Universidade do Minho
Escola de Ciências
Departamento de Física

Técnica de Investigação em Optometria e Ciências da Visão

Mestrado em Optometria Avançada
2015/2016
António Filipe Macedo

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Técnicas de Investigação em Optometria e Ciências da Visão

UNIT 1 Scientific thinking

Aula 1
12 Out 2015

Mestrado em Optometria Avançada
António Filipe Macedo

1.1. Overview

The scientific method is a body of techniques for:

- Investigating phenomena
- Acquiring new knowledge
- Correcting and integrating previous knowledge

To be termed scientific, a method of inquiry must be based on experimental and measurable evidence subject to specific principles of thinking

The Oxford English Dictionary defines the scientific method as "a method or procedure that has characterized natural science since the 17th century, consisting in systematic observation, measurement, and experiment, and the formulation, testing, and modification of hypotheses."

What do scientists seek?

Scientists seek to let reality speak for itself, supporting a theory when a theory's predictions are confirmed and challenging a theory when its predictions prove false.

- Procedures vary from one field of inquiry to another but many steps are common
- Scientific inquiry is intended to be as objective as possible in order to minimize bias
- Documentation, archiving and sharing of all data collected or produced and of the methodologies used so they may be available for careful scrutiny and attempts by other scientists

This practice, known as full disclosure, also means that statistical measures of their reliability may be made

What is scientific method?

The scientific method is the process by which science is carried out. Science builds on previous knowledge, and this can lead to improvements and refinements over time

The scientific method can function in the same way, meaning that it can become more effective at understanding, and even generating new knowledge

The current method is based on a hypothetico-deductive model formulated in the 20th century, although it has undergone significant revision since first proposed

1.1.1. The process

The overall process involves making conjectures (hypotheses), deriving predictions from them as logical consequences, and then carrying out experiments based on those predictions to determine whether the original conjecture was correct

As noted by William Whewell (1794–1866), "invention, sagacity, and genius" are required at every step

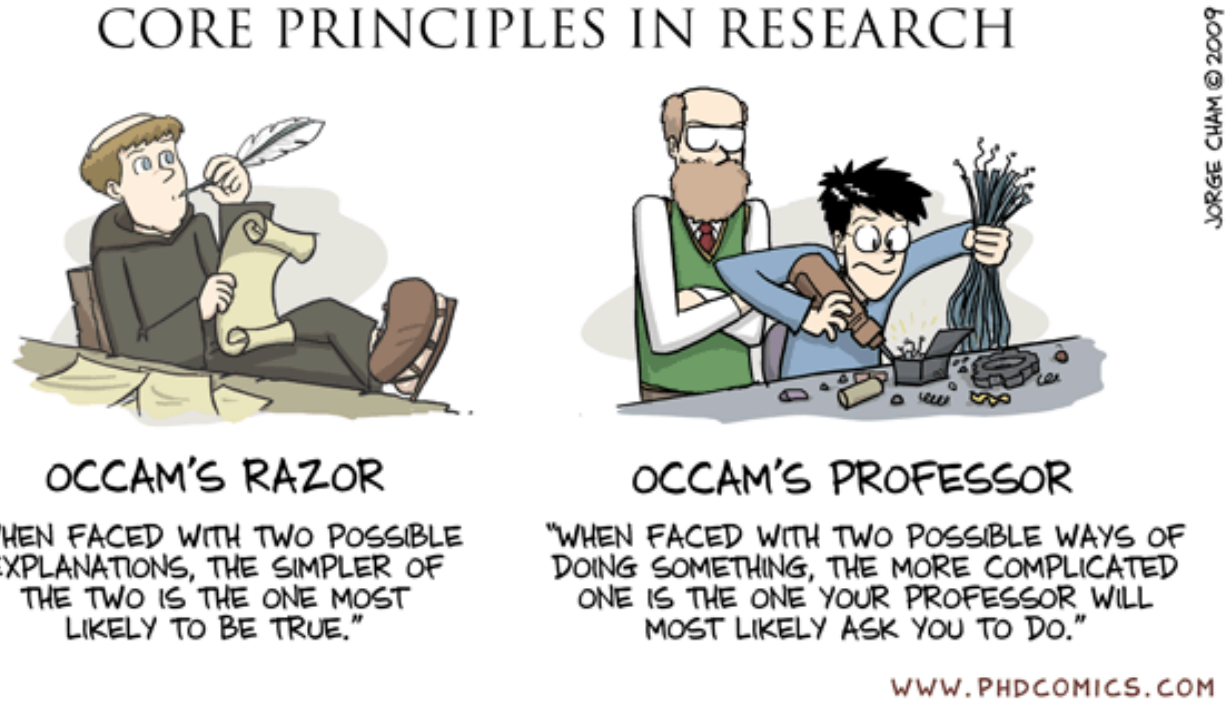
1.1.2. Formulating of a question

The overall process involves:

1. Making conjectures (hypotheses)
2. Deriving predictions from them as logical consequences
3. Carrying out experiments based on predictions to determine whether the original conjecture was correct

1.1.3. Hypothesis

An hypothesis is a conjecture, based on knowledge obtained while formulating the question, that may explain the observed behaviour of a part of our universe



The hypothesis

The hypothesis might be very specific, e.g., Einstein's equivalence principle, or it might be broad, e.g., unknown species of life dwell in the unexplored depths of the oceans

A statistical hypothesis

A statistical hypothesis is a conjecture about some population

For example, the population might be people with a particular disease. The conjecture might be that a new drug will cure the disease in some of those people

Null hypothesis and alternative hypothesis

A null hypothesis is the conjecture that the statistical hypothesis is false, e.g., that the new drug does nothing and that any cures are due to chance effects

Researchers normally want to show that the null hypothesis is false

The alternative hypothesis is the desired outcome, e.g., that the drug does better than chance

1.1.4. Prediction

This step involves determining the logical consequences of the hypothesis. One or more predictions are then selected for further testing

The more unlikely that a prediction would be correct simply by coincidence, then the more convincing it would be if the prediction were fulfilled; evidence is also stronger if the answer to the prediction is not already known
[not done very often -- unfortunately]

