3. Some concepts on experimental design

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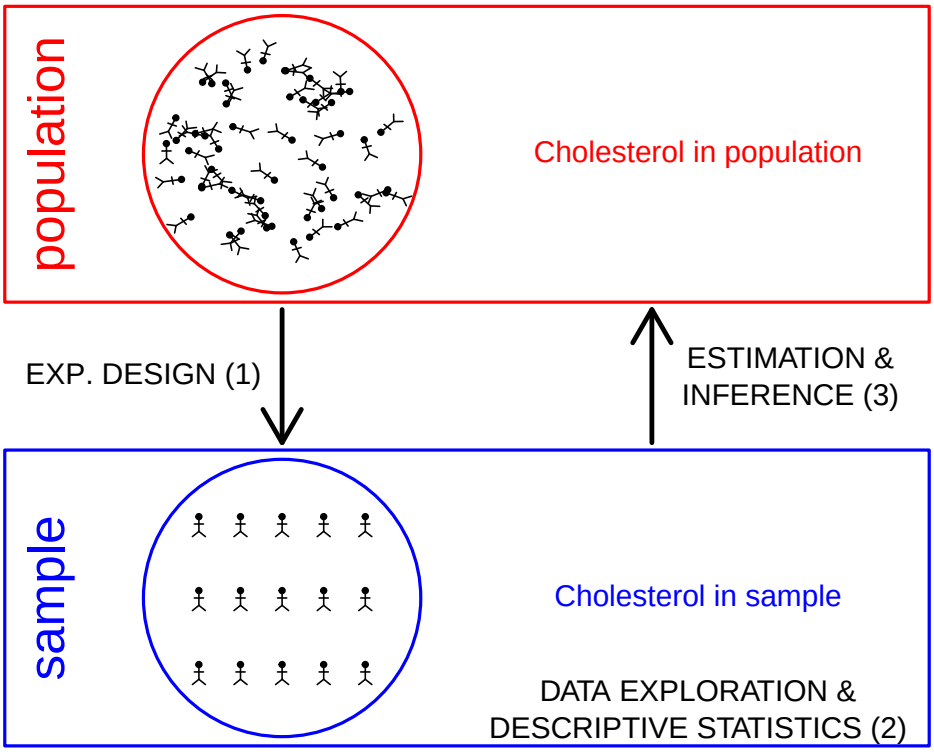

1 Need for a good control

- A good control group is crucial.
- To assess the effect of an intervention, we need to compare a test and control group.
- This is often not possible in a pretest/post-test design: e.g. effect before and after administering a drug without the use of a placebo group.
- Groups in an observational study are often not comparable: advanced statistical methods are required to draw causal conclusions.
- Double blinding
- We have to be aware of confounding!
- Randomized studies: random assignment of subjects in the study to the different treatment arms → comparable groups.

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2 Randomization

- Randomization completely at random (no systematic allocation).

2.1 Simple Randomization

- Can lead to differences in the number of experimental units in each treatment arm
- in 5% of the cases we might observe an imbalance of
  - of at least 60:40 in a study with 100 subjects, and
  - of at least 531:469 in a study with 1000 subjects.
- This imbalance is not problematic, but causes a loss in precision.

2.2 Balanced Randomization

- Equal numbers of each treatment are assigned to a block of 2 or 4 patients.
  - (1) AB, (2) BA
  - (1) AABB, (2) ABAB, (3) ABBA, (4) BABA, (5) BAAB, (6) BBAA
- Balanced Randomization ensures $\pm$ the same number of people in the control and the treatment arm of the experiment.
- Does not make that we have an equal number of males with and without the treatment, etc.
- In small studies, it is possible that the groups are unbalanced in other characteristics (e.g. gender, race, age …)
- This is not problematic because it occurs at random, but, again it causes a loss in precision.

2.3 Stratified randomization

- The imbalance according to for instance gender can be avoided using stratified Randomization: balanced randomization per stratum

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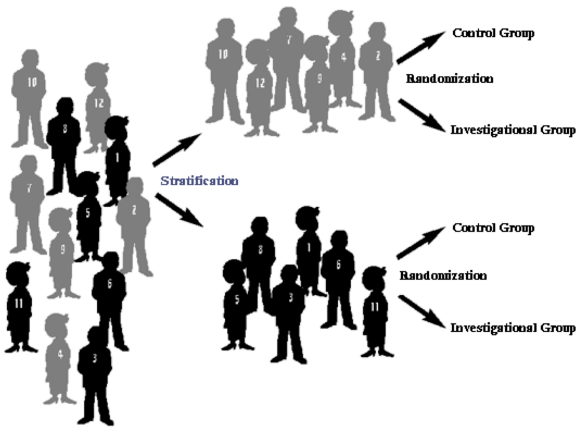


