Impacts of Research on Decision Making and Public Behavior: a Biomedical Research Perspective

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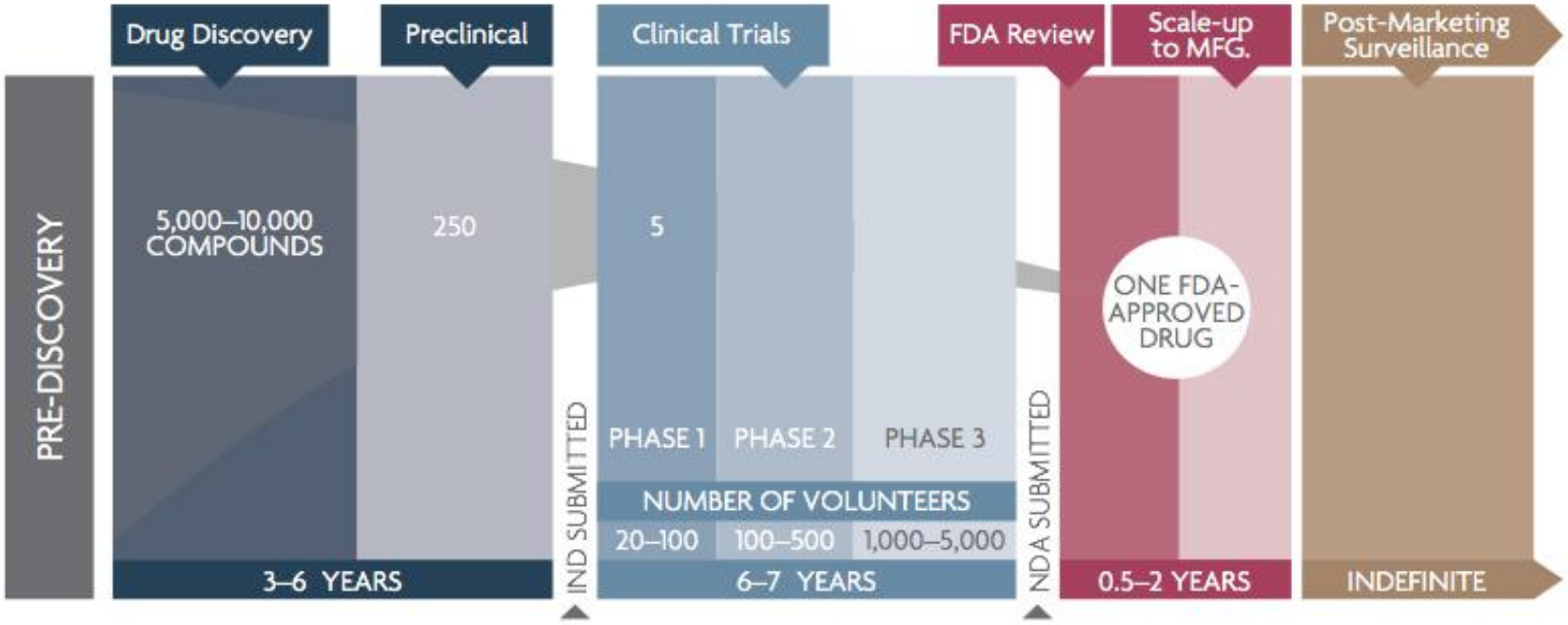
"...science is the search for truth, but it is not the search for certainty. All human knowledge is fallible and therefore uncertain" .

- Karl Popper

"Drug Development is the process of progressive removal of uncertainty".

