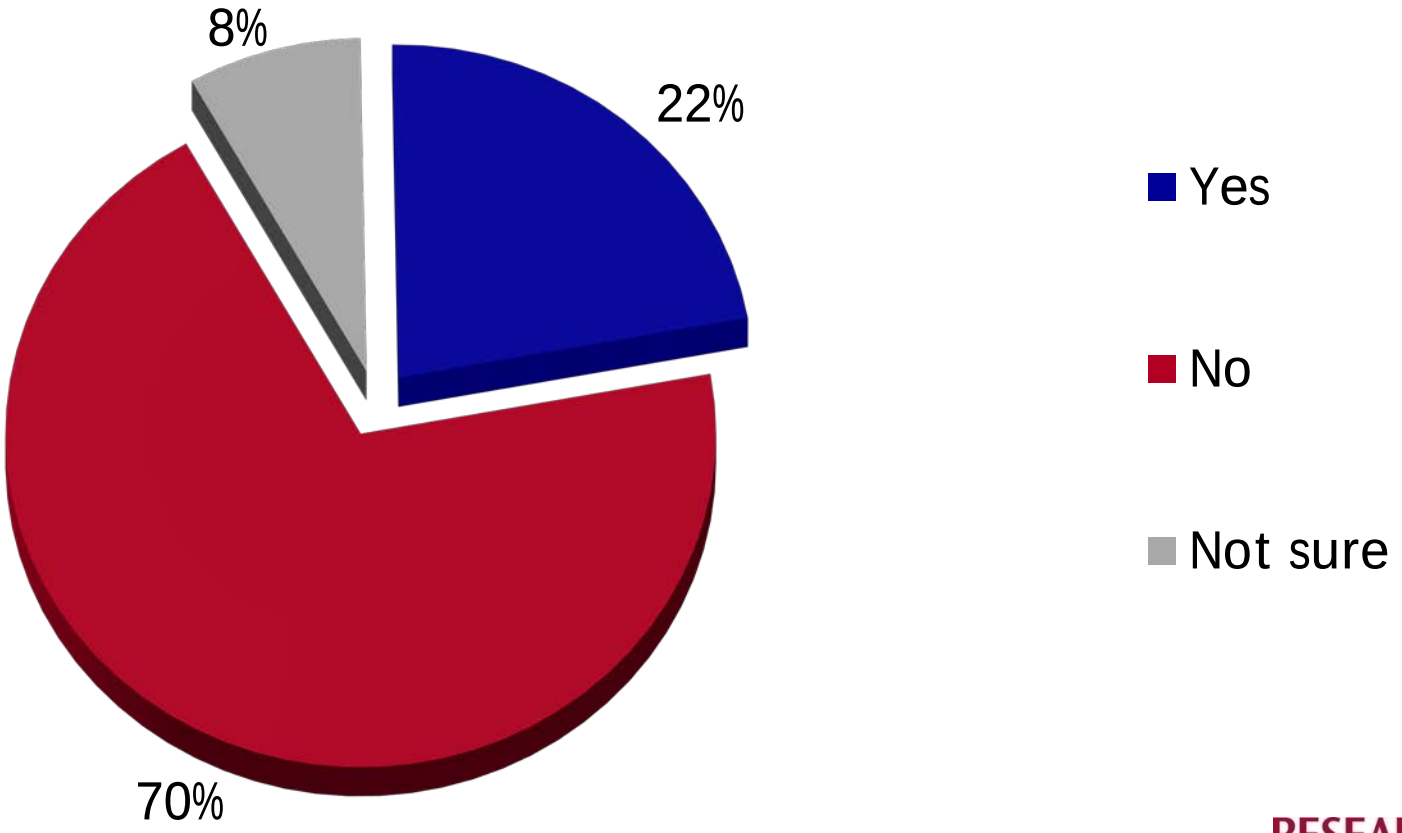


Source: Research Enterprise Poll, February 2010
CharIton Research Company for Research!America

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

Seven in 10 Say Doctors Don't Talk About Medical Research

Has your doctor or other health care professional ever talked to you about medical research?



Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.

Specific Suggestions

- Get out of the echo chamber and talk to new audiences
- Design and fund economic impact studies
- Create incentives for individual scientists to engage the non-science public; pilot test and scale
- Educate grantees about other stakeholders, including industry and patient groups — stop expecting them to make our case if we aren't making theirs
- Open dialogue with health care providers, the most trusted sources of information about research

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

Accountability is part of our contract with the public.

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

‘A Nobel in the Family: My Brother, the Genius’

“I admire and love my brother [Paul Greengard], but he lives on a higher plane, and what he does is secret, unrevealable. To me, anyway …

“Every time he took a new job — whether at Albert Einstein College of Medicine or Yale — I’d ask him about it. Then he’d get into electro-physiological properties, and it was all over …

“Now, he has won the Nobel Prize in physiology or medicine, an honor he shares with two other scientists. In reporting it, the newspapers said their work on the way brain cells communicate might one day help cure diseases like Parkinson’s and Alzheimer’s.

“I’m thrilled he won. **Now I know what he does.**”

— *Chris Chase in a* New York Times *opinion piece on October 15, 2000*

RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

"Scientists are obliged to make the case for science to lawmakers. … If I had to do it all over again I would spend more time talking to general audiences and public officials, penning op-eds."


"I work for you."
RESEARCH AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

Connect with Research!America Online

- www.researchamerica.org/blog
- www.researchamerica.org/facebook
- www.twitter.com/researchamerica
- www.youtube.com/researchamerica

RESEARCH!AMERICA
AN ALLIANCE FOR DISCOVERIES IN HEALTH

Presentation to NIH Scientific Management Review Board

October 24, 2013

Concepcion R. Nierras, Ph.D.
Assistant Vice President, International Partnerships, JDRF

JDRF Mission

- Largest charitable supporter of T1D research in the world: USD 1.7 Billion invested in research over 40+ years
- In 2012, USD 110 Million in direct support, in 18 countries
- JDRF's research mission: discover, develop & deliver drugs and devices that cure, better treat, and prevent T1D
- Goal of transforming lives:
  - Improving outcomes
  - Reducing daily burdens
  - Preventing complications
  - Accelerating progress towards curing T1D

JDRF partners with all stakeholders

JDRF partnerships:

- National Institutes of Health
- Australia NHMRC
- Canada CIHR
- EFSD
- Singapore A*STAR
- UK Wellcome Trust
- Helmsley Charitable Trust

Advocacy:

- FDA
- Australia TGA
- EMEA
- UK NICE

JDRF Research Strategy

"All T1D Stages and All Ages"

PREVENT

1st Prevention
Prevent Autoimmunity

2nd Prevention
Stop Autoimmunity
Prevent Beta cell Loss

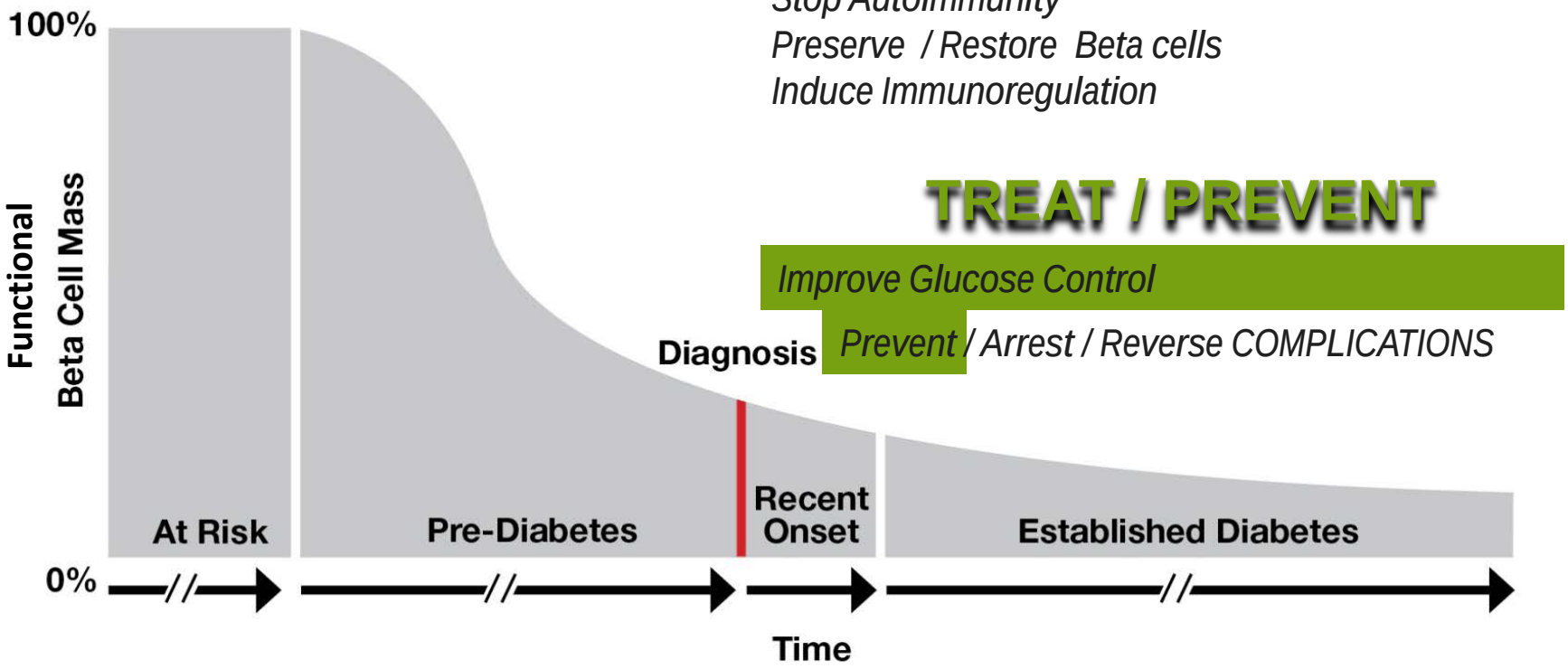
CURE

Stop Autoimmunity
Preserve / Restore Beta cells
Induce Immunoregulation

TREAT / PREVENT

Improve Glucose Control

Prevent / Arrest / Reverse COMPLICATIONS



From G Eisenbarth

How does your organization set goals?

Identifying gaps and opportunities

Innovating mechanisms

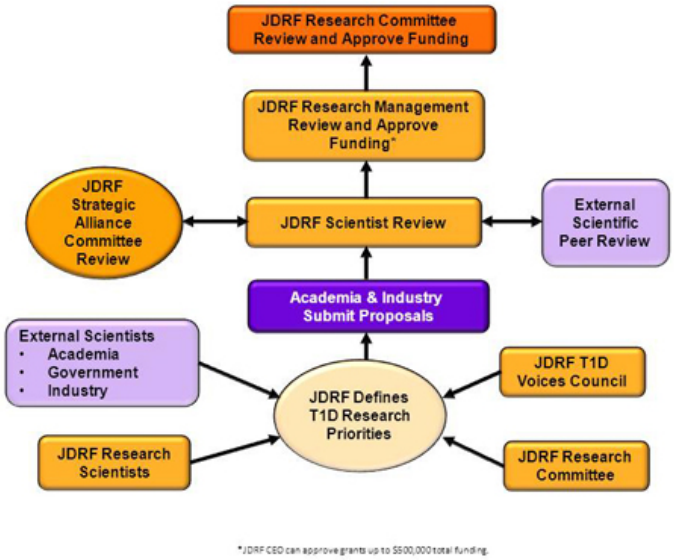
Research funding oversight

Volunteers are an important part of JDRF

- JDRF Research Committee
- T1D Voices Council

Consultation with partners (govt, other foundations, and industry)

Input from scientific experts (academia, govt and industry)



How does your organization assess whether it is meeting its goals?

Evaluation of scientific progress

Annual reporting includes evaluations/site visits

Milestone-based payments for awards

How does this research contribute to understanding of disease?

Evaluation of program effectiveness

Partnerships:

- Did it achieve its goals?
- Was the science successful?
- Are there new opportunities?

Mechanisms:

Training: did awardee make a career in diabetes research?

Communicating results

You Make A Difference – Thank You!

Learn more at: jdrf.org

- **Give** generously to speed JDRF research to cure, better treat and prevent T1D
- **Join** a JDRF walk, ride, gala or other fund-raising event
- **Volunteer** at your local JDRF chapter
- **Participate** in clinical research

Living with Diabetes: People with Type 1 Diabetes Are Living Longer, Healthier Lives

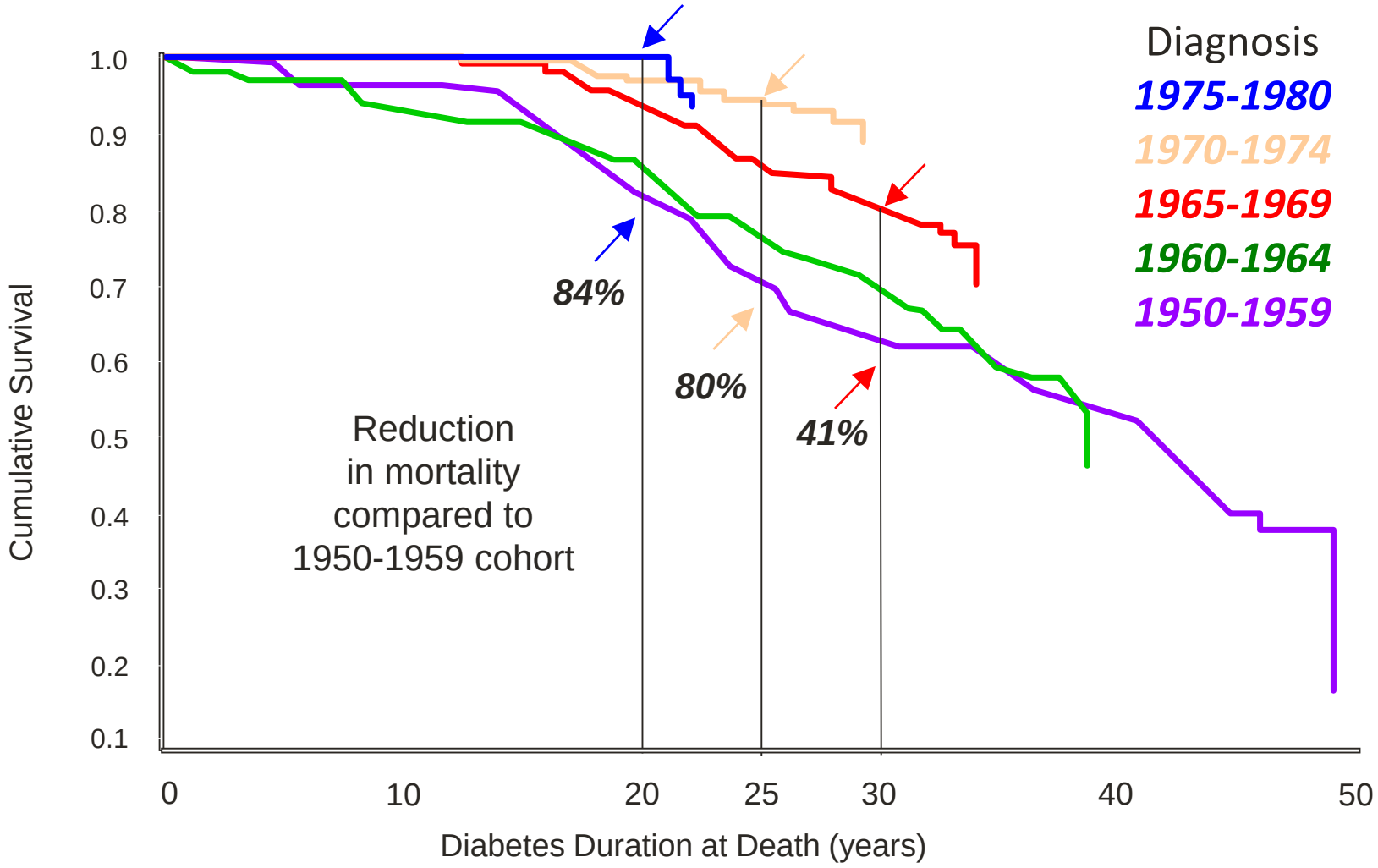


Figure adapted from *Diabetes* 55: 1463-1469, 2006

October 2013

The Economic and Health Effects of Biomedical Innovation

Peter R. Orszag
Vice Chairman, Corporate and Investment Banking
Chairman, Financial Strategy and Solutions Group
Chairman, Public Sector Group
Columnist, Bloomberg View

citi

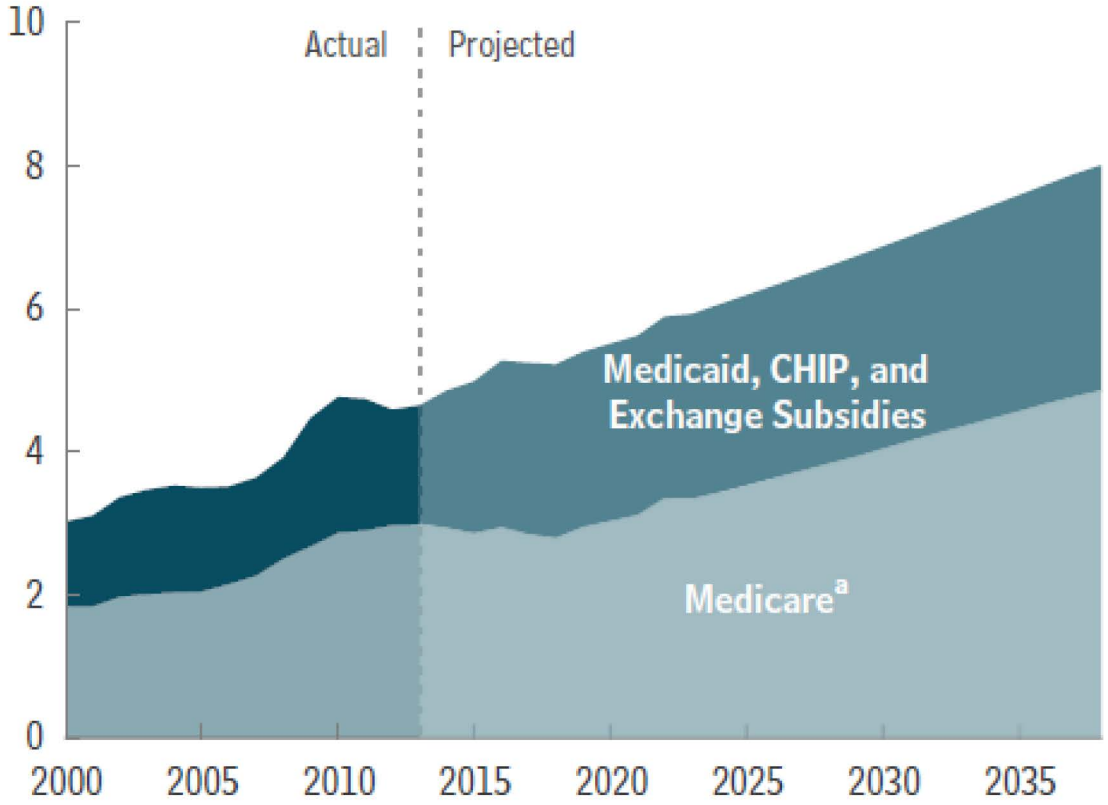
Outline

- Healthcare Spending and the Federal Budget
- Impact of Health on Productivity
- Impact of Biomedical Innovation on Health
- Life Expectancy by Education

HEALTHCARE SPENDING AND THE FEDERAL BUDGET

Federal Spending on Major Health Care Programs, by Category, Under CBO's Extended Baseline

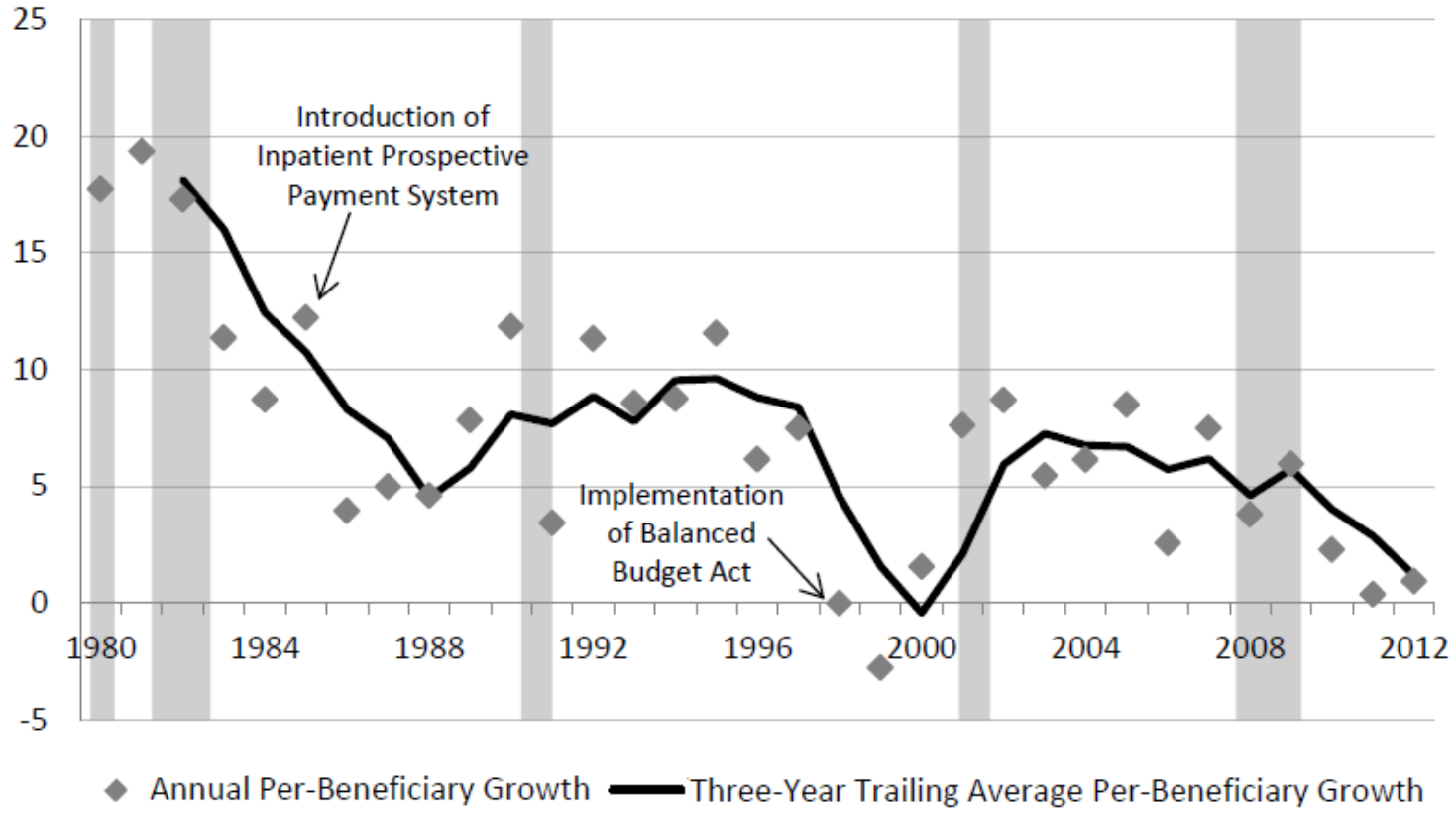
(Percentage of gross domestic product)



Source: Congressional Budget Office.

Figure 1.
Annual Growth in Per-Beneficiary Spending in Parts A and B of Medicare, Fiscal Years 1980 to 2012

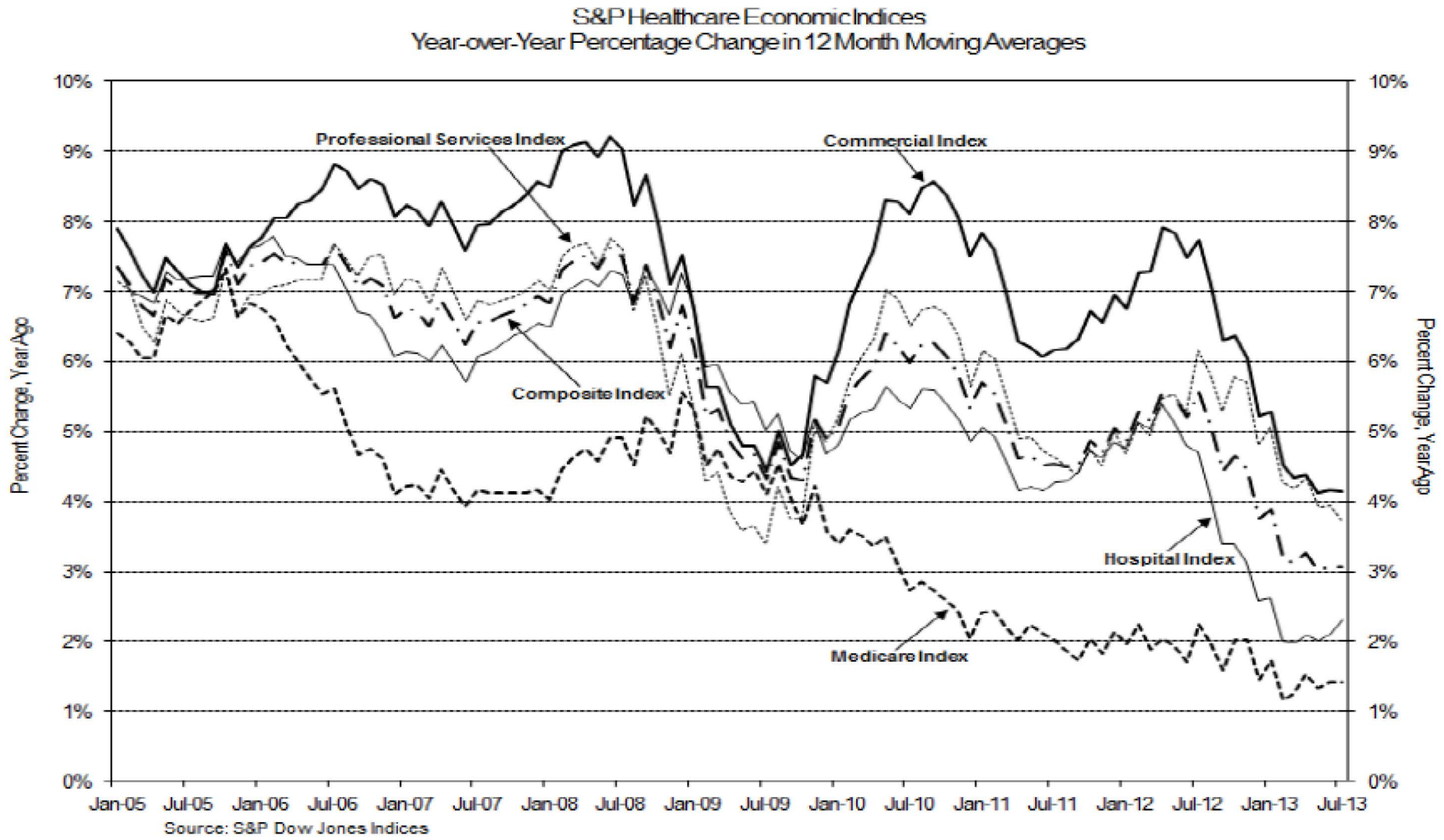
(Percent)

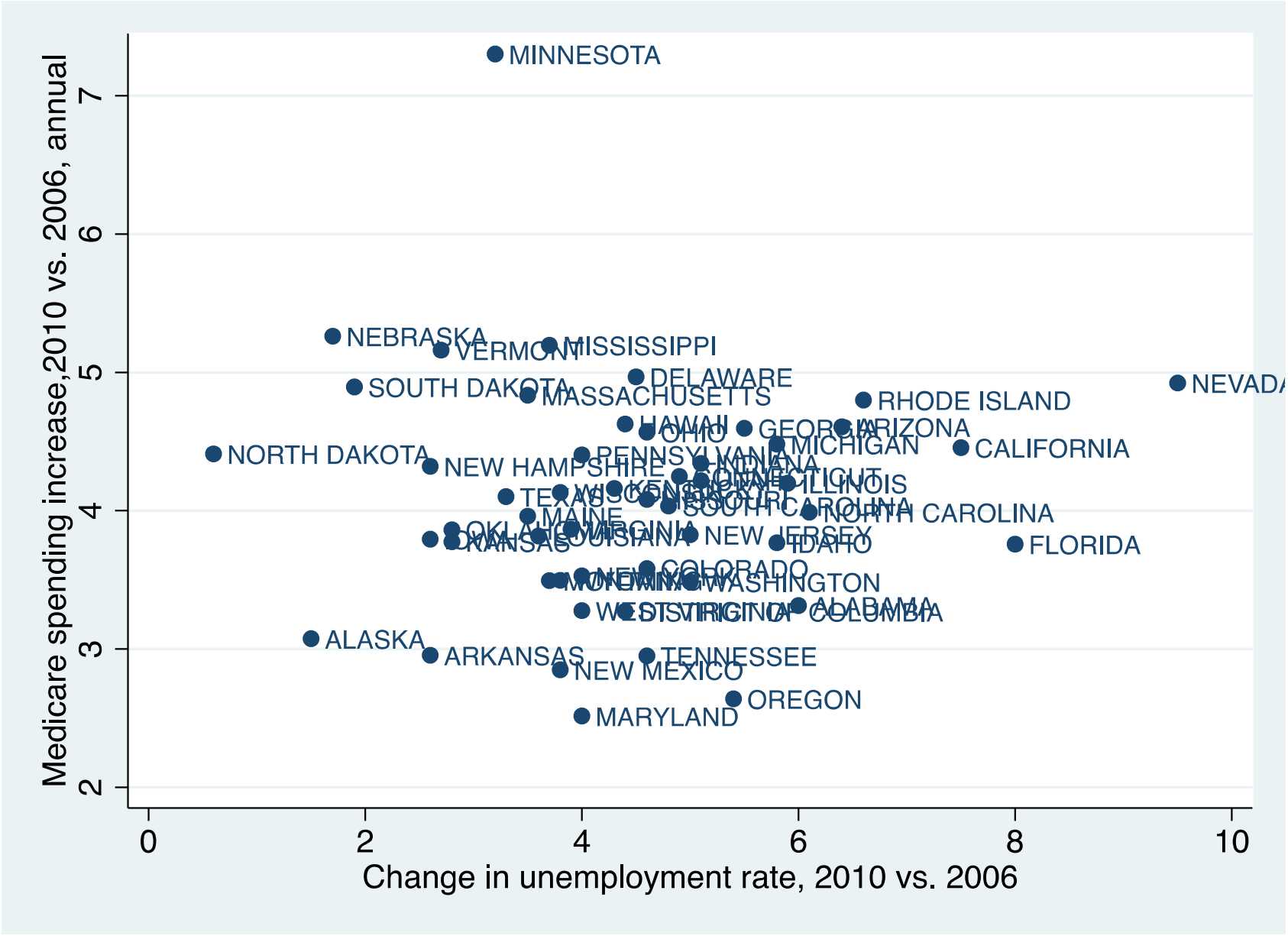


Source: Based on expenditure data provided by the Centers for Medicare and Medicaid Services, Office of the Actuary.

