



“Sprengt die Krebstherapie das Gesundheitssystem?”

Anmerkungen zur Finanzierbarkeit und ökonomischen Logik
der onkologischen Therapieforschung & -entwicklung (F&E)

Professor
Michael Schlander
M.D., Ph.D., M.B.A.

Chairman & Scientific Director
Institute for Innovation & Valuation in Health Care

Presseworkshop des DKFZ, Heidelberg, 21. Januar 2016



“Sprengt die Krebstherapie das Gesundheitssystem?”

oder:

**Können wir uns die moderne Krebsforschung
und
neue Krebstherapien überhaupt noch leisten?**



**“Hand clapping for science
is now inextricably linked to
hand wringing
over affordability.”¹**

¹Peter B. Bach

(Memorial Sloan Kettering Cancer Center, New York, NY):

New Math on Drug Cost-Effectiveness.

New England Journal of Medicine 2015 (November 05); 373 (19): 1797-1799.



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1. Medizinische Forschung & Entwicklung (F&E) im Allgemeinen und Krebsforschung im Speziellen ist aufwendig, langwierig, riskant und deshalb teuer.
2. F&E-Aufwand generiert fixe oder sprungfixe Kosten; innovative Krebstherapien können deshalb (in der Regel *zunächst*) nicht billig sein.
3. Den Kosten der Krebsforschung und -therapie müssen ihr Nutzen [*und die volkswirtschaftlichen und humanitären Kosten von Krebserkrankungen(?)*] gegenüber gestellt werden.

“Yes, We Can [Afford It]!”¹

4. Wachsende Gesundheitsausgaben (folglich auch innovative Krebstherapien) werden auch zukünftig finanzierbar bleiben.
5. Es gibt jedoch einige Voraussetzungen und Handlungsbedarf, um diesen Optimismus belastbar zu machen.

¹W.J. Baumol: *The Cost Disease – Why Computers Get Cheaper and Health Care Doesn't*. New Haven, CT: Yale University Press 2012.



Institutional Background

Who We Are

- Institute for Innovation & Valuation in Health Care (INNOVAL^{HC})
 - **Independent** Not-For-Profit Research Organization
(**Not** a Commercial Contract Research Organization)
 - Founded in Aschaffenburg / Germany in June 2005
 - Formally associated with the
University of Applied [Economic] Sciences Ludwigshafen
 - Funding of Projects
 - Under an “unrestricted educational grant” policy
 - Supported by National Institutes of Mental Health (NIMH, Bethesda, Md.), National Health and Medical Research Council (NHMRC, Canberra, ACT), Official HTA Institutions (e.g., IQWiG), Physician Organizations (e.g., FMH, KVBaWue), Sick Funds (e.g., santésuisse, vdek), Research Foundations (e.g., Deutsche Forschungsgemeinschaft, DFG, Swiss Academy of Medical Sciences, SAMW), Pharmaceutical Industry (USA, UK, CH, D, ...)
- Chairman: Professor Michael Schlander, M.D., Ph.D., M.B.A.
- Vice-Chairmen: Professor Oliver Schwarz, Ph.D.
Professor G.-Erik Trott, M.D., Ph.D.



Institutional Background

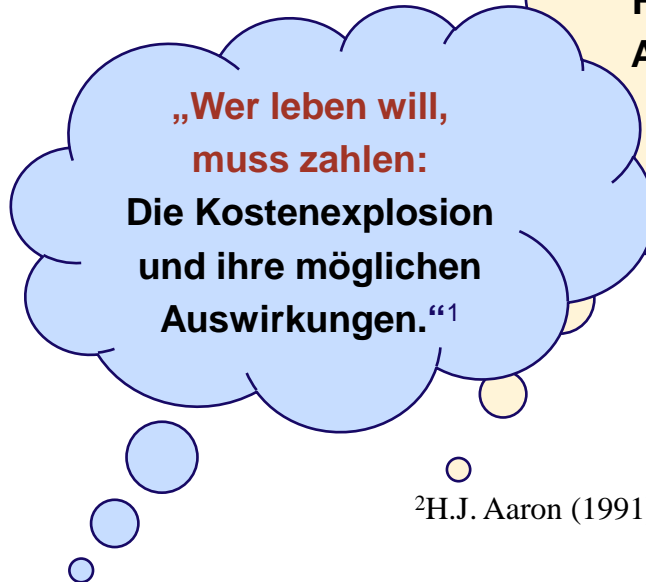
What We Do (Overview and Examples)

- Normative Analysis
 - Normative Health Economics and “Empirical Ethics”
 - Evaluation Principles for Rare & Ultra-Rare Disorders
- Health Care Policy Analysis
 - Pharmaceutical Market Regulation
 - “Appraising the Appraisers”
- Health Technology Assessment (HTA)
 - Systematic Reviews and Value Assessments
 - Swiss HTA Consensus Project
- Applied Health Economics
 - Cost Effectiveness Analyses & Modeling
 - Health Economic Methods Development
- Health Care Utilization Research
 - Nordbaden Project (using German administrative data)
- Education, Outreach & Consulting
 - Heidelberg Health Economics Summer School



Conventional Wisdom

(Not So New...)



¹W. Krämer (1982)



²H.J. Aaron (1991)

³H.J. Aaron & W.B. Schwartz (1984)



Pricing of New Drugs (2014)



It's cheaper than a new liver.

