Medical Research Skills for Optometrists

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How we should think

- a problem exists that needs to be solved.
- formulating and limiting the problem.
- facts collated pertaining to the problem.
- analyze the problem based on several issues that could be converted into several hypothesis.
- testing the hypothesis

Research

- A structured systematic process
- Investigating facts and theories.
- Examines conditions and outcomes.
- Establish relationships.
- General evidence for decision making.
- Provide improvements to understanding.

1. Exploration : Unanswered statement >>> Identify and formulate the problem

2. Deduction (General → specific) : Formulate hypothesis >>> Identify research variables

3. Structuralisation : Determine model and research design >>> Identify population, samples and instrumentation

4. induction-vertification (Specific → General) : empirical observation (measuring) >>> Data analysis >>> Making a conclusion

Study types and designs :

- The quality, reliability and possibility of publishing a study are decisively influenced by the selection of a proper study design.

- The study type is determined by the question to be answered and decides how useful a scientific study is and how well it can be interpreted.

- If the wrong study type has been selected, this cannot be rectified once the study has started.

Classification of study types :

- primary and secondary research
  - actual studies are performed in primary research.
  - secondary research summarizes available studies in the form of reviews and meta-analyses.

Three main areas are distinguished:

- basic medical research, clinical research, and epidemiological research.

- In individual cases, it may be difficult to classify individual studies to one of these three main categories or to the subcategories.

Basic research

- Basic medical research (otherwise known as experimental research)
  - animal experiments
  - cell studies
  - Biochemical
  - genetic
  - physiological investigation
  - and studies on the properties of drugs and materials.

- In almost all experiments, at least one independent variable is varied and the effects on the dependent variable are investigated.

- Laboratory conditions cannot always be directly transferred to normal clinical practice and processes in isolated cells or in animals are not equivalent to those in man (= generalizability)

- Basic research also includes the development and improvement of analytical procedures , imaging procedures—such as computed tomography or magnetic resonance imaging—, and gene sequencing—such as the link between eye color and specific gene sequences.

- The development of biometric procedures—such as statistical test procedures, modeling and statistical evaluation .

Clinical studies :

- Clinical studies include
  - interventional (or experimental) studies
  - noninterventional (or observational) studies.

  - interventional studies includes :
    - pharmacological effects of drugs >> eye drops
    - medical devices >>> spectacles lenses , prisms , CLs , low vision aids …
    - surgical, physical or psychotherapeutic procedures.

  - Non-interventional study
    - The diagnosis, treatment and monitoring are not performed according to a previously specified study protocol, but exclusively according to medical practice."

- The aim of an interventional clinical study is to compare treatment procedures within a patient population, which should exhibit as few as possible internal differences.

- This is to be achieved by appropriate measures, particularly by random allocation of the patients to the groups, thus avoiding bias in the result.

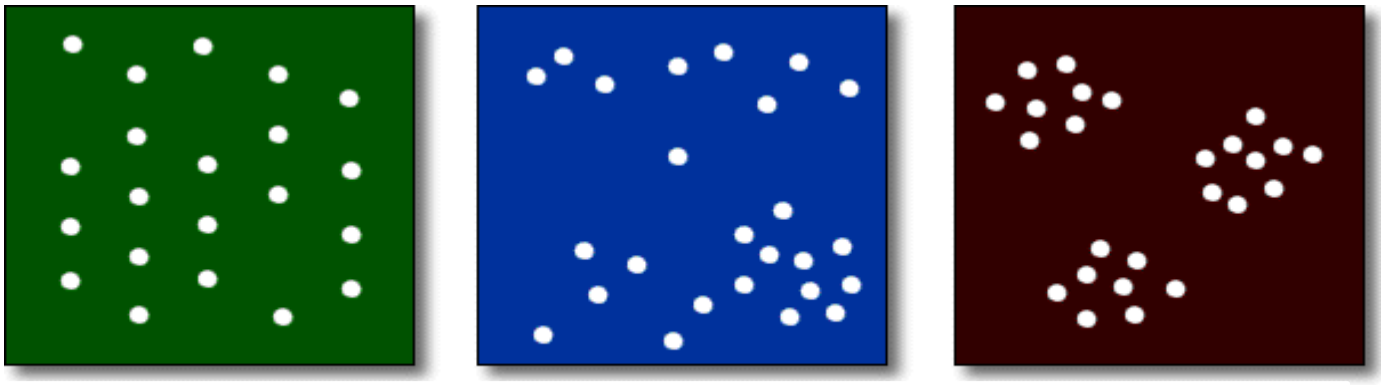
- legal and ethical requirements .

