SUMMARY OF DAY 5

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

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Großhadern, February 17, 2017

Part 1: Personalized Medicine and Study Designs

Friday 10. Feb 2017

Time	Topic	Responsible
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

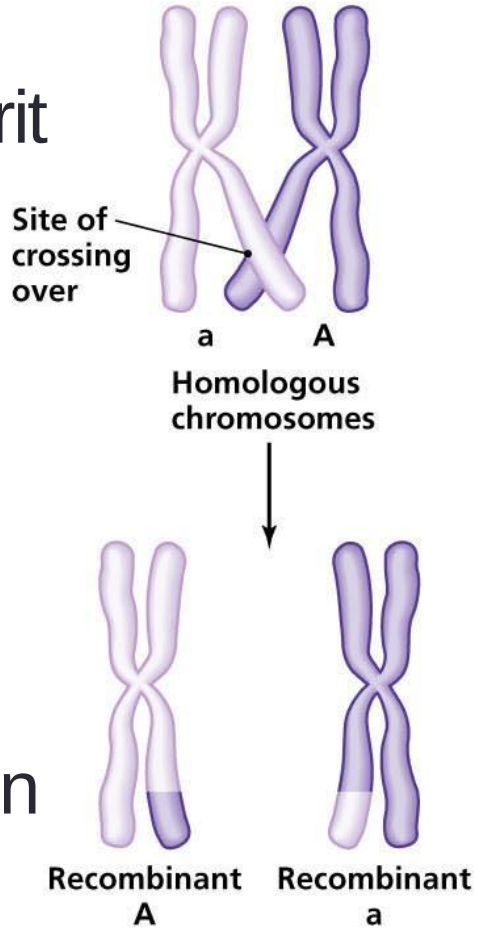
- Identification of gene(s) causing a disease NOT all genes involved in it
- Look for genetic regions DIFFERING between affected and unaffected patients

- 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 <u>family</u>
- Linkage Disequilibrium: describes events of chromosomal recombination in a <u>population</u> - > 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

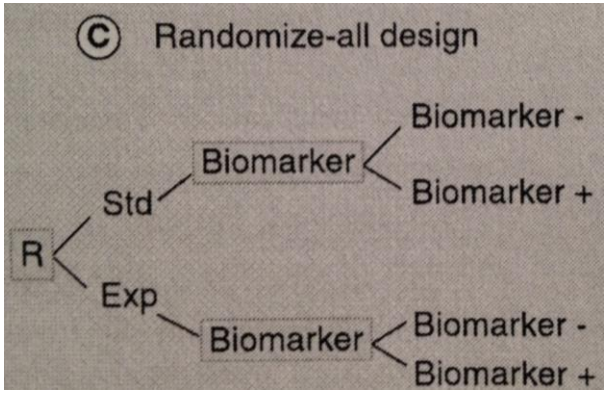
- Prognostic biomarkers: associated with outcome independent of treatment

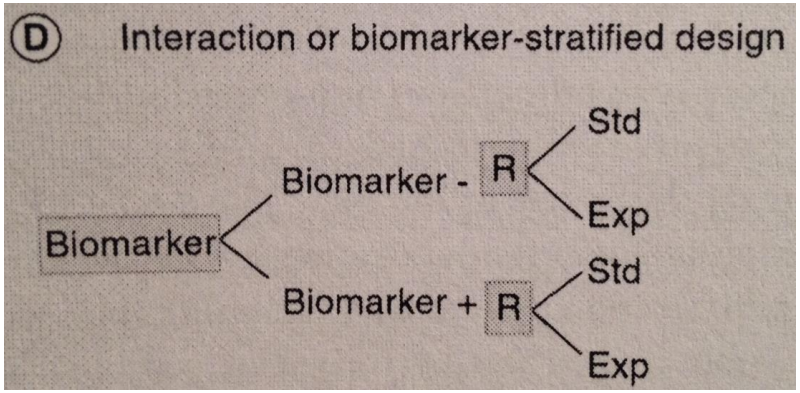
- Predictive biomarkers: predict efficacy of a certain treatment for a disease

