Post-licensing evaluation of pharmaceuticals

An international comparison

Dr. Annette Zentner MD, MPH
Dept. Health Care Management
Technische Universität Berlin, Germany

Agenda

- Pharmaceutical regulation in industrialised countries
- Pharmaceutical evaluation
  - aspects
  - Process
  - methods
- Conclusions

Dr. med. Annette Zentner, MPH
Dept. Health Care Management,
Technische Universität Berlin, Germany

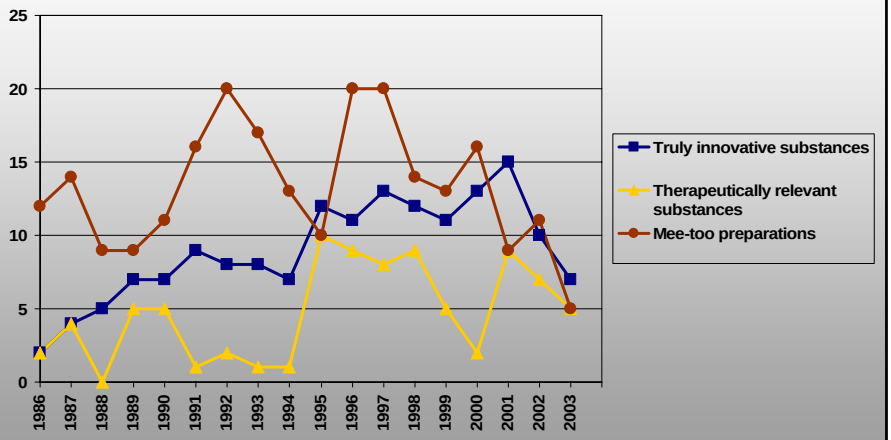
Pharmaceutical regulation in industrialised countries

Positive List	Australia Austria Canada France The Netherlands Norway New Zealand Sweden Switzerland
Negative List	Austria Germany Sweden United Kingdom
Reference Pricing	Australia Belgium Denmark Germany France New Zealand The Netherlands Norway Sweden Spain
Public Price Setting	Australia Belgium Denmark Finland Greece Italy Canada Luxembourg The Netherlands Portugal Sweden Switzerland Spain
Public Price Negotiation	Austria France Ireland New Zealand
Public Profit Control	United Kingdom

Dr. med. Annette Zentner, MPH
Dept. Health Care Management,
Technische Universität Berlin, Germany

Pharmaceutical evaluation

Rationale behind post-licensing evaluation



Source: Schwabe and Paffrath 2004

Dr. med. Annette Zentner, MPH
Dept. Health Care Management,
Technische Universität Berlin, Germany

Criteria for marketing authorisation

- Safety
- Pharmaceutical Quality
- Efficacy

→ No comparison with already available treatment options

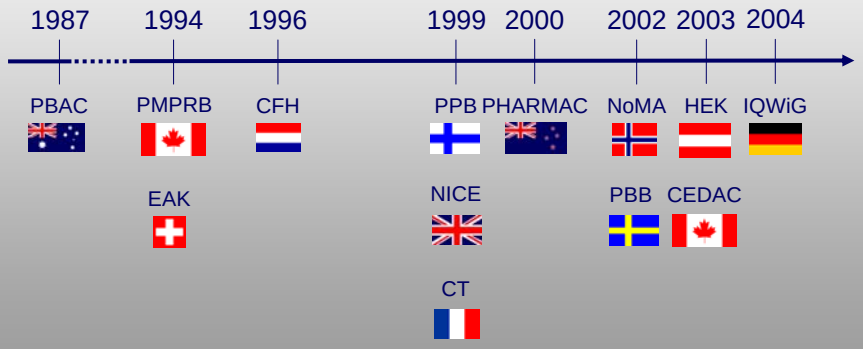
Dr. med. Annette Zentner, MPH
Dept. Health Care Management,
Technische Universität Berlin, Germany

Who is in charge for post-licensing evaluation of drugs in industrialised countries?

