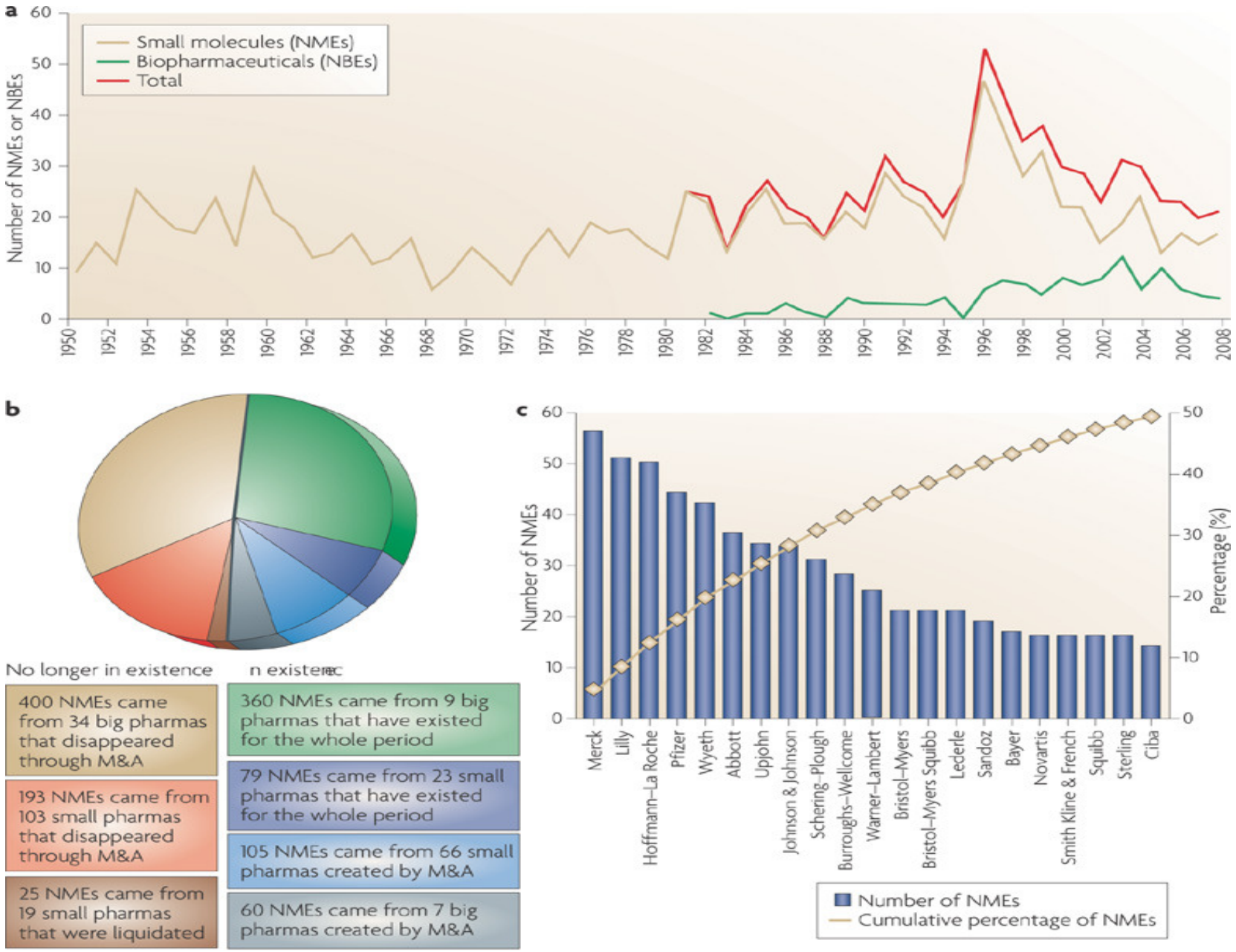
Regulatory Science and the FDA

Garret A. FitzGerald MD, University of Pennsylvania

An Existential Challenge



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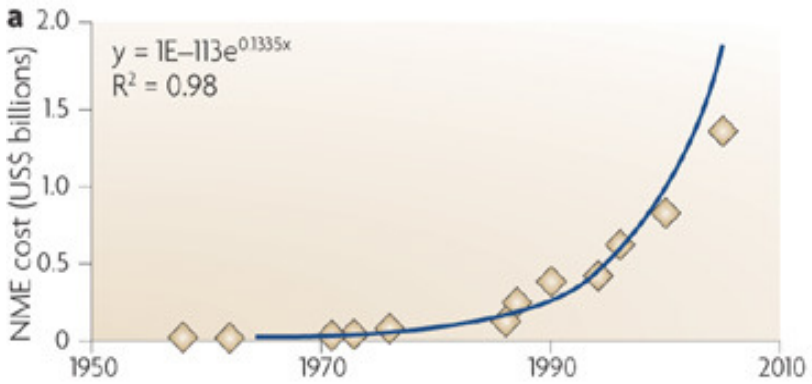
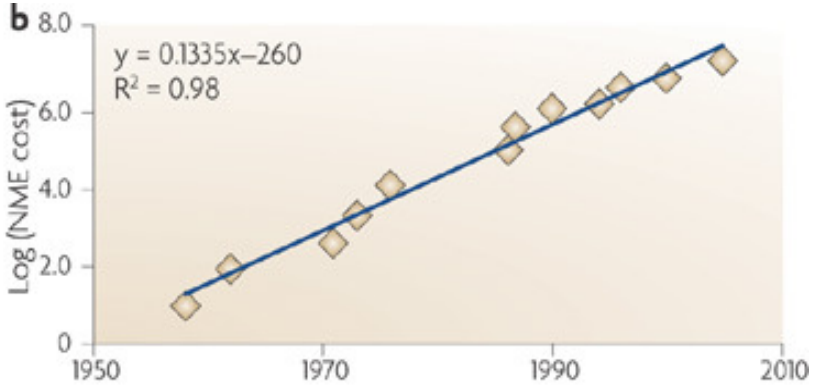
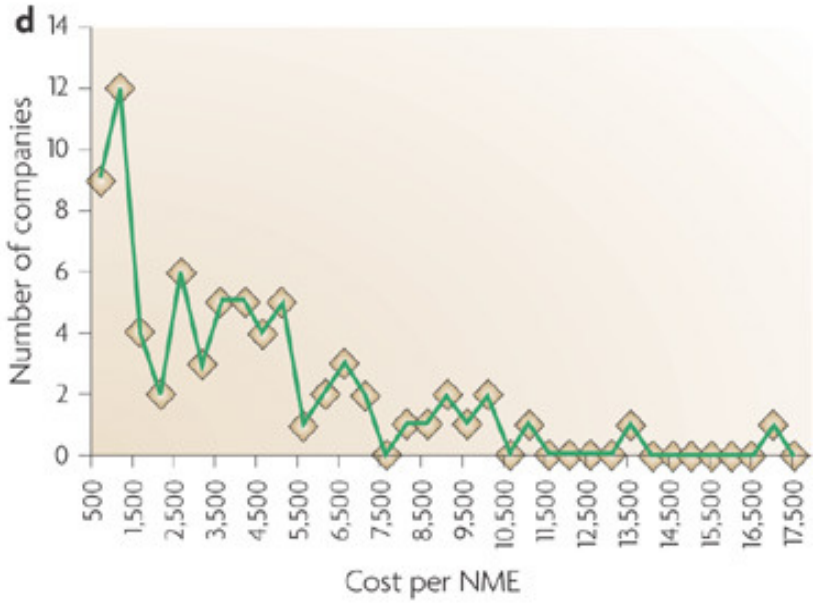




