Health Service Reimbursement: Early Benefit Assessment of New Drugs in Germany

19th Congress of the EAHP
Barcelona, 26-28 March 2014

Katrin Nink

Conflict of interest

Nothing to disclose

(Research Associate at IQWiG))

Agenda

- **IQWiG – Background**
- **Reimbursement of drugs in Germany**
- **Early benefit assessments: framework, methods, results**

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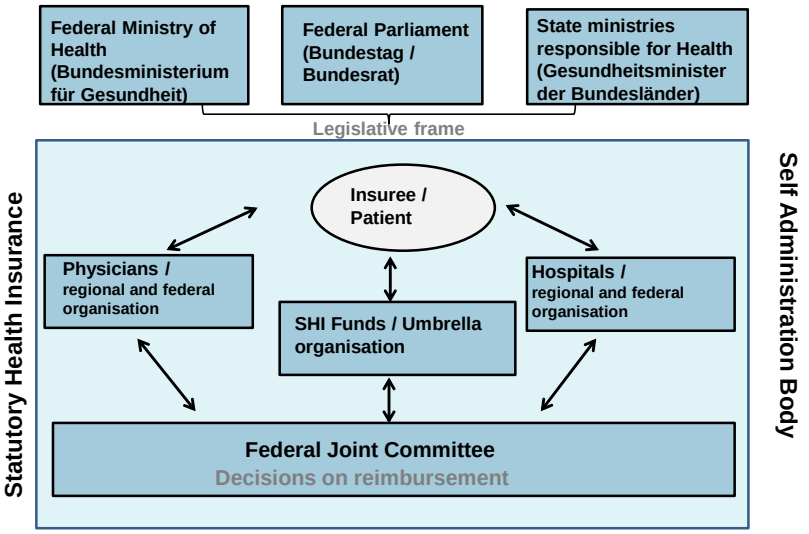
The German health care system I

- **Statutory health insurance (SHI) funds:** cover approx. 90% of population in Germany
- **Financing:** contributions by employers and employees
- **Structure:** public-law corporations, financially and organizationally independent
- **Solidarity principle:** each insured person receives the health care service that is medically necessary, regardless of income, amount of contributions paid, or morbidity risks

The German health care system II

- Large sections of the health care system are shaped by self-government via contracts that are concluded with the health care providers
- Legal basis: Social Code Book V (SGB V):
  - Provides framework for reimbursed health care services (“benefits catalogue”)

Federal Joint Committee – decision body for reimbursement



Adapted from Health Care Systems in Transition: European Observatory on Health Care Systems, WHO

Institute for Quality and Efficiency in Health Care (IQWiG)

- IQWiG was founded as an independent scientific institute by a health care reform in 2004
- The legal basis of the work of IQWiG is the Social Code Book V (SGB V)
- IQWiG runs under the umbrella of a private-law foundation, financed through levies for inpatient and outpatient medical treatment (SHI funds)

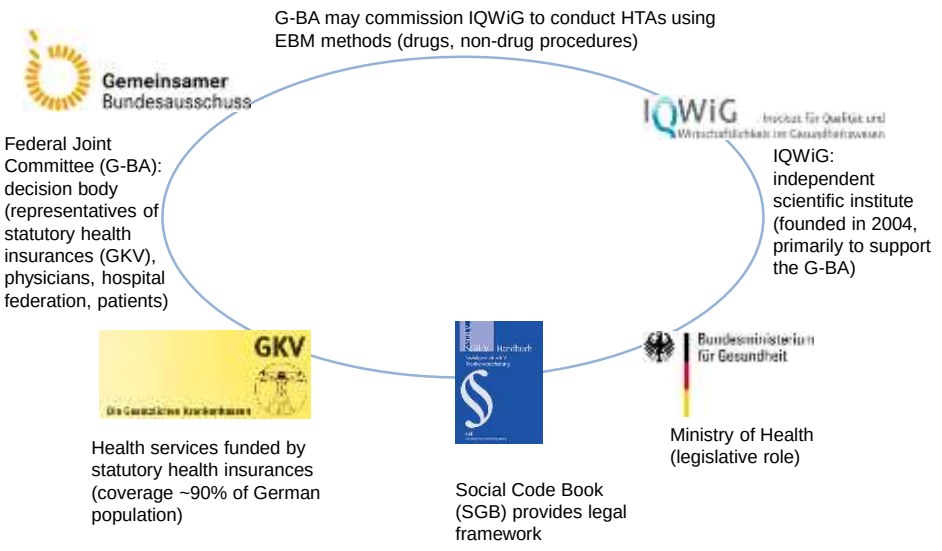
IQWiG's tasks according to § 139a SGB V

- IQWiG produces independent, evidence-based reports e.g. on:
  - Drugs (benefit and cost-benefit assessment)
  - Non-drug interventions (e.g. surgical procedures, medical devices, diagnostic and screening methods)
  - Clinical practice guidelines (CPGs) and disease management programmes (DMPs)
- In addition, IQWiG provides easily understandable health information for patients and the general public