National drug evaluating institutions and their advisory bodies

Austria	Federation of Austrian Social Insurance Institutions/Drug Evaluation Commitee (*Hauptverband der Österreichischen Sozialversicherungsträger/Heilmittel-Evaluierungs-Kommission*)
Australia	Pharmaceutical Benefits Advisory Committee/Economic Sub-Committee
Belgium	National Institute for Sickness and Invalidity Insurance/Commission for Reimbursement of Medicines (*Institut national de l'assurance maladie-invalidité/Commission de réimboursement des médicaments*)
Canada	PMPRB - Patented Medicine Prices Review Board/Human and Veterinary Drug Advisory Panels CDR - Canadian Expert Drug Advisory Committee/Common Drug Review-Directorate at Canadian Coordinating Office for Health Technology Assessment
Finland	Pharmaceuticals Pricing Board (*Lääkkeiden hintalautakunta*)
France	Economic Committee for Health Products/Transparency Commission (*Comité économique des produits de santé/Commission de Transparence*)
Germany	Federal Joint Committee/Institute for Quality and Efficienty in Health Care (*Gemeinsamer Bundesausschuss/Institut für Wirtschaftlichkeit und Qualität im Gesundheitswesen*)
The Netherlands	Health Care Insurance Board/Committee for Pharmaceutical Aid (*College voor zorgverzekeringen/Commissie Farmaceutische Hulp*)
Norway	Norwegian Medicines Agency (*Statens Legemiddelverk*)
New Zealand	Pharmaceutical Management Agency/Pharmacology and Therapeutic Advisory Committee
Sweden	Pharmaceutical Benefits Board (*Läkemedelsförmånsämnden*)
Switzerland	Swiss Federal Office of Public Health/Confederal Drug Commission (*Bundesamt für Gesundheit/Eidgenössische Arzneimittelkommission*)
United Kingdom	National Institute for Clinical Excellence

Establishing comparative post-licensing evaluation



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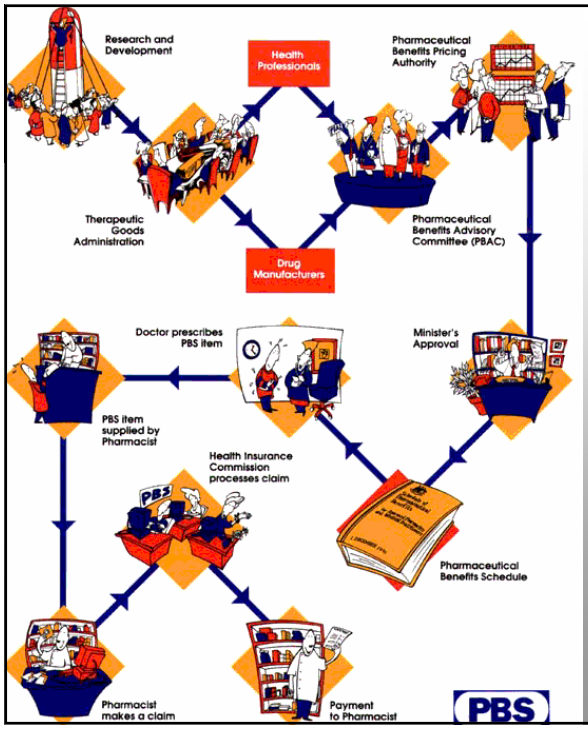
Dept. Health Care Management,
Technische Universität Berlin, Germany

Example Australia



The pathway of a new drug in Australia

Example France

Price negotions according to

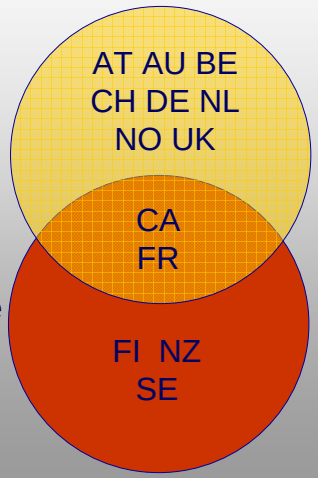
Amélioration du Service Médical Rendu-Classification

