Perspectives on cost-effectiveness thresholds in the United States

Moderated by:

- Dr. Steven Pearson, President
- Dr. Rick Chapman, Director of Health Economics

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

Webinar 1: Philosophical approaches to determining a cost-effectiveness threshold in the United States

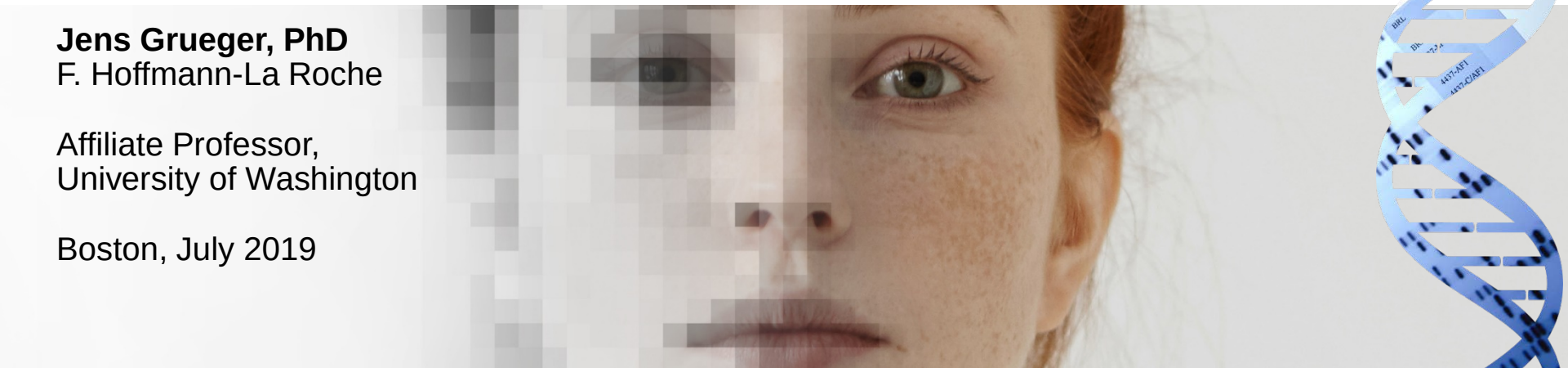
Main Presentation:

Jens Grueger, PhD

F. Hoffmann-La Roche &

University of Washington

International experience with drug price regulation; Implications for determining a cost-effectiveness threshold in the United States



Jens Grueger, PhD
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Boston, July 2019

Overview

- Experience with HTA systems ex-U.S.
  - ICER thresholds as basis for deliberative process
  - 2-step reference pricing approach: assessment + price negotiation
- Implications for the U.S.
- Summary and conclusions

Most countries have established national HTA systems
There are 2 basic archetypes: ICER or 2-step reference pricing approach

HTA using cost-effectiveness and ICER based thresholds

- C/E not the only decision criterium
- Price considered as an input, negotiated only implicitly through several rounds of appraisals
- Typically includes countries with National Health Services, focus on health as a public good rather than individual choice
- Examples: UK, Australia, Canada, Sweden, Netherlands

HTA as a 2-step reference pricing approach:

- Assessment of added patient benefit, followed by price negotiation or reference pricing (depending on added benefit)
- Often includes cost-effectiveness information, but no ICER threshold
- Decentralized healthcare systems with public health perspective
- Examples: Germany, France, Italy, Spain, Japan, Switzerland, Austria

Example Germany: Early benefit assessment and price negotiations established with AMNOG in 2011

- All medicines reimbursed at manufacturer set price immediately after marketing approval
- Standardized process for benefit assessment starting with early scientific advice (pre PIII)
- Dossier submitted by developer at launch, 6 months review by IQWiG/G-BA
  - Focus on patient relevant endpoints: mortality, morbidity, health related quality of life
  - Restriction to high quality evidence (typically randomized clinical trials)
  - Often assesses subgroups of the approved indication
  - 2-dimensional benefit assessment (IQWiG proposes, G-BA approves/modifies)
    - Extent of benefit (major, considerable, minor, non-quantifiable, none, less)
    - Level of certainty (proof, indication, hint)
- Reference price in the absence of added benefit
- Price negotiations (4-5 rounds, up to 6 months) with head association of sick funds
- If no agreement referred to arbitration committee for mandatory price decision

