

**HelmholtzZentrum münchen**

Deutsches Forschungszentrum für Gesundheit und Umwelt

## **Health economics of personalized medicine**

Winter School

“Clinical and Genetic Epidemiology – Strategies to Drive Personalized Medicine“

Dr. Larissa Schwarzkopf

Helmholtz Zentrum München

Institute for Health Economics and Health Care Management

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# Definitions of (health) economics

- ❖ “Economics analyzes the economy”
- ❖ “Economics is about money”
- ❖ “Economics is the science which studies human behavior as a relationship between ends and scarce means which have alternative uses”

Robbins L. *An essay on the nature & significance of economic science*. London, Macmillan 1937

## ❖ “Health economics”

a branch of [economics](#) concerned with issues related to efficiency, effectiveness, value and behavior in the production and consumption of [health](#) and [healthcare](#).

In broad terms, health economists study the functioning of healthcare systems and health-affecting behaviors.

*Wikipedia*

# Overview: Health economics of personalized medicine

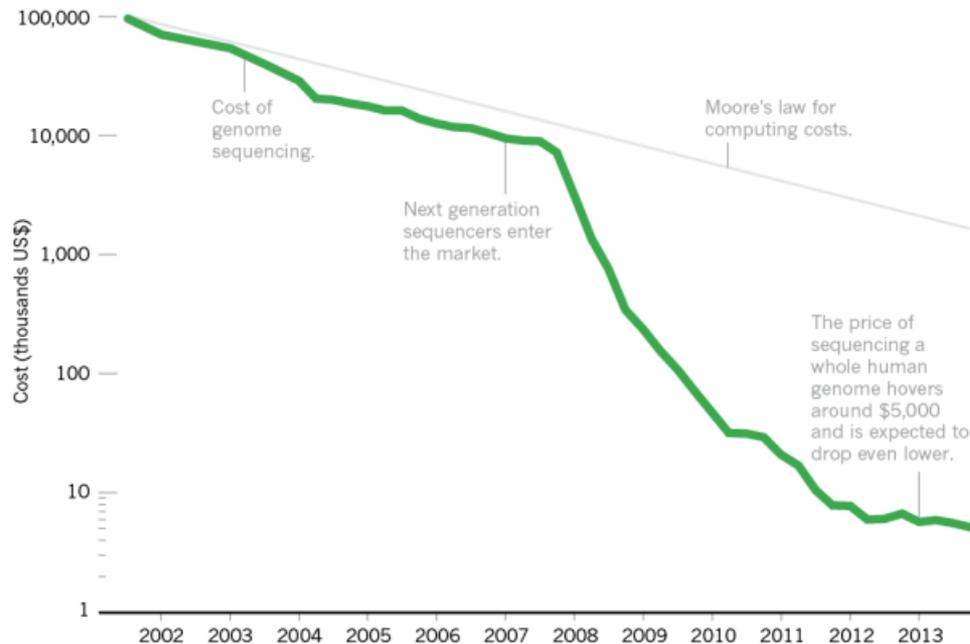
1. Background: Need for economics in health care
2. Basic concepts of health economic evaluation
3. Design of a health economic evaluation study
4. Illustrative example: Decision analytic model for personalized lung cancer therapy
5. Further considerations
6. Take home messages

**PLEASE ASK QUESTIONS  
IMMEDIATELY**

# Rapidly decreasing expenditures of Whole Genome Sequencing...

## Falling fast

In the first few years after the end of the Human Genome Project, the cost of genome sequencing roughly followed Moore's law, which predicts exponential declines in computing costs. After 2007, sequencing costs dropped precipitously.



Source: Hayden EC. "Technology: The \$1,000 genome", 2014.

- ❖ Within 15 years decrease from ca. 100 million USD to ca. 4,000 USD
- ❖ „\$1,000-Genome within reach“

## ... as driving factor of personalized medicine

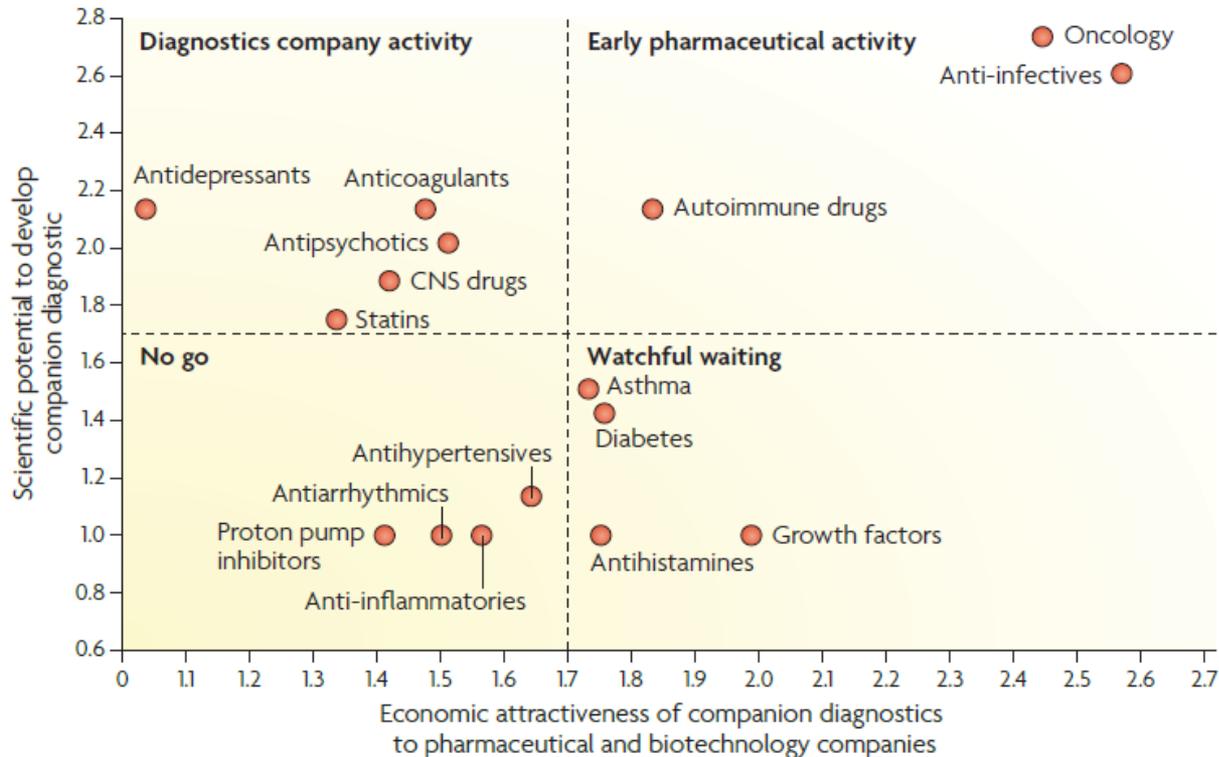
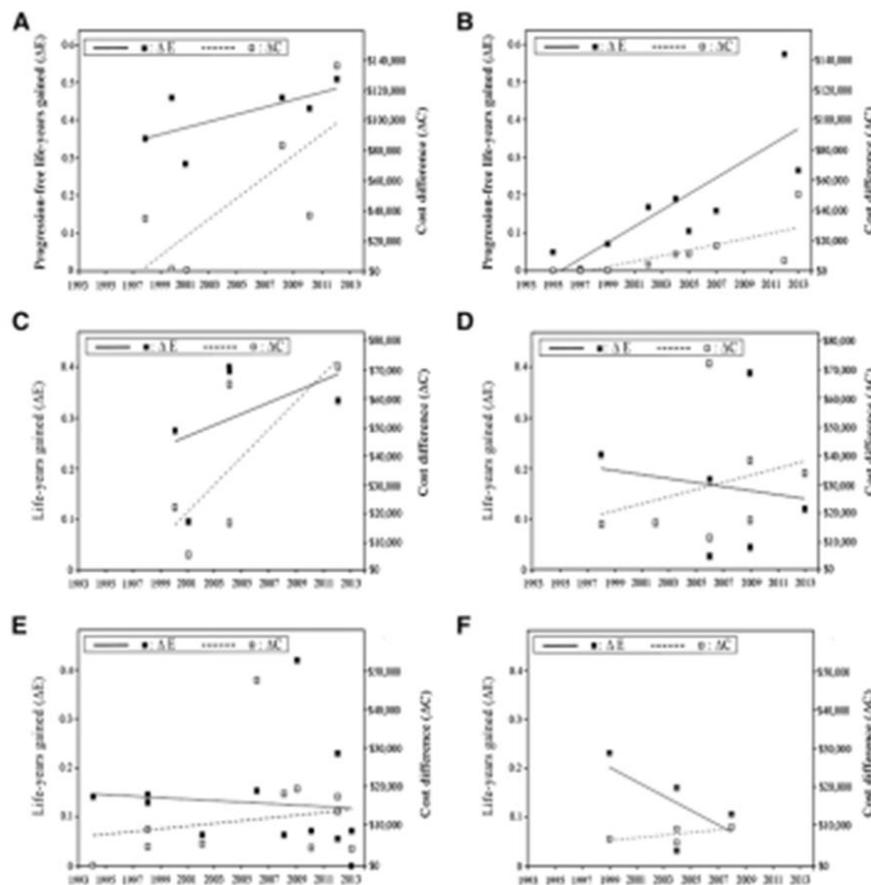


Figure 4 | **Scientific potential and economic attractiveness for companion diagnostics development across therapeutic areas.** We developed rank-order estimates for the scientific potential and economic attractiveness of the development of companion diagnostics in various therapeutic areas based on both qualitative factors (such as expert interviews) and quantitative factors (such as data on price premiums for drugs launched in the same therapeutic class). Results should be taken as directional only; for details of ranking process, see [Supplementary information S1](#) (box). CNS, central nervous system.

Source: Davis et al. "The microeconomics of personalized medicine: today's challenge and tomorrow's promise", 2009.

