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Practical Information

Scheduling:

- follow-up discussion for Monday's lab after 11am?
- note: next lab session is this Friday (Jan 12) 1-4pm.

Overview of today's lecture:

- more on descriptive analysis (2L−2), with further Minitab demonstrations,
- summary worksheets (from Stephens book) for descriptive stats,
- presentation of ideas about statistical planning/ experimentation and epidemiological reasoning:
  - causation: confounding, bias,[1]
  - design of experiments: control, randomization and replication,[2]
  - random selection, random numbers,[3]
  - surveys: sampling, stratification,[4]
- in addition, some exercises to complete together,
- no discussion of ethics in VHM 801 ($\Rightarrow$ VBS 803),
- references to skipped chapters (e.g., the correlation r): skip over for now, we'll return to those sections later.

[1] PSLS 3e: brief discussion (Chapter 7); IPS7e: Section 2.6.
[2] PSLS 3e: Chapter 8; IPS 7e: Section 3.1.
[3] PSLS 3e: Chapter 7; IPS 7e: Section 3.1.
[4] PSLS 3e: Chapter 7; S: Section 1.2; IPS 7e: Section 3.2.

More about Descriptive Stats and Outliers

Determining shape for distributions of continuous variables:

- graphically explore shape by stemplot and/or histogram (relevant distrib. curves (e.g., normal) may be overlaid),
- further assess symmetry by descriptive measures (median $\approx$ mean, Q1 and Q3 symmetrical around median),
- further assess shape by computing
  - skewness: $<0, =0, >0 \sim$ left-skew, symm., right-skew,
  - kurtosis: $<0, =0, >0 \sim$ flat/light-tailed, normal, peaked/heavy-tailed,[5]
- beware that shape may appear irregular for small samples (say, $n \leq 15$).

Outlier = observation that does not belong with the others, typically by being extreme,

- visual assessments from stemplot, dotplot or histogram,
- subject-matter knowledge may deem value implausible,
- "suspected outlier" rule based on 5-number summary:
  - screening tool for (extreme) values worth inspecting,
  - relies on assumptions of symmetry and "moderate" data size in order to correctly identify real outliers.

[5] Note that *for skewed distributions*, kurtosis is of little interest. In Stata, kurtosis values are 3 units larger; i.e., kurtosis = 3 for a normal distribution.

Association and Causation

Association between two variables x and y
= a certain pattern in the combined distribution of the two, e.g. explored by a scatterplot for two quantitative variables:

- positive association: high (low) values of x and y appear together,
- negative association: high (low) values of x appear together with low (high) values of y.

Causation = direct link between variables whereby one (say x) *causes* the other (y).

Fundamental caution for interpretations:
association *does not* always imply causation.

Example 7.2 of PSLS 3e: alcohol type (wine vs. beer) and health in UNC (Univ. North Carolina) Alumni Heart Study,[6]

- apparent health benefits of wine (compared with beer) found, but ...
- "may due to *confounding* by dietary habits and other lifestyle factors".

Definition: two variables are *confounded* when their effects on a response variable cannot be distinguished from each other.

[6] Barefoot et al. (2002), *Amer. J. Clin. Nutr.* **76**, 466-72.

Experimental and Observational Data

Experiment versus Observational study:

- an experiment deliberately imposes some *treatments* on individuals in order to observe their responses,
- an observational study observes individuals and variables of interest, but no attempt to influence responses.

Ideal method of establishing causation: experiments, because they allow comparisons *all other things being equal*, however often (depending on research field) not feasible:

- unethical to carry out experiments (e.g., on humans),
- impractical (due to cost or logistics).

Guidelines/criteria exist for establishing causation from association without experiments, e.g.: [7]

- strong association,
- consistent association (several data sources point in the same direction,
- gradual association (stronger exposure $\Rightarrow$ stronger response), often as a dose-response relation,
- time consistency (exposure before response; changes in exposure $\Rightarrow$ subsequent changes in response),
- plausible cause (e.g., established in similar setting).

[7] Discussed in Epidemiology; a brief summary is included in IPS7e, Section 2.6.

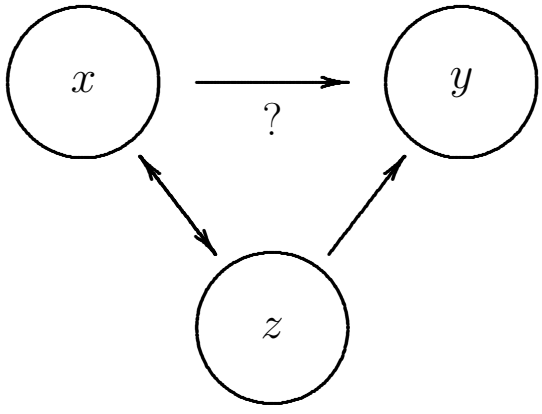
Exercise 3.6

National Halothane Study[8]: a U.S. epidemiological study from the late 1960s to evaluate halothane[9] toxicity.