Cost-effectiveness heavily debated during legislative process in Germany

- Main argument that cost-utility analysis with ICER thresholds forces trade-offs between disease/patient segments which is considered to be against German constitution *)
- Initial proposal for “efficiency frontiers” in order to review cost-effectiveness within a disease category, but was found too complex and has been abandoned *)
- Budget impact and cost-effectiveness may be reviewed during arbitration
- While there is a mandate for “Beitragssatzstabilität” (stable statutory insurance premiums), there is confidence that this can be achieved through price-pressure and savings in off-patent segment

* Caro JJ, Nord E, Siebert U, McGuire A, McGregor M, Henry D, de Pouvourville G, Atella V, Kolominsky-Rabas P. The efficiency frontier approach to economic evaluation of health-care interventions Health Econ 19, 2010, 1117-1127
Brouwer WB, Rutten FH. The efficiency frontier approach to economic evaluation: will it help German policy making? Health Econ 19, 2010, 1128-1131

2-step approach (reference pricing) considered successful

Has provided clear incentives to industry

- Focus has been on discouraging “me too” drugs
  - In the absence of an added patient benefit, price is set based on the lowest competitor in the market (reference pricing, cost minimization in C/E)
  - For Germany, medicine developers decided in around 20% of cases that added benefit was insufficient to achieve their price expectations (and consequently did not launch the product)
- Regulators and HTA/payers have different views on patient relevant endpoints and evidence
  - Germany: only lists mortality, morbidity and HRQoL; other agencies (eg NICE): ”patient relevant endpoints include mortality, morbidity and HRQoL”
  - Several examples where endpoints from pivotal studies were not considered by IQWiG*)
- Medicine developers have considered German and French added benefit assessments in their investment decision making (Eg Roche includes the target benefit rating in the Target Product Profile)

* Ruof J, Knoerzer , Dünne AA, Dintsios CM, Staab T, Schwartz FW. Analysis of endpoints used in marketing authorisations versus value assessments of oncology medicines in Germany. Health Policy. 2014 Nov;118(2):242-54.

ICER Threshold systems driven by strong focus on fixed healthcare budgets, equity and health maximization

- Maintain a fixed (healthcare) budget
- Provide equitable access to all
- Maximize health gains across all people covered by the NHS

- Opportunity cost: trade off between new and existing technologies, across patient/disease segments
- Linearity in benefits and cost
- Focus on cost rather than benefits
- Threshold represents budgetary constraints rather than willingness to pay

ICER thresholds are very consistent with the objectives of the NHS
Not clear how thresholds have affected innovation (one of NICE´s objectives)

Charlon V, Rid A. Innovation as a value in healthcare priority-setting: the UK experience. Social Justice Research (2019) 32:208–238; Kennedy, I. (2009). Appraising the value of innovation and other benefits: A short study for NICE. www.nice.org.uk/Media/Default/About/what-we-do/Research-and-development/Kennedy-study-final-report.pdf

ICER based systems have different approaches to setting thresholds

- UK (England): Original threshold of GBP 20k per QALY gained
  - Exceptions for cancer (GBP 30k), end of life (GBP 50k) and highly specialized technologies (GBP 100-300k), since 2012 “innovativeness” increasingly cited as reason for going above threshold
  - Temporary access mechanisms established, eg Cancer Drugs Fund
  - Frequently requires confidential discounts and pay for performance arrangements, still UK tends to rejects more drugs than other countries (specifically in cancer)
  - Claxton argues that marginal effectiveness of the system should result in lower threshold
- Sweden: no fixed budget, threshold depends on disease severity
  - Lowest C/E for declined therapies is around Euro80k, highest for approved Euro130k
  - 50% chance of approval at EUR 79.4k for non-severe diseases, EUR 111.7k for severe diseases

