How to design a phase-II study

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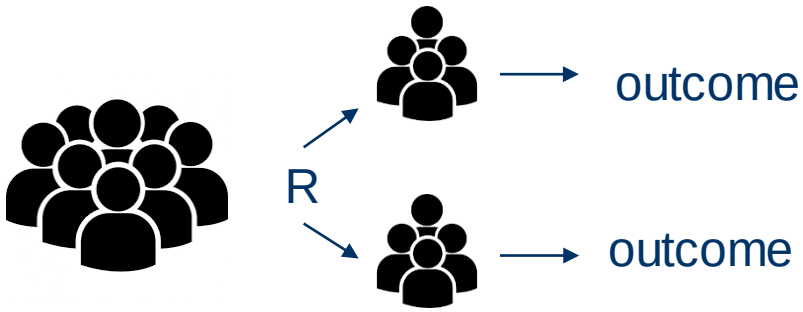
Two components



Scientific design

Operational considerations

Clinical trials

are considered the „Gold Standard“ in clinical research.

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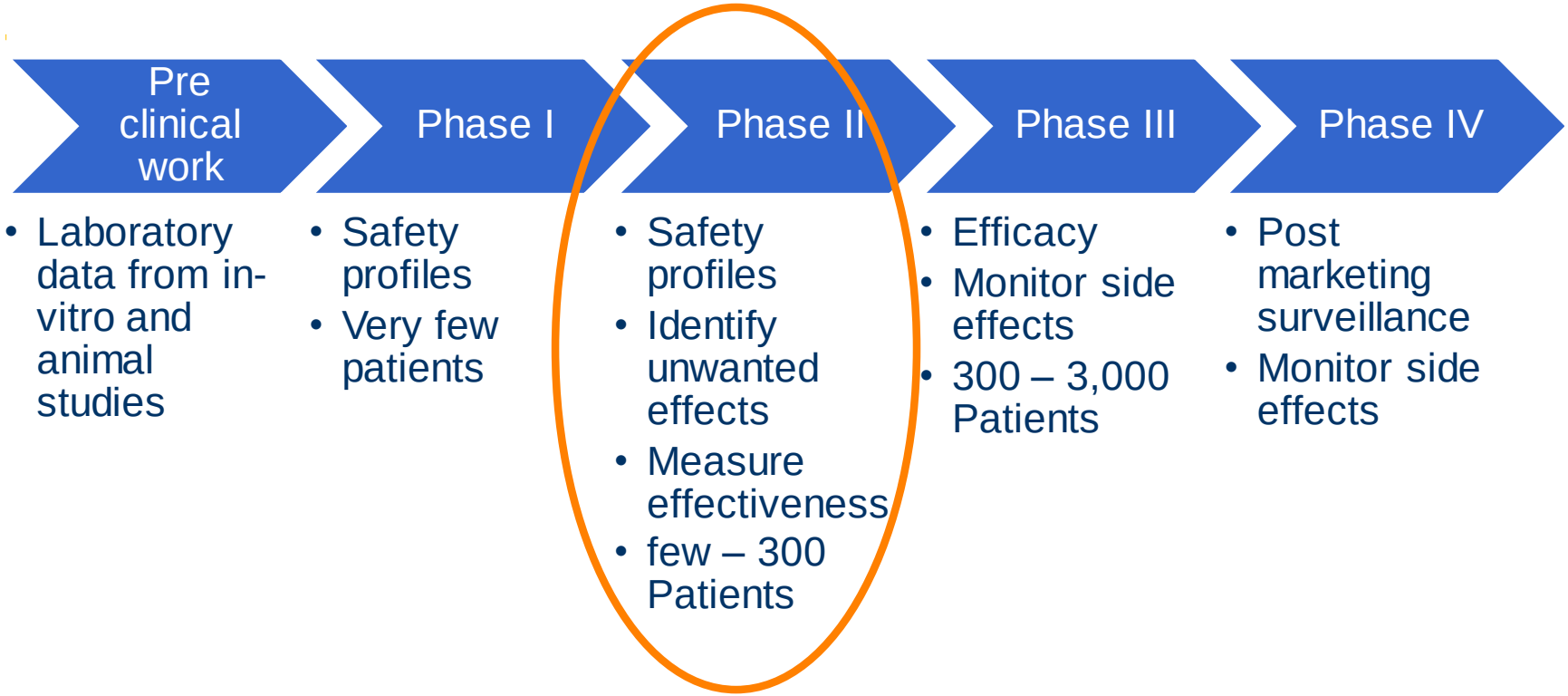

Phase II clinical trials

- Provide information to assess whether a treatment should be tested further in larger Phase III trials.