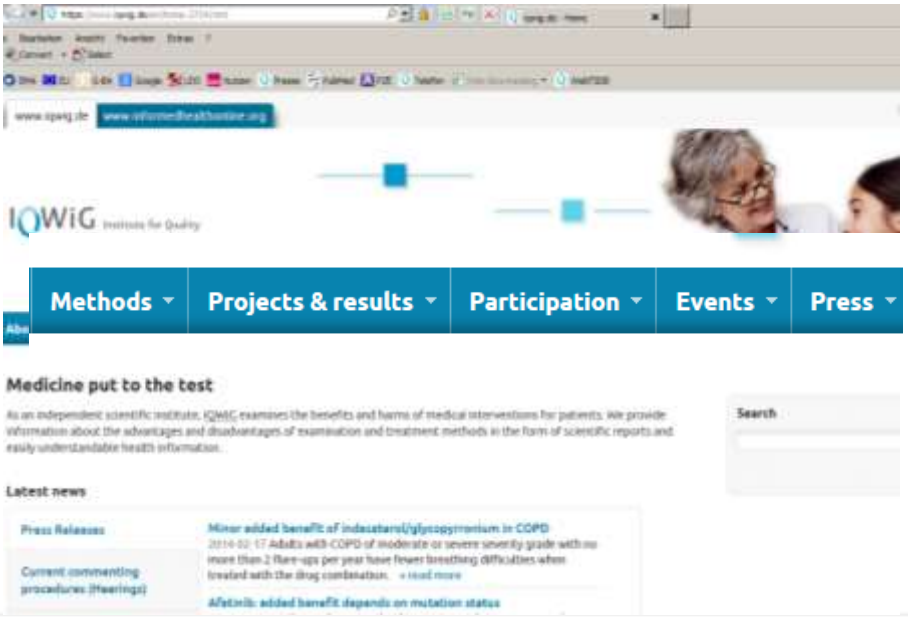
http://www.informedhealthonline.org/informed-health-online.2.en.html

http://www.gesundheitsinformation.de/startseite.2.de.html

Legal and organizational background – HTA in Germany



Transparency



IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

Institute for Quality and Efficiency in Health Care

General Methods[a]

Version 4.1 of 28 November 2013

https://www.iqwig.de/download/IQWiG_General_Methods_Version_%204-1.pdf

Agenda

- IQWiG – Background
- **Reimbursement of drugs in Germany**
- Early benefit assessments: framework, methods, results

Reimbursement of drugs in Germany

- Expenditures SHI for drugs (2012): 30 billion €
- Licensed drugs can be prescribed by physicians immediately after licensing
- Prices are specified by drug manufacturers (regulation only for margins in distribution chain)
- SHI funds must reimburse licensed drugs
- Federal Joint Committee may regulate

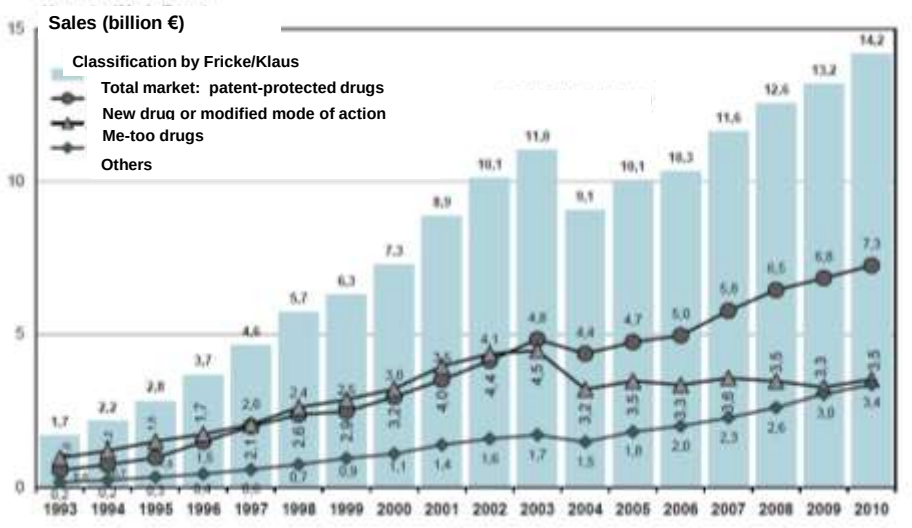
Instruments for cost-containment and price regulation

