Health economics of personalized medicine
Winter School
“Clinical and Genetic Epidemiology – Strategies to Drive Personalized Medicine“

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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”
  

- “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.

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

Source: Hayden EC. “Technology: The $1,000 genome”, 2014.
... 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.

Personalized therapies... is there a balance between effects gained and cost trends?

Potential costs and effects of personalized care

- Potential costs
  - Testing
  - Care
  - Savings from reduced side effects

- Potential effects
  - Health benefit
  - Empowerment
  - Harms

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“)
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

http://www.visionaware.org/image.ashx?ImageID=6080
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

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)

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

- 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?

http://t2.gstatic.com/images?q=tbn:ANd9GcQJZ4phjw8qJBu4JSvhF5PMSkCQB1PG1EiD_meP_tK1qBd64K_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

<table>
<thead>
<tr>
<th>Program</th>
<th>Δ Cost</th>
<th>Δ Effects</th>
<th>ACER</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Program A</td>
<td>€ 1,500,000</td>
<td>12 LYG</td>
<td>€125,000/LYG</td>
<td>€300,000/3 LYG</td>
</tr>
<tr>
<td>Program B</td>
<td>€ 1,800,000</td>
<td>15 LYG</td>
<td>€120,000/LYG</td>
<td></td>
</tr>
</tbody>
</table>

Δ Cost  Δ Effects  ACER      ICER       
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

<table>
<thead>
<tr>
<th>Factor</th>
<th>Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gene</td>
<td>Prevalence</td>
</tr>
<tr>
<td></td>
<td>• Variant allele common</td>
</tr>
<tr>
<td>Penetrance</td>
<td>• High gene penetrance</td>
</tr>
<tr>
<td>Test</td>
<td>Diagnostic accuracy</td>
</tr>
<tr>
<td></td>
<td>• High sensitivity, high specificity</td>
</tr>
<tr>
<td></td>
<td>• Fast, cheap, broad availability</td>
</tr>
<tr>
<td>Disease</td>
<td>Prevalence</td>
</tr>
<tr>
<td></td>
<td>• Widespread disease</td>
</tr>
<tr>
<td>Natural Course</td>
<td>• High mortality in case of no treatment</td>
</tr>
<tr>
<td></td>
<td>• Substantial decrement on quality of life</td>
</tr>
<tr>
<td>Treatment/Comparator</td>
<td>• Targeted application by responders only</td>
</tr>
<tr>
<td></td>
<td>• Less side effects</td>
</tr>
<tr>
<td></td>
<td>• Enhanced prognosis</td>
</tr>
<tr>
<td></td>
<td>• Small costs differences compared to standard</td>
</tr>
</tbody>
</table>
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)

Research
- burden of disease \(\rightarrow\) relevance
- existing care & therapy

Development
- Early modelling \(\rightarrow\) promising strategies
- Selected biomarker-based strategies

Selective market entry
- value proposition/drivers of value
- managed entry agreement
- Pay for performance

Health systems market entry
- formal coverage decision
- Estimating costs for reimbursement rate determination

Some strategies to answer health economic questions

- **Piggy back:** Assessment of cost components and effects along-side clinical trials (Collection Primary data)
  - **PROs**
    - Internal validity
    - Early information on promising substances
  - **CONs**
    - Generalizability limited
    - Cost

- **Desk research:** Assessment of costs components and effects out of pre-existing data (Analysis of secondary data)
  - **PROs**
    - Extended time horizon
    - External validity
  - **CONs**
    - Time lag
    - Lack of comprehensive data

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

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![Helmholtz logo](logo.png)
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

4 Steps of a health economic study

Structure problem
- relevant alternatives
- background
- research question

Assess costs
- relevant HCU
- physical units
- monetary valuation

Measure effects
- dimensions
- one primary outcome
- established tools

Analyze data
- Comprehensive synthesis
- Uncertainty
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 is 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

Steps of a health economic evaluation study:  
**Step 2a: Relevant components of health care utilization**