- Therefore they must be designed, performed and reported to allow
  - accurate interpretation of results
  - obtain the best quality data in an efficient way to
  - allow for an **unbiased decisions** regarding the subsequent development of the investigation under study

Scientific considerations

- Aim of the trial – Study objective
  - What am I trying to show with the planned trial?
    - Most promising candidate? Go/no-go decision? Evidence of activity? Dose finding? Proof of principle?
  - Biomarker
  - Is the question “answerable”?
  - How can we optimize potential benefit (and what we learn) while minimizing potential harm?

Safety profiles

Identify side effects

Measure effectiveness

Scientific considerations

- Sample population & size

  - Which patient population needs to be included?
  - How many patients need to be included into the trial in order to provide enough information to be able to make an assumption?

  - Eligibility: inclusion and exclusion criteria
    - Narrow definition
      - homogeneous patient group, fewer confounding variables
      - results applicable to narrow patient profile
      - harder to recruit patients
    - Broad definition
      - greater potential for confounding variables to affect results
      - results more broadly applicable
      - easier to recruit patients

Scientific considerations

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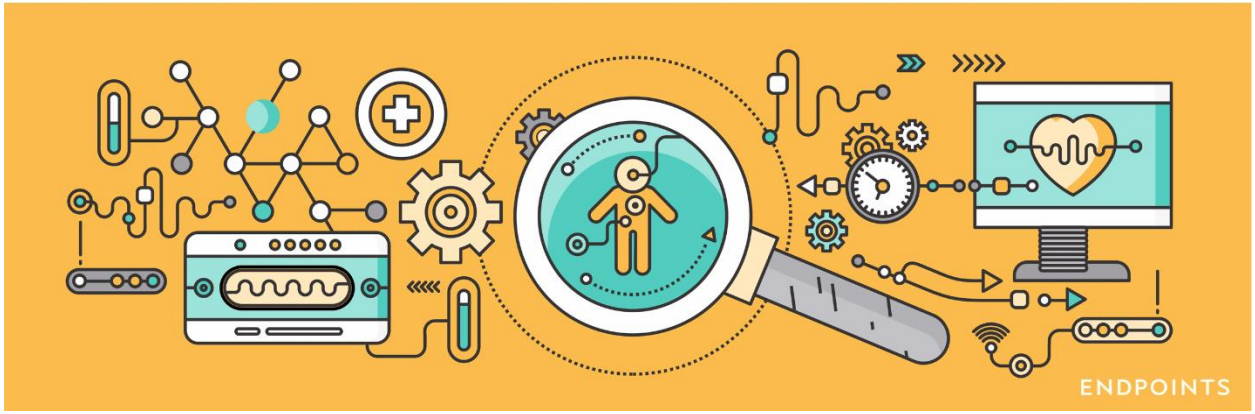
- End points and outcome measurements
  - What are the most appropriate primary endpoints? Secondary?
  - Outcomes must be quantifiable
  - Outcomes must be standardized
  - What data do I need to collect to provide information on the questions asked?
    - Adverse events



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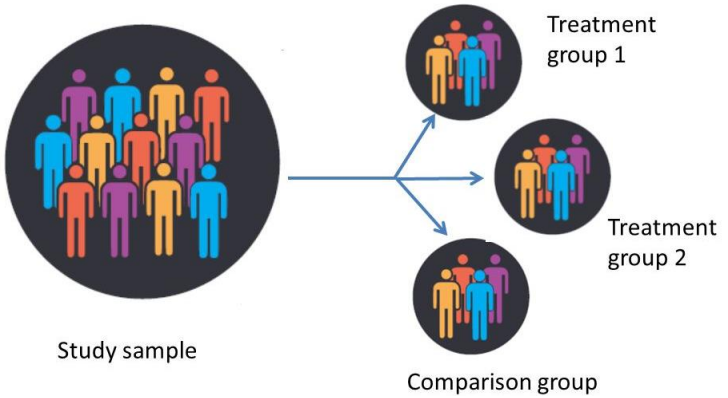
Scientific considerations

- Randomization
  - Yes/No? Blinded/non-blinded?