c

Estimate	Value of item (US$ millions)
DiMasi estimate in 2000 dollars	802
• Adjustment for post-approval R&D	95
• Adjustment for new indications and non-US approvals (20%)	160
• Adjustment for success rate (11.5% versus 21.5%)	697
Adjusted DiMasi estimate in 2000 dollars	1,754
• Adjustment for inflation (3.7% per year)	592
• Adjustment for other cost increases, such as regulation (8.3% per year)	1,565
Adjusted DiMasi estimate in 2008 dollars	3,911



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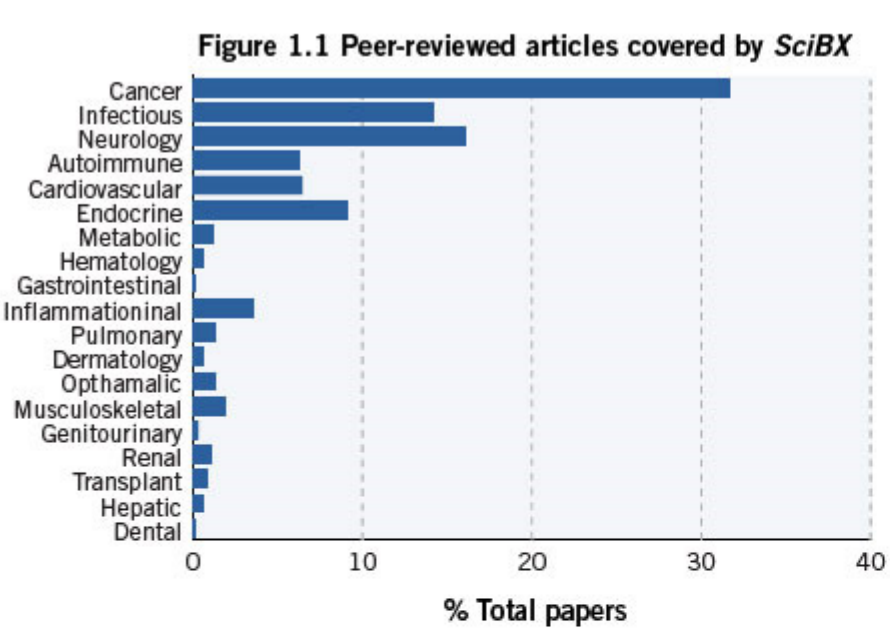
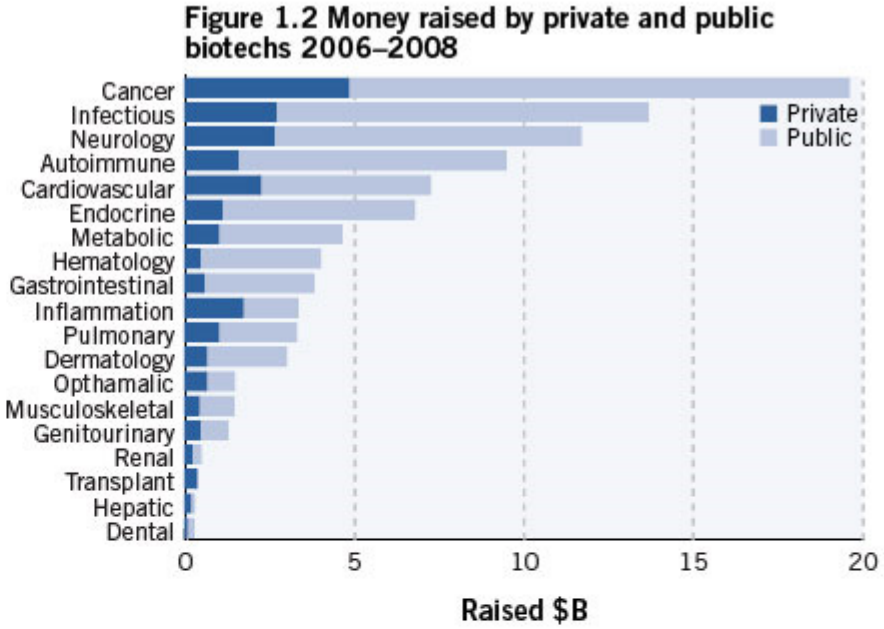
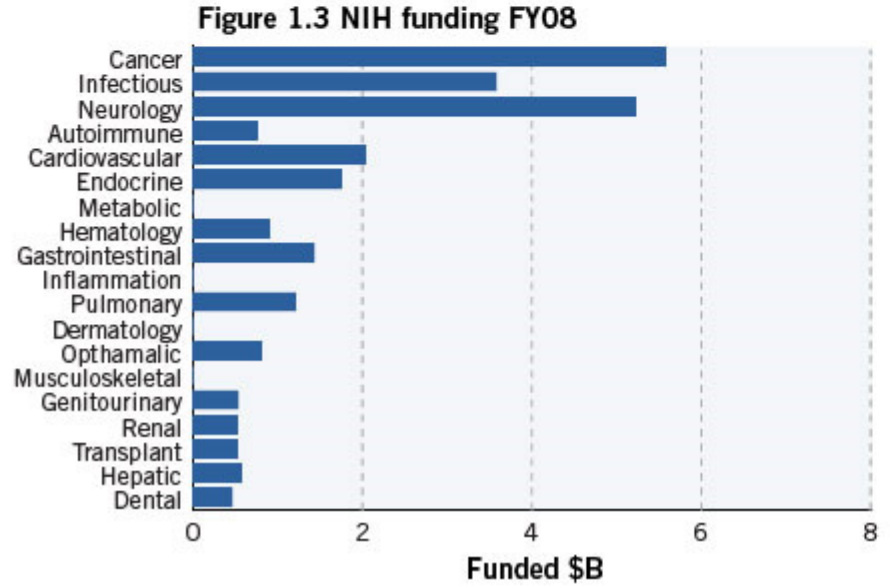
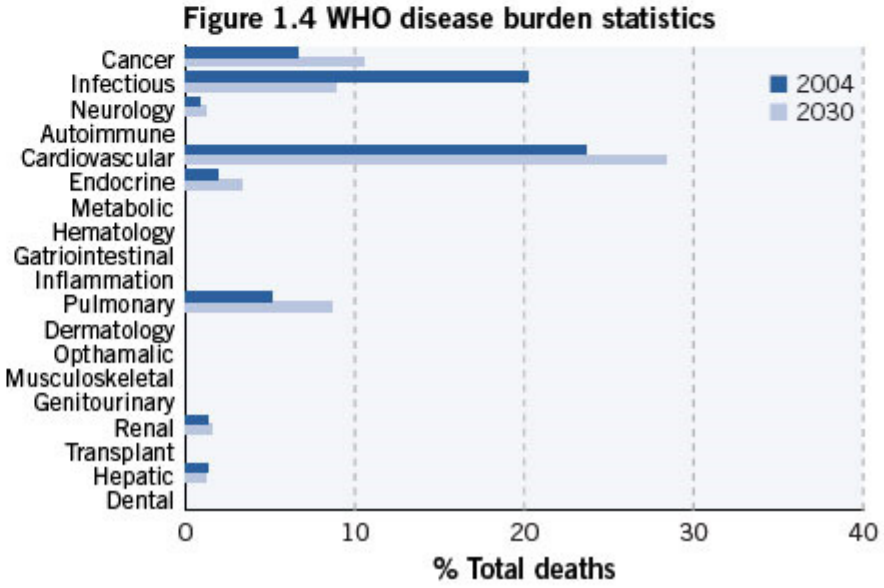
Munos B NRDD 2009; 8: 959-68.

