

# SUMMARY OF DAY 5

Clinical and Genetic Epidemiology Winter  
School (February 10, 2017)

---

Christina Strauß & Katharina Schremser

Großhadern, February 17, 2017

# Part 1: Personalized Medicine and Study Designs

Friday 10. Feb 2017

<b>Time</b>	<b>Topic</b>	<b>Responsible</b>
9:15 – 10:45	Personalized Medicine and Study Designs	Prof. Strauch
11:15 – 12:45	Personalized Medicine and Study Designs	Prof. Strauch
14:15 – 15:45	Health economics and ethics	Dr. Schwarzkopf
16:15 – 17:45	Health economics and ethics	Dr. Schwarzkopf

# Genetic Epidemiology

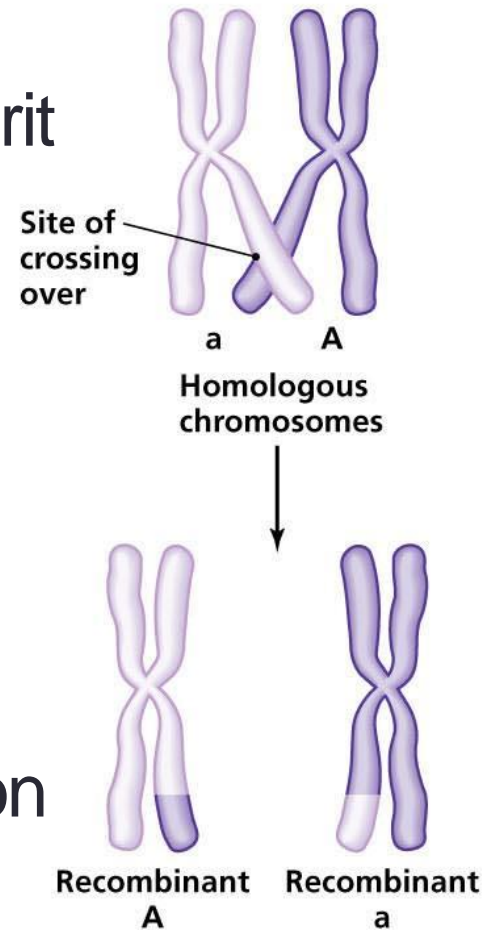
## - general idea

- Identification of gene(s) causing a disease NOT all genes involved in it
- Look for genetic regions DIFFERING between affected and unaffected patients
- Important:
  - > Mode Of Inheritance
  - > Penetrance

# Genetic Linkage

getting away from the idea that you inherit the identical chromosome you inherited from your father or your mother

- Linkage: describes events of chromosomal recombination in a family
- Linkage Disequilibrium: describes events of chromosomal recombination in a population - > tagging SNP



# Study design and type of Analyses

- Linkage Analysis vs. Association Analysis
- Population-based vs. Cohort
- Case/Control vs Family (Trio)

How rare is the disease / the genetic variant you are examining

How is your budget?

-> trend goes back to family design  
(sequencing of loci to get rare variants)

# Biomarkers

- **DIANOSTIC** – Who is sick?
- **RISK** – Who is in risk of becoming sick?
- **PROGNOSTIC** – If the person is sick, how will the course of disease be?

