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Practical Information

Overview of today's lecture:

- more on descriptive analysis with brief Minitab demonstration,
- summary worksheet (from Stephens book; Chapter 3) for descriptive statistics,
- 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",
- brief overview of ethics related to data collection,
- references to skipped chapters (e.g., the correlation r): you may skip over for now, we'll return to those sections later.

Next lab sessions: Friday (repeat of $1-$P) and Monday ($2-$P), both 1-3pm (in-class and streamed).

[1] PSLS 3e/4e: brief discussion (Chapter 7/6); IPS7e: Section 2.6.
[2] PSLS 3e/4e: Chapter 8/7; IPS 7e: Section 3.1.
[3] PSLS 3e/4e: Chapter 7/6; IPS 7e: Section 3.1.
[4] PSLS 3e/4e: Chapter 7/6; S: Section 1.2; IPS 7e: Section 3.2.

More about Descriptive Statistics and Outliers

Determining shape for distributions of continuous variables:

- graphically explore shape by stemplot, dotplot and/or histogram (relevant distribution 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-skewed, symmetrical, right-skewed, respectively,
  - kurtosis: $=0 \sim$ normal, $>0 \sim$ (often) heavy tails (for data: outliers), resp., [5]
- beware that distribution shapes may appear irregular in 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 or an outright error,
- "suspected outlier" rule based on 5-number summary:
  - screening tool for (extreme) values worth inspecting,
  - cannot be expected to correctly identify real outliers (see 1L−14).

[5] For skewed distributions, kurtosis is of no interest! In Stata, kurtosis values are 3 units larger: kurtosis = 3 for normal. Controversy exists about (in)correct interpretations of kurtosis (e.g., Westfall (2014), *Amer. Statist.* 68, 191−195).

Association and Causation

Generally in statistics, when talking about interpretations and relationships, these always refer to a population, ideally the population the data are thought to represent.

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 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 (6.2 of PSLS 4e): alcohol type (wine vs. beer & spirits) and health in UNC (University of North Carolina) Alumni Heart Study,[6]

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

Definition (IPS, PSLS): 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 does not attempt to influence responses; its results/interpretations may be subject to bias:
  - systematic favour of certain outcomes (IPS/PSLS) ⇒ potentially false conclusions,

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), (see 2L−12)
- impractical (due to cost or logistics).

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

- strong and consistent association (several data sources point in the same direction,
- gradual association (stronger exposure ⇒ stronger response, dose-response),
- time consistency (exposure before response; changes in exposure ⇒ subsequent changes in response),
- plausible cause (e.g., established in similar setting, such as another species).

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

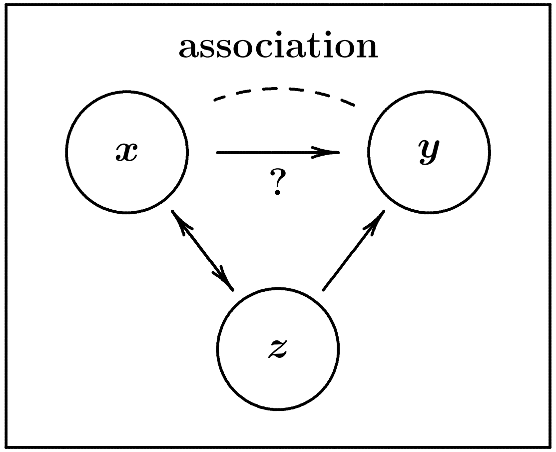
Exercise 3.6

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 unobserved (IPS,PSLS: lurking), variables z; 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, 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 of population,
- 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 "individuals" (or observational/experimental units, next slide) can also be samples.

Experimental Design

2 examples of statistical designs (both completely randomized; 2L−9):

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,[11]
- 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[12] group and/or blinding[13],

(2) randomization: random assignment of units to treatments (hence sometimes called a "randomized comparative experiment"; IPS, PSLS),

(3) replication: sufficient number of units to "drown out" randomness.

[11] Not necessarily the same as the measurement units on which measurements are taken.
[12] Placebo: control treatment that is "fake" but otherwise indistinguishable from real treatment; Placebo effect: apparent positive effect of placebo treatment.
[13] Blinding: subject and/or experimenter are not aware of the identity of treatment groups (both → double-blind).