Unmet Medical Needs?



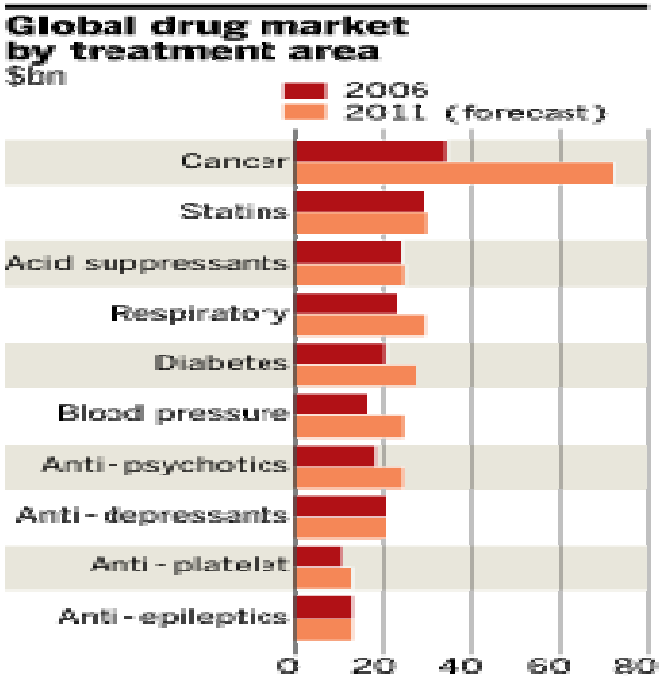


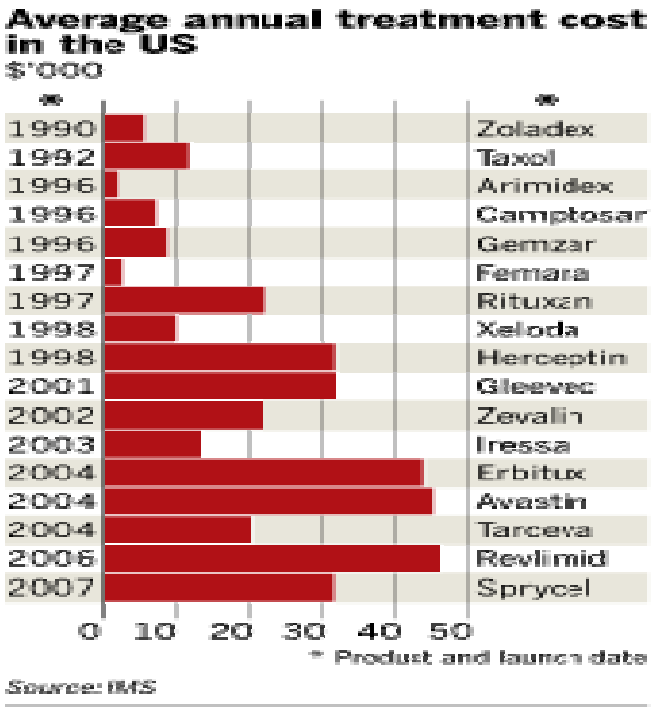




Taroncher- Oldenburg G. SciBx 2009

Not NICE


Global drug market
by treatment area
$bn
2006
2011 (forecast)
Cancer
Statins
Acid suppressants
Respiratory
Diabetes
Blood pressure
Anti-psychotics
Anti-depressants
Anti-platelet
Anti-epileptics
0
20
40
60
80


Average annual treatment cost
in the US
$'000
1990 Zoladex
1992 Taxol
1996 Arimidex
1996 Camptosar
1996 Gemzar
1997 Femara
1997 Rituxan
1998 Xeloda
1998 Herceptin
2001 Gleevec
2002 Zevalin
2003 Iressa
2004 Erbitux
2004 Avastin
2004 Tarceva
2006 Revlimid
2007 Sprycel
0
10
20
30
40
50
* Product and launch date
Source: IMS

