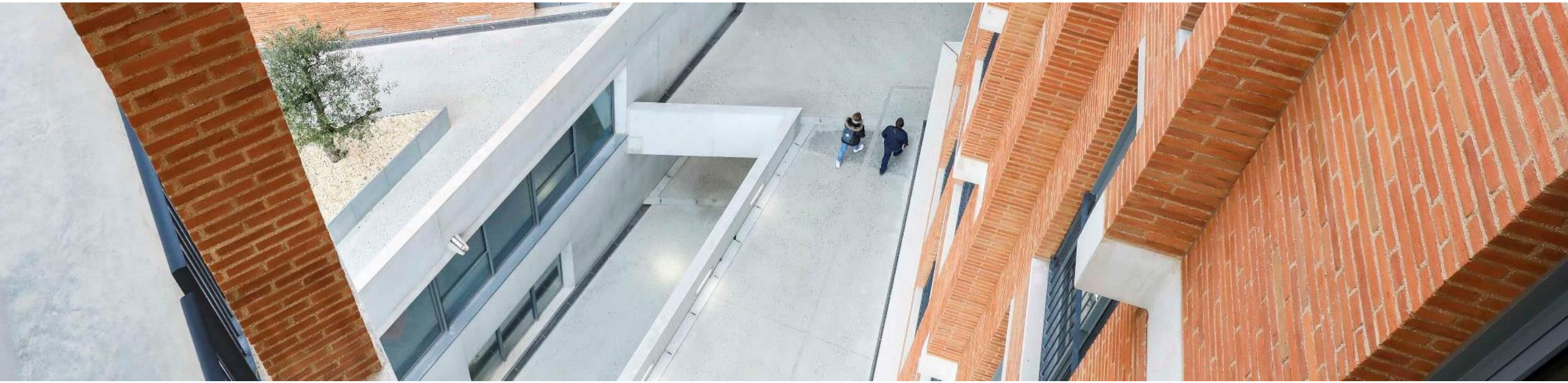
Regulation and Economics of Innovation in Health Care

Pierre Dubois



Journées SMAC

Toulouse, March 17, 2023

Toulouse School of Economics

Economics of Innovation in Health Care

- Health care systems are complex “markets”
- Each country is “specific” (health insurance organization and regulation, health care organization, heterogenous epidemiological factors, and variations in development)
- But we cannot understand the innovation process without an **international perspective** and without recognizing its **global public good** nature (non excludable, non rival)
- I will present the big picture of economists’ view, recent trends and future challenges

Health Care Innovation as a Public Good

- Innovation in health technologies are mainly "**public goods**"
- Knowledge innovations with large fixed "invention and validation" cost but with cheap replication (compared to R&D investments)
  - Most small molecules in this case
  - Biologics and advanced therapies may however have also large production costs

Financing Health Care Innovation

- As investors cannot account for the value for society of public good innovations, there is "underinvestment" without public intervention
- Need to stimulate innovation effort given large and uncertain investment costs
- R&D in health care technologies results from
  - "Push" incentives
  - "Pull" incentives

Financing Health Care Innovation

- *Push*: Grants and subsidies for fundamental research, tax incentives, bio clusters subsidies, ...
- *Pull*: Rewards depending on success/usage of innovation, potential revenue: intellectual property rights protection
- Consensus that pull incentives are more efficient with evidence of push complementarity
- Wide use of “pull” mechanisms, even if possibility to expropriate promised “rents” ex post is always tempting for regulators/governments

Financing through Push incentives

- Direct financing of fundamental research (biology, medicine, AI, RNA messenger, CRISPR-Cas9 genetic scissors, ..)
- Subsidies for R&D (BARDA, Foundations, International Organizations, clinical trials subsidies, R&D tax deductions..)
- Rationale for “Push incentives”:
  - Difficult direct appropriation of ideas
  - But it is subject to “moral hazard” because not conditional on performance, which makes it less efficient (low return on investment)