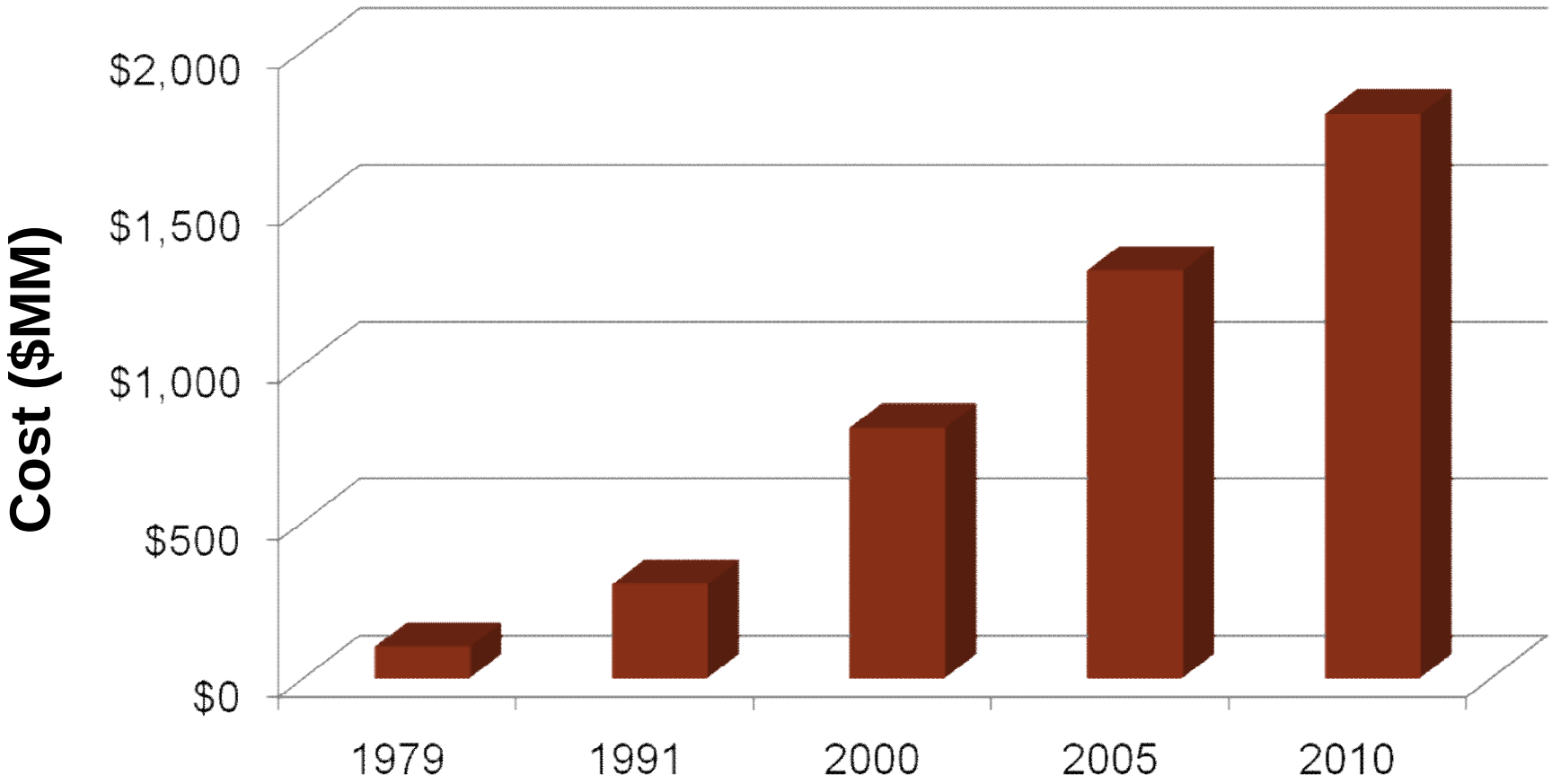
- Dr. Janet Woodcock, FDA

Drug Development Process

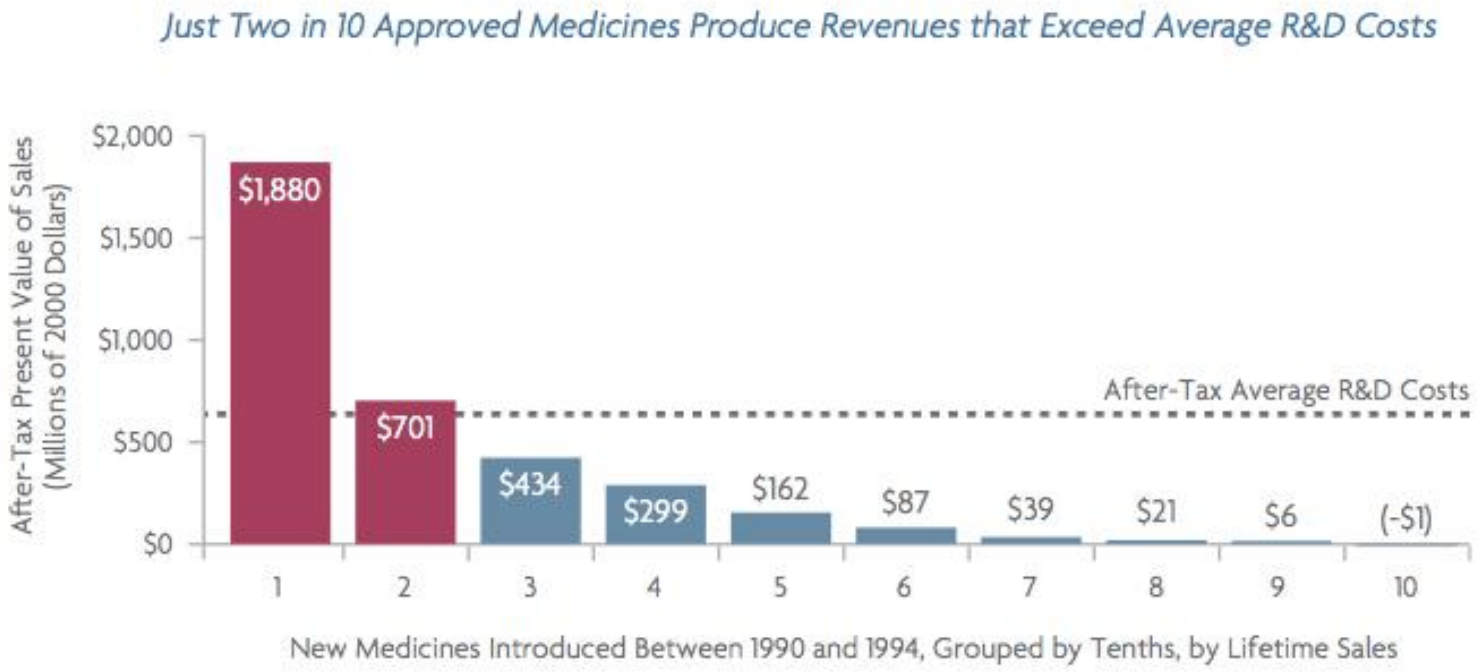


Source: PhRMA[6]