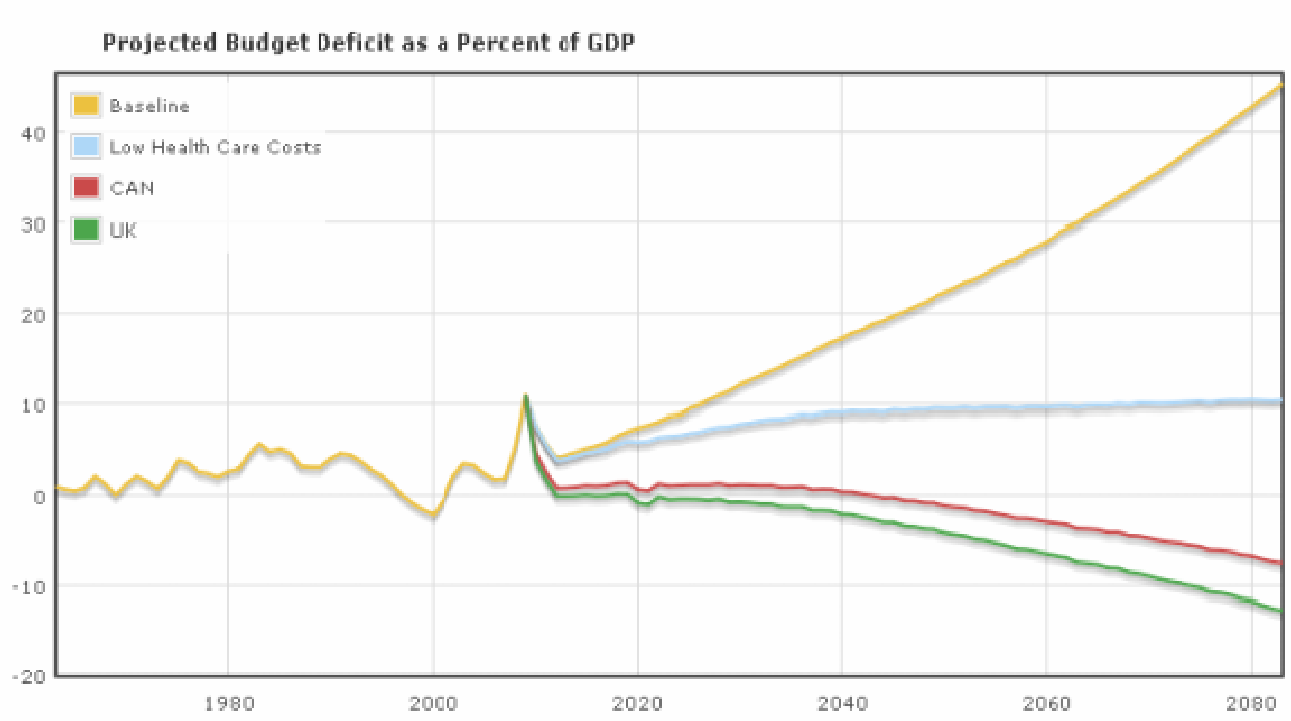
An Appeal to Reason

“If we don’t change the business models, we’re not going to survive as an industry”.

Richard Clarke, Merck CEO

Financial Times, Oct 22nd 2008

Another Existential Challenge

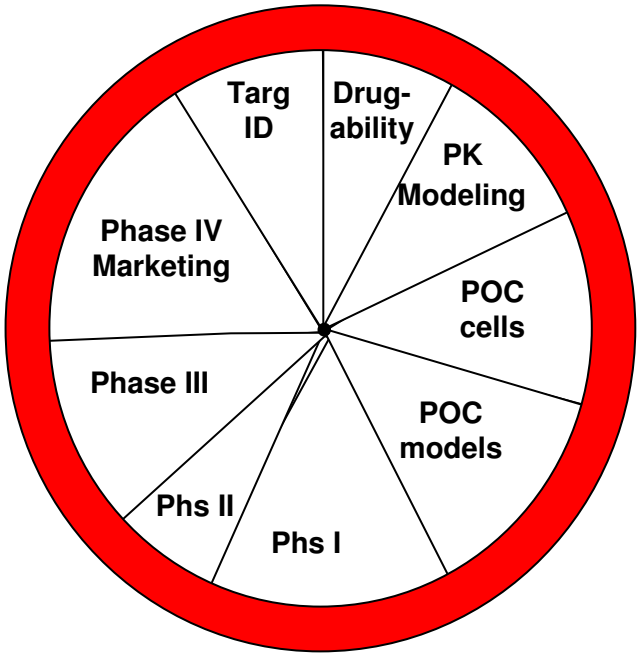


Aging population only

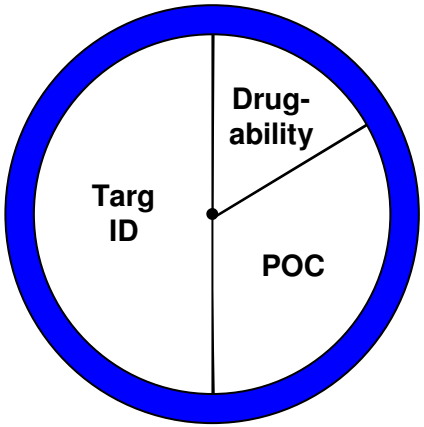
Center for Economic and Policy Research 2010