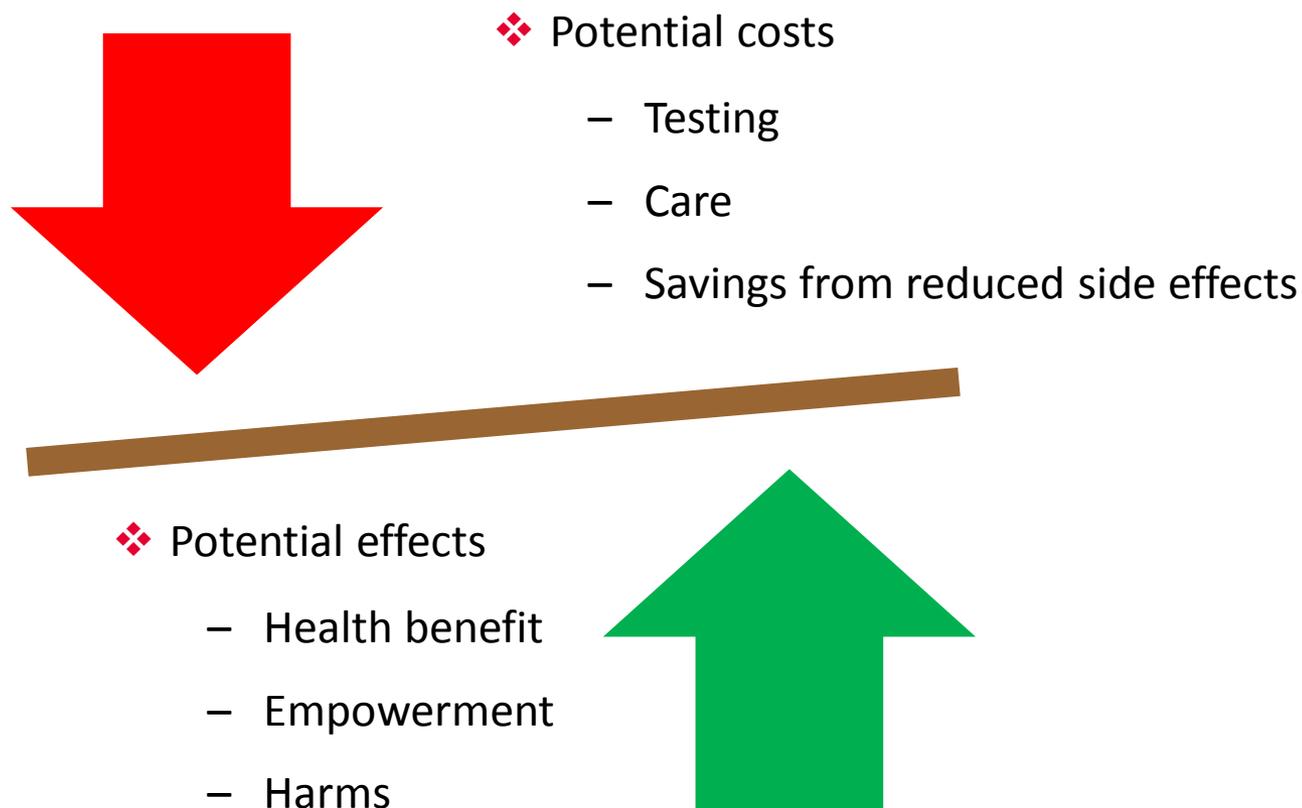
# Personalized therapies...

## is there a balance between effects gained and cost trends?



Source: Cressman S. et al. "A Time-Trend Economic Analysis of Cancer Drug Trials", 2015.

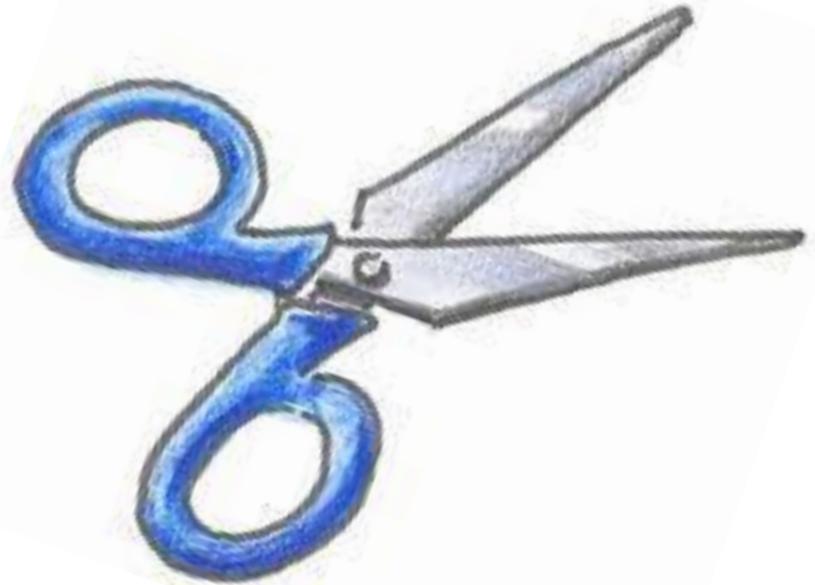
# Potential costs and effects of personalized care



➔ Costs and health effects of PM unclear; need to include total pathway of care

# Why care about costs when allocating health care resources?

- ❖ Increasing demand for health services
  - Ageing
  - Improved diagnosis
  - Technological progress
  - Providers (have to) seek for profits
- ❖ Limited funding
  - Changing demography
  - Government deficits



➔ Increasing scarcity → Need for health economic evaluation

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# Why health economic evaluation

## ❖ Scarcity:

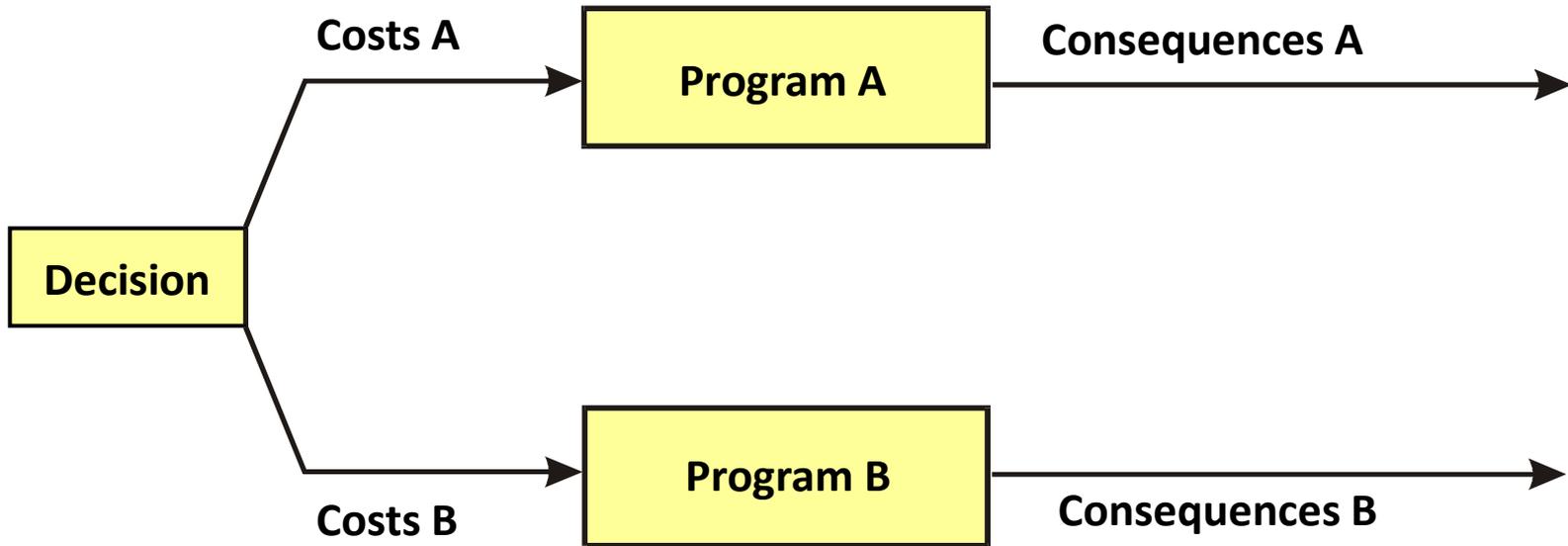
- Resources are limited but needs are not
- Resources spent on a distinct purpose are not available for other purposes

▶ Effectiveness as the one and only decision criterion is not sufficient!

## ❖ Why not a „market driven decision“?

- Market failure  
(lack of consumer sovereignty, intransparency, inconsistent preferences)
- Fairness considerations  
(„Health for all in the 21th century“)

# Simplified model of health economic evaluation



## Health economic evaluation

Consists of a **comparative analysis** of costs and consequences for (at least) two mutually exclusive alternate strategies

➔ The statement „strategy x is cost-effective“ does only make sense if the comparator is known

# Basic approaches of health economic evaluation

## 1. Cost Minimization Analysis (CMA)

- ❖ Comparison of (at least two) medical interventions aiming at the same purpose
- ❖ Identical effects assumed
- ❖ Only costs count → Decision on the cheapest alternative
- ❖ Example:  
Treating metastatic colorectal cancer with Zaltrap (Adlibercept) vs. Avastin (Bevacizumab)
  - Comparable survival benefit of ca. 1.4 months compared to standard chemotherapy
  - Similar mode of action (VEGF-A/VEGF-B Inhibition)
  - Cost per month Zaltrap \$11,000 vs. Avastin \$5,000



Sources: Bach et al. "In cancer care, cost matters", 2012.