“Lawmakers and private insurers (who also warn of Sovaldi-induced premium hikes) appear to worry that the price of Sovaldi, multiplied by the millions of Americans who now have hep C, places too heavy a financial burden on the health care system in the short-term. If it does, then the prospect of long-term savings has little appeal.”¹

¹<http://pointofcontroversy.com/2014/07/19/high-priced-hepatitis-c-drug-sovaldi/>



The Most Expensive Drugs in the World¹



¹S. Williams, The Motley Fool, June 29, 2013. <http://www.fool.com/investing/general...> [last accessed Nov. 12, 2015]



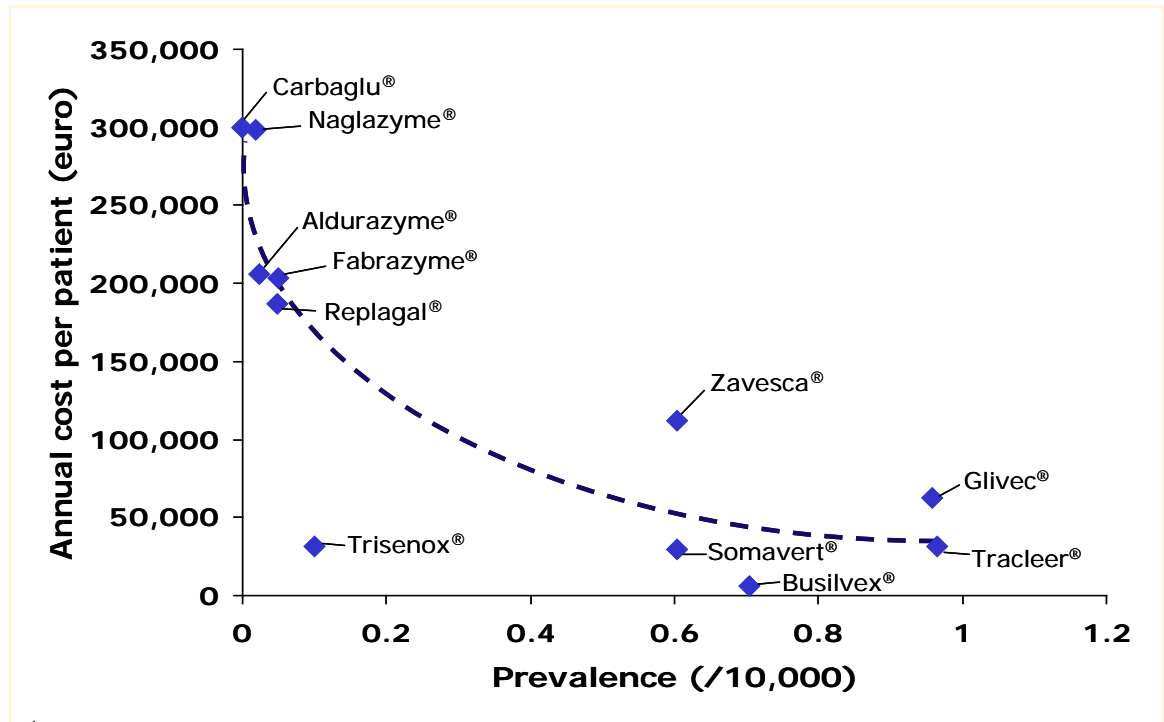
The Most Expensive Drugs in the World¹

- 1. Soliris (Alexion)**
paroxysmal nocturnal hemoglobinuria (PNH),
atypical hemolytic uremic syndrome (aHUS);
average annual cost: **US-\$ 409,500**
- 2. Elaprase (Shire)**
Hunter syndrome (ERT); **US-\$ 375,000** p.a.
- 3. Naglazyme (BioMarin)**
mucopolysaccharidosis (MPS) VI (ERT); **US-\$ 365,000** p.a.
- 4. Cinryze (ViroPharma)**
hereditary angioedema (HAE); **US-\$ 350,000** p.a.
- 5. Myozyme (Sanofi / Genzyme)**
Pompe disease (ERT); **US-\$ 300,000** p.a.

¹S. Williams, The Motley Fool, June 29, 2013. <http://www.fool.com/investing/general...> [last accessed Nov. 12, 2015]



Prevalence and Cost per Patient¹



¹M. Schlander and M. Beck: *Current Medical Research & Opinion* 2009; 25 (5): 1285-1293



Median Acquisition Costs per Year

Some New Anticancer Drugs¹



↪ Nilotinib (Tasigna [®])	€61,600
↪ Sunitinib (Sutent [®])	€50,920
↪ Cetuximab (Erbix [®])	€50,120
↪ Rituximab (MabThera [®])	€47,200
↪ Sorafenib (Nexavar [®])	€46,000
↪ Trastuzumab (Herceptin [®])	€38,200
↪ Bevacizumab (Avastin [®])	€37,200
↪ Imatinib (Glivec 400 [®])	€36,400
↪ Erlotinib (Tarceva [®])	€31,080

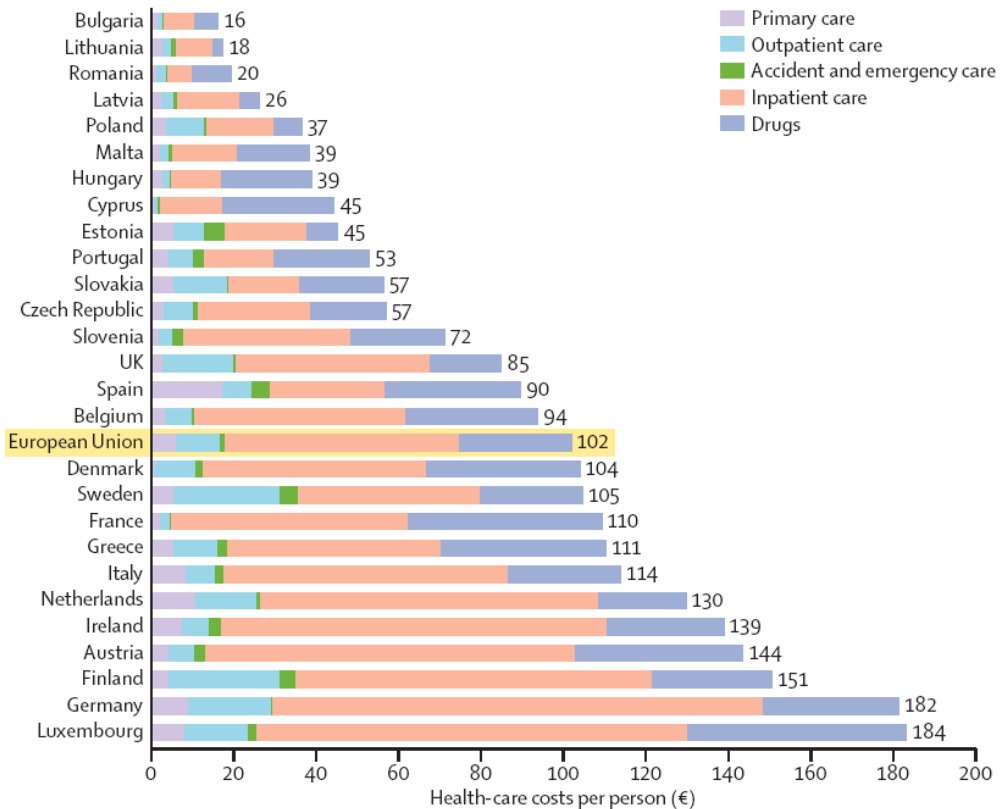
¹G. Glaeske et al. (2010)