Claxton K, Martin S, Soares M, Rice N, Spackman E, Hinde S, Devlin N, Smith PC, Sculpher M. Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold. Health Technol Assess. 2015 Feb;19(14):1-503
Svensson M, Nilsson F, Arnberg K. Reimbursement Decisions for Pharmaceuticals in Sweden: The Impact of Disease Severity and Cost Effectiveness. Pharmacoeconomics. 2015 Nov;33(11):1229

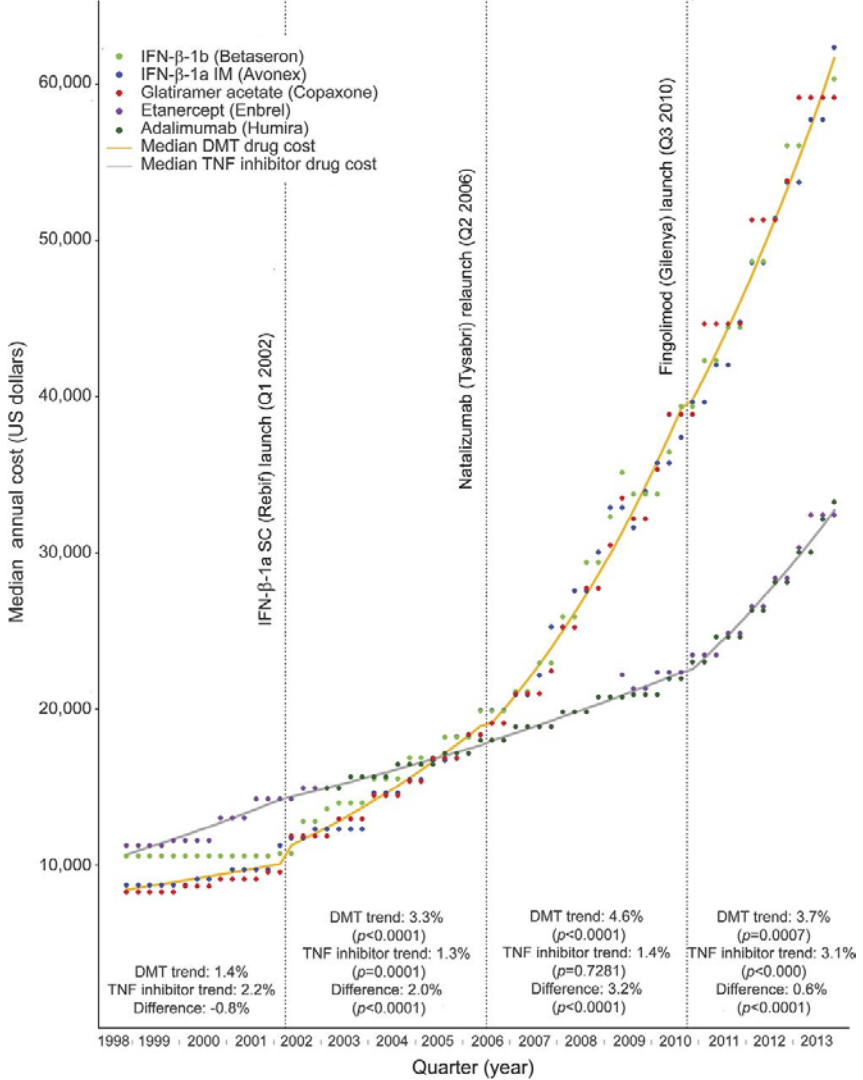
Tensions between ICER and Reference Price systems increasing in Europe, especially for innovative products

