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Interventional studies (clinical Trials)

This is similar to cohort studies , in clinical trials , individuals are included on the basis of their exposure status , but the difference is that the investigators themselves will allocate the exposure .

Advantages :

1- It is the gold standard of the epidemiological studies .

Similar to experimental studies in the lab , -- the exposure is under the investigator control , who standardized all the factors other than risk factors .

2- It can detect mild to moderate differences (this is difficult in cohort studies) .

3-It can control and manipulate many confounders .

4-It can demonstrate the temporal relation ship between the exposure and outcome with highest degree of confidence . (the same as in cohort study , we can determined the time between exposure and outcome .

5- It is the strongest and the most direct epidemiological evidence to judge the (causal association) .

Limitations

1- Expensive and time consuming .

2-Ethical problems : for certain factors there is some doubt about the benefit or harm to the study subjects .

3- It dose not represent the real life situation . (because we control all the other factors except the exposure factors , this is not the real situation in ordinary life) .

4- feasibility problem : some times it is difficult to have the control or the non –exposed group .

Types of clinical trial

1- Therapeutic or secondary prevention trials .

The study groups are (diseased) , it is conducted on patients to evaluate the effect of certain drug or procedure in minimizing symptoms , complication , or death .

2- Preventive or(primary preventive trial) .

Conducted on healthy people who are at risk or excess risk to develop outcome .

Selection of study group

1- Reference population :

Represent the group on which the results will be applicable . Then reflect on population .

2-Experimintal population :

Represent the group on which the trial will be done . They should be

a- sufficiently large .

because some of them will be excluded later . sometimes we need to detect mild to moderate difference , some times the outcome is rare .

b- sufficient outcome . there must be good number of people in the study group having the outcome .

c- complete and accurate information .

both reference and experimental groups should informed about the aim of the study , possible benefits and side-effect and the possibility of having a placebo during the study period .

Q/ How do we increase the incidence of the outcome among the experimental study group ?

A/ by including a high risk population in the study .

The process of conducting the study is as following .

Accepting group

↓

Screening for eligibility

↓

Accepting and eligible

↓

Randomization into study group and control group

Causes of exclusion .

1-Definit history of endpoint under study .

2-Definit need for the study treatment .

3-Contraindication to study treatment .

Volunteer bias ; the volunteers not being representing the true community population on which we will generalized the study results .

Blocking (stratification)

This means equal distribution of the participants into treatment group according to certain characteristic that can affect the outcome understudy . ex—age .

Randomization :

Allocation of the individuals to be included in the exposure status is random . That is to say every individual is given an equal chance to be allocated in the exposure or non-exposure groups .

It is done either by 1- use of random number table or by 2- use of computer generated randomization .

Advantages :

1-Avoid selection bias .

2-Control all variables , so by randomization control all confounders (known and unknown).

Ex: in a study on hypertension :

178.009 --------19.103 (10.7%) unwilling

↓1st screening

158.966 (89.3%)---- 135, 928 (76.4%) in eligible (excluded)

↓2nd screening

22.978 (12.9%)------5.502(3.1%) unwilling

↓ 3rd screening

17.476 (9.8%) --------- 6.536 (3.7%)

↓

10.940 ---- study population willing and eligible .

Study population
(sampling)

Study group **sample pop** **control comparison group**

↓ ↓

Randomization

1st data collection **1st data collection before intervention**
Before intervention

↓ ↓

Intervention manipulation **no manipulation**

↓ ↓

Last data collection **last data collection**

→ ←

COMPARE

NOT:- THE measure of association between disease and exposure is the

Relative risk .

Ascertainment of the outcome .

This should be as complete , accurate and uniform as possible from both study groups . So the ascertainment of the outcome can be affect by knowing the exposure status which lead to (OBSERVATIONAL BIAS) .

If the data collector (investigator) known that this person will receive placebo then this will affect the assessment of results or outcome .

Blinding technique : This is done to reduce the occurrence of observational bias .

So blinding is either :

1- SINGLE : here the investigator know what the participant receive .

2-Double ; here both investigator and participant do not know what the participant receive .

Placebo :also done to reduce the occurrence of observational bias .

Disadvantage of placebo :

1- There is a tendency of the patient to report a good result of any treatment .

2-Tendency to report side effects with treatment or placebo .
Blaming the treatment to cause certain side effect .

Maintenance and assessment of compliance :

Compliance :The commitment of the study participants by the treatment .

The non compliance is the major problem in the intervention study , it is related to the complexity and length of follow up .

Causes of non compliance

1- Development of side effect .
2-Forgetting to take treatment .
3-With draw from trials .
4-Choose the alternative method .
5- The intervention becomes contraindicated .

Enhancement of compliance is by :

1-Inclusion of interested and reliable group . (high risk group) .
2-Frequnt contact with participant .
3-Use of calendar pack of study treatment , as in contraceptive pills .
4-Provision of incentives .

How to check compliance (monitoring)

1-self report .
2-pill count of unused medication .
3-use of biochemical markers .

Ex . we give the drug and riboflavin (which is secreted in the urine --- by check riboflavin in urine .

Stopping rules :

These are criteria for early termination or modification of the trial when the appearance of extreme benefit or harm from early results .

This stopping should be :

1- done by external investigator .
2-based on experience of adequate number of subjects . (sufficient number of outcome) .
3-The statistical difference should be highly significant .

The power of clinical trials to detect mild to moderate differences depend on :

1-simple size .
2-total number of end point (outcome) this can be increase by , a- selection of high risk group . b- increase length of follow up .

In clinical trial 2 groups

1- study group , introduce intervention or new drug .
2-control group , could be a group that receive , a- no treatment , b- placebo , c- standard treatment .