Costs to develop new drugs are rising

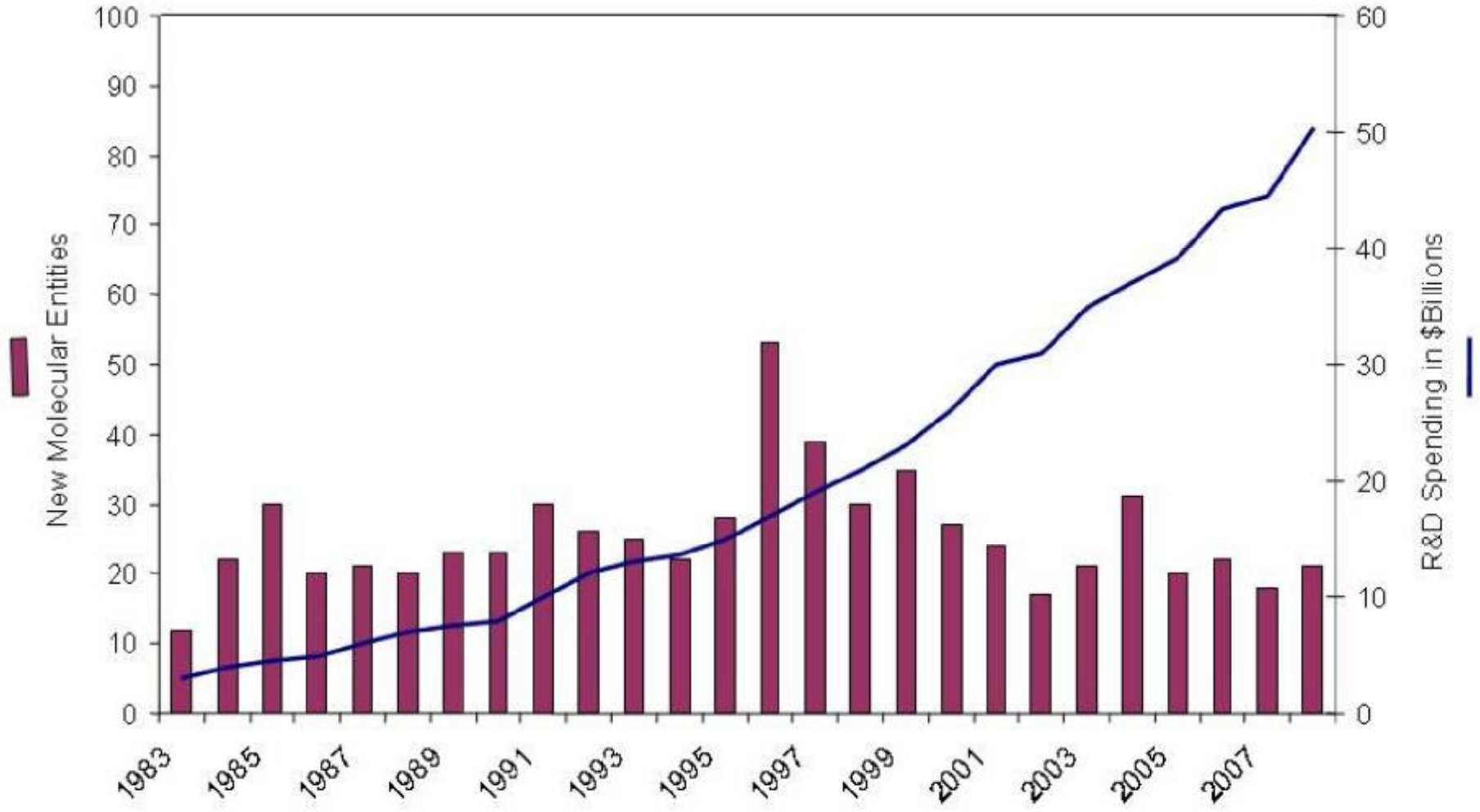


Fewer Drugs are Commercially Successful

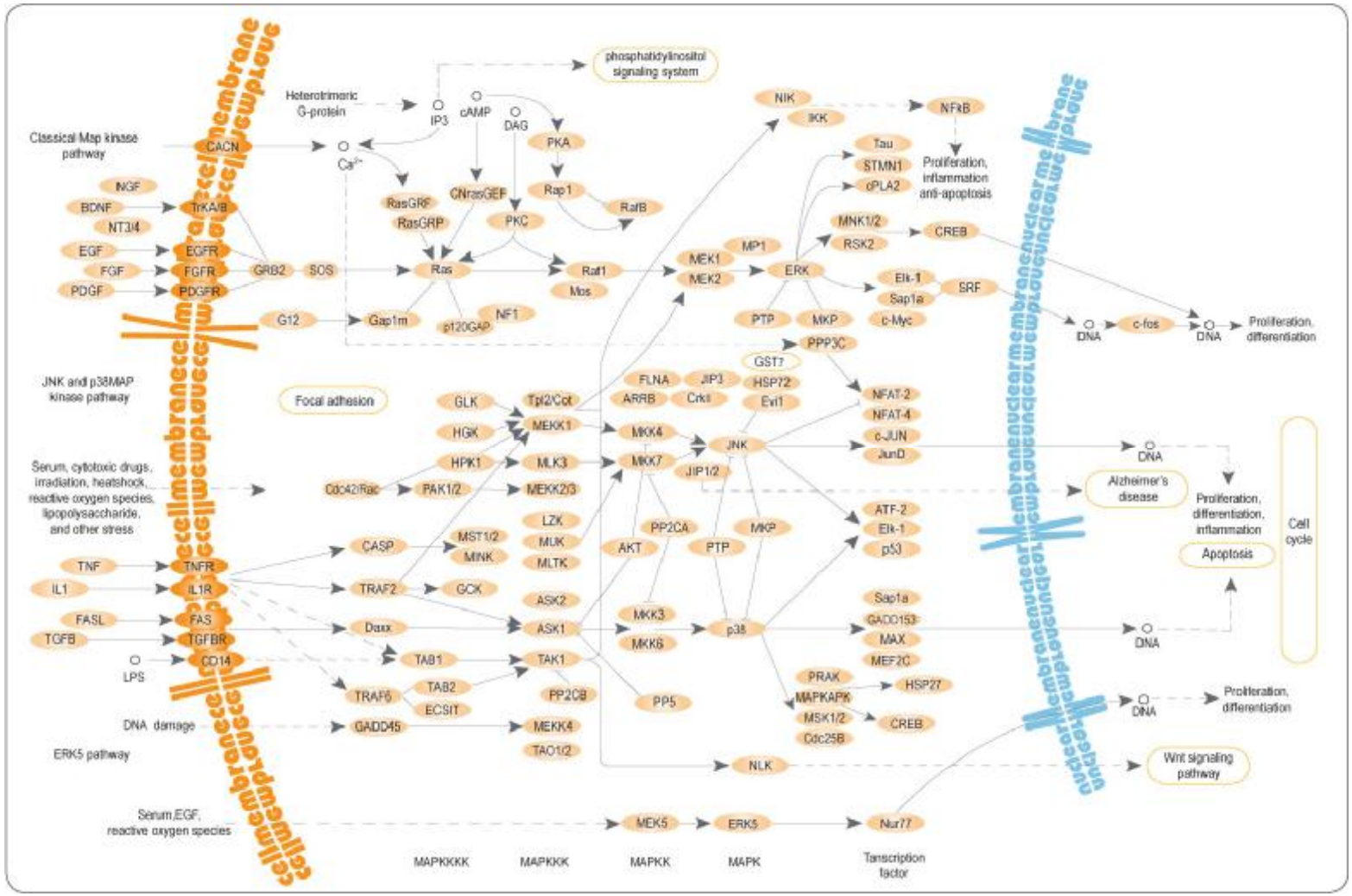


Source: J.A. Vernon, J.H. Golec, and J.A. DiMasi[2]

US Pharmaceutical R&D Spend and Productivity over time



Biological Systems are Complex – and Adaptive

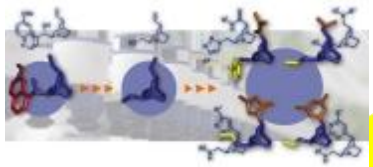


Pharma Drug Discovery Technology Cycles

1850-1960

Natural products:

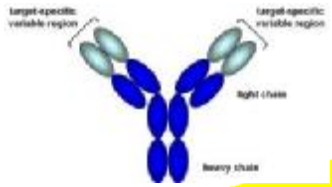
Digoxin
Insulin
penicillin



1950 - 1970

Synthetic Chemistry:

NSAIDS
antibiotics
morphine