Prescription drugs rose from 10% to 18% of health care costs from 1996 to 2006

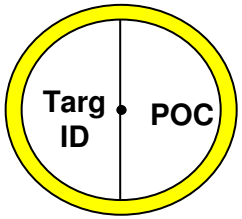
Vertical Disintegration



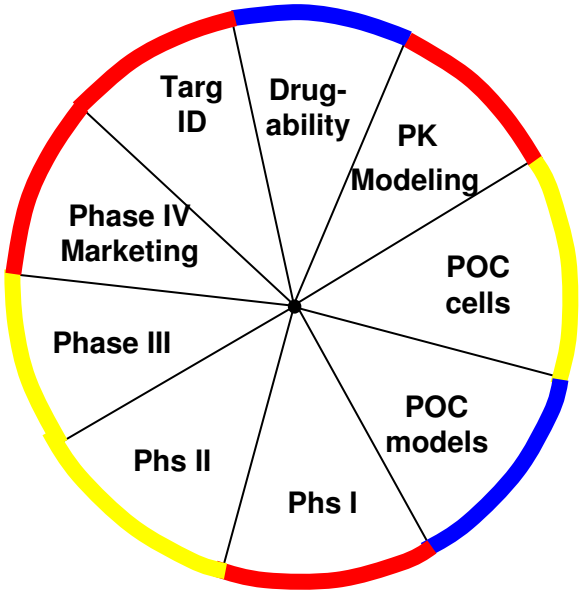
PHARMA

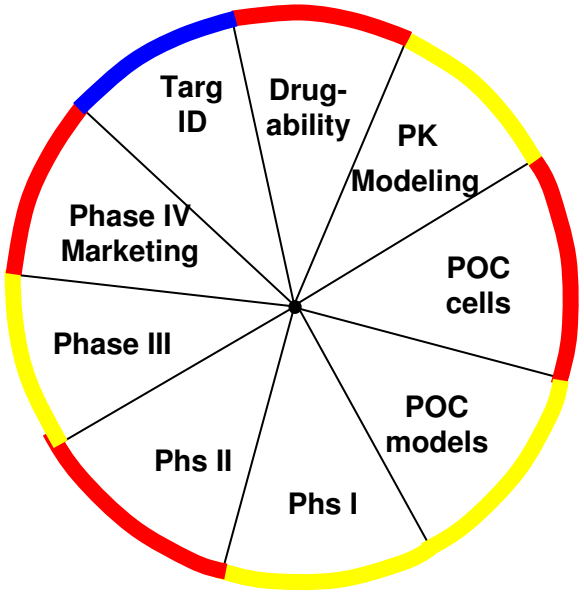


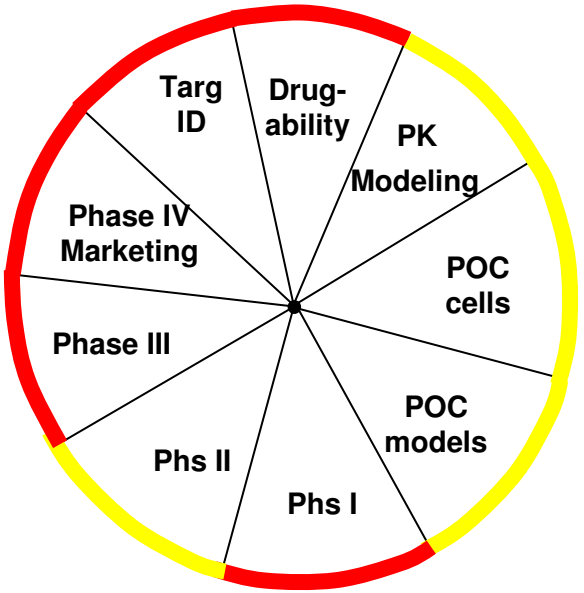
BIOTECH



ACADEMIA







Regulatory Science

Regulatory Science

The acquisition and analysis of data sufficient to inform decision making pertinent to

the approval of safe and effective therapeutics, devices and cosmetics and

ensuring the safety and nutritional value of the food supply.

What it's not…

A new set of regulations

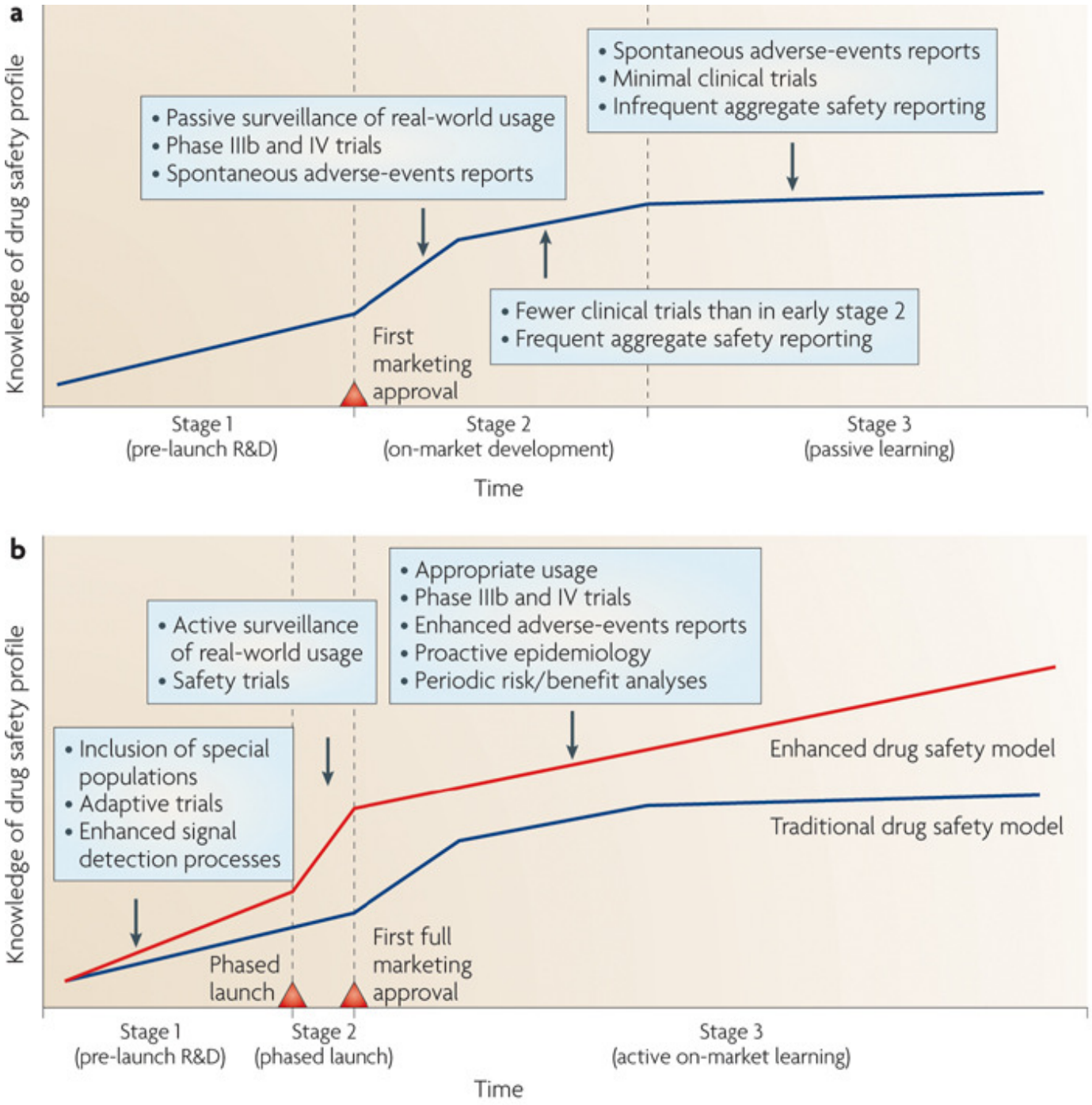
An approach to speed the approval process

An attempt to establish cutting edge biomedical science in the FDA

Why should we care?