1.1.5. Testing

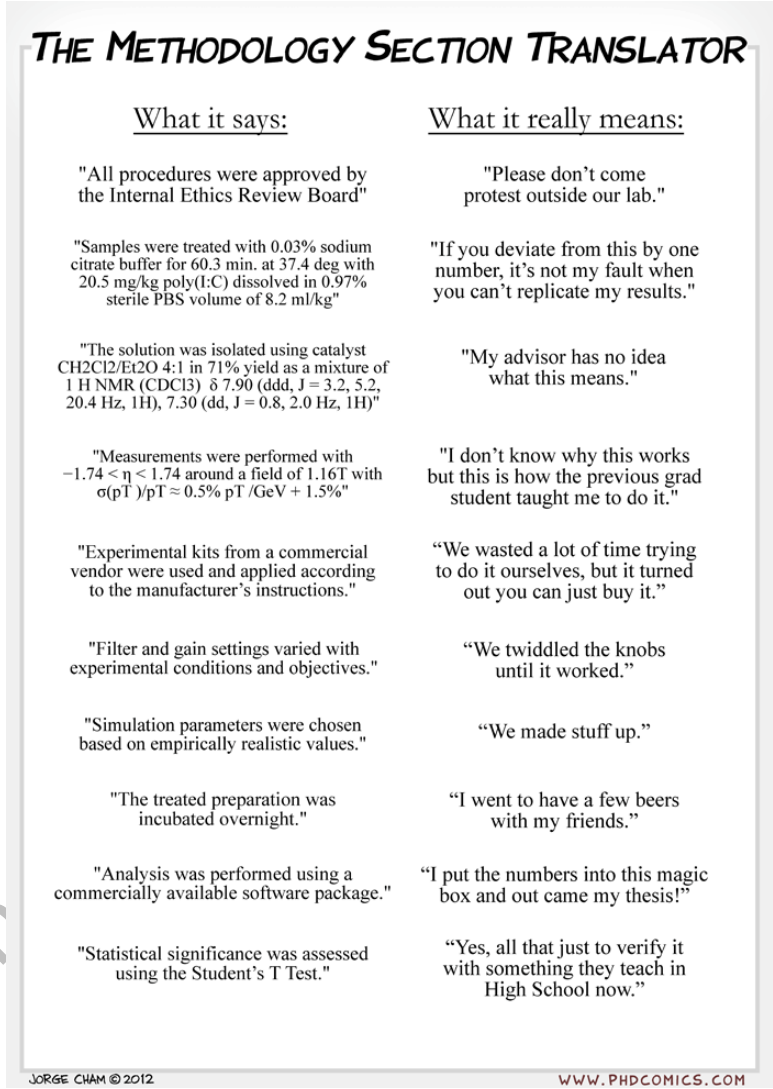
This is an investigation of whether the real world behaves as predicted by the hypothesis. Scientists (and other people) test hypotheses by conducting experiments

The purpose of an experiment is to determine whether observations of the real world agree with or conflict with the predictions derived from an hypothesis

Agreement does not assure that the hypothesis is true; future experiments may reveal problems. Karl Popper advised scientists to try to falsify hypotheses, i.e., to search for and test those experiments that seem most doubtful. Large numbers of successful confirmations are not convincing if they arise from experiments that avoid risk

Experiments should be designed to minimize possible errors, especially through the use of appropriate scientific controls

Failure of an experiment does not necessarily mean the hypothesis is false. Experiments always depend on several hypotheses, e.g., that the test equipment is working properly, and a failure may be a failure of one of the auxiliary hypotheses


THE METHODOLOGY SECTION TRANSLATOR
What it says:
What it really means:
"All procedures were approved by the Internal Ethics Review Board"
"Please don't come protest outside our lab."
"Samples were treated with 0.03% sodium citrate buffer for 60.3 min. at 37.4 deg with 20.5 mg/kg poly(I:C) dissolved in 0.97% sterile PBS volume of 8.2 ml/kg"
"If you deviate from this by one number, it's not my fault when you can't replicate my results."
"The solution was isolated using catalyst CH2Cl2/Et2O 4:1 in 71% yield as a mixture of 1 H NMR (CDCl3) δ 7.90 (ddd, J = 3.2, 5.2, 20.4 Hz, 1H), 7.30 (dd, J = 0.8, 2.0 Hz, 1H)"
"My advisor has no idea what this means."
"Measurements were performed with −1.74 < η < 1.74 around a field of 1.16T with σ(pT)/pT ≈ 0.5% pT /GeV + 1.5%"
"I don't know why this works but this is how the previous grad student taught me to do it."
"Experimental kits from a commercial vendor were used and applied according to the manufacturer's instructions."
"We wasted a lot of time trying to do it ourselves, but it turned out you can just buy it."
"Filter and gain settings varied with experimental conditions and objectives."
"We twiddled the knobs until it worked."
"Simulation parameters were chosen based on empirically realistic values."
"We made stuff up."
"The treated preparation was incubated overnight."
"I went to have a few beers with my friends."
"Analysis was performed using a commercially available software package."
"I put the numbers into this magic box and out came my thesis!"
"Statistical significance was assessed using the Student's T Test."
"Yes, all that just to verify it with something they teach in High School now."
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WWW.PHDCOMICS.COM

1.1.6. Analysis

This involves determining what the results of the experiment show and deciding on the next actions to take

The predictions of the hypothesis are compared to those of the null hypothesis, to determine which is better able to explain the data

Evidence from other scientists and experience are frequently incorporated at any stage in the process

Many iterations may be required to gather sufficient evidence to answer a question with confidence, or to build up many answers to highly specific questions in order to answer a single broader question

1.1.7. Other components

1.1.7.1. Replication

If an experiment cannot be repeated to produce the same results, this implies that the original results might have been in error.

As a result, it is common for a single experiment to be performed multiple times, especially when there are uncontrolled variables or other indications of experimental error

For significant or surprising results, other scientists may also attempt to replicate the results for themselves, especially if those results would be important to their own work.

1.1.7.2. External review

The process of peer review involves evaluation of the experiment by experts, who typically give their opinions anonymously.

Peer review does not certify correctness of the results, only that, in the opinion of the reviewer, the experiments themselves were sound (based on the description supplied by the experimenter).

The specific journal that publishes the results indicates the perceived quality of the work.

1.1.7.3. Data recording and sharing

Scientists typically are careful in recording their data, a requirement promoted by Ludwik Fleck (1896–1961) and others. Though not typically required, they might be requested to supply this data to other scientists who wish to replicate their original results (or parts of their original results), extending to the sharing of any experimental samples that may be difficult to obtain.

1.2. Scientific enquiry

Scientific inquiry generally aims to obtain knowledge in the form of testable explanations that can be used to predict the results of future experiments.

The most successful explanations, which explain and make accurate predictions in a wide range of circumstances, are called often called scientific theories.

Most experimental results do not result in large changes in human understanding. In general, explanations become accepted by a scientific community as evidence in favour is presented, and as presumptions that are inconsistent with the evidence are falsified.

1.2.1. Properties of scientific inquiry

Scientific knowledge is closely tied to empirical findings, and typically remains subject to falsification if new experimental observation incompatible with it is found. That is, no theory can ever be considered completely certain, since new evidence falsifying it might be discovered.

