Colloque «L’insoutenabilité,
un défi incontournable
pour l’avenir de la cancérologie»

«Should New Drug Prices Be Based On Cost?»

Michael Schlander (Heidelberg / Germany)

Centre Léon Bérard, Lyon / France, May 21, 2025

Contact: ms@michaelschlander.com

Personal & Professional Background

Michael Schlander

[Academic]
- Professor of Health Economics – Heidelberg University (since 2017)
- *on leave of absence to lead the* «Division of Health Economics» at the German Cancer Research Center [«DKFZ»] (since 2017)
- Chairman & Scientific Director – InnoVal^{HC} / Wiesbaden (since 2005)
- Professor [em.] of [Health Care & Innovation] Management (2002-[2016])

[Professional]
- C.E.O. – Biopharmaceutical Industry (MEDICE; D; 1999-2002)
- Director of Strategic Business Unit – Biopharmaceutical Industry (Byk Gulden; Johnson & Johnson; D, B, USA; 1993-1999)
- Head of German and European Clinical Research & Development (Sandoz AG; Takeda Euro R&D Centre; D, CH; 1987-1993)

[Academic]
- Exp. Brain Research and Clinical Neurology – Frankfurt University (1982-1987)

[Education]
- Ph.D. (*Habilitation*) – Health Economcis, Heidelberg (2007)
- Diploma – Health Economics, Stockholm School of Economics (2002)
- M.B.A. (*Valedictorian of Class of 1994*) – General Management & International Marketing, City University of Seattle, Washington (1994)
- M.D. (Dr. med., *summa cum laude*) – Brain Research, Frankfurt Univ. (1985/87)

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Relevance

«In case after case,
our citizens pay massively
higher prices than other nations pay for the same exact pill, ...»

Donald J. Trump
(The White House Fact Sheet, Washington, D.C., May 12, 2025):
President Donald J. Trump Announces Actions to Put American Patients First by Lowering Drug Prices and Stopping Foreign Free-riding on American Pharmaceutical Innovation

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Relevance

«**Hand clapping for science** is now inextricably linked to hand wringing over affordability.»

Peter 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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Relevance

«Hand Clapping for Science…»

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Relevance

«Hand Clapping for Science…»

Neue Gentherapie von Novartis soll über 2 Millionen Dollar kosten

Der Pharmakonzern hat für die neuartige Genersatztherapie Zolgensma in den USA die Zulassung erhalten. Der Preis für eine einmalige Injektion wird Debatten auslösen.

Basler Zeitung

«Wir halten unseren Preis für angemessen und fair»

BaZ, 24. Mai 2019

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Relevance

Outrageous prices of orphan drugs: a call for collaboration

Lucio Luzzatto, Hanna I Hyry*, Arrigo Schieppati, Enrico Costa, Steven Simoens, Franz Schaefer, Jonathan C P Roos, Giampaolo Merlini, Helena Kääriäinen, Silvio Garattini, Carla E Hollak, Giuseppe Remuzzi, on behalf of the Second Workshop on Orphan Drugs participants*

The Lancet, 20. Juli 2018

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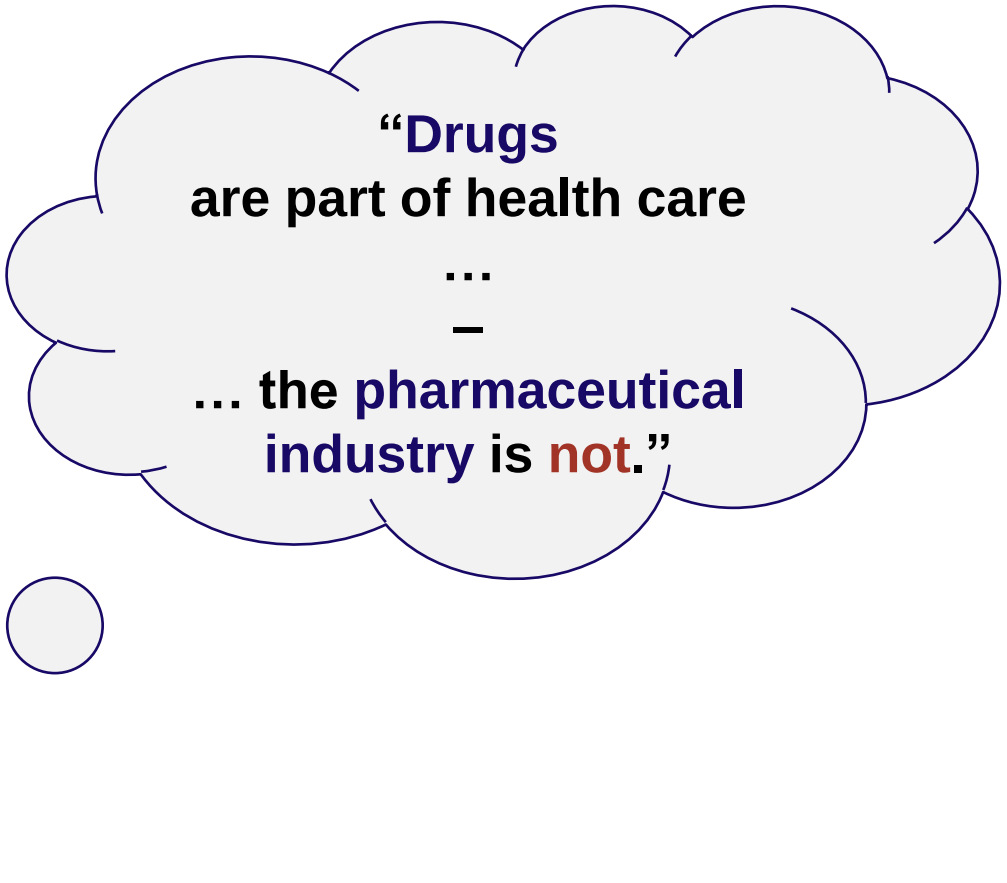
Relevance

Frequently forgotten:



Heinz Redwood (1992)

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Analysis

Cost Structure

of the [Research-Based] Biopharmaceutical Industry

- **Fixed Costs**:
  - Research & Development
  - Marketing & Sales
  - Administration
  - Capital Investment
- **Variable Costs**:
  - [Parts of] Manufacturing
  - [Parts of] Distribution
- **Contribution Margins**:
  - Strategic Implications
  - Pricing [& Reimbursement] Policies
- **Value-Based Pricing**:
  - Is there a role for R&D cost, and if so, which?