Financing through Push incentives

- Free riding in “Push incentives”:
  - International “free riding” (crowding out across countries - 10% increase in US government funding for a disease leads to 2-3% reduction in funding for that disease by another government - Kyle, Ridley, Zhang, 2017)
  - Development of emerging markets (BRICS) may lead to more “free riding” (US concentration of global revenue is good for dynamic efficiency) (Egan and Philipson, 2013)

Financing through Pull incentives

- “Pull” incentives are more “efficient” because reward performance only, but depend on worldwide factors:
  - Future diseases prevalence, demographics
  - Regulations (prices but also promotion/advertising, off label use, ..)
  - IP protection laws
  - Competition policies/ Antitrust

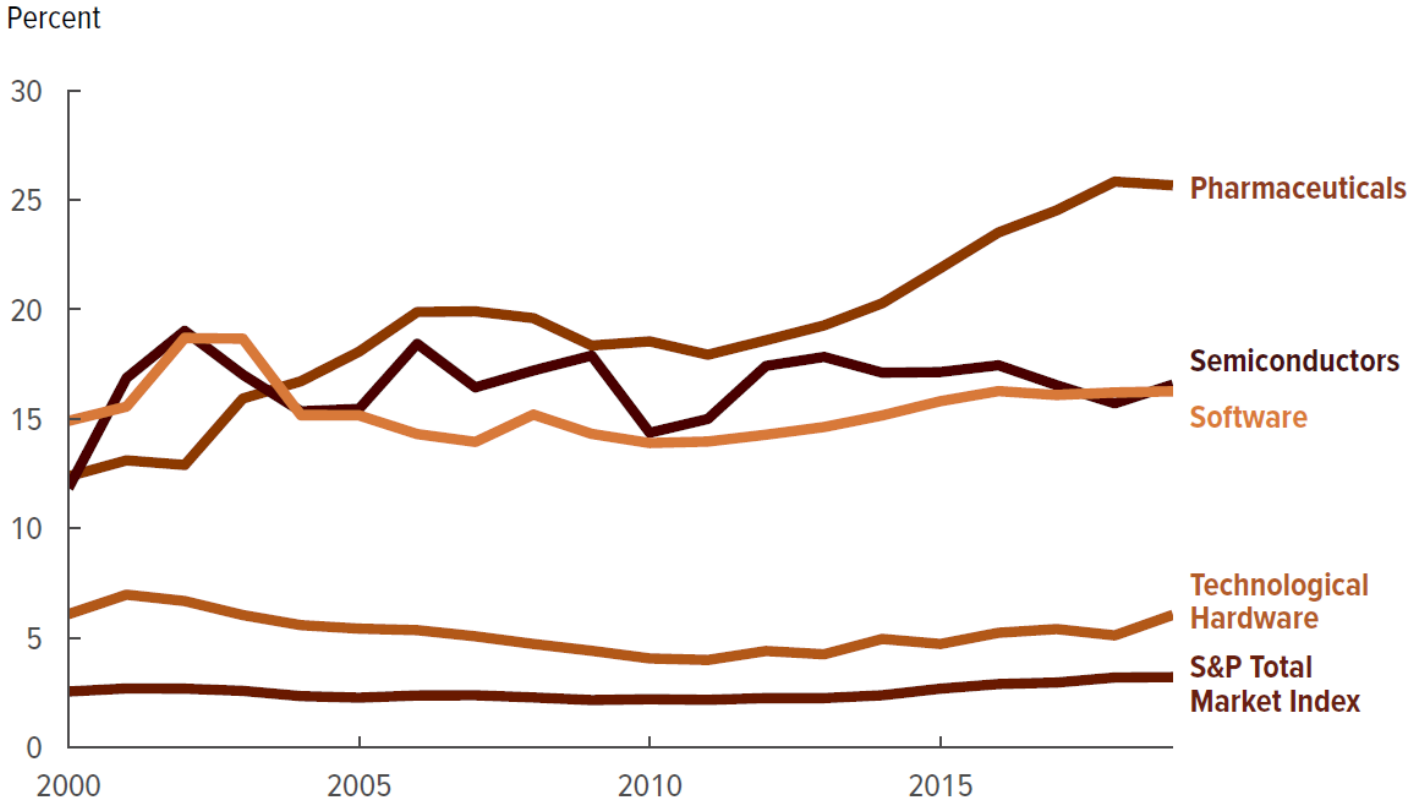
R&D investment and Innovation

- Recent trends in pharmaceutical R&D and drug approvals:
  - R&D spending increased 50% between 2015 and 2019
  - Number of new drugs approved per year has increased
  - Many new drugs are specialty drugs, biologics, often treat chronic complex and rare conditions
- Many recently approved drugs are high priced specialty drugs for relatively small number of potential patients vs low price drugs with large patient populations in the 90s

R&D investment and Innovation

- Pharmacy invests more than other knowledge-based industries

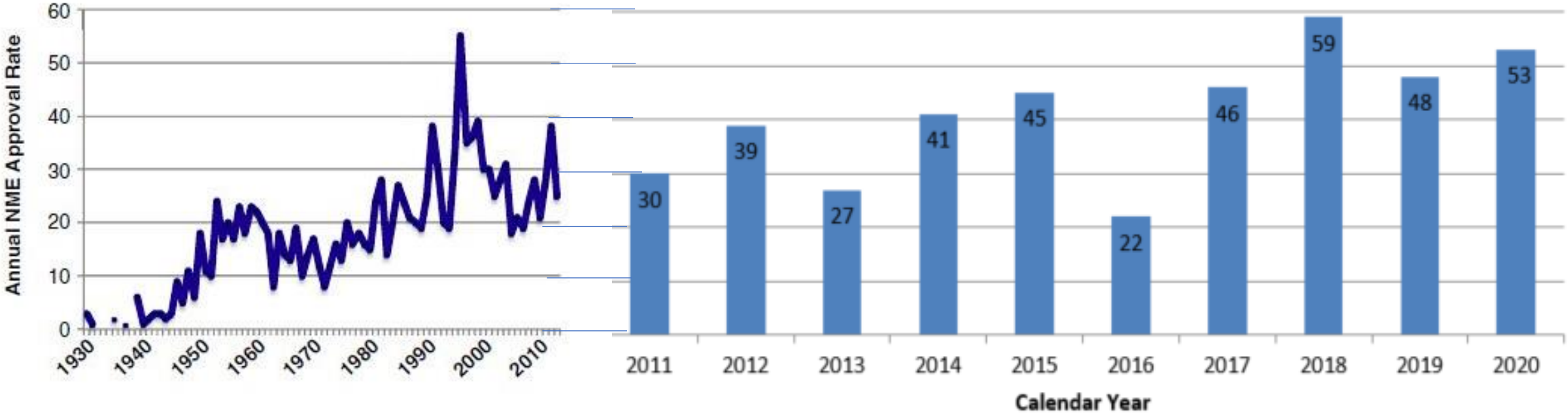
Average R&D Intensities (revenue share) for Publicly Traded U.S. Companies



