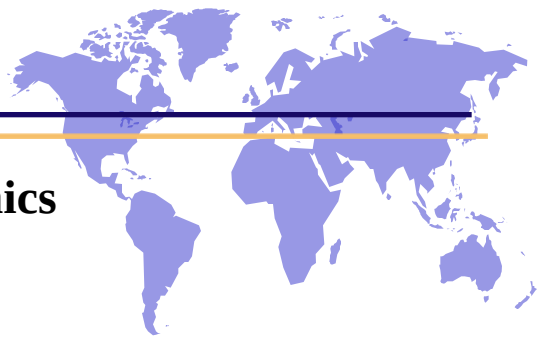

The Burning Platform

Health Economics Global Congress 2015

Hilton London Kensington Hotel, December 07, 2015

The Burning Platform



Credibility of Corporate Health Economics

Michael Schlander

Ruprecht Karls University of Heidelberg
& Institute for Innovation & Valuation in Health Care (INNOVAL[HC])

Institutional Background

- **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.

WHAT WE DO

Practice, Process, and Policy

- **Normative Analysis**
  - Normative Health Economics and "Empirical Ethics"
  - Evaluation Principles for Ultra-Rare Disorders
- **Health Care Policy Analysis**
  - Pharmaceutical Market Regulation
  - "Appraising the Appraisers"
- **Health Technology Assessments**
  - Systematic Reviews and Value Assessments
  - Swiss HTA Consensus Project
- **Applied Health Economics**
  - Cost Effectiveness Evaluations
  - Health Economic Methods Development
- **Health Care Utilization Research**
  - Administrative Database (Nordbaden / Germany)
- **Strategic Consulting & Executive Education**
  - Strategic Consulting
  - Market Access Master Class
  - Heidelberg Health Economics Summer School

Example

Normative Analysis

Measures of efficiency in healthcare: QALMs about QALYs?

Michael Schlander[a,b,c,*]

[a]Institute for Innovation & Valuation in Health Care (InnoVal[HC])
[b]Universität Heidelberg, Medizinische Fakultät Mannheim (Institut für Public Health)
[c]Hochschule für Wirtschaft Ludwigshafen

Z. Evid. Fortbild. Qual. Gesundh. wesen 104 (2010) 209-226

Summary

Comparative economic evaluations are concerned with the relative efficiency of alternative uses for scarce resources. Cost-benefit analysis (CBA) is grounded in economic welfare theory and attempts to identify alternatives with a net social benefit, measuring the created value in terms of individual willingness to pay (WTP). In applied health economics, cost-effectiveness evaluation (CEA) is more widely used than CBA, adopting a modified efficiency criterion, minimization of incremental costs per quality-adjusted life year (QALY) gained ("cost-utility analysis," CUA).

CBA has been greeted with skepticism in the health policy field, primarily owing to resistance to a monetary measure of benefit and owing to concerns that WTP may be unduly influenced by ability to pay. The move to CUA, however, has not been without problems. The framework deviates from economic theory in important aspects and rests on a set of highly restrictive assumptions, some of which must be considered as empirically falsified. Results of CUAs do not seem to be aligned with well-documented social preferences and the needs of healthcare policy makers acting on behalf of society. By implication, there is reason to assume that a context-independent value of a QALY does not exist, with potentially fatal consequences for any attempt to interpret CUAs in a normative way. Policy makers seem well advised to retain a pragmatic attitude towards the results of CUAs, while health economists should pay more attention to the further development of promising alternative evaluation paradigms as opposed to the application of algorithms grounded in poor theory.

Key words: efficiency, cost-benefit analysis, cost-effectiveness analysis, cost-utility analysis, willingness to pay. quality-adjusted life year (QALY)

Evaluation Principles for Ultra-Rare Disorders

INNOVAL HC
Institute for Innovation & Valuation in Health Care

International Expert Consensus

"DETERMINING THE VALUE OF MEDICAL TECHNOLOGIES TO TREAT ULTRA-RARE DISORDERS (URDs)"

CONSENSUS STATEMENT

based upon an International Expert Workshop
held in
Berlin / Germany, November 08, 2012

Final Version of July 19, 2013

by

Michael Schlander, Silvio Garattini, Peter Kolominsky-Rabas, Erik Nord, Ulf Persson, Maarten Postma, Jeff Richardson, Steven Simoens, Oriol de Solà Morales, Keith Tolley, Mondher Toumi

Disclaimer:

This document summarizes the consensus emerging from debate during the workshop as well as an exchange of thoughts on two preliminary versions describing the results of the workshop. It does not necessarily represent in detail the individual views of its authors. The final version of the document was completed by July 19, 2013.

UNIVERSITÄT HEIDELBERG
Mannheim Medical Faculty

UNIVERSITÄT HEIDELBERG

Incremental Cost per Quality-Adjusted Life Year Gained?

The Need for Alternative Methods to Evaluate Medical Interventions for Ultra-Rare Disorders

Michael Schlander,
Silvio Garattini, Peter Kolominsky, Erik Nord, Ulf Persson, Maarten Postma, Jeffrey Richardson, Steven Simoens, Oriol de Solá-Morales, Keith Tolley, and Mondher Toumi

16th ISPOR Annual European Congress
Dublin / Ireland, November 04, 2013

Value in Health 16 (7), November 2013: A324

INNOVAL HC
Institute for Innovation & Valuation in Health Care

& Mannheimer Institut für Public Health – www.miph.uni-hd.de

Example

Health Care Policy Analysis: "Appraising the Appraisers"

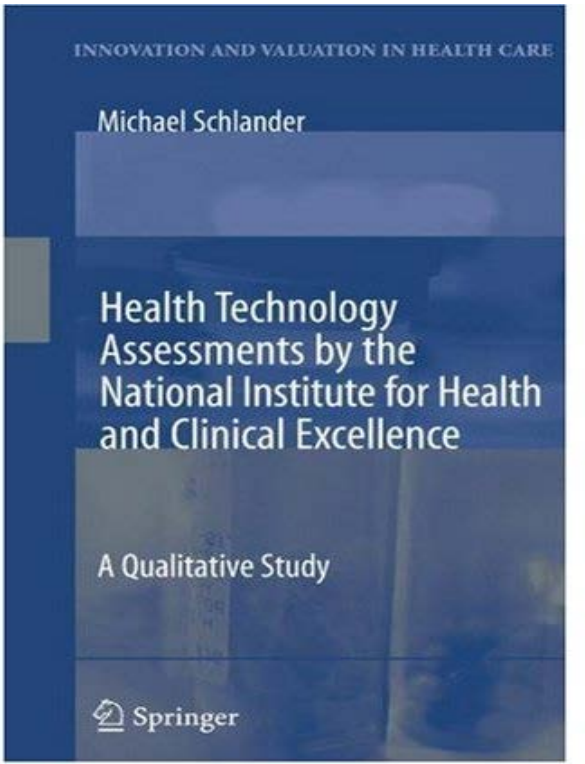
Market Access and Regulatory Context

Quotes from the Introduction:

Results of Health Technology Assessments (HTAs) have become increasingly relevant to health care policy makers worldwide.

The National Institute for Health and Clinical Excellence (NICE) in London, England, is widely regarded as a role model for the implementation of HTAs, incorporating economic evaluation based on the logic of cost-effectiveness.

However, international health care policy makers contemplating to adopt NICE-like approaches appear well advised to consider both strengths and limitations of the NICE approach, in addition to the specific value judgments underlying NICE technology appraisals, which they may or may not share.