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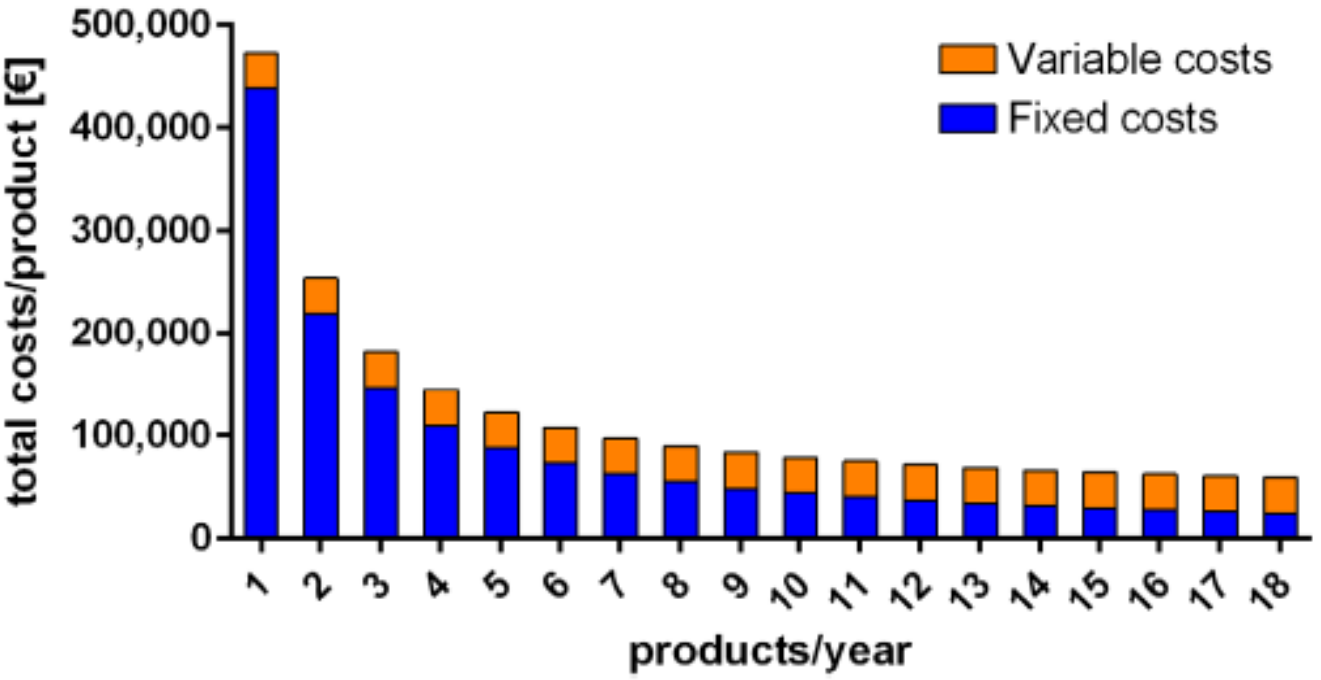
Analysis

Cost of Decentralized CAR T Cell Production

in a Not-for-Profit Setting

Economies of scale



Analysis:
T. Ran et al. (2019);
M. Schlander et al. (2020)

in cooperation
with Stefan B. Eichmüller
and Patrick Schmidt

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Analysis

Can We Reduce the Acquisition Cost of CAR T Cell Therapies?

For a clean room facility with one automated cell manufacturing platform, annual fixed costs were €438,098. The variable cost per production was estimated at €34,798. At maximum capacity of one machine, total cost per product was close to €60,000. We used scenario analyses to estimate (1) the impact of production **upscaling** and (2) the impact of likely **technological improvements**.

(1) If three machines were to be installed in one clean room facility, per production total cost could be as low as **€45,000** (2019).

(2) If cheaper plasmid-based vectors were used as a substitute for currently applied lentiviral vectors, per production total cost could be further reduced to **€33,000** (2019).

Abstracting from potential issues related to intellectual property rights, decentralized T cell production might be a less-costly and more efficient alternative to the commercially available centralized production mode.

We might anticipate production costs to further decrease in the future with

- ***increased standardization of processes,***
- ***economies of scale,***
- ***economies of scope, and***
- ***learning curve effects.***

This expectation is commensurate with the early life cycle stage of this new technology.