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Cost of Cancer Treatment¹



¹R. Luengo-Fernandez, J. Leal, A. Gray, and R. Sullivan: Economic burden of cancer across the European Union: a population-based cost analysis. *Lancet Oncology* 14; 2013: 1165-1174.

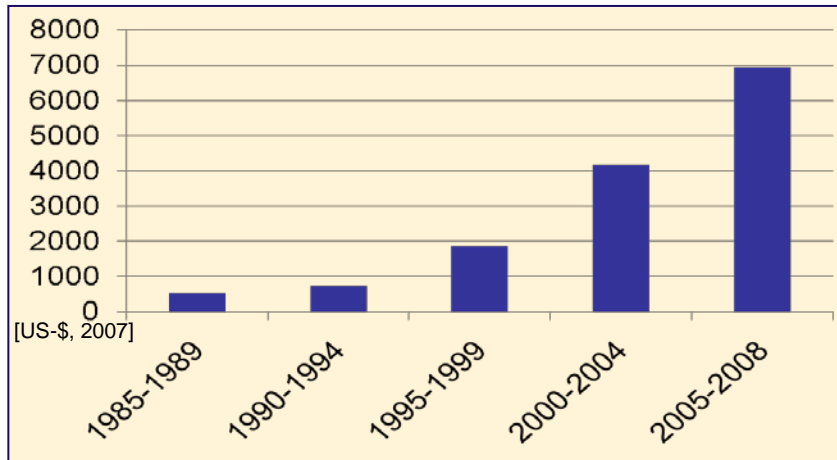




Cost of Cancer Drug Treatment

- Average costs per month of some newer cancer drugs is now US-\$ 10,000 to US-\$ 30,000 per month.¹
- Combinations of checkpoint inhibitors cost as much as US-\$ 100,000 per month.¹

Median Monthly Costs of New Anticancer Drugs (by Year of Launch²)

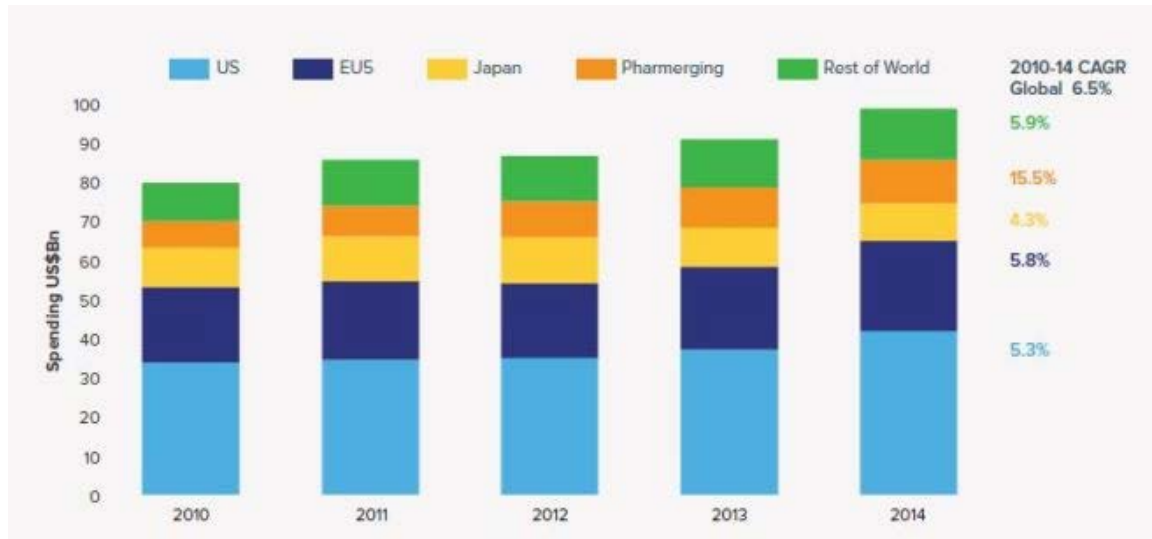


¹R.C. Young (2015); ²P.B. Bach (2009)