1.2.2. Beliefs and biases

Scientific methodology typically directs that hypotheses be tested in controlled conditions which can be reproduced by others. The scientific community's pursuit of experimental control and reproducibility can diminish the effects of any one individuals' cognitive biases.

For example, pre-existing beliefs can alter the interpretation of results, as in confirmation bias; this is a heuristic that leads a person with a particular belief to see things as reinforcing their belief, even if another observer might disagree (in other words, people tend to observe what they expect to observe).

1.3. Elements of the scientific method

There are different ways of outlining the basic method used for scientific inquiry. The scientific community and philosophers of science generally agree on the following classification of method components. The cycle of formulating hypotheses, testing and analysing the results, and formulating new hypotheses, will resemble a cycle

Four essential elements of the scientific method are iterations, recursions, interleavings, or orderings of the following:

1) Characterizations

Observations, definitions, and measurements of the subject of inquiry

2) Hypotheses

Theoretical, hypothetical explanations of observations and measurements

3) Predictions

Reasoning including logical deduction from the hypothesis or theory

4) Experiments

Tests of all of the above

The elements above are often taught in the educational system as "the scientific method".

The scientific method is not a single recipe: it requires intelligence, imagination, and creativity. In this sense, it is not a mindless set of standards and procedures to follow, but is rather an ongoing cycle, constantly developing more useful, accurate and comprehensive models and methods.

A linearized, pragmatic scheme of the four points above is sometimes offered as a guideline for proceeding:

1) Define a question
2) Gather information and resources (observe)
3) Form an explanatory hypothesis
4) Test the hypothesis by performing an experiment and collecting data in a reproducible manner
5) Analyse the data
6) Interpret the data and draw conclusions that serve as a starting point for new hypothesis
7) Publish results
8) Retest (frequently done by other scientists)

The iterative cycle inherent in this step-by-step method goes from point 3 to 6 back to 3 again. This cycle is not an unanimous way of doing science.

1.3.1. Models of scientific enquiry

1.3.1.1. Classical model

** information not relevant for exams **

1.3.1.2. Pragmatic model

** information not relevant for exams **

…

The scientific method – the method wherein inquiry regards itself as fallible and purposely tests itself and criticizes, corrects, and improves itself.

1.4. Communication and community

Frequently the scientific method is employed not only by a single person, but also by several people cooperating directly or indirectly. Such cooperation can be regarded as one of the defining elements of a scientific community. Various techniques have been developed to ensure the integrity of scientific methodology within such an environment.

1.4.1. Peer review evaluation

Scientific journals use a process of peer review, in which scientists' manuscripts are submitted by editors of scientific journals to (usually one to three) fellow (usually anonymous) scientists familiar with the field for evaluation.

The referees may or may not recommend publication, publication with suggested modifications, or, sometimes, publication in another journal.

This serves to keep the scientific literature free of unscientific or pseudoscientific work, to help cut down on obvious errors, and generally otherwise to improve the quality of the material.

The peer review process can have limitations when considering research outside the conventional scientific paradigm: problems of "groupthink" can interfere with open and fair deliberation of some new research.

1.4.2. Document and replication

Sometimes experimenters may make systematic errors during their experiments, unconsciously veer from scientific method (pathological science) for various reasons, or, in rare cases, deliberately report false results.

Consequently, it is a common practice for other scientists to attempt to repeat the experiments in order to duplicate the results, thus further validating the hypothesis.

1.4.2.2. Archiving

As a result, researchers are expected to practice scientific data archiving in compliance with the policies of government funding agencies and scientific journals.

Detailed records of their experimental procedures, raw data, statistical analyses and source code are preserved in order to provide evidence of the effectiveness and integrity of the procedure and assist in reproduction.

These procedural records may also assist in the conception of new experiments to test the hypothesis, and may prove useful to engineers who might examine the potential practical applications of a discovery.

1.4.2.4. Data sharing

When additional information is needed before a study can be reproduced, the author of the study is expected to provide it promptly. If the author refuses to share data, appeals can be made to the journal editors who published the study or to the institution that funded the research.

1.4.2.6. Limitations

Since it is impossible for a scientist to record everything that took place in an experiment, facts selected for their apparent relevance are reported.

This may lead, unavoidably, to problems later if some supposedly irrelevant feature is questioned.

For example, Heinrich Hertz did not report the size of the room used to test Maxwell's equations, which later turned out to account for a small deviation in the results. The problem is that parts of the theory itself need to be assumed in order to select and report the experimental conditions. The observations are hence sometimes described as being 'theory-laden'.

1.4.3. Dimensions of practice

The primary constraints on contemporary science are:

Publication, i.e. Peer review
Resources (mostly funding)

It has not always been like this: in the old days of the "gentleman scientist" funding (and to a lesser extent publication) were far weaker constraints.

Both of these constraints indirectly require scientific method – work that violates the constraints will be difficult to publish and difficult to get funded. Journals require submitted papers to conform to "good scientific practice" and this is mostly enforced by peer review. Originality, importance and interest are more important – see for example the author guidelines for Nature.

1.5. Philosophy and sociology of science

** information not relevant for exams **

Philosophy of science looks at the underpinning logic of the scientific method, at what separates science from non-science, and the ethic that is implicit in science. There are basic assumptions, derived from philosophy by at least one prominent scientist, that form the base of the scientific method – namely, that reality is objective and consistent, that humans have the capacity to perceive reality accurately, and that rational explanations exist for elements of the real world.

These assumptions from methodological naturalism form a basis on which science may be grounded. Logical Positivist, empiricist, falsificationist, and other theories have criticized these assumptions and given alternative accounts of the logic of science, but each has also itself been criticized.

1.6. History

** information not relevant for exams **

The development of the scientific method is inseparable from the history of science itself. Ancient Egyptian documents describe empirical methods in astronomy, mathematics, and medicine.

In the 7th century BCE, Daniel, a Jewish captive of the Babylonian king Nebuchadnezzar, conducted a scientific experiment complete with a hypothesis, a control group, a treatment group, and a conclusion. The control group partook of the king's delicacies and wine, whereas Daniel's test group limited themselves to vegetables and water.

At the end of the test, Daniel's hypothesis was proven true.

1.7. Relationship with mathematics

Science is the process of gathering, comparing, and evaluating proposed models against observables. A model can be a simulation, mathematical or chemical formula, or set of proposed steps.
Science is like mathematics in that researchers in both disciplines can clearly distinguish what is known from what is unknown at each stage of discovery. Models, in both science and mathematics, need to be internally consistent and also ought to be falsifiable (capable of disproof).

