

Module II: The Trial Landscape

Unit: Main Features of Clinical Trial Design

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- Why clinical trials?

■ Main features of clinical trial design

- The history of clinical trials
- The drug development process
- Phases of clinical trials
- Clinical trial players
- Trial guidelines - GMP, GLP and GCP
- Quality assurance – audits and inspections
- Research ethics
- Risk and benefits of trial participations

Main features of clinical trial design

■ Biomedical Study Design

■ Cross sectional - Longitudinal

- Retrospective - Prospective
- Observational - Experimental

The cross-sectional study design can be used to determine disease prevalence in the community such as asthma, construction of clinical reference values such as child weight growth chart values or the evaluation of a diagnostic test such as diagnosis of cancer.

The longitudinal study is especially useful to define disease incidence over a certain time period, construction of longitudinal clinical reference values, evaluation of prognostic tests, describe natural history of a disease and to identify risk factor association.

Main features of clinical trial design

■ Biomedical Study Design

■ Cross sectional - Longitudinal

■ Retrospective - Prospective

- Observational - Experimental

The most well-known retrospective study design is the case-control.

Most other longitudinal studies are prospective in nature whereby the data is collected when time passes along.

Main features of clinical trial design

■ Biomedical Study Design

- Cross sectional - Longitudinal
- Retrospective - Prospective

Observational - Experimental

Most biomedical studies at least clinical studies are observational in nature, i.e. without introducing any intervention such as a medical treatment or a clinical procedure.

The experimental study is used to evaluate the effect of new medical treatments or prevention health programs. Typical examples are drug trials and surgical procedure studies.

Main features of clinical trial design

■ Clinical Trial Design

- Cross sectional - Longitudinal
- Retrospective - Prospective
- Observational - Experimental

Explorative trials Confirmatory trials

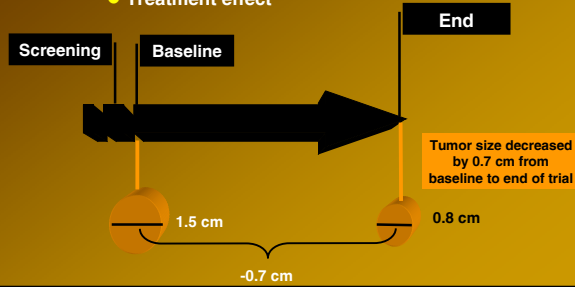
Main features of clinical trial design

■ Clinical trial design - phrases

- Endpoint or outcome measure
- Efficacy, safety or quality of life
- Primary versus secondary outcome(s)
- Clinical versus surrogate outcome
- Biases of study results
- Parallel design versus cross-over design
- Controls
- Randomisation
- Blinding

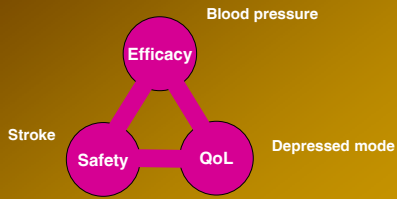
Main features of clinical trial design

- Endpoint or outcome measure
 - Screening value
 - Baseline value
 - Study end value
 - Treatment effect



Main features of clinical trial design

- Efficacy, safety or quality of life (QoL)



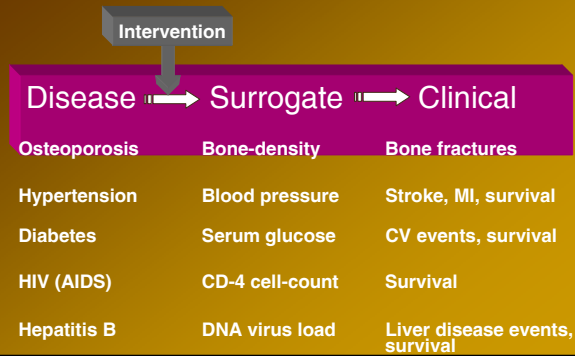
Main features of clinical trial design

- Primary versus secondary outcome

Type 1 diabetes mellitus - Insulin trial	
Primary	Incidence of severe hypoglycaemia
Secondary	Change in laboratory test – HbA _{1c}
Secondary	Self monitored blood glucose
Secondary	Change in body weight
Secondary	Changes in treatment satisfaction