- Reference pricing (since 1989), predominantly for generic drugs
- Discount agreements between individual SHI funds and drug manufacturers (since 2007: obligation for pharmacies to dispense discounted drugs)
- Temporary cost-containment measures: price moratorium (until 2017), price reductions, legally implemented discounts (drug manufacturers, pharmacies), co-payments of insured persons

Regulations on drugs in the hospital sector

- Hospital-specific positive lists for drugs
- Diagnosis-Related-Groups (DRG) system: drug costs included in flat-rate reimbursement
- Special prices for expensive drugs (e.g. cancer drugs)

Turnover of patent-protected drugs before AMNOG*



*Act on the Reform of the Market for Medicinal Products
Source: WIdO 2011 http://www.wido.de/fileadmin/wido/downloads/pdf_arzneimittel/wido_arz_pk_avr2011_0911.pdf

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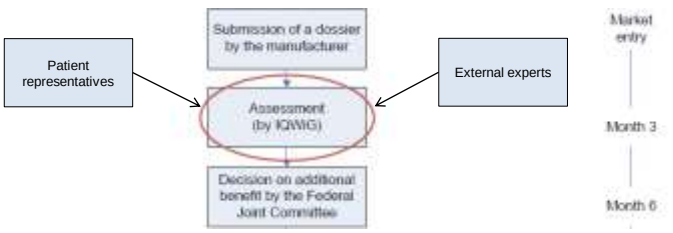
- **Early benefit assessments: framework, methods, results**

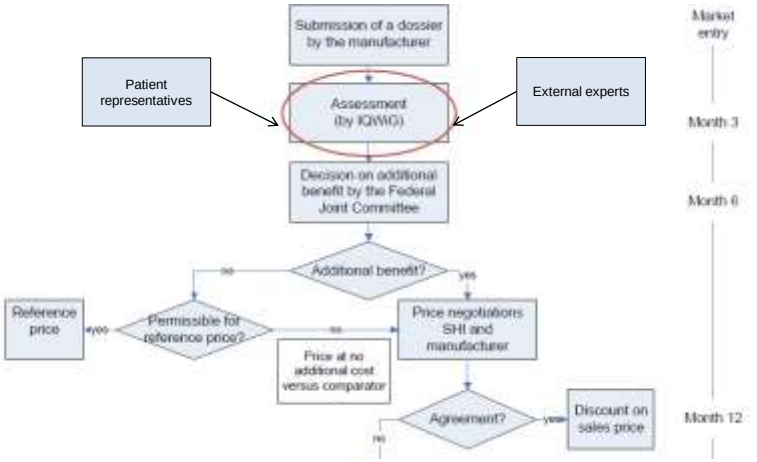
AMNOG – new legislation, new HTA products

- New law to reorganize pharmaceutical market for SHI
- Came into force on 01/01/2011
- § 35a SGB V directly concerns early benefit assessment of drugs:
  - For new chemical entities / new indications
  - Requirement linked to market entry
  - Now onus of proof on drug manufacturer to demonstrate added benefit (vs. an appropriate comparator) – submission of a dossier
  - Results used for price negotiations (not for the decision: reimbursement yes/no)