Analysis:
T. Ran et al. (2019);
M. Schlander et al. (2020)

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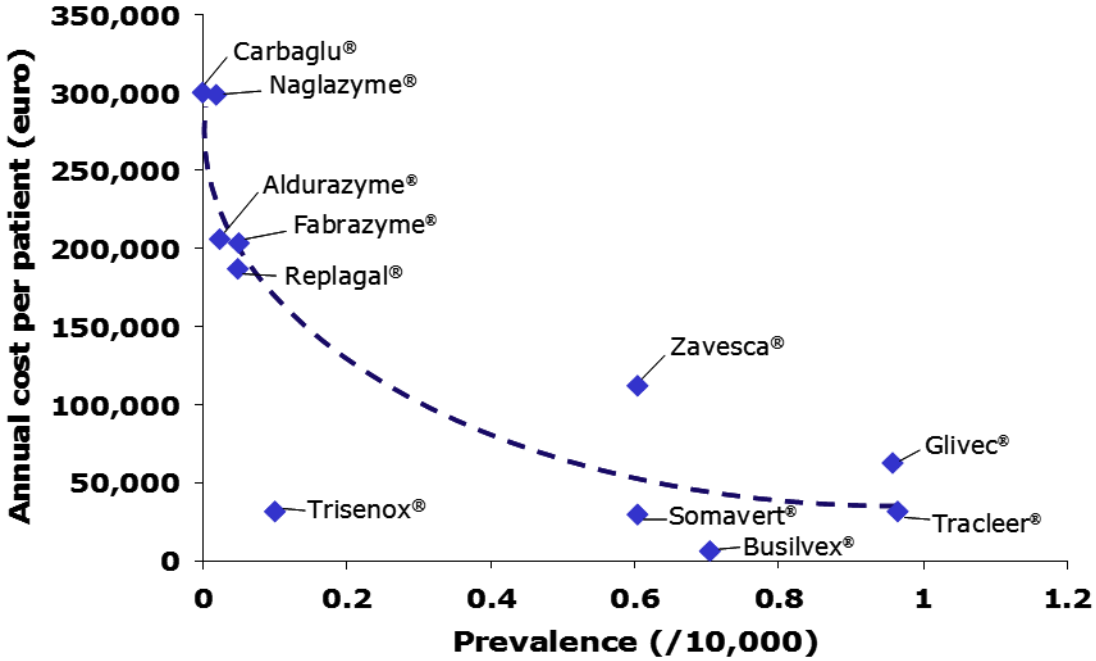
Analysis

Hypothesis: Annual Cost per Patient



M. Schlander. S. Garattini, S. Holm et al. *J. Comp .Eff. Res.* 2014; 3 (4): 399-422. (p.402)
M. Schlander, M. Beck. *Curr. Med. Res. Opin.* 2009; 25 (5): 1285-1293; A. de Varax, M. Letellier, G. Börtlein. *Alcimed Study I*, Paris 2005.

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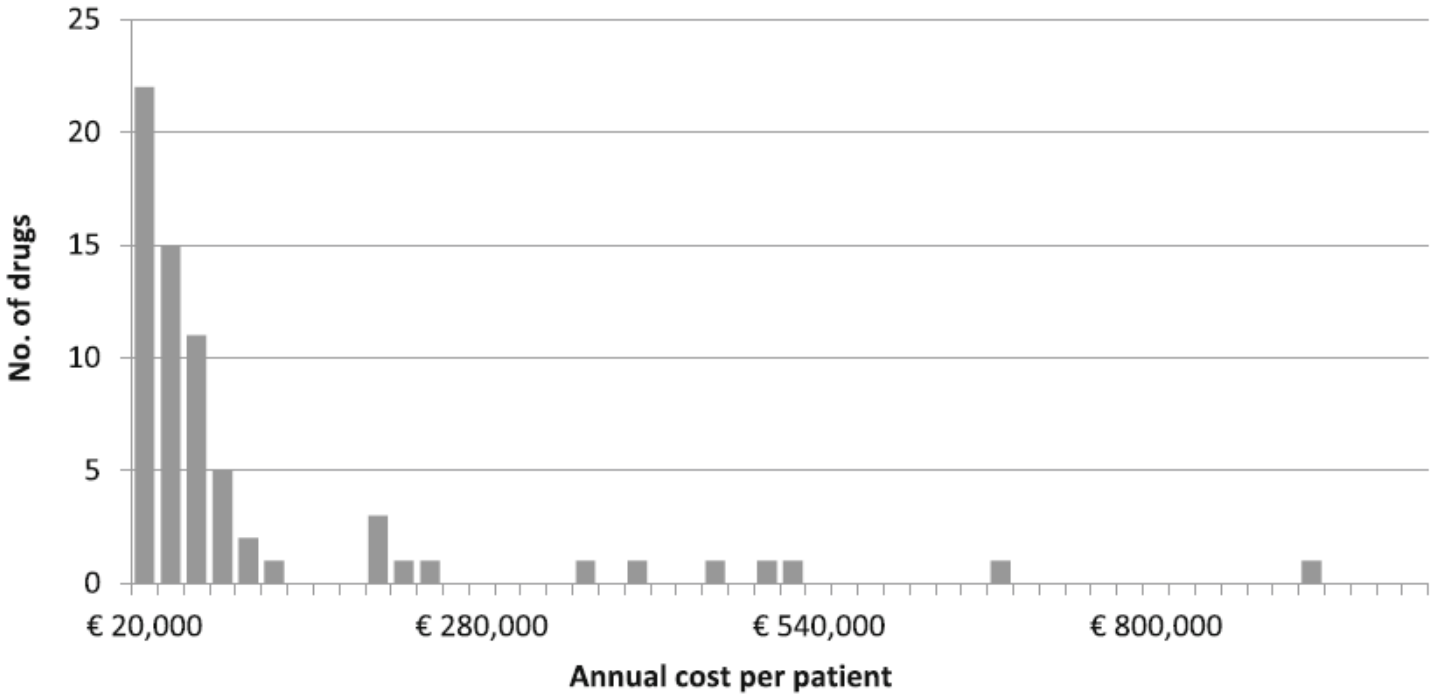
Analysis

Annual Cost per Patient

[based on 68 orphan drugs in France]



Median, €96,518 p.a.
Source: Daria Korchagina et al. *Orphanet Journal of Rare Diseases* (2017) 12:75

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Analysis

Annual Cost per Patient

[based on 68 orphan drugs in France]

- **Cost Drivers** *identified in French study*:
  - (Non-) Availability of alternative treatments
  - Therapeutic area
  - Prevalence (p=0.02)