<table>
<thead>
<tr>
<th>Component</th>
<th>Relevant elements</th>
</tr>
</thead>
</table>
| **Utilization of medical care**  | - Physician services  
| (direct medical costs,           | - Drugs  
| i.e. economic value of services  | - Non-physician services  
| within the health care system)   | - Medical Aids  
|                                  | - Hospital services  
|                                  | - Rehabilitation services  
|                                  | - Formal Nursing care                                                          |
| **Resource**                     | - Time of patients  
| (direct non-medical costs,       | - Time of relative/social environment  
| i.e. economic value of services  | - Home help  
| provided outside the health care | - Travel costs  
| sector)                          | - Convenience goods                                                            |
| **Productivity loss**            | - Reduced productivity  
| (indirect costs)                 | - (Temporary) inability to work  
|                                  | - Premature death                                                             |
### Steps of a health economic evaluation study: Step 2b: measurement and valuation

<table>
<thead>
<tr>
<th>Relevant elements</th>
<th>Valuation</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Physician services</td>
<td>- Cost per contact</td>
</tr>
<tr>
<td>- Drugs</td>
<td>- Pharmacy prices less discounts</td>
</tr>
<tr>
<td>- Non-physician services</td>
<td>- Negotiated prices (list)</td>
</tr>
<tr>
<td>- Medical Aids</td>
<td>- Negotiated prices (list)</td>
</tr>
<tr>
<td>- Hospital services</td>
<td>- DRG + capital costs</td>
</tr>
<tr>
<td>- Rehabilitation services</td>
<td>- Daily cost rate (department)</td>
</tr>
<tr>
<td>- Formal Nursing care</td>
<td>- Negotiated prices</td>
</tr>
<tr>
<td>- Time of patients</td>
<td></td>
</tr>
<tr>
<td>- Time of relatives/social environment</td>
<td>- Net income, market prizes similar services</td>
</tr>
<tr>
<td>- Home help</td>
<td>- Net income, market prizes similar services</td>
</tr>
<tr>
<td>- Travel costs</td>
<td>- Market prices</td>
</tr>
<tr>
<td>- Convenience goods</td>
<td>- Rates from income tax legislation</td>
</tr>
<tr>
<td>- Reduced productivity</td>
<td>- Market prices</td>
</tr>
<tr>
<td>- Permanent inability to work</td>
<td></td>
</tr>
<tr>
<td>- Temporary inability to work</td>
<td></td>
</tr>
<tr>
<td>- Premature death</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Step</th>
<th>Important aspects</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Measurement</strong></td>
<td>▪ Health is multi-dimensional</td>
<td>▪ EuroQol 5D values:11111-33333</td>
</tr>
<tr>
<td></td>
<td>▪ Generic instruments less sensitive</td>
<td>▪ Mobility; Self-care; General activities; Pain / discomfort; Anxiety / depression</td>
</tr>
<tr>
<td></td>
<td>▪ Competing, tested instruments</td>
<td>▪ 3 value scale =&gt; 243 health states</td>
</tr>
<tr>
<td><strong>Valuation</strong></td>
<td>▪ Aim: compare across dimensions</td>
<td>▪ EuroQol tarif, based on VAS</td>
</tr>
<tr>
<td></td>
<td>▪ Index 0-1</td>
<td>▪ Similar evaluations across different countries</td>
</tr>
<tr>
<td></td>
<td>▪ Standard gamble, Time-trade-off, Visual analogue scale</td>
<td></td>
</tr>
<tr>
<td><strong>(Weighting)</strong></td>
<td>▪ Priority e.g. for severe diseases</td>
<td>Methodologically not solved yet</td>
</tr>
</tbody>
</table>

EQ 5D 5-Level Version

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

BEWEGLICHKEIT / MOBILITÄT
- ich habe keine Probleme herumzugehen
- ich habe leichte Probleme herumzugehen
- ich habe mäßige Probleme herumzugehen
- ich habe große Probleme herumzugehen
- ich bin nicht in der Lage herumzugehen

FÜR SICH SELBST SORGEN
- ich habe keine Probleme, mich selbst zu waschen oder anzuziehen
- ich habe leichte Probleme, mich selbst zu waschen oder anzuziehen
- ich habe mäßige Probleme, mich selbst zu waschen oder anzuziehen
- ich habe große Probleme, mich selbst zu waschen oder anzuziehen
- ich bin nicht in der Lage, mich selbst zu waschen oder anzuziehen