Driven by different WTP and external reference pricing

- While countries like Germany and France have been difficult for “me-too” products, they have given more generous prices for innovative products
  - However, granting the highest added patient benefit categories (ASMR 1 and 2) has significantly decreased in France over the last 10 years
- Difference between UK on the one hand, and Germany and France on the other is less on ability to pay but more on willingness to pay (UK healthcare spend only 8% of GDP, 20% less than DE or FR)
  - Despite stretching the thresholds, UK system is struggling with innovative products
  - In the presence of international reference pricing and parallel trade, difficult to offer differential prices to UK
  - In order to facilitate patient access complex discount and “pay for performance” agreements emerged, specifically in the UK for innovative products

United States needs some form of price regulation

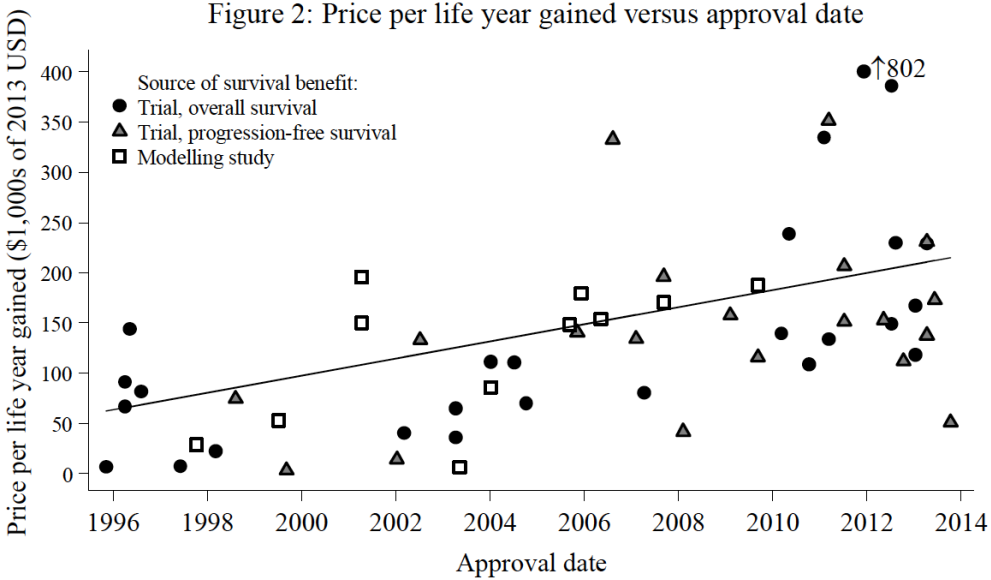
- Dramatic price increases in large drug categories in the absence of evidence of increased value
- Sets the anchor for new drug launches



Hartung DM, Bourdette DN, Ahmed SM, Whitham RH. The cost of multiple sclerosis drugs in the US and the pharmaceutical industry. Too big to fail? Neurology May 26, 2015; 84 (21)

For Oncology drugs, year of approval is the only predictor of “price per life year gained”

Figure 2: Price per life year gained versus approval date



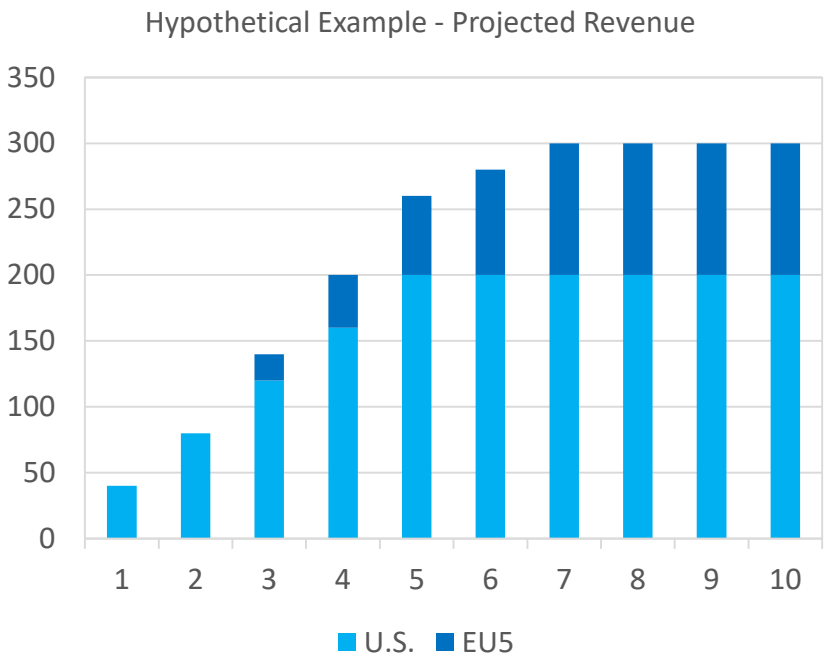
The best fit line is: Price per life year gained = $54,100 + $8,500 x Approval year.
Approval Year = 0 for 1995, 1 for 1996, etc. For purposes of display, we re-coded one value from $802,000 to $400,000.
Source: Authors