Note: Shaded bars indicate recessions.

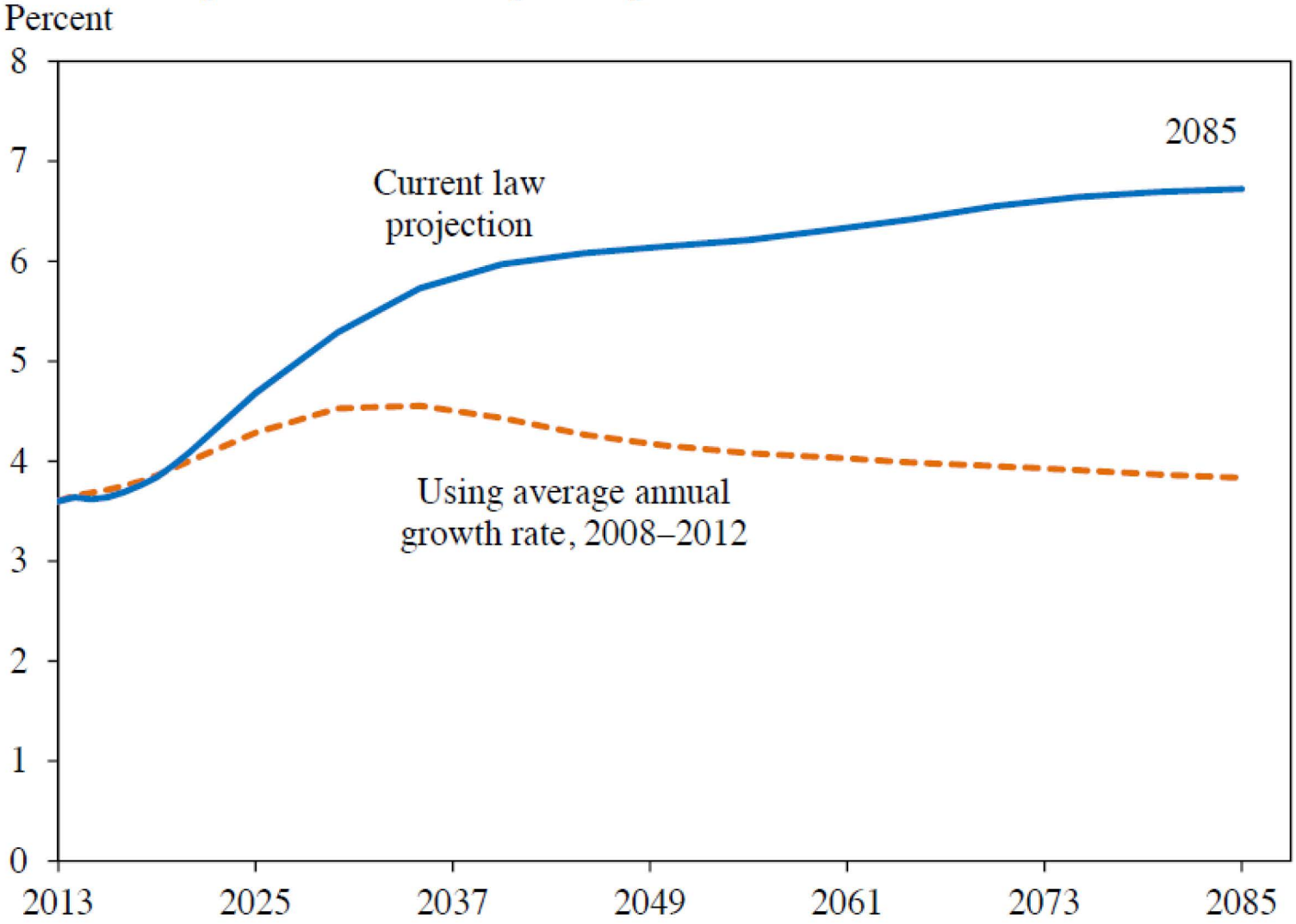
Source: CBO Working Paper


S&P Healthcare Economic Indices
Year-over-Year Percentage Change in 12 Month Moving Averages
Professional Services Index
Commercial Index
Composite Index
Hospital Index
Medicare Index
Percent Change, Year Ago
10%
9%
8%
7%
6%
5%
4%
3%
2%
1%
0%
Jan-05
Jul-05
Jan-06
Jul-06
Jan-07
Jul-07
Jan-08
Jul-08
Jan-09
Jul-09
Jan-10
Jul-10
Jan-11
Jul-11
Jan-12
Jul-12
Jan-13
Jul-13
Source: S&P Dow Jones Indices



Source: CMS, BLS

Projected Medicare Spending as a Share of GDP, 2013–2085



Source: Medicare Trustees (2012); Social Security Trustees (2012); CEA calculations.

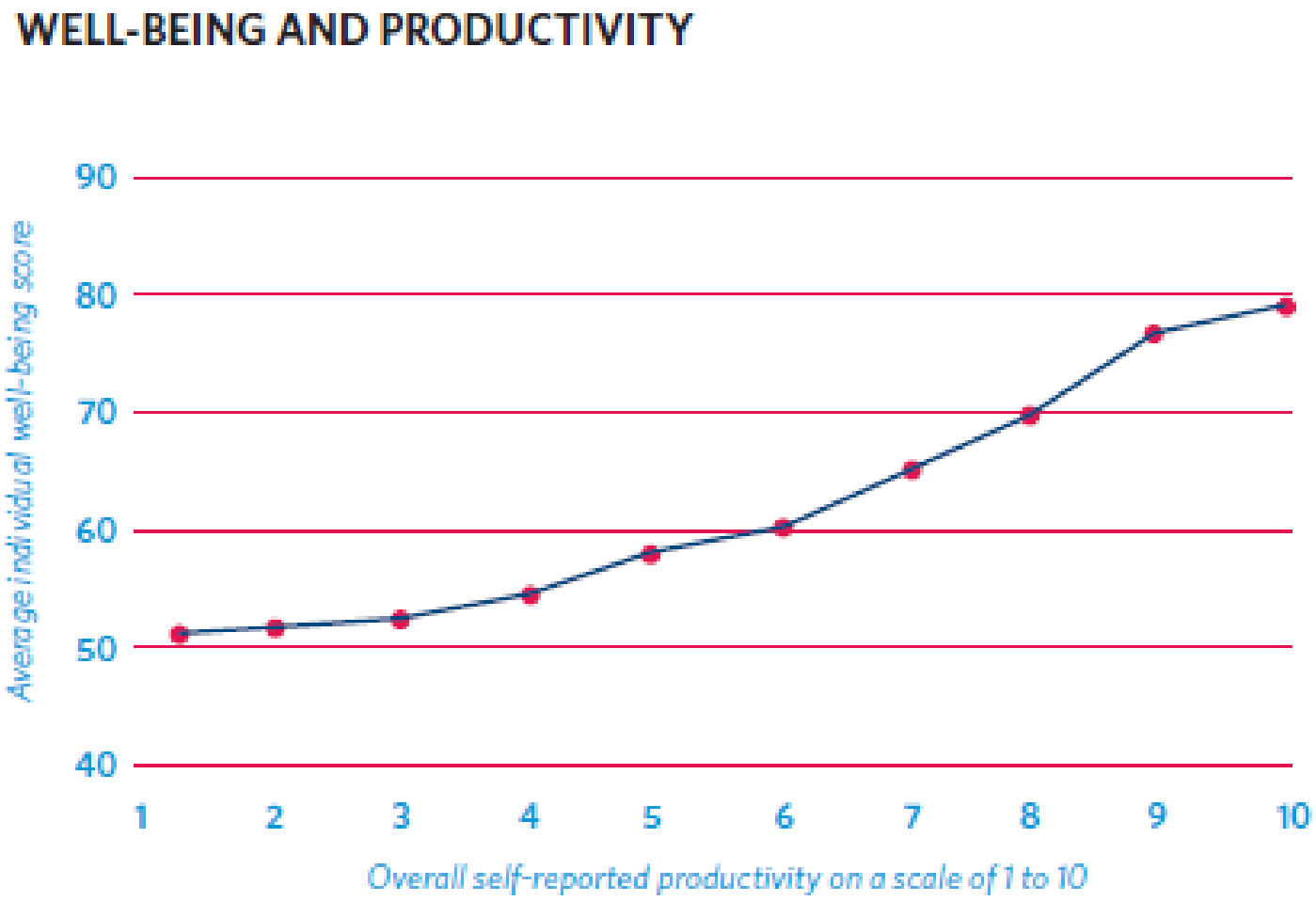
Changes in Projected Medicare and Medicaid Spending Between March 2010 and May 2013

	Medicare[a]		Medicaid[b]	
	Technical Revisions (Billions of dollars)	*Percent Change*	Technical Revisions (Billions of dollars)	*Percent Change*
2010	-14	*-3%*	0	*0%*
2011	-26	*-5%*	-1	*-1%*
2012	-30	*-6%*	-11	*-4%*
2013	-45	*-8%*	-17	*-6%*
2014	-63	*-10%*	-32	*-10%*
2015	-69	*-11%*	-48	*-13%*
2016	-78	*-11%*	-53	*-13%*
2017	-91	*-13%*	-59	*-13%*
2018	-106	*-14%*	-63	*-13%*
2019	-125	*-15%*	-74	*-15%*
2020	-137	*-15%*	-85	*-16%*
Total 2010-2020	**-785**	***-11%***	**-445**	***-11%***

a. Medicare spending is net of offsetting receipts.
b. The comparison for the Medicaid baseline is to August 2010, as the March 2010 baseline did not include the effects of the Affordable Care Act (ACA). Only minor changes were made in that August baseline beyond those related to the ACA.

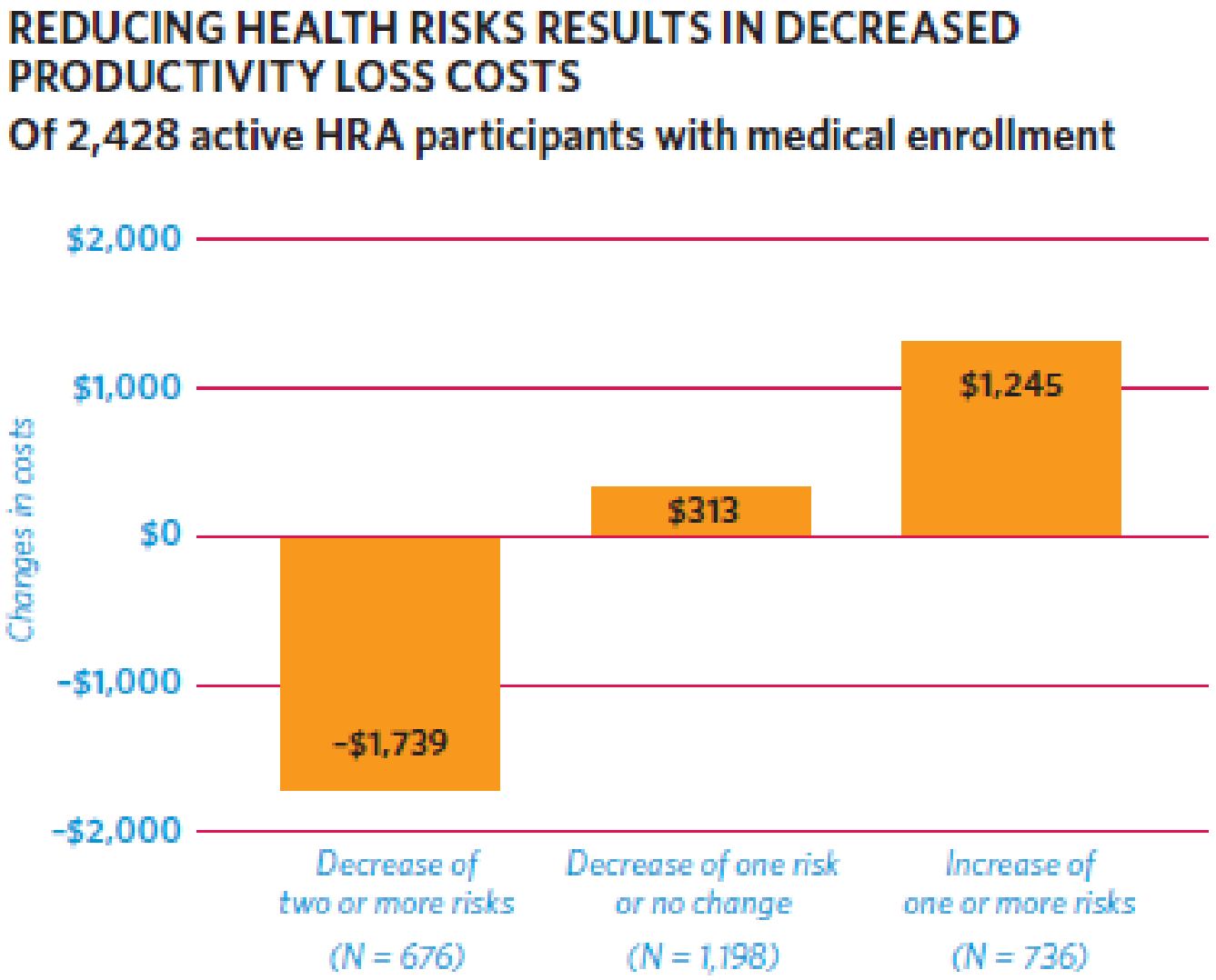
IMPACT OF HEALTH ON PRODUCTIVITY

Caterpillar



Source: IBI, 2011

Baystate Health



Source: IBI, 2011

Gallup – Lost Productivity by Occupation

- Gallup surveyed 14 different occupation types to calculate productivity losses from poor health of workers. Poor health was defined as being above normal weight or having one or more chronic conditions. They found that the productivity lost per year due to absenteeism in those job types equaled $84 billion.
- The findings were based on more than 94,000 interviews of U.S. adults working 30+ hours per week. The Gallup-Healthways Well Being Index gets self-reported information on height and weight to calculate BMI, and asks about certain chronic health conditions.
- To calculate the number of unhealthy days Gallup asked respondents “During the past 30 days, for about how many days did poor health keep you from doing your usual activities?" and "How many actual work days in the last month did you not work due to poor health?”
- The cost of absenteeism is estimated at $341 per day and that figure is used to calculate yearly productivity losses from absenteeism.

Source: Gallup, 2013

Gallup – Lost Productivity by Occupation

Cost of Lost Productivity Per Year by Major U.S. Occupations

Profession	% Above normal weight or 1+ chronic conditions	Extra missed work days each month among those with subpar health	Cost of lost productivity per year due to absenteeism (in billions)
Professional (excluding physicians, nurses, and teachers)	74.8	0.30	$24.2
Managers or executives	78.8	0.29	$15.7
Service workers	76.4	0.31	$8.5
Clerical or office	76.5	0.39	$8.1
Sales	75.2	0.29	$6.8
School teachers (K-12)	72.6	0.30	$5.6
Nurses	73.7	0.36	$3.6
Transportation	86.0	0.41	$3.5
Manufacturing or production	82.0	0.24	$2.8
Business owners	79.2	0.34	$2.0
Installation or repair	83.0	0.23	$1.5
Construction or mining	80.5	0.11	$1.3
Physicians	67.9	0.04	$0.25
Farmers, foresters, fishers	78.8	0.08	$0.16

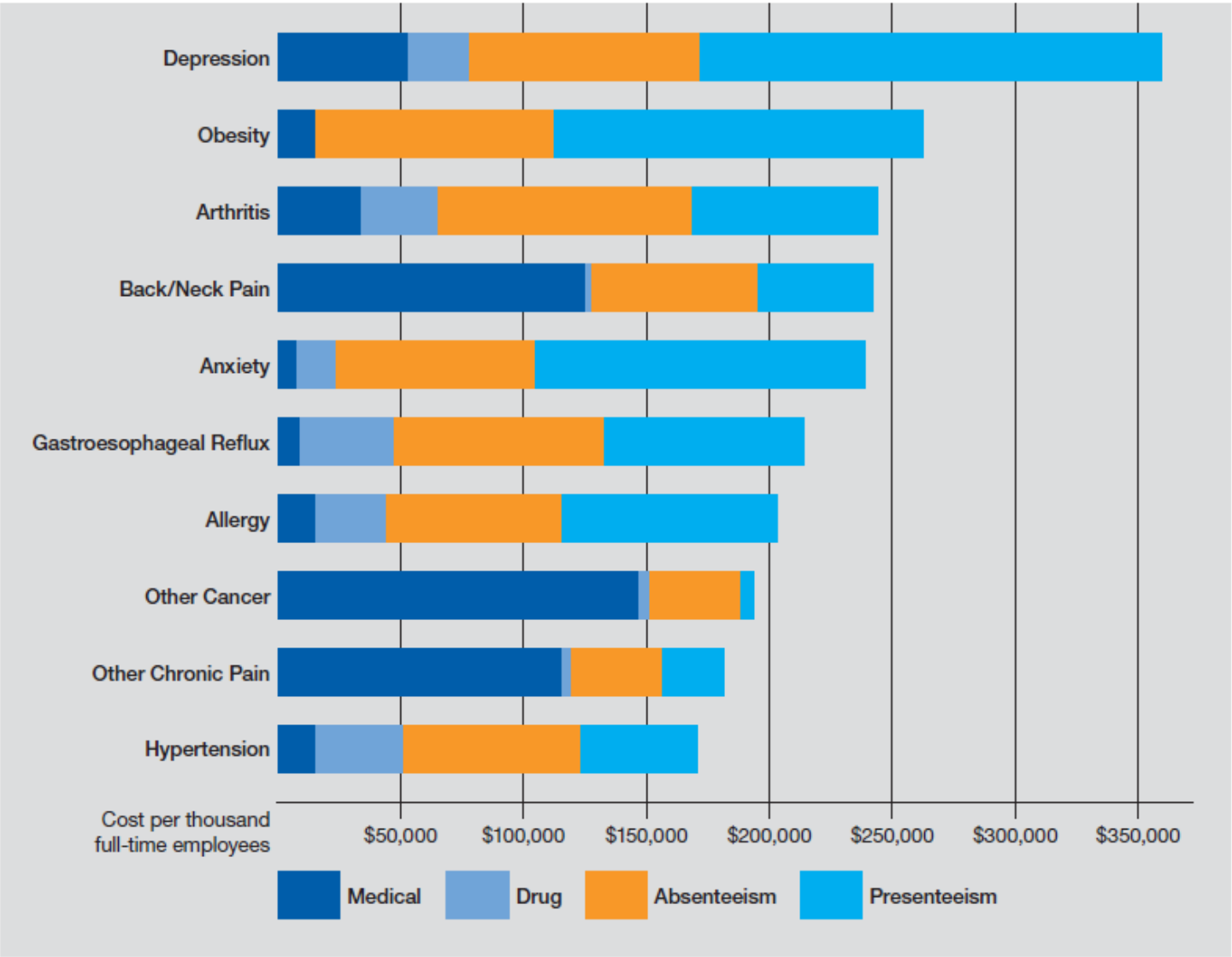
Source: Gallup, 2013

Annual Costs per 1000 FTEs by Health Condition

- Ronald Loeppke and co-authors surveyed ten companies with 144,400 employees and integrated medical and pharmacy claims data with self-reported data on absenteeism and presenteeism to get a measure of the “full cost” of health. The Health and Work Performance Questionnaire (HPQ) survey was used to get the self-reported data on absenteeism and presenteeism.
- Using this data the authors were able to rank the ten most costly health conditions.

Source: Loeppke et al.

Annual Costs per 1000 FTEs by Health Condition



Source: Loeppke R, et al., pp. 140-152. Results of survey of 10 companies with 144,400 employees from the following business sectors: manufacturing, telecom, hospitality, energy, consulting and insurance.

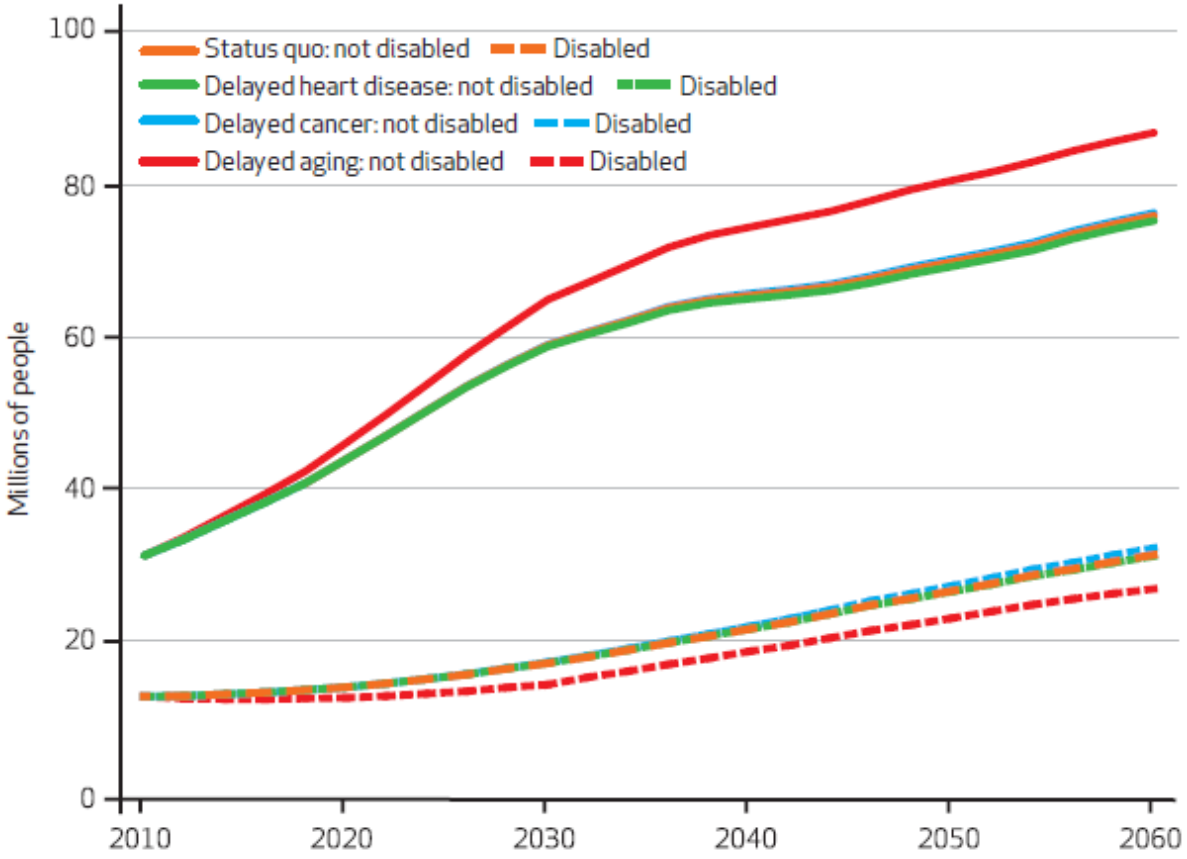
The Value of Delayed Aging

- Most medical research is still focused on fighting specific diseases, but investment in research to delay aging could yield greater benefits.
- Delayed aging could lead to an increase of life expectancy of 2.2 years resulting in an economic value of $7.1 trillion over fifty years.
- The $7.1 trillion figure is calculated by looking at the present discounted value of additional quality adjusted life years from delayed aging. The authors use a (relatively) conservative value of $100,000 per QALY.
- Although the social return is large, delayed spending would increase entitlement spending.

Source: Dana Goldman et. al, Health Affairs, 2013.

The Value of Delayed Aging

Millions Of Nondisabled And Disabled Elderly Americans In Various Scenarios, 2010–60



SOURCE Authors' calculations using the Future Elderly Model. **NOTES** The exhibit shows the number of elderly Americans (age sixty-five or older) projected to be either disabled or not disabled according to the various medical progress scenarios. *Disabled* is defined as having one or more limitations in instrumental activities of daily living, having one or more limitations in activities of daily living, living in a nursing home, or a combination of the three. The delayed aging scenario resulted in a substantially higher percentage and number of nondisabled people than the delayed heart disease or delayed cancer scenario.

Source: Dana Goldman et. al, Health Affairs, 2013.

Murphy and Topel: The Value of Health and Longevity

- Gains in life expectancy since 1900 were worth $1.2 million to a typical American in 2000.
- Gains since 1970 added $3.2 trillion annually to GDP.
- Future gains could be very large; for example, a permanent reduction of 1% in mortality from cancer has a present value for Americans of nearly $500 billion.
- Murphy and Topel value health improvements based on individuals' "willingness to pay". They distinguish between two types of health improvements: extension of life and improvement in quality of life. Life extension means that goods and leisure are enjoyed for a longer period of time. Improvements to quality life increase utility from goods and leisure. The framework allows for a calculation of the value of life years.
- The table on the next page shows the projected value of life-years gained from a 10% reduction in mortality from various diseases.
- The social value of a health advance from date t forward is calculated from the following equation:

$$W_\alpha(\tau) = \int_{a=0}^{\infty} N(a, \tau) V_\alpha(a) da + N^f(\tau) V_\alpha(0).$$

- $V_\alpha(a)$ based on value of a statistical life, spread over multiple ages

Source: Murphy and Topel, 2006

Murphy and Topel: The Value of Health and Longevity

TABLE 8
CURRENT VALUE OF A 10 PERCENT REDUCTION IN MORTALITY FROM MAJOR DISEASES
(Billions of 2004 Dollars)

MAJOR CAUSE OF DEATH	MALES (1)	FEMALES (2)	TOTAL (3)	COMPLEMENTARITY EFFECT Value (4)	COMPLEMENTARITY EFFECT Share (5)
All causes	$10,651	$7,885	$18,536	$3,278	.18
Cardiovascular diseases	$3,254	$2,471	$5,725	$1,288	.22
Heart disease	$2,676	$1,852	$4,529	$1,013	.22
Cerebrovascular diseases	$393	$460	$852	$194	.23
Malignant neoplasms	$2,415	$2,261	$4,675	$863	.18
Respiratory and intrathoracic	$847	$557	$1,404	$278	.20
Breast	$3	$444	$447	$51	.11
Genital and urinary	$301	$302	$603	$126	.21
Digestive organs	$575	$431	$1,006	$200	.20
All other infectious diseases	$500	$148	$649	$60	.09
Obstructive pulmonary disease	$343	$331	$674	$153	.23
Pneumonia and influenza	$214	$194	$408	$98	.24
Diabetes	$237	$249	$486	$91	.19
Liver disease and cirrhosis	$217	$102	$319	$46	.14
Accidents and adverse effects	$977	$421	$1,398	$133	.10
Motor vehicle accidents	$519	$247	$767	$62	.08
Homicide and legal intervention	$324	$90	$415	$29	.07
Suicide	$411	$102	$513	$50	.10

NOTE.—The social value of a 10 percent reduction in mortality from the indicated disease, calculated using eq. (18). Calculations use 2000 population values and census predictions of future birth cohorts, discounted at 3.5 percent.

Source: Murphy and Topel, 2006

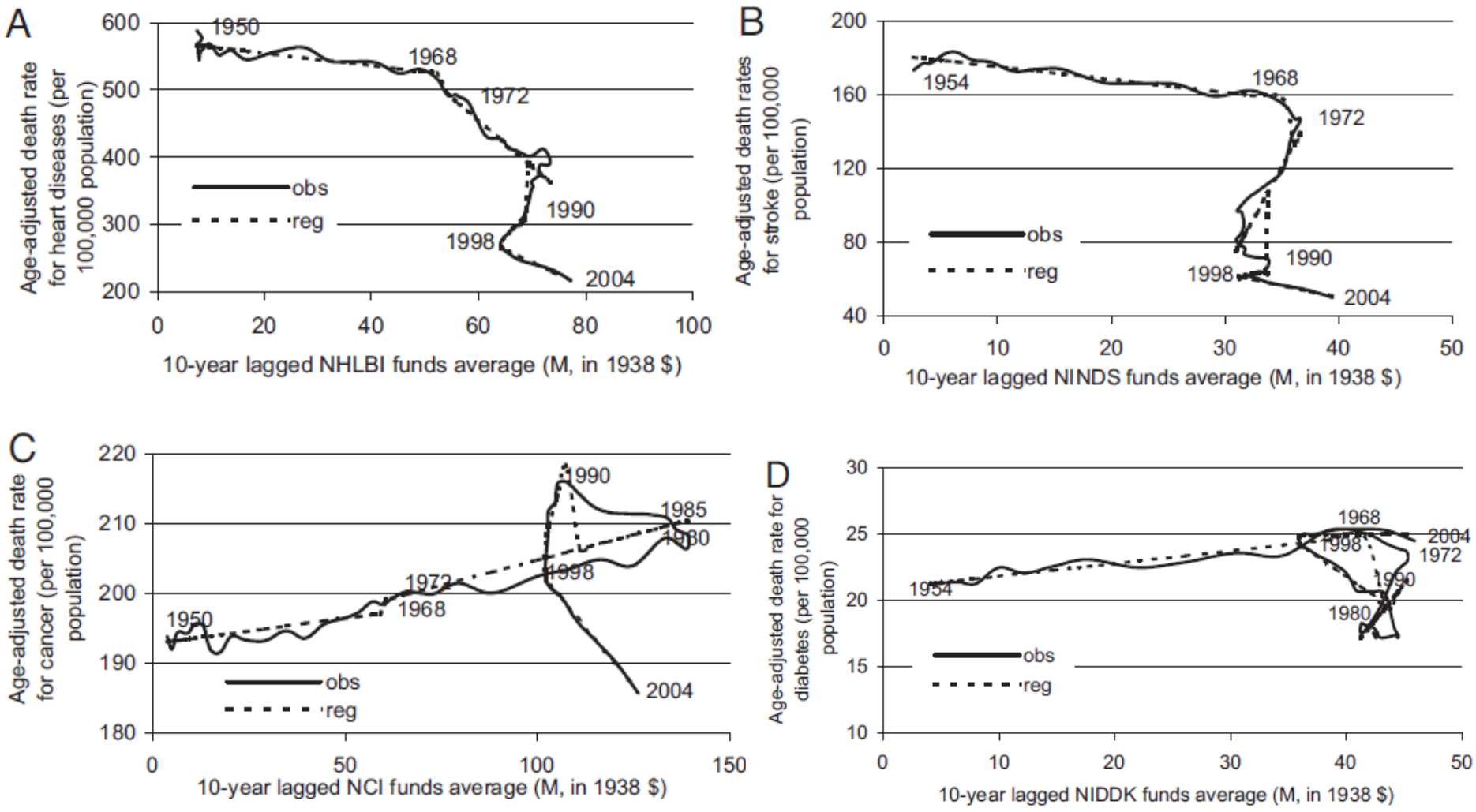
IMPACT OF BIOMEDICAL INNOVATION ON HEALTH

NIH Funding and US Health Dynamics

- Kenneth Manton and co-authors analyzed the longitudinal correlation between level of investment in NIH research and changes in the risk of certain diseases to the population. They look at four major chronic diseases: cardiovascular disease (CVD), stroke, cancer, and diabetes.
- They analyzed inflation adjusted annual expenditures for the relevant NIH institutes and age-adjusted mortality rates for the specific diseases. NIH expenditures were aggregated over a ten year window because the typical time between changes in NIH budgets and health effects is 10 to 15 years.