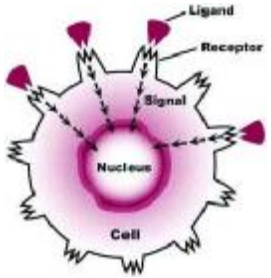


1970 - 1990's

Receptors/ enzyme biology:

Beta blockers
H2 inhibitors
ACE inhibitors
statins

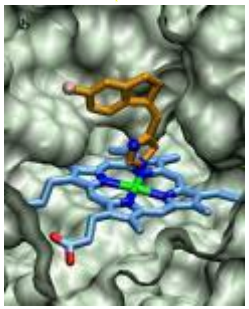
Mab



2000 -

Genomics/ proteomics:

HTS
Combi chem
Bioinformatics/Systems Biology



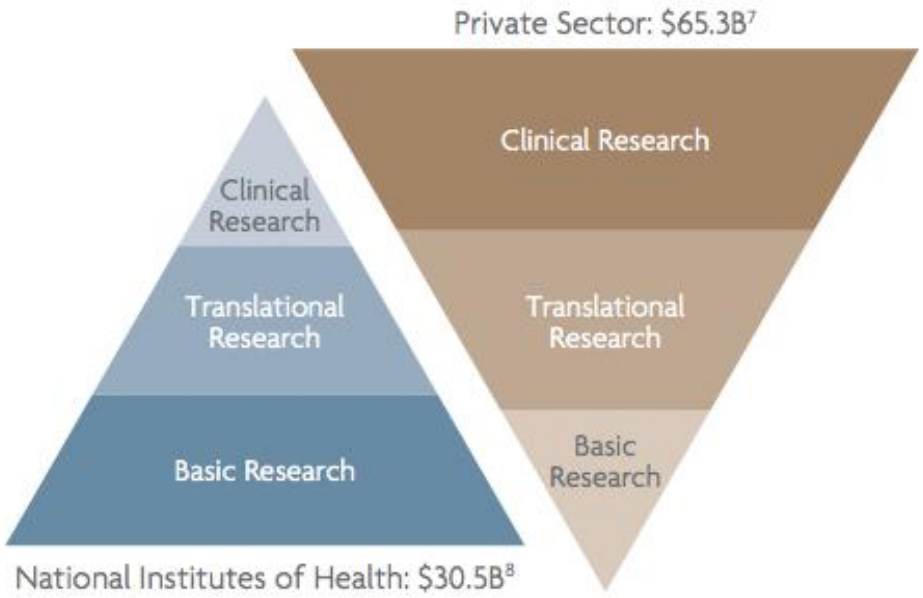
We need something big!

Source: Steve Plag, Credit S

Private and Public R&D Spending Over Time

Source: Burrill & Company, PhRMA, NIH Office of Budget[10]

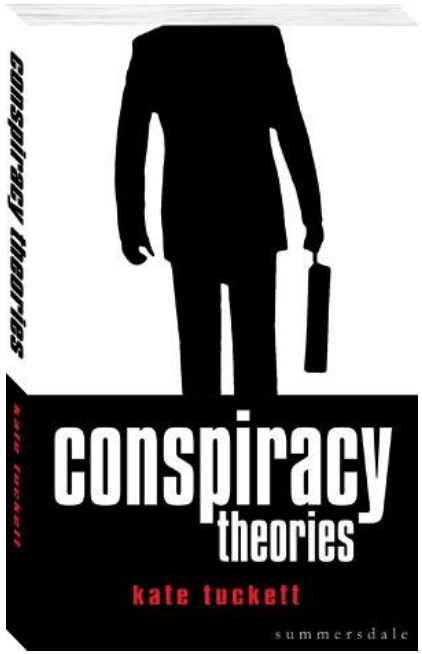
US Private and Public Sector R&D Funding are Complementary