- A control group is included in most clinical studies.

This group receives another treatment regimen and/or placebo.

- Clinical studies should ideally include randomization.

Randomization is intended to maximize homogeneity between the groups and prevent, for example, a specific therapy being reserved for patients with a particularly favorable prognosis .



- Blinding is another suitable method to avoid bias.
  - single and double blinding.

- single blinding, the patient is unaware which treatment he is receiving

- double blinding, neither the patient nor the investigator knows which treatment is planned.

- Blinding the patient and investigator excludes possible subjective (even subconscious) influences on the evaluation of a specific therapy (e.g. drug administration versus placebo).

- Thus, double blinding ensures that the patient or therapy groups are both handled and observed in the same manner.

- The highest possible degree of blinding should always be selected.

- The study statistician should also remain blinded until the details of the evaluation have finally been specified.
  - Triple blinding

- A well designed clinical study must also include case number planning.
  - Sample size calculation

- the randomized controlled and blinded clinical trial with case number planning is accepted as the gold standard for testing the efficacy and safety of therapies or drugs

- noninterventional clinical studies are patient-related observational studies, in which patients are given an individually specified therapy.

- The responsible physician specifies the therapy on the basis of the medical diagnosis and the patient's wishes.

- include
  - noninterventional therapeutic studies
  - prognostic studies
  - observational drug studies
  - secondary data analyses
  - case series and single case analyses .

- Similarly to clinical studies, noninterventional therapy studies include comparison between therapies; however, the treatment is exclusively according to the physician’s discretion. The evaluation is often retrospective.

- Prognostic studies examine the influence of prognostic factors on the further course of a disease.

- Diagnostic studies are another class of observational studies, in which either the quality of a diagnostic method is compared to an established method (ideally a gold standard)

- or an investigator is compared with one or several other investigators (inter-rater comparison) or with himself at different time points (intra-rater comparison)

- If an event is very rare (such as a rare disease or an individual course of treatment), a single-case study, or a case series, are possibilities.
  - A case series is a study on a larger patient group with a specific disease.
  - The lack of a control group is a disadvantage of case series.
  - For this reason, case series are primarily used for descriptive purposes

Epidemiological studies :

- The main point of interest in epidemiological studies is to investigate the distribution and historical changes in the frequency of diseases and the causes for these.

- Analogously to clinical studies, a distinction is made between experimental and observational epidemiological studies

- Interventional epidemiological studies :
  - field studies (sample from an area, such as a large region or a country)
  - group studies (sample from a specific group, such as a specific social or ethnic group).

- On the other hand, many interventions are unsuitable for randomized intervention studies, for ethical, social or political reasons, as the exposure maybe harmful to the subjects

- Observational epidemiological studies can be further subdivided into

  - cohort studies (follow-up studies)
  - case control studies
  - cross- sectional studies (prevalence studies)
  - ecological studies (correlation studies or studies with aggregated data)

- studies with only descriptive evaluation are restricted to a simple depiction of the frequency (incidence and prevalence) and distribution of a disease within a population.

- The objective of the description may also be the regular recording of information (monitoring, surveillance).

- cohort studies involve the observation of two healthy groups of subjects over time. One group is exposed to a specific substance and the other is not exposed.

- It is recorded prospectively how often a specific disease occurs in the two groups . The incidence for the occurrence of the disease can be determined for both groups.

- Moreover, the relative risk (quotient of the incidence rates) is a very important statistical parameter which can be calculated in cohort studies.

- For rare types of exposure, the general population can be used as controls.

- All evaluations naturally consider the age and gender distributions in the corresponding cohorts.

