Experimental Study
Wrap- Up

Definition

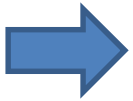
- Experiment = Observation + Control Circumstance + Manipulate
- In an experiment investigators apply treatments to experimental units (people, animals, plots of land, etc.) and then proceed to observe the effect of the treatments on the experimental units.
- Limitation (Extraneous Factor)
  - Other Co-intervention
  - Placebo effect
  - Regression to mean phenominum etc.

Design Consideration

- Research question
- Selection of participant
- Selection of intervention and control
- Selection of outcome
- Data Analysis and sample size
- Measure to reduce bias
- Ethical consideration

Research question

- Primary Research Question? (want to answer)
- Second Research Question? (hypothesis generation)



FINER (Feasible, Interesting, Novel, Ethical and Relevant)

Selection of Participants

Eligible criteria

- Inclusive Criteria
- Exclusive Criteria

Why exclusive?

- Study treatment clearly indicated.
- Study treatment is contraindicated or would be harmful
- Unlikely to benefit from study treatment
- Practical problem with participating protocol
  - impair mental status,
  - language barrier

Selection of intervention and control

Intervention

- knowledge of trial (primary trial) Intensity, duration and frequency
- Need to balance
  - the effectiveness (highest tolerable dose)
  - Safety (lowest effective dose, vaccine) in the mild condition or prevention

- Control:
  - Should have concurrent standard of care including placebo + no treatment and (always) supportive care.
  - Specify allowance or restriction of co-intervention

Outcome (Endpoint)

- Single Event(total mortality, occurrence of condition (stroke,..)
- Combination of event = Composite outcome (usually primary outcome)

- Primary outcome:
- Secondary outcome:
- Adverse outcome:

Data Analysis and Sample Size

- Is the intervention effective?
- Does the intervention make any difference between the group?
  - Absolutely no difference = intervention is not effective (this situation is rare)
  - Some degree of difference: what prob. that observe difference between 2 group of study? P-value To prove effectiveness (but not enough) to make the clinical decision.

What is Magnitude of effect (to patient)?

- Measure the effect Parameter estimation (approach)
  - point estimate (RD, RR, OR, HR,..)
  - interval estimate (95%CI)

Parameter required for calculation of Sample size

1. Acceptable type 1 error (level of significance) 5%
2. Acceptable type 2 error (complement of power) 10-20%
3. Smallest clinically important effect that need to be detected = is clinical judgment of disease. (Ex. Difference =1% reduced mortality when using new drug.
4. Expected variability of outcome variable
   - From other trial or a pilot study
5. Expected magnitude of outcome in one group (usually) control group
   - From other trial or a pilot study

Measure to reduce bias

- Treatment allocation by randomization (simple, blocked, stratified, adaptive, and cluster). Recommendation of randimization method:
  - Large studies (one center- block randomization; multi center –stratifed by center (blocked)
  - Small studies (n=100) (one center- block or stratifed randomization (by 1-2 risk factor; multi center –stratifed by center + risk factor(blocked)
  - Very small studies (n=50) one center – adaptive minimization
- Concealment of randomization
  - Concealed randomization
  - Unconcealed randomization
  - Pseudo-(Quasi) randomization
- Blinding of treatment of allocation
- Maximizing adherence and follow-up
- Analysis using intention-to-treat principle

Ethical consideration

- Is randomization ethical?
- Is using placebo ethical?
- Inform consent

Conclusion

- Experimental study is most suitable for studying the effectiveness of a therapeutic or preventive intervention
- Main features
  - Control group
  - Similar prognosis between experimental and control group
  - Investigator manipulate or control assignment of subject to group using randomization technique
- Measures used to reduce bias
  - Treatment allocation by randomization
  - Concealment of randomization
  - Blinding of treatment allocation
  - Maximizing adherence and follow-up
  - Analysis using intention-to-treat principle

Thank you