- **Cost Drivers** *not confirmed in French study*:
  - Severity of condition
  - Age of targeted population
  - Marketing authorization date (time span, 2002-2015)
  - Clinical evidence (phase II or III data)
  - Clinical endpoint (surrogate or «hard»)

Source: Daria Korchagina et al. *Orphanet Journal of Rare Diseases* (2017) 12:75

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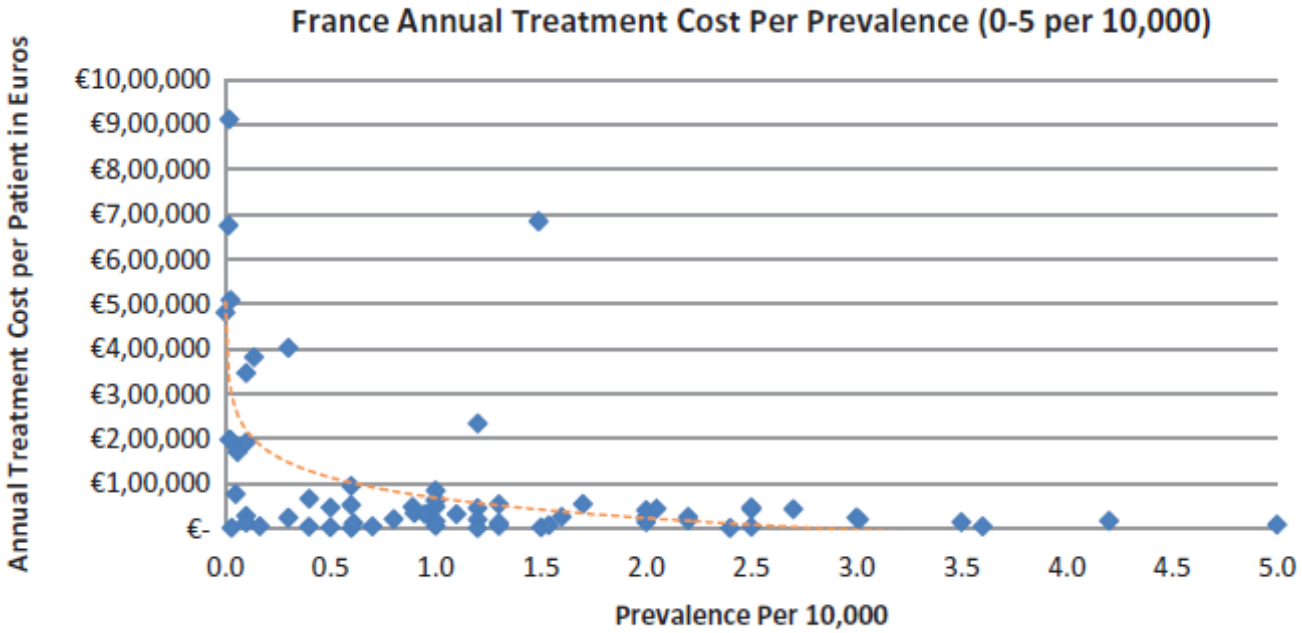
Analysis

Evidence: Prevalence and Cost per Patient



Goran Medic et al., *Journal of Market Access & Health Policy* (2017)

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Analysis

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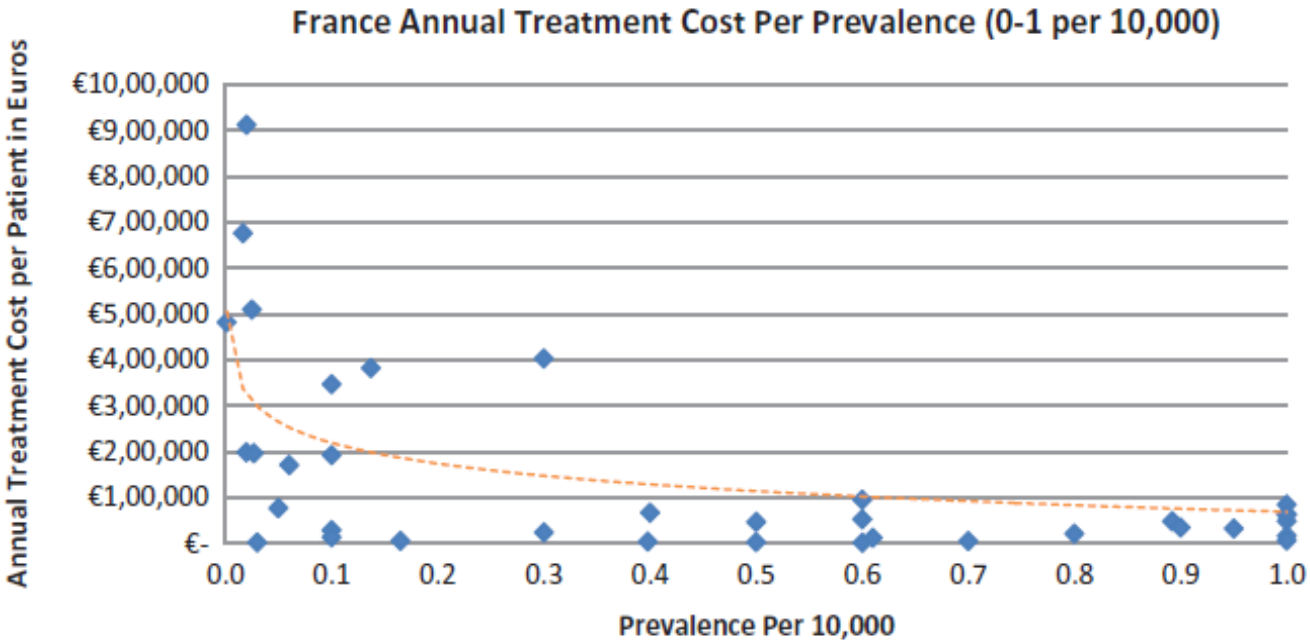