	Mathematical method	Scientific method
1	Understanding	Characterization from experience and observation
2	Analysis	Hypothesis: a proposed explanation
3	Synthesis	Deduction: prediction from the hypothesis
4	Review/Extend	Test and experiment

Técnicas de Investigação em Optometria e Ciências da Visão

UNIT 2 Anatomy and physiology of clinical research

Aula 2
26 Outubro 2015

Mestrado em Optometria Avançada
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2.1. The anatomy of research: what it's made of…

Research follows a protocol, the protocol will help the researcher to stay organized the research in a logical, focused and efficient way.

Table 2.1: Elements of a study protocol

Element	Purpose
Research questions	What questions will the study address?
Significance (background)	Why are these questions important?
Design	How is the study structured?
Time frame	
Epidemiologic approach	
Subjects	Who are the subjects and how will they be selected?
Selection criteria	
Sampling design	
Variables	What measurements will be made?
Predictor variables	
Confounding variables	
Outcome variables	
Statistical issues	How large is the study and how will it be analysed?
Hypotheses	
Sample size	
Analytic approach	

2.1.1. Research question

Imagine you are interested in environmental factors determining myopia progression

Initial question
Should children spend more time outdoors?

This is a good initial question but we need to be more specific and focused. Often making a more clear question involves breaking the whole question into its constituent parts and singling out one or two of these to build the protocol.

A good research question should pass the “so what?” test.

Getting this answer should contribute usefully to our state of knowledge. The acronym FINER denotes five essential characteristics of a good research question: that is (F) feasible, (I) interesting, (N) novel, (E) ethical, and (R) relevant.

Exercise (5 min)
Please take group please bring alternative questions

Study tips
Go to your notes from class, it is likely that you wrote very interesting

2.1.2. Significance

The significance section of a protocol sets the proposed study in the context and gives its rationale:

What is known about that topic at hand?
What kind of answers will the study provide?

This section cites previous research that is relevant and indicates the problems with that research (gaps) and what questions remains.

It must be clear how the findings of the current study will help resolve these uncertainties, leading to new scientific understanding and influencing clinical or other applied knowledge.

Time Outdoors and Physical Activity as Predictors of Incident Myopia in Childhood- A Prospective Cohort Study

Exercise (5 min)

Identify the significance in the paper: Time Outdoors and Physical Activity as Predictors of Incident Myopia in Childhood- A Prospective Cohort Study

Study tips
Go to your notes from class, it is likely that you wrote very interesting

2.1.3. The design

The design can be subject to lots of discussion. However, to get started a fundamental decision is whether to take a passive role in observing the events taking place in the study subjects in an observational study or apply an intervention and examine its effects on these events in a clinical trial. Some designs are explained in Table 2.2.

Specific aspects of each study design will be debated in Unit 5.

Table 2.2: Elements of a study protocol

Study design	Key feature	Example
Observational designs		
Cohort study	A group is followed over time	Examine a cohort of children for several years, observing the incidence (new cases) of myopia
Cross-sectional study	A group examined at one point in time	One investigate the prevalence of myopia in children that play outdoors and children that do not play
Case-control study	Two groups, based on the outcome	One investigate the "cases" of myopia and compare then with those without ("controls") for the time spent playing outdoors
Experimental designs		
Randomized blinded trial	Two groups created by a random process, and a blinded intervention	One decide to take a uniform group and split it in two and force one to play outdoors (treatment) and the other group don't (placedo). Participants do not know which group they are in to

The design that best fits your needs depends on your question. The randomized control trials is typically the gold standard in establishing causality and the cost effectiveness of interventions, but there are situations for which an observational study is better choice or the only feasible option. The relatively low-cost of case control studies and their suitability for uncommon outcomes makes them attractive for many questions.

The study of a topic starts typically with observational studies of a type that is called descriptive

Observational descriptive studies are usually followed by analytic studies that evaluate associations to discover cause-and-effect relationships

The final step is often a clinical trial to establish the effects of an intervention

2.1.4. The study subjects

Two major decisions

First

Specify selection criteria that define the target population

Second

How best to recruit enough

2.1.5. The variables

The choice of which variables to measure, this will be debated again units 5 and 6. In a descriptive study the investigator looks at individual variables one at a time

In an analytic study the investigator studies the associations among two or more variables in order to predict outcomes and to draw inferences about cause and effect. The variable that precedes (or is presumed on biological grounds to be antecedent) is called the predictor variable; the other is called the outcome variable.

Most observational studies have many predictor variables (age, race, diabetes) and several outcome variables (glaucoma, high IOP, retinopathy)
Experiments study an intervention (a special kind of predictor variable because is manipulated by the investigator) such as treatment and placebo

2.1.6. Statistical issues

The investigator must develop plans for managing and analysing the study data. For experiments this always involves specifying a hypothesis, a version of the research question that provides the basis for testing the statistical significance of the findings.

Hypothesis: Children that spend more time outdoors have less myopia

The hypothesis also allow the investigator to estimate the SAMPLE SIZE, the number of subjects needed to observe the expected difference in the outcome between study groups with a reasonable degree of probability, or POWER.

2.2. The physiology of research: How it works…

The goal of clinical research is to draw inferences from the study results about the nature of truth in the universe, as shown in Figure 2.1