ALLTÄGLICHE TÄTIGKEITEN (z. B. Arbeit, Studium, Hausarbeit, Familien- oder Freizeitaktivitäten)
- ich habe keine Probleme, meinen alltäglichen Tätigkeiten nachzugehen
- ich habe leichte Probleme, meinen alltäglichen Tätigkeiten nachzugehen
- ich habe mäßige Probleme, meinen alltäglichen Tätigkeiten nachzugehen
- ich habe große Probleme, meinen alltäglichen Tätigkeiten nachzugehen
- ich bin nicht in der Lage, meinen alltäglichen Tätigkeiten nachzugehen

SCHMERZEN / KÖRPERLICHE BESCHWERDEN
- ich habe keine Schmerzen oder Beschwerden
- ich habe leichte Schmerzen oder Beschwerden
- ich habe mäßige Schmerzen oder Beschwerden
- ich habe starke Schmerzen oder Beschwerden
- ich habe extreme Schmerzen oder Beschwerden

ANGST / NIEDERGESCHLAGENHEIT
- ich bin nicht ängstlich oder deprimiert
- ich bin ein wenig ängstlich oder deprimiert
- ich bin mäßig ängstlich oder deprimiert
- ich bin sehr ängstlich oder deprimiert
- ich 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 •
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

- Philosophical questions
- Susceptible to bias
- Measuring/valuing health states
- Lack of evidence on $\lambda$
Particular issues regarding economic evaluation of Personalized Medicine

Personalization of medicine

By physiological/clinical characteristics (e.g. biomarkers)
- Impact on model structure
  - Complex care pathways
  - Spill-over effects
  - Evidence gaps

- Data requirements
- Heterogeneity of the treatment effect
- Impact of test characteristics on cost-effectiveness

By individual preferences (e.g. clinician and patient)
- Analysis of uncertainty
  - Value of further research
  - Appropriate time horizons

- Revealed preferences
  - Uptake of test and intervention
  - Impact of personalization on adherence

- Stated preferences
  - Impact of heterogeneity in preferences
  - Perception of risk versus benefit

- Evaluative framework
  - Welfarist viewpoint
  - Extra-welfarist viewpoint

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

HelmholtzZentrum münchen
Deutsches Forschungszentrum für Gesundheit und Umwelt
Increasing relevance of health economics in personalized medicine...

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

<table>
<thead>
<tr>
<th>Indication</th>
<th>Disease area, # of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer, 38 Studies</td>
<td>Breast cancer 18; HNPCC 9; hereditary breast/ovarian, cervical, non-small-cell lung cancer, colorectal cancer 2; lung, prostate, lymphoblastic leukemia 1</td>
</tr>
<tr>
<td>Cardio-vascular diseases, 20 Studies</td>
<td>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</td>
</tr>
<tr>
<td>Other, 26 Studies</td>
<td>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</td>
</tr>
</tbody>
</table>
...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

NICE technology appraisal guidance

TA192 Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer

1 Guidance

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:

- they test positive for the epidermal growth factor receptor tyrosine kinase (EGFR -TK) mutation and
- the manufacturer provides gefitinib at the fixed price agreed under the patient access scheme.
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

Broader view on further principles for resource allocation...

<table>
<thead>
<tr>
<th>Utilitarianism:</th>
<th>Egalitarianism:</th>
<th>Proceduralism:</th>
<th>Priotarianism:</th>
<th>Social usefulness:</th>
<th>Liberalism/ Libertarianism:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No. Of life years saved</td>
<td>• No. Of life years prognoses</td>
<td>• Lottery • First-come, first served</td>
<td>• Sickest first • Youngest first</td>
<td>• Instrumental values • Reciprocity</td>
<td></td>
</tr>
</tbody>
</table>

- 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...

- Quality of evidence regarding effects
- Political aspects
- Size of effect
- Level of innovation
- Difficulties in establishing general threshold value
- Safety
- Legal aspects
- Budget impact (system vs. individual)
- Relevance of disease area
- Size of effect
- Budget impact (system vs. individual)
- Relevance of disease area
- Legal aspects
- Level of innovation
- Difficulties in establishing general threshold value
... 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

... 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

... 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 ≠ 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

- Adams PC, Barton JC. “Haemochromatosis” 2007. http://t2.gstatic.com/images?q=tbn:ANd9GcQJZ4phjw8qJBu4JSvhF5PM SkCQB1PG1EiD_meP_tK1qBd64K_0zv4G


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Thank you!

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