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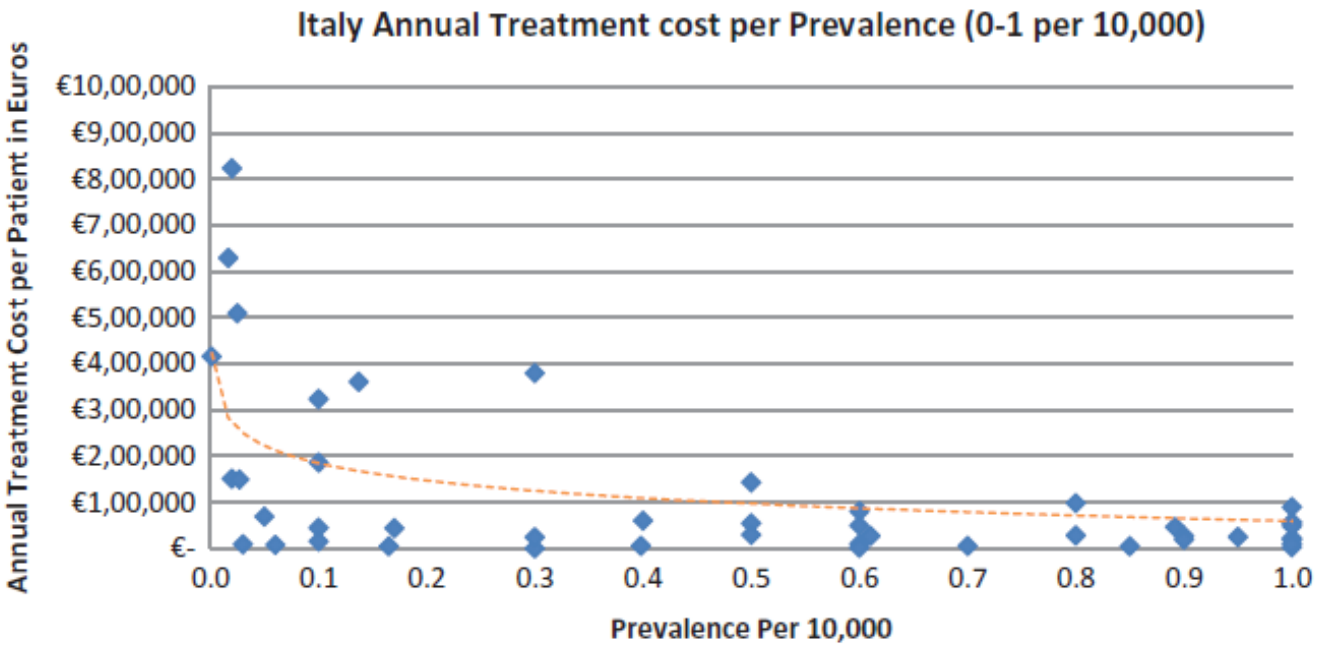

Goran Medic et al., *Journal of Market Access & Health Policy* (2017)

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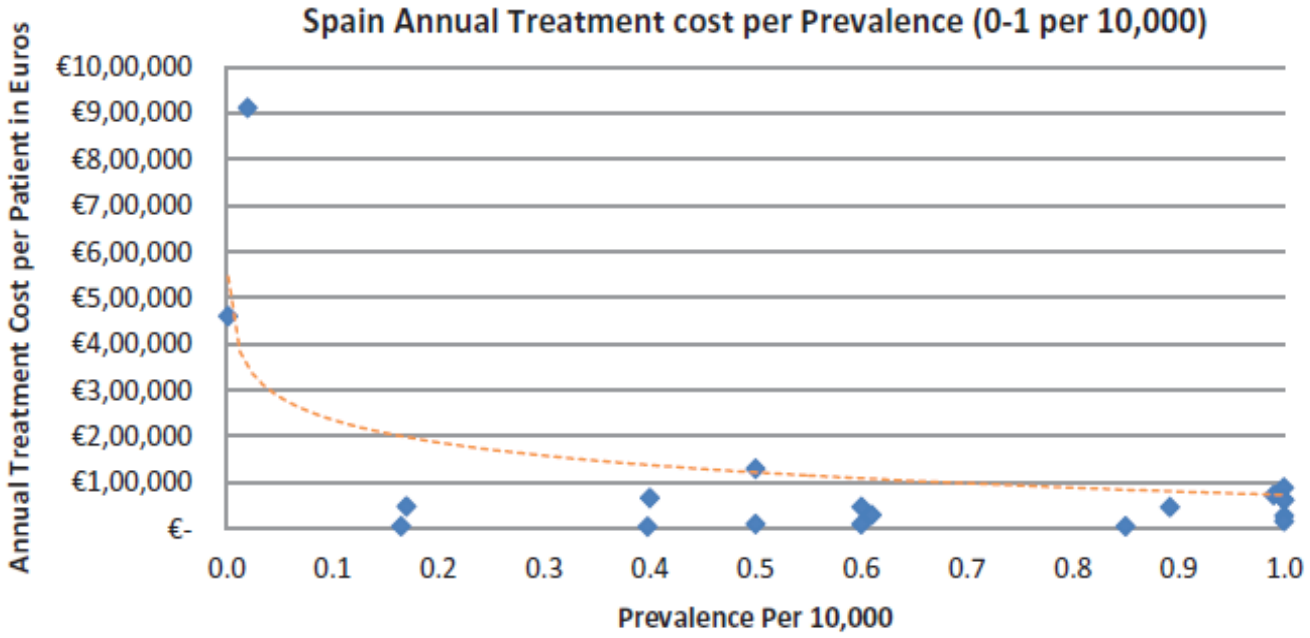

Goran Medic et al., *Journal of Market Access & Health Policy* (2017)

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Analysis

Once Again: **Cost Structure** of the [Research-Based] Biopharmaceutical Industry

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  - Is there a role for R&D cost, and if so, which?