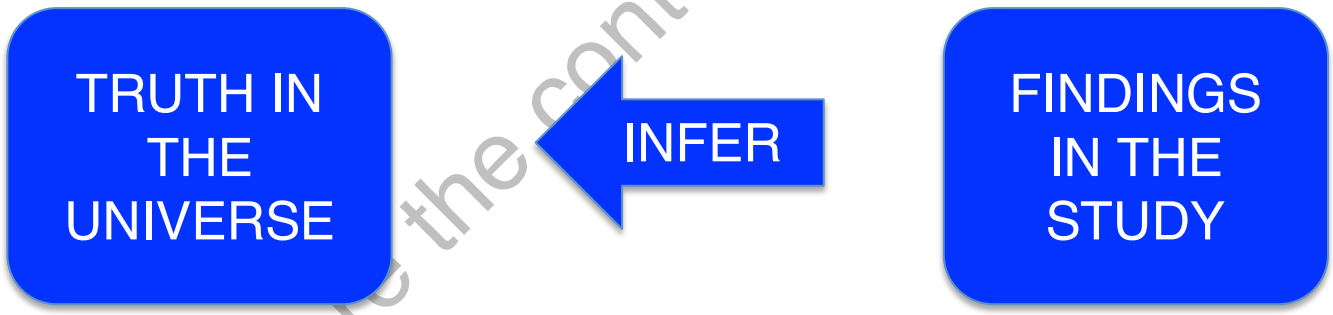


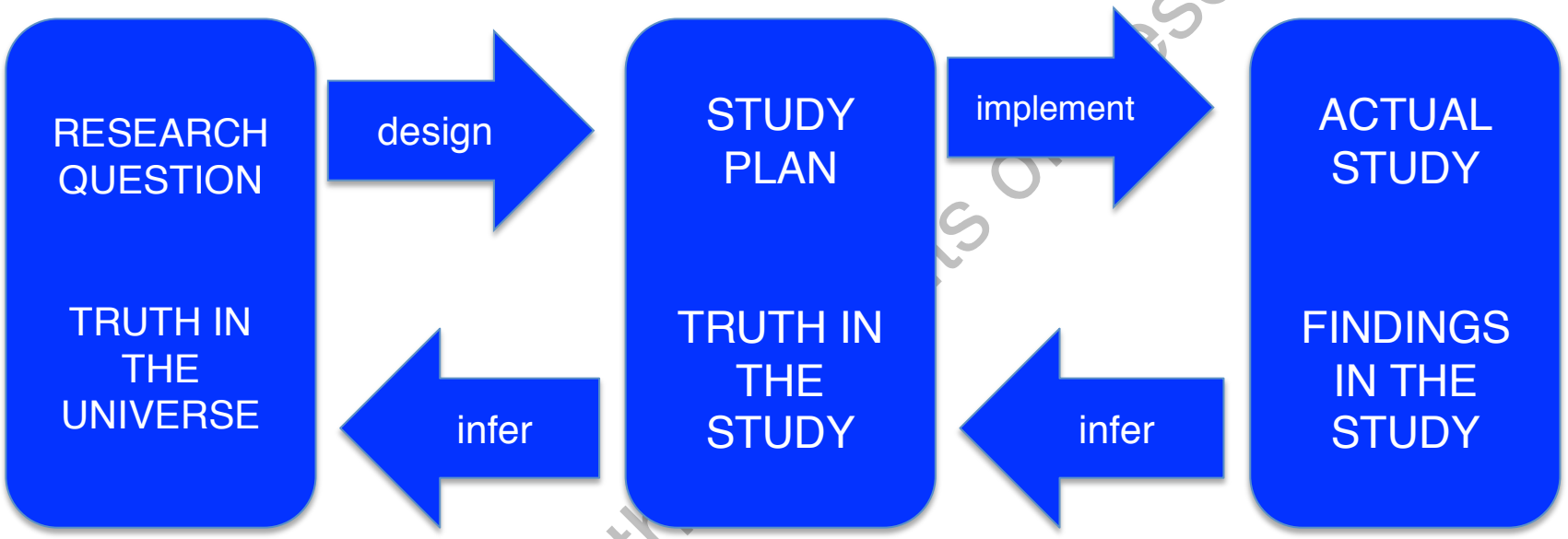
Figure 2.1: The findings of a study lead to inferences about the universe outside.

To start a study that will answer the research question the investigator needs to follow two steps show in Figure 2.2.

Design a study plan with subjects and measurements chosen to enhance the process of appropriately answering the research question

Carry out the study in a way that enhances the likelihood of getting the right answer, that is, to draw the correct conclusions about what actually happened in the study

Figure 2.2: The process of designing and implementing a research project sets the stage for drawing conclusions from the findings



2.3. Designing the study

Initial question
Should children spend more time outdoors to avoid myopia?

We cannot study all children, if the question is given this way it would be impossible to achieve

Exercise (5 min)

Please put this question in a way that the study can be conducted and results can be used

The transformation from research question to study is shown in Figure 2.3

The choice of a sample

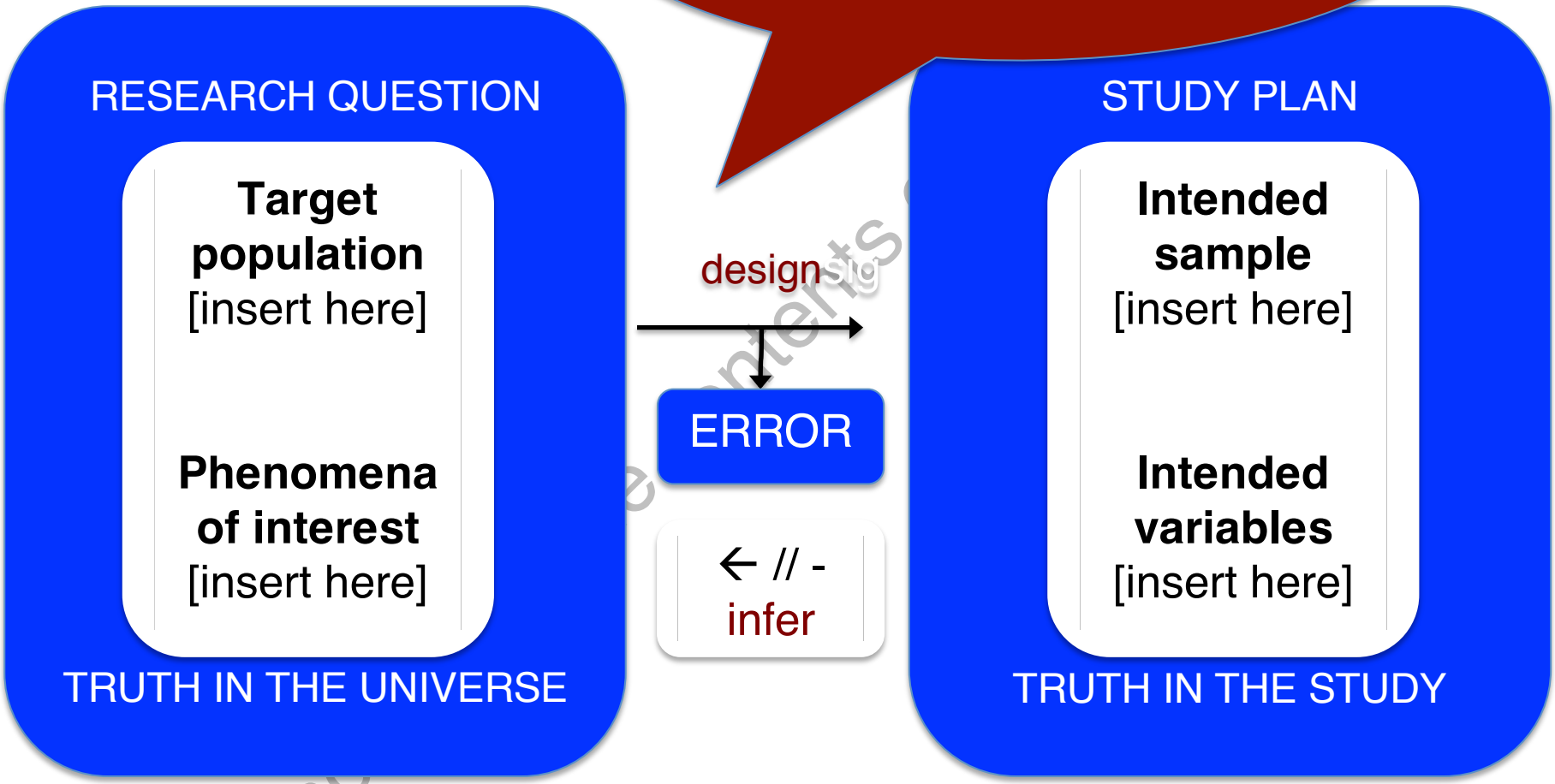
The group of participants specified for the protocol can only be a sample of the population of interest because there are practical barriers to studying the entire population