M. Schlander: *Health Technology Assessments by the National Institute for Health and Clinical Excellence: A Qualitative Study*.
New York, NY: Springer Science and Business Media, 2008

Example

Health Care Policy Analysis: "Appraising the Appraisers"

House of Commons
Health Committee

National Institute for Health and Clinical Excellence (NICE)

Written evidence

Ordered by The House of Commons to be printed 26 April 2007

Expert Report on National Institute for Health and Clinical Excellence, NICE, London / England

NHS National Institute for Health and Clinical Excellence

M. Schlander: *House of Commons Health Committee Inquiry into aspects of the work of the National Institute for Health and Clinical Excellence. Evidence submitted by the Institute for Innovation & Valuation in Health Care.* In: House of Commons Health Committee (ed.): National Institute for Health and Clinical Excellence (NICE) – Written Evidence. Published on 17 May 2007 by authority of the House of Commons: London, The Stationery Office, pp. 118-122.

HC 503-II
Published on 17 May 2007
by authority of the House of Commons
London: The Stationery Office Limited
£0.00

GALEN INSTITUTE
A not-for-profit health and tax policy research organization

Briefing Document

Comparative Effectiveness Programs:

A Global Perspective: Discussing Germany and the UK

By Michael Schlander

(Institute for Innovation & Valuation in Health Care, InnoVal-HC)

Washington, DC, March 09, 2009

Example

Health Technology Assessments: "Appraising the Appraisers"

Review of IQWiG Pilot Cost-Benefit Study

Zusammenfassende Würdigung (Studienauftrag)

1. Der Endbericht adressiert eine – abweichend vom Auftrag[1] – selbst definierte Forschungsfrage.
2. Der vorliegende Endbericht vom 20. Mai 2009 beinhaltet
   a. eine unvollständige und nicht mängelfreie Bearbeitung der mit dem Auftrag gestellten Forschungsfrage(n), u.a. wegen fehlender Berücksichtigung von Komplikationen und eines sehr einfachen, nicht extrapolations-fähigen Markov-Modells, dessen Validität äußert zweifelhaft erscheint
   b. ….
3. Die mit dem Endbericht aufgeworfenen Fragen können nicht schon deshalb als irrelevant abgetan werden.


UNIVERSITÄT HEIDELBERG

Machbarkeitsstudie
zur Kosten-Nutzenbewertung (KNB)
von Thrombozytenaggregationshemmern

Aufgeforderter Diskussionsbeitrag
zu den Ergebnissen einer Machbarkeitsstudie
für das Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG)
vorgelegt von J. Wasem et al. (2009)

Michael Schlander

Kaiserin-Friedrich-Haus Berlin, 30. Juni 2009

INNOVAL HC

Project supported by IQWiG, Cologne / Germany IQWiG

& Mannheimer Institut für Public Health – www.miph.uni-hd.de

Example

Cost-Benefit Analysis for IQWiG

Kosten-Nutzen-Bewertung von Clopidogrel bei der peripheren arteriellen Verschlusskrankheit und beim akuten Koronarsyndrom

Berichtsplan

Project supported by
IQWiG, Cologne / Germany

IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

INNOVAL HC
Institute for Innovation & Valuation in Health Care

Institut für Innovation & Evaluation im Gesundheitswesen

"VALUE & VALUATION OF HEALTH TECHNOLOGIES"

SCHWEIZER HTA-KONSENSUS-PROJEKT

ECKPUNKTE FÜR DIE WEITERENTWICKLUNG IN DER SCHWEIZ

Health Technology Assessment (HTA):
Systematische Bewertung medizinischer Interventionen in der sozialen Krankenversicherung

Lesehinweis:
Die Ziffern in [eckigen] Klammern verweisen jeweils auf die Dezimalgliederung des ausführlichen Dokuments (Fokusset): „Thesen (Schweizer Konsensus)" Finale Version („FV") vom 19. Oktober 2011 (= korrespondierende Folien).

vorgelegt am 19. Oktober 2011 für **FMH, Interpharma, SAMW** und **santésuisse** unter Beteiligung des **BAG** von

Christian Affolter (santésuisse), **Thomas Cueni** (Interpharma), **Pius Gyger** (Helsana), **Ansgar Hebborn / Claude Cao** (Roche), **Daniel Herren** (FMH), **Stefan Kaufmann** (santésuisse), **Heiner Sandmeier** (Interpharma), **Michael Schlander** (Universität Heidelberg) und **Peter Suter** (SAMW)
unter Mitarbeit von **Andreas Faller**[1] (BAG)

[1]projektbeteiligt im Beobachterstatus]

INNOVAL HC
Institute for Innovation & Valuation in Health Care

Institut für Innovation & Evaluation im Gesundheitswesen

"VALUE & VALUATION OF HEALTH TECHNOLOGIES"

SWISS HTA CONSENSUS

GUIDING PRINCIPLES

Objectives

Scope
A Broad Technology Focus
HTA at the National Level

Stakeholder Involvement
Governance and Process Development
Technology Assessments

Evaluation Criteria
Beyond Clinical Efficacy:
A Prior Normative Commitment
Social Preferences
Swiss "WZW" Criteria

Evidence of Clinical Effectiveness
Reasonable Evidence Expectations:
Expected Level of Evidence
Grading of Clinical Evidence

Economic Viability
Budgetary Impact
Technical and Allocative Efficiency
Setting Limits
Managing Uncertainty

Evolutionary Options
Research Needs
Methods Development

Swiss HTA Consensus Project 2010-2013
www.swisshta.ch

Example

Applied Health Economics / Cost Effectiveness Analysis (The Example of ADHD)

Current Pharmaceutical Design, 2010, *16*, 2443-2461

The Pharmaceutical Economics of Child Psychiatric Drug Treatment

Michael Schlander[1-3,*]

Michael Schlander

Long-acting medications for the hyperkinetic disorders

A note on cost-effectiveness

European Child & Adolescent Psychiatry
16 (7), 2007: 421-429

Treatment for ADHD: Is More Complex Treatment Cost-Effective for More Complex Cases?

E. Michael Foster, Peter S. Jensen, Michael Schlander, William E. Pelham Jr., Lily Hechtman, L. Eugene Arnold, James M. Swanson, and Timothy Wigal

Health Services Research
42 (1), 2007: 165-182

Example

Health Economic Methods Development

HRQoL Multi-Instrument Comparison (MIC) Study

UNIVERSITÄT HEIDELBERG

The Measurement of Health-Related Quality of Life (HRQoL)

First German Findings from the Multi-Instrument Comparison (MIC) Study

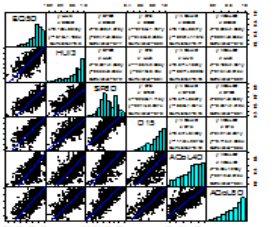
Michael Schlander, Munir A. Khan, Angelo Iezzi, Aimee Maxwell, Oliver Schwarz, Jeff Richardson

16th ISPOR Annual European Congress
Dublin / Ireland, November 04, 2013

INNOVAL HC Institute for Innovation & Valuation in Health Care

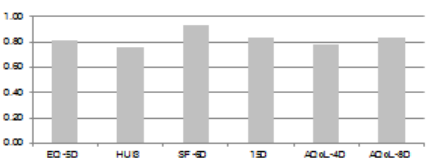
MIC Study: Linear Relationships

Pairwise geometric regression results (total, n=1,269):



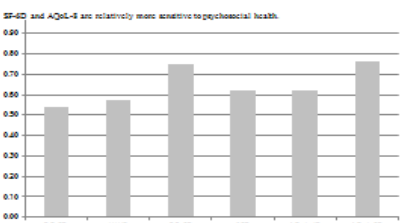
MIC Study: Pearson Correlations with SF-36

Pearson correlation of MAU Instruments with SF-36 (total, n=1,269):