**PREDICTING THE OUTCOME** – the ultimate aim

# Biomarkers

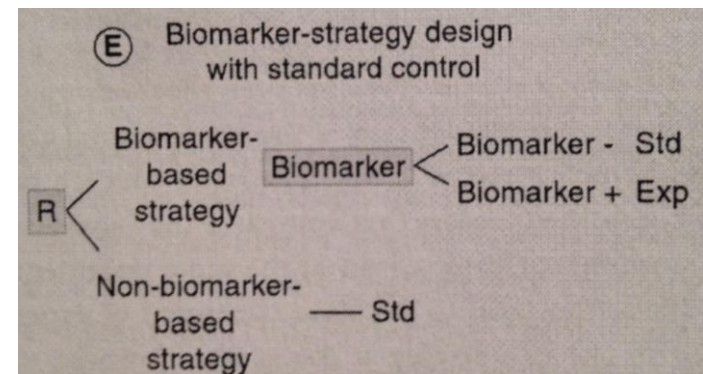
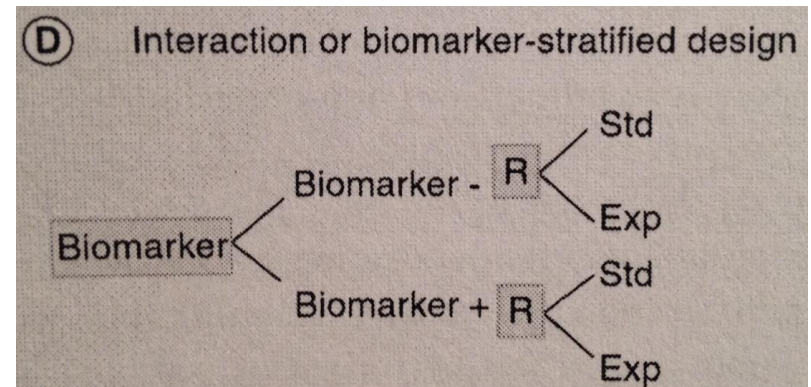
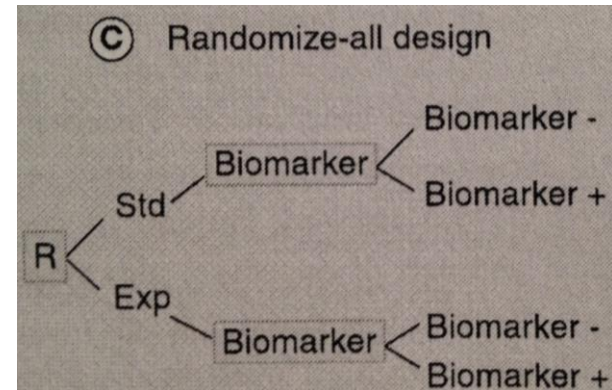
## Retrospective identification and prospective validation

- Prognostic biomarkers: associated with outcome independent of treatment
- Predictive biomarkers: predict efficacy of a certain treatment for a disease

# Biomarkers

Randomization  
designs for Phase III  
trials have low  
statistical power

when Biomarker is  
reliable: targeted trial  
design to reduce patient  
number





# Part 2: Health economics and ethics

Friday 10. Feb 2017

<b>Time</b>	<b>Topic</b>	<b>Responsible</b>
9:15 – 10:45	Personalized Medicine and Study Designs	Prof. Strauch
11:15 – 12:45	Personalized Medicine and Study Designs	Prof. Strauch
14:15 – 15:45	Health economics and ethics	Dr. Schwarzkopf
16:15 – 17:45	Health economics and ethics	Dr. Schwarzkopf

# Types of health economic studies



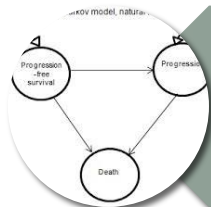
Piggy back

Primary data



Routine data (e.g. claims data, registries)

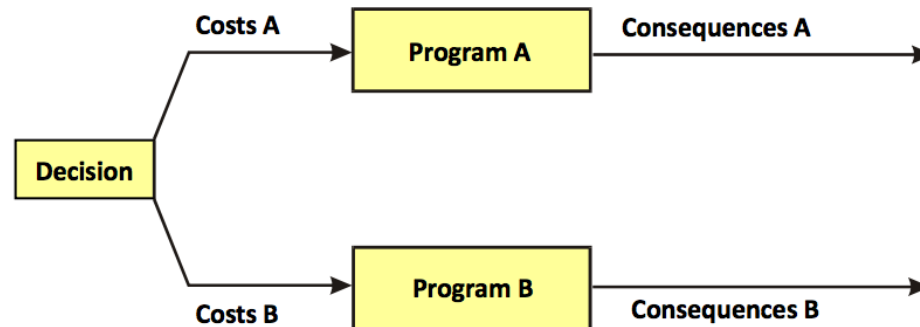
Secondary data



Health analytic modeling

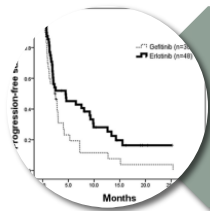
Synthesis of sources

# Basic approaches of health economic evaluation



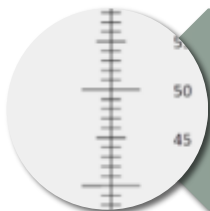
Cost Minimization Analysis  
→ *only costs count*