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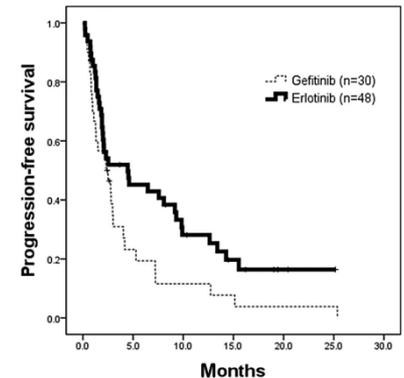
[http://www.zaltrap.com/images/3-0\\_packaging.jpg](http://www.zaltrap.com/images/3-0_packaging.jpg)

# Basic approaches of health economic evaluation

## 2. Cost Effectiveness Analysis (CEA)

- ❖ Assessment of effects in physical units  
(e.g. kgs lost, life-years gained, avoided hospitalizations, length of rehab, etc..)
- ❖ Comparison focused on one pre-specified primary outcome  
(e.g. progression-free life-years (PFLYG) gained )
- ❖ Example:  
Personalized lung cancer treatment with Erlotinib vs. Gefitinib

- Erlotinib:
  - 1.15 PFLYG, \$ 31,434 → PFLYG \$ 27,340
- Gefitinib:
  - 0.79 PFLYG, \$ 17,376 → PFLYG \$ 21,995



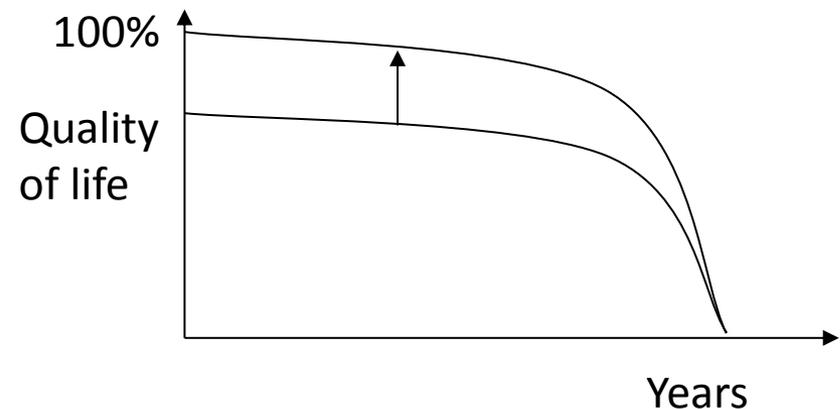
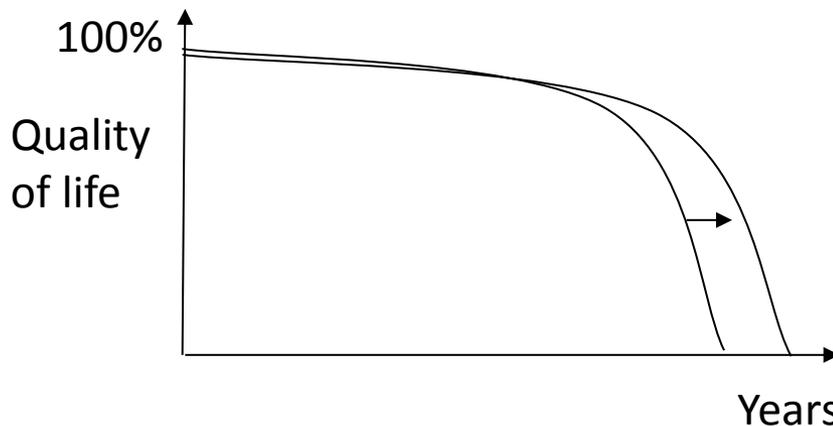
- ❖ **Cave: Comparison of alternatives requires focus on the same primary outcome**

Source: Lee et al. "Effectiveness and cost-effectiveness of erlotinib versus gefitinib in first-line treatment of epidermal growth factor receptor-activating mutation-positive non-small-cell lung cancer patients in Hong Kong ", 2014.

# Basic approaches of health economic evaluation

## 3. Cost Utility Analysis (CUA)

- ❖ Combination of all effects within one multidimensional outcome parameter (**utility**)
- ❖ Most common tool in health economics: **QALY** → quality adjusted life year
  - combination of health-related quality of life and lifespan



- Trade-off between quantity and quality feasible
- Comparison of interventions across different indications

# Basic idea of health economic evaluation

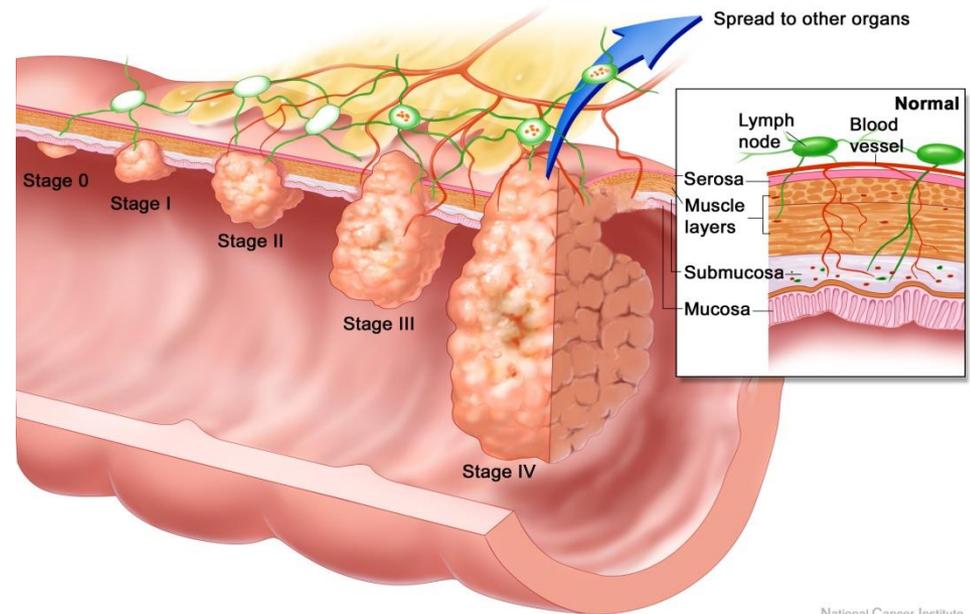
- ❖ Comparison of costs and effects of two alternate strategies
- ❖ Calculation of incremental costs and incremental effects (not average ones)
  - costs (A) – costs (B) =  $\Delta$  costs
  - effects (A) – effects (B) =  $\Delta$  effects
- ❖ Combination of both endpoints in a single parameter  
e.g. incremental cost effectiveness ratio (ICER)

$$\text{ICER} = \frac{\Delta \text{ costs}}{\Delta \text{ effects}}$$

- ❖ ICERs as support for policy decision making on resource allocation
  - a) distinct threshold  $\lambda$  for cost-effectiveness (e.g. NICE £20,000-30,000/QALY)
  - b) spending a fixed budget on different options with increasing ICERs (league table)

# Example (I): Colorectal cancer (CRC)

- ❖ Tumor growth over 10-15 years
- ❖ 5-year survival depends on stage at diagnosis
- ❖ Colonoscopy associated with milder distribution of stages
- ❖ Screening in Germany:
  - Colonoscopy every 10 years 55+
  - FOBT (bi)annually 50+ (55+)
  - Low uptake (16%)
- ❖ Benefit though personalization (?)



# Example (I): Hereditary hemochromatosis (HH)

## ❖ Hereditary defect of iron metabolism

- Increased absorption and excessive storage of iron in body tissue

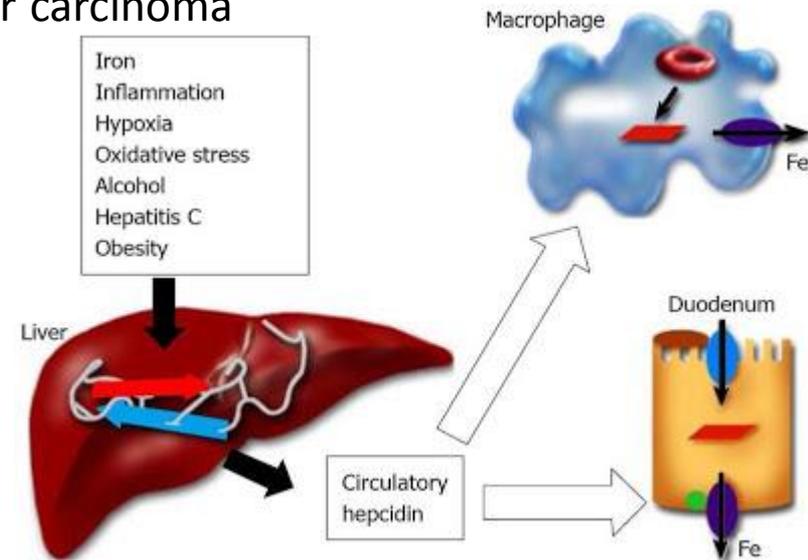
## ❖ Complications: liver cirrhosis and hepatocellular carcinoma

## ❖ Phlebotomy effective

## ❖ Detection of HH

- Phenotype tests
- 90% homozygous for mutation
- Genetic test
- Screening feasible and acceptable

➔ **Both CRC and HH screening can save lives – which program should be funded?**



Sources: Adams PC, Barton JC. "Haemochromatosis" 2007.