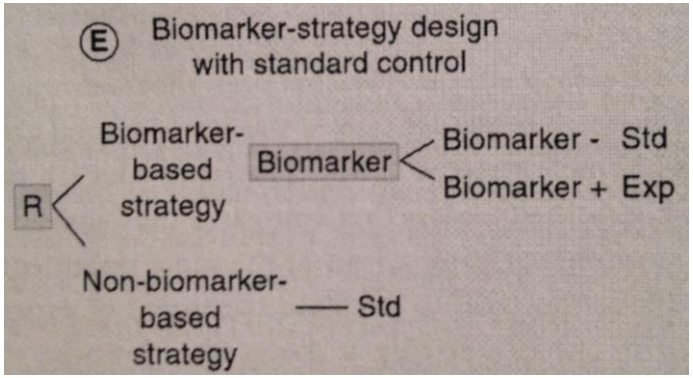
Biomarkers

<u>Randomization designs for Phase III trials have low statistical power</u>

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







Part 2: Health economics and ethics

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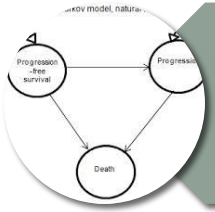
Types of health economic studies

Piggy back

Primary data

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

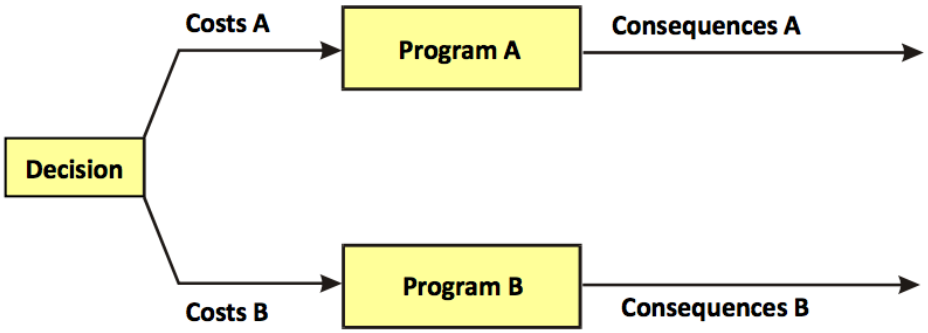
Secondary data



Health analytic modeling

Synthesis of sources

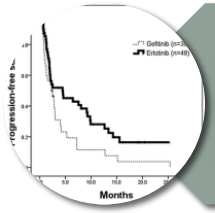
Basic approaches of health economic evaluation