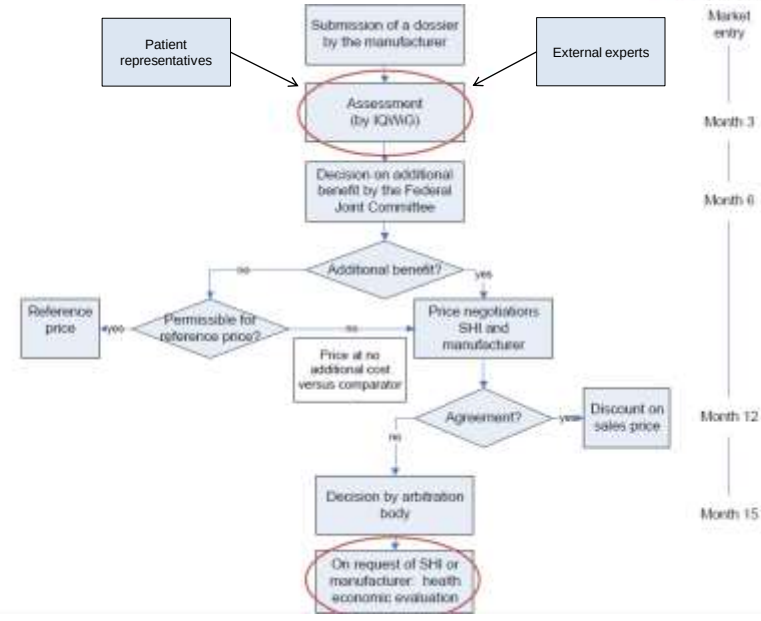
Drug assessment according to AMNOG



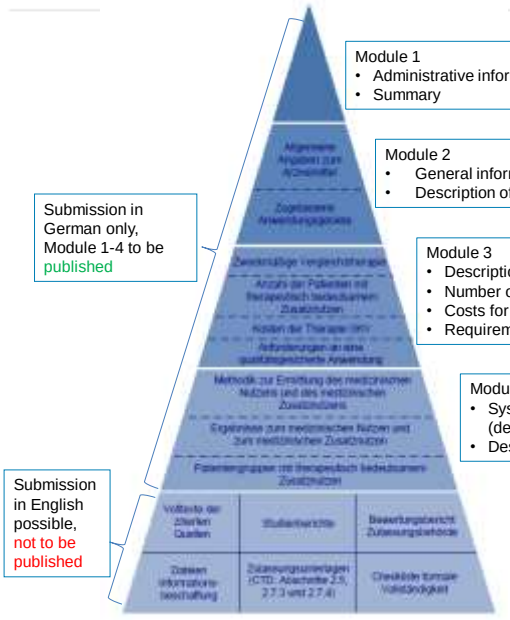
Drug assessment according to AMNOG



Drug assessment according to AMNOG



Dossier structure



Module 1
- Administrative information
- Summary

Module 2
- General information on the drug
- Description of approved indication

Module 3
- Description of appropriate comparator
- Number of patients with relevant additional benefit
- Costs for the SHI
- Requirements for quality-assured application

Module 4
- Systematic review of the benefit and additional benefit (description of methods and results)
- Description of patient groups with a relevant additional benefit

Module 5
- Full texts of references
- Data on the documentation of information retrieval
- Study reports for all manufacturer-sponsored trials
- Approval documents (CTD 2.5, 2.7.3, 2.7.4)
- Evaluation report of the regulatory authority
- Checklist for the review of formal completeness

Submission in German only, Module 1-4 to be published

Submission in English possible, not to be published

Appropriate comparator therapy (ACT)

- Specified by G-BA
- If requested, advice on ACT is offered by G-BA to drug manufacturer
- Precondition for ACT: approved and reimbursable
- Decision criteria for selection of ACT:
  - Evidence of benefit for patients; tested in clinical practice

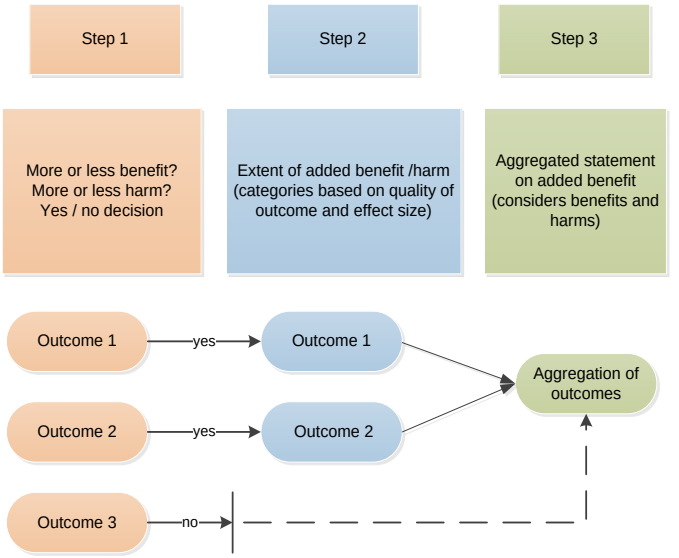
Early benefit assessments

- Legal obligation for the manufacturer of the drug under assessment to provide all available evidence for the HTA
  - Study reports (including study protocols) of all studies on the drug under assessment which have been sponsored by the manufacturer
  - All available information on ongoing and terminated studies which have been sponsored by the manufacturer or in which the manufacturer was financially involved
  - Assessment reports of regulatory authorities
  - Corresponding information about studies by third parties as available