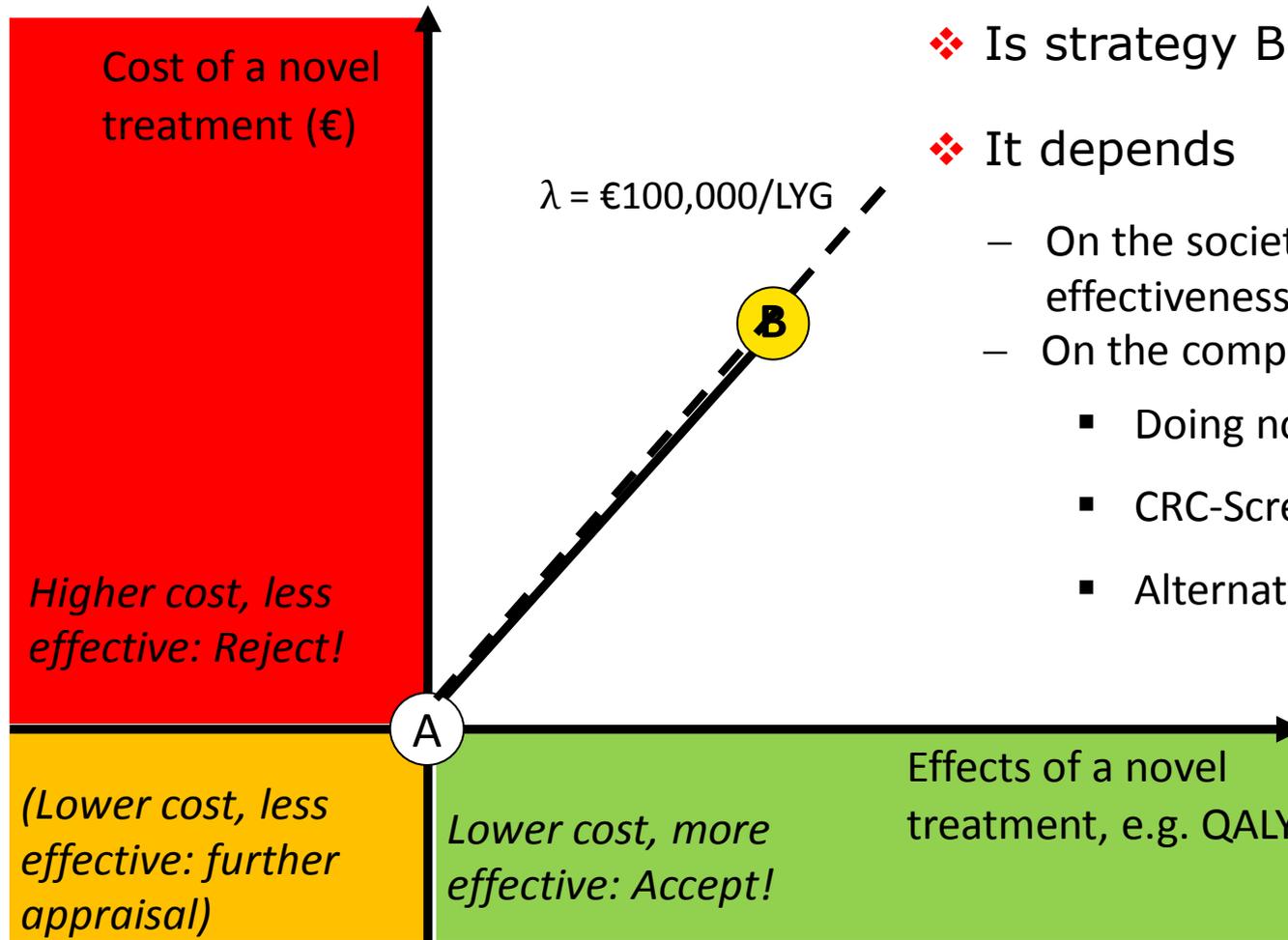
[http://t2.gstatic.com/images?q=tbn:ANd9GcQJZ4phjw8qJBu4JSvhF5PMSkCQB1PG1EiD\\_meP\\_tKlqBd64K\\_0zv4G](http://t2.gstatic.com/images?q=tbn:ANd9GcQJZ4phjw8qJBu4JSvhF5PMSkCQB1PG1EiD_meP_tKlqBd64K_0zv4G)

# Comparison of strategies for HH / CRC screening (fictive figures)

- ❖ Strategy A: Family analysis and personalized colonoscopy CRC screening
  - Cost per test in 10,000 individuals: €150
  - 3 premature death prevented with life prolongation by 4 years
- ❖ Strategy B: HH screening, two independent phenotype tests
  - Cost per test in 10,000 individuals: €180
  - 30 premature death prevented with prolongation by 6 months
- ❖ Cost-Effectiveness of both strategies
  - Average cost-effectiveness (compared to doing nothing) → ACER
  - Incremental cost-effectiveness (B vs. A) → ICER

	Δ Cost	Δ Effects	ACER	ICER
Program A	€ 1,500,000	12 LYG	€125,000/LYG	
Program B	€ 1,800,000	15 LYG	€120,000/LYG	
	Δ € 300,000	Δ 3 LYG		

# ICER: Incremental cost of a health gain (compared to alternative)



❖ Is strategy B cost-effective?

❖ It depends

- On the societally accepted cost effectiveness threshold  $\lambda$
- On the comparator chosen
  - Doing nothing
  - CRC-Screening
  - Alternate Screening program

# Factors enhancing cost-effectiveness of personalized medicine

- ❖ Basic rule:  
The lower the ICER the higher the probability for being cost effective

	<b>Factor</b>	<b>Requirement</b>
<b>Gene</b>	Prevalence Penetrance	<ul style="list-style-type: none"><li>• Variant allele common</li><li>• High gene penetrance</li></ul>
<b>Test</b>	Diagnostic accuracy Cost	<ul style="list-style-type: none"><li>• High sensitivity, high specificity</li><li>• Fast, cheap, broad availability</li></ul>
<b>Disease</b>	Prevalence Natural Course	<ul style="list-style-type: none"><li>• Widespread disease</li><li>• High mortality in case of no treatment</li><li>• Substantial decrement on quality of life</li></ul>
<b>Treatment/ Comparator</b>		<ul style="list-style-type: none"><li>• Targeted application by responders only</li><li>• Less side effects</li><li>• Enhanced prognosis</li><li>• Small costs differences compared to standard</li></ul>

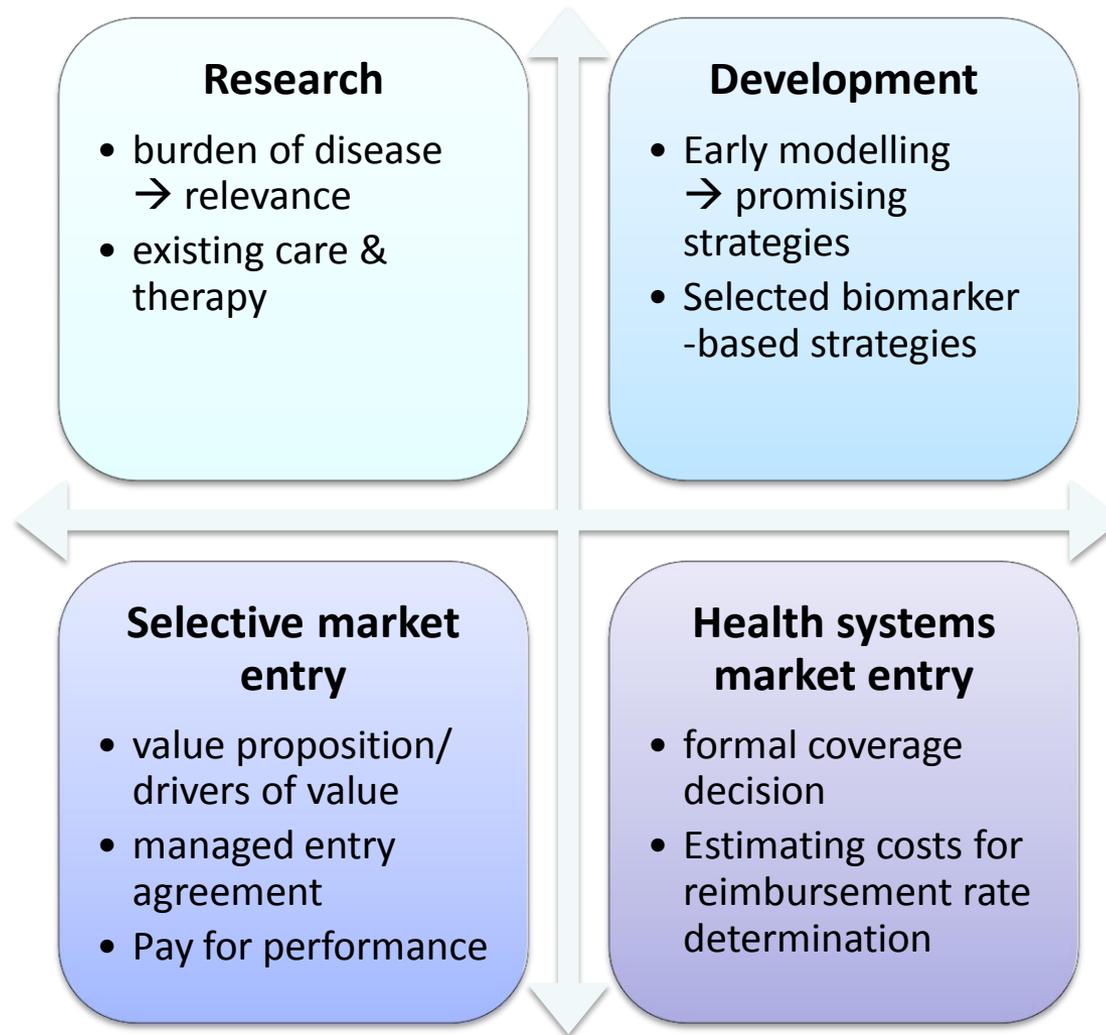
# Take home messages for Session I

- ❖ Budget constraints require the implementation of economic considerations in health care
- ❖ Health economic evaluation compares costs and effects of mutually exclusive alternatives
  - Additional costs need to be „justified“ by additional effects
- ❖ Interventions which do not exceed a pre-specified (societally) accepted threshold / budget can be accepted
- ❖ Distributional considerations are not a part of health economic evaluation per se but need to be taken into consideration by decision makers

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# Why economic evaluation for personalized interventions? (I)



Source: Koerber F, et al. "Early evaluation and value-based pricing of regenerative medicine technologies.", 2013.