Cost of Cancer Drug Treatment

Global Oncology Drug Spending 2010-2014¹

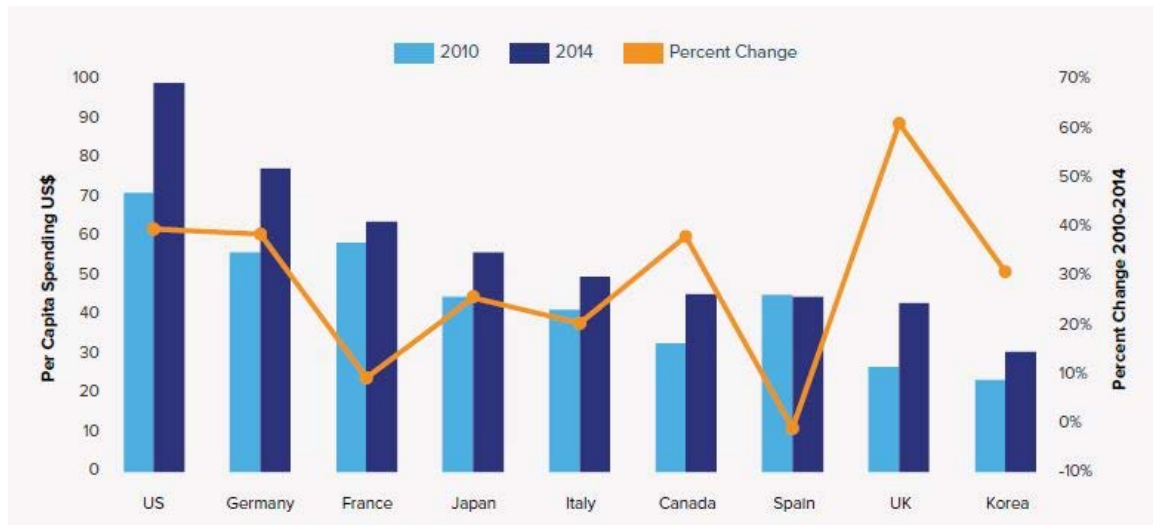


¹K. Leonard (2015), based on ims data



Cost of Cancer Drug Treatment

Cancer Drug Spending per Capita 2010-2014¹



¹K. Leonard (2015), based on ims data



Cost of Cancer Drug Treatment



- **Value-Based Cancer Care** (Current *Examples*¹)
 - **Institute of Medicine**: six elements – safety, effectiveness, patient-centeredness, timeliness, efficiency, equity
 - **ASCO**: three elements – clinical benefit (effectiveness), toxicity (safety), cost (efficiency)
 - **NCCN**: “patient-oriented value formula” – efficacy, safety, quality of evidence, consistency of evidence, affordability



- **International Price Comparisons**

- Germany, Sweden and Switzerland vs. Greece, Portugal, and Spain²
- but: limited to official list prices and by inaccessibility of confidential, discounted price data: *“the end of the international reference pricing system?”*³

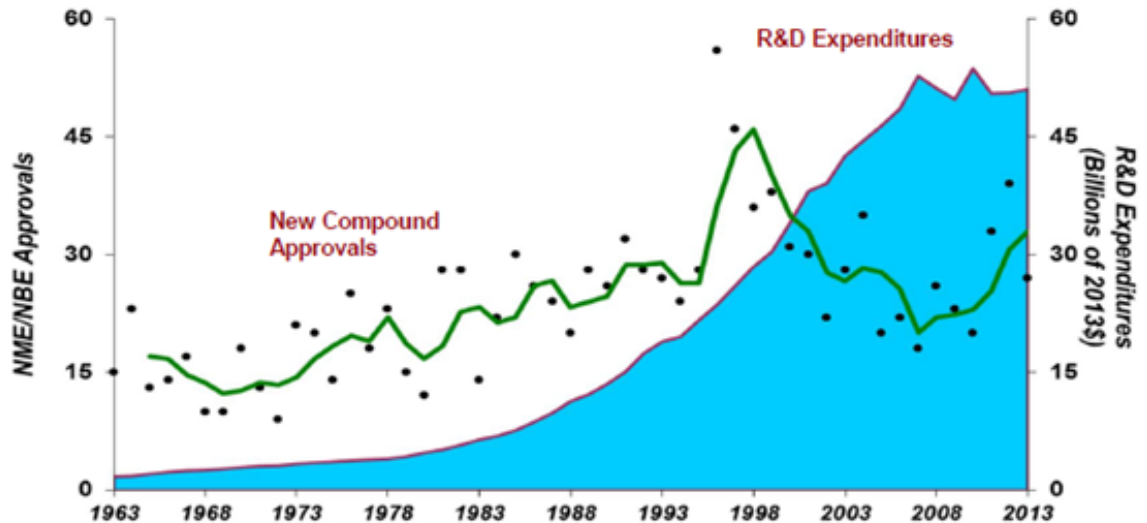
¹R.C. Young: Value-based cancer care. *New England Journal of Medicine* 2015 (Dec. 31), 373 (27): 2593-2595.

²S. Vogler, A. Vitry, Z.-U.-D. Babar: Cancer drugs in 16 European countries, Australia, and New Zealand: a cross-country price comparison study. *Lancet Oncology* 17; 2016: 39-47.

³U. Persson, B. Jönsson: The end of the international reference pricing system? *Appl. Health Econ. Health Policy* 2015 (Jun. 26)



Biopharmaceutical R&D: New Drug Approvals and R&D Spending



R&D expenditures are adjusted for inflation; curve is a 3-year moving average for NME/NBEs
 Sources: Tufts CSDD; PhRMA, 2014 Industry Profile

Source: J.A. DiMasi. “Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs”, Tufts Center for the Study of Drug Development, November (2014). Available: at http://csdd.tufts.edu/news/complete_story/pr_tufts_csdd_2014_cost_study, s.l.: s.n.