The choice of variables

The variables specified in the study plan are usually proxies for these phenomena

If the intended sample and variables do not represent the target population and phenomena of interest, these errors may distort inferences about the answer to the research question

Figure 2.3: DESIGN ERRORS



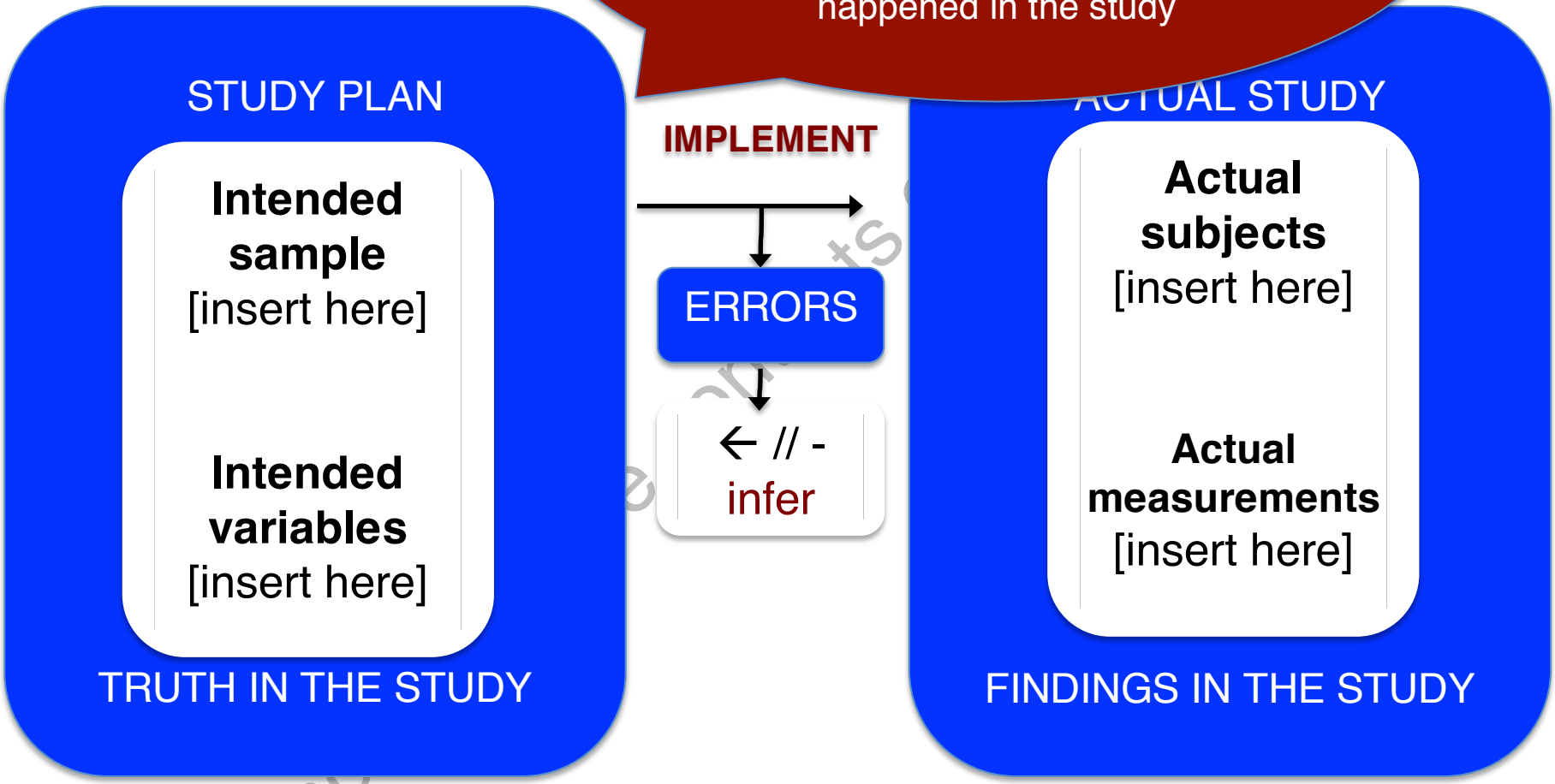
2.4. Implementing the study

In Figure 2.2, right-hand side is concerned with the implementation of the study and the match between implementation and study plan.

The differences between the study plan and the actual study can alter the answer to the research question, as it is represented in Figure 2.4.

Implementation errors: if the actual subjects and measurements do not represent the intended sample and variables, these errors may distort inferences about what actually happened in the study

Figure 2.4: Implementation errors



2.4.1. Drawing a causal inference

A this question will be debated in later in the course

2.4.2. Errors in research

A this question will be debated in later in the course

2.5. Summary

2.6. Exercises: Outline of a study (case study)

Outline of the study

Técnica de Investigação em Optometria e Ciências da Visão

UNIT 3 Literature review and critical analysis

Many material of this class have been taken from the Study Advice website, University of Reading: http://www.reading.ac.uk/internal/studyadvice/

Aula 3
02 Nov 2015

Mestrado em Optometria Avançada
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3.1. Why write a literature review

New discoveries don't materialise out of nowhere; they build upon the findings of previous experiments and investigations

A literature review shows how the investigation you are conducting fits with what has gone before and puts it into context

A literature review demonstrates to your reader that you are able to:

- Understand and critically analyse the background research
- Select and source the information that is necessary to develop a context for your research

What else?