Source: Manton et. al, 2009

NIH Funding and US Health Dynamics



Source: Manton et. al, 2009

NIH Funding and US Health Dynamics

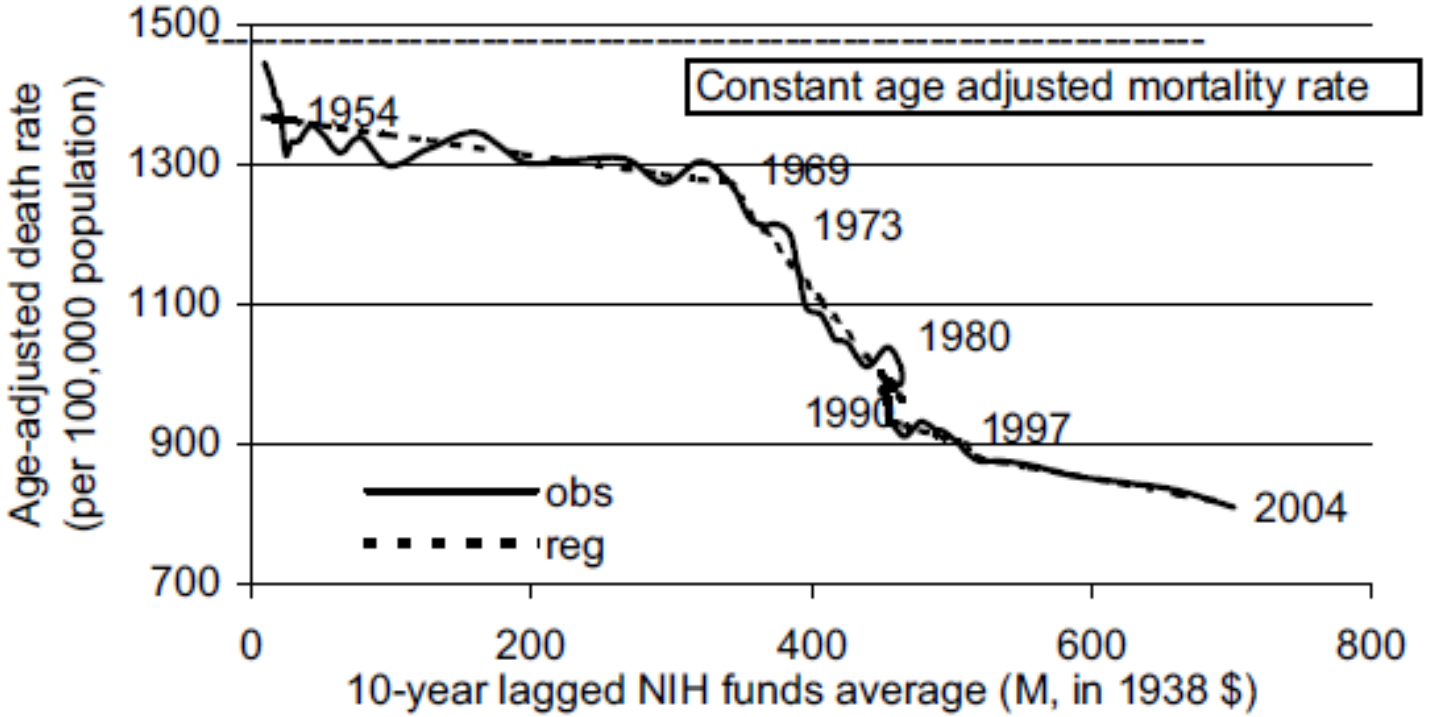


Fig. 4. Age-adjusted death rates as a function of 10-year lagged NIH funds average.

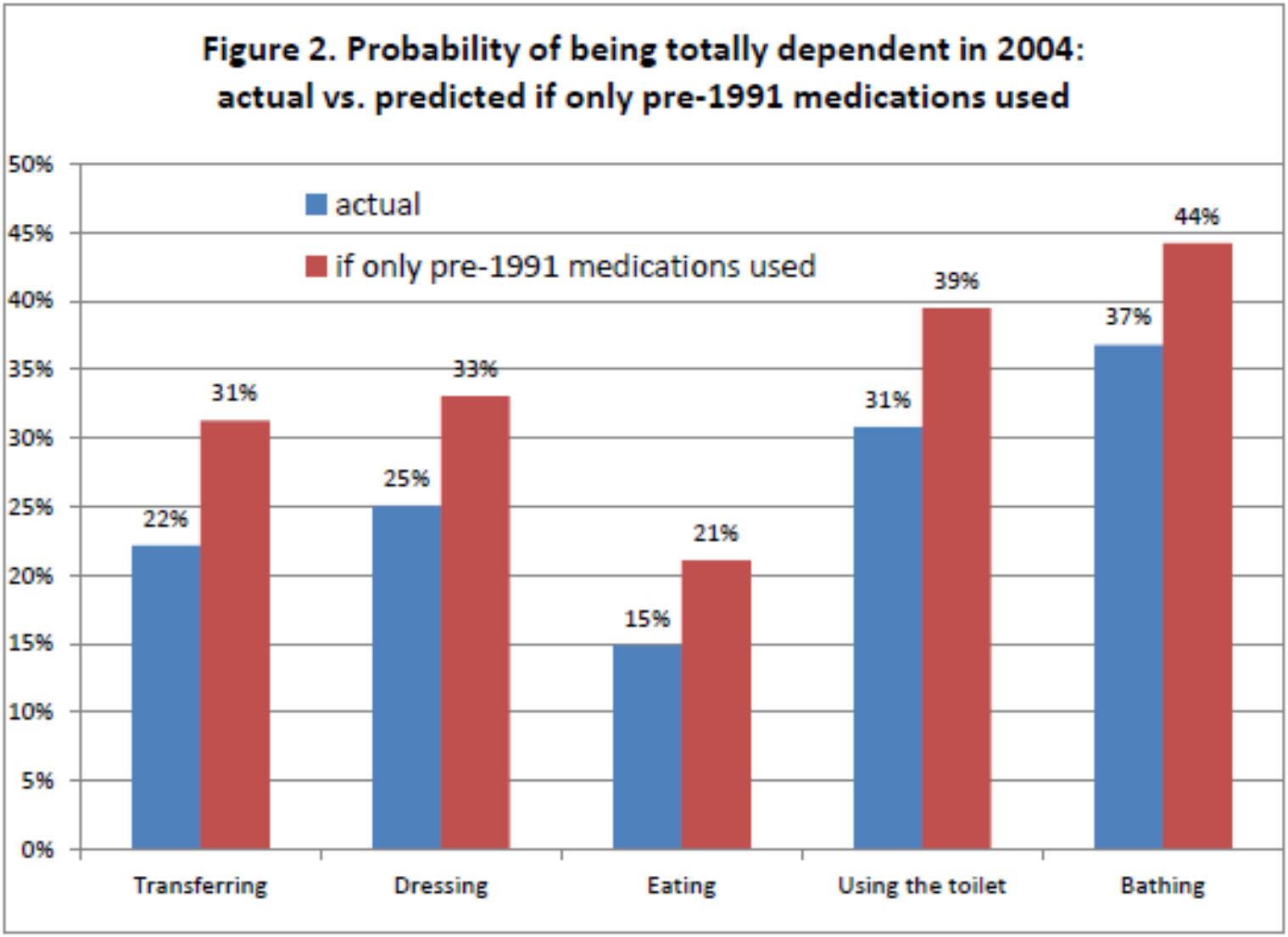
Source: Manton et. al, 2009

Pharmaceutical Innovation and Daily Living Activities

- Frank Lichtenberg analyzed cross-sectional, patient level data from the 2004 National Nursing Home Survey that contained information on medication use and functional status.
- Nursing home residents using newer medications and a higher share of priority review medications were more likely to be able to complete the five activities of daily living.
- Their ability to perform these five activities was positively associated with the number of new (post-1990) medications they take; it is unrelated to the number of old medicines they take.
- From 1990 to 2004, the functional limitations of nursing home residents was reduced by 1.2% to 2.1% per year.

Source: Lichtenberg, 2012

Pharmaceutical Innovation and Daily Living Activities



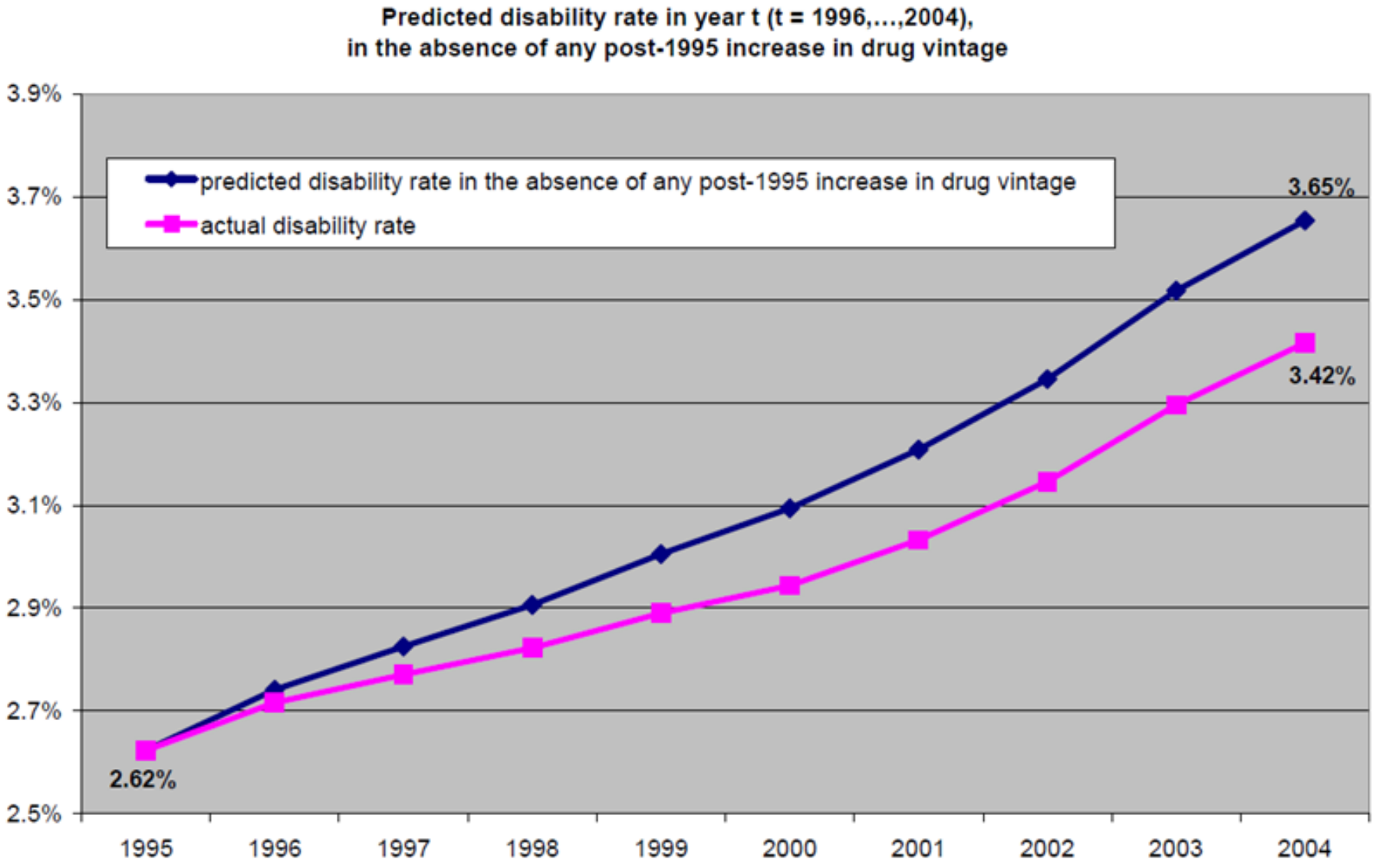
Source: Lichtenberg, 2012

Pharmaceutical Innovation and Disability

- Frank Lichtenberg used longitudinal state level data from 1995 to 2004 to study the impact of pharmaceutical innovation on disability. His measure of disability was the ratio of workers receiving disability insurance to the working age population. The author included drug vintage measures in his econometric model and found a consistent inverse relationship between disability and drug vintage.
- The increase in the share of workers receiving Social Security disability insurance would have been 30% larger if drug vintage (FDA approval year) had not increased since 1995. In 2004, 418,000 more workers would have been on DI costing $4.5 billion in additional Social Security benefits.

Source: Lichtenberg, 2011

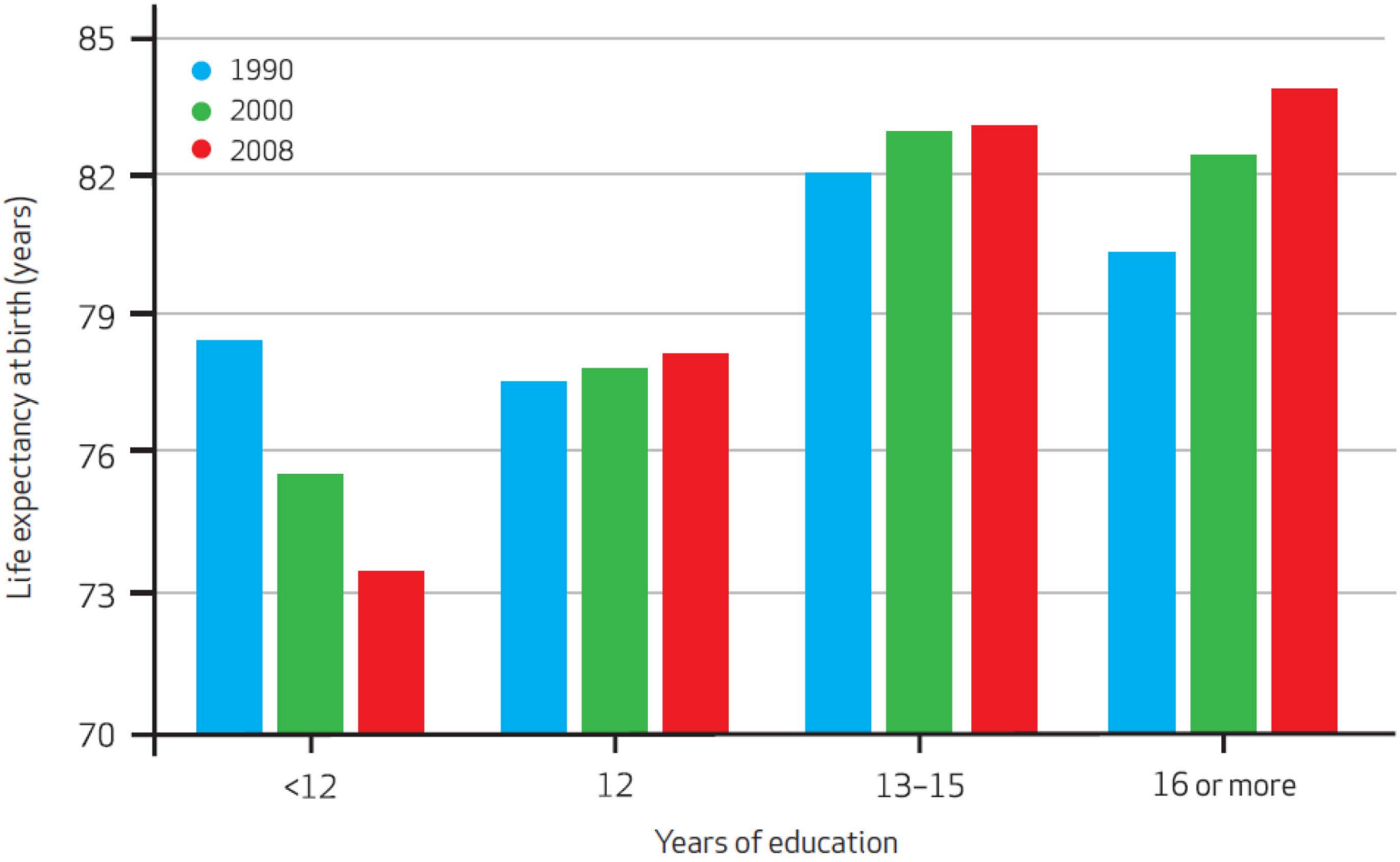
Pharmaceutical Innovation and Disability



Source: Lichtenberg, 2011

LIFE EXPECTANCY BY EDUCATION

Life Expectancy At Birth, By Years Of Education At Age 25 For White Females, 1990–2008



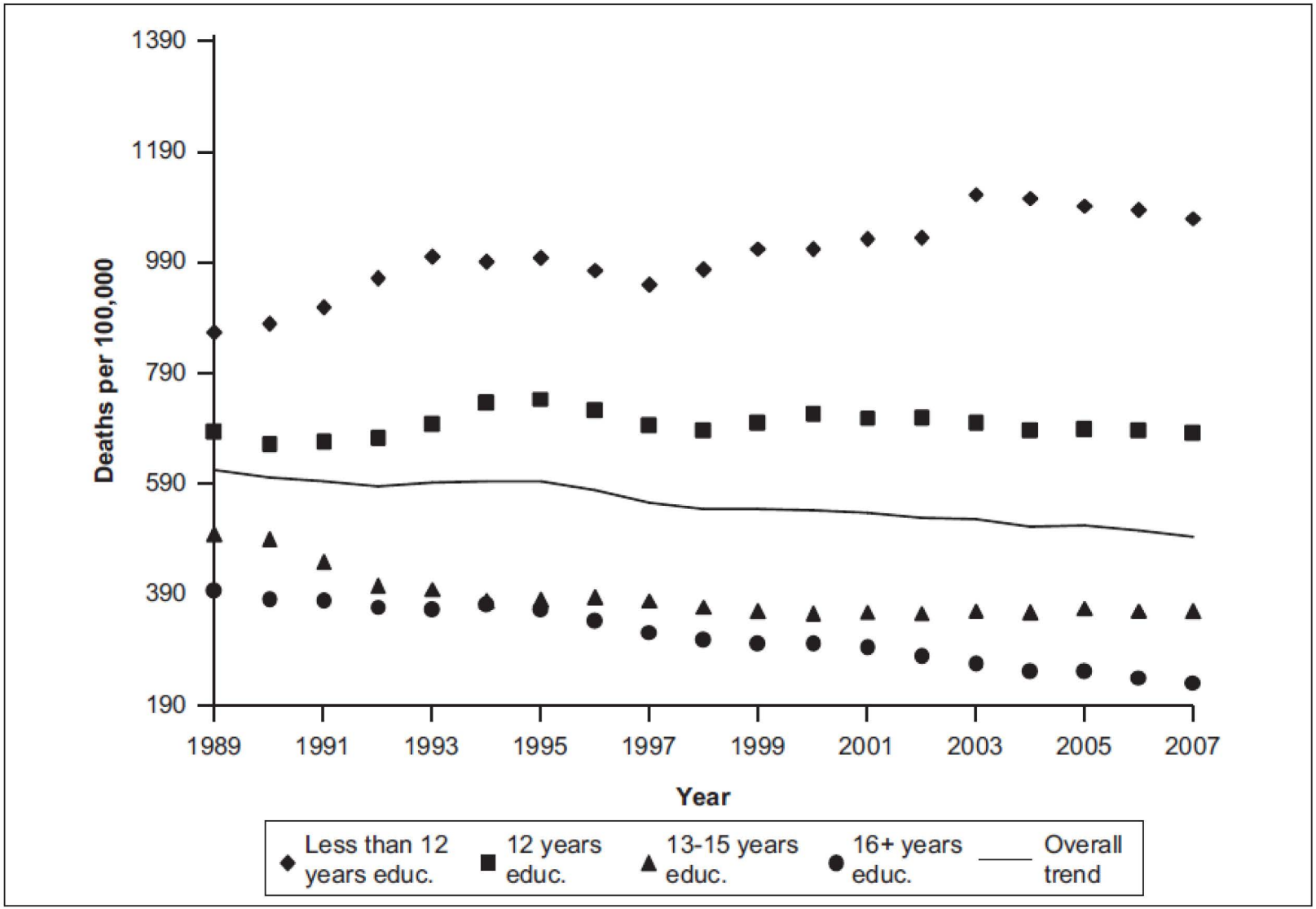
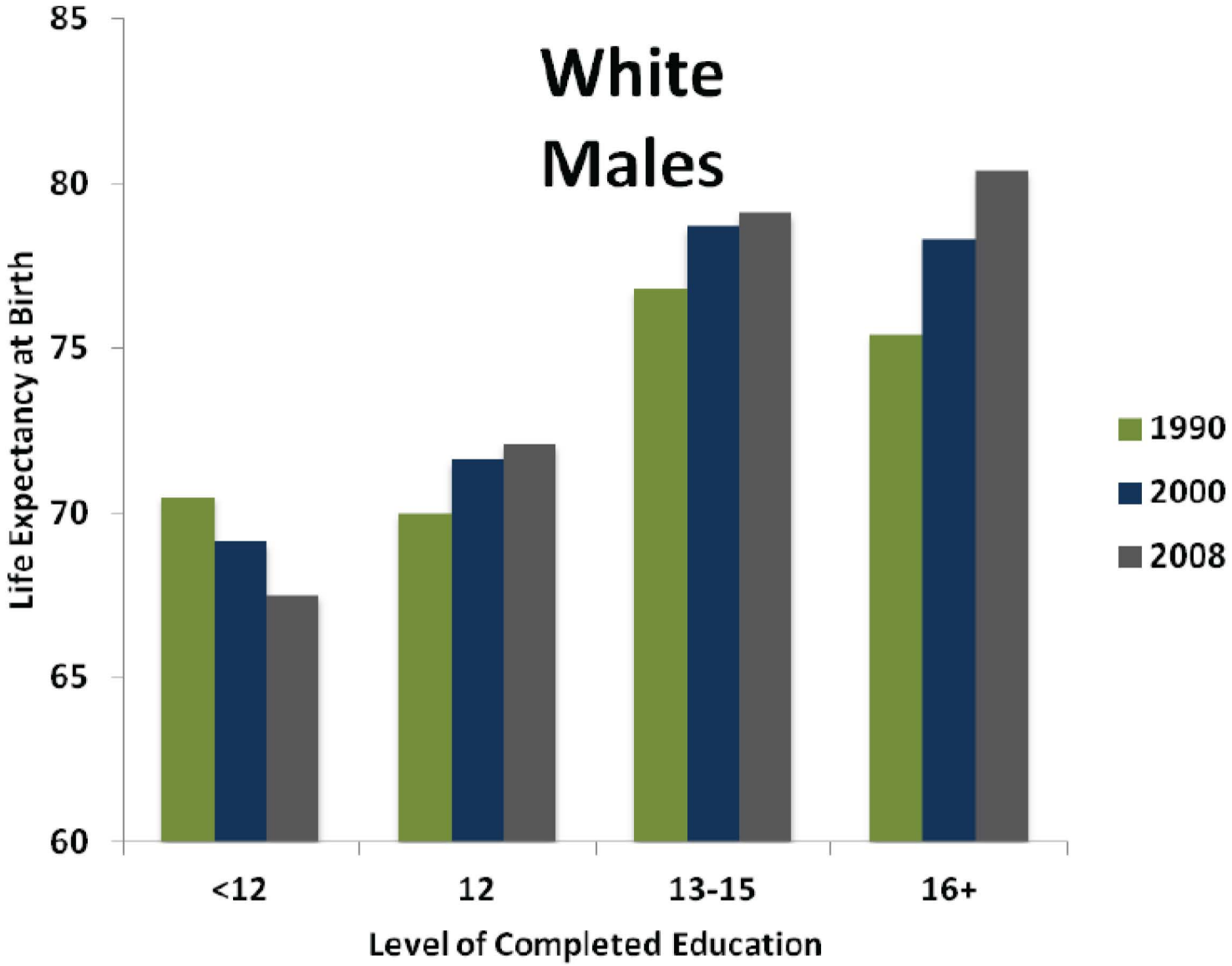


Figure 1. Trends in U.S. Mortality Levels by Education for Individuals Age 40 to 64 Years, 1989 to 2007


White
Males
85
80
75
70
65
60
Life Expectancy at Birth
<12
12
13-15
16+
Level of Completed Education
1990
2000
2008

The Accountability Conundrum for Biomedical Research

NIH Scientific Management Review Board

October 24, 2013

AAAS

ADVANCING SCIENCE, SERVING SOCIETY

Never Discuss Floods With Noah In the Audience

You have covered most of the major ways to demonstrate the value of biomedical research

- My thoughts surround an overlay of accountability demands on top of demonstrating overall value

The conundrum is that we tend to focus on overall value of our enterprise

- Many people are now asking for more granularity
  - Accountability at the level of “programs” or even individual grants

Start with the context in which all of this occurs….

- The societal context for science and technology

As Dickens might say…..

- The scientific enterprise is experiencing the best of times
- And some of the worst of times
  - That's an exaggeration
    - But things are pretty tough in some quarters

On the one hand

We're living in the best of scientific times

Advances in science are coming at a fantastic pace

- The rate of incremental advance is accelerating
- New technologies are enabling quantum jumps in understanding
  - With great practical significance
- “Transformative” or “breakthrough” research is getting (somewhat) easier to get funded

Science and technology have never been more important or prominent in modern life

Some major global societal issues

- Environmentally sustainable development
- Need for renewable energy sources
- Information and communications technology
- Universal access to education
- Poverty and economic opportunity
- Technology-based manufacturing and jobs
- Intellectual property rights
- Terrorism
- International security
- Natural disasters
- Science and technology capacity building
- Vaccines and medical therapies against infectious diseases
- Quality and accessibility of health care

Corollaries:

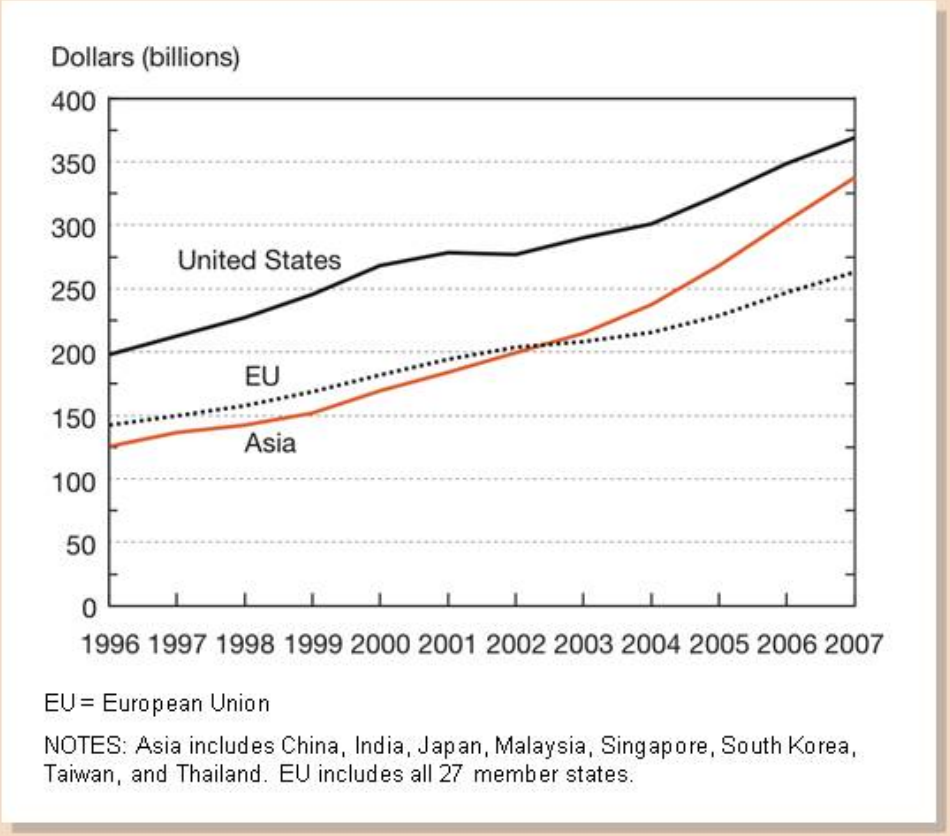
- For people to prosper in modern society, they need fundamental understanding and comfort with S&T
- For nations to prosper they need
  - Scientific capacity
  - National policies that reflect the best science
- For science to prosper, the science-society relationship must be positive and strong

More and more countries are investing in science and building a *national* science enterprise

The motivation is typically tied to

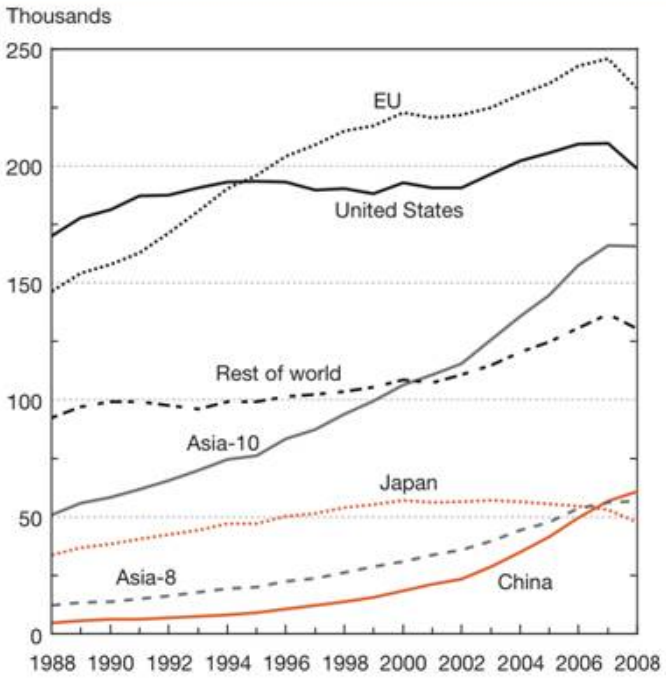
- Solving local problems
- Overall health and quality of life of their people
- Innovation and the economy

R&D expenditures for United States, EU, and Asia: 1996–2007



SOURCE: National Science Board, *Science and Engineering Indicators 2010*

S&E journal articles produced by selected regions/countries: 1988–2008



EU = European Union

NOTES: Asia-8 includes India, Indonesia, Malaysia, Philippines, Singapore, South Korea, Taiwan, and Thailand. Asia-10 includes Asia-8 plus China and Japan. Internationally coauthored articles credited fractionally to authors' countries/locations. Counts for 2008 are incomplete.

SOURCE: National Science Board, *Science and Engineering Indicators 2010*

Conclusion: Science is going on in more and more parts of the world

- The distribution and balance are shifting

Is this globalization good or bad?

- If you're particularly nationalistic – no!
  - US is no longer #1 in every area of S&T
- On the other hand
  - "Science anywhere is good for science everywhere"

NSF Director, Subra Suresh, 2012

In general, things are going extremely well

- So what's the problem?