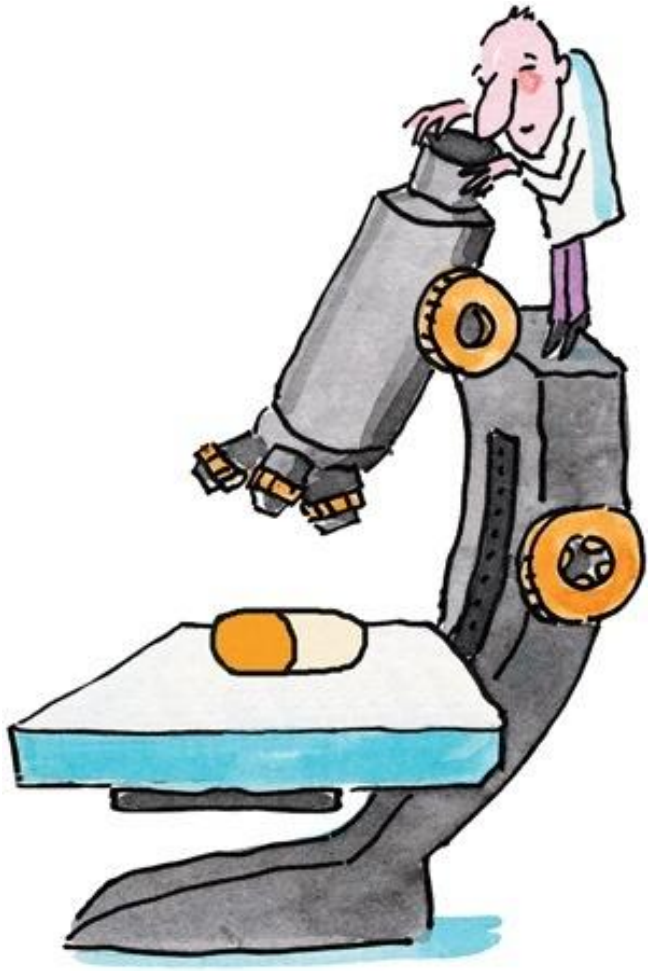
Spending is for 2009. Private Sector is estimated.

Source: Adapted from E. Zerhouni[9]

Public confidence in the industry and regulators has eroded

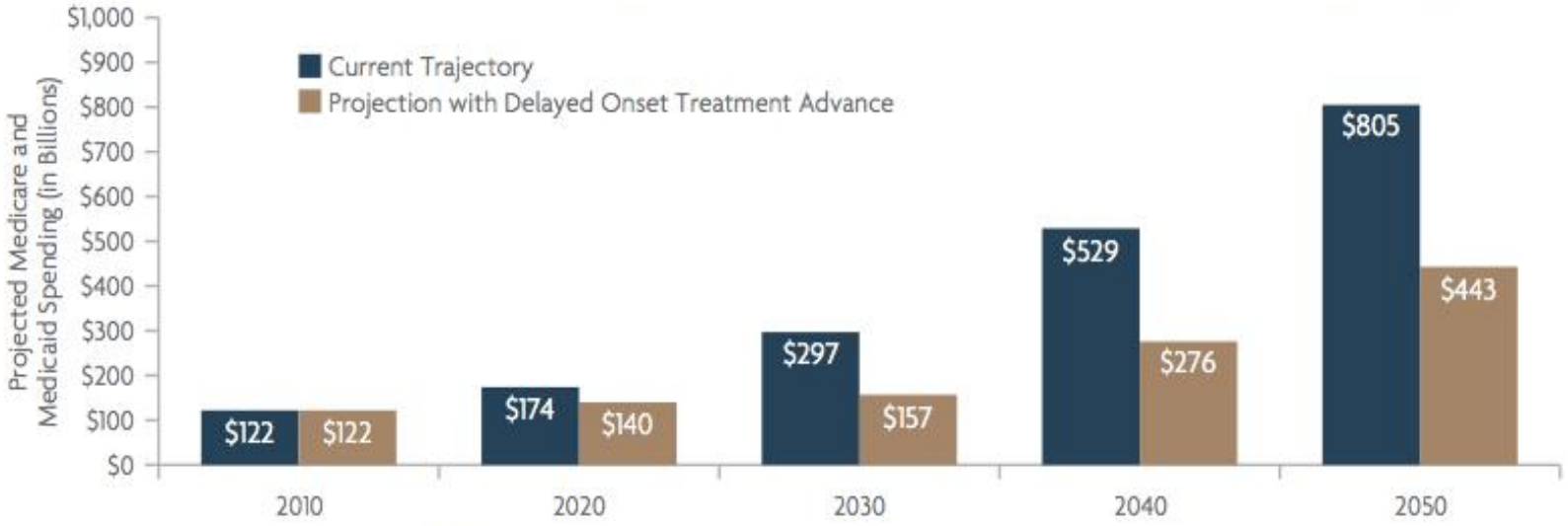


Regulatory Standards are Higher



Alzheimer's Unmet Need

Projected Annual Medicare & Medicaid Spending, With and Without New Treatment Advances (billions)[13]