Biopharmaceutical R&D: Determinants of Fully Allocated R&D Cost / NME

- ↪ **Out-of-pocket costs**
 - ↪ Clinical development
 - ↪ Preclinical research & development
 - ↪ Discovery research

- ↪ **Clinical success and attrition rates**

- ↪ **Capitalization**
 - ↪ Development times (“Time-to-Market”, TTM)
 - ↪ Cost of capital

NME: New Molecular Entity





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Biopharmaceutical R&D:

Overall Success Rates for Clinical Development

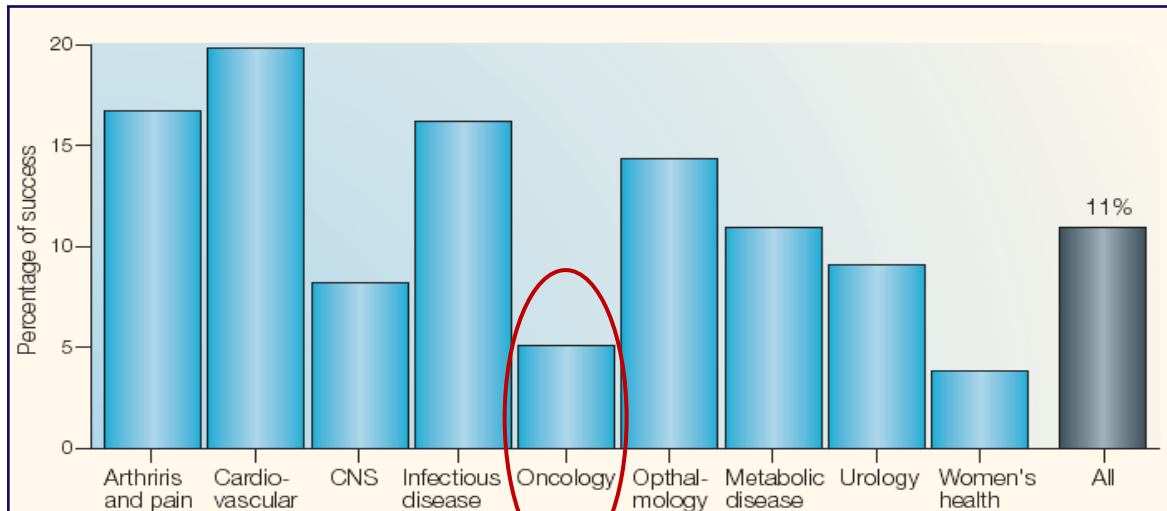


Figure 1 | **Success rates from first-in-man to registration.** The overall clinical success rate is 11%. However, if the analysis is carried out by therapeutic areas, big differences emerge. The data are from the ten biggest drug companies during 1991–2000. (The companies are AstraZeneca, Bristol-Myers Squibb, Eli Lilly, F. Hoffman-LaRoche, GlaxoWellcome, Johnson & Johnson, Novartis, Pfizer, Pharmacia, Schering-Plough and SmithKline Beecham; data were obtained by Datamonitor in the Pharmaceutical Benchmarking Study). CNS, central nervous system.

Source: I. Kola and J. LandisC: Can the pharmaceutical industry reduce attrition rates?
Nature Reviews Drug Discovery, August 2004; 3: 711-715.



Biopharmaceutical R&D:

Variables Influencing Clinical Success Rates

- **Therapeutic area:**
currently best: cardiovascular estimated at 20% on average;
currently worst: neurology and cancer/oncology at 5-8% on average
- **Compound origin:**
statistically, self-originated projects carry a higher risk of failure
(compared to licensed-in projects)
- **Biologics and biopharmaceutical projects:**
associated with higher overall success rates (vs. small molecules),
but also with longer development times and higher costs of capital
- **Firm size:**
“Big Pharma” overall success rates slightly lower, but phase III better;
development times substantially shorter for Big Pharma
- **Development time:**
development cost is heavily influence by clinical development time,
with cancer projects at 7.6 years (CNS, 10.0y; AIDS antivirals, 5.1y)

Primary data sources:

*Office of Health Economics (OHE),
London, 2012.*

*Kola and Landis, Nature Reviews
Drug Discovery 2004*

*Abrantes-Metz, Adams and Metz,
Journal of Pharmaceutical Finance,
Economics and Policy 2005*

*Centre for Medicines Research
International (CMR-I), London,
2015*

*Tufts Center for the Study of Drug
Development, Boston, Mass. 2014*



Biopharmaceutical R&D: Attrition Rate and Project Termination Trends

- **Overall success rates** of NMEs entering into clinical development have remained stable, approximately in the 10-25% range.
- **To minimize attrition costs**, it is crucial that unsuccessful NMEs fail as quickly as possible (i.e., before clinical phase III).
- Biopharmaceutical companies have moved to integrate health economics into **early strategic assessments** of NMEs.
- Reasons for premature project termination show a persistent trend to increasing importance of **commercial and economic criteria**.



Biopharmaceutical R&D: Fully Allocated Cost / NME

Study Reference	Sample of New Molecular Entities	Cost of Capital (real)	Discovery Research (included?)	Geography	Estimated cost of R&D [US\$m, 2011 prices]
Hansen, 1979	First tested in humans between 1963 and 1975	8%	No	USA	199
Wiggins, 1987	1970-1985	8%	No	USA	226
DiMasi et al, 1991	First tested in humans between 1970 and 1982	9%	Yes (estimated)	USA	451
OTA, 1993	-	-	-	-	625
Myers and Howe, 1997	-	-	-	-	664
DiMasi et al, 2003	First tested in humans between 1983 and 1994	11%	Yes (estimated)	USA	1,031
Gilbert, Henske and Singh, 2003	Estimated first tested in humans between 1995 and 2002	-	Yes	Global	(1995–2000) 1,414
					(2000–2002) 2,185
Adams and Branter, 2006	Drugs entering human clinical trials for the first time 1989-2002	11%	Use DiMasi et al 2003	Global	1,116
Adams and Branter, 2010	Drugs entering human clinical trials for the first time 1989-2002	11%	No	Global	1,560
Paul et al, 2010	Estimated 1997-2007	11%	Yes	Global	1,867
Mestre-Ferrandiz et al, 2012					1,506
DiMasi, 2014					2,600 †

Adapted from: J. Mestre-Ferrandiz, J. Sussex and A. Towse. *The R&D Cost of a New Medicine*. London: Office of Health Economics, Dec. 2012.
 †J.A. DiMasi. *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, Tufts Center for the Study of Drug Development (2014).