ASMR I	major therapeutic progress
ASMR II	great improvement in terms of efficacy and/or reduction of side effects
ASMR III	modest improvement
ASMR IV	minor improvement
ASMR V	no improvement but a lower treatment cost
ASMR VI	no improvement: no inclusion of the product on the positive list

Drug Review Bodies: Role and Structure

advisory-type bodies

regulatory-type bodies



- Physicians
- Health economists
- Pharmacists, clinical pharmacologists
- Epidemiologists
- Government/insurance fund representatives
- Consumers (AU, SE, UK)
- Industry (UK)

Dr. med. Annette Zentner, MPH
Dept. Health Care Management,
Technische Universität Berlin, Germany

Which pharmaceuticals are subject to evaluation?

- **all newly licensed** (AT, AU, NL)
- those with **new chemical substances** (CA [CDR])
- **all patented** (CA [PMPRB])
- all **newly** licensed for **outpatient** care (FI)
- **newly** licensed **prescription drugs** for **outpatient** care (FR)
- **new and "old" prescription drugs** (SE)
- specific **products** according to **priority setting** (UK)

Dr. med. Annette Zentner, MPH
Dept. Health Care Management,
Technische Universität Berlin, Germany

Aspects of pharmaceutical evaluation in industrialised countries

Criteria for Assessment and Decision-Making

Criteria	AT	AU	BE	CA	CH	DE	FI	FR	NL	NO	NZ	SE	UK
Therapeutic benefit	X	X	X	X	X	X	X	X	X	X	X	X	x
Patient benefit	X	X	X	X	X	X	X	X	X	X	X	X	X
Cost-effectiveness	X	X	X	X			X		X	X	X	X	X
Budget impact		X	X	X			X	X	X	X	X		X
Pharmacological/innovative characteristics	X		X	X				X	X				X
Availability of therapeutic alternatives	X	X							X		X	X	X
Equity considerations				X						X	X	X	X
Community need		X									X		
Public health impact				X				X					
R&D		X					X						
Government priorities											X		

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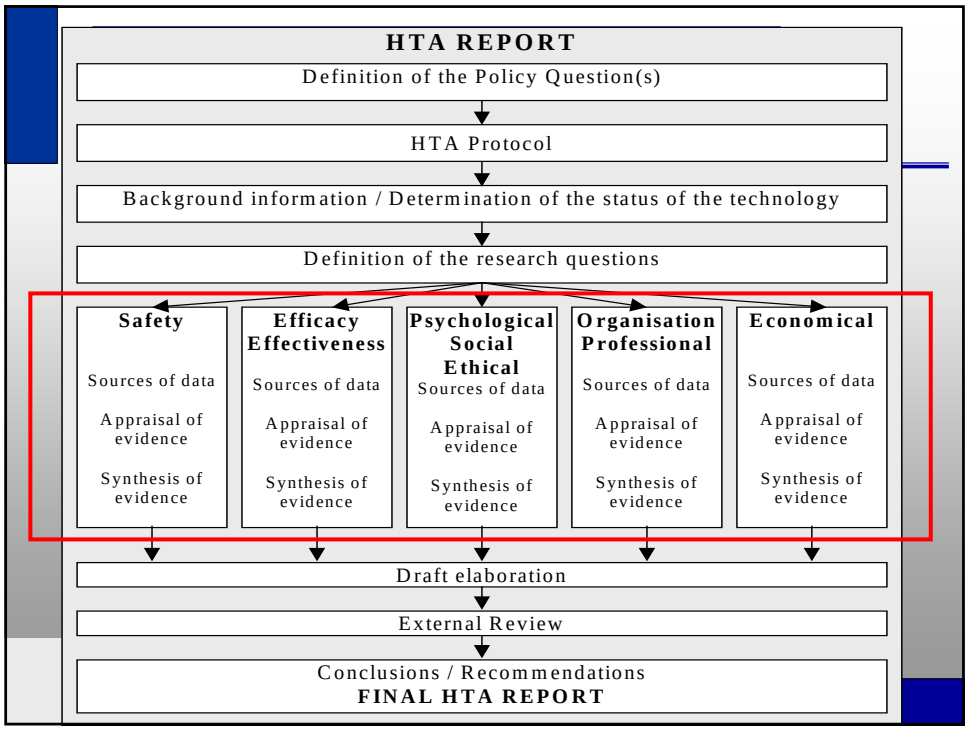
Dept. Health Care Management,
Technische Universität Berlin, Germany



Process of pharmaceutical evaluation in industrialised countries

Who provides and analyses the data?