Regulatory Science

- Provide purpose, focus and respect for the scientific mission of the agency
- Encourage and reward innovation
- Enhance risk detection and conserve value
- Leverage the resources of the academic sector to refine decision making at the FDA


a
Knowledge of drug safety profile
• Passive surveillance of real-world usage
• Phase IIIb and IV trials
• Spontaneous adverse-events reports
• Spontaneous adverse-events reports
• Minimal clinical trials
• Infrequent aggregate safety reporting
• Fewer clinical trials than in early stage 2
• Frequent aggregate safety reporting
First marketing approval
Stage 1 (pre-launch R&D)
Stage 2 (on-market development)
Stage 3 (passive learning)
Time
b
Knowledge of drug safety profile
• Active surveillance of real-world usage
• Safety trials
• Appropriate usage
• Phase IIIb and IV trials
• Enhanced adverse-events reports
• Proactive epidemiology
• Periodic risk/benefit analyses
• Inclusion of special populations
• Adaptive trials
• Enhanced signal detection processes
Enhanced drug safety model
Traditional drug safety model
Phased launch
First full marketing approval
Stage 1 (pre-launch R&D)
Stage 2 (phased launch)
Stage 3 (active on-market learning)
Time

Elements of Regulatory Science

- Exploit the lifecycle approach to approval and withdrawal of novel therapeutics and devices: graded introduction and graded withdrawal
- Incentivize innovation and early, unrestricted exploration of drug action and mechanisms of SAEs: a safe haven for systems pharmacology and physiology

Elements of Regulatory Science

- Broaden the approach to risk detection

Lessons of Vioxx, Tegenero and Avandia: look beyond pharmacoepidemiology and meta-analyses

- Catalyze development of orphans; drugs and diseases. FDA as a unique repository of information
- FDA – Academia Centers of Excellence

FDA Centers of Excellence

Add value by leveraging academic expertise to Agency needs:

- Adaptation of trial design
- Informatics for collation, storage, interpretation and communication
- Translational Medicine and Therapeutics
- Emerging therapeutic modalities – stem cell biology, nanotechnology

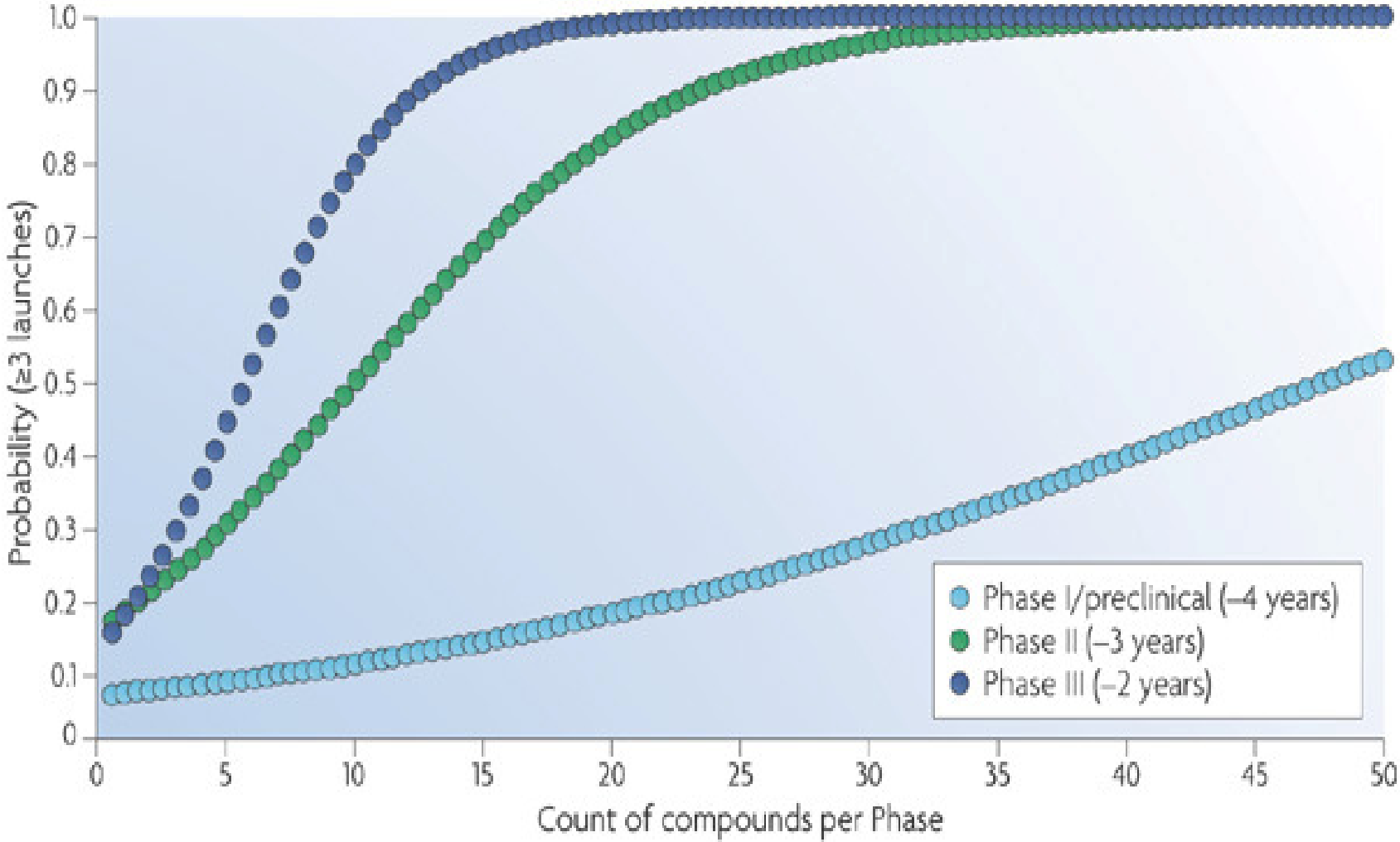
FDA Centers of Excellence

- A source of incremental expertise in partnership with FDA investigators
- A neutral testing ground – a JPL for the FDA
- A bi-directional educational opportunity
- Lessons from CPI and CERTS – sufficient incremental resource to attract engagement and demand delivery
- Leverage NIH peer review system

A Parallel Initiative…

A coincident role for NIH, Academia and Industry; Rebuild Capacity in Human Pharmacology