MIC Study: Instrument Content

Correlation with SF-36 Mental Component Summary (MCS) (total, n=1,269):



Example

Health Care Utilization Research: The Nordbaden Project

July 07, 2013

European Society for Child and Adolescent Psychiatry
ESCAP
15th International ESCAP Congress
Dublin, Ireland, July 06 - 10, 2013

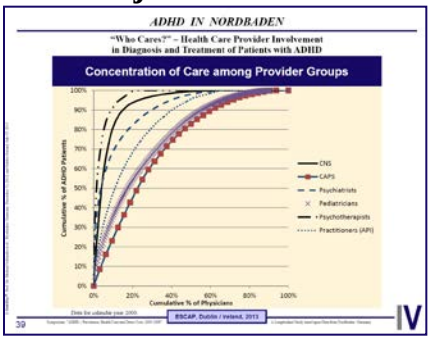
ADHD: A Longitudinal Analysis (2003-2009) of Prevalence, Health Care, and Direct Cost based upon Administrative Data from Nordbaden / Germany

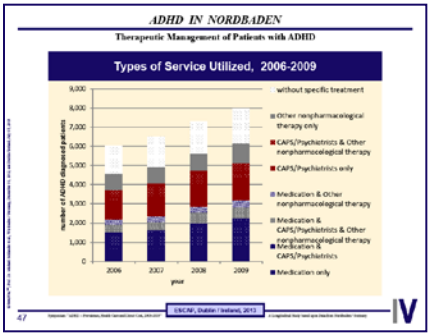
Michael Schlander[1], Oliver Schwarz[2], Götz-Erik Trott[3], and Tobias Banaschewski[1]

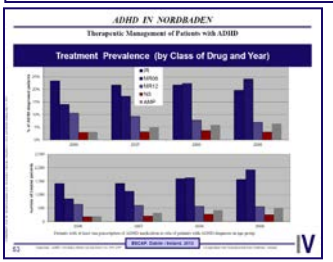
[1]University of Heidelberg
[2]Heilbronn University
[3]University of Würzburg

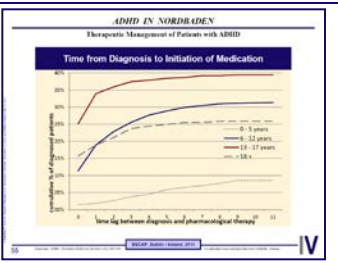
and

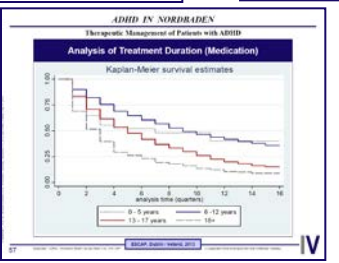
Institute for Innovation & Valuation in Health Care (INNOVAL[HC])
University of Heidelberg & University of Applied Economic Sciences Ludwigshafen

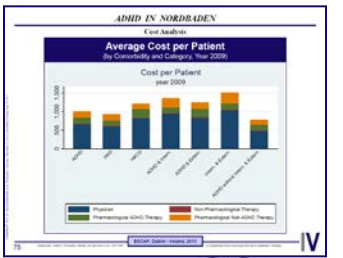












Research Translation & Outreach

Strategic Consulting:

Health Economics
Market Access
Reimbursement
Value Identification
Value Demonstration
Comprehensive Value Dossiers
Value Communication
Pricing Policies

Executive Education:

Heidelberg Health Economics Summer School

Market Access Master Class
(in conjunction with **LSE**, *London School of Economics*)

RESEARCH & DEVELOPMENT

A Strategic Role for CROs

External contractors are playing an increasingly significant role in the drug development process. But pharmaceutical companies need to learn how to use them to the greatest advantage.

PHARMACEUTICAL EXECUTIVE FEBRUARY 1994

Research Translation & Outreach

Strategic Consulting:

Health Economics
Market Access
Reimbursement
Value Identification
Value Demonstration
Comprehensive Value Dossiers
Value Communication
Pricing Policies

Executive Education:

Heidelberg
Health Economics
Summer School

Market Access
Master Class
(in conjunction with **LSE**,
London School of Economics)

Health Economics Summer School

- **Modeling in Theory and Practice**
  (Workshop incl. Decision Analytic Software Training)
  Heidelberg, 2006, 2007, 2008
- **Current Concepts & Controversies**
  and International HTA Experience
  Heidelberg, 2006, 2007, 2008, 2015, 2016, …

  Economic Theory and Extrawelfarism; Normative Issues; The Ethics of HTA; Focus on Due Process; Measuring "Social" (Non-Selfish) Preferences

  Experience: Australia (PBAC), Canada (CDR), USA (Academy of Managed Care), England (NICE), Sweden (LFN), France (HAS), Germany (IQWiG), …
- Faculty incl. F. Breyer, M.J. Buxton, J.J. Caro, G. de Pouvourville, S. Holm, P.G. Kanavos, P.J. Neumann, E. Nord, U. Persson, J. Richardson, R. Viney, et al.

Credibility

"How Leaders Gain and Lose It,
Why People Demand It"

James M. Kouzes and Barry Z. Posner,
San Francisco: Jossey-Bass Publishers 1993

PERCEPTIONS & POLITICAL CLIMATE

IV

Credibility: Perceptions of Industry

Scandals (Non-Pharmaceuticals)

- **Volkswagen Emissions Scandal (2015)**
- **FIFA Corruption Crisis (2015)**
- **Petrobas Corruption Scandal (2014)**
- **LIBOR Rigging Scandal (2012)**
- **Olympus Accounting Fraud (2011)**
- **Bernie Madoff's Ponzi Scheme (2008)**
- **WorldCom Accounting Scandal (2002)**
- **Enron Accounting Scandal (2001)**

FIFA
For the Game. For the World.

Credibility: Perceptions of Industry

Scandals

"In the last three years, global pharma giants have paid fines to the tune of $11 billion for criminal wrongdoing, including withholding safety data and promoting drugs for use, beyond any licensed condition."[1]

BioSpectrum the business of bioscience

[1]Source: http://www.biospectrumasia.com/biospectrum/analysis/192973/worlds-big-pharma-frauds

Credibility: Perceptions of Industry

BioSpectrum the business of bioscience

Reputation of the Pharmaceutical Industry: Some Big Scars (~2013)[1]

- GSK China Bribery Scandal (2013)
- GSK / FDA $3 billion Fraud Settlement (2013)
- Merck & Co. MMR / Mumps Vaccine Scandal (2013)
- Roche Medicine Safety Reporting System (2012)
- Pfizer's "Harmful Deceit" (2012)
- Abbott's "Unlawful Drug Promotion" (2012)
- Takeda accused of suppressing Actos safety data (2012)
- John Le Carré's The Constant Gardener (2001):
  - "Profits don't buy reforms.
    They buy corrupt government officials and Swiss bank accounts."