General steps from formulating question to decision on therapeutic value

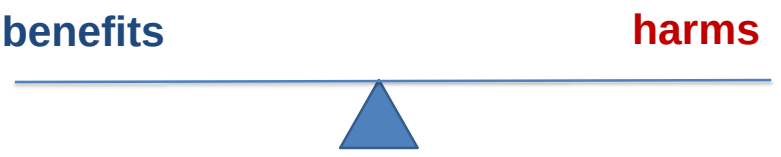
- Identify PICO
- Appropriate comparator used?
- Identify relevant clinical trials (direct / indirect comparison)
- Identify patient-relevant outcomes (selection and assessment of outcomes following EbM methods)
- Determine treatment effects
- Consider benefits **and** harms
- Consider uncertainty / risk of bias
- Aggregate information on various outcomes

Process of assessing "added benefit"



GOAL:

⇒ Adequately capture benefits *AND* harms…



AMNOG – extent of 'added benefit'

Criteria in accordance with AM-NutzenV*

Major added benefit → sustained and great improvement[#] (cure, major increase in survival time, long-term freedom from serious symptoms, extensive avoidance of serious side effects)

Considerable added benefit

Minor added benefit

No added benefit has been proven

Less benefit

*Regulation for Early Benefit Assessment of New Pharmaceuticals

[#]in the therapy-relevant benefit, which has not previously been achieved versus the appropriate comparator

AMNOG – extent of 'added benefit'

Criteria in accordance with AM-NutzenV*

Major added benefit

Considerable added benefit → marked improvement[#] (perceptible alleviation of the disease, moderate increase in survival time, alleviation of serious symptoms, relevant avoidance of serious adverse effects, important avoidance of other adverse effects)

Minor added benefit

No added benefit has been proven

Less benefit

*Regulation for Early Benefit Assessment of New Pharmaceuticals

[#]in the therapy-relevant benefit, which has not previously been achieved versus the appropriate comparator

AMNOG – extent of 'added benefit'

Criteria in accordance with AM-NutzenV*

Major added benefit

Considerable added benefit

Minor added benefit

No added benefit has been proven

Less benefit

sustained and great improvement[#] (cure, major increase in survival

marked improvement[#] (perceptible alleviation of the disease, moderate increase in survival time, alleviation of serious symptoms, relevant

moderate and not only marginal improvement[#] (reduction in non-serious symptoms, relevant avoidance of side effects)

*Regulation for Early Benefit Assessment of New Pharmaceuticals

[#]in the therapy-relevant benefit, which has not previously been achieved versus the appropriate comparator

AMNOG – extent of 'added benefit'

Criteria in accordance with AM-NutzenV*

Major added benefit

Considerable added benefit

Minor added benefit

Added benefit not quantifiable

No added benefit has been proven

Less benefit

sustained and great improvement[#] (cure, major increase in survival

marked improvement[#] (perceptible alleviation of the disease, moderate increase in survival time, alleviation of serious symptoms, relevant

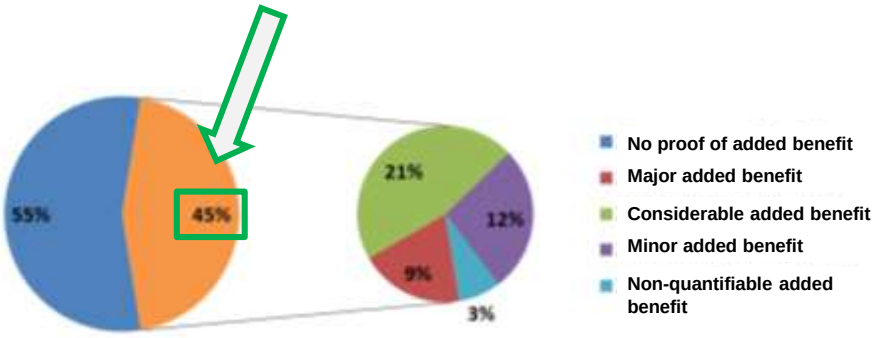
moderate and not only marginal improvement[#] (reduction in non-serious symptoms, relevant avoidance of side effects)

*Regulation for Early Benefit Assessment of New Pharmaceuticals

[#]in the therapy-relevant benefit, which has not previously been achieved versus the appropriate comparator