The scientific enterprise is experiencing some significant turbulence

An array of forces are converging to make the overall climate for science rocky, at best

- And these are contributing to more and more calls for “accountability”
  - More than just showing the value of the enterprise

Some of the forces are *internal* to science…

An array of issues *within* science are not going so well…and negatively affect the broader (societal) context for science

- Incidents of scientific misconduct
- Human subjects concerns
- Animal welfare issues
- Conflict of interest problems
- Publishing by press release
- Hyperbolic or exaggerated claims
- Appearing to suppress dissenting views
- Mistakes in scientific papers

We need to ensure our house is in order!

These are factors *internal* to science

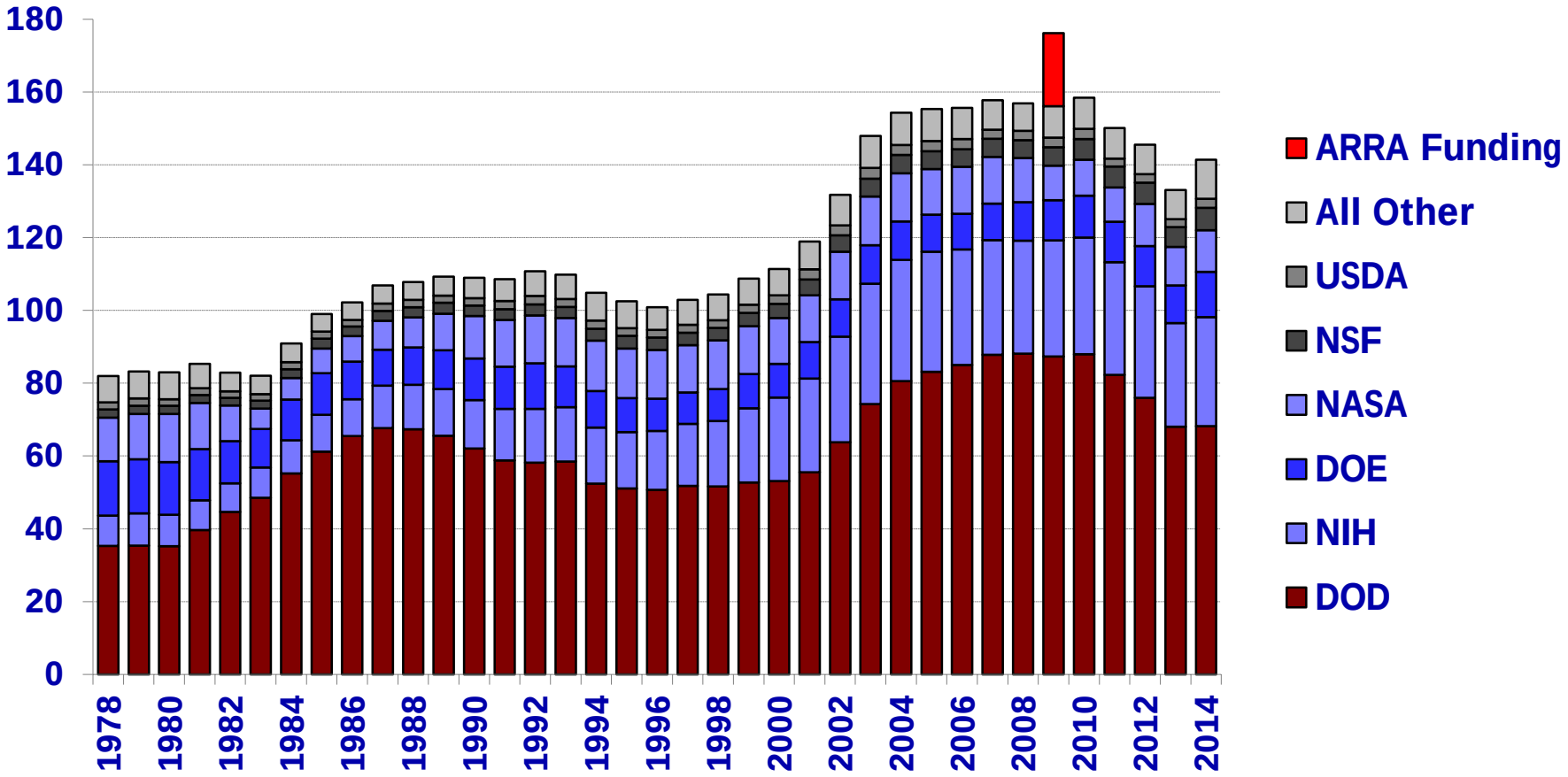
- There are *external pressures* as well
  - Not all are bad
    - But shouldn't be ignored

Funding is the BIG external factor

- Prospects are iffy at best

Trends in R&D by Agency

in billions of constant FY 2013 dollars



Source: *AAAS Report: Research & Development* series.
FY 2013 and FY 2014 figures are latest estimates.
1976-1994 figures are NSF data on obligations in the Federal Funds survey.
© 2013 AAAS

Other factors are making things tough

- American eminence in some fields is at risk

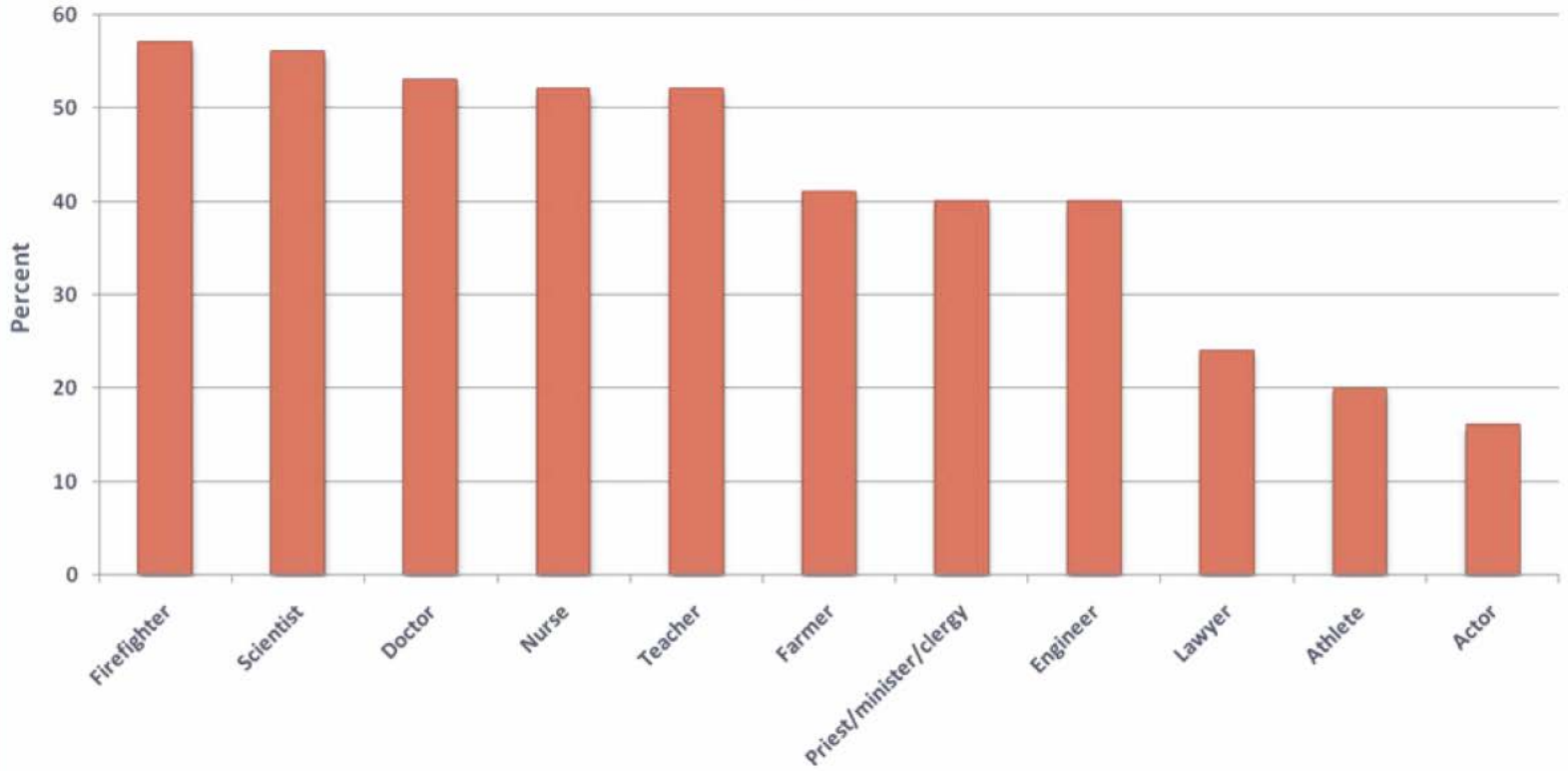
Losing eminence can have consequences

- Fewer foreign students coming to the US
- Potential brain drain of American scientists(?)
- Fewer US-based science and technology breakthroughs
- Fewer US start-up companies and jobs
- Loss of public respect and trust

The broader science-society relationship is not so smooth

People generally still respect science and technology….

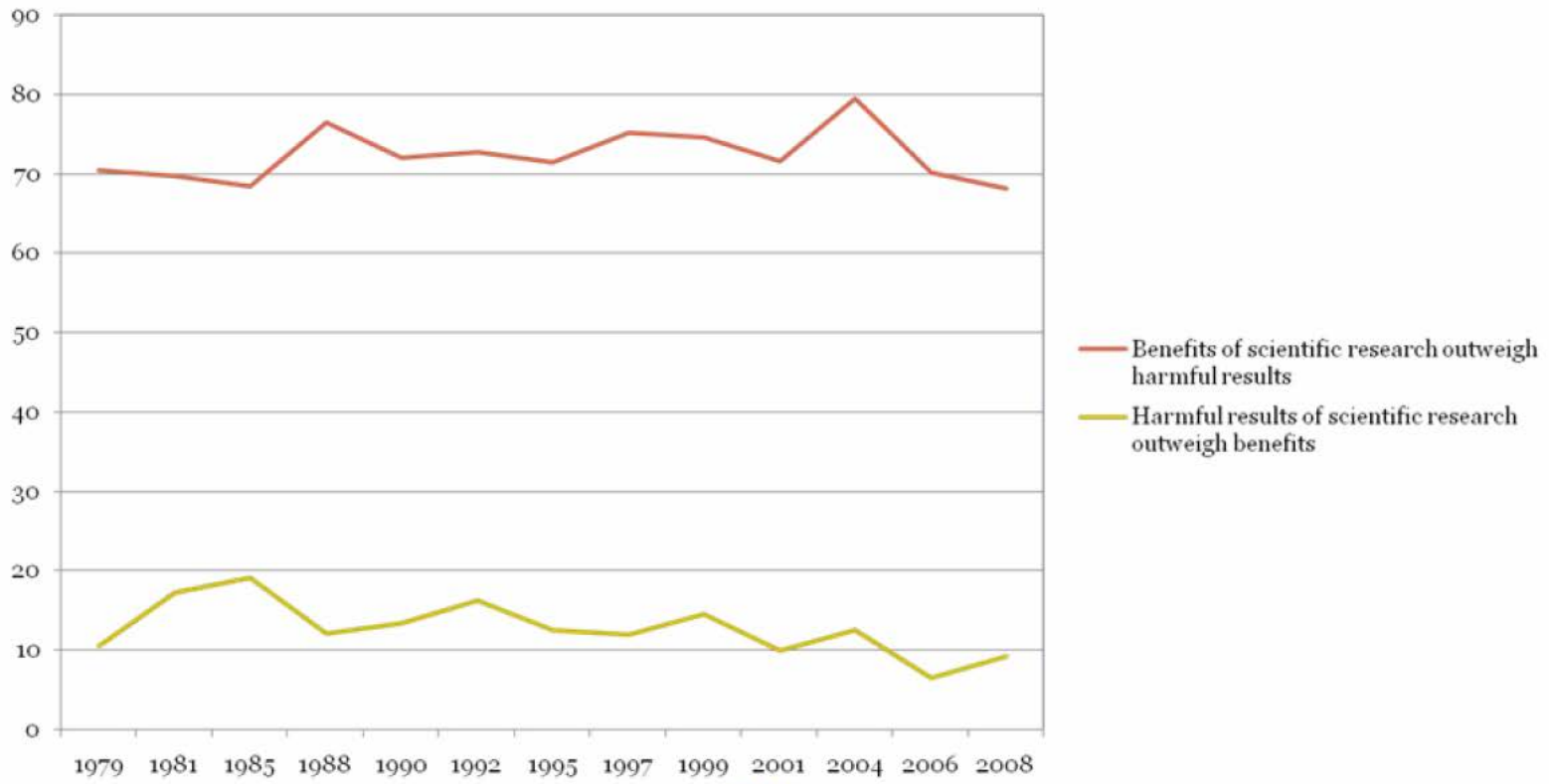
Prestige of Scientists and Engineers



Science and Engineering Indicators 2010

www.nsf.gov/nsb/sei/

Public Attitudes Toward Scientific Research



Science and Engineering Indicators 2010

They have little understanding of what is and is not science

- 60% of Americans believe in extrasensory perception
- 47% still do not answer "*true*" to the statement: "Human beings developed from earlier species of animals"
- 41% think astrology is somewhat scientific

Science and Engineering Indicators, 2004

Science-society tension can result from

- Widespread misunderstanding
  - Vaccines and autism
  - GMO's
- Political or economic inconvenience
  - Climate change
- Conflict with peer group beliefs
- Conflict with core human values

Only scientists are stuck with what science says

- The rest of the public can disregard, deny, or distort findings
  - With relatively little immediate consequence

This science-society tension has consequences

- Science is less able to serve societal needs
- Society wants to exert influence on what science is (or is not) done
- Public support of science is undermined
- Public trust of science seems to be weakened

And is contributing to increasing calls for value and accountability

- “What are we getting for all that money?”
- “What are we getting for that (big) grant?”

Traditional measures of scientific productivity don't satisfy most constituents

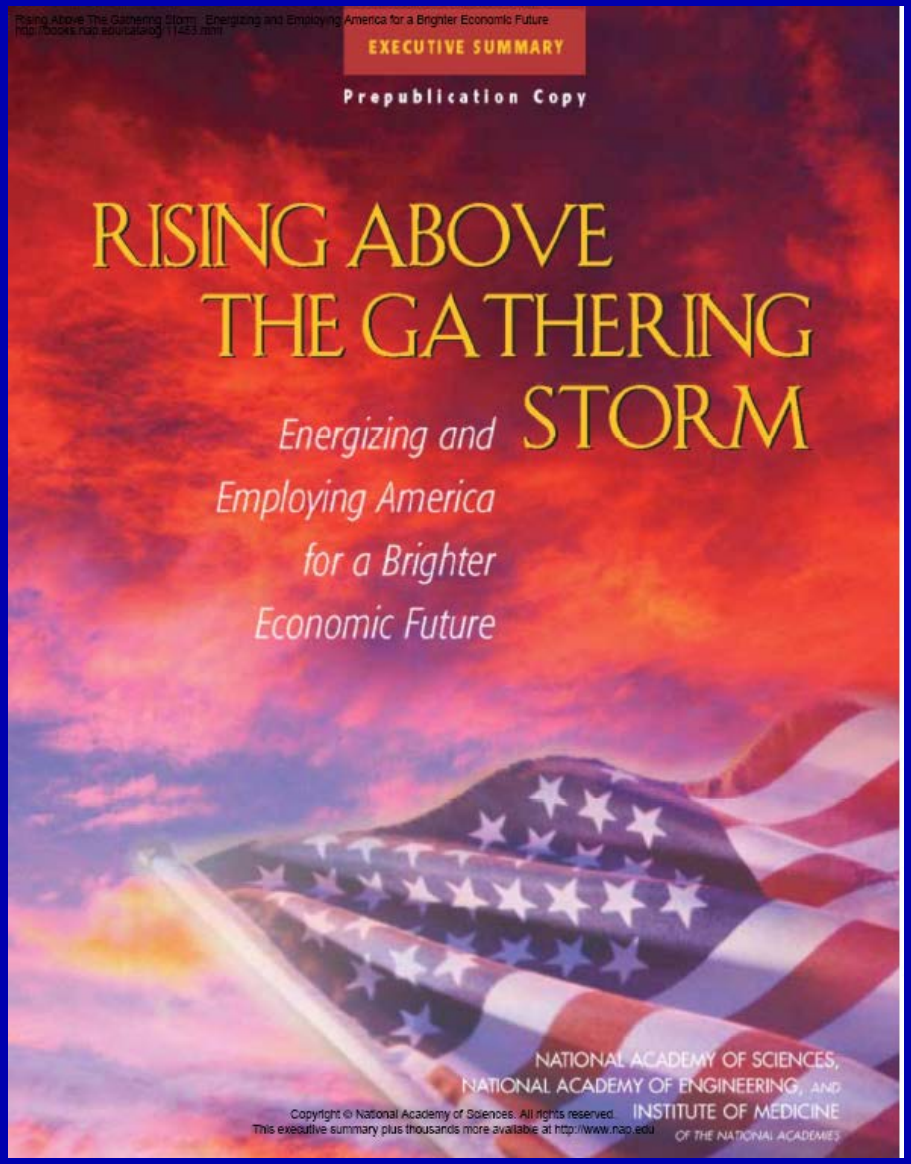
- Number of grants
  - E.g.,Number of R01s tied to Centers
- Numbers of publications
- Number of citations
- Impact factors

“Tracebacks” often generalize (with examples) about contributions of the enterprise

- Economic growth and competitiveness
- National security
- Health of the public

“Traceback studies” only help minimally

- They’re the norm for the arguments
  - But only go so far
  - Can’t account on an individual or program level


Rising Above The Gathering Storm: Energizing and Employing America for a Brighter Economic Future
http://books.nap.edu/catalog/11463.html
EXECUTIVE SUMMARY
Prepublication Copy
RISING ABOVE THE GATHERING STORM
Energizing and Employing America for a Brighter Economic Future
NATIONAL ACADEMY OF SCIENCES,
NATIONAL ACADEMY OF ENGINEERING, AND
INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES
Copyright © National Academy of Sciences. All rights reserved.
This executive summary plus thousands more available at http://www.nap.edu

"Traceback studies" don't seem to be convincing enough

- Many stakeholders now want to be assured that every grant (or grant program) will have impact

That philosophy led to

- America COMPETES Act
  - Called on NSF to develop a Broader Impacts criterion for proposal review and funding
- Could well happen to NIH

Sec. 526 of America COMPETES Reauthorization Act of 2010

- Instructs NSF to have a Broader Impacts review criterion for every grant to address one or more of several societal goals:
  - Increased economic competitiveness of the United States.
  - Development of a globally competitive STEM workforce.
  - Increased participation of women and underrepresented minorities in STEM.
  - Increased partnerships between academia and industry.
  - Improved pre-K-12 STEM education and teacher development.
  - Improved undergraduate STEM education.
  - Increased public scientific literacy.
  - Increased national security.

NSF's Merit Review Criteria: Review and Revisions

A Report of the National Science Board

Broader Impacts Criterion

- Strengths:
  - Ensures the connection between scientific research and society

- Weaknesses:
  - Guidance is very unclear on:
    - Expectations for nature of, and support for, proposed activities
    - How to review the proposed activities

Three Merit Review Principles

1. All NSF projects should be of the highest quality and have the potential to advance, if not transform, the frontiers of knowledge.

2. NSF projects, in the aggregate, should contribute more broadly to achieving societal goals. These "Broader Impacts" may be accomplished through the research itself, through activities that are directly related to specific research projects, or through activities that are supported by, but are complementary to, the project.

Three Merit Review Principles (continued)

3. Meaningful assessment and evaluation of NSF funded projects should be based on appropriate metrics, keeping in mind the likely correlation between the effect of broader impacts and the resources provided to implement projects. If the size of the activity is limited, evaluation of that activity in isolation is not likely to be meaningful. Thus, assessing the effectiveness of these activities may best be done at a higher, more aggregated, level than the individual project.

How did that work out?

- We're not sure yet
- Draft of the "High Quality Research Act"
  - Asked NSF Director to certify every grant is relevant to
    - National Security
    - Economic competitiveness
    - Health of the public
- Reauthorization of America COMPETES is now on the table

Not just happening in the US

- RC-UK asks scientists to delineate impact plans
  - Plus pathways to impact
    - How help the beneficiary benefit
  - RC will help pay to make the impacts happen

Will this level of accountability be asked of biomedical research?

- While we are worrying the “value of biomedical research”
  - Should we be worrying more about showing the value of specific research projects and programs?

Should we be better attending to pressures on other fields of science?

- And view “value” in a much narrower sense than we have traditionally

We can no longer get away with asserting productivity by citing

- Traditional scientific productivity standards
- Examples of historical (traceback) outcomes

We need to better articulate concrete outcome measures for

- Contributions to the progress of science
- Improvements in health care and health practice

And then evaluate “programs of research” against them

- Hopefully we can avoid greater granularity

There's a growing community of scholars working on this set of issues

- NSF's Science of Science Policy

Should this approach be more formalized for biomedical research?

Overview of Private Funder Approaches: The Health Research Alliance

Kate Ahlport

Executive Director, HRA

Scientific Management Review Board Meeting

October 24, 2013

HRA Member Organizations

- AACR Foundation for the Prevention and Cure of Cancer
- Alzheimer's Association
- Alzheimer's Drug Discovery Foundation
- American Brain Tumor Association
- American Cancer Society
- American Diabetes Association
- American Federation for Aging Research
- American Heart Association
- Arthritis Foundation
- Autism Speaks
- Avon Foundation for Women
- The Breast Cancer Research Foundation
- Burroughs Wellcome Fund
- Cancer Research Institute, Inc.
- Children's Tumor Foundation
- Conquer Cancer Foundation of ASCO
- CURE | Citizens United for Research in Epilepsy
- Damon Runyon Cancer Research Foundation
- The Donaghue Foundation
- Doris Duke Charitable Foundation
- The Ellison Medical Foundation
- The Flinn Foundation
- Fondation Leducq
- Foundation Fighting Blindness, Inc.
- The Gerber Foundation
- Heart Rhythm Society
- The Leona M. & Harry B. Helmsley Charitable Trust
- Howard Hughes Medical Institute
- Hydrocephalus Association
- Iacocca Family Foundation
- JDRF
- W. M. Keck Foundation
- The Klarman Family Foundation
- Susan G. Komen for the Cure
- Leukemia & Lymphoma Society
- LUNGevity Foundation
- Lupus Foundation of America
- Lymphoma Research Foundation
- March of Dimes Foundation
- The Medical Foundation, *a division of Health Resources in Action*
- Melanoma Research Alliance
- MPN Research Foundation
- Mt. Sinai Health Care Foundation
- Multiple Myeloma Research Foundation
- New York Stem Cell Foundation
- Pancreatic Cancer Action Network
- Parent Project Muscular Dystrophy
- Parkinson's Disease Foundation
- Patient-Centered Outcomes Research Institute (PCORI)
- The Pew Biomedical Programs
- Physicians' Services Incorporated Foundation
- Rheumatology Research Foundation
- Rita Allen Foundation
- Simons Foundation
- Samuel Waxman Cancer Research Foundation

Membership as of October, 2013

HRA Mission Statement

HRA member organizations work together to maximize the impact of investment in biomedical research and training to improve human health.

Strategies by which HRA achieves its mission:

The Health Research Alliance brings together not-for-profit, non-governmental funders of biomedical research and training committed to supporting and enhancing the continuum of biomedical research and training to:

- Foster open communication and collaboration among members.
- Provide comprehensive data and analysis about the funding of biomedical research and training by HRA members.
- Identify gaps in funding and facilitate innovative grantmaking.
- Address issues key to accelerating research discovery and its translation.

Diversity of HRA Membership

- Large voluntary health organizations:
  - American Cancer Society
  - American Diabetes Association
  - American Heart Association
- Private foundations:
  - Burroughs Wellcome Fund
  - Doris Duke Charitable Foundation
  - Simons Foundation
- Disease-specific public charities:
  - Foundation Fighting Blindness
  - Melanoma Research Alliance
  - Multiple Myeloma Research Foundation

SMRB questions for funders:

- How does your organization set goals?
- How does your organization assess whether it is meeting its goals?
- How does your organization communicate the results of assessments to stakeholders and the public?

Challenges recognized by the HRA membership:

- Length of the “translation lag:”
  - Of 101 promising claims in major basic science journals of new discoveries with clear clinical potential, only 5 had resulted in interventions with licensed clinical use 10 years later
    - *Ioannidis D et al (2008). “Life Cycle of Translational Research for Medical Interventions,” **SCIENCE**. 321, 1298-99.*
- Difficulty of attributing success to one specific award/funding stream

Challenges recognized by the HRA membership:

- No ideal comparison group for awardees:
  - Unsuccessful applicants to same award program
  - Matched applicants or awardees from another organization
- Difficulty disentangling the effects of selection bias – what accounts for differences in outcomes:
  - The difference in the awardee group (those selected are in fact different from those not selected), OR
  - The award itself

Traditional approach for career development awards:

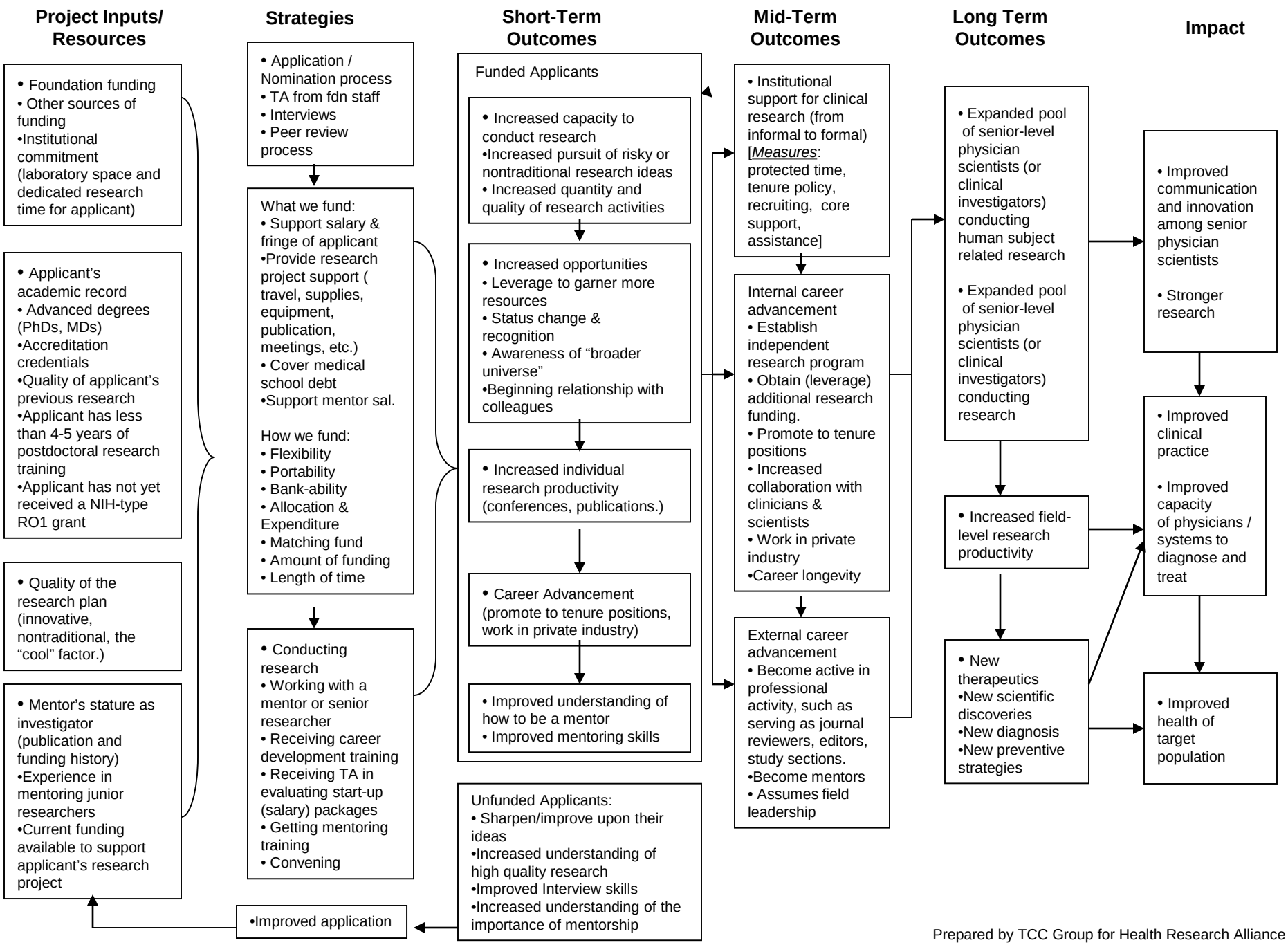
- Comparison group: highly-ranked but unsuccessful applicants (same funder)
- Intermediate/proxy outcome measures:
  - Scientific productivity (publications & citations)
  - Research support (external funding received)
  - Current faculty position (institutional prestige, tenure status)

- *Mavis B and Katz M (2003). "Evaluation of a Program Supporting Scholarly Productivity for New Investigators."* ***Academic Medicine.*** *78(7), 757-765.*

Traditional approach for career development awards – other examples:

- Leukemia & Lymphoma Society
  - *Lichtman MA and Oakes D. (2001). The productivity and impact of the Leukemia & Lymphoma Society Scholar Program: the apparent positive effect of peer review.* ***Blood Cells Mol Dis****. 27(6): 1020-7.*
- Burroughs Wellcome Fund
  - *Pion G and Ionescu-Pioggia M. (2003). Bridging postdoctoral training and a faculty position: Initial outcomes of the Burroughs Wellcome Fund Career Awards in the Biomedical Sciences.* ***Academic Medicine****. 78(2), 177-186.*
  - *Pion G and Cordray DS. (2008). The Burroughs Wellcome Career Award in the Biomedical Sciences: Challenges to and Prospects for Estimating the Causal Effects of Career Development Programs.* ***Eval Health Prof****. 31, 335-369.*
- Doris Duke Charitable Foundation
  - *Escobar-Alvarez S and Myers E. (2013). The Doris Duke Clinical Scientist Development Award: Implications for Early-Career Physician Scientists.* ***Academic Medicine****. 88(11), 1-7.*

DRAFT Career Development Award Logic Model



Prepared by TCC Group for Health Research Alliance

“Evolved” Consensus

- Accept that we will never be able to disentangle whether success is due to:
  - Picking the best candidates OR
  - Characteristics of the award itself
- Accept that we will never be able to attribute success to a specific funder/funding stream with full certainty
- Monitor/track awardees to insure they are doing what they promised to do
- Decide on acceptable proxy measures for outcome and impact

Howard Hughes Medical Institute

- **A science philanthropy whose mission is to advance biomedical research and science education for the benefit of humanity.**
- $7.1 billion invested in research and science education since 2003
  - $695 million for research and research support in 2012
  - $114 million for science education, international research in 2012
- Current endowment of $16.1 billion

HHMI Board of Trustees

Kurt L. Schmoke, Esq., Chairman. Dean, Howard University School of Law

James A. Baker, III, Esq., Senior Partner, Baker Botts L.L.P.; former U.S. Secy. of State

Ambassador Charlene Barshefsky, Esq.,Senior International Partner Wilmer Hale

Susan Desmond-Hellman, M.D.,M.P.H., Chancellor, University of California, San Francisco

Joseph L. Goldstein, M.D., Regental Professor and Chairman, Department of Molecular Genetics, University of Texas Southwestern Medical Center at Dallas

Garnett L. Keith, Chairman,SeaBridge Investment Advisors, L.L.C.; Former Vice Chairman and Chief Investment Officer, The Prudential Insurance Company of America

Fred R. Lummis, Chairman and CEO, Platform Partners LLC

Sir Paul Nurse, F.R.S., President, The Royal Society, Director,The Francis Crick Institute

Dame Alison Richard, Ph.D., Senior Research Scientist and Professor Emerita, Yale University

Clayton S. Rose, Ph.D., Senior Lecturer of Business Administration, Harvard University; Former Head of Global Investment Banking, J.P. Morgan & Co.