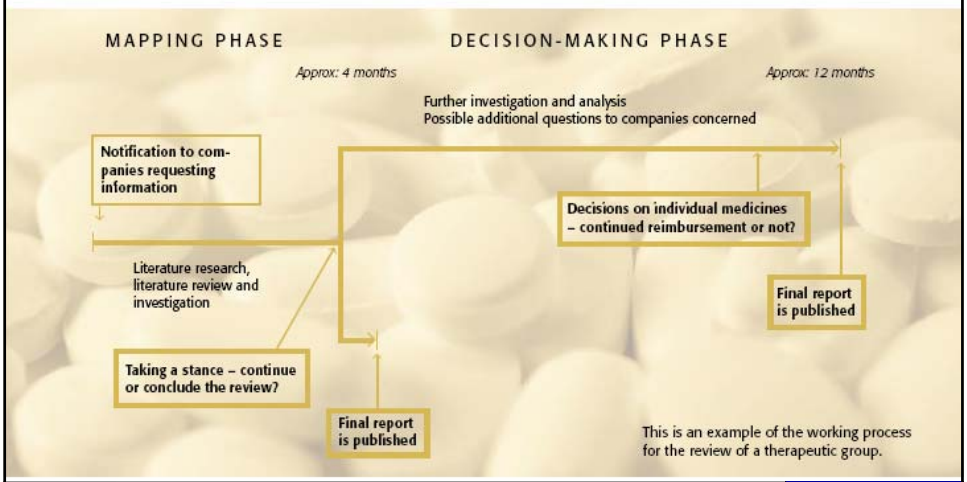
AU, NO, NL: Review bodies check and validate data provided by industry. Manufacturers are required to submit a comprehensive summary of the drug's effectiveness and cost-effectiveness data that is based on a systematic search and synthesis of published and unpublished evidence.

CA (CDR), NZ, SE, UK: Review bodies themselves perform systematic review of clinical and economic evidence independently of studies and data provided by companies.

AT, CA (PMPRB), CH, FI, FR: Assessments are mainly based on a definite number of clinical or economic studies which are submitted by pharmaceutical companies. Systematic reviews are preferred but not required.

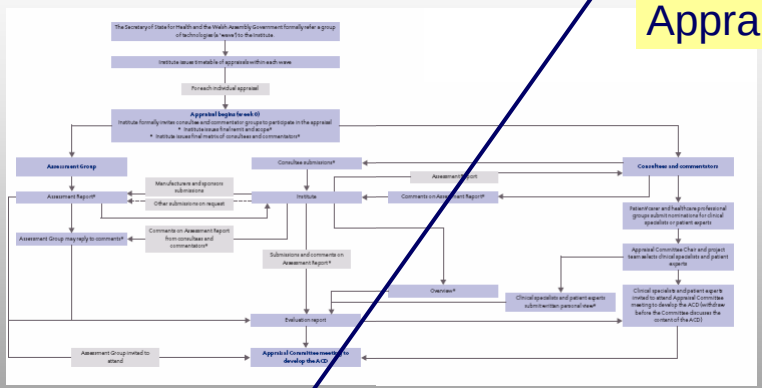
Example Sweden

Evaluation process at PBB



Example England and Wales

Evaluation process at NICE



Appraisal

Assessment

Methods for pharmaceutical evaluation in industrialised countries

Everything is relative...