Results of IQWiG's early benefit assessments

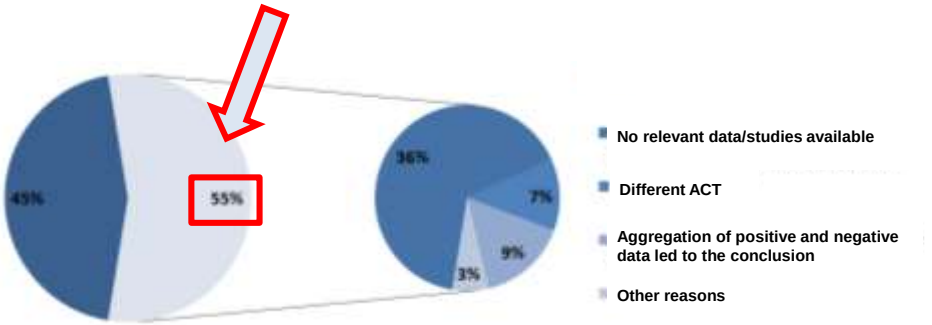
- Added benefit determined in 45% of assessments



Status: 9 Jan 2014 (without orphan drugs): maximum added benefit due to consideration of addenda (n = 58)

Results of IQWiG's early benefit assessments

- No added benefit determined in 55% of assessments



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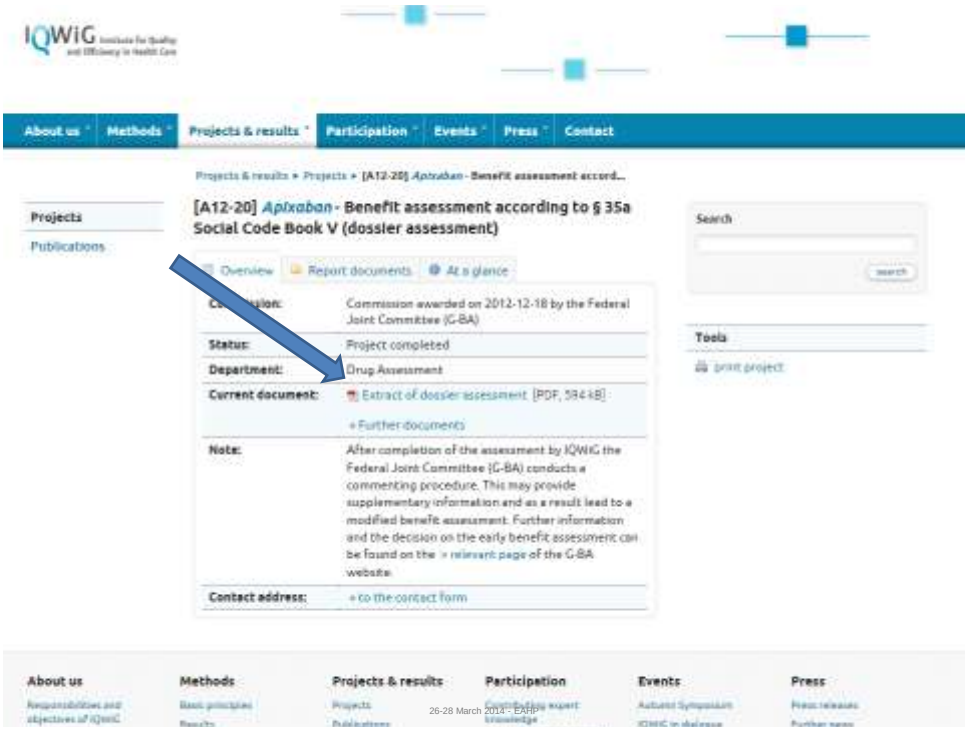
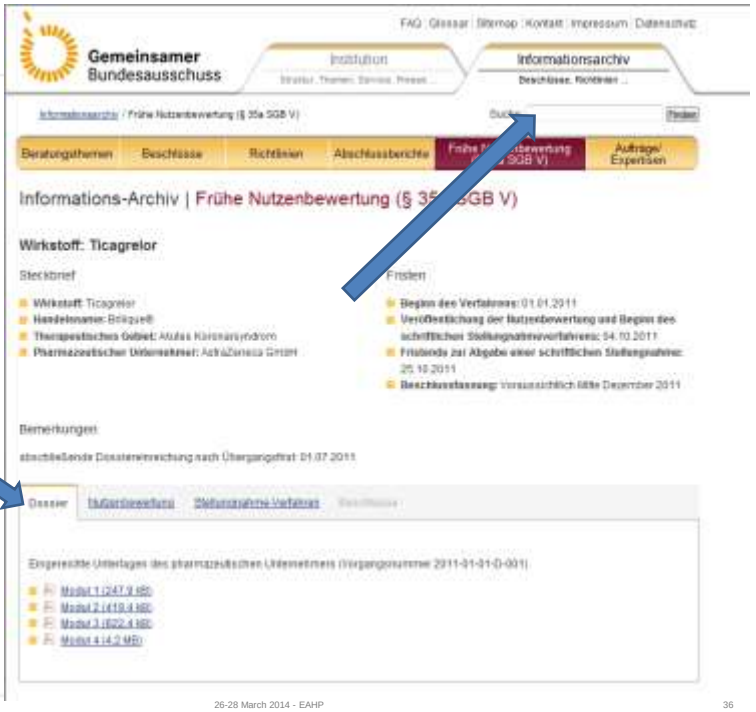