[1]http://www.biospectrumasia.com/biospectrum/analysis/192973/worlds-big-pharma-frauds

Cost of Interventions:
Median Costs per Year of New Anticancer Drugs (Germany)

Some New Anticancer Drugs[1]

¬ **Nilotinib (Tasigna®)**	**€ 61,600**
¬ **Sunitinib (Sutent®)**	**€ 50,920**
¬ **Cetuximab (Erbitux®)**	**€ 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

[1]G. Glaeske et al. (2010) "The Burning Platform"

Credibility: Perceptions of Industry

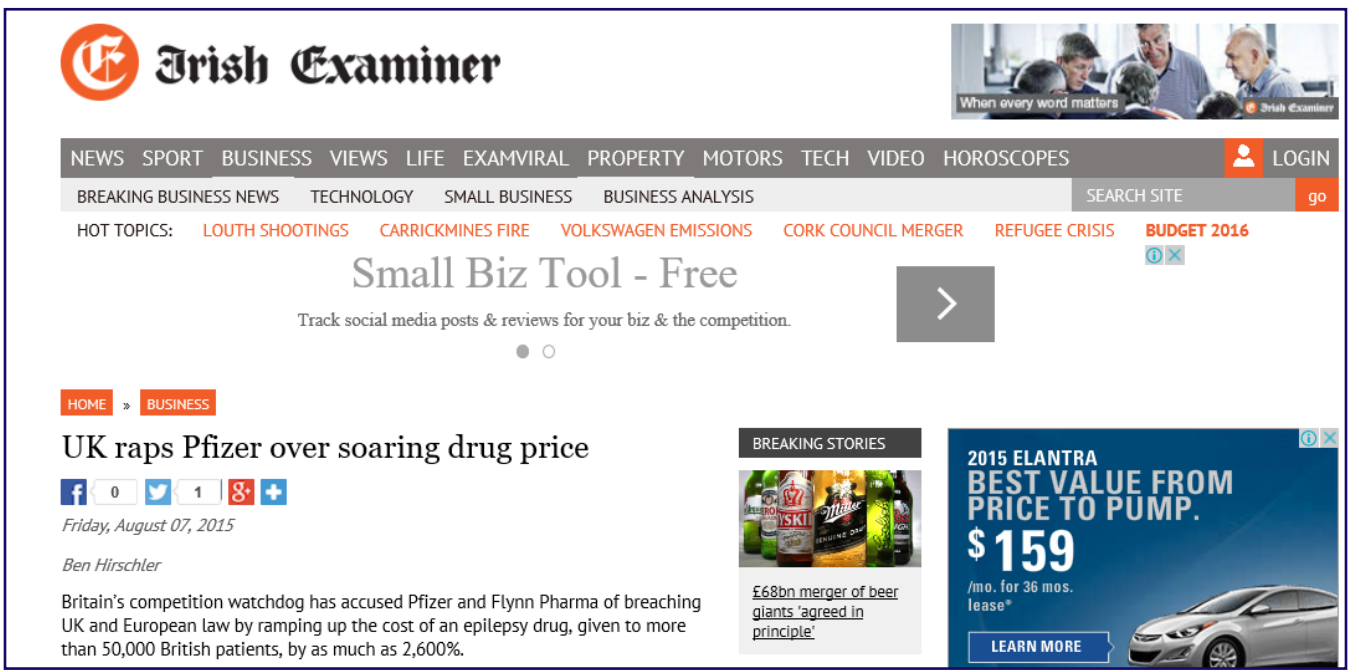
Pricing of New Drugs (2014)

"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."

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

Credibility: Perceptions of Industry

Recent Examples from the Media



http://www.irishexaminer.com/business/uk-raps-pfizer-over-soaring-drug-price-346857.html

Credibility: Perceptions of Industry

Recent Examples from the Media

sign in subscribe search jobs more International

theguardian

UK world sport football opinion culture business lifestyle fashion environment tech travel browse all sections

home › opinion columnists

Pharmaceuticals industry
Comment is free

The Guardian view on the NHS and soaring drugs prices
Editorial

The cancer drugs fund has become a way of escaping constraints carefully established by the National Institute for Health and Care Excellence

http://www.theguardian.com/commentisfree/2014/aug/11/guardian-view-nhs-soaring-drugs-prices

Credibility: Perceptions of Industry

Frequently forgotten:

"Drugs
are part of health care …
–
… the pharmaceutical industry is not."

Heinz Redwood (1992)

Credibility: Perceptions of Industry

Pharmaceutical Industry Profitability

"The spectacle of a drug company wringing its hands as a victim of government whilst proudly reporting 'our 15th successive year of record profits' **is as zoologically bizarre as a cat sitting pretty in a mouse trap, quietly eating the cheese**."[1]

[1]Picture: "*off the mark*", courtesy of Mark Parisi

[2]Heinz Redwood; "*The Dynamics of Drug Pricing and Reimbursement in the European Community*." Richmond (1992)

CASE STUDY IN BRIEF: ORPHAN MEDICINAL PRODUCTS

IV

Case Study: Drugs for Rare and Ultra-Rare Disorders

International Orphan Drug Legislation

- USA: Orphan Drug Act (1983); Orphan Drug Regulation (1993)
- Japan: Orphan Drug Regulation (1993)
- Australia: Orphan Drug Policy (1997)
- European Union: Regulation CE No. 141/2000 (2000)

Some Measures:

- R&D grants, tax credits, protocol assistance, accelerated review, market exclusivity (USA, 7y; Japan and EU, 10y; Australia, 5y)

Some Definitions:

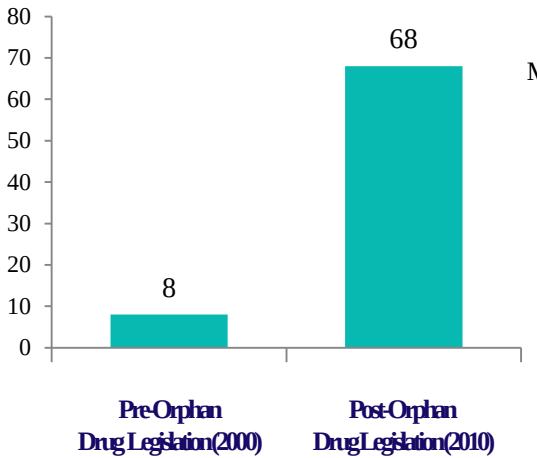
- USA: prevalence < 7.5/10,000 (i.e., <200,000)
- Japan: prevalence <4/10,000
- Australia: prevalence <1.1/10,000
- European Union: prevalence <5/10,000
- England / Wales: “ultra-orphan” disorders, prevalence <1/50,000

Case Study: Drugs for Rare and Ultra-Rare Disorders

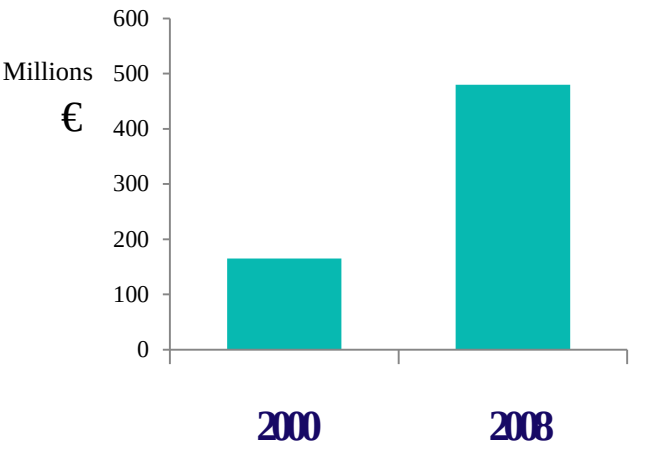
EU Orphan Drug Regulation

Impact on Research & Development

No. of Drugs for rare diseases receiving marketing authorization in Europe



European investment in orphan drug R&D, 2000 and 2008



Source: Office of Health Economics (OHE). *Assessment of the Impact of OMPs on the European Economy and Society. Consulting Report November 2010*.
Available at http://www.ohe.org/publications/article/assessment-of-the-impact-of-orphan-medicinal-products-on-europe-15.cfm.
Last accessed 14/11/15.