Cost Minimization Analysis

→ *only costs count*

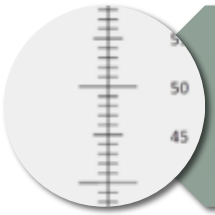
Zaltrap vs. Avastin in mCR



Cost-Effectiveness Analysis

→ *Effects in physical units*

Erlotinib vs Gefitinib in EGFR M+ NSCLC

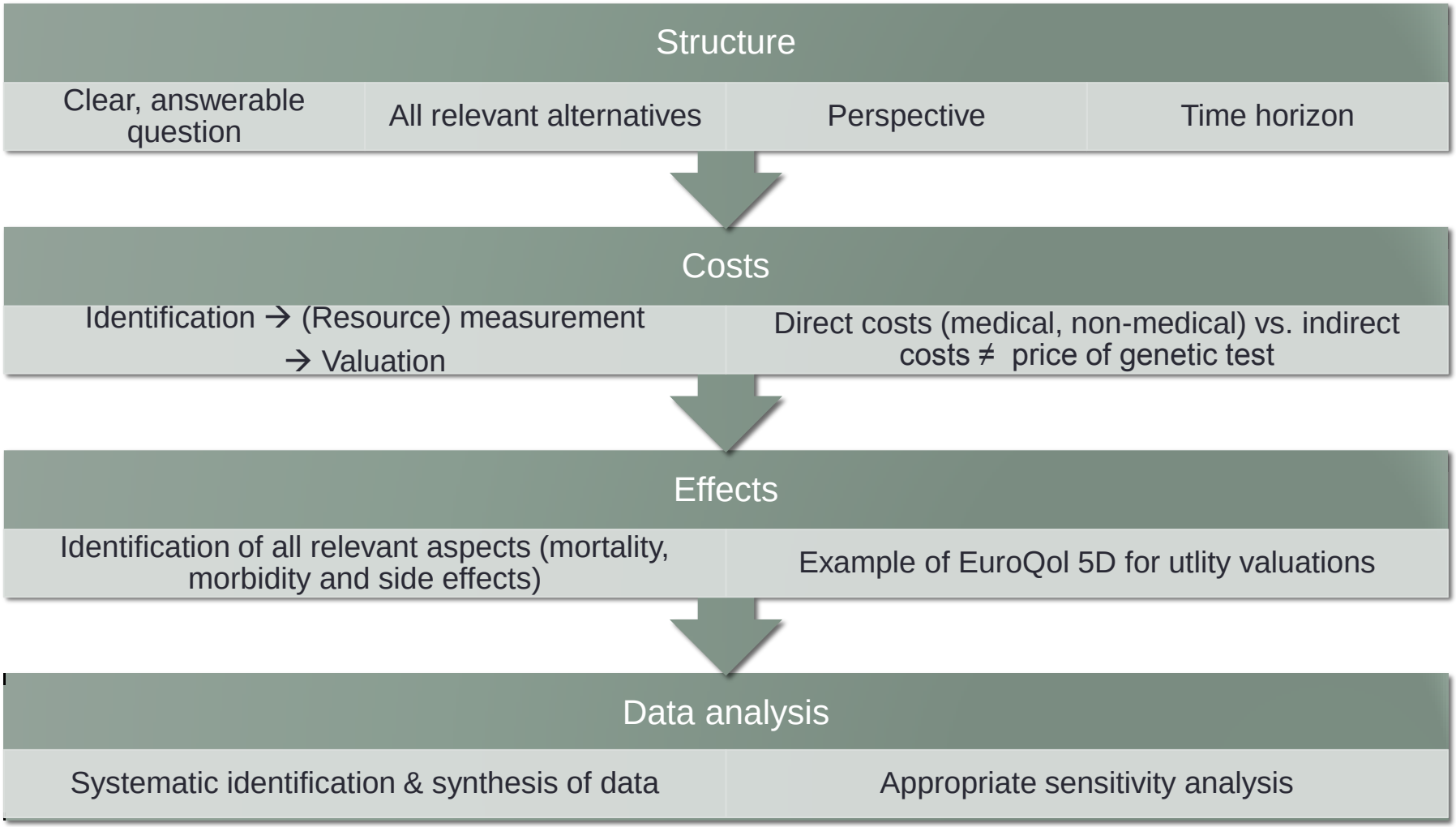


Cost-Utility Analysis

→ *Multidimensional outcome parameter (QALY)*

CRC/HH screening Case study

Steps of health economic evaluation



Factors enhancing the cost-effectiveness of personalized medicine

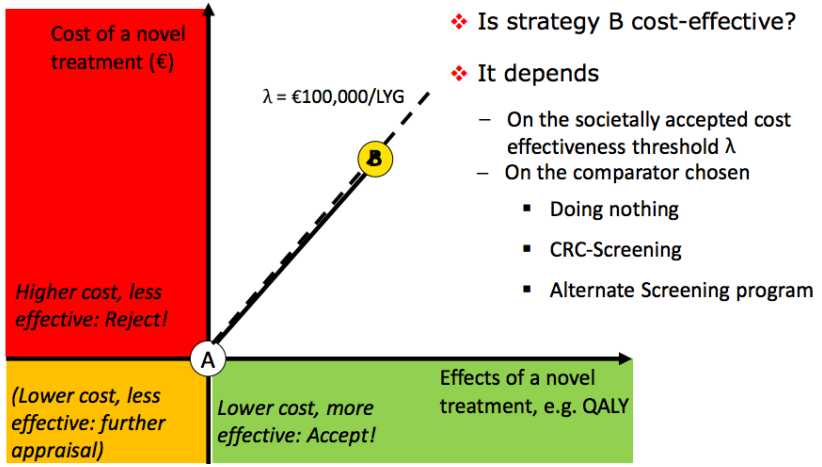
	Factor	Requirement
Gene	Prevalence	• Variant allele common
	Penetrance	• High gene penetrance
Test	Diagnostic accuracy	• High sensitivity, high specificity
	Cost	• Fast, cheap, broad availability
Disease	Prevalence	• Widespread disease
	Natural Course	• High mortality in case of no treatment • Substantial decrement on quality of life
Treatment/ Comparator		• 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)