How to access the manufacturers' dossiers

www.g-ba.de

Only German versions available



Summary

- Early benefit assessments:
  - provide basis for price negotiations for outpatient sector (price discounts negotiated are not binding in inpatient sector)
  - close the evidence gap in the assessment of new drugs
  - support informed decision-making by physicians and patients
- So far, 58 early benefit assessments (or “dossier assessments”) have been performed: 45% show added benefit

Institute for Quality and Efficiency in Health Care (IQWiG)

- Im Mediapark 8
- D-50670 Cologne

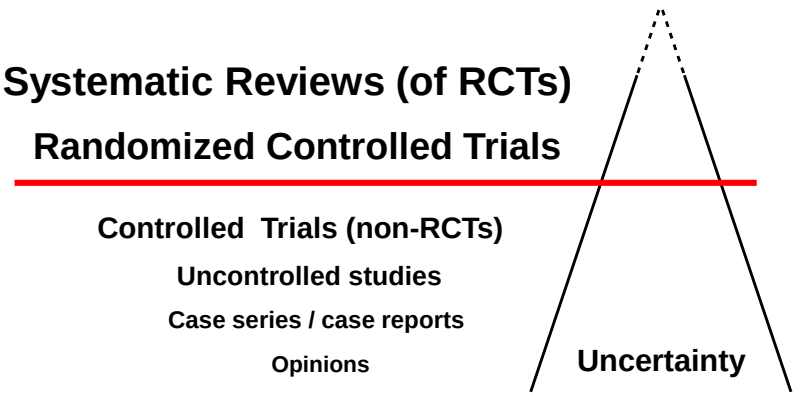
- Telefon +49-221/3 56 85-0
- Telefax +49-221/3 56 85-1

- info@iqwig.de
- www.iqwig.de

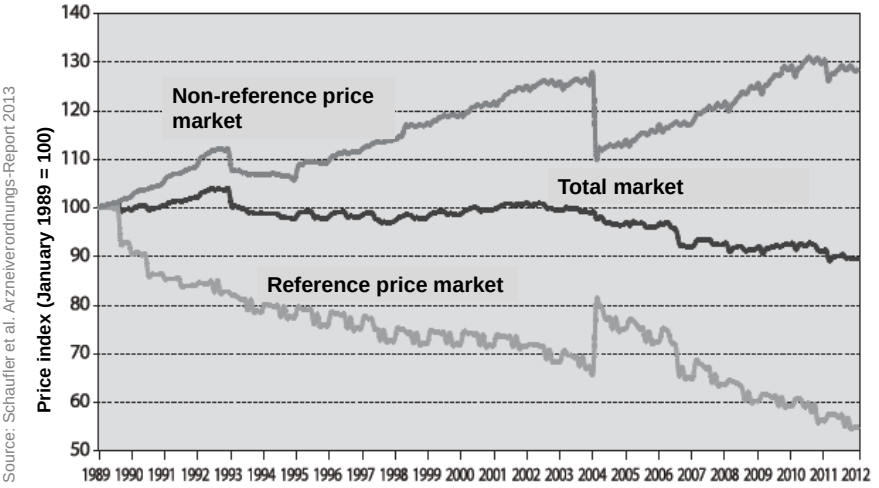
Evidence-based medicine

- Precise formulation of questions to be addressed (Patient Intervention Comparator Outcome)
- Systematic (i.e. reproducible, transparent) procedure (search and evaluation of clinical trials)
- Reliability assessment of the result as the basis for a recommendation ('How credible are the results?')
  - Qualitative component (risk of bias)
  - Quantitative component (precision, significance level)
  - Magnitude (and nature) of the (observed) effect