Critical to the development of NMEs



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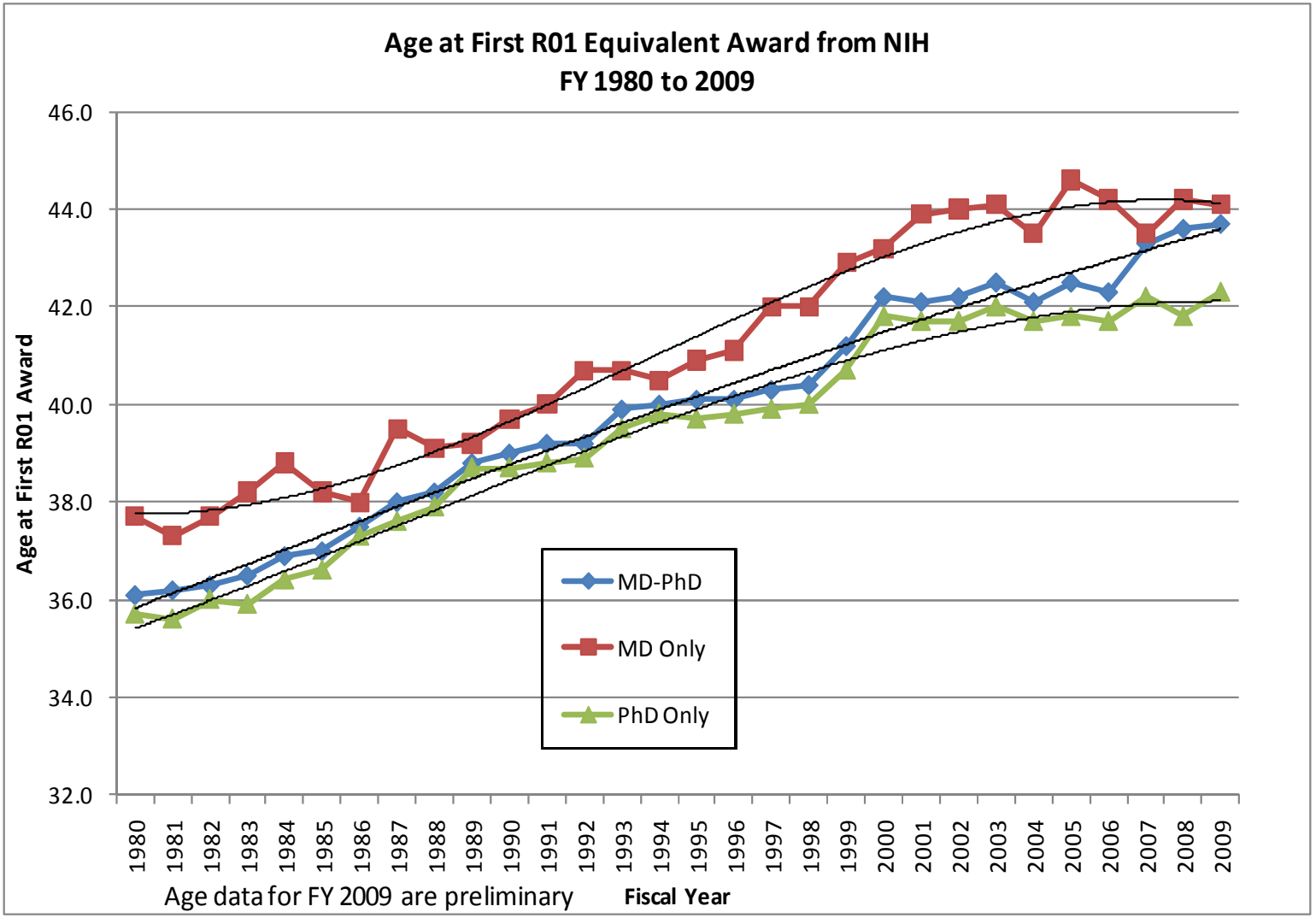
The Prescribing Physician's Primary Source of Drug Information

A coincident role for NIH, Academia and Industry; Rebuild Capacity in Human Pharmacology

- Critical to the role of the FDA in determining benefit and risk
- Critical to comparative effectiveness
- Critical to the education of doctors
- Deficient or absent in industry, academia and the FDA

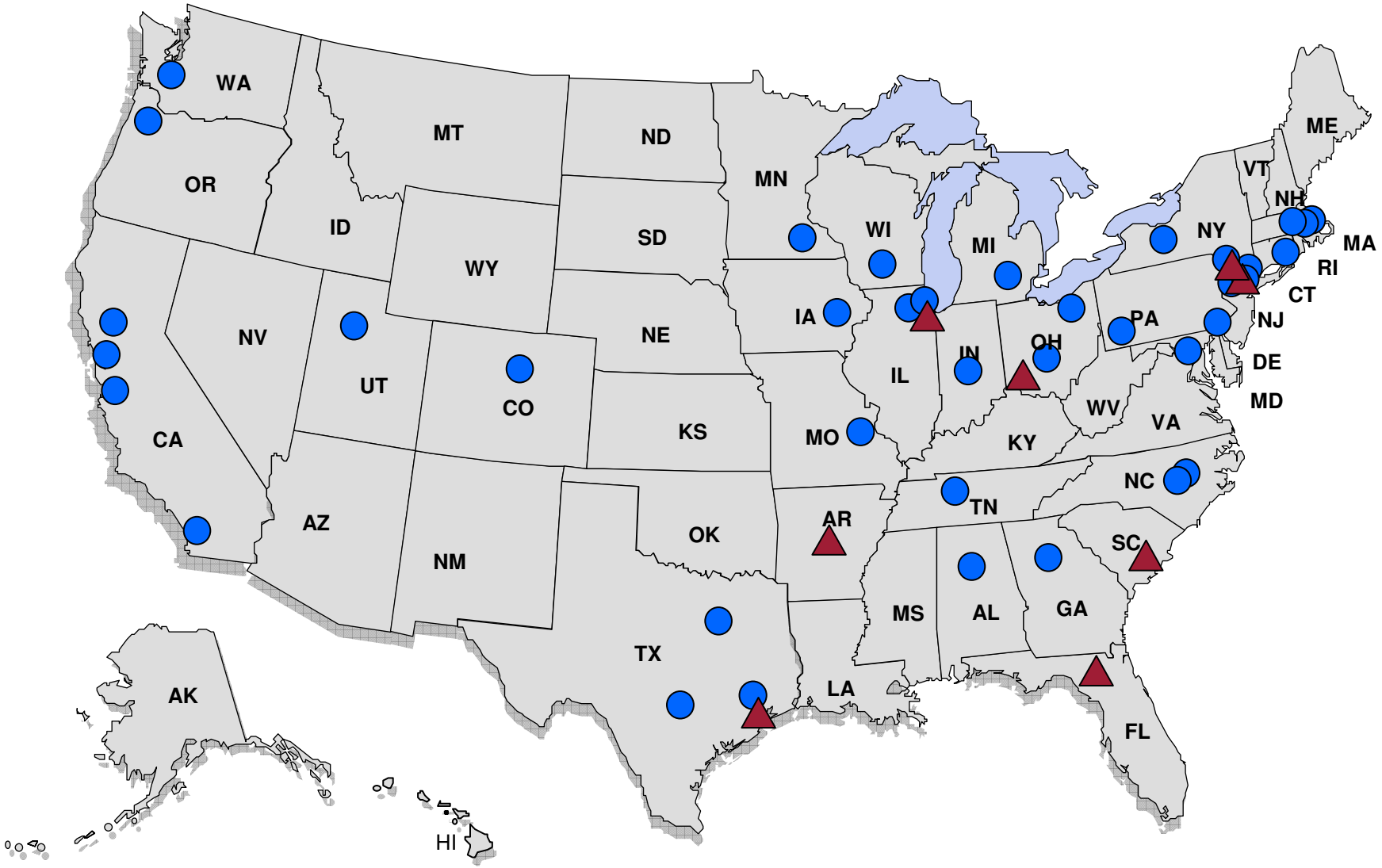
Recapture the imagination of the Young(er)