- In case control studies, cases are compared with controls.
  - Cases are persons who fall ill from the disease in question.
  - Controls are persons who are not ill, but are otherwise comparable to the cases.

- A retrospective analysis is performed to establish to what extent persons in the case and control groups were exposed .

- Possible exposure factors include close work, nutrition and pollutant load.

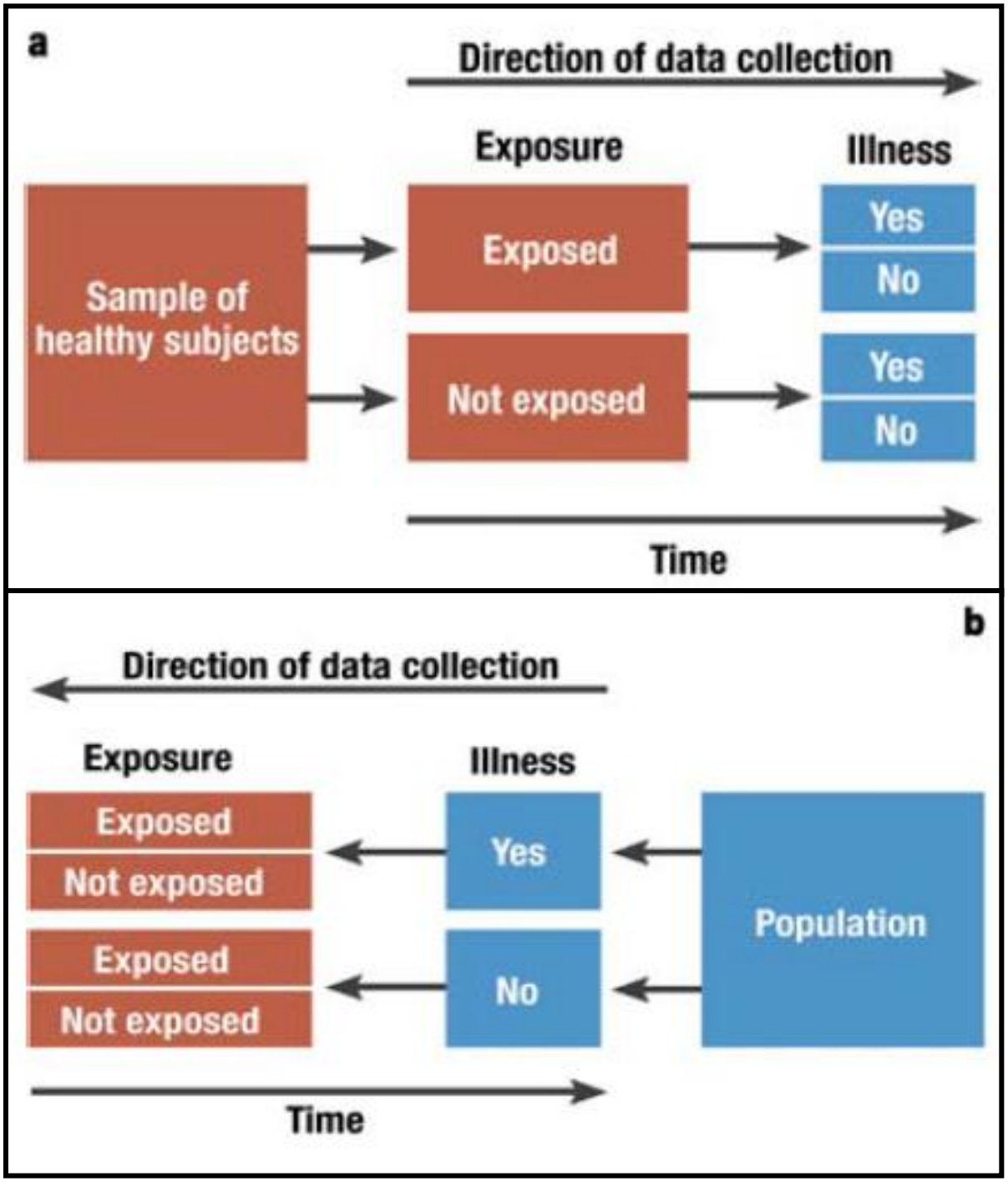
- Care should be taken that the intensity and duration of the exposure is analyzed as carefully and in as detailed a manner as possible.