Case Study: Drugs for Rare and Ultra-Rare Disorders

"The Most Expensive Drugs in the World"[1]

The Motley Fool

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

Case Study: Drugs for Rare and Ultra-Rare Disorders

"The 5 Most Expensive Drugs in the World"[1]

1. **Soliris** (Alexion)
   (8,000 [PNH] + 300 [aHUS]) x US-$ 409,500 =
   = **US-$ 3,400 million p.a.** (U.S. alone)
2. **Elaprase** (Shire)
   2,000 [Hunter s.] x US-$ 375,000 = **US-$ 750 million p.a.** (WW)
3. **Naglazyme** (BioMarin)
   1,100 [MPS VI] x US-$ 365,000 = **US-$ 400 million p.a.** (WW)
4. **Cinryze** (ViroPharma)
   6,000 [HAE] x US-$ 350,000 = **US-$ 2,100 million p.a.** (U.S.)
5. **Myozyme** (Sanofi / Genzyme)
   900 [Pompe dis.] x US-$ 300,000 = **US-$ 270 million p.a.** (WW)

Five Drugs (back of the envelope estimate): ≥ US-$ 6.9 billion p.a.

[1]S. Williams, The Motley Fool, June 29, 2013. http://www.fool.com/investing/general...

Case Study: Drugs for Rare and Ultra-Rare Disorders

Orphan Drugs and the NHS: Should We Value Rarity?

Christopher McCabe, Karl Claxton, Aki Tsuchiya

The growing number and costs of drugs for rare diseases are straining healthcare budgets. Decisions on funding these treatments need to be made on a sound basis

[…]

The justification for special status for rare diseases must rest on the question: should we value the health gain to two individuals differently because one individual has a common disorder and the other has a rare disorder?

[…]

While orphan drugs were rare, healthcare systems were able to deal with them in an ad hoc manner. But there are now over 6000 orphan diseases with over 200 treatments approved by the US Food and Drugs Administration and 64 trials currently sponsored by the US Office of Orphan Products Development. […] Genomics is expected to disaggregate currently prevalent diseases into many genetically defined distinct conditions. Orphan status is thus likely to become increasingly common.

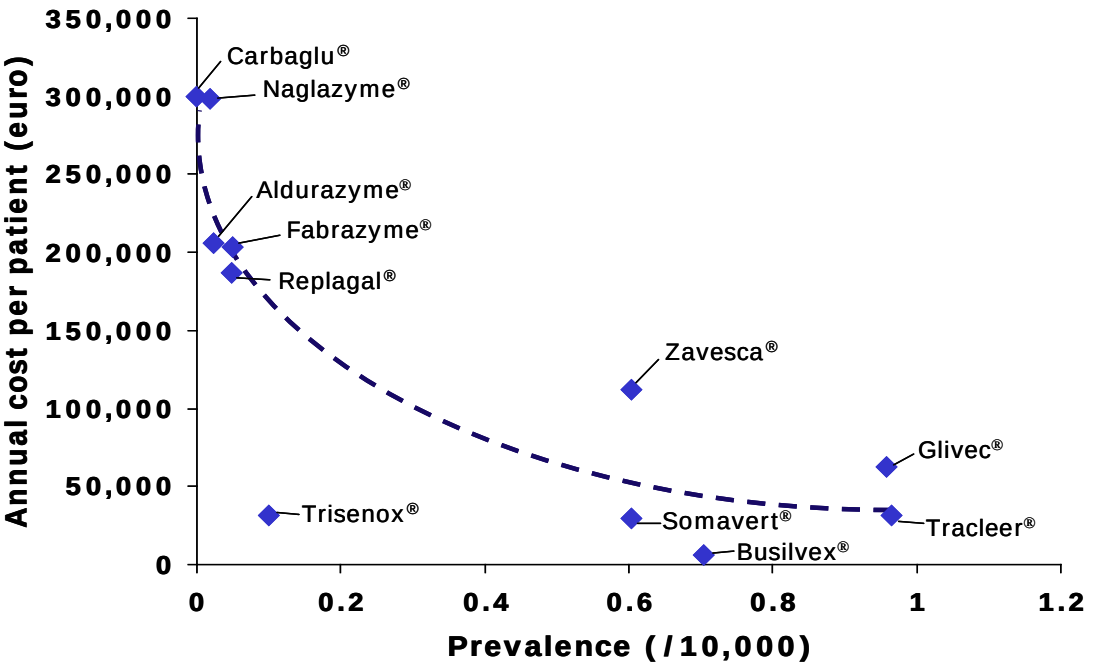
[…]

Special status for orphan drugs in resource allocation will avoid difficult and unpopular decisions, but it may impose substantial and increasing costs on the healthcare system. The costs will be borne by other, unknown patients, with more common diseases who will be unable to access effective and cost effective treatment as a result.

British Medical Journal 2005, 331: 1016-1019

Case Study: Drugs for Rare and Ultra-Rare Disorders

Prevalence and Cost per Patient



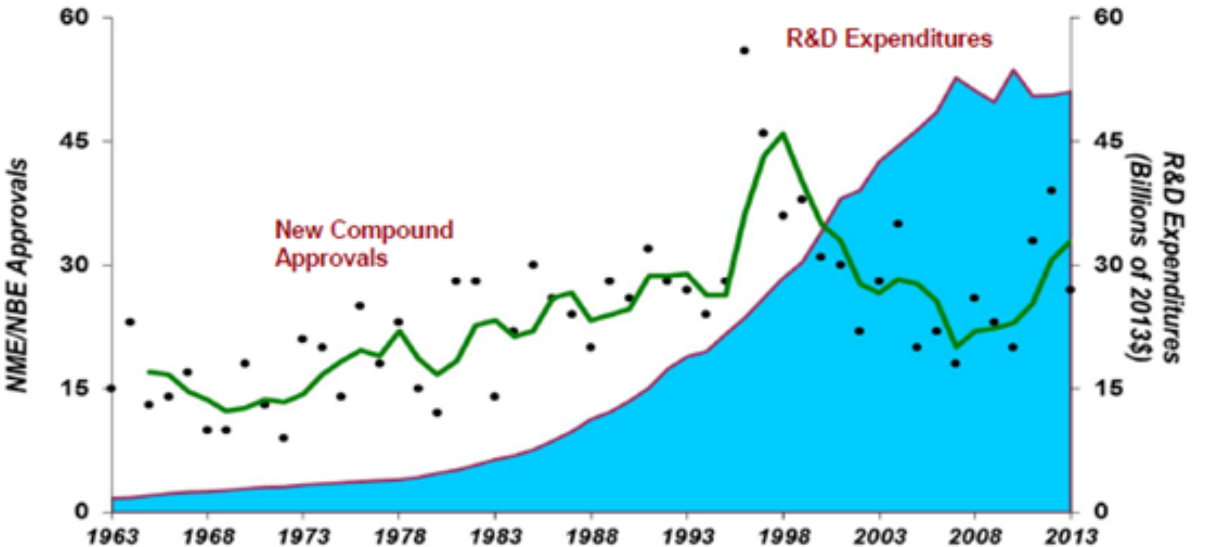
[1]M. Schlander and M. Beck, *Current Medical Research & Opinion* 2009; 25 (5): 1285-1293

BIOPHARMACEUTICAL RESEARCH & DEVELOPMENT (R&D)

IV

R&D Productivity

Pharmaceutical R&D:
New Drug and Biologics 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.