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Analysis

Research & Development (R&D):

Effective Project Management

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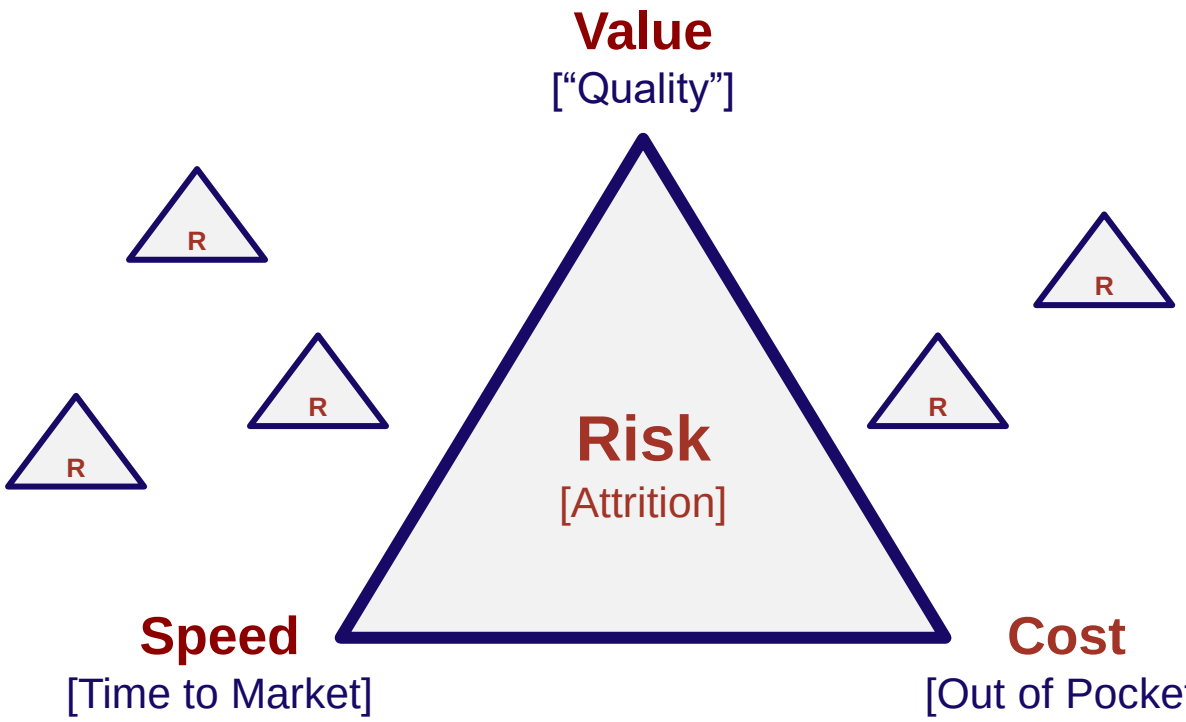
Industry Challenge: Effective R&D-Management

Strategic Portfolio Management



Decision Processes

Integrated Project Management

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Analysis

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

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Analysis

Trends in Biopharmaceutical R&D

Clinical Cost / Patient

- **Context: Organizational Setting** (commercial / public sector / …)
  - Research versus development
  - Public or private sector
  - Shared values
  - Strategy and strategic fit (including managerial decision-making)
  - Structures (and interdepartmental interfaces)
  - Systems & processes (including effective project management)
  - Skills (experience; including standardized support processes)
  - Staff & incentives (intrinsic and extrinsic motivation)
  - Style (leadership and organizational culture)
- Note that all of the above are interdependent and will impact both success and cost of clinical research and development, but none of the above can be compensated for by a mere budget increase.

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Trends in Biopharmaceutical R&D

Clinical Cost / Patient in Commercial Cancer Drug Trials

«Total costs [for oncology drug trials] can be staggeringly high, but they are also highly variable…» (McGuire, 2013)

- **Study design**
  - Clinical phase (volunteers / patients; phase I/II; IIIa; IIIb; IV)
  - Proof-of-concept or confirmatory design
    (single arm < placebo-controlled < active control arm; cf. Hsiue et al., 2020)
  - Study endpoints (OR < PFS < OS; cf. Hsuie et al., 2020)
  - Single center / multi-center; eligible patient pool
  - Parallel development of companion diagnostics
  - Objectives (clinical effectiveness / cost effectiveness / access and reimbursement)
    (e.g., «pivotal study» for authorization? => for U.S. pivotal studies, cost per patient in *commercial* oncology trials (2015-2017) varied between 80,000 US-$ and 155,000 US-$, with a median of **100,000 US-$**; cf. Moore et al., 2020)

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Trends in Biopharmaceutical R&D

Clinical Cost / Patient in Public Sector Cancer Drug Trials

Example: estimate of the total cost per patient in multicenter clinical trials in an Italian National Cancer Institute (NCI) (Pascarella et al., 2019)

- **Cost drivers**
  - Role of financial sources and study sponsorship;
    direct cost of care **savings** may amount to 10,000€ per patient on average
    (cf. Fireman et al., 2000; Ferrández et al., 2021)
  - European data from nine *randomized clinical trials* with anticancer biological agents from 2014 to 2016 (setting, National Cancer Institute of Napoli, Italy) suggest
    an average total cost of all “per patient” activities of a clinical trial
    amounting to **~11,000€** …
  - … with estimates of treatment costs (4,800€/patient) followed by cost of pre-study activities (1,400€/patient) and audit costs (1,300€/patient), plus 20% overhead …
  - … however excluding the actual costs of the drugs used,
    since those were entirely supplied by the study sponsors

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Trends in Biopharmaceutical R&D

Risk / Attrition Rates & Project Termination

- Overall 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 HTA regulation and health economics into early strategic assessments of NMEs.
- Reasons for premature project termination show a continuing trend to an increasing importance of economic criteria.