Anne M. Tatlock, Director, Retired Chairman and CEO, Fiduciary Trust Company International

Senior Scientific Leadership

Robert Tjian, Ph.D.
President, HHMI
and
Professor of Biochemistry &
Molecular Biology
University of California-Berkeley

Gerald M. Rubin, Ph.D.
Vice President and Director,
Janelia Farm Research Campus

Erin O'Shea, Ph.D.
Vice President and Chief Scientific Officer, HHMI
and
Paul C. Mangelsdorf Professor,
Molecular and Cellular Biology,
and Chemistry and Chemical Biology
Harvard University

Sean Carroll, Ph.D.
Vice President for
Scientific Education, HHMI
and
Allan Wilson Professor of Molecular Biology, Genetics, and Medical Genetics
University of Wisconsin-Madison

Medical Advisory Board: A Committee Guiding Scientific Review and Policy

David Baltimore, Ph.D.
President Emeritus and Robert Andrews Millikan Professor of Biology
California Institute of Technology

J. Michael Bishop, M.D.
Director, G.W. Hooper Foundation and University Professor
University of California, San Francisco

Michael Botchan, Ph.D.
Richard and Rhoda Goldman Distinguished Professor of Biochemistry and Co-Chair of the Department of Molecular and Cell Biology
University of California, Berkeley

Gerry Fink, Ph.D.
Herman and Margaret Sokol Professor
Whitehead Institute for Biomedical Research
Massachusetts Institute of Technology

Carol Greider, Ph.D.
Daniel Nathans Professor & Director
Molecular Biology & Genetics
Johns Hopkins University School of Medicine

Rowena Matthews, Ph.D.
G. Robert Greenberg Professor Emeritus of Biological Chemistry
and Research Professor Emeritus, Life Sciences Institute
University of Michigan

Elizabeth Nabel, M.D.
President
Brigham and Women's/Faulkner Hospitals, Boston

Janet Rossant, Ph.D., F.R.S.
University Professor of Molecular Genetics and of Obstetrics and Gynecology, University of Toronto
Chief of Research
The Hospital for Sick Children, Toronto

Phillip Sharp, Ph.D.
Institute Professor, Koch Institute for Integrative Cancer Research
Massachusetts Institute of Technology

Bruce Stillman, Ph.D., F.R.S.
President, Cold Spring Harbor Laboratory

Marc Tessier-Lavigne, Ph.D.
President, The Rockfeller University

Craig Thompson, M.D.
President and Chief Executive Officer
Memorial Sloan-Kettering Cancer

HHMI's Major Programs

- HHMI Investigators and Early Career Scientists
- Janelia Farm Research Campus
- International Research
- Science Education

HHMI Investigator Program

- "People, not
- Transformin
- High risk, hi
- Flexible, gen

HHMI Investigator Program

- Science department budget: ~$650M/year (exclusive of Janelia Farm)
- ~$1.4M per investigator, although the individual amounts vary
- 312 Investigators (12 others to be appointed in 2013)
- 40 Early Career Scientists
- 41 Janelia Farm Laboratory Groups
- 70 Host Institution Sites + Janelia Farm Campus

Strategies to maximize an HHMI investigator's impact

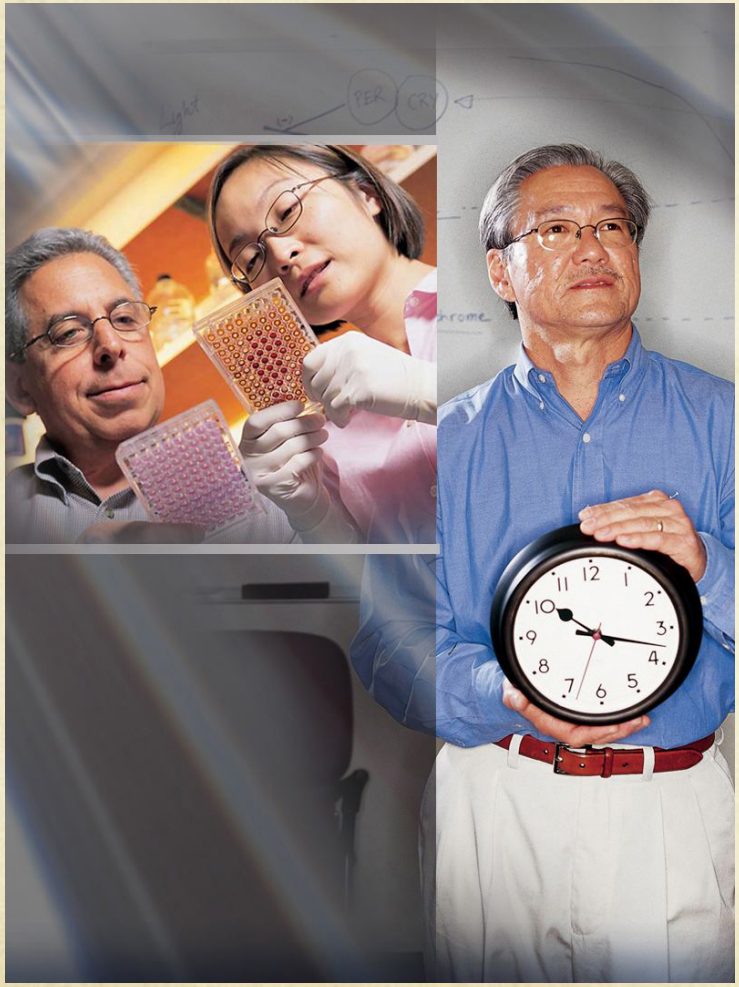
1. "People, not projects" - promote freedom to focus on projects driven by passion, incentive to emphasize creativity and a sense of responsibility to harness resources to study risky but high-impact questions
2. Minimize non-research requirements; 75% of time to be spent on "active conduct of research"
3. Provide extensive administrative, legal, operational and scientific assistance
4. Provide complete salary and benefits for investigators and other employees
5. Investigator controls generous budgets for laboratory personnel and supplies
6. Investigators can apply for equipment purchases during four rounds of capital funding annually
8. Annual scientific meetings foster critical review and scientific collaborations

Current Investigators	Year of Award
Susumu Tonegawa	1987
Thomas Cech	1989
Eric Wieschaus	1995
Gunter Blobel	1999
Eric Kandel	2000
Robert Horvitz	2002
Roderick MacKinnon	2003
Linda Buck	2004
Richard Axel	2004
Craig Mello	2006
Mario Capecchi	2007
Roger Tsien	2008
Jack Szostak	2009
Thomas Steitz	2009
Robert Lefkowitz	2012
Randy Shekman	2013
Thomas Sudhof	2013
And six alumni investigators	

Members of the National Academy of Science (NAS)

- as of 2013: 172 (out of 354 investigators and early career scientists)
- since 1994, HHMI investigators accounted for approximately
  - 19% of all new NAS members in the Life Sciences
- 65 members of the Institute of Medicine

A Model That Fosters Invention



- 2,477 inventions
- 1,270 active licenses
- 1,242 patents
- 976 pending patent applications
- 100+ startup companies
- As of 2012

Reviewing the HHMI Investigator

Does Our Review Process Retain Only the Best People?

"The most important single task that Jack Dixon and I have at HHMI is to review the reviewers."

Robert Tjian, President of HHMI

What are the criteria for an investigator review?

“The Howard Hughes Medical Institute expects not only that its investigators be talented and productive scientists, but also that they demonstrate some combination of the following attributes to an extent that clearly distinguishes them from other highly competent researchers in their field:

(1) They identify and pursue significant biological questions in a rigorous and deep manner.

(2) They push their chosen research field into new areas of inquiry, being consistently at its forefront.

(3) They develop new tools and methods that enable creative experimental approaches to biological questions, bringing to bear, when necessary, concepts or techniques from other disciplines.

(4) They forge links between basic biology and medicine.

(5) They demonstrate great promise of future original and innovative contributions.”

Scientific Review

The Review Process

- Reviews take place every 5 years; no review for ECS (a six year appointment)
- All reviewer panel votes are counted for each investigator
- No progress reports are required between formal reviews

The Reviewers:

- A mixture of experts in a specific field and “knowledgeable generalists”
- Especially important to include skilled evaluators of scientific talent
- Members of the Scientific Review Board, Medical Advisory Board and *ad hoc* distinguished scientists (*No HHMI Investigators participate in the review)*

HHMI Investigator Reviews
Materials Submitted in Advance of the Review Meeting

- *Curriculum vitae*.
- Bibliography, in reverse chronological order
- Information about all graduate students and postdoctoral fellows affiliated with the investigator's research group during the past 10 years
- Description of research performed during the current appointment term, as well as a description of future goals and plans
- PDF's of the five most significant publications during the current appointment term, and a statement describing the impact and significance of each publication
- Investigators are encouraged to update their laboratory web site as well as their HHMI public web site pages, well in advance of the review.

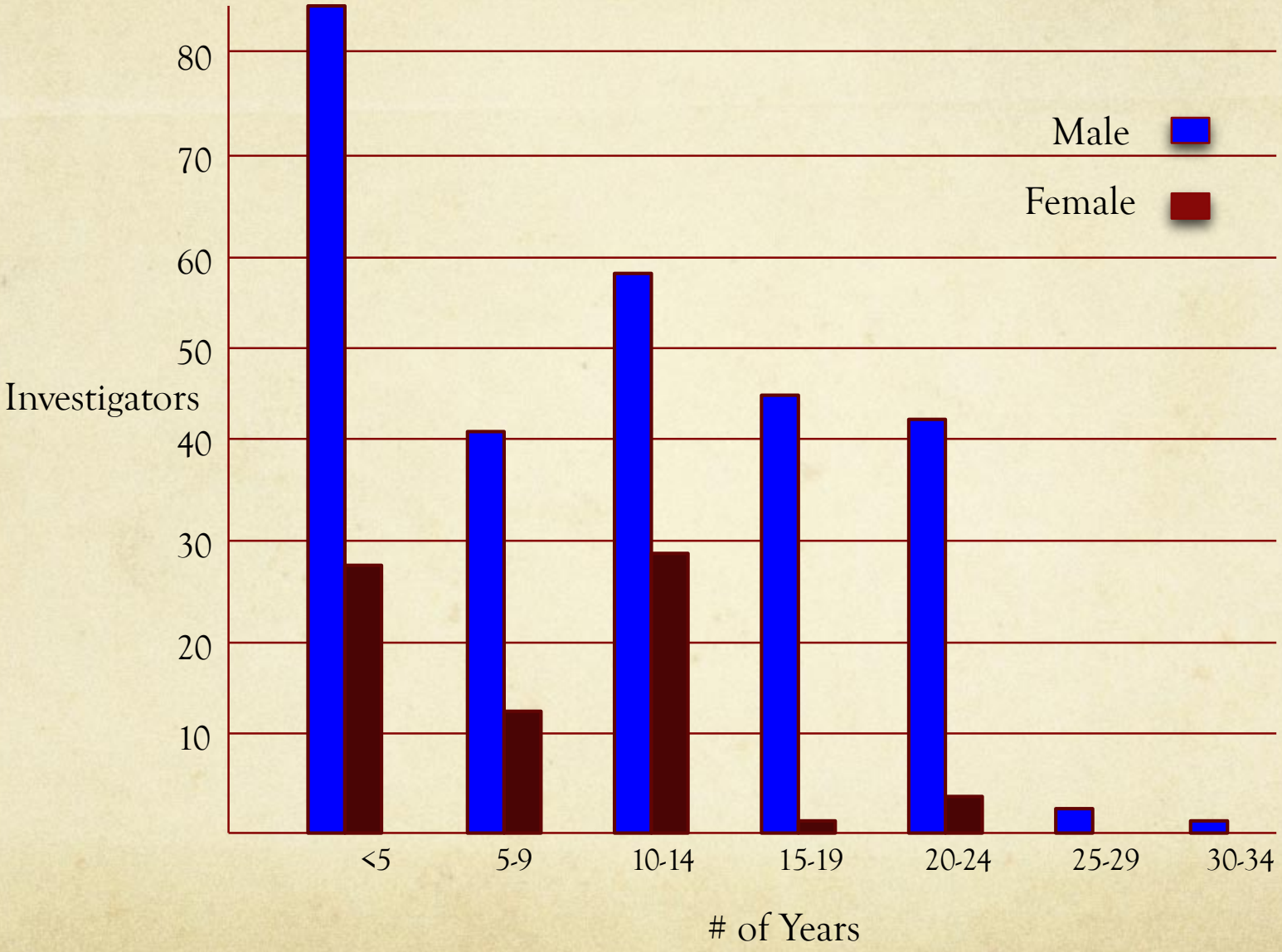
Review Meeting - at HHMI Headquarters in Chevy Chase, Maryland

- Investigator Presentation – 35 minutes
- Questions and Discussion – 20 minutes
- Executive Session and Development of Recommendation for Appointment
- Final Decision made by HHMI Science Department and the President
- For Reappointment for a Renewable Five-Year Term
- Or Nonrenewable Appointment for a Two-Year Term

Investigator Review Outcomes: 2000 – 2012

Year	# Reviews	# Terminated	% Terminated
2000	28	5	18
2001	36	7	19
2002	65	17	26
2003	67	16	24
2004	74	14	19
2005	58	6	10
2006	30	4	13
2007	60	7	12
2008	41	10	24
2009	48	10	21
2010	60	12	20
2011	59	10	17
2012	44	14	31
Total	**670**	**132**	**20**

2012: length of HHMI appointment periods



HHMI News

[October 6, 2013]

RNAi Protects Mice from Deadly Heart Condition

Summary

HHMI researchers have designed an inhibitor that can reduce the expression of the mutated gene that causes hypertrophic cardiomyopathy, a potentially fatal heart condition.

Highlights

- Hypertrophic cardiomyopathy is a potentially fatal disease that is caused by malformation of the heart muscle.
- In experiments in mice, HHMI researchers have shown that they could deliver RNAi to mice prone to developing hypertrophic cardiomyopathy.
- Mice receiving the RNAi were protected from disease for months.

When a young athlete dies suddenly on a sports field, the cause is more often than not hypertrophic cardiomyopathy, a genetic disease that leads to malformation of the heart muscle. Now, Howard Hughes Medical Institute (HHMI) researchers have designed an inhibitor that can reduce the expression of the mutated gene that causes the condition. When mice prone to hypertrophic cardiomyopathy received the inhibitor, they were protected from disease—and the associated cardiac electrical abnormalities—for months, the team reported October 4, 2013 in the journal *Science*.

"This is a really exciting opportunity to address the root genetic cause of a disease rather than the resulting symptoms," says Christine Seidman, an HHMI investigator at Brigham and Women's Hospital and senior author of the new study.

Hypertrophic cardiomyopathy (HCM) results from mutations in genes that encode components of myosin, proteins integral to heart muscles. The mutations cause enlargement of not only individual contractile elements that help the heart pump blood, but thickening of an entire side of the heart. The symptoms of HCM can go unnoticed for years, until it causes sudden cardiac arrest. The disease, which affects up to one in 500 people, is the leading cause of nonviolent deaths in young adults.

More than a thousand unique mutations in myosin genes have been linked to HCM, and it takes just one mutated copy of the gene—inherited from only one parent—to cause symptoms. In an attempt to test new treatment strategies, Seidman's group decided to first focus on a mutation for which they had a well-researched mouse model, in a gene called *Myh6*. Mice with the *Myh6* mutation develop thickening of the heart muscle and measurable changes, at a molecular level, to the functioning of proteins and cells that make up the muscle tissue.

Seidman's group aimed to target the mutated copy of *Myh6* with RNAi, strands of RNA which bind to matching RNAs and block them from being used to encode proteins.

Scientist Profile

Christine E. Seidman, MD

Brigham and Women's Hospital

Related Links

Spontaneous Mutations Play a Key Role in Congenital Heart Disease

Sensitive Genetic Analysis Reveals Vast Changes Associated with Hypertrophic Cardiomyopathy

Recent NIH Activities: A Brief Update

NIH Scientific Review Board Meeting

October 24, 2013

Lawrence Tabak, D.D.S., Ph.D.

Principal Deputy Director, NIH

Department of Health and Human Services

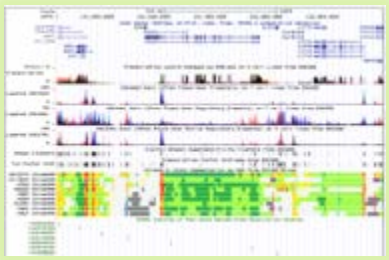
Furthering the NIH Mission

- Enhancing the translation of data into knowledge
  - Big Data to Knowledge (BD2K)
  - Reproducibility activities and pilot programs
- Accelerating development of in-depth understanding of human brain
  - BRAIN Initiative
- Ensuring a robust and diverse biomedical workforce
  - Biomedical Workforce and Diversity Initiatives
- Supporting the best science through a dynamic and efficient peer review system

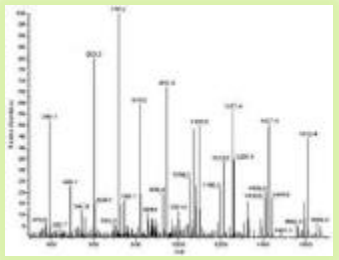
Furthering the NIH Mission

- Enhancing the translation of data into knowledge
  - Big Data to Knowledge (BD2K)
  - Reproducibility activities and pilot programs
- Accelerating development of in-depth understanding of human brain
  - BRAIN Initiative
- Ensuring a robust and diverse biomedical workforce
  - Biomedical Workforce and Diversity Initiatives
- Supporting the best science through a dynamic and efficient peer review system

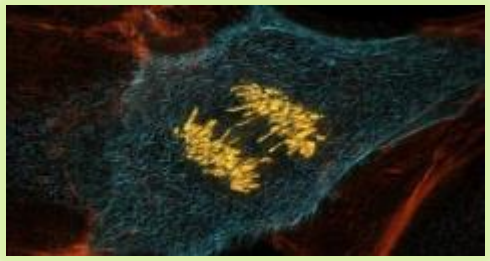
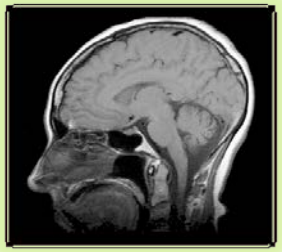
Myriad Data Types

Genomic




Other ‘Omic

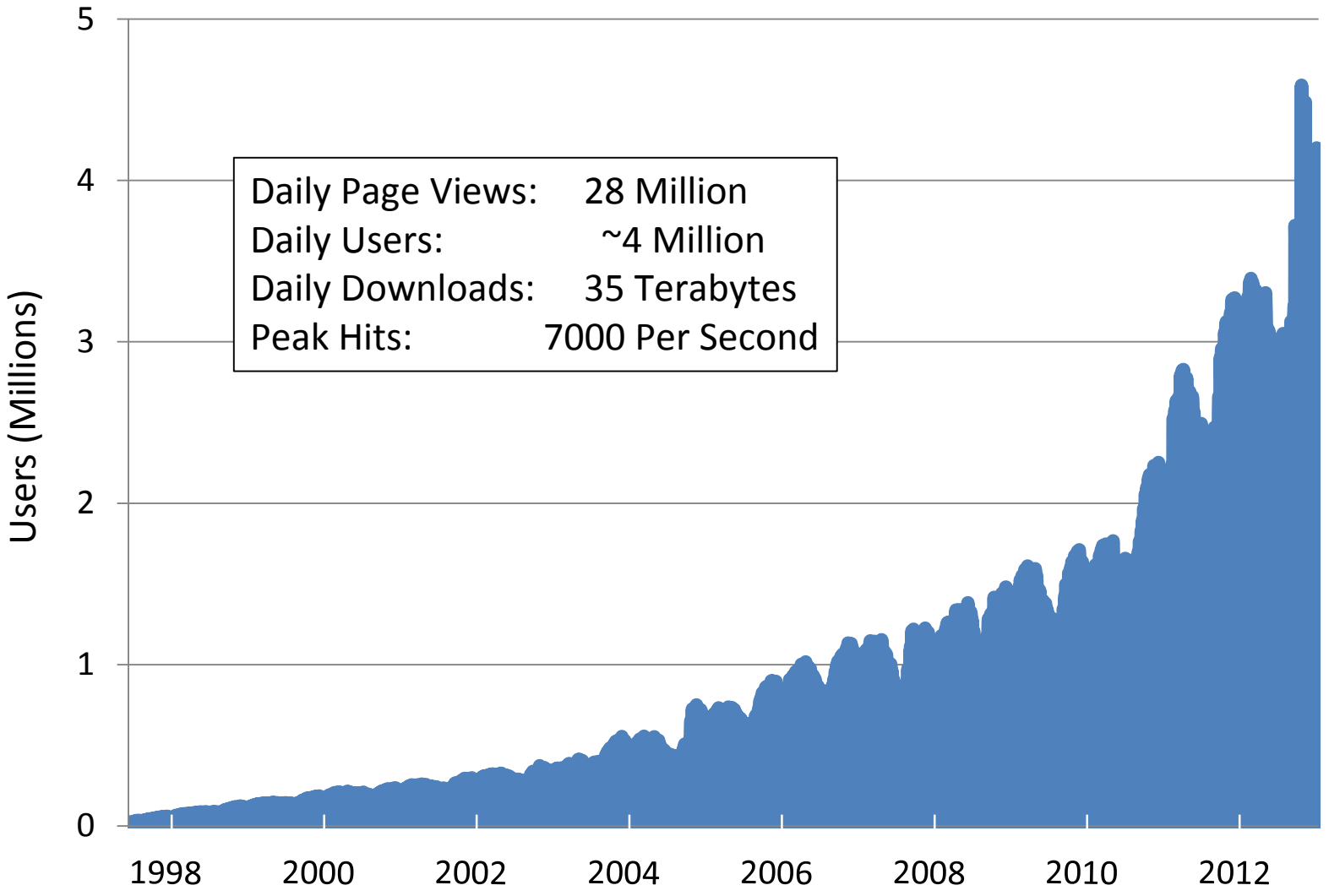
Imaging


Phenotypic

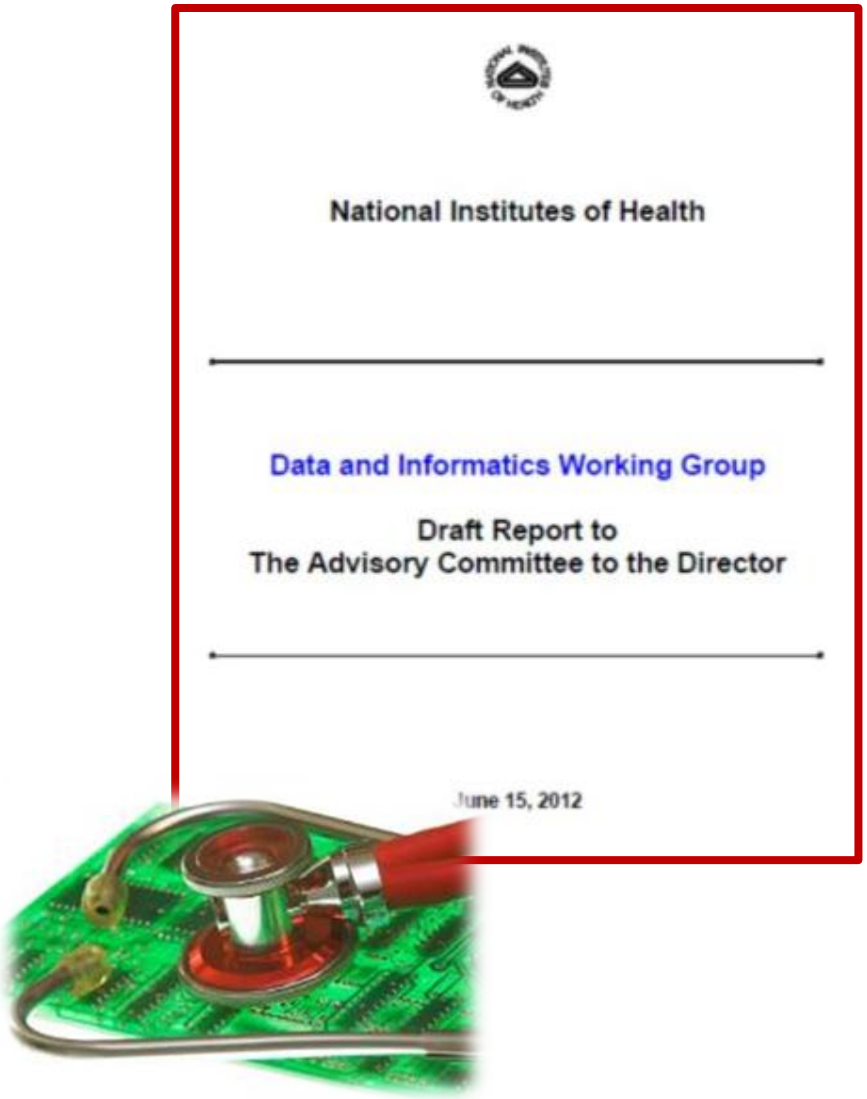

Exposure


Clinical

Daily Users - NCBI Web Site



Data and Informatics Working Group of Advisory Committee to the NIH Director



Major Themes in Report:

- At a pivotal point:
  - At risk of failing to capitalize on technology advances
- Cultural changes at NIH are essential
- Aim to develop new opportunities for:
  - Data sharing
  - Data analysis
  - Data integration
- Long-term NIH commitment is required

NIH is Tackling the "Big Data" Problem

1. New NIH Leadership Position:
   - Associate Director for Data Science
2. New Internal NIH Governing/Oversight Body:
   - Scientific Data Council
3. New Trans-NIH Initiative:
   - Big Data to Knowledge

Furthering the NIH Mission

- Enhancing the translation of data into knowledge
  - Big Data to Knowledge (BD2K)
  - Reproducibility activities and pilot programs
- Accelerating development of in-depth understanding of human brain
  - BRAIN Initiative
- Ensuring a robust and diverse biomedical workforce
  - Biomedical Workforce and Diversity Initiatives
- Supporting the best science through a dynamic and efficient peer review system

Beware the creeping cracks of bias

Evidence is mounting that research is riddled with systematic errors. Left unchecked, this could erode public trust, warns **Daniel Sarewitz**.

Believe it or not: how much can we rely on published data on potential drug targets?

Florian Prinz, Thomas Schlange and Khusru Asadullah

Statistical Design Considerations in Animal Studies Published Recently in *Cancer Research*

Kenneth R. Hess

Raise standards for preclinical cancer research

lenn Begley and **Lee M. Ellis** propose how methods, publications and incentives must change if patients are to benefit.

Why animal research needs to improve

Many of the studies that use animals to model human diseases are too small and too prone to bias to be trusted, says **Malcolm Macleod**.

False-Positive Psychology: Undisclosed Flexibility in Data Collection and Analysis Allows Presenting Anything as Significant

Helping editors, peer reviewers and authors improve the clarity, completeness and transparency of reporting health research

David Moher*[1,2], Iveta Simera[3], Kenneth F Schulz[4], John Hoey[5] and Douglas G Altman[3]

and Cultural Reforms

Drug targets slip-sliding away

The starting point for many drug discovery programs is a published report on a new drug target. Assessing the reliability of such papers requires a nuanced view of the process of scientific discovery and publication.

Translating animal research into clinical benefit

Poor methodological standards in animal studies mean that positive results may not translate to the clinical domain

Courtesy of Dr. S. Silberberg, NINDS

Reproducibility and Transparency of Research Findings

- Reproducibility and transparency of research findings have been noted as an issue in multiple publications.
  - This is a problem in all areas of research, not just specific types of studies.
  - This has also been observed in both clinical and preclinical research, though the focus here is on reproducibility of preclinical research.

Background

- Topic discussed in workshops by NINDS and NCI in 2012.
- IC leadership supportive of further focus on reproducibility.
- Ad-hoc group formed by Francis Collins to develop approaches to redressing these issues.
- Group's deliberations brought to IC Directors for feedback.
- IC Director input used to inform plans for Trans-NIH and IC-level next steps.

Underlying Issues

- Poor training
- Poor evaluation
- Perverse reward incentives

Principles for Addressing the Underlying Issues

1. Raise community awareness.
2. Enhance formal training.
3. Improve the evaluation of applications.
4. Protect the quality of funded and published research by adoption of more systematic review processes.
5. Increase stability for investigators.

Trans-NIH Actions and Pilots

- ICs and OD Offices will discuss reproducibility and transparency of research findings with their stakeholder communities to alert them to the issues and solicit feedback.
- OIR to create and pilot a new module on research integrity as it relates to experimental biases and study design to ethics training course required for NIH intramural fellows.
- Once tested, OER will make available on the web and encourage adoption (or equivalent) by extramural training programs for fellows and trainees.

Trans-NIH Actions and Pilots (cont.)