Howard DH, Bach PB, Berndt ER, Conti RM. Pricing in the Market for Anticancer Drugs. J Econ Perspect. 2015;29(1):139-62.

Any change in U.S. pricing will have significant impact on industry

U.S. funds 80% of pharmaceutical innovation

Typical U.S./EU5 revenue scenario for new medicine



- Similar patient numbers U.S./EU5 (325mn)
- 5 years to peak sales
- U.S. price at 2x EU5 price (200 vs. 100)
- U.S. approval/reimbursement 2 years earlier
- Discounted cumulative revenue CHF 1,720
  - U.S. CHF 1,350 (78%), EU5 CHF 370 (22%)
- If U.S. price constrained to 1.5x EU5 price, revenue reduced by CHF 340

- Developers focus on U.S. and are opportunistic in EU (as long as there is no penalty for US price)
- From an ex-US payer perspective: can decline the product and wait for additional data (free-rider)

Introduction of HTA with ICER and thresholds needs to address a number of specific issues in the U.S.

- Which parts of U.S. healthcare have similar objectives like England or Australia: Health maximization and equitable access within fixed budgets?
- Each plan may have a different threshold, which will affect the insurance premium. What would be the selection effects?
- Do we have to be concerned about transparency around differential access that are currently hidden – Uwe Reinhardt´s question about the poor family child?
- Need to address litigation if you really want to include some form of rationing

Does the U.S. need to go all the way to ICER thresholds?

Rather focus on increased price competition between similar products

- Starting point could be a reference price system that anchors launch prices to the price of current standard of care in the absence of evidence of added benefit – similar to France and Germany
  - But potentially taking a broader perspective on value and evidence
- Can be the basis for competitive purchasing
  - Express Scripts has already exercised its purchasing power for HepC drugs
  - Consumers choosing other products would need to pay the difference
- Coverage with Evidence Development (in case the evidence is uncertain) and price adjustments (once certainty has been increased) are already possible in the U.S.
- Several complex issues need to be addressed in a reference price system:
  - Pricing for products with multiple indications
  - Annual reference price adjustments
  - Will competition be enough to adjust inflated prices in some drug categories (eg MS) ?

Summary and conclusions

- Some form of price regulation is required for the U.S., in order to create sustainable financing environment that continues to incentivize true innovation
- All countries in Europe (whether they use an ICER threshold or not) follow a reference pricing approach that limits prices for products without demonstrated added patient benefit
- Innovative products seem to fare better in countries without threshold
- Any change in U.S. pricing system will have significant implications for drug developers
- U.S. needs to consider creating more price competition between products with similar/equal benefit (price referencing)
- Formal introduction of thresholds will highlight differential WTP between different parts of the U.S. health care system

Discussion

Responders: Dave Vanness, Patricia Danzon

Next webinar:

Wed, Jul 24, 2019 12:00 PM - 1:00 PM EDT

Webinar 2: Willingness to pay as a basis for a cost-effectiveness threshold in the United States: Using per capita GDP and/or individual surveys to determine a specific threshold range

Hosts: Steve Pearson and Rick Chapman
Lead Presentation: Chris McCabe
Responders: Jens Grueger, David Meltzer, Lou Garrison