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

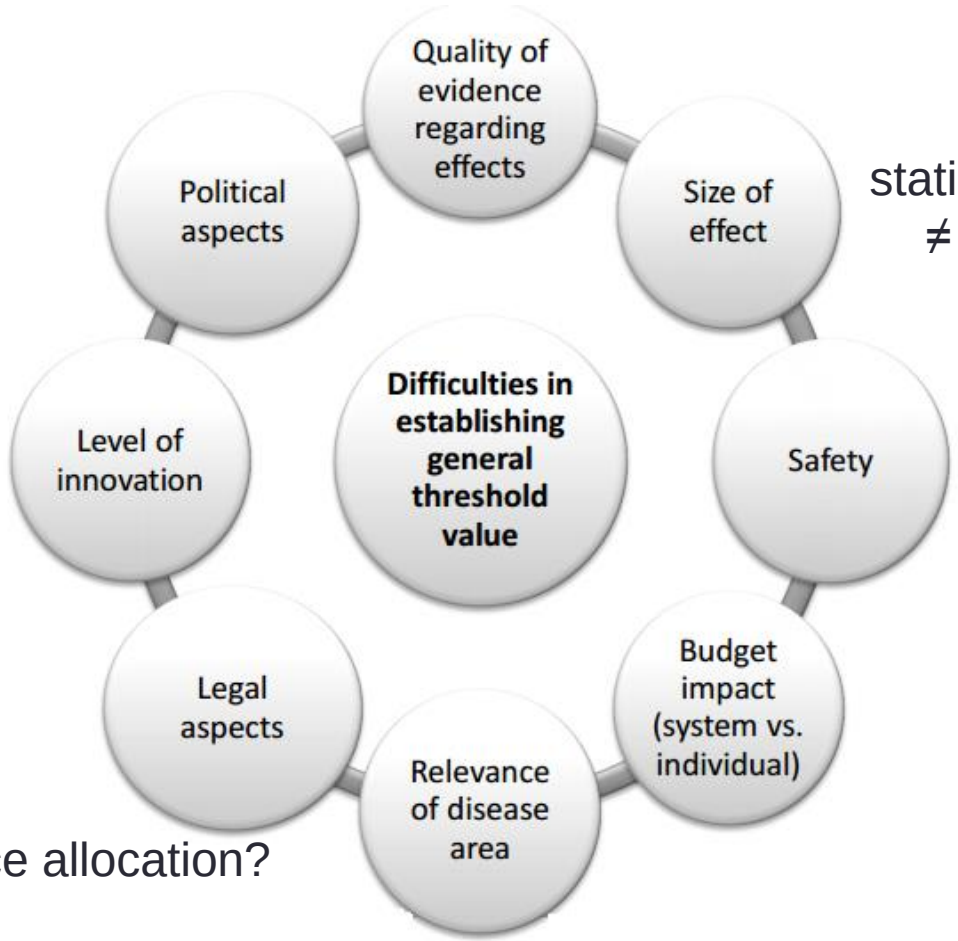


- NHS: 20,000-30,000£
- WHO: three times a country‘s gross domestic product

Is it enough?

→ no willingness-to-pay threshold in Germany

Potentially relevant aspects for decision making



statistical significance ≠ clinical relevance

Ethical issues in resource allocation?

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