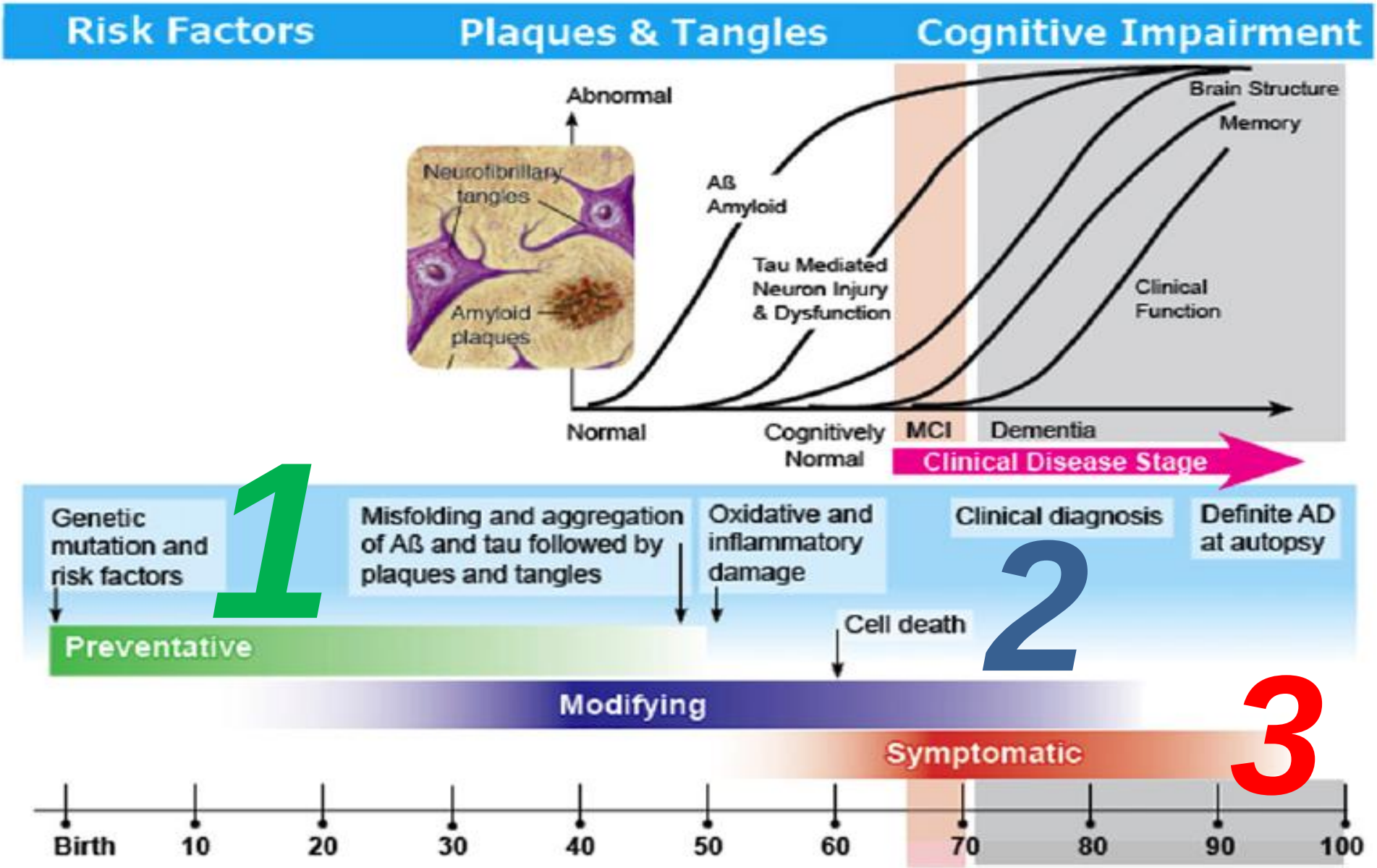


* Assumes research breakthroughs that delay the average age of onset of Alzheimer's disease by five years beginning in 2010.

Source: Alzheimer's Association[14]

Where do we want to play?

J.Q. Trojanowski et al. / Alzheimer's & Dementia 6 (2010) 230–238



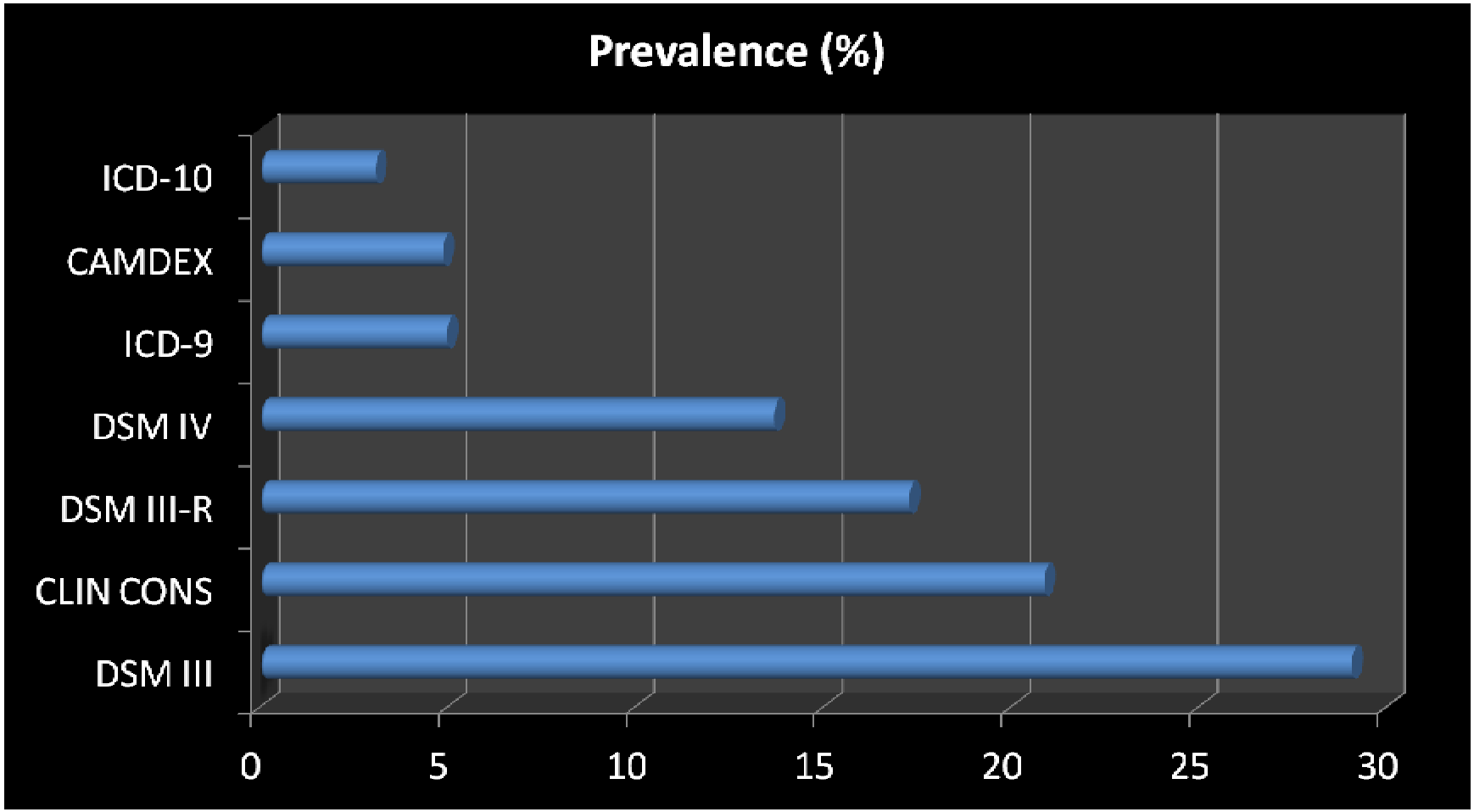
What treatment intervention should we go after?