LAUNCHING A NEW DISCIPLINE IN ACADEMIA: TRANSLATIONAL MEDICINE AND THERAPEUTICS

- Develop and project mechanism based quantitative biomarkers from model systems into humans.
- Evoking phenotypic responses in humans to guide individualization of rational dose selection
- Harness the unbiased technologies to select amongst molecules directed against a single target
- Complements the emergence of Regulatory Science

National CTSA Consortium

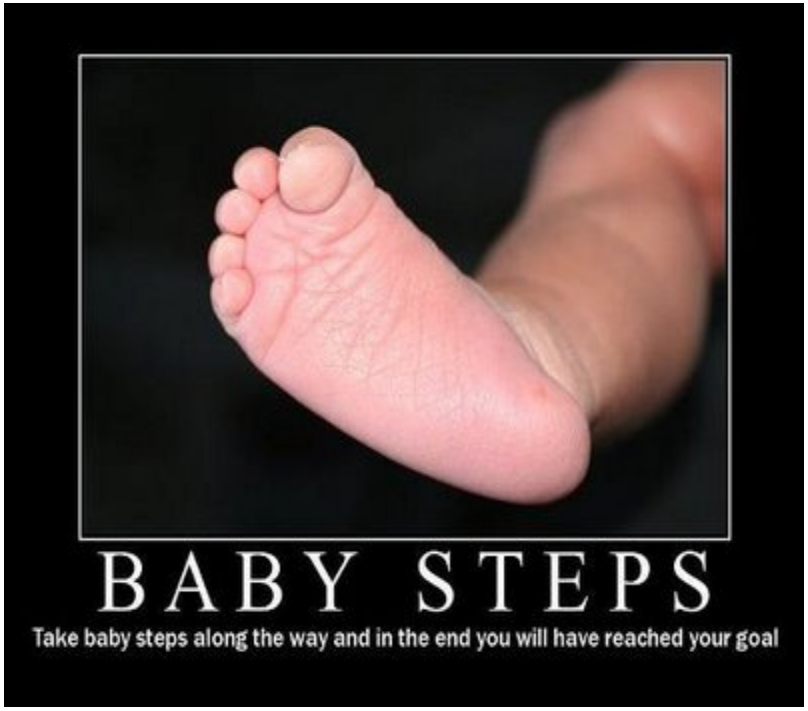


Participating Institutions

- New members 2009
- Members

CTSA Clinical & Translational® Science Awards

Steps in the right direction…



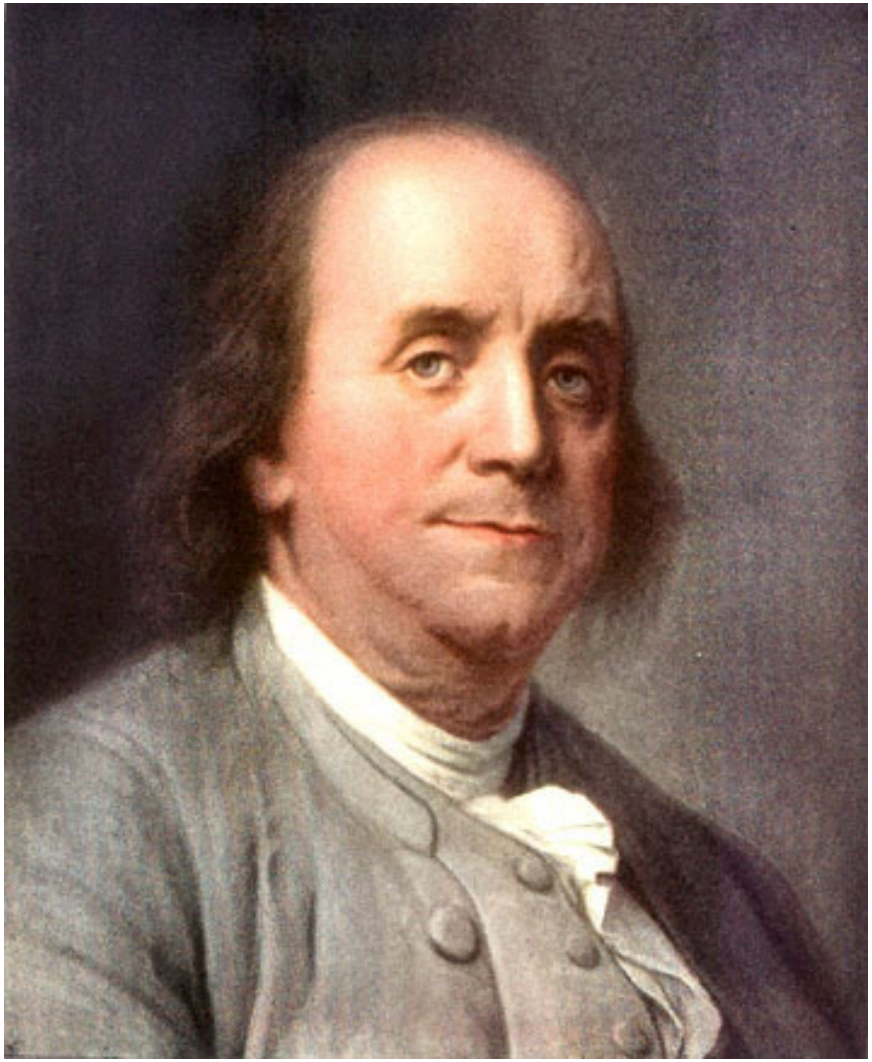
- **A Joint NIH-FDA Leadership Council**

•The NIH and the FDA will jointly make 2-3 awards of $450,000 - $675,000 per year, each for 3 years.

Final Message

- Academia and its funders, the Pharma and Biotech industries and the FDA face serious and integrated challenges
- How we address them will directly impact both the health and wealth of the US and the wider world
- Shared problems demand imaginative approaches to developing shared solutions

A word from Philadelphia…..



Let’s not hang together