(a) The anesthetic used was not imposed, but rather chosen by the doctors caring for each patient.

(b) The higher death rate for anesthetic C could be due to confounding (possibly *lurking*/unobserved) variables; some possibilities: nature and seriousness of condition/surgery, the patient's overall physical condition and age.

Schematic for potential confounding scenario by variable z:



x = type of anesthetic, y = mortality

[8] Bunker JP, Forrest WH, Mosteller F, et al (Eds). National Halothane Study. A study of the possible association between halothane anesthesia and postoperative hepatic necrosis. U.S. Government Printing Office, Washington, DC 1969.

[9] Halothane is an inhaled anesthetic, introduced in the 1950s and in the early years suspected to be associated with increased risk of hepatitis (liver disease).

Planning a Study

Data sources:

- anecdotal evidence: rarely useful, unrepresentative,
- available data, often in registers:
  - produced/collected for other purposes,
  - quality and usefulness not evident!
- designed sample surveys (samples): address a subset of entire population, as opposed to censuses,
- designed experiments may use data generated exclusively for study or routinely recorded data (e.g. use of register data for clinical field trials).

Statistical design = procedures for collecting data:

(1) Which individuals to be studied? and how many?[10]

(2) What variables to record?

(3) What patterns to explore and hypotheses to test?

(4) Method af analysis.

Many statistical designs include only (1)−(2); however the statistical analysis and any statistical assessment of necessary sample size (to be discussed later in course) benefit from or require information about (3)−(4).

[10] Recall that observational/experimental units can also be samples.

Experimental Design

2 examples of statistical designs (completely randomized):

Parasite exposure in Lithuania		
Calves	Pasture	
	safe	infected
	10	10

Advertising study (Exercise 13.22)			
Subjects	Repetitions (times)		
Familiarity	1	2	3
familiar	15	15	15
unfamiliar	15	15	15

Some terminology for experimental design:

- treatment: specific experimental condition applied by the experimenter,
- experimental units: subjects/individuals/samples to which treatments are applied,
- factor: (controlled) explanatory variable in experiment,
- level: specific value of factor/treatment.

3 basic principles of experimental design:

(1) control of lurking variables, by control/placebo group,

(2) randomization: random assignment of units to treatments to avoid unexpected patterns,

(3) replication: sufficient number of units to "drown out" randomness, or repetitions of experiment.

Violation of (1) or (2) may result in bias = systematic favour of certain outcomes ($\Rightarrow$ potentially false conclusions).

Random Selection

In practice: how to select individuals for a treatment group? e.g., 10 (m) calves for safe pasture out of 20 (n).

First number individuals 1,...,20 (n). Then, employ one of the following methods,

- use one's own random generation, e.g. draw 10 (m) cards from pile of 20 (n),
- using random digits (Table A in PSLS; Table B in IPS):
  - choose starting point in table (arbitrarily),
  - read off digits (along rows) to form numbers 1–20 (n), until 10 (m) different numbers encountered,
- using Minitab:
  - generate column with numbers 1,...,20 (n) (`Calc-Make Patterned Data-Simple...`),
    - *easy way*: sample from column without replacement (`Calc-Random Data-Sample from Columns`),
    - *other way*: generate column of same length with random numbers (`Calc-Random Data-Uniform`), and sort both columns by the random numbers (`Data-Sort`),
  - use first 10 (m) numbers in new or sorted column,
  - procedure is reproducible using a *seed* (Minitab: base),
- using Simple Random Sample applet (not reproducible).

Completely Randomized Design

In a completely randomized design, all treatments are allocated at random among the experimental units (using a method for random selection). In all other respects, the units are treated as equally as possible.

$\Rightarrow$ (idea/rationale:)

Differences in response must be due to either treatment effects or play of chance in random assignment of units.

Comments:

+ simple/easy to understand, carry out and analyze,
+ flexible (allows any number of levels and replications),
+ randomization as safeguard against syst. errors (bias),
− all experimental units need to be "homogeneous", otherwise the random variation will be large,
− if a good grouping of experimental units exists (either in their state before treatments are applied or in general conditions during the experiment), other designs will be more efficient (give better precision),
$*$ primarily for small designs with no obvious grouping (as described above) that could be used as blocks $\rightarrow$ 2L−10.