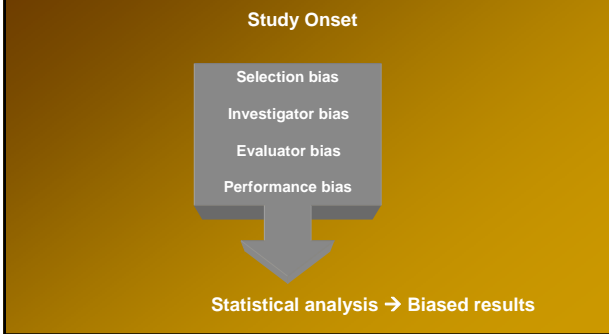
Main features of clinical trial design

■ Clinical versus surrogate endpoints



Main features of clinical trial design

■ Biases of study results



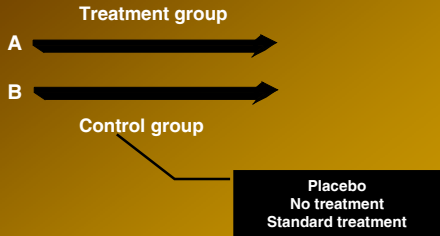
Main features of clinical trial design

■ Parallel design versus cross-over design



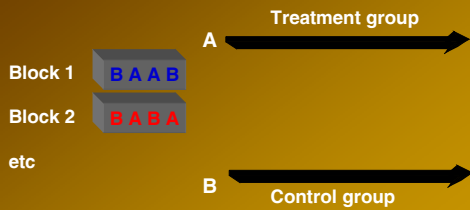
Main features of clinical trial design

Controls



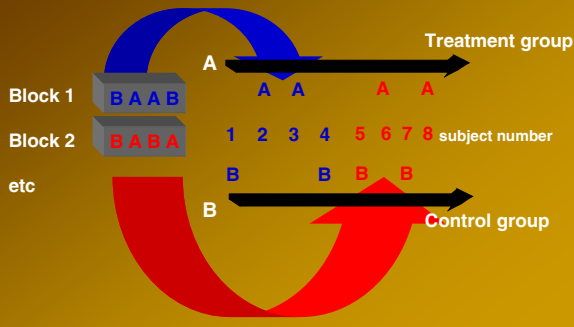
Main features of clinical trial design

Randomization



Main features of clinical trial design

Randomization



Main features of clinical trial design

Blinding

- Single 1 or 2 or 3
- Double 1+2+3
- Triple 1+2+3+4



- 1. Trial participant =the patient
- 2. Trial investigator =the doctor, nurse or other health care worker
- 3. Trial outcome assessor =commonly the treating doctor
- 4. Trial data evaluator =medical statistician

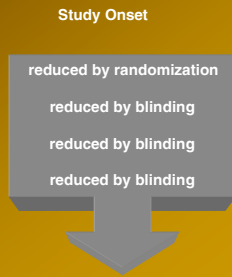
Main features of clinical trial design

With no randomisation and no blinding the study result for the new treatment may be exaggerated by 50%

Biases of study results

Biases

- Selection bias
- Investigator bias
- Evaluator bias
- Performance bias

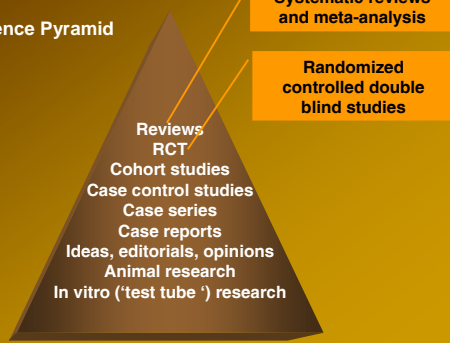


Statistical analysis → Results

Main features of clinical trial design

Evidence Based Medicine

The Evidence Pyramid



Conclusion

Main features of clinical trial design

- A clinical trials is longitudinal, prospective and experimental in nature
- A clinical trial should preferably use controls, random allocation and blinded procedures to avoid biases that can influence the results
- The outcome of a trial can be related to efficacy, safety and/or quality of life
- A clinical trial includes primary and secondary outcomes that can be intermediate (surrogate) or clinical
- The randomized controlled double blind study design is the highest ranked clinical study design