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Trends in Biopharmaceutical R&D

Risk / Attrition Rates in Our Analysis[1]

- Clinical Approval Success Rates (*examples*)
  - Cancer NMEs (Wouters et al., 2020) 3%
  - Cancer NMEs (Falconi et al., 2014) 11%
  - All in most recent study (Wouters et al., 2020) 14%
  - All in most recent Tufts analysis (DiMasi et al., 2016) 12%
  - Orphan NMEs (Jayasundara et al., 2019) 33%
  - Non-Orphan NMEs (Jayasundara et al., 2019) 10%
  - Antibacterials, model (Sertkaya et al., 2014) 9%
  - Vaccines, model (Sertkaya et al., 2014) 39%
  - Seasonal influenza vaccines (Chit et al., 2014) 20%

[1]Michael Schlander et al.: How Much Does It Cost to Research and Develop a New Drug? A Systematic Review and Assessment. *PharmacoEconomics* 2021; 39: 1243-1269.

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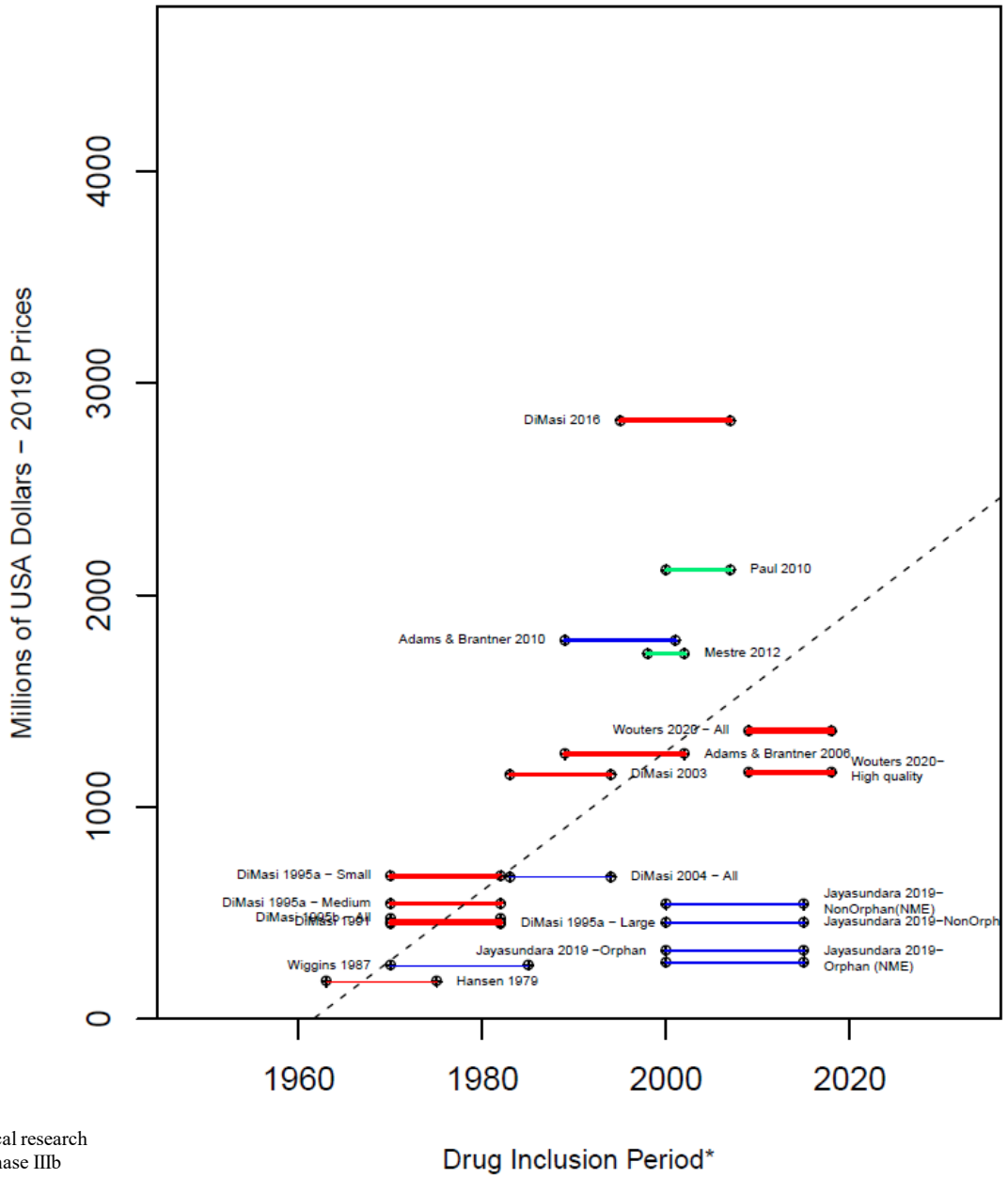
Results

R&D Costs / NME

integrating multiple disease categories (20 out of 36studies),

average capitalized



Blue lines: clinical phases only
Red lines: plus discovery and preclinical research
Green lines: plus R&D costs during phase IIIb

Michael Schlander et al.: How Much Does It Cost to Research and Develop a New Drug? A Systematic Review and Assessment. *PharmacoEconomics* 2021; 39: 1243-1269.