Biopharmaceutical R&D: Fully Allocated Cost / NME (2012)

- **most plausible estimate: ~ 1.5 billion US-\$**
- **plausible range from 1.1 to 1.9 billion US-\$**

while the time, risk, and cost profiles of individual projects may substantially deviate from the average ...

... fully allocated economic costs / NME

will invariably include opportunity costs (driven by time to market), cost of failures, and non-allocated costs (e.g., discovery research)

- **Effective R&D management** is a critical success factor, making the most important difference between companies, adding or destroying value.

NME: New Molecular Entity



Burden of Disease and Cost of Cancer¹



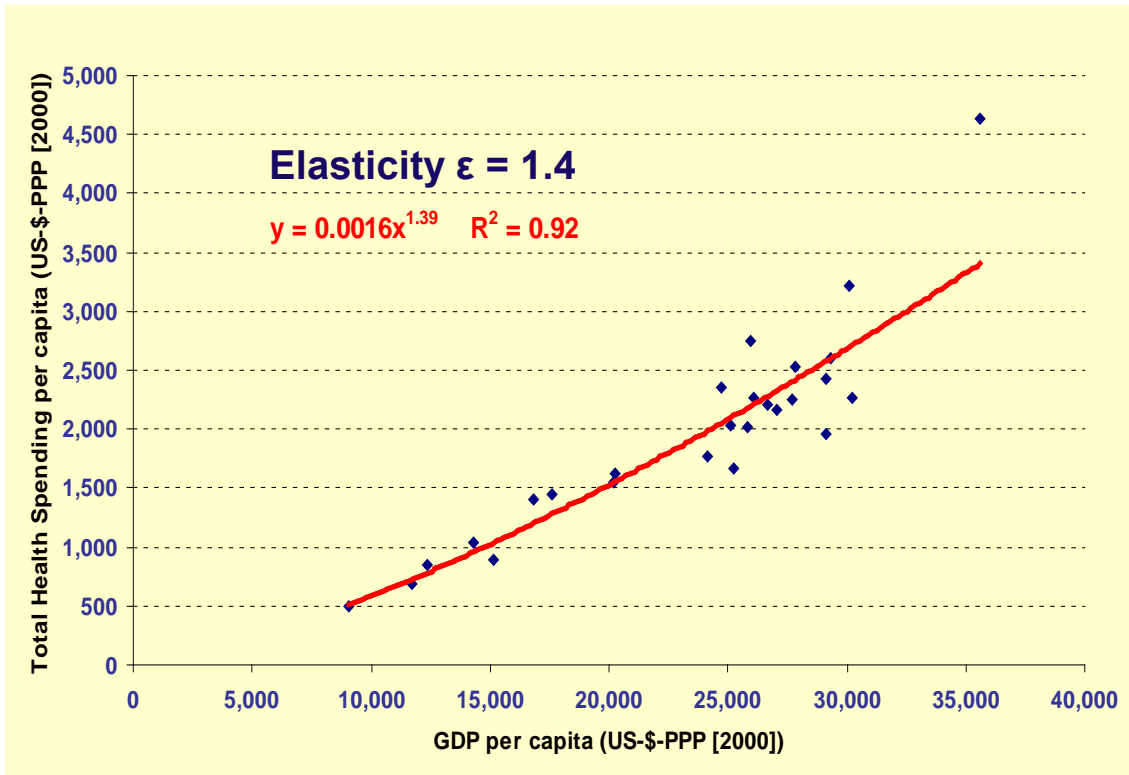
- **Burden of Disease** (p.a., EU 2008)
 - 2.45 million people diagnosed with cancer
 - 1.23 million people died because of cancer

- **Cost of Cancer** (p.a., EU 2009)
 - estimated at 126 billion € in total
 - health care accounting for 40%
(i.e., ~51.0 billion €, or 102€ per citizen)
 - productivity loss due to premature deaths ~42.6 billion €
 - productivity loss due to lost working days ~9.43 billion €
 - leading causes of economic cost: lung cancer (18.8 bn €),
breast cancer (15.0 bn €), colorectal cancer (13.1 bn €),
and prostate cancer (8.4 bn €)

¹R. Luengo-Fernandez, J. Leal, A. Gray, and R. Sullivan: Economic burden of cancer across the European Union: a population-based cost analysis. *Lancet Oncology* 14; 2013: 1165-1174.



National Income and Health Expenditures¹



¹Cross-sectional analysis based on OECD Health Data 2002 (26 OECD member states); cf. Kleiman (1974) and Newhouse (1977); from Schlander and Schwarz (2005)



Baumol’s Disease (or “Bowen’s Curse”)¹

- **“Progressive Sector” of Economy**
 - mass-manufactured products
 - productivity growth as a labor-saving change in a production process
- **“Stagnant Sector” of Economy**
 - personal services
 - health care, education, the live performing arts
 - the quantity of labor required to produce these services is difficult to reduce