Zaltrap vs. Avastin in mCR



Cost-Effectiveness Analysis  
→ *Effects in physical units*

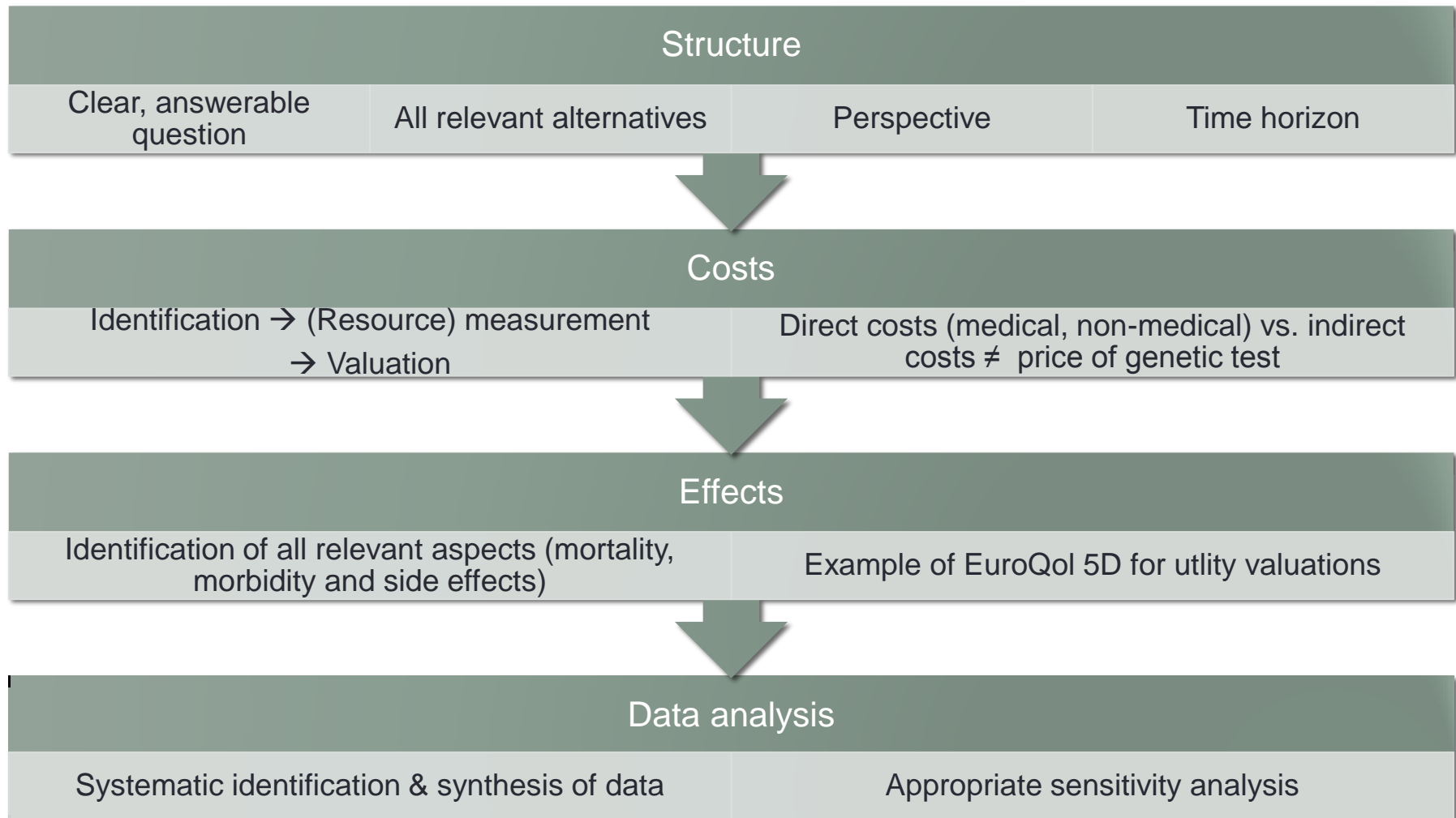
Erlotinib vs Gefitinib in EGFR M+ NSCLC



Cost-Utility Analysis  
→ *Multidimensional outcome parameter (QALY)*

CRC/HH screening Case study

# Steps of health economic evaluation



# Factors enhancing the cost-effectiveness of personalized medicine

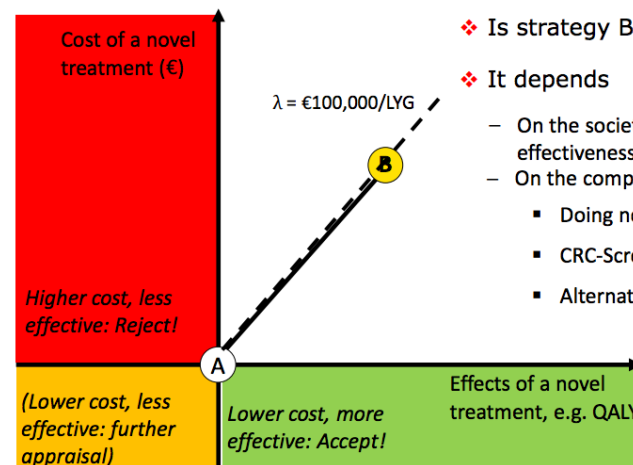
	<b>Factor</b>	<b>Requirement</b>
<b>Gene</b>	Prevalence	• Variant allele common
	Penetrance	• High gene penetrance
<b>Test</b>	Diagnostic accuracy	• High sensitivity, high specificity
	Cost	• Fast, cheap, broad availability
<b>Disease</b>	Prevalence	• Widespread disease
	Natural Course	• High mortality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