# Some strategies to answer health economic questions

- ❖ **Piggy back:**  
Assessment of cost components and effects along-side clinical trials  
(Collection Primary data)

- ❖ **Desk research**  
Assessment of costs components and effects out of pre-existing data  
(Analysis of secondary data)

Study Type	PROs	CONs
Piggy-back design	<ul style="list-style-type: none"><li>▪ Internal validity</li><li>▪ Early information on promising substances</li></ul>	<ul style="list-style-type: none"><li>▪ Generalizability limited</li><li>▪ Cost</li></ul>
Routine data analysis	<ul style="list-style-type: none"><li>▪ Extended time horizon</li><li>▪ External validity</li></ul>	<ul style="list-style-type: none"><li>▪ Time lag</li><li>▪ lack of comprehensive data</li></ul>

- ❖ ....or **Decision analytic modelling**  
Bringing together information on costs components and effects from various sources in a theoretically found model

# Some thoughts on Decision Analytic Modelling

## ❖ Quite common in personalized medicine

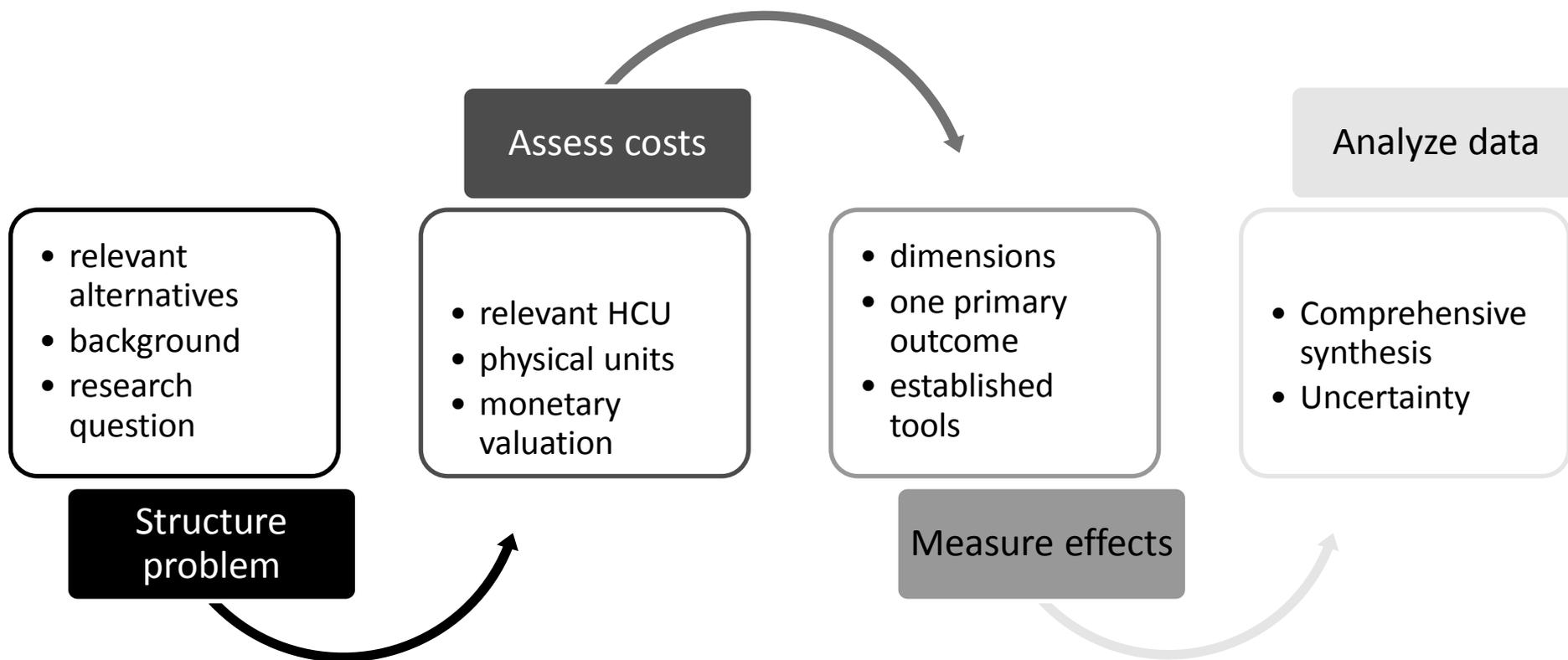
- Early evidence on highly innovative approaches
- Description of dynamic pathways (interaction Diagnosis, treatment, etc.)
- Simultaneous comparison of multiple strategies

## ❖ General issues

- Clear statement of decision problem
- Structure consistent with theory of health condition
- Clear definition of options under evaluation, inclusive incorporation
- Appropriate time horizon

Source: Philips Z, et al.: “Good practice guidelines for decision-analytic modelling in health technology assessment: a review and consolidation of quality assessment.”, 2006.

# 4 Steps of a health economic study



# Steps of a health economic evaluation study:

## Step 1a: Defining a precise research question

- ❖ Does personalized lung cancer treatment save money?
  - effect side ignored
- ❖ How efficient is personalized lung cancer treatment?
  - comparator not specified
- ❖ What the cost per life year gained of Erlotinib based lung cancer treatment in comparison to platinum-based
  - Well defined health economic research question
- ❖ [...] from the perspective of the statutory health insurance in Germany?
  - ... relevant for health care practice?
  - ... does the clinician understand whether the clinical practice corresponds with practice in her own setting?

# Steps of a health economic evaluation study:

## Step 1b: Comprehensive assessment of background

- ❖ Epidemiological background of the target condition
  - Widespread diseases vs. orphan diseases
  - Natural course of the disease
  
- ❖ Currently available interventions
  - Target population
  - Accessibility/Relevance for daily routine
  - Clinical pathways
    - Care setting (e.g. outpatient vs. inpatient)
    - Consequences (e.g. life-long medication intake, rehab....)
  
- ❖ Intervention (in the same detail as currently available approaches)

# Steps of a health economic evaluation study:

## Step 2: Costs

### ❖ “Costs”

- Valued resource consumption of an intervention
- Not necessarily linked to cash-flow

### ❖ Steps in cost measurement

- Identification
- Measurement
- Valuation

### ❖ Valuation preferably based on opportunity costs

- Money can be spent only once
- benefit forgone (because best alternate option cannot be realized)
- Market prices as accepted proxy for true opportunity costs

Source: Krauth C. et al. “Empirical standard costs for health economic evaluation in Germany -- a proposal by the working group methods in health economic evaluation)“, 2005.

# Steps of a health economic evaluation study:

## Step 2a: Relevant components of health care utilization

Component	Relevant elements
<b>Utilization of medical care</b> (= <b>direct medical costs</b> , i.e. economic value of services within the health care system)	<ul style="list-style-type: none"><li>- Physician services</li><li>- Drugs</li><li>- Non-physician services</li><li>- Medical Aids</li><li>- Hospital services</li><li>- Rehabilitation services</li><li>- Formal Nursing care</li></ul>
<b>Resource</b> (= <b>direct non-medical costs</b> , i.e. economic value of services provided outside the health care sector)	<ul style="list-style-type: none"><li>- Time of patients</li><li>- Time of relative/social environment</li><li>- Home help</li><li>- Travel costs</li><li>- Convenience goods</li></ul>
<b>Productivity loss</b> (= <b>indirect costs</b> )	<ul style="list-style-type: none"><li>- Reduced productivity</li><li>- (Temporary) inability to work</li><li>- Premature death</li></ul>

# Steps of a health economic evaluation study:

## Step 2b: measurement and valuation

Relevant elements	Valuation
<ul style="list-style-type: none"> <li>- Physician services</li> <li>- Drugs</li> <li>- Non-physician services</li> <li>- Medical Aids</li> <li>- Hospital services</li> <li>- Rehabilitation services</li> <li>- Formal Nursing care</li> </ul>	<ul style="list-style-type: none"> <li>- Cost per contact</li> <li>- Pharmacy prices less discounts</li> <li>- Negotiated prices (list)</li> <li>- Negotiated prices (list)</li> <li>- DRG + capital costs</li> <li>- Daily cost rate (department)</li> <li>- Negotiated prices</li> </ul>
<ul style="list-style-type: none"> <li>- Time of patients</li> <li>- Time of relatives/social environment</li> <li>- Home help</li> <li>- Travel costs</li> <li>- Convenience goods</li> </ul>	<ul style="list-style-type: none"> <li>- Net income, market prizes similar services</li> <li>- Net income, market prizes similar services</li> <li>- Market prices</li> <li>- Rates from income tax legislation</li> <li>- Market prices</li> </ul>
<ul style="list-style-type: none"> <li>- Reduced productivity</li> <li>- Permanent inability to work</li> <li>- Temporary inability to work</li> <li>- Premature death</li> </ul>	<ul style="list-style-type: none"> <li>- No recommendation</li> <li>- gross income</li> <li>- gross income * friction period</li> <li>- Lifetime gross income / friction costs</li> </ul>

Source: Bock J.-O. et al.: "Calculation of Standardised Unit Costs from a Societal Perspective for Health Economic Evaluation", 2015.

# Steps of a health economic evaluation study:

## Step 3: Identification of relevant effects

### ❖ Life span

- Hard endpoint: Exact quantification feasible
- Increased life expectancy/reduced mortality

### ❖ Quality of life

- Soft endpoint: Subjective valuation
- Morbidity aspects
  - Side effects of treatment/pain
  - Participation in social life
  - Disability
  - Etc.

# Measurement and valuation of health

Step	Important aspects	Example
<b>Measurement</b>	<ul style="list-style-type: none"> <li>▪ Health is multi-dimensional</li> <li>▪ Generic instruments less sensitive</li> <li>▪ Competing, tested instruments</li> </ul>	<ul style="list-style-type: none"> <li>▪ EuroQol 5D values:11111-33333</li> <li>▪ Mobility; Self-care; General activities ; Pain / discomfort; Anxiety / depression</li> <li>▪ 3 value scale =&gt; 243 health states</li> </ul>
<b>Valuation</b>	<ul style="list-style-type: none"> <li>▪ Aim: compare across dimensions</li> <li>▪ Index 0-1</li> <li>▪ Standard gamble, Time-trade-off, Visual analogue scale</li> </ul>	<ul style="list-style-type: none"> <li>▪ EuroQol tarif, based on VAS</li> <li>▪ Similar evaluations across different countries</li> </ul>
<b>(Weighting)</b>	<ul style="list-style-type: none"> <li>▪ Priority e.g. for severe diseases</li> </ul>	Methodologically not solved yet

Source: Brazier J,et al. "Measuring and valuing health benefits for economic evaluation", 2007.