Allocation of treatments is carried out using a chance mechanism so that neither the patient nor the physician know in advance which therapy will be assigned



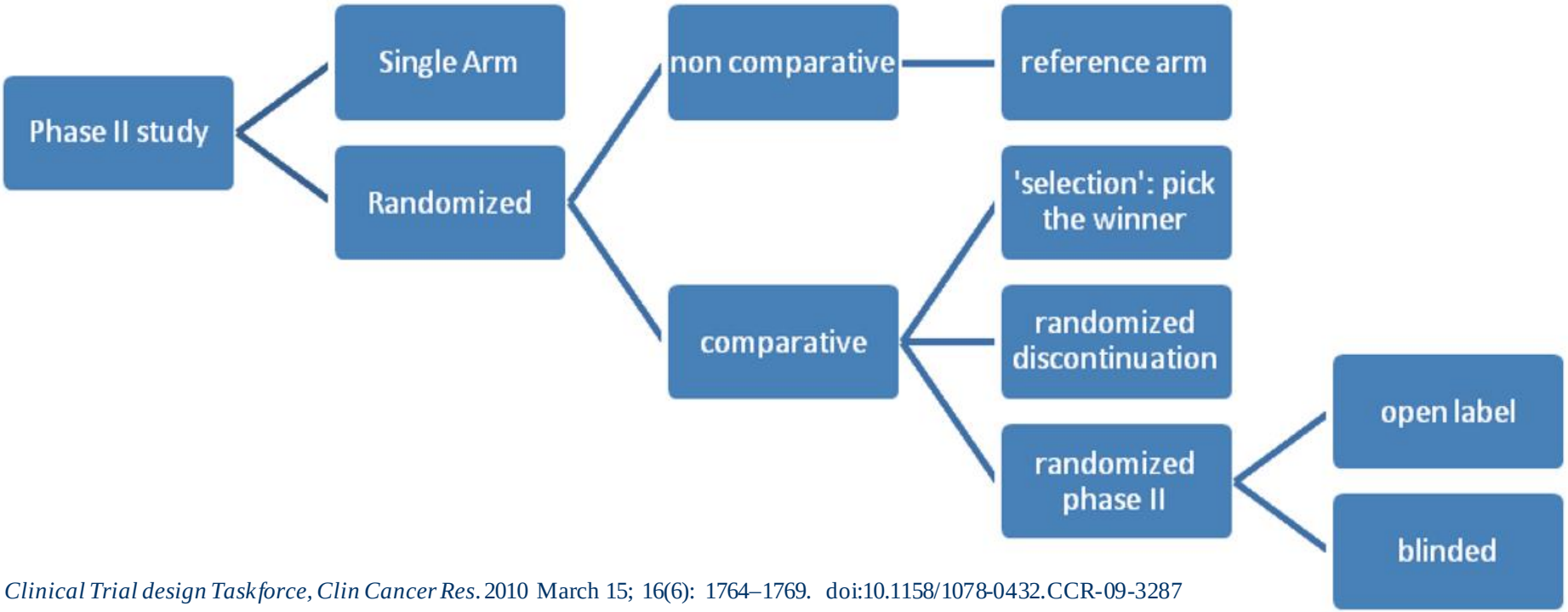
Considerations:

- Simple Randomization: May result in substantial imbalance
- Block and/or stratified randomization
- Alternatives: Historical controls, non-randomized concurrent controls, standard of care, etc

- Blinding/Placebo

Scientific considerations

- Trial designs
  - Choose most appropriate design: e.g. single-arm, parallel, cross-over, factorial, etc.



Clinical Trial design Taskforce, Clin Cancer Res. 2010 March 15; 16(6): 1764–1769. doi:10.1158/1078-0432.CCR-09-3287

Scientific considerations

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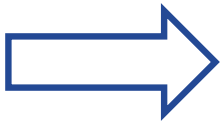
- Trial designs
  - The design of any clinical trial should always be carefully evaluated and justified based on the characteristic specific to the situation.
  - There is no

Be informed regarding design choices, considering all aspects of trial design from trial aims and outcomes, to randomization and the type of design to use.

Scientific considerations

- Aim of the trial
- End points
- Sample size
- Randomization
- Trial designs



STATISTICIAN

"To call in the statistician after the experiment is done may be no more than asking him to perform a postmortem examination: he may be able to say what the experiment dies of."

-R.A. Fisher, Indian Statistical Congress, Sankhya, ca 1938

Two components

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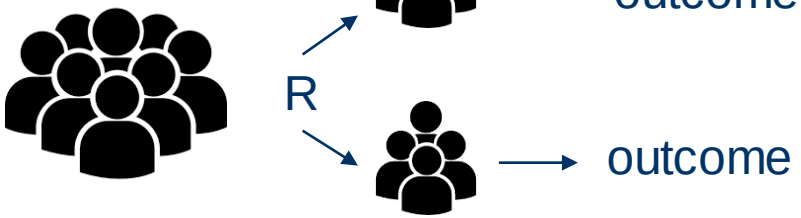

Scientific design

Operational issues to consider during the design of a clinical trial

First things first

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Keyplayers

- Patient
- Principal Investigator
- Sponsor
- Study team
- Institutions / Clinical trial site
- Cooperations, Translational research
- Clinical Research Organizations (CRO), Monitors
- Pharmaceutical companies
- Authorities / Independent Review Boards / Ethical Committees

Core Document

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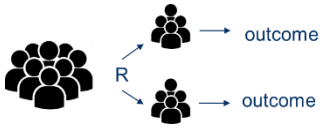
STUDY PROTOCOL

Protocols are necessary to organize research in a logical, focused, and efficient way.