Pharmaceutical 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

R&D Productivity

Pharmaceutical R&D:

Overall Success Rates for Clinical Development

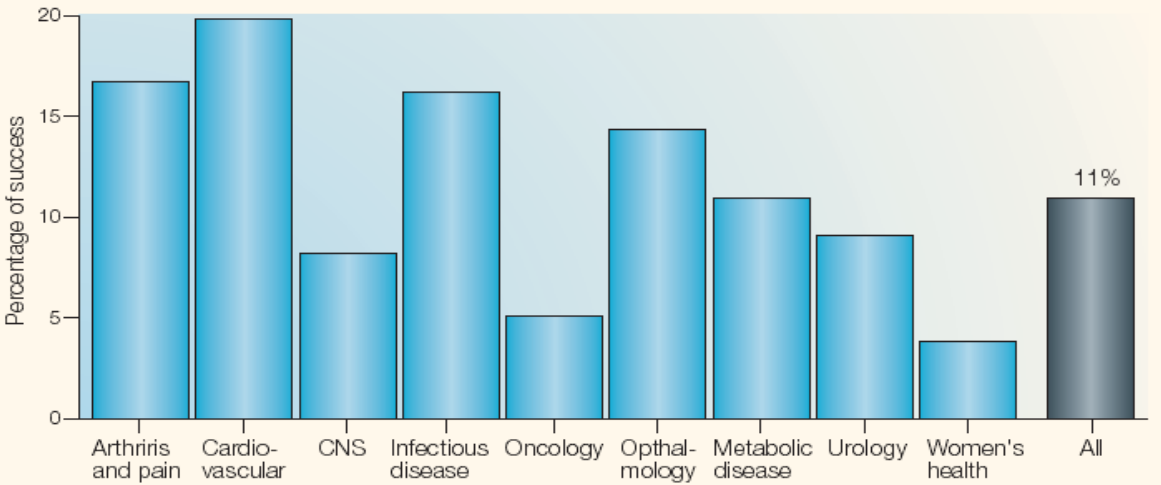


Figure 1 | **Success rates from first-in-man to registration.** The overall clinical success rate is 11%. However, if the analysis is carried out by therapeutic areas, big differences emerge. The data are from the ten biggest drug companies during 1991–2000. (The companies are AstraZeneca, Bristol-Myers 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. Landis. Can the pharmaceutical industry redice attrition rates?
Nature Reviews Drug Discovery, August 2004; 3: 711-715.

Pharmaceutical 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-Ferrandez et al, 2012					**1,506**
DiMasi, 2014					**2,600 †**

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

Pharmaceutical R&D: Trends in Attrition and Project Termination

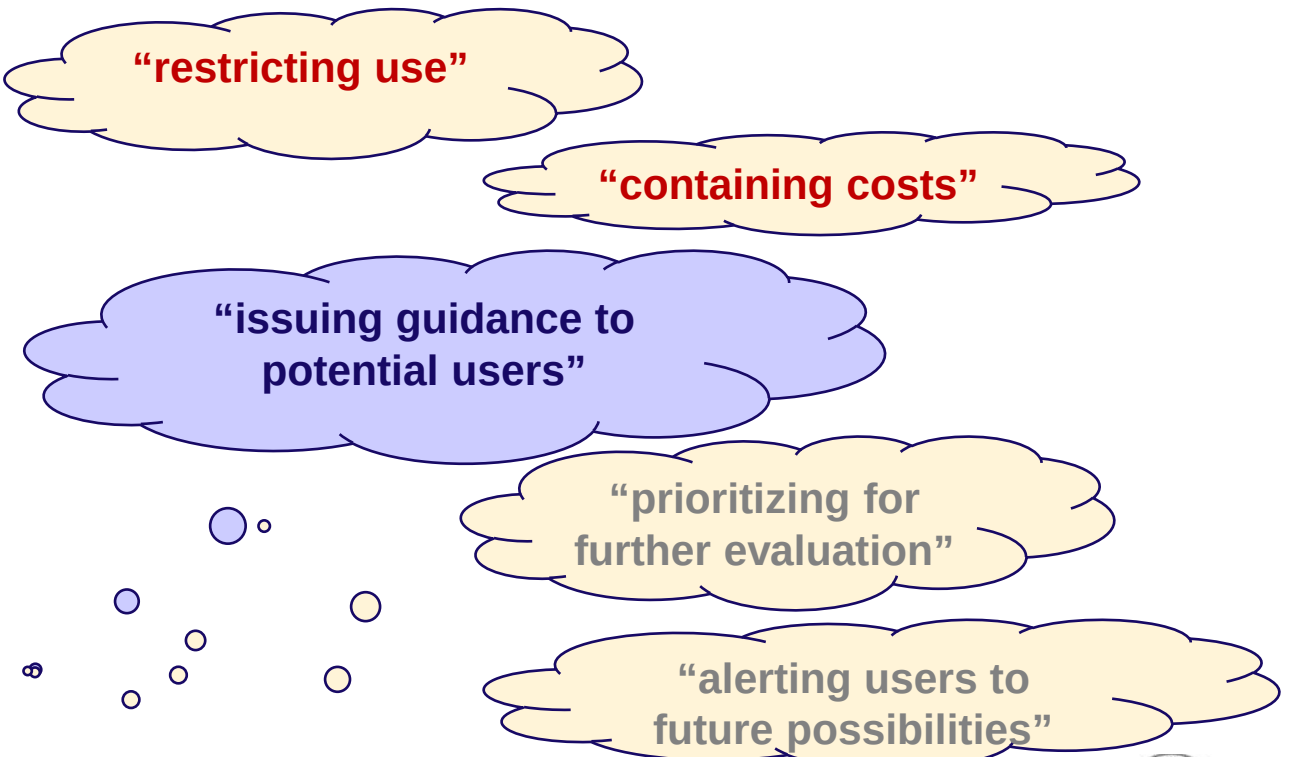
- **Success rates** of NMEs entering into clinical development have remained stable, in the 10-25% range.
- **Biotechnology-derived NMEs** carry a lower attrition risk and are associated with shorter development times.
- **To minimize attrition costs**, it is crucial that unsuccessful NMEs fail as quickly as possible (in particular given that phase III development is very expensive).
- Pharmaceutical companies have moved to integrate health economics into **early strategic assessments** of NMEs.
- Reasons for premature project termination show a trend to **increasing importance of economic criteria**.

IN SEARCH OF "VALUE FOR MONEY"