Source: CBO

R&D investment and Innovation

New drugs approved (FDA)



Innovation in the Pharmaceutical Industry

- Types of New Drugs in Development:
  - Treatments for cancer and nervous system disorders (Alzheimer and Parkinson diseases)
  - In 2018, those two therapeutic classes accounted for more than twice clinical trials than drugs in next three classes (vaccines; pain, including arthritis therapies; and dermatologic)

R&D investment and Innovation

- Small and large firms focus on different R&D activities
  - Small companies: greater share of their research to developing and testing new drugs (many ultimately sold to larger companies)
  - Larger companies: greater share in clinical trials and incremental line extension improvements
- Large companies (>US$ 1 billion) still account for more than half of new drugs approved since 2009 and even greater share of revenues, but have only initiated about 20% of drugs currently in phase III clinical trials (CBO, 2021)

R&D Investment and M&A

- Make or buy: 20% of drugs in development have been acquired by another company over last 30 years
- Acquisitions by larger firms sometimes motivated by desire to limit competition ("Killer acquisitions" Cunningham, Ederer, Ma, 2021)
- Competition policy may become stricter on M&A (risk for biotechs)
- May 2021: FTC Announces Multilateral Working Group to Build a New Approach to Pharmaceutical Mergers (US FTC, US DoJ, Canadian Competition Bureau, EC DG Comp, UK CMA)