Block Design

Blocks = groups of homogeneous experimental units, i.e., units are more alike within than between groups, before and during experiment.

In a (randomized) block design, treatments are assigned randomly to the units within each block, typically such that each treatment occurs once in each block.

$\Rightarrow$ (idea/rationale:)

More accurate to compare similar units (in same block).

Special cases:

- matched pairs design: blocks of size 2,
- cross-over design: multiple treatments on same subject (= block).

Examples of factors used to form blocks:

- agriculture: areas in fields,
- animal science: litters, groups (age/weight/sex), environment (herd),
- human medicine: twins, family, groups (as above + condition, social status, lifestyle...),
- general: time, operator (surgeon, technician).

Comments on block designs:

\+ improvement in precision if efficient groups available,

\+ randomization as safeguard against systematic errors (bias),

+/− minor added complexity in design and analysis,

− less flexible (block size should match number of treatments),

∗ very useful and very much used.

Surveys and Sampling

In surveys we select a subset of individuals from a population to draw inference *about populations*,

- population: entire group of individuals of interest,
- sample: subset from population,
- sample design: method to extract sample,
- common example: opinion polls.

The main reasons for preferring survey to census are costs and feasibility.

Some common causes of bias (systematic errors) by favouring certain parts of the population:

- voluntary response sample (respondents rarely representative),
- in general, non-random selection (often a convenience sample: the individuals/samples at hand),
- undercoverage (some parts of population left out of sampling process),
- non-response (non-response may be more likely for certain parts of population).

Response bias = answers incorrect due to "circumstances",

- particular example: wording of questions.

Sampling Schemes

Simple random sampling:

- choose n individuals from population such that every subset of n individuals has equal chance of selection,[11]

\+ simplest to understand and analyze,

− impractical if entire population cannot be enumerated, so often statistically and practically inefficient.

Systematic random sampling:

- assume samples ordered (say $1, \ldots, N$), and choose a *sampling interval* I, typically to achieve a desired sample size $n = N/I$,
- select the first sample *randomly* among samples $1, \ldots, I$, and thereafter select every Ith sample,
- often the logistically simplest probabilistic sampling method, but not a simple random sample $\Rightarrow$ biases may occur.

Stratified sampling:

- split population into homogeneous groups (strata, e.g. geographical), use simple random sampling in each group,[12]
- similar to a block design (strata $\sim$ blocks), and with similar advantages and disadvantages.

Multistage sampling: (including cluster sampling)

- sampling in several stages, often corresponding to population's hierarchical structure; for example, sampling of cows in two stages — first herds, then cows within selected herds,
- practical and economical advantages (but more complex analysis).

[11] The same principle as with random selection in completely randomized designs.

[12] Note: The strata need not be represented equally in data; this would then be accounted for in analysis by a weighting procedure.

Exercise 3.52

Word lengths in writings of Tom Clancy.

Answers:

- population: words in Tom Clancy novels,
- sample: 250 words on one page in one novel,
- variable measured: length (number of letters).

Do you think the sample is representative for the population?

* maybe need more pages in same book,
* certainly need more books,
* all in all too small.

Study and Experimental Design Terminology

- Studies do not always use individuals (subjects, samples) that are drawn directly from the population of interest (PoI); this raises the issue of whether the study findings are representative for the PoI (in epidemiology, termed external validity).
- Observational study types (in epidemiology):
  - cross-sectional study: based on survey at single point in time,
  - cohort study: study groups (e.g. exposure) followed over time,
  - case-control study: cases and control selected separately, and their characteristics are compared,
  - retrospective study: using past data (often as a case-control study), contrasting a prospective study.
- Randomized comparative designs involve several (≥ 2) treatment groups and random allocation of subjects to treatments.
- Placebo: control treatment that is "fake" but otherwise indistinguishable from real treatment; placebo effect: apparent positive effect of placebo treatment.
- Blinding: subject and/or experimenter are not aware of the identity of treatment groups (both $\Rightarrow$ double-blind).

Summary Notes

2 aims of statistical methods:

- detect pattern(s) in a data set, without prior knowledge about which patterns the analysis will focus on,
  $\Rightarrow$ exploratory data analysis,
- confirm or disprove certain theories (hypotheses) about relationships in the data, typically with the aim of generalizing the conclusions to a more general context,
  $\Rightarrow$ formal statistical inference.

Any generalization from specific to common relies on assumptions! (in particular, representativity)

Key words and concepts:

- descriptive statistics to quantify distribution shape,
- causation, confounding/lurking variable, bias,
- experimental design terminology, control, randomization (incl. methods for), replication,
- completely randomized design, block design,
- survey and sampling terminology, simple random sample, stratification.