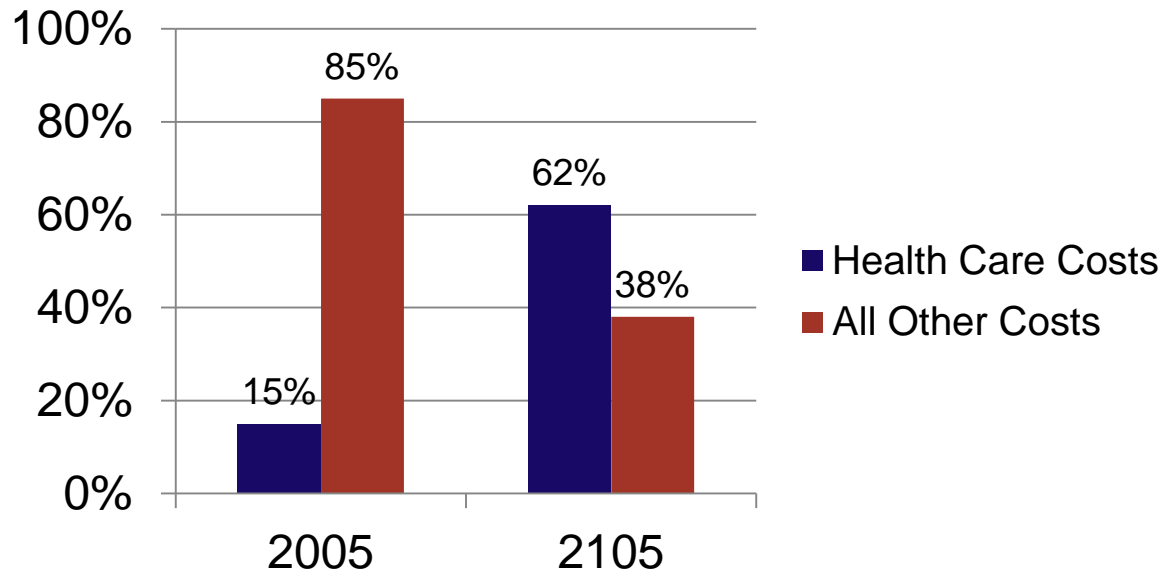
¹W.J. Baumol: *The Cost Disease – Why Computers Get Cheaper and Health Care Doesn’t*. New Haven, CT: Yale University Press 2012.



Baumol's Disease:

Health Care and All Other Spending

(extrapolated, as a percentage of U.S. GDP¹)



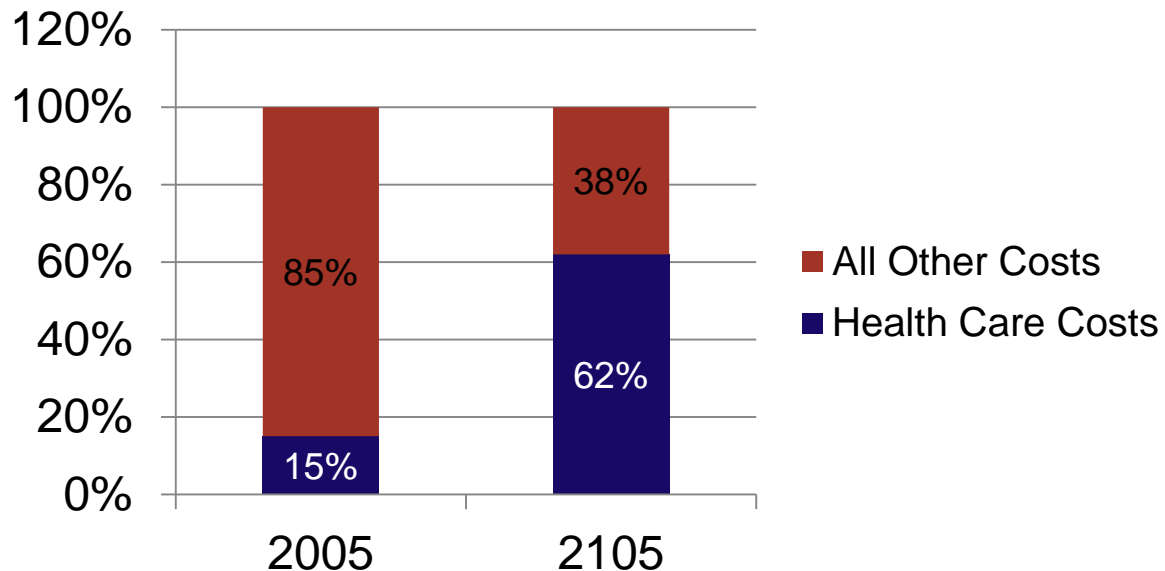
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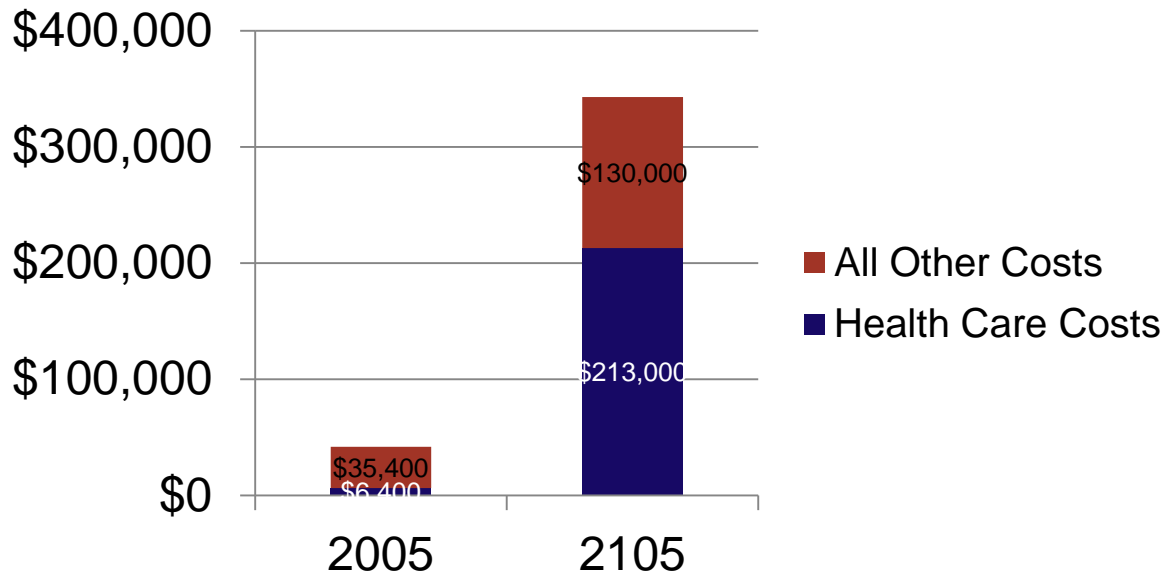
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Baumol's Disease:

Health Care and All Other Spending

(extrapolated spending per capita¹)



¹W.J. Baumol: *The Cost Disease – Why Computers Get Cheaper and Health Care Doesn't*. New Haven, CT: Yale University Press 2012.