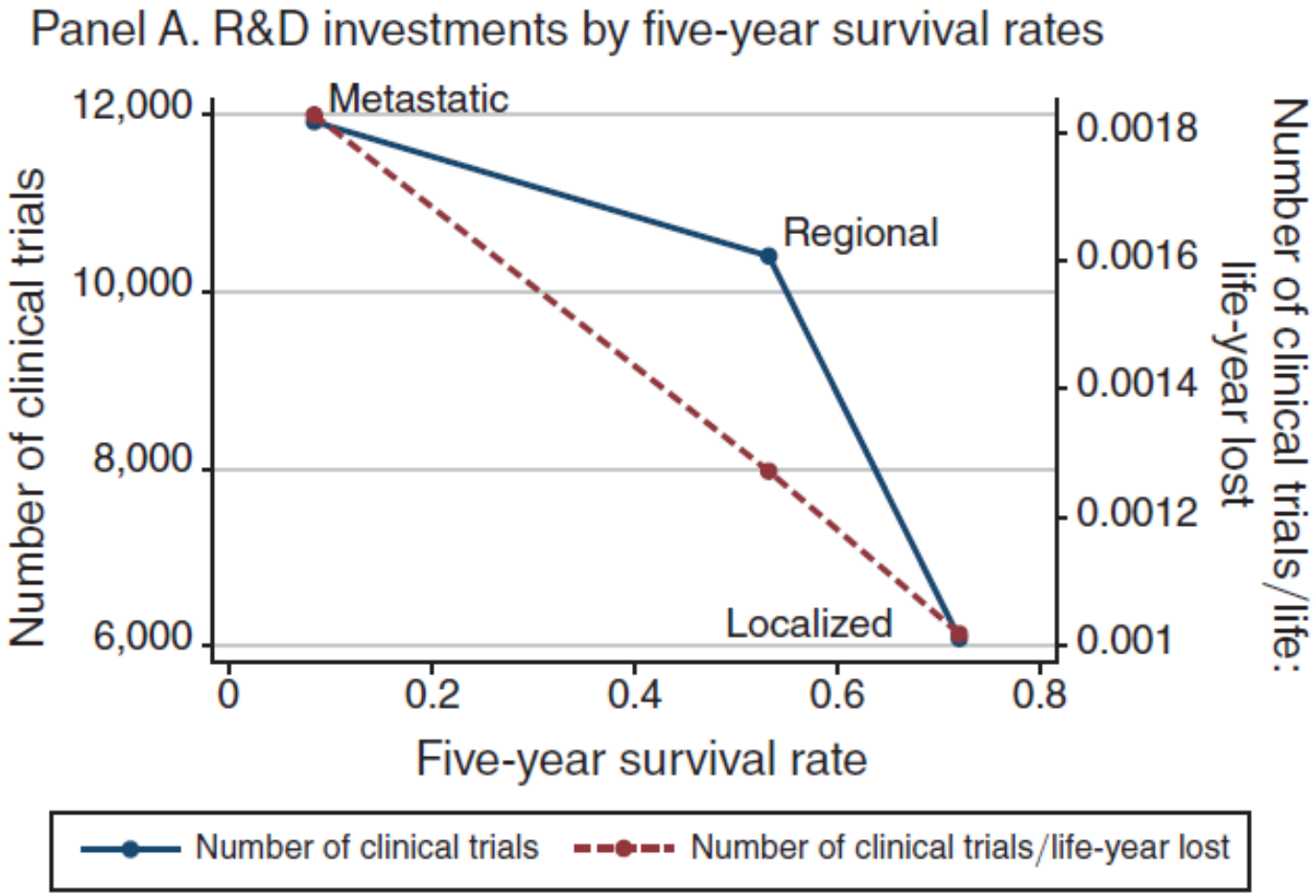
Trends in R&D costs

- R&D costs increased by about 8.5% per year over past decade
  - Changes in types of drugs developed (success rates for new biologic drugs lower than for traditional small-molecule drugs)
  - Become harder to recruit candidate patients into clinical trials
  - Oncology treatments have extended cancer patients' expected lifespans: need longer clinical trials