### EQ 5D 5-Level Version

Bitte kreuzen Sie unter jeder Überschrift DAS Kästchen an, das Ihre Gesundheit HEUTE am besten beschreibt.

#### BEWEGLICHKEIT / MOBILITÄT

- ch habe keine Probleme herumzugehen
- ch habe leichte Probleme herumzugehen
- ch habe mäßige Probleme herumzugehen
- ch habe große Probleme herumzugehen
- ch bin nicht in der Lage herumzugehen

#### FÜR SICH SELBST SORGEN

- ch habe keine Probleme, mich selbst zu waschen oder anzuziehen
- ch habe leichte Probleme, mich selbst zu waschen oder anzuziehen
- ch habe mäßige Probleme, mich selbst zu waschen oder anzuziehen
- ch habe große Probleme, mich selbst zu waschen oder anzuziehen
- ch bin nicht in der Lage, mich selbst zu waschen oder anzuziehen

#### ALLTÄGLICHE TÄTIGKEITEN (z. B. Arbeit, Studium, Hausarbeit, Familien- oder Freizeitaktivitäten)

- ch habe keine Probleme, meinen alltäglichen Tätigkeiten nachzugehen
- ch habe leichte Probleme, meinen alltäglichen Tätigkeiten nachzugehen
- ch habe mäßige Probleme, meinen alltäglichen Tätigkeiten nachzugehen
- ch habe große Probleme, meinen alltäglichen Tätigkeiten nachzugehen
- ch bin nicht in der Lage, meinen alltäglichen Tätigkeiten nachzugehen

#### SCHMERZEN / KÖRPERLICHE BESCHWERDEN

- ch habe keine Schmerzen oder Beschwerden
- ch habe leichte Schmerzen oder Beschwerden
- ch habe mäßige Schmerzen oder Beschwerden
- ch habe starke Schmerzen oder Beschwerden
- ch habe extreme Schmerzen oder Beschwerden

#### ANGST / NIEDERGESCHLAGENHEIT

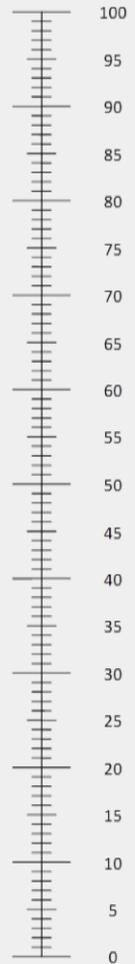
- ch bin nicht ängstlich oder deprimiert
- ch bin ein wenig ängstlich oder deprimiert
- ch bin mäßig ängstlich oder deprimiert
- ch bin sehr ängstlich oder deprimiert
- ch bin extrem ängstlich oder deprimiert

Wir wollen herausfinden, wie gut oder schlecht Ihre Gesundheit HEUTE ist.

- Diese Skala ist mit Zahlen von 0 bis 100 versehen.
- 100 ist die beste Gesundheit, die Sie sich vorstellen können.
- 0 (Null) ist die schlechteste Gesundheit, die Sie sich vorstellen können.
- Bitte kreuzen Sie den Punkt auf der Skala an, der Ihre Gesundheit HEUTE am besten beschreibt.
- Jetzt tragen Sie bitte die Zahl, die Sie auf der Skala angekreuzt haben, in das Kästchen unten ein.

IHRE GESUNDHEIT HEUTE =

Beste Gesundheit, die Sie sich vorstellen können



Schlechteste Gesundheit, die Sie sich vorstellen können

# Steps of a health economic evaluation study:

## Step 4: Dealing with uncertainty

- ❖ Health economic analyses rely on distinct assumptions
  
- ❖ Validity of pre-specified assumptions unknown
  
- ❖ Sensitivity analyses to deal with uncertainty and to check robustness of results
  - Variation of pre-specified assumptions  
(e.g. target population, size of effects, size of costs)
  - Information about existing care & comparators

# Take home messages: Session II

## 1) Structure

- ❖ Clear, answerable question
- ❖ Incorporating all relevant alternatives

## 2) Costs

- ❖ Identification of all relevant resources
- ❖ Measurement in physical units
- ❖ Valuation, ideally at market prices

## 3) Effects

- ❖ Identification of all relevant effects
- ❖ Evidence-based measurement
- ❖ Valuation (esp. cost-utility analyses)

## 4) Data analysis

- ❖ Systematic identification & synthesis of data
- ❖ Appropriate sensitivity analysis

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# Health Economic Evaluation of Personalized Medicine

## - a case study

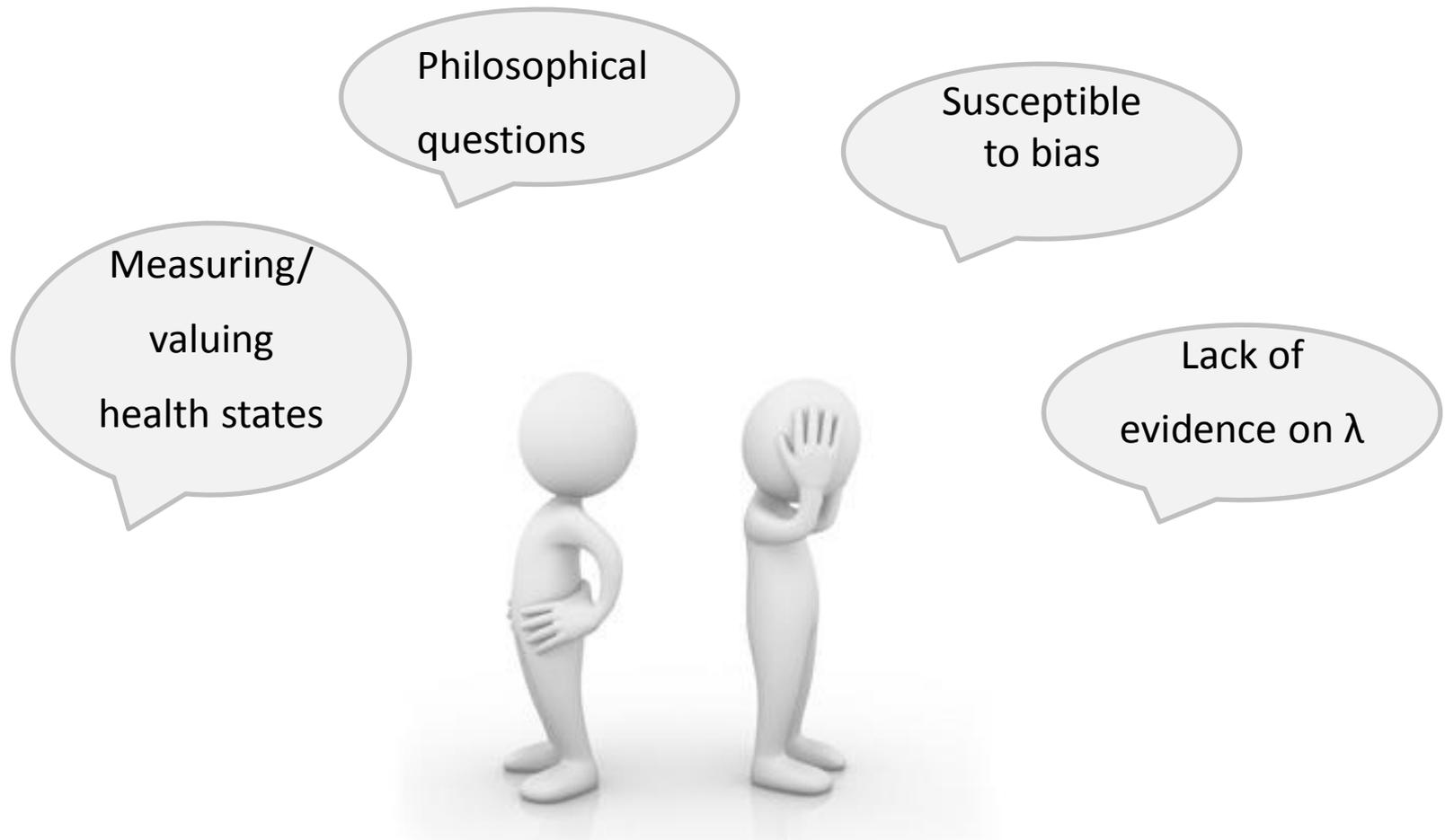
Read through the paper of Schremser et al. with particular focus on methods and results and try to answer the following questions

- ❖ What is the main research question of the study and which way is chosen to answer the question?
- ❖ How are costs incorporated in the study with which final result?
- ❖ How is the effect side assessed in the study with which final result?
- ❖ What is the conclusion on cost-effectiveness and uncertainty around the ICER?