- Shows how your investigation relates to previous research
- Reveals the contribution that your investigation makes to this field (fills a gap, or builds on existing research, for instance)
- Provides evidence that may help explain your findings later

3.2. What is a literature review

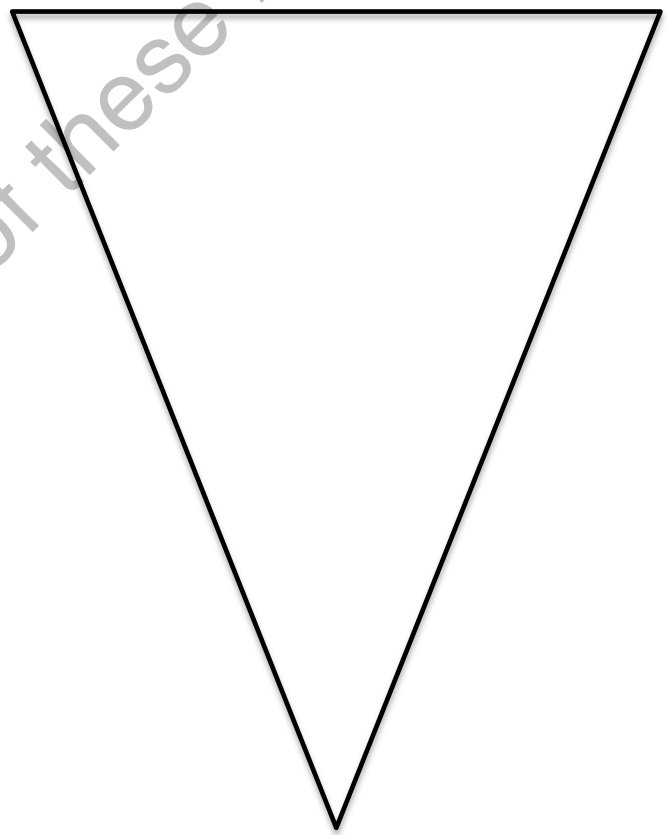
A literature review is a select analysis of existing research which is relevant to your topic, showing how it relates to your investigation. It explains and justifies how your investigation may help answer some of the questions or gaps in this area of research

A literature review is not a straightforward summary of everything you have read on the topic and it is not a chronological description of what was discovered in your field

A longer literature review may have headings to help group the relevant research into themes or topics. This gives a focus to your analysis, as you can group similar studies together and compare and contrast their approaches, any weaknesses or strengths in their methods, and their findings

3.2.1. Think of a literature review as an inverted triangle

- First briefly explain **the broad issues** related to your investigation; you don't need to write much about this, just demonstrate that you are aware of the breadth of your subject
- Then narrow your focus to deal with the **studies that overlap with your research**
- Finally, hone in any research, which is **directly related to your specific investigation**. Proportionally you spend most time discussing those studies which have most direct relevance to your research



Myopia arises from a mismatch between the axial length of the eye and the focal power of its refractive elements, the cornea and crystalline lens. This produces blurred distance vision that requires the use of spectacles, contact lenses or refractive surgery for correction. A high degree of myopia is associated with a number of sight-threatening pathologies.[1,2] Myopia is rare in infancy, but increases steadily in prevalence to affect approximately 25–50% of young adults in Western countries, and up to 80% of young adults in parts of South East Asia.[3,4]

Experiments in animals from a range of taxonomic orders, including primates, have shown that the visual environment can influence refractive development.[5-8] For instance, the deprivation of sharp vision ("form deprivation") induces axial myopia, as does the hyperopic defocus imposed by wearing a minus-power spectacle lens.[9,10] Genetic factors also have been shown to be important, because—at least in chickens—they are the major determinant of an individual animal's susceptibility to myopia induced by the visual environment.[11] The level of illumination during the day (and, indeed, the timing or complete absence of a light or dark phase) also can affect refractive development.[12-21]

3.3. How do I get started

Start by identifying what you will need to know to inform your research:

1. What research has already been done on this topic?
2. What are the sub-areas of the topic you need to explore?
3. What other research (perhaps not directly on the topic) might be relevant to your investigation?
4. How do these sub-topics and other research overlap with your investigation?

3.3.1. Identify your goals

Identifying what you want to find out from your reading before you start will help you to focus and make your reading more active

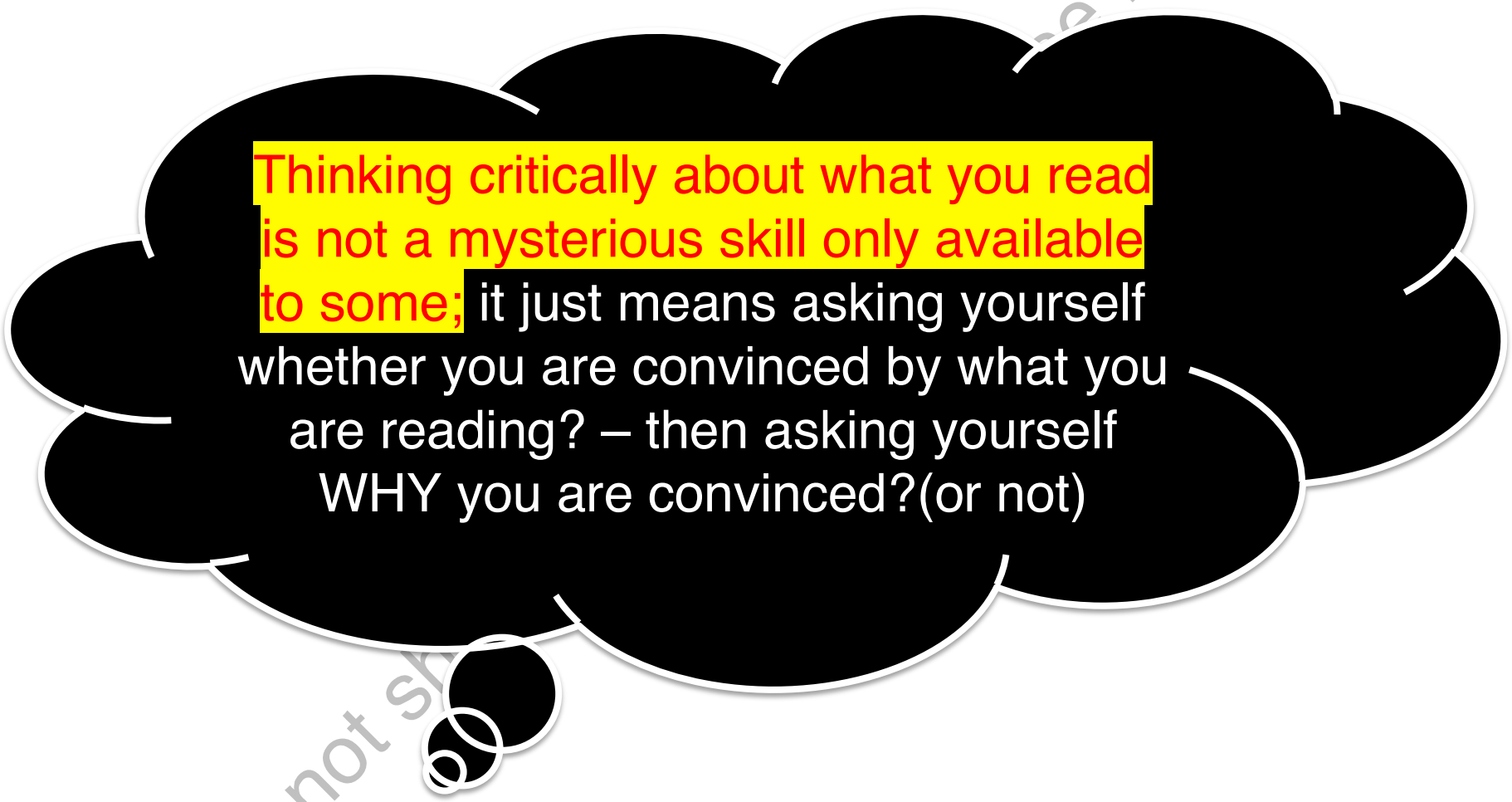
Decide what you need to read up on and perhaps write a few questions to seek answers to whilst reading