Clinical Trials Costs

- FDA recently allowed use of “surrogate endpoints” in drug trials for certain illnesses (HIV and some cancers) to shorten some clinical trials
- Surrogate endpoints: indirect predictive indicators (blood pressure, cholesterol level, tumor size, T-cell counts, test results)
- Surrogate endpoints helped neutralize tendency to emphasize treatments that can be commercialized more quickly (result in *too little investment in longer clinically valuable treatments*)

Underinvestment in Long-Term Research



Budish, Roin, Williams (2015)

Innovation Pull Mechanism

- Expected costs to develop a new drug
  - Development risk: 12% of drugs entering clinical trials are ultimately approved (part of this risk is strategic and not scientific)
  - Estimates of average R&D cost per new drug: *1 billion to 2 billions* (including company's capital costs) but price does not depend on these sunk costs
  - Anticipated lifetime global revenues from a drug

Innovation Pull Mechanism

- Lifetime revenue of innovative drug depends on:
  - Expected sales volumes and prices, depending on willingness to pay, insurance plans, ..
  - Patent life duration
- Revenues of existing drugs inform about potential market size for new drugs (consumers' and insurance plans' willingness to pay) and source of funding for R&D for large companies
- Little outside financing for large companies but venture capital for small companies

Innovation Pull Mechanism

- Overall "Market Size" matters (positive elasticity of innovation – Acemoglu and Linn 2004, Blume-Kohout and Sood, 2013, Dubois et al. 2015)
- Medicare Part D (prescription drug benefit) in 2006:
  - Increased sales of prescription drugs to enrolees
  - Encouraged industry to develop new drugs for Medicare population (observed in Phase I trials in therapeutic classes with high Medicare enrolees)
- Elasticity of new drugs introduction to expected market size