Time trajectory	*Normal, no known risk factors*	*Normal, but known risk factors*	*Asymptomatic amyloid deposition (imaging), no signs of neurodegeneration, no detectable clinical deficit*	*Signs of Neurodegeneration (e.g. pTau in CSF, NMR spectroscopy), in addition to amyloid deposition, No detectable clinical deficits*	*Early clinical deficit (detectable only by sensitive neuropsychological testing, e.g paired association learning), in addition to amyloid deposition and signs of neurodegeneration*	*Prodromal AD: Amnestic MCI (e.g. California verbal learning) plus biomarker (e.g. low Abeta, high tau, volumetric MRI)*	*AD (DSM-IV)*
Amyloid			X	X	X	X	X
Tau			X	X	X	X	X
Oxidative stress		?	X	X	X	X	X
Inflammation		?	?	?	?	X	X
Mitochondrial dysfunction		?	?	?	?	X	X
Loss of synapses		?	X	X	X	X	X
As yet unidentified pathological event	?	"Inciting pathology"	?	?	?	?	?

Biologically plausible

Feasible

An Example with Dementia Definitions



Created from Erkinjuntti T, Masbye T, Steenhuis R, Hachinski V: The effect of different diagnostic criteria on the prevalence of dementia. N Engl J Med 337:1667-1774, 1997

Investments Required

- Better understanding of basic biology, targets, validation
- Tool set for translational medicine
- Clinical trials/evidence infrastructure
- Safety/performance monitoring and decision support in market and at point of care
- Regulatory science

Planned Regulatory Adaptation

- Revision of rules when relevant new knowledge appears, and steps taken to produce/acquire such improved knowledge.
- Still rare, but used by:
  - EPA
  - FAA
  - FDA for pharmacovigilance

McCray et al 2011

- Regulates 25% of US economy
  - $466 Billion food
  - $275 Billion drugs
  - $100 Billion medical devices/diagnostics
  - $60 Billion cosmetics
  - $18 Billion vitamins
  - *1/3 of all imports*

FDA Regulatory Science Needs

- Contemporary tools and techniques to evaluate emerging technologies
  - pre and post marketing evaluation
  - Multi-drug, multi-modality solutions
  - Personalized medicine
- Risk assessment tools
- Better engagement of patient communities
- Decision support and communication tools

Risk Assessment

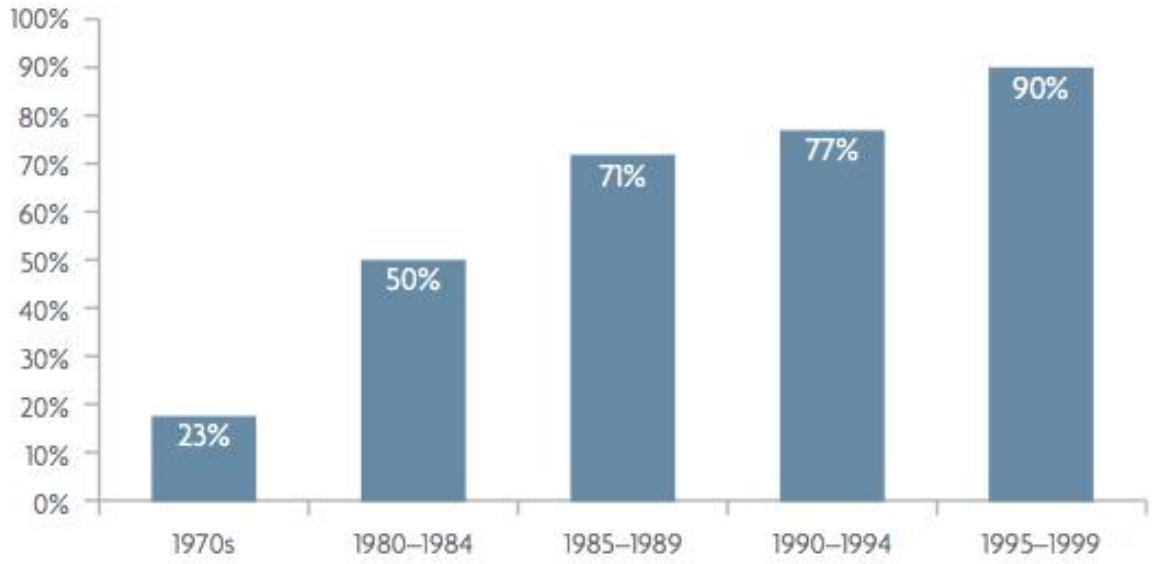
Risk/Benefit

Risk/Risk!