→ the lower the ICER, the higher the probability of being cost-effective

# It's all about the increments...

Combination of both (cost and effect) parameters in a single outcome e.g. incremental cost effectiveness ratio (ICER)

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



- ❖ 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



20,000-30,000€

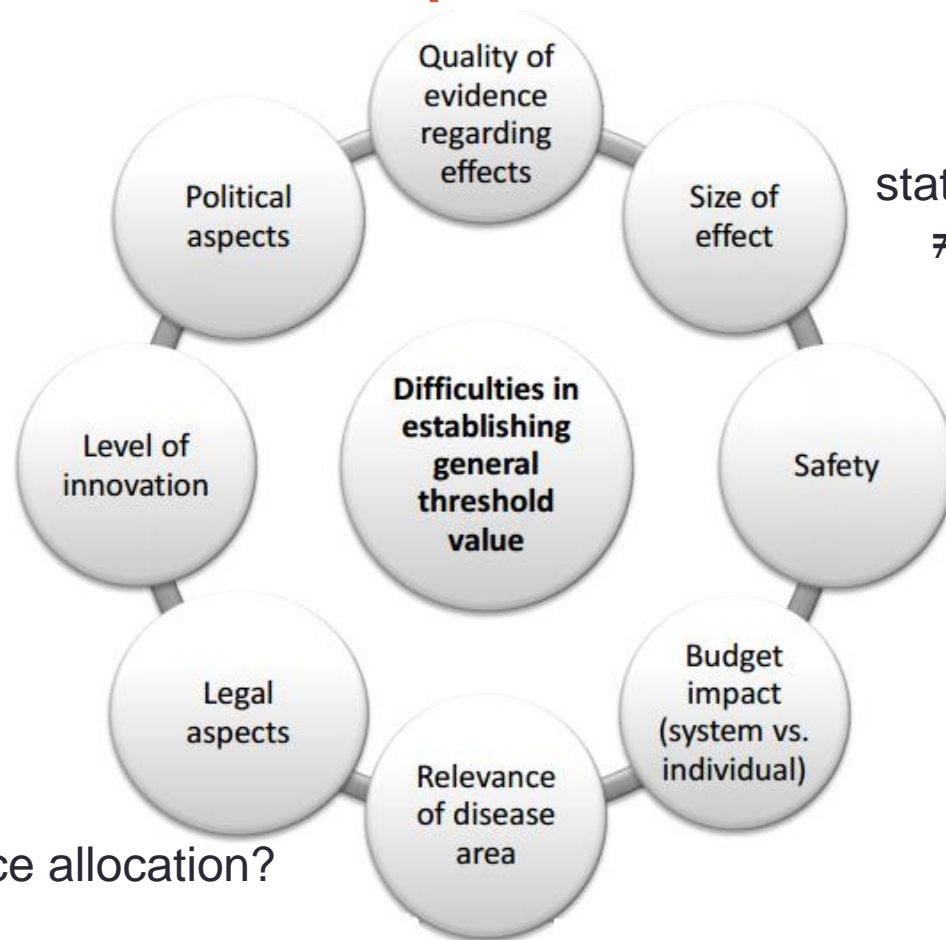


three times a country's gross domestic product

Is it enough?

→ no willingness-to-pay threshold in Germany

# Potentially relevant aspects for decision making



Ethical issues in resource allocation?

→ different principles ranging from liberalism (US) over prioritarianism to utilitarianism (e.g. QALY maximisation)