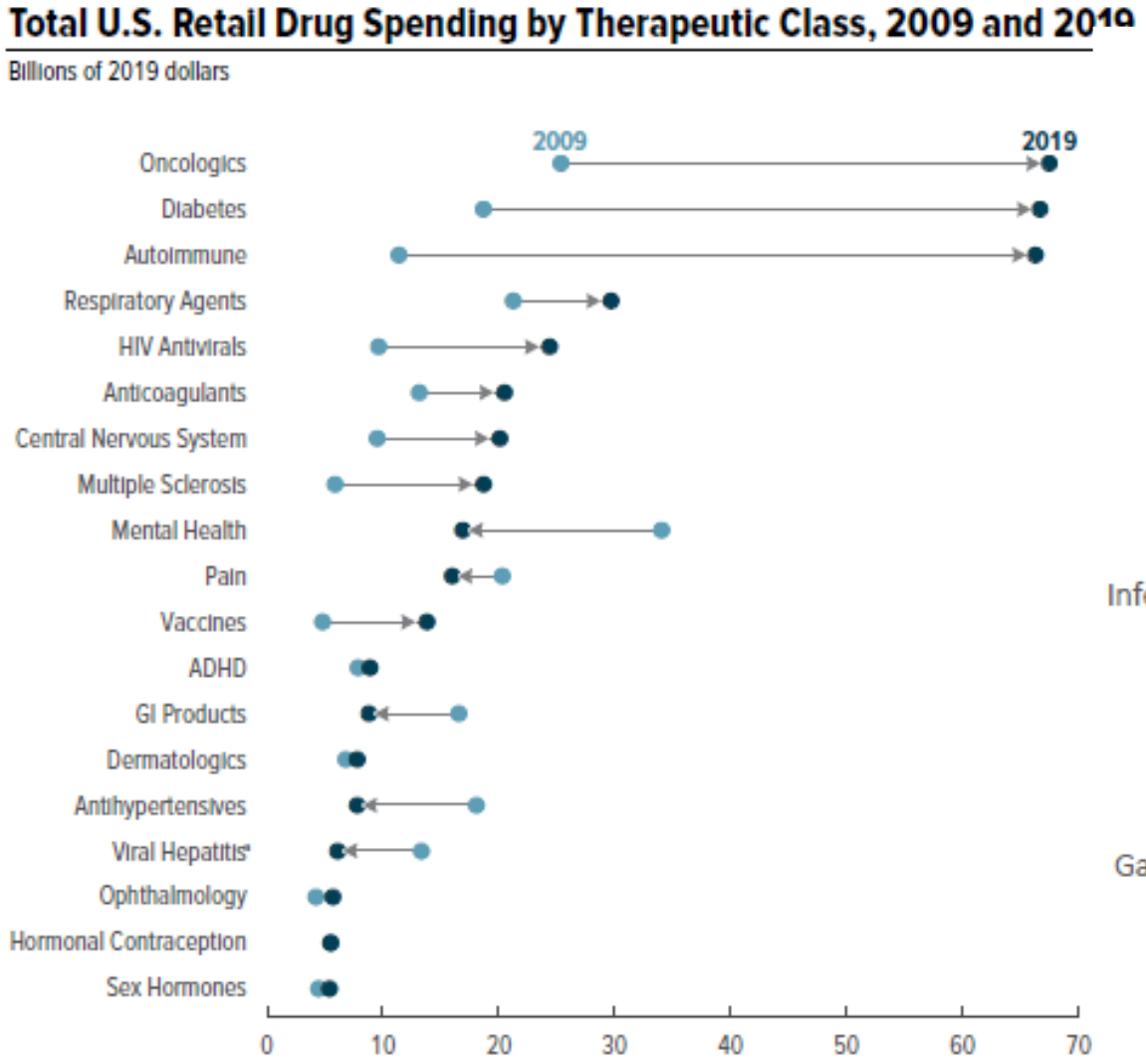
Innovation Pull Mechanism

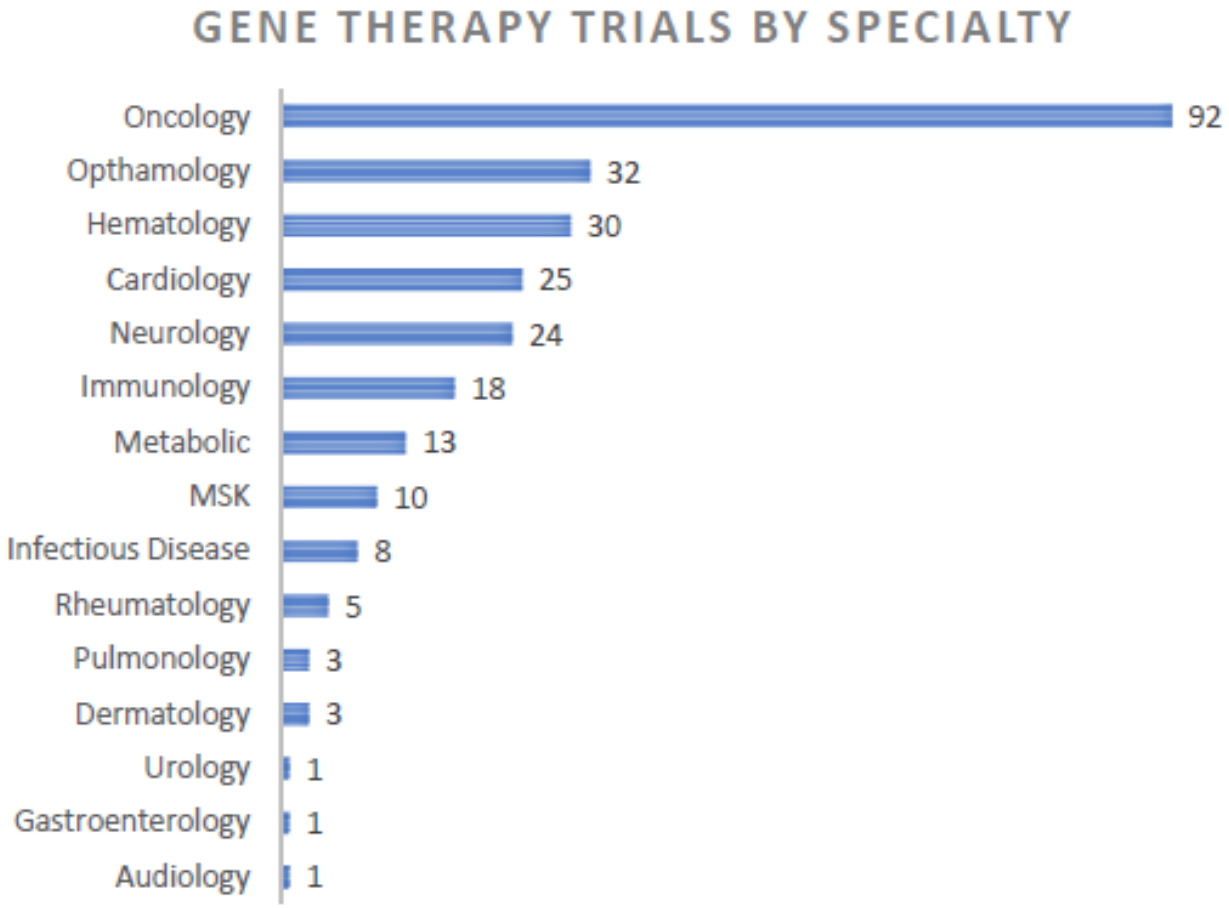
TABLE 8 Elasticities and Market Size Generating One Innovation per Class