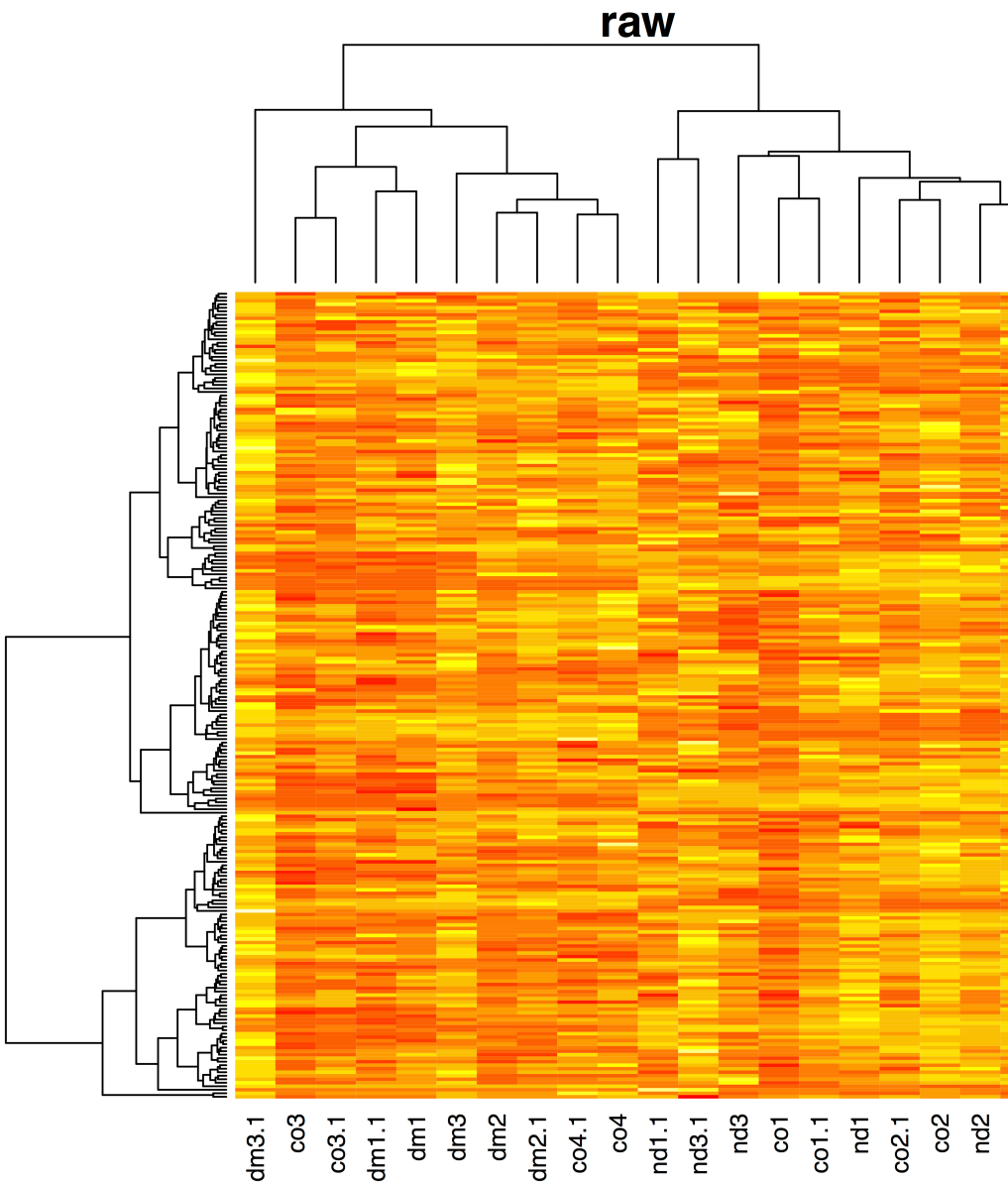
Figure 1: Stratified Randomization

3 Sample size

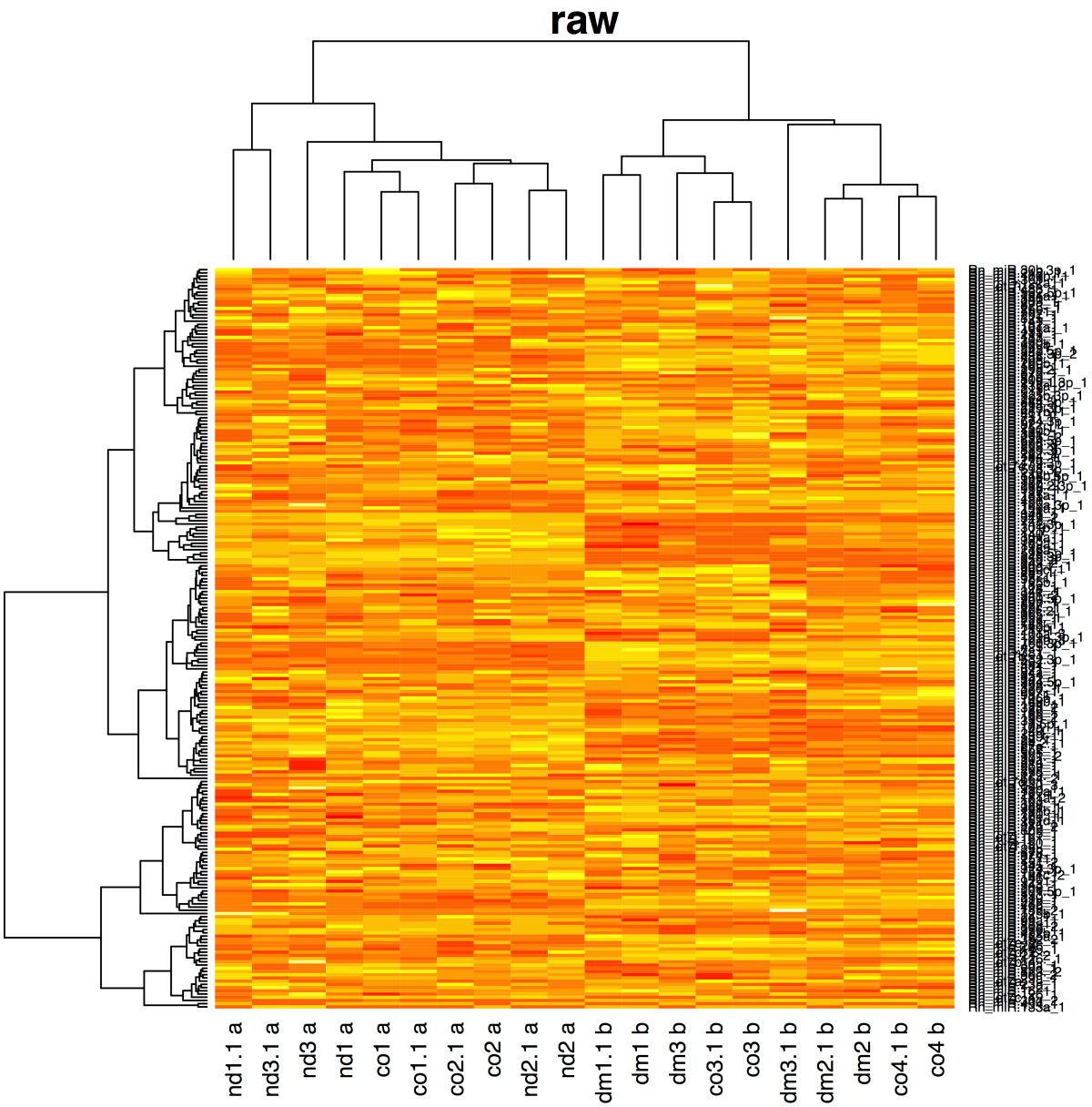
- The sample size and the design are crucial.
- The larger the sample size, the more precise the results.

4 Bad design example

- dm: diabetic medium, nd: non diabetic medium, co: control



- 4 bio-reps, 2 techreps/biorep
- dm: diabetic medium, nd: non diabetic medium, co: control
- 4 bio-reps, 2 techreps/biorep, 2 plates A & B
- Treatment and plate almost entirely confounded



5 Wrap-up

- Sample size is very important.
- To assess the effect of a treatment, we should compare comparable and representative groups of subjects with and without the treatment (a good control!).
- In observational studies, the researcher cannot choose the treatment. It was the patient or their MD who had chosen it
- In experimental studies, the researcher assigns the treatment.
- Confounding can be avoided via randomization.

- We can also correct for confounding in the statistical analysis for the confounders that have been registered.