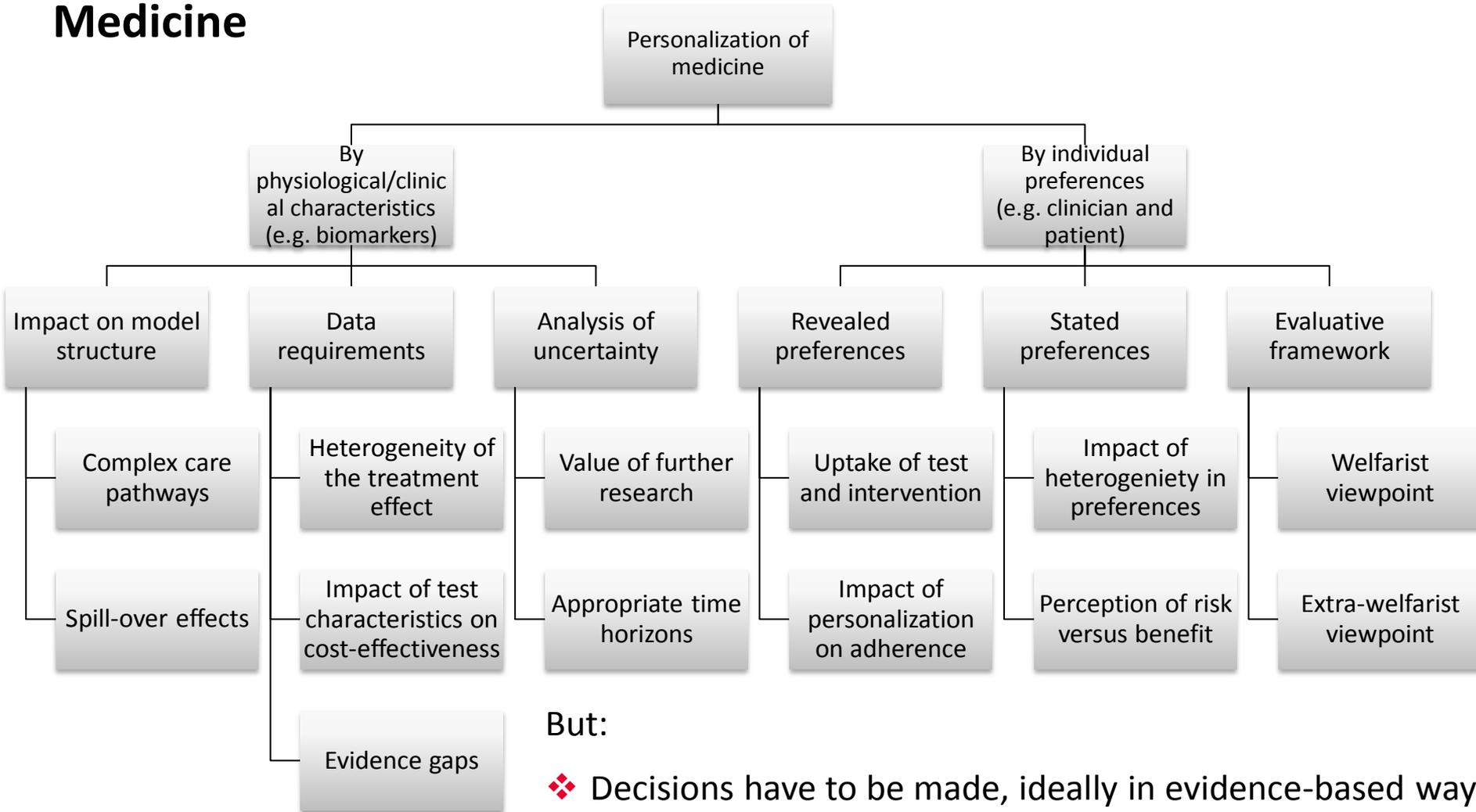
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# General limitations of (not only) model-based economic evaluation



# Particular issues regarding economic evaluation of Personalized Medicine



But:

- ❖ Decisions have to be made, ideally in evidence-based way
- ❖ Alternative to explicit economic evaluation: implicit one

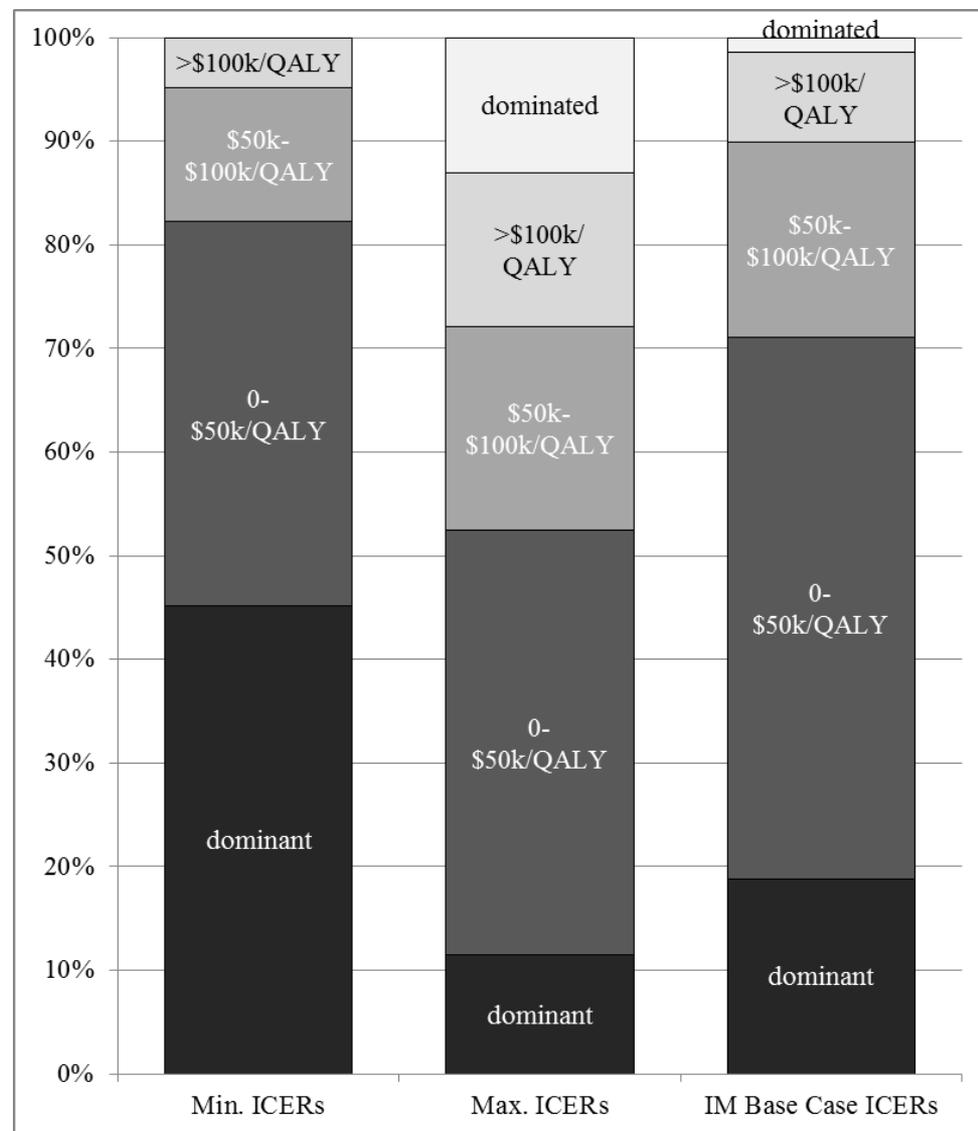
# Increasing relevance of health economics in personalized medicine...

❖ Body of evidence on cost-effectiveness studies in PM (status 206)

Indication	Disease area, # of studies
<b>Cancer, 38 Studies</b>	Breast cancer 18; HNPCC 9; hereditary breast/ovarian, cervical, non-small-cell lung cancer, colorectal cancer 2; lung, prostate, lymphoblastic leukemia 1
<b>Cardio-vascular diseases 20 Studies</b>	Atrial fibrillation, vein thrombosis 4; familial hypercholesterolemia 3; hypertrophic cardiomyopathy, long QT syndrome 2; acute coronary syndrome, thromboembolic events, cardio-vascular disease, hypercholesterolemia, hypertension 1
<b>Other 26 Studies</b>	HIV 10; chronic hepatitis C 5; smoking cessation 2; nephropathies, kidney failure, periodontal disease, MAP, epilepsy, major depressive disorder, schizophrenia, cystic fibrosis, idiopathic pulmonary fibrosis 1

## ...with heterogeneous results....

- ❖ Personalized Medicine in some-cases cost-effective
- ❖ Framework of application decisive
  - screening
  - therapy
- ❖ Overall cost per QALY comparable to those of alternate options



## ... also regarding coverage decision practice...

- ❖ Importance internationally increasing
  
- ❖ Example: National Institute of Health and Care Excellence (NICE), UK
  - Explicit methodological guideline
  - Threshold area
  - Transparent, evidence-based, participative decision process
  - Deliberative inclusion of further aspects
  
- ❖ Example: Non-small cell lung cancer (NSCLC)
  - Epidermal growth factor receptor tyrosine kinase mutation in tumor tissue
  - Intervention: high-cost tyrosine kinase inhibitors
  - Coverage only at reduced price of patient access scheme

# Detailed information available on the NICE website

The screenshot shows a web browser window displaying the NICE website. The address bar shows the URL: <http://publications.nice.org.uk/gefitinib-for-the-first-line-treatment-of-locally-advanced-or-metastatic-non-small->. The browser tabs include "Search Guidelines", "Smoking cessation...", "Pemetrexed for the...", "Gefitinib for the...", and "Lung cancer (non-...". The NICE logo and name "National Institute for Health and Care Excellence" are visible at the top. The navigation menu includes "Home", "News", "Get involved", and "About NICE". Below the navigation menu, there are links for "Find guidance", "NICE Pathways", "Quality standards", "Into practice", and "QOF". A search bar is also present. The main content area displays "NICE technology appraisal guidance Issued: July 2010". The title of the guidance is "TA192 Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer". There is a button to "View the summary and implementation tools" and a "Next" button. A table of contents on the right side lists the following sections: 1 Guidance, 2 The technology, 3 The manufacturer's submission, 4 Consideration of the evidence, 5 Implementation, 6 Related NICE guidance, 7 Review of guidance, and Appendix A: Appraisal Committee members and NICE project team. The main text under "1 Guidance" states: "1.1 Gefitinib is recommended as an option for the first-line treatment of people with locally advanced or metastatic non-small-cell lung cancer (NSCLC) if:" followed by two bullet points: "• they test positive for the epidermal growth factor receptor tyrosine kinase (EGFR -TK) mutation and" and "• the manufacturer provides gefitinib at the fixed price agreed under the patient access scheme." The Windows taskbar at the bottom shows various application icons and the system clock indicating 21:57 on 18.02.2014.