ATC Class (*C*)	Mean Elasticity	Mean Market Size per Innovation
A: Alimentary tract and metabolism	0.155	1,729,303
B: Blood and blood-forming organs	0.069	15,637,100
C: Cardiovascular system	0.098	3,134,607
D: Dermatologicals	0.245	160,228
G: Genitourinary system and sex hormones	0.269	726,358
J: Anti-infectives for systemic use	0.281	3,033,395
L: Antineoplastic & immunomodulating agents	0.377	2,313,080
M: Musculoskeletal system	0.151	3,950,014
N: Nervous system	0.398	386,187
R: Respiratory system	0.109	1,258,170
S: Sensory organs	0.406	148,508
All	0.231	2,471,139

Dubois et al. (2015)

Oncology: first spending area





Free riding and International externalities

- As world profits drive innovation, spending growth in a given country is affected by health care policies of other countries
- But reimbursements are “strategic substitutes” (“free riding”)
- A small country has no price-innovation trade-off
  - ➡ low prices (gets same innovations regardless of price)
- Despite being largest buyer, US pays highest reimbursements
- Free riding counteracts standard positive impact of larger world markets on innovation when health care spending concentration falls (Egan and Philipson, 2013)

Advanced therapies economic challenges

- Challenges for public finances:
  - Difficult transition in shifting of resources from chronic disease management to more intense acute episodic care
  - Manufacturing cost higher than with old small molecules: biosimilars will not be as cost savings as generics
  - Increase of complexity of required IP and manufacturing know-how
  - Expansion of biopharmaceutical companies into service-based business models

Advanced therapies economic challenges

- Challenges for public finances:
  - Drastic innovations saving lives
  - Pay for ex post profitability of investments and for paying high variable costs
  - Need long term evaluation of innovation value
  - Long term budget allocation problem: commitment
  - Pay for performance models for risk sharing

Conclusion and Lessons

- Economic policy at international level will affect profitability and geographical distribution of sales value
- US may not continue to let others free ride
- Need to develop a European BARDA, and harmonize European Health Insurance and financing of innovation
- M&A may become more scrutinized
- Personalized medicine and pay for performance may allow smoothing health care expenses over time with new reimbursement models
- Advanced cell and gene therapies are promising but will raise the bar for economic sustainability

Health Center

Economics for the Common Good

www.tse-fr.eu/health