

Introduction:

The evidence base (EB) is the base for any profession concerned with treatment and prevention of diseases. The EB practice require:

- gathering evidence ← CLINICAL RESEARCH.
- critically interpreting evidence ← BIOSTATISTICS.

We cannot intended biostatistics without COMPUTING. ← no blackbox

Note: Statistics is based on probabilistic assumption and provides quantification of variability around the estimates.

Design of Experiment

There are two main type of study in medical research:

1. Observational: Aspects of an existing situation are observed ← we try to interpret data to give of the the fact we are observing.
2. Experimental: We do something (for example we give a drug) and observe the result of our action (trials of treatment on human beings are called CLINICAL TRIALS).

Example:

We want to compare if a new treatment is more efficient than a standard one. Possible approach:

- compare results of new treatment on new patients with results of the old treatment. ← Not so good patient could be very different from each other.
- We can compare old and new treatments concurrently ← example by comparing pts of our facility with pts of another. ← again there may be differences between the patient group of the two hospital.
- We could ask people to volunteer for the new treatment and give the standar treatment to those who don't volunteer ← again, same problem.
- We can allocate patient for a treatment and patient for the standar treatment and observe the outcome. The allocation can really influence the results enormously this because the allocation method may produce groups of subjects that are not comparable.

So we need a allocation method for which the characteristics of the patients will not affect their chance of belonging to one particular group. This method is called random allocation!

RANDOM ALLOCATION (RANDOMIZATION):

If we want that the chance that to people will receive an advantage (for example a vaccine) we just toss a coin. Doing that for each pair of people we end up having two group. The only differences between this two group will be those due to chance. ← we like it!

Randomization can be performed in a number of ways, for example:

- Pseudo random table ← And for example we put odd pts to group A and even pts to group B.
- blocks ← are small equal size group and in each block allocate same numbers of A and B.

Note: of course we can have more than two group.

Note 2: The biggest limitation is due to its principal characteristics, the random chance.

We can see the same problem when we are trying to sample a large population.

Sometime it is better to divide the population into STRATA (for example age, sex,...) and take random sample within this strata.

So a stratin: a mutually exclusive group.

Intention to treat (ITT)

We analyze the data according to the way we intended to treat, not the way in which they were actually treated.

Example

We are trying to evaluate the effectiveness of a health check-up. The subjects are randomly split in a screening or control group. The subjects can accept or decline the invitation. So when we analyze the data we have to keep that in mind.

The opposite is to analyze just the actually received ← this is called ON TREATMENT analysis

Intention to treat VS on treatment (analysis)

ITT is bias because some patients may receive the other treatment so the DIFFERENCE may be smaller than they should be.

On treatment is biased because it favours the differences.

Response bias

Placebo effect ← the response of the treatment could depend on the knowing that the person is being treated.

So in any trial it is desirable that subjects should not be able to tell which treatment is which.

Note: Placebo is not always possible or ethical (ex: surgery is a treatment, there is no placebo surgery).

Assessment bias and double blind test

The response of pts to treatments are not the only things affected by the knowledge of the treatment. Also the assessment of response by the researcher

A way of avoiding this bias is BLIND ASSESSMENT ← the assessors don't know which treatment the subject is receiving.

Double Blind: both the pt and the assessor don't know which treatment the pt is receiving

Cluster Randomized Trial

Are type of trial where groups of subjects, instead of single units, are randomized.

- They are trials where EXPERIMENTAL unit (the smallest group of subjects whose response cannot be affected by other subjects) play the role of the individual

NB: we need to know the amount of natural variation existing between experimental units before we can decide whether the treatment effect is distinguishable from this natural variation.

Pros:

Reduced cost in

survey

Cons:

Greater complexity in study design

More participants are needed to obtain the same power

We must include bias in the analysis