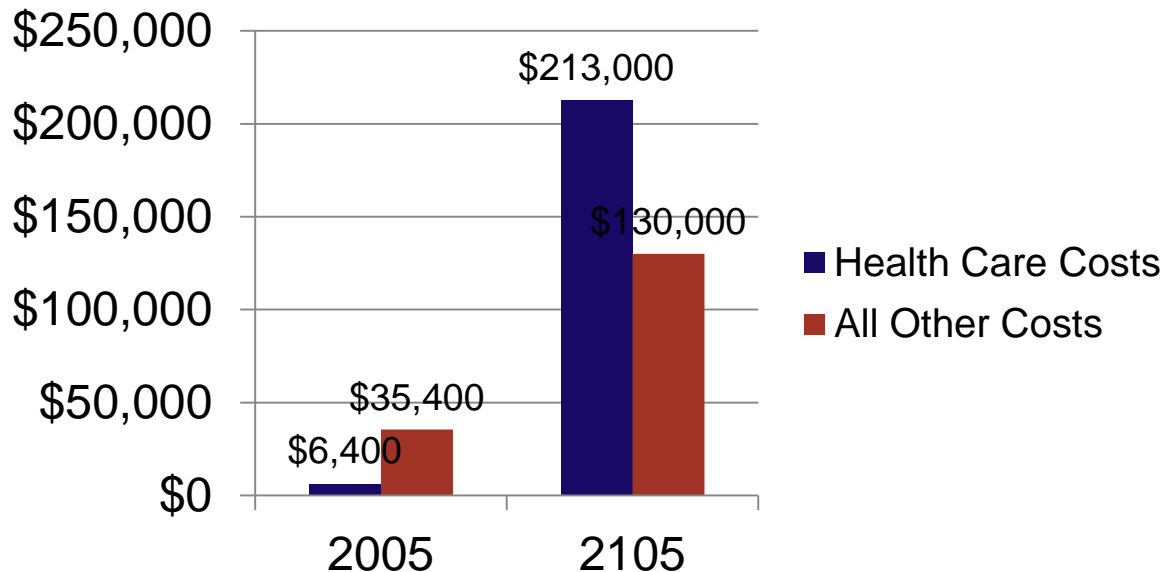
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Baumol's Disease:

Health Care and All Other Spending

(extrapolated spending per capita¹)



¹W.J. Baumol: *The Cost Disease – Why Computers Get Cheaper and Health Care Doesn't*. New Haven, CT: Yale University Press 2012.



Affordability

(“Yes, but...”)

- **Affordability vs. Financing**
 - equity issues
- **Increasing Public Sector Share of GDP**
 - will productivity continue to accelerate?
- **Educating the Public and Politicians**
 - financial vs. physical measurement of manufacturing output



Affordability

(“Yes, but...”)

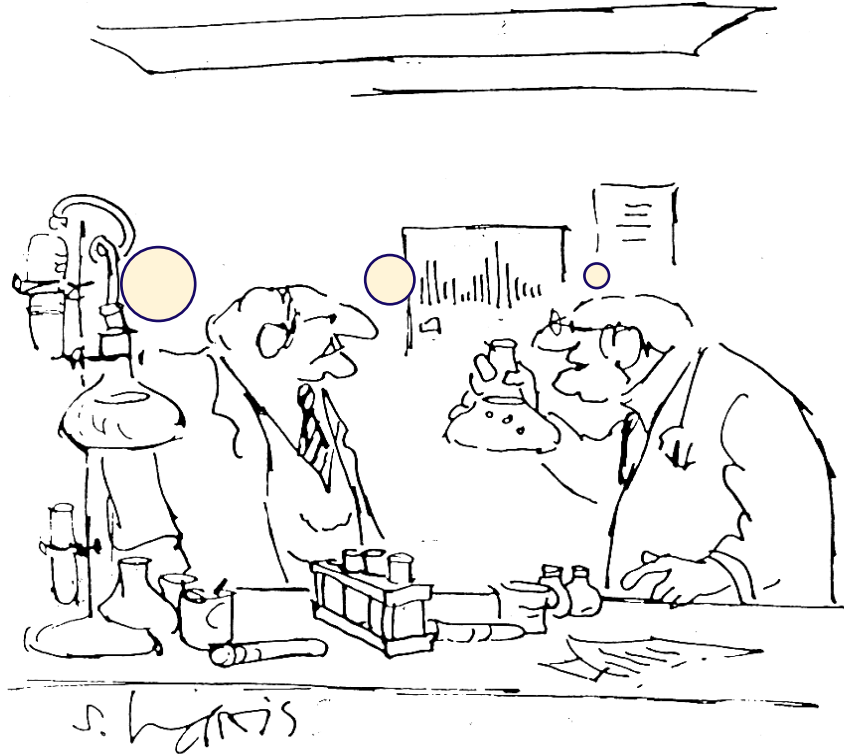
Some Moral (if not Economic) Imperatives:

- **Elimination of Ineffective Care**
 - avoidance of harmful or unnecessary interventions
- **Targeting Interventions (including Prevention)**
 - by using genetic information
- **Systematic Health Technology Assessments (HTAs)**
 - ensuring “**Value for Money**”
 - ... searching cost saving alternatives, “choosing wisely”,
life style changes, medical education, ...



Health Technology Assessment (HTA)

**“It may well
bring about
immortality
–
but it will
take forever
to test
it.”**





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Thank You for Your Attention!

Professor **Michael Schlander**, M.D., Ph.D., M.B.A.

Contact

www.innoval-hc.com

www.michaelschlander.com

michael.schlander@innoval-hc.com

michael.schlander@medma.uni-heidelberg.de

Address

An der Ringkirche 4

D-65197 Wiesbaden / Germany

INNOVAL^{HC}
Institute for Innovation & Valuation
in Health Care