Hierarchy of evidence



Reference prices - most effective instrument for stabilizing drug prices



Source: Schaufler et al. Arzneiverordnungs-Report 2013

Outcomes

German Social Code Book V

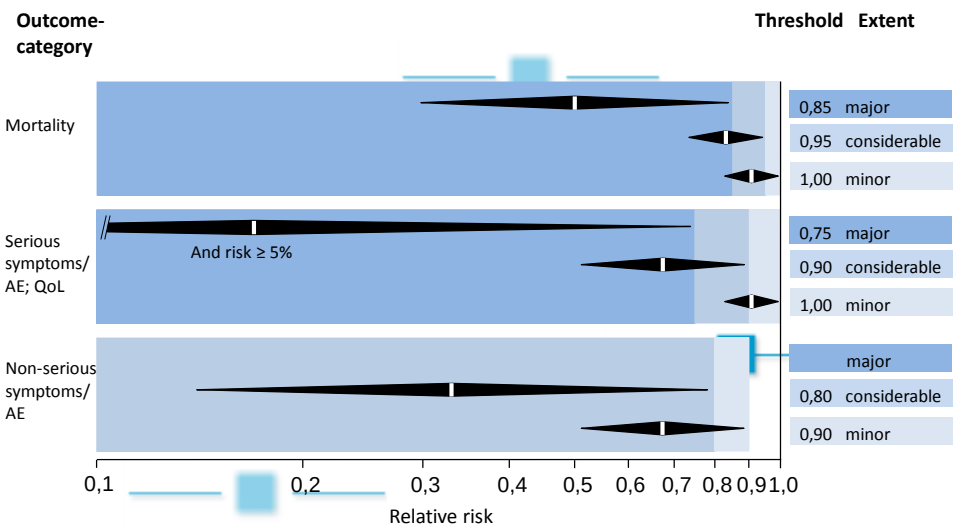
'… Regarding patient benefit, an

- improvement of the medical condition,
- a shortening of the duration of the disease,
- an increase in life expectancy,
- a reduction in side effects, as well as
- an improvement of the quality of life are especially to be considered. …'

Benefits catalogue of SHI

- Health care services must be sufficient, appropriate and efficient (12 SGB V)
- Approved drugs are basically reimbursable; exceptions (acc. to G-BA):
  - OTC drugs for adults (only in exceptional cases)
  - Lifestyle drugs (e.g. for improvement of erectile dysfunction, smoking cessation, weight reduction)
- Therapy advice, reimbursement restrictions and exclusions by the G-BA must be considered

Determination of the extent of added benefit



Determination of the extent of added benefit

Added Benefit		Outcome Category: Survival Time (Mortality)	Outcome Category: Serious (or Severe) Symptoms (or Late Complications) and Adverse Effects	Outcome Category: Quality of Life	Outcome Category: Non-Serious (or Non-Severe) Symptoms (or Late complications) and Adverse Effects
	Major **sustained and great improvement** in the therapy-relevant benefit, which has not previously been achieved versus the appropriate comparator	Major increase in survival time **CI_E: 0.85** (RR_I = 0.50)	Long-term freedom or extensive avoidance **CI_E: 0.75** (RR_I = 0.17) **and risk ≥ 5%**[2]	*Major improvement*[1] **CI_E: 0.75** (RR_I = 0.17) **and risk ≥ 5%**[2]	Not applicable
	Considerable **marked improvement** in the therapy-relevant benefit, which has not previously been achieved versus the appropriate comparator	Moderate increase in survival time **CI_E: 0.95** (RR_I = 0.83)	Alleviation or relevant avoidance **CI_E: 0.90** (RR_I = 0.67)	*Important improvement*[1] **CI_E: 0.90** (RR_I = 0.67)	Important avoidance **CI_E: 0.80** (RR_I = 0.33)
	Minor **moderate and not only marginal improvement** in the therapy-relevant benefit, which has not previously been achieved versus the appropriate comparator	*Any (statistically significant) increase in survival time* **CI_E: 1.00**	*Any (statistically significant) reduction* **CI_E: 1.00**	*Relevant improvement*[1] **CI_E: 1.00**	Relevant avoidance **CI_E: 0.90** (RR_I = 0.67)

Additions to AM-NutzenV in *italics*

1: The precondition is the use of a validated instrument and a validated response criterion. Values count for non-response.

2: For at least one of the groups to be compared.

AM-NutzenV: Regulation for Early Benefit Assessment of New Pharmaceuticals, CI_E: threshold value for the upper limit of the 95% confidence interval, RR_I: actual relative risk

*: Table 32 in the German Appendix