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 a 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 the column without replacement[14],
    - (flexible way): generate a column of the same length with random numbers[14], and sort both columns by the random numbers (`Data-Sort`),
  - use the first 10 (m) numbers in new or sorted column,
  - procedure is reproducible using a seed (Minitab: base),
- using Simple Random Sample applet (not reproducible).

[14] Minitab menus: `Calc-Random Data-Sample from Columns` and `Calc-Random Data-Uniform`, respectively.

Completely Randomized Design

In a completely randomized design (or trial), 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 systematic errors (bias), e.g. by randomly re-ordering the experimental units (easy in statistical software),

– the 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 (→ next slide).

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[15] ⇒ idea/rationale:

> it should be more accurate to compare similar units (within same block), and to aggregate such comparisons across blocks.

Some special cases:

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

Examples of factors used to form blocks:

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

Comments on block designs:

+ improvement in precision if efficient groups available,

+/− minor added complexity in design and analysis,

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

∗ very useful and very much used.

[15] Not a strict requirement, and even incomplete blocks are possible; → VHM 802 for discussion of block designs.

Observational Study Types and Terminology

Brief overview of observational study types:[16]

- cross-sectional study: based on survey at a single point in time,
- cohort study: study groups (e.g. exposure) followed over time,
- case-control study: cases and control selected separately (⇒ each individual's status as a case or control is predetermined), and their characteristics are compared,
  - main advantage when cases (or events) are rare,[17]
  - needs special analytical methods to get proper inference about the population,
- controlled study: an experiment carried out on subjects in their usual environment (and possibly utilizing routinely recorded data),
- retrospective study: using past data (often as a case-control study), contrasting a prospective study (often a cohort study).

Concepts and terminology from epidemiology:

- 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),
- Different bias types distinguished, e.g. selection, information, and confounding bias.

[16] Detailed coverage can be found in courses in Epidemiology.
[17] If cases are rare, it may be impractical to get enough cases by sampling randomly from the population.

Data Ethics

Aim: brief overview of concepts and questions
— more detailed coverage should be available for your program.[18]

4 major principles of research involving humans:

* An institutional review board must review all planned studies in advance in order to protect the study subjects.[19]
* All individuals must give their informed content in writing before data are collected.
* All individual data must be kept confidential, meaning for example that only summaries for groups of subjects may be made public.
* A guiding principle for ethics questions is: "the interests of the subject must always prevail over the interests of science and society".

Further questions involving ethics:

- Is it ethical to include a placebo group when safe and efficient treatments exist?
- Must a trial be stopped or altered if early results indicate adverse effects or clear superiority of one group?[20]

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[18] In the past, ethics was part of the mandatory course VBS 803 (Principles of Biomedical Research); as this course is undergoing changes, the topic may be covered in a workshop.
[19] UPEI has separate bodies for human and animal research: Research Ethics Board (human participants), and Animal Care Committee (animal participants).
[20] Research in biostatistics deals with both stopping rules and methodology for analysis of altered trials.

SURVEYS AND SAMPLING

In surveys, we select a subset of individuals from a population to draw inference about the entire population,

- population: all the 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 (for entire population) are costs and feasibility.

Some common causes of selection bias by favouring certain parts of the population in the sampling:

- voluntary response sample (respondents rarely representative),
- 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 (often SRS):

- ∘ choose n individuals from population such that every subset of size n has same chance of selection,[21]
- + simplest to understand and analyze,
- − impractical if entire population cannot be enumerated.

Systematic random sampling:

- ∘ assume population (units) 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 units $1, \ldots, I$, and thereafter select every Ith unit,
- ∘ a (logistically) simple probabilistic sampling method, but not SRS ⇒ biases may occur.

Stratified sampling:

- ∘ split population into homogeneous groups (strata, e.g. geographical), then use SRS (or other approaches) in each group,[22]
- ∘ similar to a block design (strata ∼ 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).

[21] The same principle as with random selection in completely randomized designs.
[22] 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?

Answer:

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

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 ⇒ exploratory data analysis,
- confirm or disprove certain theories (hypotheses) about relationships in the population (ideally population of interest) the data are thought to represent ⇒ formal statistical inference.

Any generalization from specific (sample) to common (population) relies on assumptions! (e.g., representativity and ability to avoid/control bias).

Key words and concepts:

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