Thank You!

Drug Competition is Increasing

Percent of First-in-Class Medicines with a Competitor Already in Phase II Clinical Testing at Time of Approval

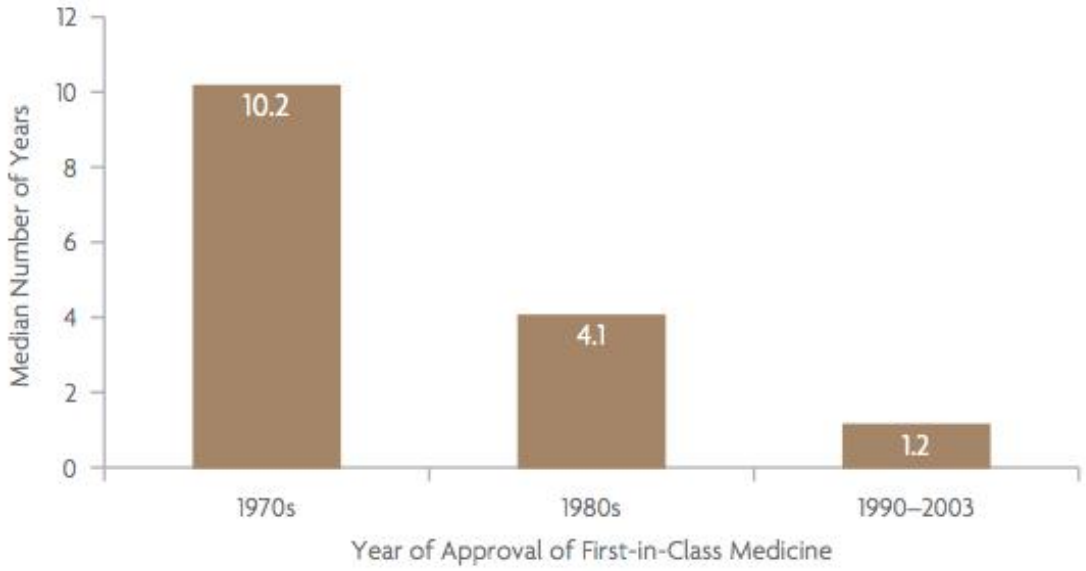


Source: J. DiMasi and L. Faden[19]

Time Between First and Second in Class Entry has Decreased

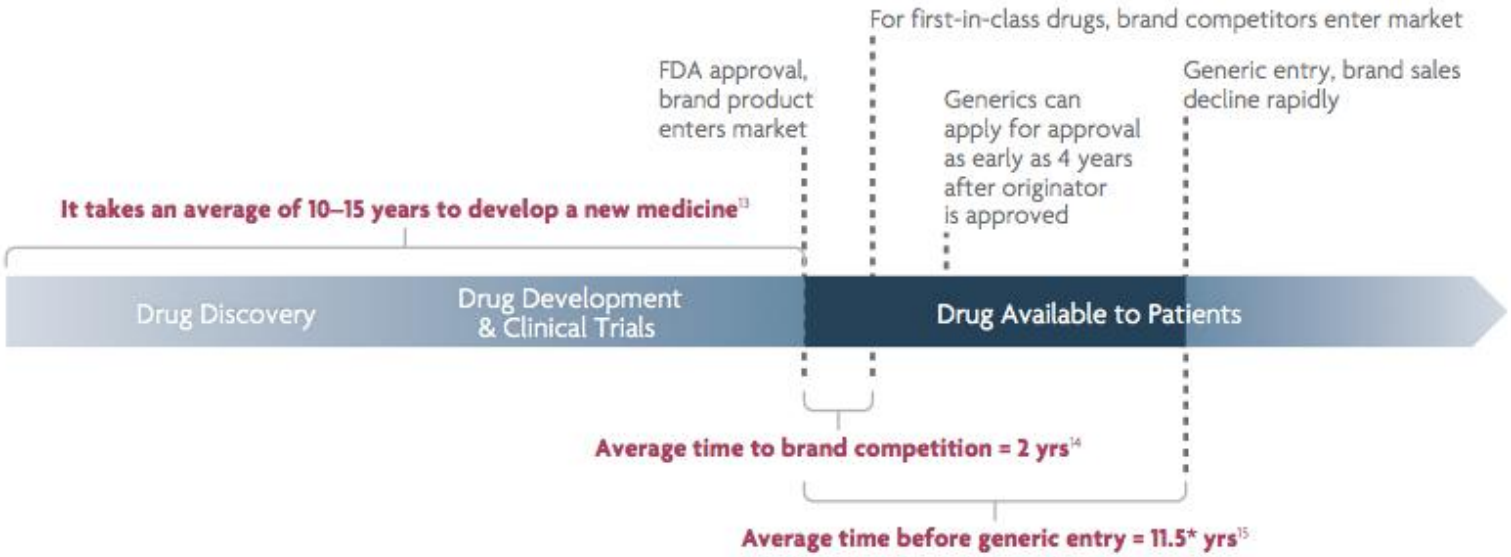
The average time a medicine is the only drug available in its therapeutic class has declined dramatically — from more than 10 years in the 1970s to less than two years by 1998.

Time Between Approval of First and Second Drugs in a Therapeutic Class



Source: Tufts CSDD[20]

Typical Drug Lifecycle



* Refers to pharmaceuticals with annual sales in 2005 of more than $100 million, which accounted for 90% of the sales of medicines exposed to generic competition.

Sources: J. DiMasi and C. Paquette[14]; H. Grabowski and M. Kyle[15]; PhRMA[16]