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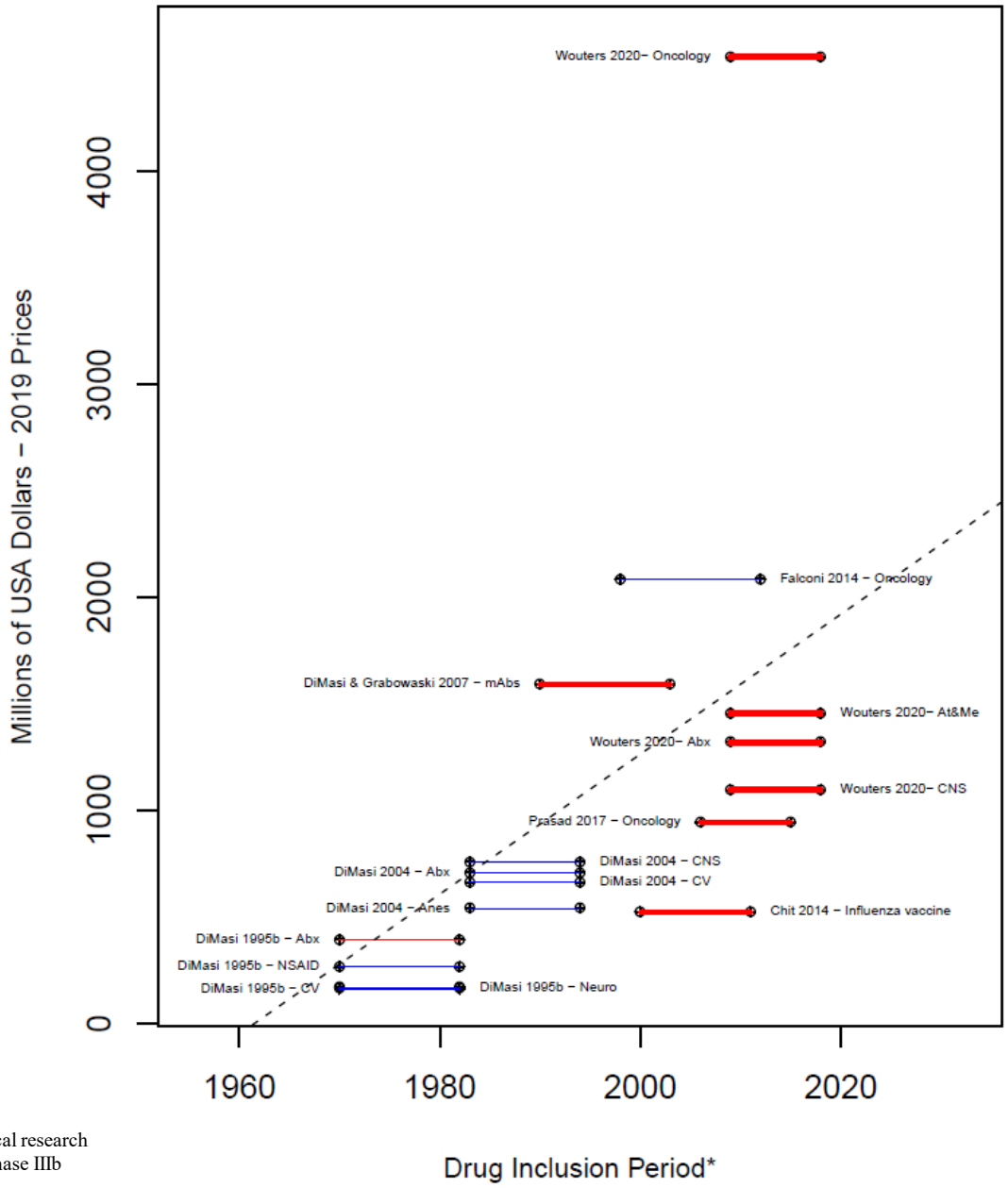
Results

R&D Costs / NME

each based on one particular therapeutic area or disease category (16 out of 36 studies),

average capitalized



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Results and Conclusions

Potential Sources of Variation

of Fully Allocated R&D Cost / NME

- Therapeutic Area
- Orphan / Nonorphan NMEs
- Firm Size
- Self-Originated versus Licensed-In
- NCE or NBE

Michael Schlander et al.: How Much Does It Cost to Research and Develop a New Drug? A Systematic Review and Assessment. *PharmacoEconomics* 2021; 39: 1243-1269.

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Some Limitations

- **Impact on *Future* Estimates**
  - The role of public investment
  - Post-authorization R&D costs
  - Disparities in regulations
    and length of time for approval over time
  - Variations in the complexity of clinical trials
    (e.g., protocol design) over time

- **Technology Changes**
  - «Precision Medicine»
    and its potential impact on R&D effectiveness

- **Formal quantitative analyses**
  - Hindered by differences in models
  - Hindered by limited number of observations

Michael Schlander et al.: How Much Does It Cost to Research and Develop a New Drug? A Systematic Review and Assessment. *PharmacoEconomics* 2021; 39: 1243-1269.

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Some Implications for Pricing

- **The Need to Set Limits**
  - Fairness and distributional justice versus allocative efficiency
  - Due process and transparency (in Health Technology Assessments)
- **Cost-Based Pricing?**
  - How to adjust for risk (project attrition rates)?
  - Average cost of R&D – which modifiers might be applied?
  - Allowance for admin, marketing and sales?
  - Accounting for manufacturing costs?
  - Incentives for developers & appropriate rates of ROI?
- **Value-Based Pricing?**
  - Applying «Cost Effectiveness Thresholds» *[not addressed today]* relying on the (controversial) «logic of cost effectiveness»**?**
  - Social Cost Value Analysis considering institutional environment and citizens' preferences**?** *[not addressed today]*

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Interested in More Background & Application?

Heidelberg Health Economics Summer School 2025

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Brunico, Alto Adige, Italia
Bruneck, South Tyrol, Italy
Brunico, Tyrol du Sud, l'Italie
11.-19. September 2025

Information:
(a) ms@michaelschlander.com
(b) www.innoval-hc.com / Summer School

Many Thanks Indeed for Your Attention!

Univ.-Prof. Prof. [em.] Dr. med. **Michael Schlander**, M.B.A.

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