- Protocol lays out who, what, why, when, where, how
- Safeguards participants
- Safeguards study integrity

Key elements:



Study design

Objectives & Inclusion/exclusion criteria

Procedures

Schedule of Assessments

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Not to forget

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Timelines

Finances

- Schedule of Assessments
- Number of patients and sites
- Supplies
- Case report form (CRF, electronic/paper)
- Insurance
- Investigational product
- Monitoring

Legal issues & Guidelines

- Laws and regulations (local & international)
- Contracting
- Good Clinical Practice (GCP)

Road to success

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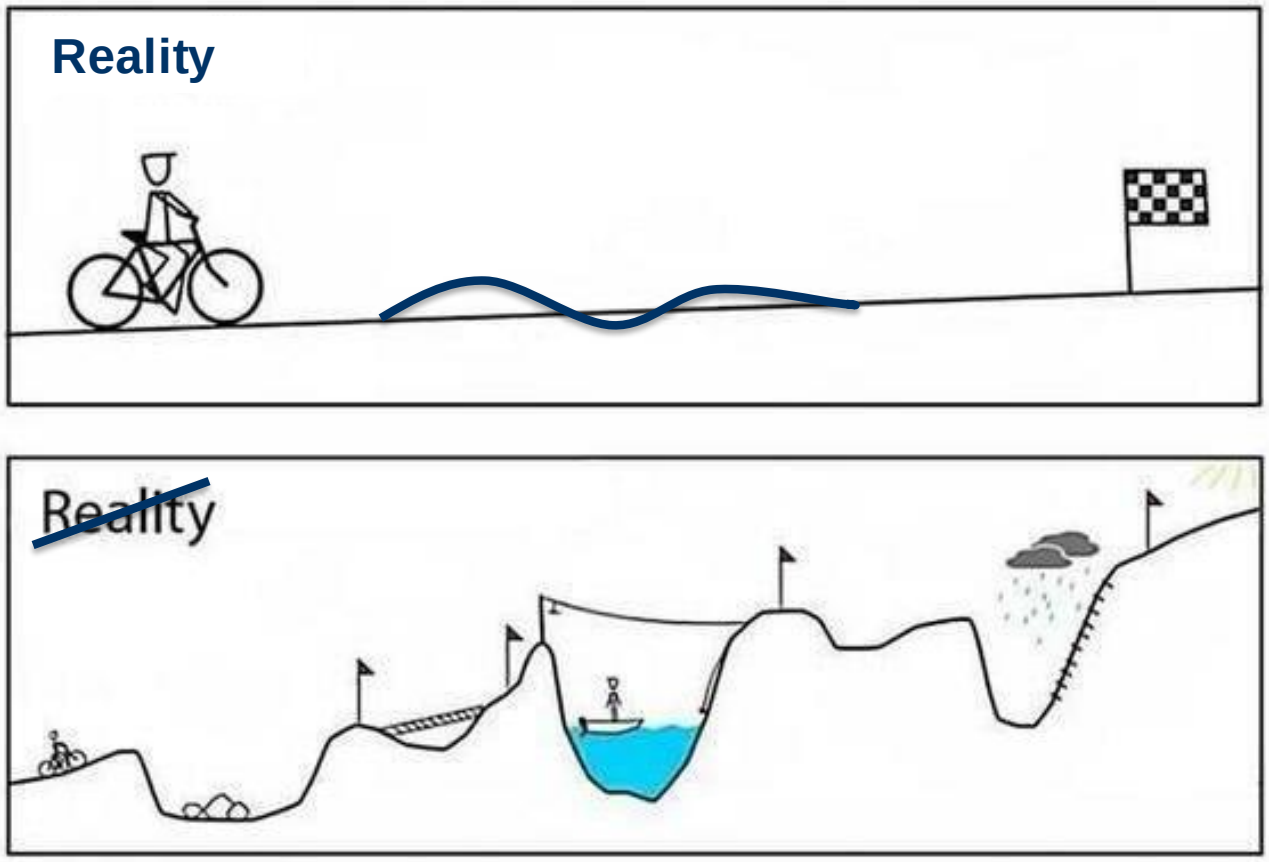

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Useful links

EMA

http://www.ema.europa.eu/ema/

FDA

https://www.fda.gov/

ICH-GCP

http://www.ich.org/products/guidelines/efficacy/efficacy-single/article/good-clinical-practice.html

TAKE HOME MESSAGE

Careful planning, cooperations & networking are the key to a successfull clinical trial