- If it is observed that ill people are more often exposed than healthy people, it may be concluded that there is a link between the illness and the risk factor.

- Case control studies usually require less time and fewer resources than cohort studies.

- The disadvantage of case control studies is that the incidence rate (rate of new cases) cannot be calculated.

- There is also a great risk of bias from the selection of the study population ("selection bias") .


a
Direction of data collection
Exposure
Illness
Sample of healthy subjects
Exposed
Not exposed
Yes
No
Yes
No
Time
b
Direction of data collection
Exposure
Illness
Exposed
Not exposed
Exposed
Not exposed
Yes
No
Population
Time

Evidence pyramid

Clinical research, providing results that are relevant for the actual clinical practice

Least relevant sources of information
(background information, generating hypotheses for more serious studies, etc.)

- Sample vs. census

- Why sample ??
  - Time
  - Cost
  - Impossibility of conducting a census

Power and Sample Size

- Many analytics problems are setup to compare one hypothesis versus another
  - H_0: $\theta=\theta_0$
  - H_1: $\theta\neq\theta_0$
- how many people do we need in our sample?
  - Type I error
  - Type II error.
  - A Type I error happens when we wrongly conclude that the null hypothesis H_0 is false when it is actually true.
  - A Type II error happens when we wrongly conclude that the null hypothesis H_0 is true when it is actually false.

	H_0 is actually true	H_0 is actually false
We conclude H_0 is true	We made correct conclusion	We made a Type II error
We conclude H_0 is false	We made a Type I error	We made correct conclusion

In reality, we're not so lucky.

	H_0 is actually true	H_0 is actually false
We conclude H_0 is true	We made correct conclusion	We made a Type II error β
We conclude H_0 is false	We made a Type I error α	We made correct conclusion $1-\beta$

- To answer the question of how many people need to be in our sample, we note that sample size is related to our desired Type I and Type II error rates.

- $\alpha = 0.05$
- Power = $1-\beta$, 80 , 90 or 95 %

- In simple terms, a small sample size gives us little power to reject the null hypothesis, whereas a large sample size gives us more statistical power.

For descriptive studies :

- In order to determine a sample size ,you need to specify:
  - Population
  - Confidence interval
  - Confidence level
- Use sample size calculator websites

To compare means :

- In order to determine a sample size for a given hypothesis test, you need to specify:
  - The desired α level, that is, your willingness to commit a Type I error.
  - The desired power ,your willingness to commit a Type II error.
  - A meaningful difference from the value of the parameter that is specified in the null hypothesis.
  - The standard deviation of the sample statistic or, at least, an estimate of the standard deviation (the "standard error") of the sample statistic.
- Use power and sample size program software
- Use formula

Sampling methods

- Random and nonrandom samples.

- Random sampling techniques :
  - Simple random sampling
  - Systematic random sampling
  - Stratified random sampling
    - Subpopulations called strata
    - Sample randomly selected from each stratum

Types of Variables

- Variable assumes different values for different subjects .
  - Vision
  - Refraction
  - Color vision
  - Accommodation
  - Gender
  - Age
  - CDR
  - Deviation angle

- Types of variables :

- Quantitative variables
  - Can be measured numerically
    - Discrete >> countable
      - Number of CL / year
    - Continuous >> assume any numerical value
      - RNFL
      - Refractive errors

- Qualitative variables
  - Cannot assume a numerical value
    - Categories
      - Eye color
      - Refractive state
      - Gender

Data manipulation

- Raw data
  - Gender
  - Age
  - Vision
  - Refraction
  - Symptoms
  - Disease
  - Refractive state
  - Signs, Fundus exam findings

Data Manipulation

- Data entry >> create file to practice
- Compute
  - recode
- Missing data
  - Replace missing data
- Split file
- Select cases

- If condition
  - And
  - Or
  - Range : from low to high

Summarizing and displaying data

- Data entry >> create file to practice
- Frequencies
- Descriptive
- Explore
  - Normality test
  - Extreme values and outliers

Ready to test hypothesis !