# Use of cost-effectiveness for decision making in Germany

- ❖ Level of health care providers: comparison of reimbursement rate and own costs
- ❖ Level of single health insurance funds
  - Criterion of “efficiency”
  - Examples of cost saving contracts with manufacturers or providers
- ❖ Level of health care system
  - Use of other criteria
  - Cost-effectiveness analysis introduced as §35b, Fifth German Social Code Book
  - Currently debate about methods

 Methodology and use still in infancy, importance likely to increase

## ...despite equity and fairness issues

- ❖ Framework for decision maker → maximizing health subject to budget constraint
- ❖ Theoretical framework: societal decision maker
  - Objective function: health (e.g. LYG)
  - Opportunity costs in the face of fixed budget: health forgone
  - Decision: Adopt if  $\Delta C/\Delta E < \text{threshold value } \lambda$
  - Look at society as a whole (not at the individual person)
- ❖ Distributional effects (10 LYG for 1 = 1 LYG for 10 people) are not relevant (sum ranking rule)
- ❖ Both adoption of cost-ineffective technology and uncertainty induce expected costs

Sources: Claxton, K., „The irrelevance of inference: a decision-making approach to the stochastic evaluation of health care technologies.“, 1999;  
Stinnett, A.A., J. Mullahy, „Net health benefits: a new framework for the analysis of uncertainty in cost-effectiveness analysis“, 1998.

# Broader view on further principles for resource allocation...

## Utilitarianism:

- No. Of life years saved
- No. Of life years prognoses

## Egalitarianism:

## Proceduralism:

- Lottery
- First-come, first served

## Priortarianism:

- Sickest first
- Youngest first

## Social usefulness:

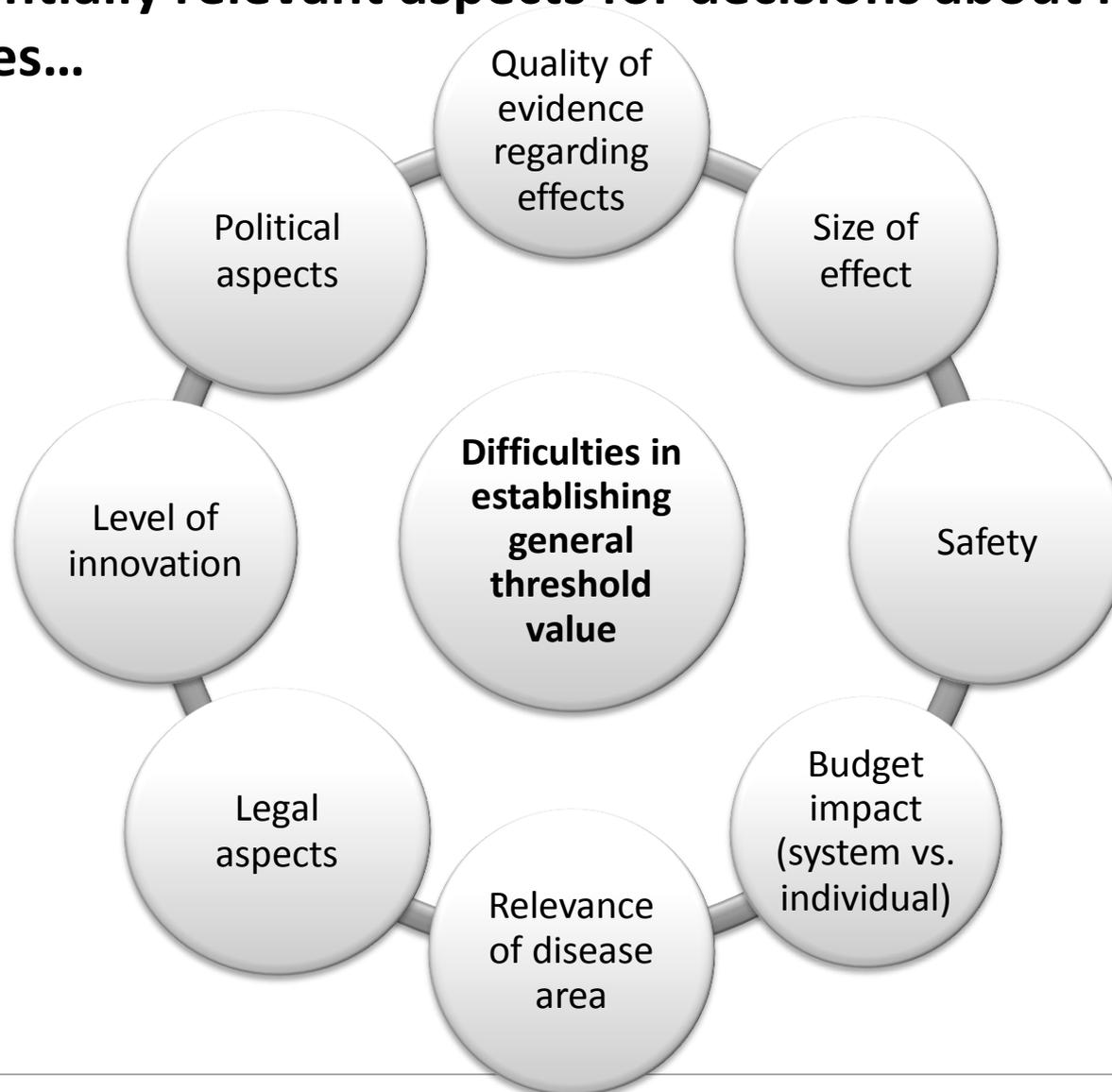
- Instrumental values
- Reciprocity

## Liberalism/ Libertarianism:

- ❖ All approaches with distinct advantages and disadvantages
- ❖ Decision dependent on cultural background and social norms
- ❖ “Perfect” solution cannot be achieved
  - but alternative is implicit / bedside rationing or lobbyism

Sources: Rogowski WH et al. „Criteria for fairly allocating scarce health-care resources to genetic tests: which matter most?“, 2014;  
Persad G et al. „Principles for allocation of scarce medical interventions“, 2009.

# ... and potentially relevant aspects for decisions about new health technologies...



# ... with particular focus on needs-based claims to health care funding...

## ❖ Health need e.g.

- Severity of disease
- Immediacy of need

## ❖ Care need e.g.

- Evidence of benefit
- Availability of alternatives

 Equitable coverage decision requires weighting different criteria

Source: Rogowski W et al. „Using need-based frameworks for priority setting: An application to genetic tests Health Policy”, 2014.

# ... keeping ethical, legal and social implications of personalized medicine in mind (I)

- ❖ Implications of establishing Personalized Medicine into health care
  - Increased amount of health information
    - Privacy
    - Discrimination
    - Physician-patient relationships
    - Liability
  - Exacerbation of existing disparities in healthcare
    - Input-Output problem
    - Cost of health care
    - Access to health care
    - Access to information technologies

Sources: Brothers KB/Rothstein MA. "Ethical, legal and social implications of incorporating personalized medicine into healthcare", 2015; Juengst ET, et al. "After the revolution? Ethical and social challenges in 'personalized genomic medicine'", 2012.

## ... keeping ethical, legal and social implications of personalized medicine in mind (II)

- ❖ Implications of establishing personalized medicine into health care
  - Awareness for drawbacks 4P of personalized medicine
    - Prediction (→ Medicalization, Stigmatization)
    - Prevention (→ Genotypic prevention, Eugenics)
    - Personalization (→ Classification, Essentialism)
    - Participation (→ Personal responsibility, Exploitation)
  - Further evidence on stakeholders, their interest and interactions required
    - Promoters
    - Monitors
    - Providers
    - Users

# Overview: Health economics of personalized medicine

1. Background: Need for economics in health care
2. Basic concepts of health economic evaluation
3. Design of a health economic evaluation study
4. Illustrative example: Decision analytic model for hemochromatosis screening
5. Discussion of the case study
6. Further considerations
7. Take home messages

# Take home messages (I)

- ❖ Health economics offers relevant view on Personalized Medicine
  - Expected costs
  - Total effect on health & resource consumption frequently unclear
    - Sensitivity analysis as tool to account for uncertainty!
- ❖ Costs as monetary valuation of resource consumption (not necessarily cash flows)
  - Direct and indirect costs of care  $\neq$  price of technology (e.g. genetic test)!
  - Perspective of costs can have large impact on cost-effectiveness results
- ❖ Relevance of opportunity costs for prioritizing medical interventions
  - Scarce resources could be used for alternative purposes
  - In health care: other health services are displaced, thus health is forgone

## Take home messages (II)

- ❖ Health economic evaluation as comparison of mutually exclusive alternatives
  - Comparison of costs and effects (clinical endpoints or utilities)
  - QALYs: scientifically controlled aggregation of different dimensions of health
  - Open methodological issues e.g. limited sensitivity of generic health measures
- ❖ Health economic evaluation deals with assessment (i.e. issues of measurement) and appraisal (i.e. issues of valuation) of medical technologies
  - Focus on efficient resource allocation
  - Welfarism: only individual preference rankings, measured in WTP
- ❖ Comprehensive health care decision making requires more than bare results of health economic evaluations
  - Ethical considerations
  - Societally accepted distribution rules

# Take home messages (III)

- ❖ Selected benefits of using health economic evidence in process of translation
  - Research: e.g. measure of (economic) burden of disease
  - Development: e.g. assessing the most valuable use of biomarker
  - Regional market entry: Assessing cost savings for managed entry agreements
  - National market entry: Assessing cost-effectiveness for coverage decision
  
- ❖ Selected issues in the economic evaluation of personalized medicine
  - Structure: complexity, dynamic pathways of care, spill-over effects
  - Effects: limited evidence, economics of changing diagnostic thresholds
  - Costs: small budget impact of diagnostics, potentially large impact of care
  - Data: decreasing sample sizes and technology life cycles complicate general remarks

 Promises of personalized medicine need to be critically assessed case by case

# Literature

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- ❖ Stinnett, A.A., J. Mullahy, „Net health benefits: a new framework for the analysis of uncertainty in cost-effectiveness analysis“, 1998.



"BUT IF YOU WANT THE REAL LOWDOWN, WE'LL  
NEED SOME OF YOUR DNA."

**Thank you!**

[l.schwarzkopf@helmholtz-muenchen.de](mailto:l.schwarzkopf@helmholtz-muenchen.de)