Comparator

• "**common practice**" in most countries (i.e. most frequently prescribed medicine or mo cal treatm

• **best** NO, NZ, U

• **least expensive** therapeutic alternative (e.g. CA, FR, NZ)

Choice of comparator is crucial for result of assessment! Methological guidelines require close adherance

Study designs

- preferably "head-to-head" randomized controlled trials (direct comparisons)
- majority favours final outcome parameters (change in mortality, morbidity, quality of life) and studies in "natural" and country specific setting
- cost-utility analyses are most frequently recommended, required in AU, NZ, UK; quality-adjusted life years (QALYs) required as outcome in 4 countries

Australia (PBAC)-
benefit versus harm versus costs

effectiveness

Toxicity

	more	alike	less
less	cost-effectiveness-/ utility-analysis		?
alike		cost-minimisation-analysis	STOP
More		STOP	STOP

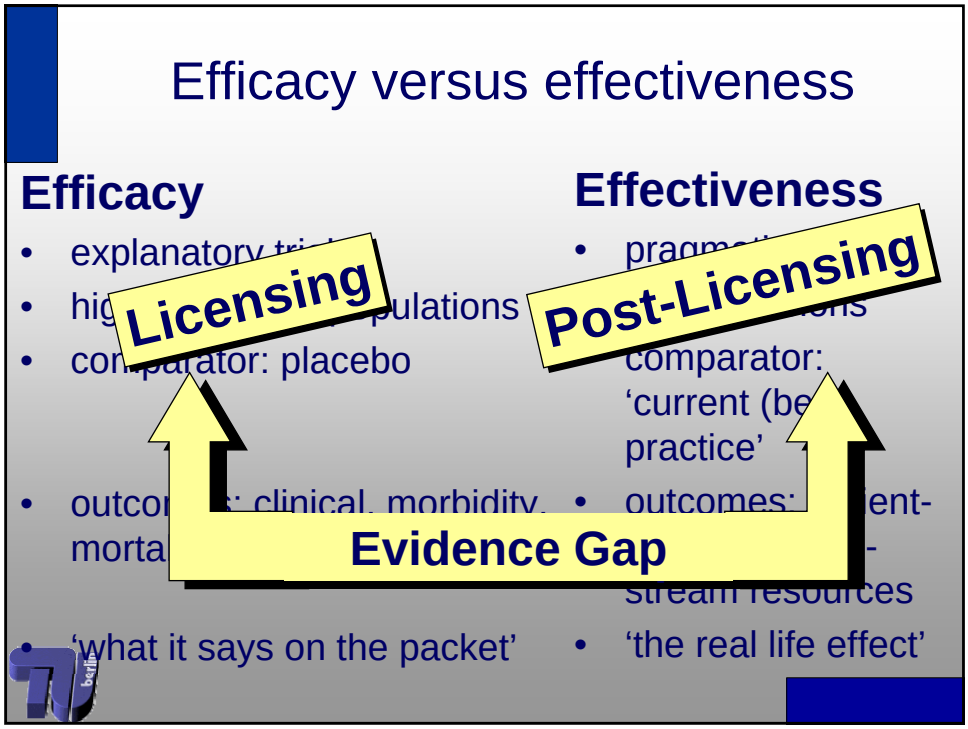
Dr. med. Annette Zentner, MPH
Dept. Health Care Management,
Technische Universität Berlin, Germany

Final outcomes versus surrogatparameters

Coronary thrombosis (thrombolysis)	Quality-adjusted survival	Number surviving	Number with specified level of left ventricular function	Number achieving coronary reperfusion
Unstable angina (various interventions)	Quality-adjusted survival	Number surviving	Number with myocardial infarction	Number with adequate relief of pain
Stable angina (various interventions)	Quality-adjusted survival	Number with acceptable quality of life	Number who can walk a specified distance	Number with adequate relief of pain
Asthma (various drugs)	Quality-adjusted survival	Number surviving	Number with adequate control of bronchial hyperreactivity	Number achieving a target level of airways function
Depression (various drugs)	Quality-adjusted survival	Number avoiding suicide	Quality of life (may be improved by drugs)	Number achieving a target Hamilton or Montgomery-Asberg Depression Rating Scale
Hypertension (various drugs)	Quality-adjusted survival	Number avoiding stroke	Quality of life (may be worsened by drugs)	Number achieving a target blood pressure