- Pilots will be conducted by ICs
  - Evaluation process of the "scientific premise" of a grant application
  - Checklist to systematically evaluate grant applications
  - Changes to bio-sketch
  - Approaches to reduce "perverse incentives"
  - Supporting replication studies
- Convene meetings with Journal Editors, Study Section Chairs, and BSC Chairs

Furthering the NIH Mission

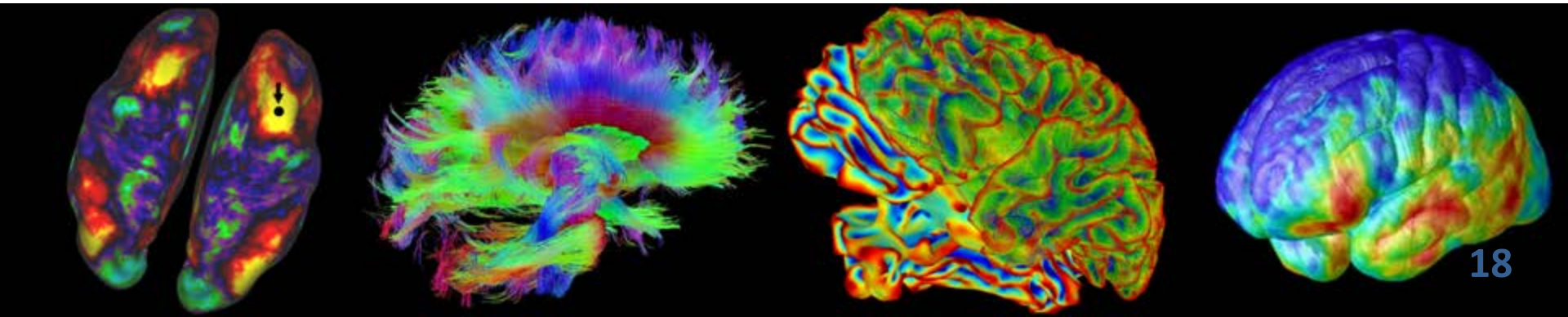
- Enhancing the translation of data into knowledge
  - Big Data to Knowledge (BD2K)
  - Reproducibility activities and pilot programs
- Accelerating development of in-depth understanding of human brain
  - BRAIN Initiative
- Ensuring a robust and diverse biomedical workforce
  - Biomedical Workforce and Diversity Initiatives
- Supporting the best science through a dynamic and efficient peer review system

Brain Disorders Affect Us All

- Neurodegenerative disorders
  - Alzheimer's, Parkinson's, ALS, Huntington's…
  - Annual cost of dementia care in the U.S. is ~200 billion
- Cognitive and affective disorders
  - Schizophrenia, Bipolar Disorder, Depression, Anxiety, OCD…
- Neurodevelopmental disorders
  - Autism, Attention-deficit disorder, Epilepsy, Intellectual disability…
- Injury- and insult-induced disorders
  - PTSD, Traumatic brain injury, Stroke…

BRAIN Initiative: Goals

- Accelerate development, application of innovative technologies to construct dynamic picture of brain function that integrates neuronal and circuit activity over time and space
- Build on growing scientific foundation – neuroscience, genetics, physics, engineering, informatics, nanoscience, chemistry, mathematics, etc. – to catalyze interdisciplinary effort of unprecedented scope



BRAIN Working Group Interim Report: High-Priority Research Areas for FY14

1. Generate a census of cell types
2. Create structural maps of the brain
3. Develop new large-scale network recording capabilities
4. Develop a suite of tools for circuit manipulation
5. Link neuronal activity to behavior
6. Integrate theory, modeling, statistics, and computation with experimentation
7. Delineate mechanisms underlying human imaging technologies
8. Create mechanisms to enable collection of human data
9. Disseminate knowledge and training

Furthering the NIH Mission

- Enhancing the translation of data into knowledge
  - Big Data to Knowledge (BD2K)
  - Reproducibility activities and pilot programs
- Accelerating development of in-depth understanding of human brain
  - BRAIN Initiative
- Ensuring a robust and diverse biomedical workforce
  - Biomedical Workforce and Diversity Initiatives
- Supporting the best science through a dynamic and efficient peer review system

Biomedical Research Workforce: Challenges

- Increasingly difficult to launch traditional, independent academic research career:
  - Rising number of Ph.D.s
  - Number of established researchers staying longer in field

- Long training time and relatively low early-career salaries make biomedical research careers less attractive than other professions
- Training programs offer little preparation for careers outside academia–despite decreasing likelihood of finding an academic position

http://acd.od.nih.gov/bwf.htm

DP7 BEST Program – Broadening Experiences in Scientific Training

- Common Fund program seeking innovative approaches to complement traditional research training in biomedical sciences at institutions that receive NIH funds
  - http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-12-022.html
  - One application per institution
  - Up to $250,000 in direct costs per year
  - Closed May 10, 2013
  - Over 100 applications
  - Awards were announced on September 23 - http://www.nih.gov/news/health/sep2013/od-23.htm

- Encourage institutions to leverage funds with existing institutional offices and programs, local resources outside the institution, or that partner with industry or other entities
- Must include rigorous analysis to demonstrate impact
- Proven approaches will be widely disseminated throughout the biomedical research community; awardees will meet to exchange ideas

Other Workforce Initiatives

- Improve graduate student and postdoctoral training
- Increase postdoctoral stipends – to be implemented in FY2014
- Consider policies on benefits – developing comprehensive survey
- Shorten eligibility period and increase support for K99/R00 – implemented for applications received after February 2014
- Develop a simple and comprehensive tracking system for trainees
  - Automate training grant tables to include structured data
  - Develop SciENCV
  - Incorporate unique identifier
- Initiate discussion with the community to assess NIH support of faculty salary – developing pilot survey
- Create functional unit at NIH to assess the biomedical research workforce

Diversity: The Challenges We Must Solve

http://acd.od.nih.gov/06142012_DBR_ExecSummary.pdf

Diversity: The Challenges We Must Solve

- **Time:** no one set of initiatives will diversify NIH-funded workforce overnight
- **Mistrust:** we must gain trust within many communities
- **Develop partners:** success will require collaboration and cooperation of extramural partners

Diversifying the NIH-funded workforce and ensuring the fairness of the peer review system are collective responsibilities across NIH

Diversity Initiative: Overarching Strategy

Four interrelated approaches will be implemented:

- NIH Building Infrastructure Leading to Diversity (BUILD) Program
- National Research Mentoring Network (NRMN)
- Ensuring Fairness in Peer Review
- Increased Engagement by all NIH Leadership – Create Steering Committee WG on Diversity and Recruit Chief Officer for Scientific Workforce Diversity

Furthering the NIH Mission

- Enhancing the translation of data into knowledge
  - Big Data to Knowledge (BD2K)
  - Reproducibility activities and pilot programs
- Accelerating development of in-depth understanding of human brain
  - BRAIN Initiative
- Ensuring a robust and diverse biomedical workforce
  - Biomedical Workforce and Diversity Initiatives
- Supporting the best science through a dynamic and efficient peer review system

Improving the NIH Systems for Reviewing and Awarding Grants

- Brief Background on Peer Review
- Ongoing Efforts
- New Charge to the SMRB

Improving the NIH Systems for Reviewing and Awarding Grants

- Brief Background on Peer Review
  - Origins, Scope, and Core Values
- Ongoing Efforts
- New Charge to the SMRB

NIH Review and Award Process: Fundamental to the NIH Mission

- The NIH two-tier review system is the foundation on which the agency's funding of extramural research is based.
- The majority of the NIH budget goes to extramural research grants.
- It is vital that NIH continue to innovate and optimize the process by which grant applications are submitted, reviewed, processed, and awarded.

NIH Review and Award Process: Scope of NIH Peer Review

- Each year, NIH:
  - Issues 1,000 – 1,100 Funding Opportunity Announcements
  - Reviews 70,000 – 80,000 applications
  - Recruits ~22,500 reviewers (average = two review meetings per reviewer)
  - Runs ~2500 meetings

NIH Review and Award Process: Origins of NIH Peer Review

- The Public Health Service Act (Sec. 492 [289a]) requires the technical and scientific peer review of applications for grants and contracts
  - Requires the reviewing entity be provided with a written description of the research under review
  - The reviewing entity provides the advisory council with this description and the results of the review

NIH Review and Award Process: Origins of NIH Peer Review (cont.)

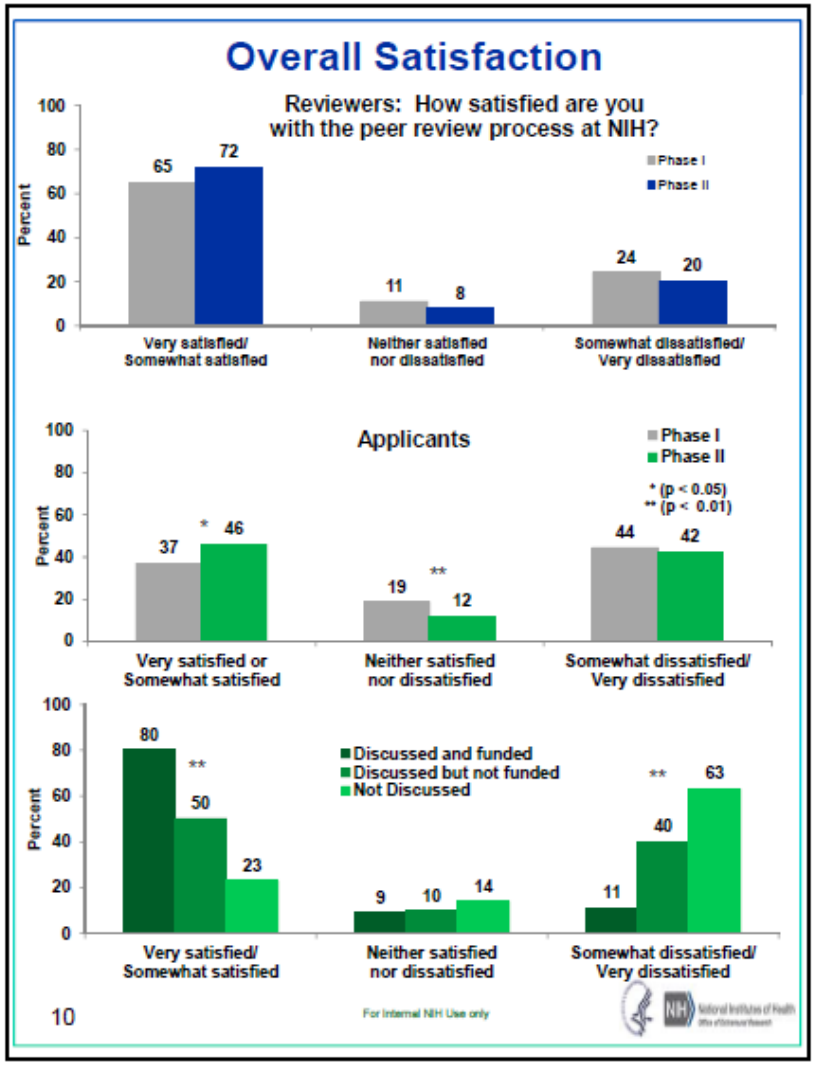
- Federal regulation at 42 CFR 52h "Scientific Peer Review of Research Grant Applications and Research and Development Contract Projects"
  - Invokes the Federal Advisory Committee Act
  - Defines the membership of review groups and expertise
  - Defines conflicts of interest for reviewers
  - Outlines review criteria for research projects

NIH Review and Award Process: Core Values of NIH Peer Review

- Expert assessment
- Transparency
- Impartiality
- Fairness
- Confidentiality
- Integrity
- Efficiency

*See NIH Peer Review: Grants and Cooperative Agreements

Continuous Review of Peer Review



http://enhancing-peer-review.nih.gov/docs/Enhancing_Peer_Review_Report_2012.pdf

Continuous Review of Peer Review (cont.)

ACD Working Group on Diversity in the Biomedical Research Workforce

- NIH should establish a WG of the ACD comprised of experts in behavioral and social sciences and studies of diversity with a special focus on determining and combating real or perceived biases in the NIH peer review system (Recommendation #9)
- NIH should first, pilot different forms of validated implicit bias/diversity awareness training for NIH scientific review officers and program officers to determine the most efficacious approaches. Once the best training approaches have been identified with NIH staff, pilot these programs with members of study sections to ascertain if their value is sustained. If they are, provide to all study section members (Recommendation #10)

http://acd.od.nih.gov/06142012_DBR_ExecSummary.pdf

Improving the NIH Systems for Reviewing and Awarding Grants

- Brief Background on Peer Review
- Ongoing efforts
  - Develop new approaches for ensuring that NIH peer review is a dynamic process responsive to important and emerging scientific trends and opportunities
- New charge to the SMRB

Current NIH Efforts to Enhance the Responsiveness of Peer Review to Emerging Scientific Opportunity

- In January 2013, the NIH Director convened a team of NIH experts to:
  - Develop methods for identifying emergent, highly active, areas of science as well as those areas that may have stagnated
  - Recommend approaches for coupling the "state" of scientific fields with study section organization in order to yield a dynamic system responsive to scientific trends

Improving the NIH Systems for Reviewing and Awarding Grants

- Brief Background on peer review
- Ongoing effort
- New charge to the SMRB
  - Complementary to, but distinct from, the ongoing effort
    - Will need to ensure that both groups are kept abreast of each other's activities
    - Focused on streamlining and shortening the process while maintaining high quality review

NIH Review and Award Process: Challenges and Opportunities

- Today, the research enterprise faces additional challenges due to economic constraints that have resulted in decreases in application success rates
- At the same time, advances in technology may be capitalized on to improve overall efficiency and effectiveness in the grant awarding process

NIH Review and Award Process: Charge to the SMRB

NIH requests that the SMRB recommend ways to further optimize the process of reviewing and awarding grants.

In addressing this charge, the scope of the SMRB deliberations should focus on ways in which NIH can:

1. Streamline the grant-making process and shorten the length of time from application to allocation of funds, and
2. Address the administrative burden on applicants and their institutions, scientific reviewers, Council members, and NIH staff while maintaining a high-quality review process

NIH Review and Award Process: Charge to the SMRB (cont.)

NIH requests that the SMRB provide:

- Recommended strategies and options for improving the process (i.e., streamlining procedures, shortening time frames, reducing burden) as well as the rationale for these recommendations

Discussion

Address to NIH
Scientific Management Review Board

Presented by

Philip Yeo, **SINGAPORE**

Chairman, **Standards, Productivity and Innovation for Growth**
SPRING, www.spring.gov.sg, 2007-to-date

Chairman, **Agency for Science, Technology and Research**
A*STAR, www.a-star.edu.sg, 2001-2007)

Chairman, **Economic Development Board**
EDB, www.edb.gov.sg, 1986-2006

Measuring the Impact and Value of Biomedical Research

- **Industrial Capital –** ***Promote Economic Growth***

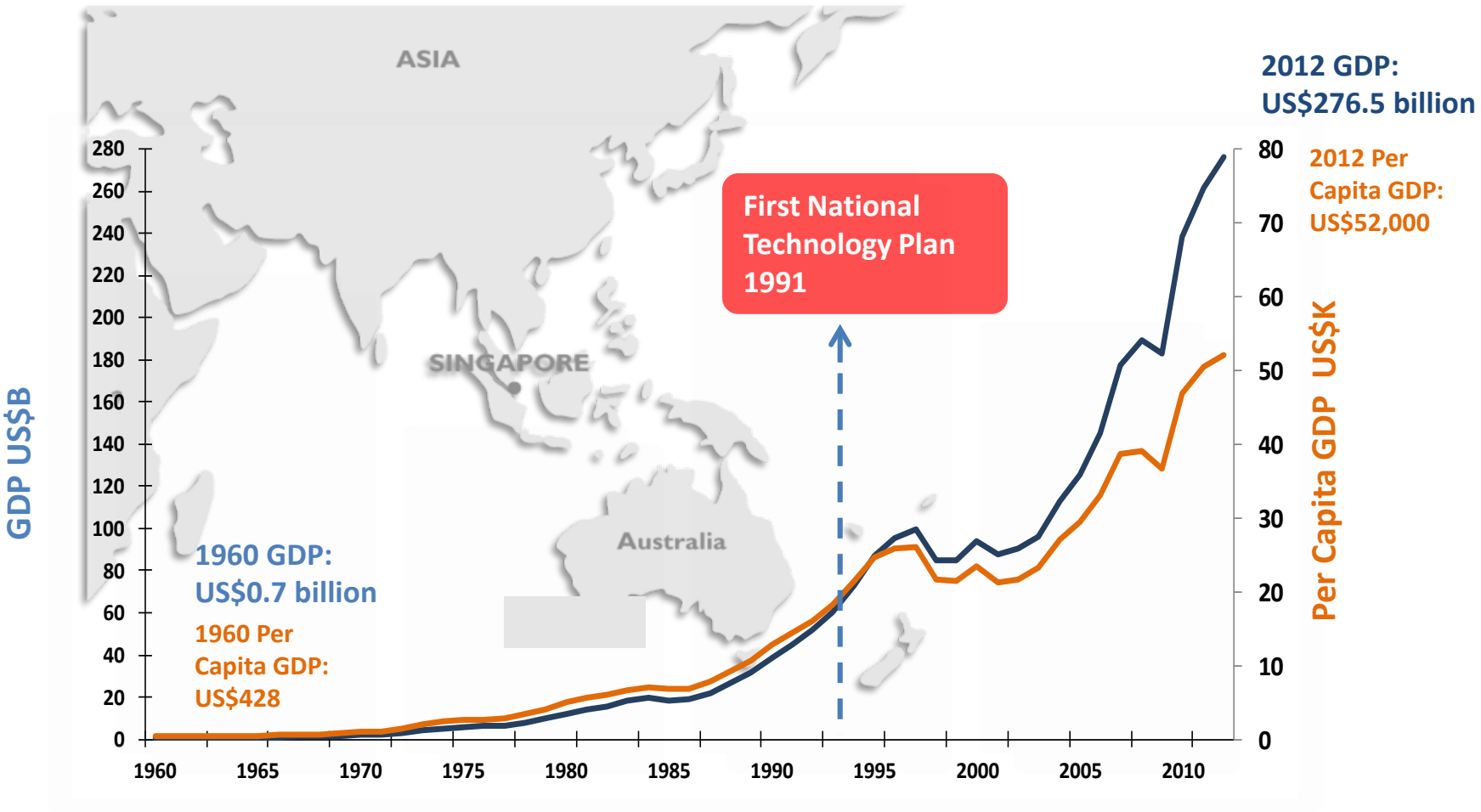
- **Knowledge Capital –** ***Encourage Scientific Excellence and Innovation - Encourage Networks/Collaboration in the Research Community***

- **Clinical and Healthcare Capital –** ***Support Clinical Trials and Healthcare Outcomes***

- **Human Capital –** ***Invest in and Nurture R&D Talent***

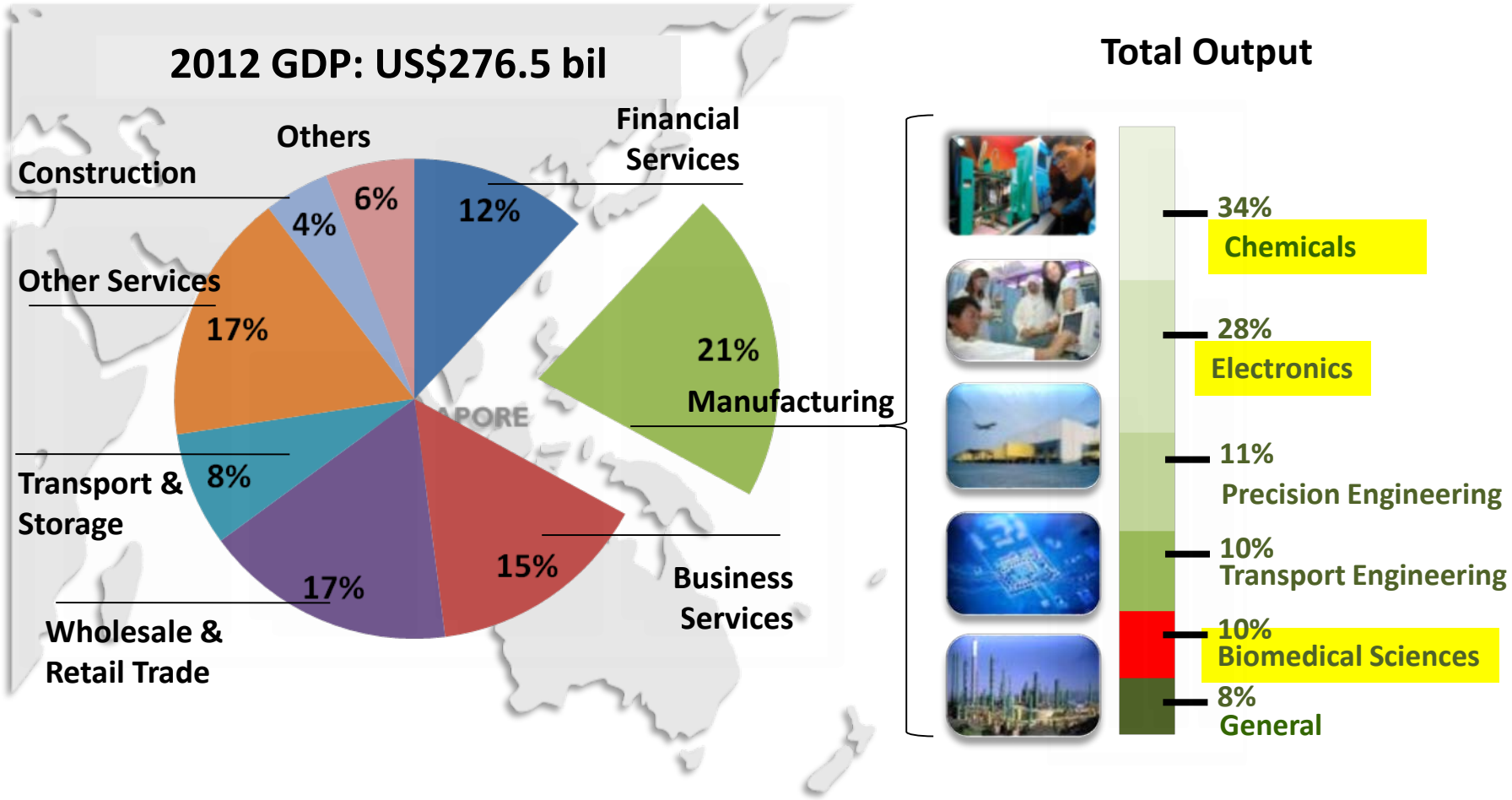
- **Communications:** ***Value of Scientific Knowledge to Economic Growth***

Growth of Singapore's Economy

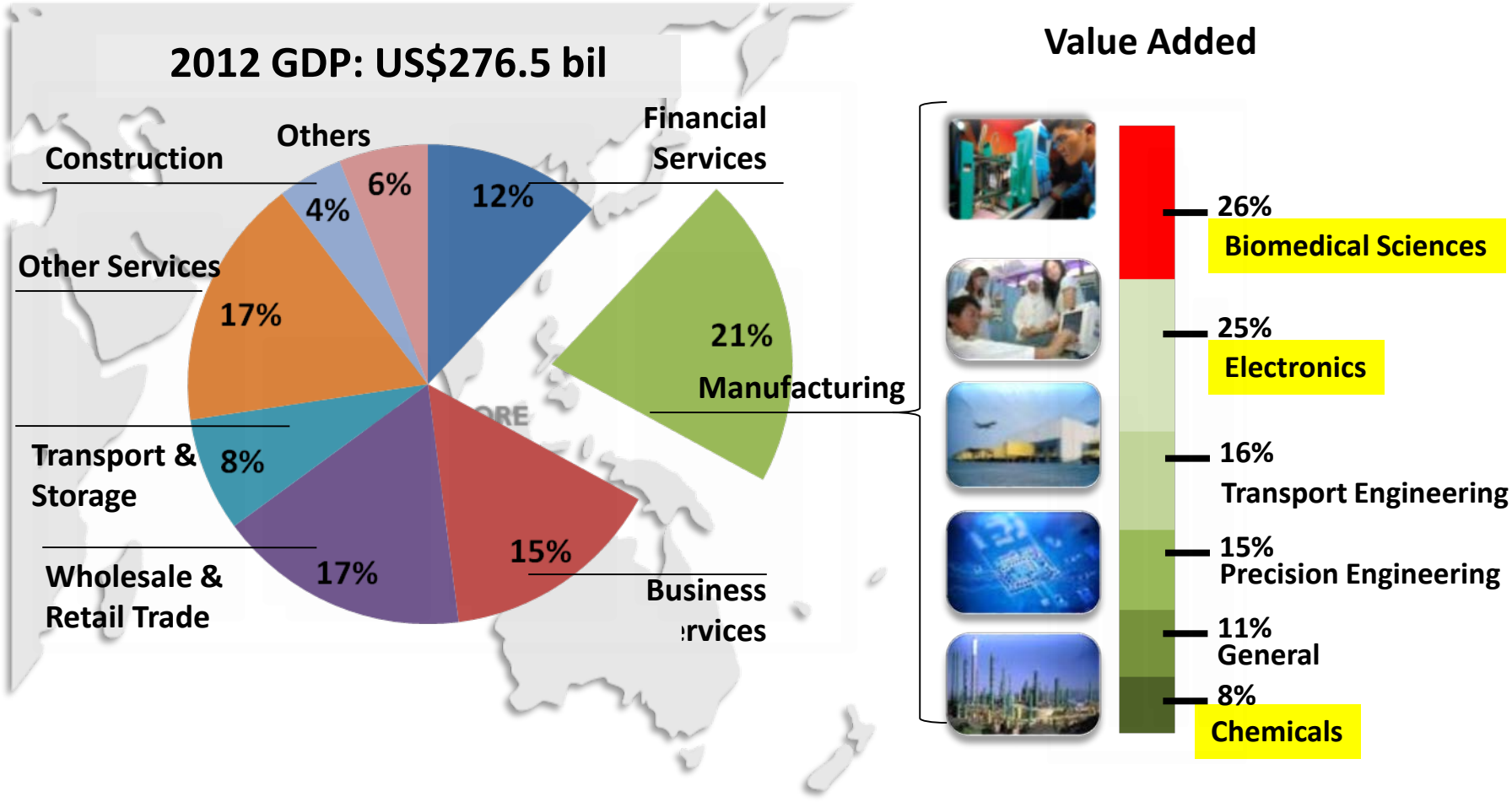


1960s	1970s	1980s	1990s	2000…
Labour intensive	Skill intensive	Capital intensive	Technology Intensive	Knowledge & Innovation Based Economy

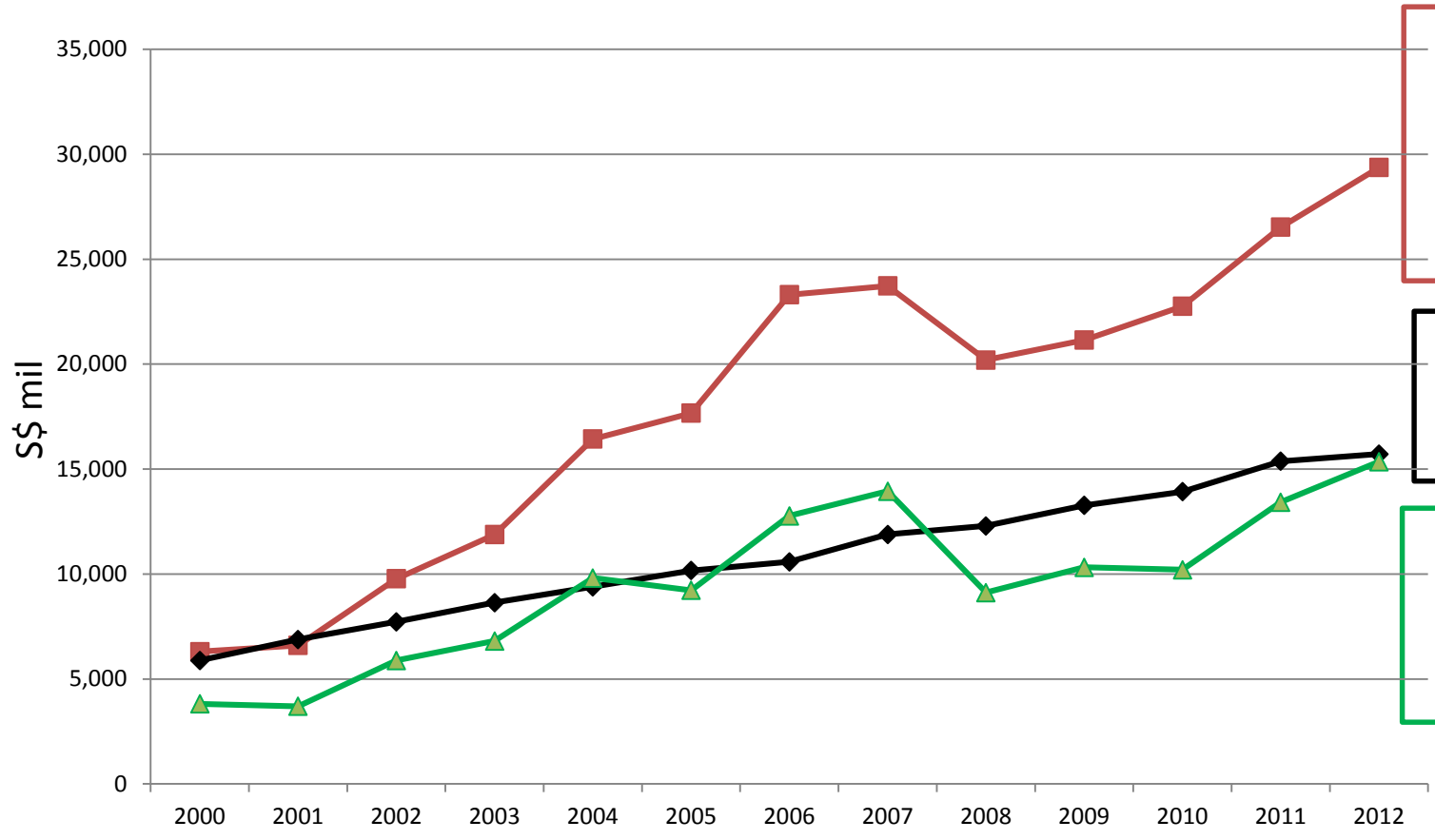
Singapore's Economy Today



Singapore's Economy Today



BioMedical Sciences (BMS) in Singapore



Manufacturing Output*
S$29.4 billion
(US$22.9 billion)

Manufacturing Employment
15,700 employees

Value-Added*
S$15.3 billion
(US$ 11.9 billion)