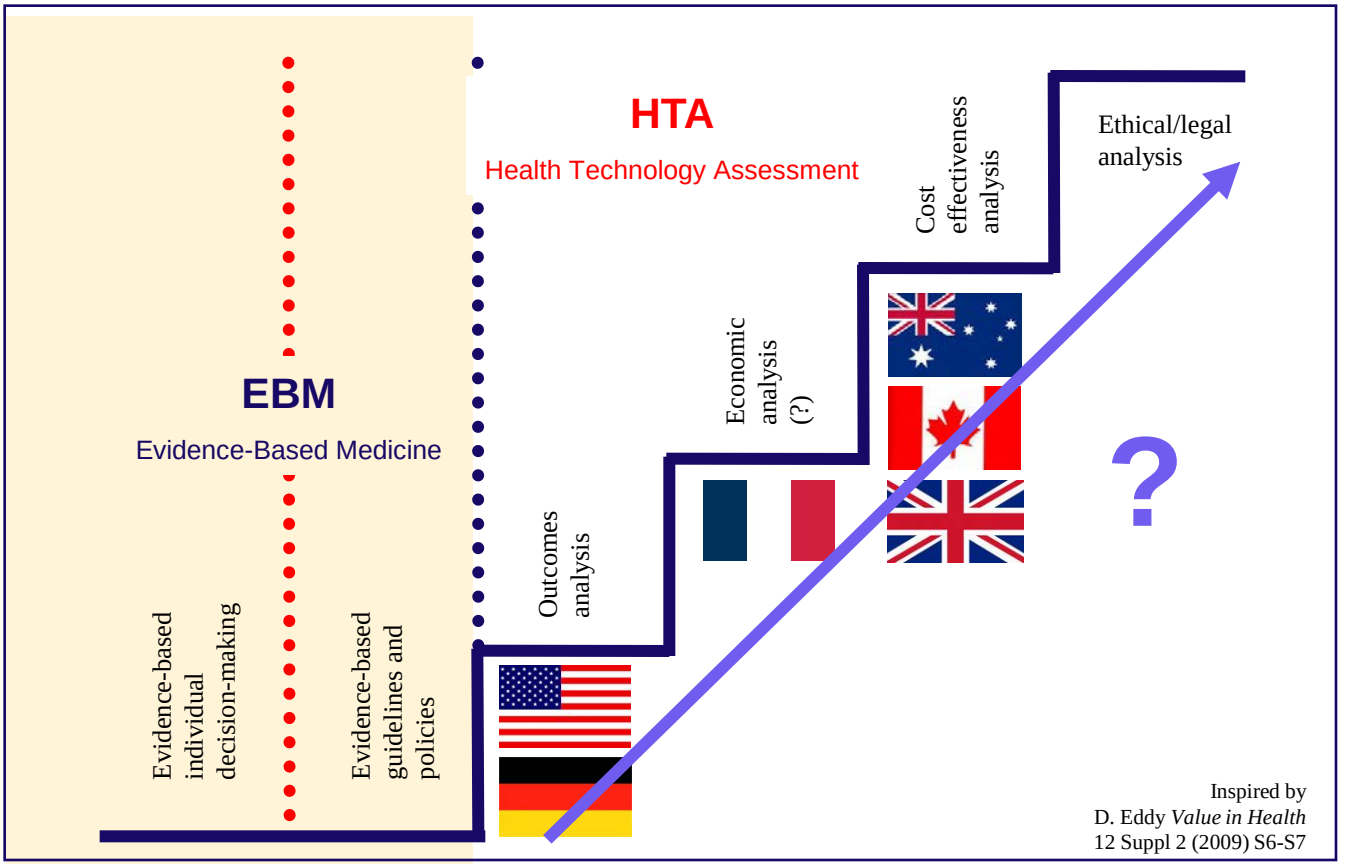
IV

A broad range of expectations (and fears) …

What are Technology Assessments for?



An Evolutionary Process?[1]



A High Profile

"What Could Be Nicer Than NICE?"[1]

- **Pearson and Rawlins (2005)[2]:**

  "The conditions seem ripe for a NICE in the United States …"

- **Smith (2004)[3]:**

  "*The triumph of NICE"*:

  "NICE is conquering the world … and may prove to be one of Britain's greatest cultural exports along with Shakespeare, Newtonian physics, The Beatles, Harry Potter, and the Teletubbies …"

- **WHO (2003)[4]:**

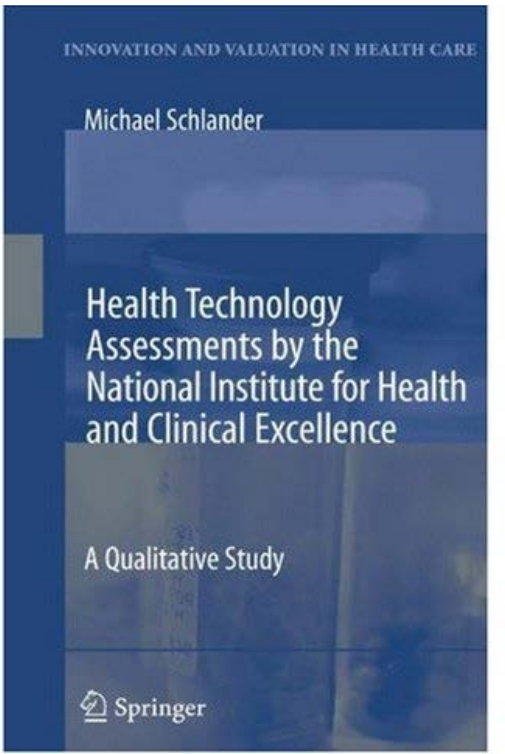
  "Published technology appraisals are already being used as international benchmarks …"

[1] A. Williams (2004)

How Robust Are NICE Technology Appraisals?

Some Issues

- Timing of Technology Appraisals?
- Approach to Uncertainty?
- Integration of Clinical and Economic Expertise?
- Availability of Sufficient Resources?
- Efficiency-First Approach?
- (Almost) Exclusive Reliance on QALYs?
- Enforcement:
  Internal Quality Assurance?
  Implementation of Guidance?



HAS NICE GOT IT RIGHT?

"What More Could Anyone Ask For?"

NICE is **"the closest anyone has yet come to fulfilling the economist's dream of how priority-setting in health care should be conducted."**

Alan Williams (1927 – 2005)

… "[NICE] is transparent, evidence-based, seeks to balance efficiency with equity, and uses a cost-per-QALY benchmark as the focus for its decision-making. *What more could anyone ask for*?"

HAS NICE GOT IT RIGHT?

"What More Could Anyone Ask For?"

NICE is **"the closest anyone has yet come to fulfilling the economist's dream of how priority-setting in health care should be conducted."**

Alan Williams (1927 – 2005)

However:
"Experience has taught me that it is not uncommon for an-economist's-dream-come-true to be seen as a nightmare by everyone else."

Key Assumptions of the Conventional Logic:

Quality-Adjusted Life Years (QALYs)

- (fully) capture the value of health care interventions;
- are all created equal ("A QALY is a QALY is a QALY…").

Maximizing the number of QALYs "produced"

- ought to be the primary objective of collectively financed health schemes,
- leading to the concept of thresholds (or benchmarks) for the maximum allowed cost per QALY gained.

Decreasing cost per QALY

- implies increasing social desirability of an intervention.

A Fundamental Premise

"Social Desirability of an Intervention is Inversely Related to its Incremental Cost per QALY Gained"

but this assumption may create **Reflective Equilibrium** issues:

- Sildenafil for elderly diabetics with erectile dysfunction
- Removal of Tattoos

  compared to
- Palliative Care,
- Interventions for people with comorbid conditions (in "Double Jeopardy", like the chronically disabled)
- Orphan Medicinal Products (OMPs) for (very) rare disorders

A Canadian Policy Analysis[1]

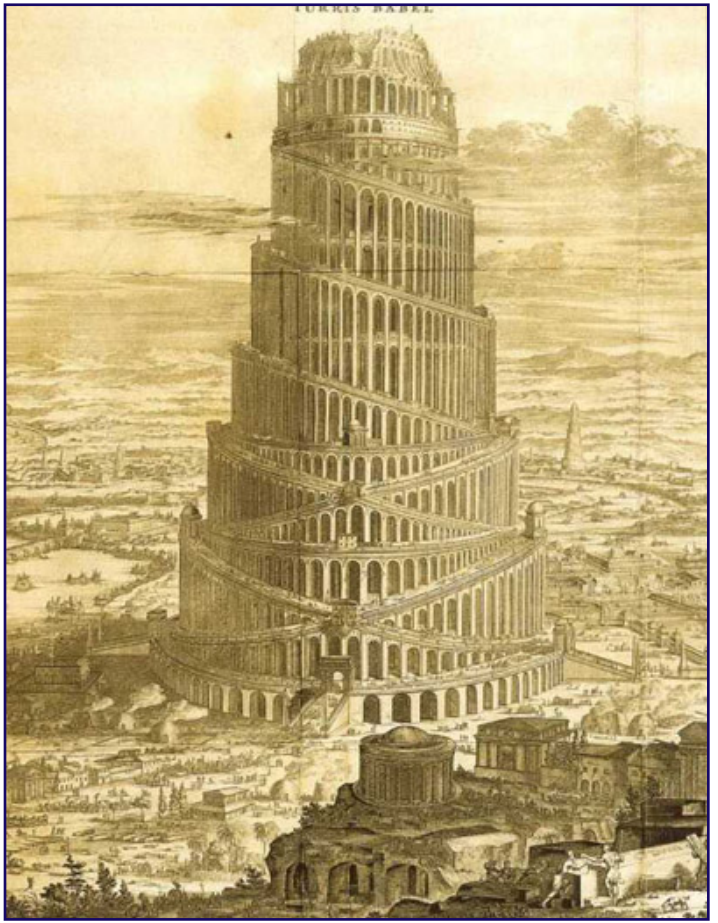


Illustration by Athanasius Kircher

A Tower of Babel …

Referral to many different and often incommensurate things…

A key paradox:

The discourse about values is both very important and very ambiguous…

Stakeholders may be tempted to react to this problem with either

reductionism
(focusing on one particular definition of values to the neglect of other relevant types)

or

nihilism…
(either rejecting all values analyses as equally unreliable, or accepting all as equally credible)

[1]M. Giacomini et al. (2004)

THE STRATEGIC IMPORTANCE OF HEALTH ECONOMICS

IV

An old German saying ...

“Wer am Wege baut, hat viele Meister“[1]

[1]**Martin Luther (1530)**

“A house built by the wayside is either too high or too low.”

The increasing strategic importance of HE&P

The Enhanced Strategic Role of HE&P

- **International Pharmaceutical Industry:**

1950s – 1970s	The Research-Driven Paradigm
1980s	The Market-Driven Paradigm
1990s	The Value-Driven Paradigm
2000s	New Definitions of Value & New International Heterogeneity

} ever increasing complexity

- **The New Challenge:**

  Redefining the business model

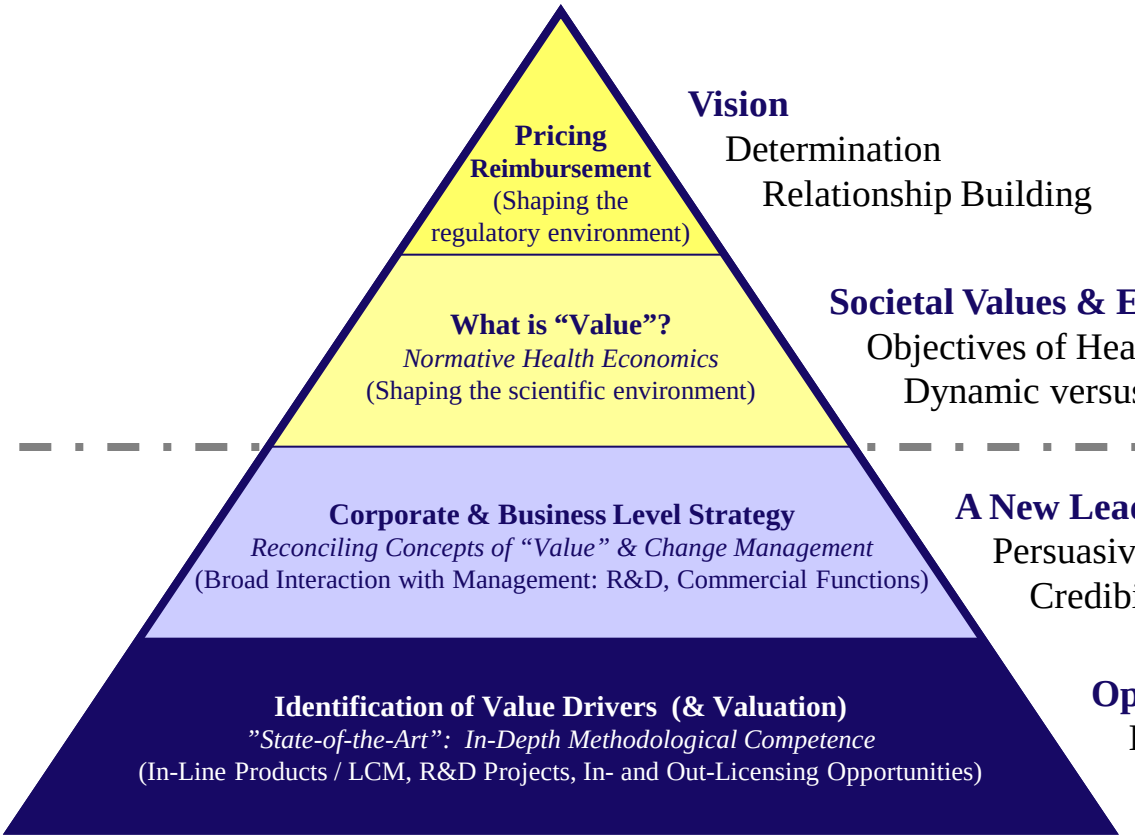
  Reconciling different perspectives of value

- **Health Economics, Pricing & Market Access** capabilities as critical success factors

STRATEGIC IMPLICATIONS

Working with stakeholders

Shaping the environment in a cooperative spirit



Vision
Determination
Relationship Building

Societal Values & Economic Analysis
Objectives of Health Care
Dynamic versus Static Efficiency

A New Leadership Role
Persuasiveness
Credibility & Integrity

Operational Excellence
Impeccable Execution
Team Management

Working with stakeholders

Shaping the environment in a cooperative spirit

Key Stakeholder Groups

- **Traditional Target Groups**
  - Physicians
  - Pharmacists
  - Patient Advocacy Groups
- **… ?**
- **Payer Representatives**
- **Health Care Policy Makers**
  - Regulators & HTA Agencies
- **Academic Thought Leaders**
  - Health Economists
  - HTA Specialist Networks
  - Scholars of Evidence-Based Medicine

Working with stakeholders

Shaping the environment in a cooperative spirit

Integrity and Credibility[1]

- ***citius, altius, fortius*?**
- **Leadership is a Relationship**
- **Credibility Makes a Difference**
- **Discovering Your Self**
- **Appreciating Constituents and Their Diversity**
- **Affirming Shared Values**
- **Developing Capacity**
- **Serving a Purpose**
- **Taking Charge**
- **The Struggle to Be Human**

[1]adapted from Kouzes and Posner (1993)

Working with stakeholders

Shaping the environment in a cooperative spirit

Networking

- **Health Economcis, Pricing & Reimbursement**
  - a key strategic capability (and core competence) of research-based biopharmaceutical corporations
  - honesty and integrity, educating (and communicating with) internal and external stakeholders
  - payers, policy makers, patient **a**dvocacy groups
  - **are you ready for the challenges ahead?**
- **Normative Analysis & Methods Development**
  - sources of value, such as “social” (non-selfish) preferences
- **Need for a New Paradigm**
  - a compelling and credible narrative for the research-based industry
  - novel value(s)-based health economic evaluation methods; **A**lliance for the **A**dvancement of **A**pplied **H**ealth **E**economics (www.**A³HE**.org)

Need to Address Three (or more) Distinct Areas:

- **Health Politics**
  - Political Climate — Prevailing Attitudes and Beliefs
  - Political Power & Will — Cost Containment / "Value for Money"
  - Regulatory Environment — HTA Agencies, Pricing & Reimbursement
- **Health Policy**
  - Theory — Quality, Equity, Access, Efficiency
  - Practice — Managed Care (?), "Personalized" Medicine
- **Health Economics**
  - Normative — The Logic of Cost-Effectiveness **(?)**
  - Positive — Utilization and Cost; Outcomes Research

There is (or should be!) a difference between Health Economics, Health Policy, Health Care Politics, and Health Care Cost Containment

Cartoon © The New Yorker (1989)

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