source: PBAC

Efficacy versus effectiveness



Methodology: Details

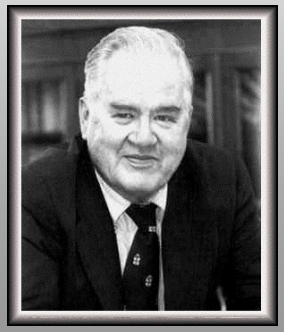
Methodologies further differ on:

sub-group analysis, time horizon, preferred outcome parameter (clinical, patient benefit, combined), use of „community effectiveness" data (mostly preferred), indirect comparisons (mostly no), instruments to measure quality of life, perspective of economic analysis, costs included in analysis, calculation of drug costs, incremental analysis, discounting (0%-15%), use of modelling techniques, sensitivity analysis, dealing with missing and unreliable data …

Dr. med. Annette Zentner, MPH
Dept. Health Care Management,
Technische Universität Berlin, Germany

Dealing with missing or unreliable data

Far better an approximate answer to the right question, which is often vague, than an exact answer to the wrong question, which can always be made precise.



Tukey JW, 1962

Methodological approaches

- inclusion of various study designs and expert opinion (RCT is not a dogma)
- indirect comparisons
- modelling

Dr. med. Annette Zentner, MPH
Dept. Health Care Management,
Technische Universität Berlin, Germany

Restrictions for use of pharmaceutical

to specific indications, type and severity of diseases or conditions, populations (e.g. age, sex), therapeutic strategies (e.g. first line

attempt to target limited resources to populations that are likely to benefit most (or to those for whom evidence is available)

e.g. inpat
care)
NZ)
or pre-authorisation through sickness fund (AT, BE)

Dr. med. Annette Zentner, MPH
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Technische Universität Berlin, Germany

Example United Kingdom

Recommendations of NICE

Bewertungskategorie		alle Leistungen		nur Arzneimittel	
		absolut	in %	absolut	in %
A	empfohlen	66	90,4	45	95,7
	davon: für alle Indikationen	20	27,4	18	38,3
	indikationsspezifisch bzw. nur für bestimmte Patientengruppen	46	63,0	27	57,4
B	nur im Kontext begleitender Studien empfohlen	5	6,9	2	4,3
C	nicht empfohlen	2	2,7	0	0,0
	Summe aller Entscheidungen	73	100,0	47	100,0

source: Rothgang 2004

Dr. med. Annette Zentner, MPH
Dept. Health Care Management,
Technische Universität Berlin, Germany

Conclusion I: Criteria and Process

Post-licensing evaluation of drugs is a valuable policy tool

IF...

- ...it follows a systematic, evidence-based, comparative approach,
- ...it is independently performed and supplemented by other criteria in the decision-making process

Dr. med. Annette Zentner, MPH
Dept. Health Care Management,
Technische Universität Berlin, Germany

Conclusion II: Methodological Challenges

Post-licensing evaluation of drugs is a valuable policy tool

IF...

- ...decision-makers are aware of its methological strenghts and limitations,
- ...it is repeated according to gain in new evidence.

Dr. med. Annette Zentner, MPH
Dept. Health Care Management,
Technische Universität Berlin, Germany

Conclusion III: Policy Challenges

Post-licensing evaluation of drugs is a valuable policy tool

IF...

- ...it has reliable impact on rewarding manufacturers in terms of full reimbursement and/or free or premium pricing,
- ...if potential for international collaboration to increase transparency and acceptability is increasingly used.

Dr. med. Annette Zentner, MPH
Dept. Health Care Management,
Technische Universität Berlin, Germany

Thank you for your attention!

More details are available:

Zentner A, Velasco-Garrido M, Busse, R. Methods for comparison of pharmaceuticals – an international review. GMS Health Technol Assess 2005; 1:Doc09 (20051115) (abstract and executive summary in English)

www.egms.de/en/journals/hta/2005-1/hta000009.shtml

Dr. med. Annette Zentner, MPH
Dept. Health Care Management,
Technische Universität Berlin, Germany