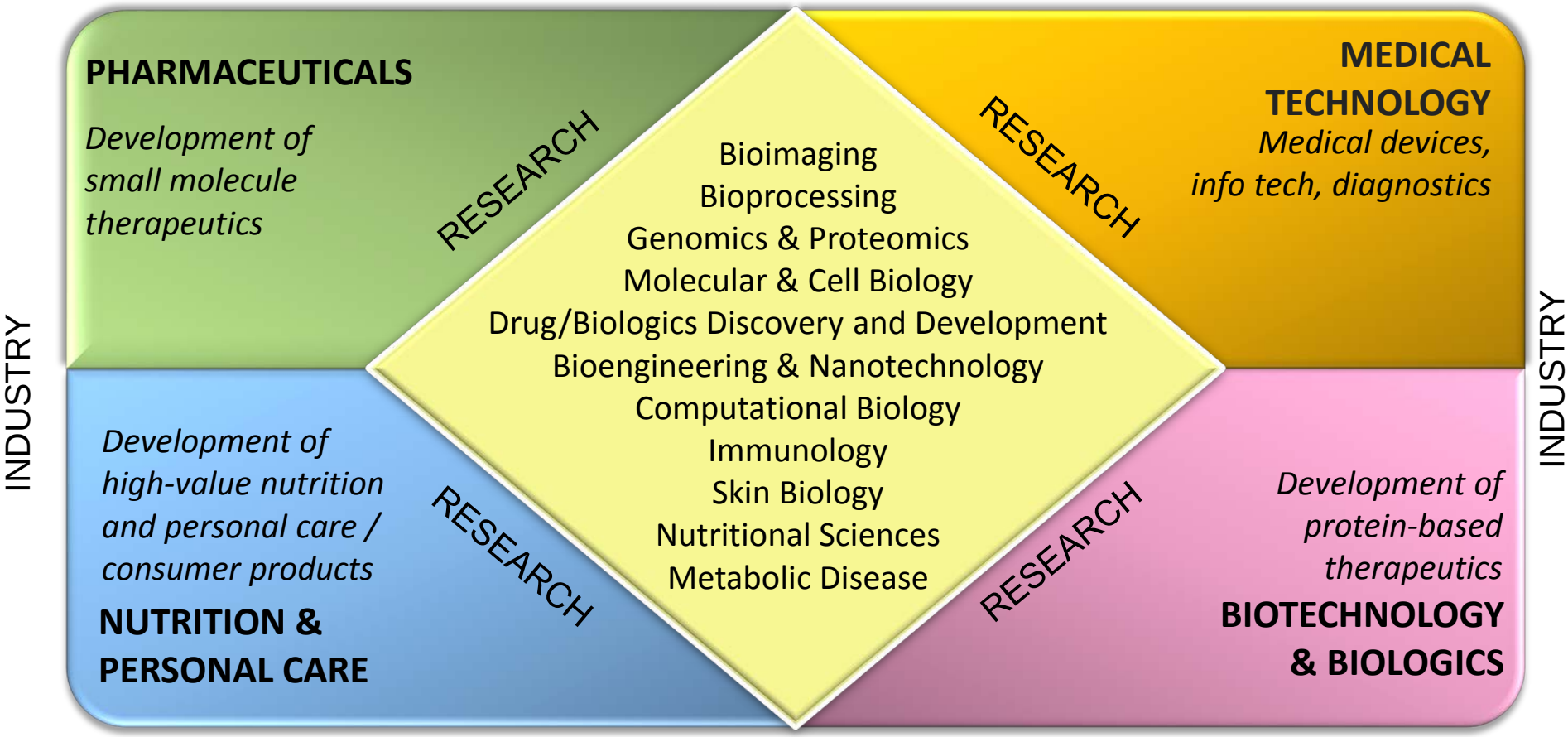
Launch of BMS Initiative

Opening of Biopolis

GDP Share (2012): 5.25%
Total Employment: >20,000
CAGR (2012): 13%

Compounded Annual Growth Rates (CAGR) computed over 5 years
**Value-Add = Labour Cost + Depreciation + Interest Cost + Profit before Tax + Land Cost*

BioMedical Sciences (BMS) Initiative



Breaking Ground in Dec 2001: Biopolis Phase 1

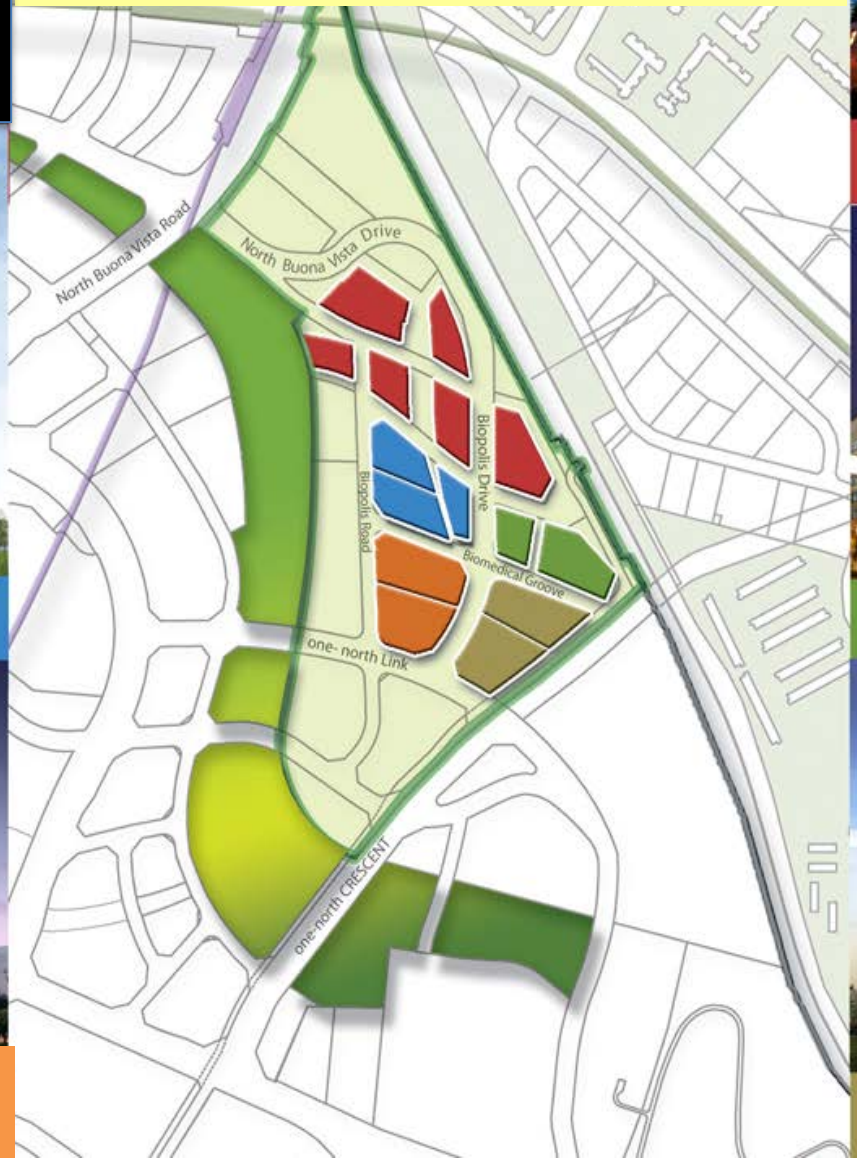
BIOPOLIS MASTERPLAN
(537, 625 SQ M)
5,787,000 SQ FT

- Developed :
5.6 ha of land
264,000 sqm GFA

- In-process :
9.5 ha of land
273,625 sqm GFA

Biopolis Phase 4
(under construction)

Biopolis Phase 5
(under construction)



Biopolis Phase 1
First Biopolis development seeded by JTC

Biopolis Phase 2
Completed in 2006

Biopolis Phase 3
Completed in Jan 2011

Pharma HQs in Singapore

Pharmaceutical companies with Regional HQs in Singapore

Johnson & Johnson, gsk, Abbott, NOVARTIS, SANOFI, Roche, MSD, QUINTILES TRANSNATIONAL, AstraZeneca, Takeda

Highlights of Headquarters in Singapore

gsk GlaxoSmithKline

GSK's Emerging Markets & Asia-Pacific Hub

Regional headquarters and control tower for all of GSK's operations in Asia-Pacific, Latin America, and African regions

QUINTILES TRANSNATIONAL

Quintiles's Asia-Pac Regional Headquarters

Quintiles Singapore functions as Asia-Pac headquarters providing a full range of clinical development and commercialization services

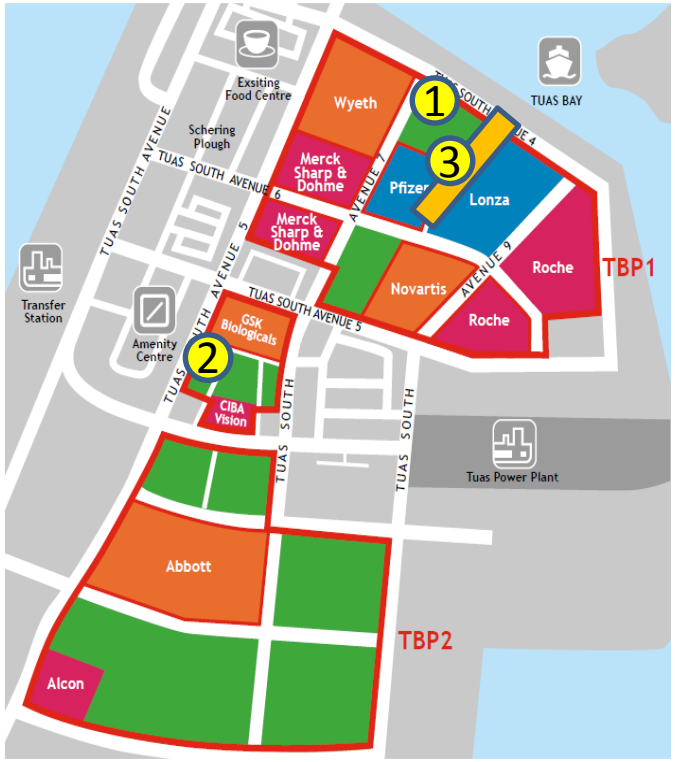
NOVARTIS

Novartis's Regional Headquarters for Asia Cluster

Regional headquarters for pharmaceutical operations across Asia cluster

Pharma Manufacturing Plants

Tuas Biomedical Park



MERCK

Bulk API and secondary manufacturing plants

Lonzagroup

Bulk biologics manufacturing plant
Cell Therapy Facility

Roche

Microbial and mammalian bulk biologics facility

gsk GlaxoSmithKline

Bulk API plants with pilot facility and pediatric vaccines plant

NOVARTIS

Tablet facility
Biologics Manufacturing Facility

Abbott
A Promise for Life

Bulk nutritionals plant

Pfizer

Bulk API and nutritionals plant

Baxter

Biologics and recombinant therapies plant

kaneka

Bulk API intermediates plant

gsk GlaxoSmithKline Biologicals

Vaccines plant

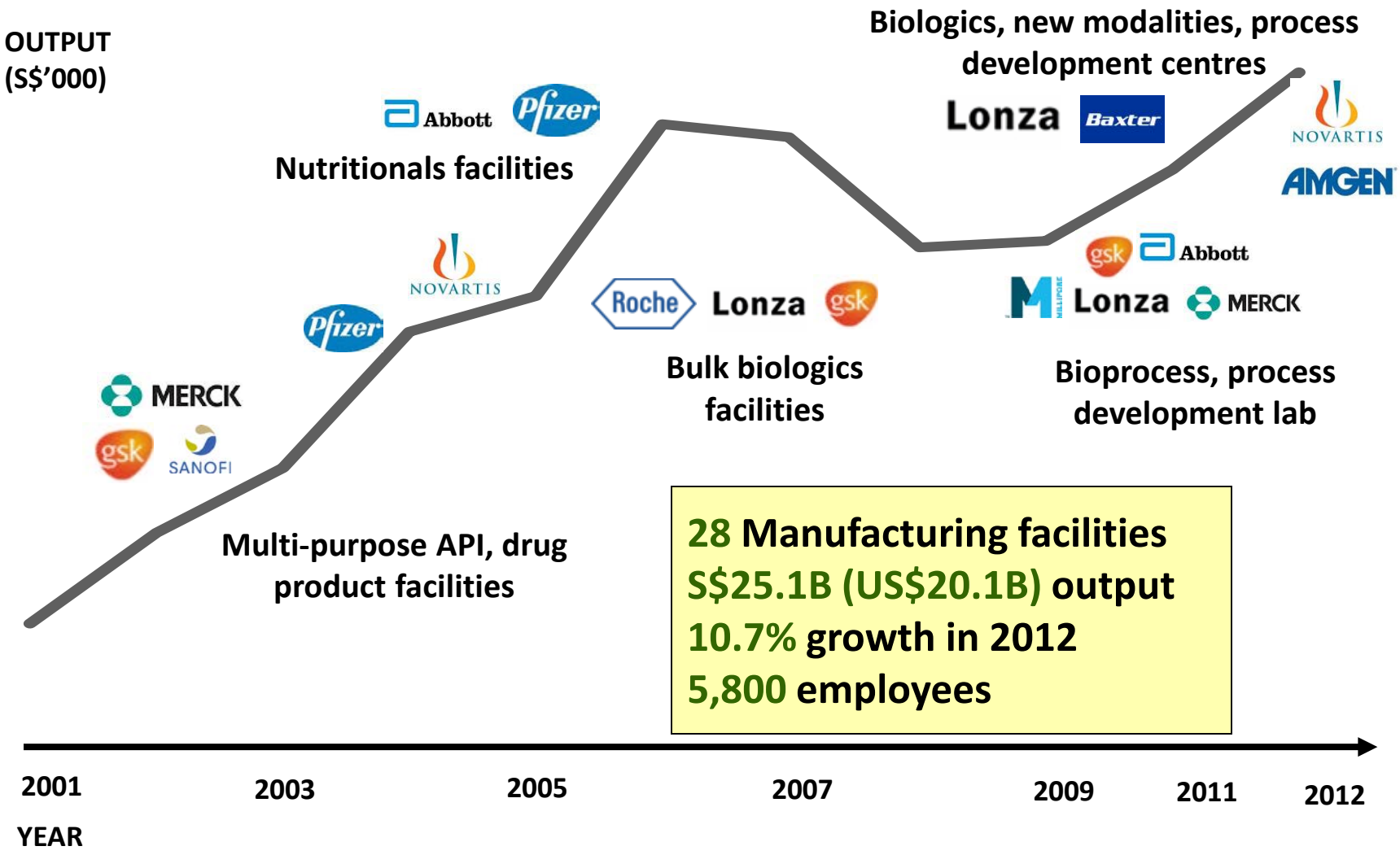
Quality & Operational Excellence

- Zero major observations with regulators
- Track record producing for global markets
- Strong global logistics
- Secure business environment
- Access to talent

Manufacturing for the world

-28 commercial scale manufacturing facilities
-7 of the top 10 Big Pharma
-API, biologics, cell therapy, nutrition

Pharma Manufacturing Growth in Singapore



MedTech Company HQs

The Top 10 Medical Device Companies have Regional HQs in Singapore

COVIDIEN · BD · Abbott · Baxter · Medtronic · GE · Johnson & Johnson · PHILIPS · SIEMENS · Boston Scientific

Highlights of Headquarters in Singapore

BD

Becton Dickinson's Shared Services Centre

Shared services hub supports all BD's operations in Asia-Pacific region.

Siemens Medical Instruments Global Headquarters

Global HQ for hearing aids business. Singapore R&D and Manufacturing facility supplies 30% of the world's hearing aids

ESSILOR

Essilor's Asia-Pacific Headquarters and R&D Hub

Asia-Pacific R&D centre and coordination hub developing lenses for Asian consumers.

MedTech Cluster in Singapore

35 Manufacturing Plants

9,666 employees

26 R&D Centers

500 Researchers & Engineers

29 Regional HQs

1,500 employees

Recent MedTech Investments

Manufacturing

Medtronic Pacemaker Manufacturing Facility

Medtronic opens manufacturing facility for cardiac rhythm disease management (CRDM), which will produce pacemakers and leads.

Agilent Instrument Manufacturing

Agilent Technologies opens its new life sciences manufacturing facility to produce Liquid Chromatography/Mass Spectrometry instruments for global markets.

R&D and Innovation

Menicon R&D Centre and Manufacturing Facility

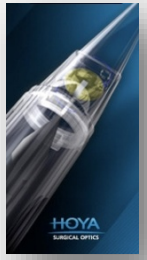
Menicon established its first R&D and manufacturing facility for its new line of daily disposable “Flat Pack” contact lenses in Singapore.

Life Technologies Global Instrument Centre of Excellence

Life Technologies established its Global Instrument Centre of Excellence in Singapore.

Headquarters

Hoya Surgical Optics Global Headquarters



Hoya Surgical Optics relocates its global headquarters from California, US to Singapore.

Siemens Medical Instruments Global Headquarters

Siemens Healthcare relocates its Audiology Group global headquarters in Singapore under Siemens Medical Instruments

BIOMEDICAL SCIENCES DIRECTION

BENCH → BEDSIDE

Basic

Research Institutes

- Institute of Molecular & Cell Biology
- Genome Institute of Singapore
- Institute of Bioengineering & Nanotechnology
- Bioprocessing Technology Institute
- Bioinformatics Institute
- NUS School of Medicine
- NUS Cancer Science Institute
- Duke-NUS Graduate Medical School

Translational

Institute of Medical Biology

- Skin Basic & Translational biology
- Genetic Diseases
- Regenerative Medicine (including stem cells)

Experimental Therapeutics Centre

- Drug Discovery & Development from target validation to early phase clinical trials

Consortia

- Singapore BioImaging Consortium
- Singapore Immunology Network
- Singapore Stem Cell Consortium (now subsumed into IMB)

Singapore Institute for Clinical Sciences

- Develop programmes in translational & clinical medicine
- Focus on Growth, Development & Metabolism
- Develop Clinician Scientists

Clinical

Ministry of Health

- Ethical regulations/framework for clinical research, e.g. IRBs
- HSA – Evaluation capabilities for new technologies

National Medical Research Council

- Clinical research strategy
- Grant management
- Manpower development
- Getting research outcomes into usage in patient care

Hospital Institutions

1. Tertiary Centres
   - National University Hospital
   - National University Cancer Institute
   - National University Heart Centre

   Outram Campus
   - Singapore General Hospital
   - National Cancer Centre
   - National Heart Centre
   - National Neuroscience Institute
   - Singapore National Eye Centre
   - Duke-NUS Graduate Medical School

2. Others with specific capabilities
   - KK Women and Children's Hospital
   - Tan Tock Seng Hospital

Service Delivery

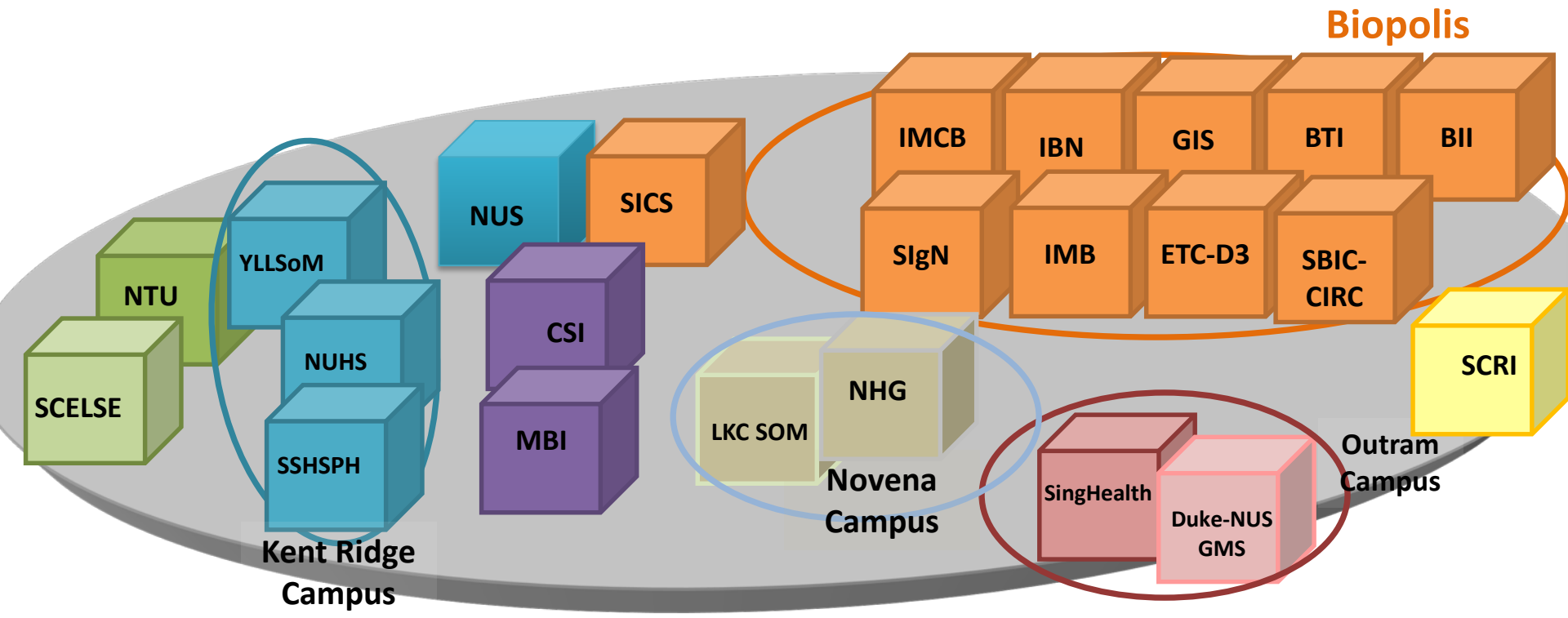
Public Sector Healthcare Groups

1. **Singapore Health Services**
   - Singapore General Hospital
   - KK Women and Children's Hospital
   - National Cancer Centre
   - National Dental Centre
   - National Heart Centre
   - National Neuroscience Institute
2. **National Healthcare Group**
   - Tan Tock Seng Hospital
   - Institute of Mental Health
   - National Skin Centre
   - Communicable Disease Centre
3. **National University Health System**
   - National University Hospital
   - National University Cancer Institute
   - National University Heart Centre
4. **Alexandra Health**
   - Khoo Teck Phuat Hospital
5. **Jurong Health**
   - Alexandra Hospital
   - Ng Teng Fong General Hospital
6. **Eastern Health Alliance**
   - Changi General Hospital

Private Sector Healthcare Groups

- Parkway Group
- Raffles Medical Group
- Thomson Medical

Public Research Infrastructure

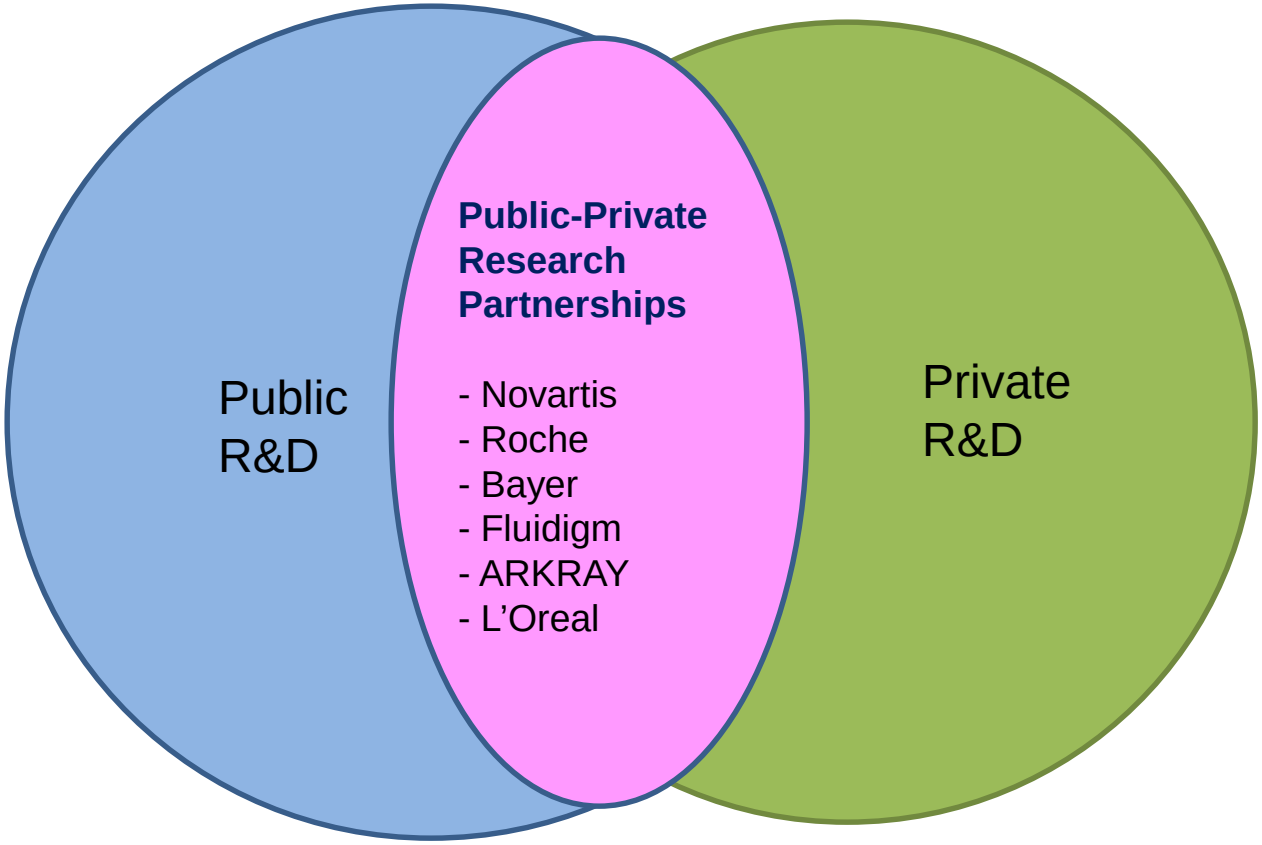


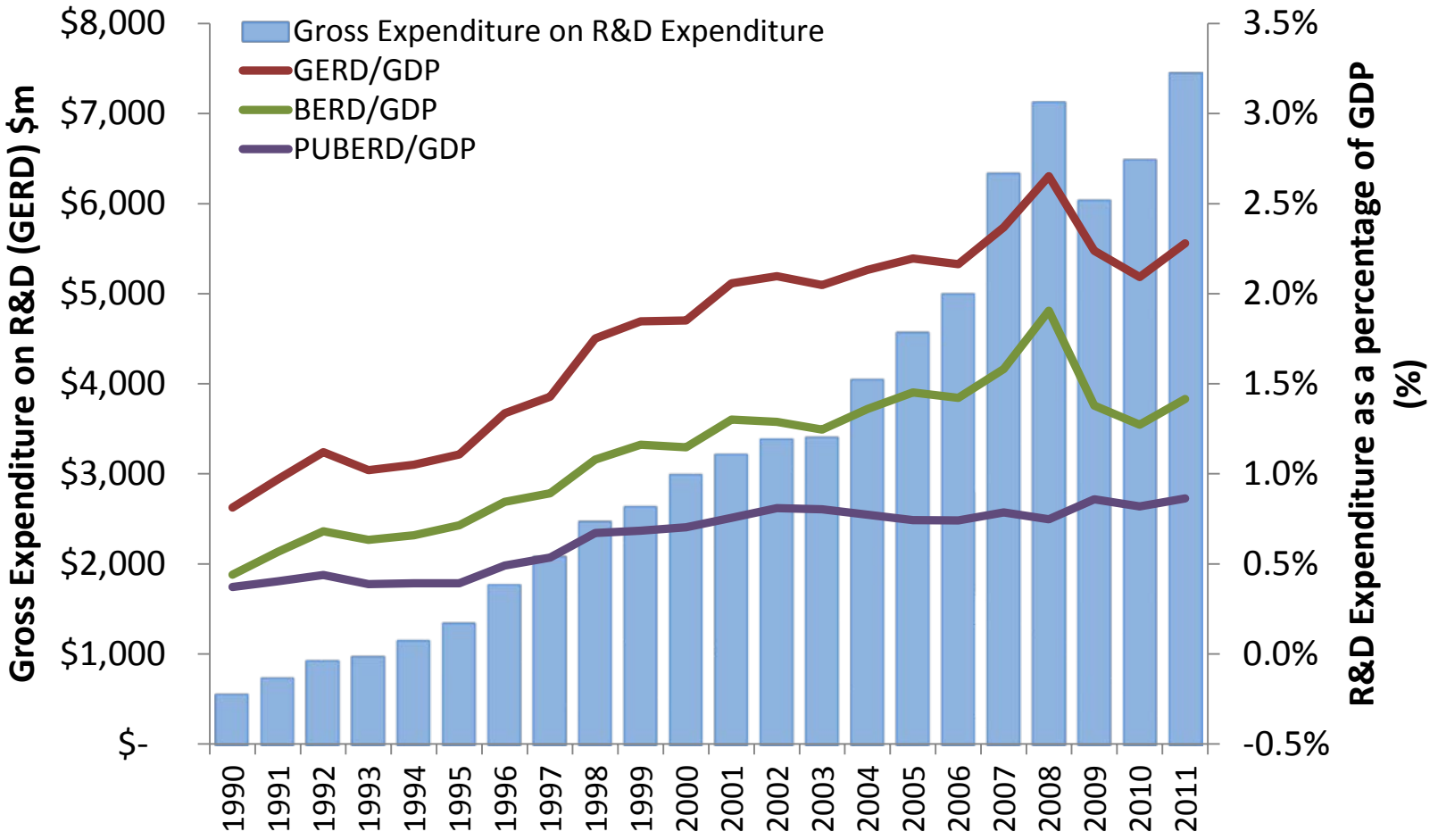
NTU - Nanyang Technological University
SCELSE – Singapore Centre on Environmental Life Sciences Engineering
YLLSoM - Yong Loo Lin School of Medicine
NUHS - National University Healthcare Singapore
SSHSPH – Saw Swee Hock School of Public Health
NUS - National University of Singapore
SICS - Singapore Institute for Clinical Sciences
CSI - Cancer Science Insittute
MBI - MechanoBiology Institute

IMCB – Institute of Molecular & Cell Biology
IBN – Institute of Bioengineering & Nanotechnology
GIS - Genome Institute of Singapore
BTI - Bioprocessing Technology Institute
BII - BioInformatics Institute
SigN – Singapore Immunology Network
IMB – Institute of Medical Biology
ETC-D3 – Experimental Therapeutics Centre-Drug Discovery & Development
SBIC-CIRC – Singapore BioImaging Consortium-Clinical Imaging Research Centre
SCRI – Singapore Clinical Research Institute
LKC SOM – Lee Kong Chian School of Medicine
NHG - National Healthcare Group

Public Research Collaborations With Hospitals, Industry, Academia

Public-Private R&D Partnerships





GERD – Gross Expenditure on R&D
BERD – Business Expenditure on R&D
PUBERD – Public Expenditure on R&D

Commitment to R&D

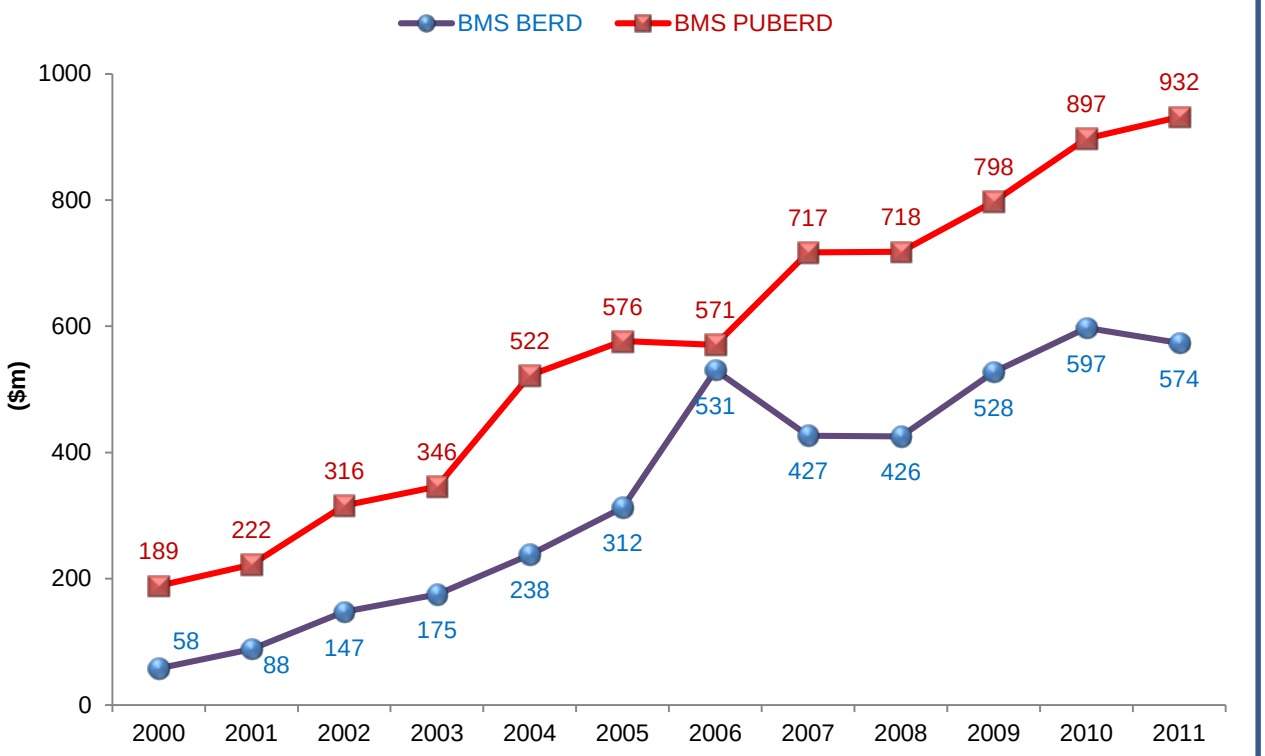
5-year S&T Plans

National Technology Plan (1991-1995) **US$1.5 bn**	National Science & Technology Plan (1996-2000) **US$3 bn**	Science & Technology Plan 2005 (2001-2005) **US$4.8 bn**	Science & Technology Plan 2010 (2006-2010) **US$10.7 bn**	Research, Innovation & Enterprise Plan (2011-2015) **U$12.3 bn**

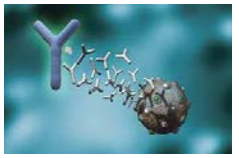
Gross Expenditure on BMS R&D

Moving up the value chain from manufacturing to innovation

BUSINESS EXPENDITURE ON R&D for BMS
US$460 mil (2011)
CAGR (2011): 26%



Source: National R&D survey 2011, Singapore



CHUGAI

Chugai Pharmbody Research
Established in July 2012
S$200M (US$160.3M), 60 jobs

P&G

P&G Innovation Centre
TOP in Nov 2013
S$250M (US$200.4M), 500 jobs

arkray

First Asian research center outside Japan
S$9.1M (US$7.3M) over 5 years

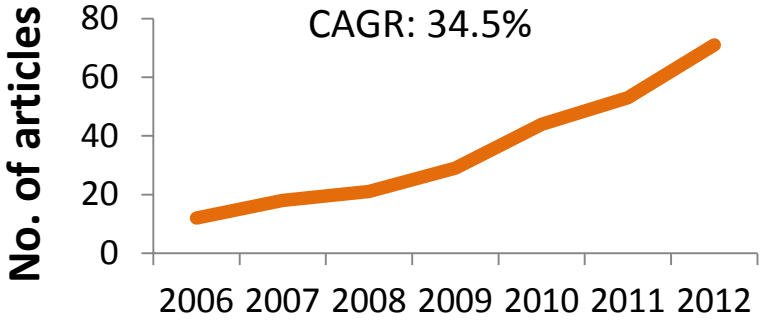
Knowledge & Innovation Capital

Papers

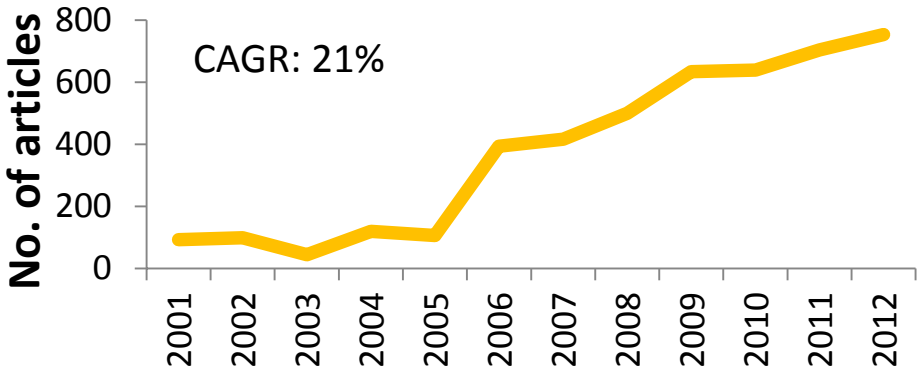
nature asia-pacific
Highlighting the best research from the Asia-Pacific

Country Rankings 2012
Overall: 5th
Most productive among top 5 countries

NATURE PUBLICATIONS SINGAPORE

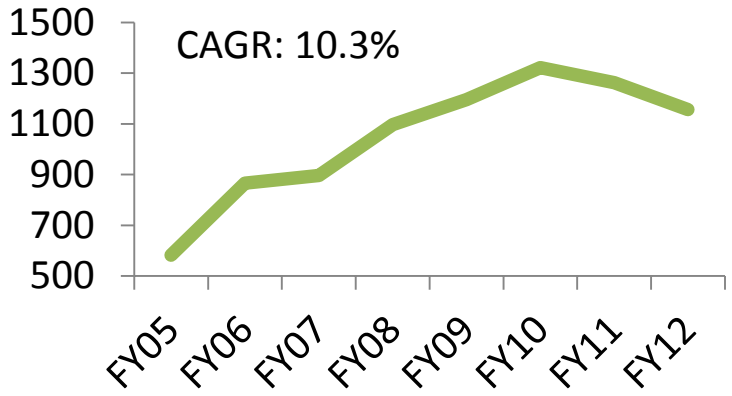


A*STAR Biomedical Publications



Patents

Number of BMS applications filed



*Based on A*STAR & extramural projects managed by A*STAR ETPL*

Start-Ups

Since 2000

>20 **BMS Start-ups**

*(From A*STAR only)*

Financing & Support Programmes for Start-ups

Support

YES! Schools

Provides schools with grants to put in place a entrepreneurship learning programme for their students.

Incubator Development Programme (IDP)

Grant support for incubators & venture accelerators that assist innovative startups.

Grant

Action Community for Entrepreneurship (ACE) Start-ups

Provides grant support to entrepreneurial Singaporeans to set up their business on a $7 : $3 matching basis

Technology Enterprise Commercialisation Scheme (TECS)

Support early-stage Proof-of-Concept (POC) and Proof-of-Value (POV) projects

Equity

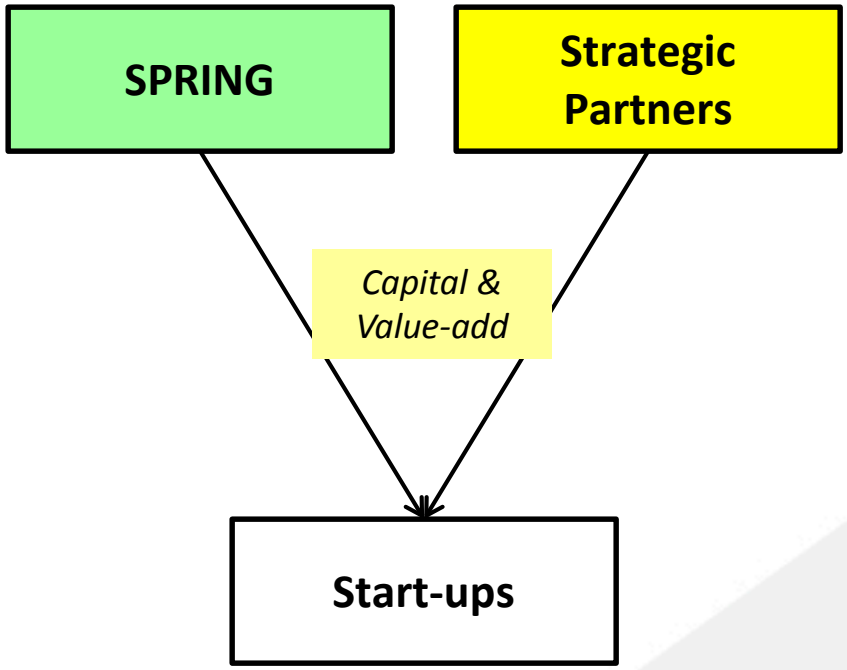
Equity-based co-financing for Singapore-based start-ups with innovative products and /or processes.

*at least 30% equity owned by Singapore citizens / permanent residents

YES : Young Entrepreneurs Scheme

Equity Related Programs

Co-Investment Approach



Programs

SPRING SEEDS	Biomedical Sciences Accelerator (BSA)
Broad-based program for start-ups in multiple sectors	Medtech start-ups raising first round of institutional funds
Co-invest up to SGD$1.5 Mil (US$1.2 Mil)	**Co-invest up to SGD$4 Mil (US$3.3 Mil)**

Our partners include…

bansea · jungle ventures · Clearbridge Accelerator · SMA Singapore MedTech Accelerator · SMALL WORLD GROUP

MedTech Start-ups Supported by SPRING

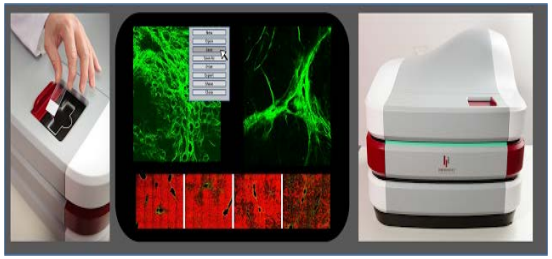
- Supported through TECS Proof-of-Concept / Proof-of-Value Grants and /or SPRING SEEDS investment
- ~ 40 local Med Tech Start-ups currently being helped

Clearbridge BioMedics

- Spin-off from National University of Singapore (NUS); advisors include founder of Biosensors Int'l.
- Developed non-invasive "liquid biopsy" platform using a microfiltration biochip to isolate rare CTCs from whole patient blood.
- Raised institutional round in 2013 from Vertex Venture

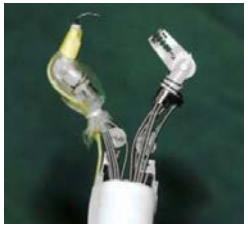
HISTOINDEX
New Standard | New Life

- Spin-off from A*STAR's Institute of Bioengineering & Nanotechnology.
- World's first stain-free, 3D, quantitative imaging solution for visualizing and staging liver fibrosis.
- This provides critical information not currently available with existing stain-based imaging techniques



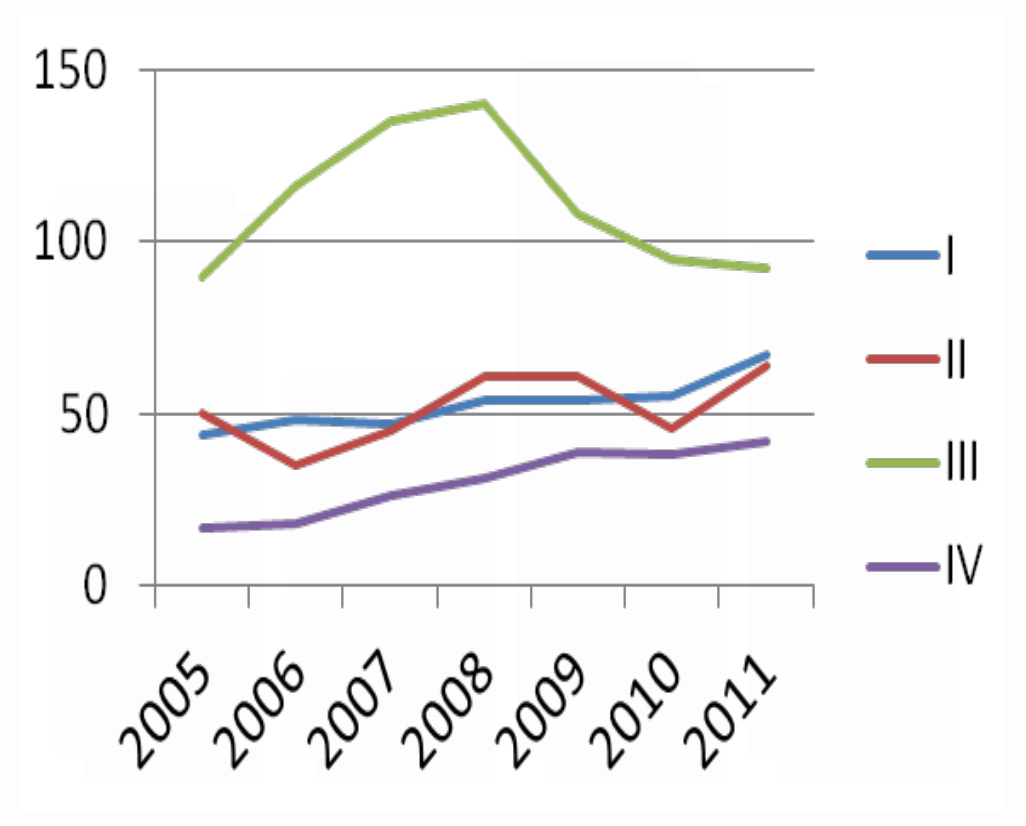
EndoMaster

- Spin-off from Nanyang Technological University
- Robot-assisted surgical system in which a surgeon uses a joystick controller to control 2 robot arms mounted on a tip of an endoscope, guided by images sent from a camera mounted on the same tip.
- Limited human trials with positive results – less discomfort, faster healing time.
- Secured strategic investment from Hoya Group in Aug 2013



Clinical and Healthcare Outcomes

Clinical trials



Total of 265 clinical trials in 2011

Healthcare Outcomes

Evidence-based dengue hospital admission criteria

- 40% reduction in hospitalisation rate, $1.8 mil (US$1.4 mil) savings

HLA-screening before treatment with carbamezipine

- Drop in severe adverse drug reactions

Clinical and Healthcare Outcomes

- Systemic health outcomes:
  - Includes healthcare cost savings, improved patient care and better population health outcomes
  - Highest value-added outcomes but also the most long-term
- Current measures of research outcomes in Singapore:
  - Quantitative indicators e.g. publications, patents, licenses and industry funding
  - Represent *short to mid-term* outcomes, not long-term outcomes
- As we plan the next 5-year R&D plan - *Research, Innovation and Enterprise (RIE) 2020* - the framework for evaluating the value of biomedical research is being reviewed:
  - Strong consensus among the Singapore BMS community that *quantitative KPIs should be complemented by qualitative measures* e.g. narrative on *how R&D derives benefits for patients*
  - Expertise in public healthcare economics needs to be developed; *not easy to measure economic value and healthcare cost savings yielded from BMS research*

Clinical and Healthcare Outcomes

BMS Initiative, besides contributing to the economy and creating quality jobs, has helped Singapore and our region's health outcomes. Examples :

1. A much greater understanding that there is such an entity as the ***"Asian Phenotype",*** where diseases such as *lung cancer, heart failure, dementia, diabetes* have a different presentation and thus treatment and outcome, compared with the same disease in largely Caucasian populations in the West. It also highlights the need to invest in pharmaco-genomics and pharmaco-vigilance after drugs are approved and widely marketed.

2. Enhanced international collaboration:

* Singapore has helped improve pediatric leukemia survival in Malaysia by sharing of clinical protocols as part of a multi-center clinical trial

* Stimulated basic science collaboration with , e.g. Genome Institute of Singapore-National University of Singapore (NUS)/National University Hospital System(NUHS)-Harvard collaboration in *lung cancer stem cells* (Cell), and NUS/NUHS-Harvard collaboration in *liver cancer* (New England Journal of Medicine)

Basic Research is an investment in the future

- Determining the structure of DNA

- Relenza, the world's first cure for influenza, arose from the crystal structure determination of the enzyme, neuraminidase used by the influenza virus to get into cells.

- New England Biolabs (NEB) 1975 : " many of those early restriction enzymes were discovered at my lab in CSHL…Rich Roberts "

- ZFRs, TALENs, CRISPRs -- Explosion in genome engineering tools for stem cells/mouse model research came from basic research in Plants (early 2000), Bacteria and Bioinformatics tools (2005), thus changing the drug discovery pipeline.

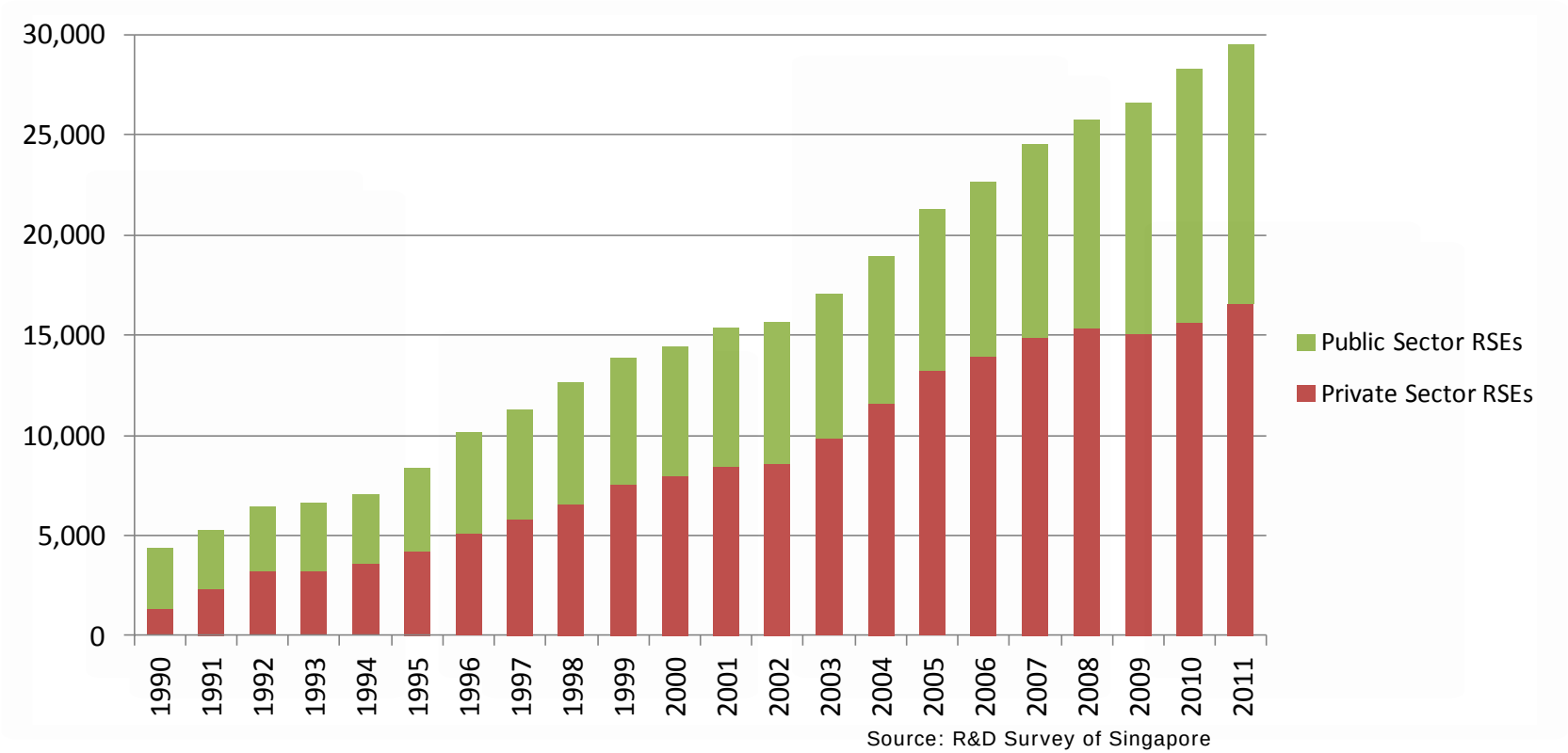
- **Commercializing research discoveries is a present necessity; the funding of basic research must be a long term pursuit.**

Keep the line between Basic and Applied "Blurry"

ZFRs	Zinc finger recombinases
TALENs	Transcription activator-like effector nucleases
CRISPRs	Clustered regularly interspaced short palindromic repeats

Building Up R&D Human Capital

Research Scientists & Engineers (RSEs) grew from 4,300 to 29,480 (between 1990-2011)
RSEs in the private sector grew more than tenfold from 1,360 to 16,540

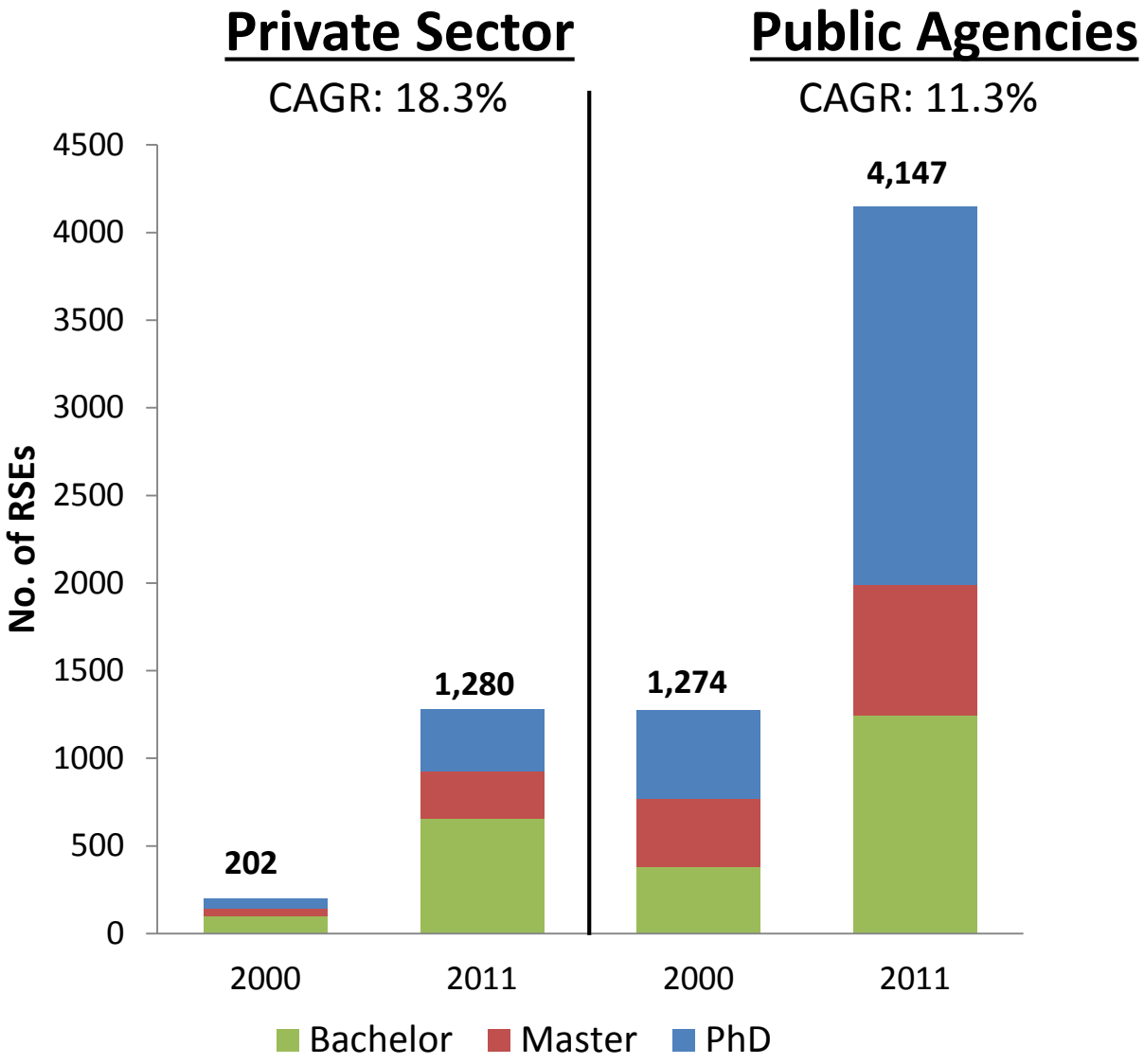


Source: R&D Survey of Singapore

Manpower Growth	Public	Private	Total
CAGR 1990-2011(PhD)	9.6%	16.4%	**10.4%**
CAGR 1990-2011(Overall)	7.3%	12.6%	**9.6%**

56% of total RSEs work in the private sector

BMS R&D Human Capital



Source: National R&D survey 2011

Building up Human Capital: Catch a few Whales

Senior Scientific Leaders to help develop local talent

Dr Philippe Kourilsky
Chairman, SIgN

Dr Alan Colman
Exec Dir, SSCC

Dr Sydney Brenner
Scientific Adviser, A*STAR

Dr David Srolovitz
Exec Dir, IHPC

Prof Charles Zukoski
Chmn, SERC

Sir George Radda Chmn, BMRC

Dr Edward Holmes
Exe Dy Chmn (TCSG), BMRC &
Chmn, NMRC

Dr Judith Swain
Exec Dir, SICS

Prof Paola Castagnoli
Scientific Dir, SIgN

Dr Dale Purves
Exec Dir, NRP

Prof Dim-Lee Kwong
Exec Dir, IME

Dr Keith Carpenter
Exec Dir, ICES

Dr Pantelis Alexopoulis,
Exec Dir, DSI

Dr Phil Ingham
Dy Dir, IMCB

Sir David Lane
Chief Scientist

Dr Birgitte Lane
Exec Dir, IMB

Dr Frank Eisenhaber
Director, BII

Dr Alex Matter
Director, ETC

Dr Edison Liu
Exec Dir, GIS

Dr Jackie Ying
Exec Dir, IBN

Prof Stephen Quake
Consultant

Dr Jean Paul Thiery
Dy Dir, IMCB

Prof Peter Gluckman
PI, SICS

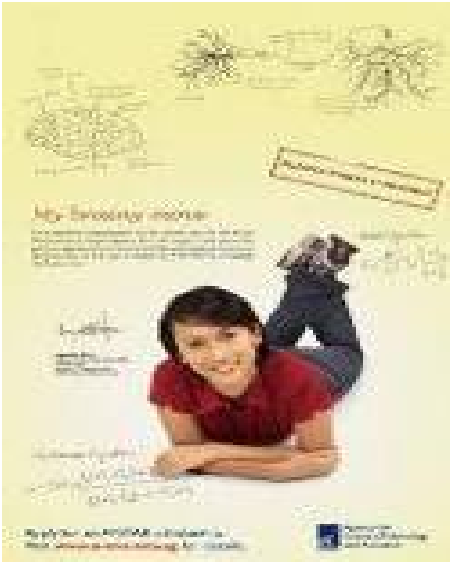
Dr Davor Solter
PI, IMB

Prof David Townsend
Head of PET and SPECT Group, SBIC

Dr Stephen Cohen
Acting Exec Dir, IMCB

Local Human Capital – Grow PhD Guppies

Guppy – 0.03 meters



Long Term Human Capital Pipeline

Evelyn Thangaraj
2005 A*STAR YRAP Scholar from India (currently A*STAR Scholar, Medicine, Imperial College, London)

Le Ngoc Phuong Lan
2005 A*STAR YRAP Scholar from Vietnam (currently A*STAR Scholar, Pharmacy, University of London)

10-14 yrs	15-18 yrs	19-23 yrs	24-30 yrs	< 35 yrs
Youth Science	YRAP & A*STAR Science Awards	NSS(BS) PGS	NSS(PhD) AGS SINGA	AIF AGS (Post-doc)

YRAP - Young Researchers Attachment Programme
A*STAR - Agency for Science & Technology Research
NSS - National Science Scholarship
PGS - Pre-Graduate Scholarship

AGS - A*STAR Graduate Scholarship
SINGA - Singapore International Graduate Award
AIF - A*STAR International Fellowship

Nurturing a Pipeline of >1,200 Singaporean PhD Talent

Dr Karen Crasta
Lee Kong Chian School of Medicine,
Nanyang Technological University (NTU)
A*STAR International Fellow
NRF Fellow 2013

Dr Cheok Chit Fang
Principal Investigator, IFOM-p53 Lab
National Science Scholar (PhD)

Dr Melissa Fullwood
Yale-NUS College
Principal Investigator, Cancer Science Institute
National Science Scholar (BS-PhD)
NRF Fellow 2013

Dr Jonathan Loh Yuin Han
Principal Investigator, Institute of Molecular & Cell Biology (IMCB)
A*STAR Graduate Scholar

Dr Seah Kwang Hwee
Associate Patent Examiner,
Intellectual Property Office of Singapore (IPOS)
A*STAR Graduate Scholar

Communicating the Value of Scientific Knowledge

Importance of **Public Outreach** in S&T:

- *Future of the scientific enterprise depends on public support for R&D*
- *Develop the next generation of scientists and engineers*
- *Build capacity for sustained long-term economic growth and improved quality of life*

Role of Different **Stakeholders** in Public Outreach Efforts

- *Public policy-makers, scientists, teachers with the influence, corporations as part of Corporate Social Responsibility efforts*

Communicating the Value of Scientific Knowledge

How Singapore Does It:

- *Framing the "**Economic Development**" story*
  - Instilling the positive economic impact of our research (i.e. high value-added job creation) in the public mindset
- *Reiterating positive **Societal outcomes** which are relatable to the public e.g. 2003 SARS outbreak, Genome Institute of Singapore co-developed a sensitive and accurate SARS Diagnostic Kit with Roche*

Communicating the Value of Scientific Knowledge

How Singapore Does It:

- *Enhancing public understanding of increasingly complex and urgent societal issues, and the role of R&D in addressing these issues*
  - e.g. Ageing and Healthcare - Cutting-edge R&D (especially in telehealth) can potentially transform and improve the delivery of healthcare for millions, but the impact would be minimal if the public did not embrace the technologies

Communicating the Value of Scientific Knowledge

How Singapore Does It:

- *Platforms to reach out to students and the public and enhance appreciation of Science :*
  - Partnership with Singapore Science Centre and Ministry of Education
  - Singapore Science Festival, STAR Lecture, Science in the Mall, Centre for Research and Applied Learning in Science, Singapore Academy of Young Engineers and Scientists, Teachers Local Research Attachment Program

STAR Lecture 2013
'The Modern Alchemist'
Dr Peter Wothers, Cambridge University

SINGAPORE SCIENCE FESTIVAL 2013

Science in the Mall

CRADLE
Centre for Research and Applied Learning in Science

Communicating the Value of Scientific Knowledge

Singapore Science Festival

- Annual carnival spanning several weeks with events for students, parents and the general public to understand the application of science in our daily lives
- Celebrates achievements of local innovators

STAR Lecture

- A*STAR and Science Centre bring the Royal Institution's Christmas Lecture to Singapore
- Designed to bring Singaporean youths on a journey of scientific discovery and inspiration through an interactive discussion with a world-renowned scientist
- Brings the attention of the nation's youth to the 'big picture' questions in Science

Centre for Research and Applied Learning in Science (CRADL∑)

- An open learning and research lab at the Science Centre Singapore
- Develops teacher-mentors and enhance the capacity of teachers and schools in science research and innovation
- Collaboration between Science Centre, A*STAR, DSO and MOE