Start by reading a basic introduction, encyclopaedia article, or general textbook first. This will give you an overview and broad framework on which to hang more complex information, making it easier to process and stay focused

3.3.2. Reading to find out…

- Wide background information or contexts
- Previous or most recent research on a defined area
- Theories or methods to underpin (reinforce) your work
- Evidence to support your ideas

3.3.3. Critical and reflective reading



3.3.3.1. When reading a paper consider the following

- What is the main line of thought?
- Is there a hidden plan?
- What evidence is being used?
- Are there any limitations in the evidence or research methods?
- What are the conclusions?
- Does it fit in with other academic research or line of thought?
- Does it alter / strengthen your own view – and why?

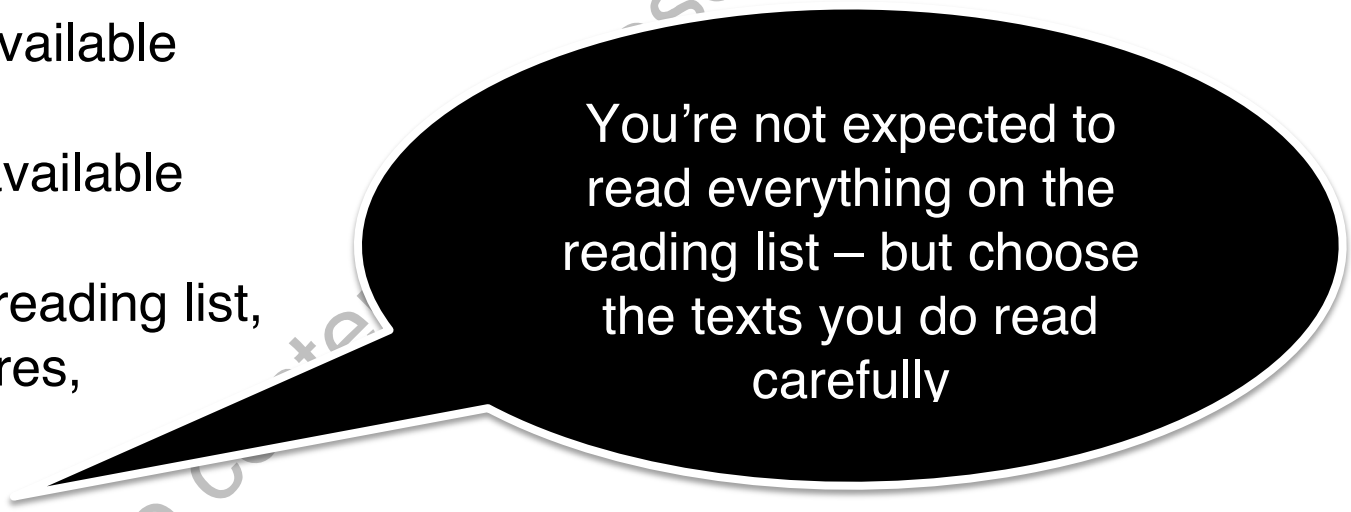
3.3.4. Staying focused

- What do I want to know about? (your reading goals?)
- What is the main idea – or what are the major findings?
- How does this fit in with my own ideas, theory, and experience?
- Am I surprised – or do I agree and what is making me agree?

Read actively by asking yourself what you think about the information you are reading. This will keep you actively engaging with what you are reading, rather than just passively absorbing it

3.3.5. Selecting what you read

- The amount of time available
- What resources are available
- Any guidance given (reading list, references from lectures, supervisor etc)



3.3.5.1. Check for relevance & usefulness by asking questions

- Look at the summary, abstract, introduction or contents page. Does it cover your goals?
- Is it sufficiently up-to-date?
- Look up an item from the index and / or read through a couple of paragraphs – is it at the right level?
- Are the examples, illustrations, diagrams etc. easy to follow and helpful for your purpose?
- Check the references – what is the range of the author's sources?

3.4. Searching for sources

It's easy to think that the best way to search for texts is to use the Internet – to 'Google it'. There are useful online tools that you may use, like Google Scholar.

However, for most literature reviews you will need to focus on academically authoritative texts like academic books, journals, research reports, and government publications

Searching Google will give you thousands of hits, few of them authoritative, and you will waste time sorting through them

A better idea is to use databases. These are available through the Library in paper and electronic (usually online) forms

3.4.1. Examples of recommended databases

_Medline
www.pubmed.com

_Scopus
www.scopus.com

_Science Direct
www.sciencedirect.com

_Cochrane Reviews
http://www2.cochrane.org/reviews/

_Google Académico
http://scholar.google.pt

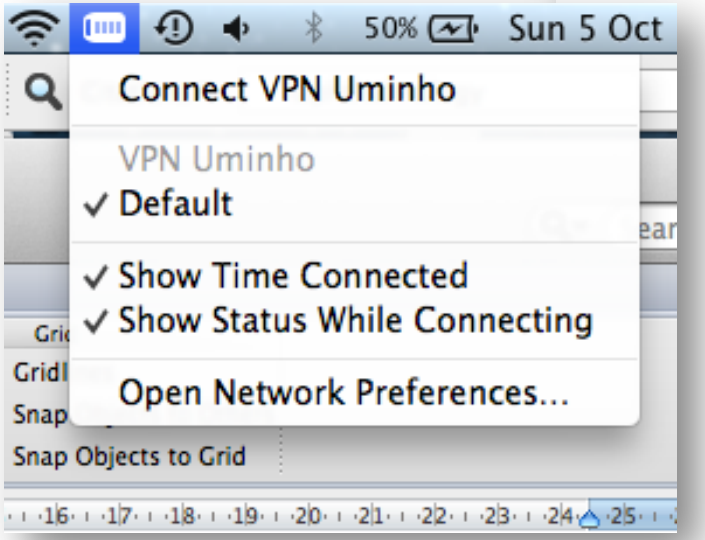
_Clinical Trials
http://clinicaltrials.gov

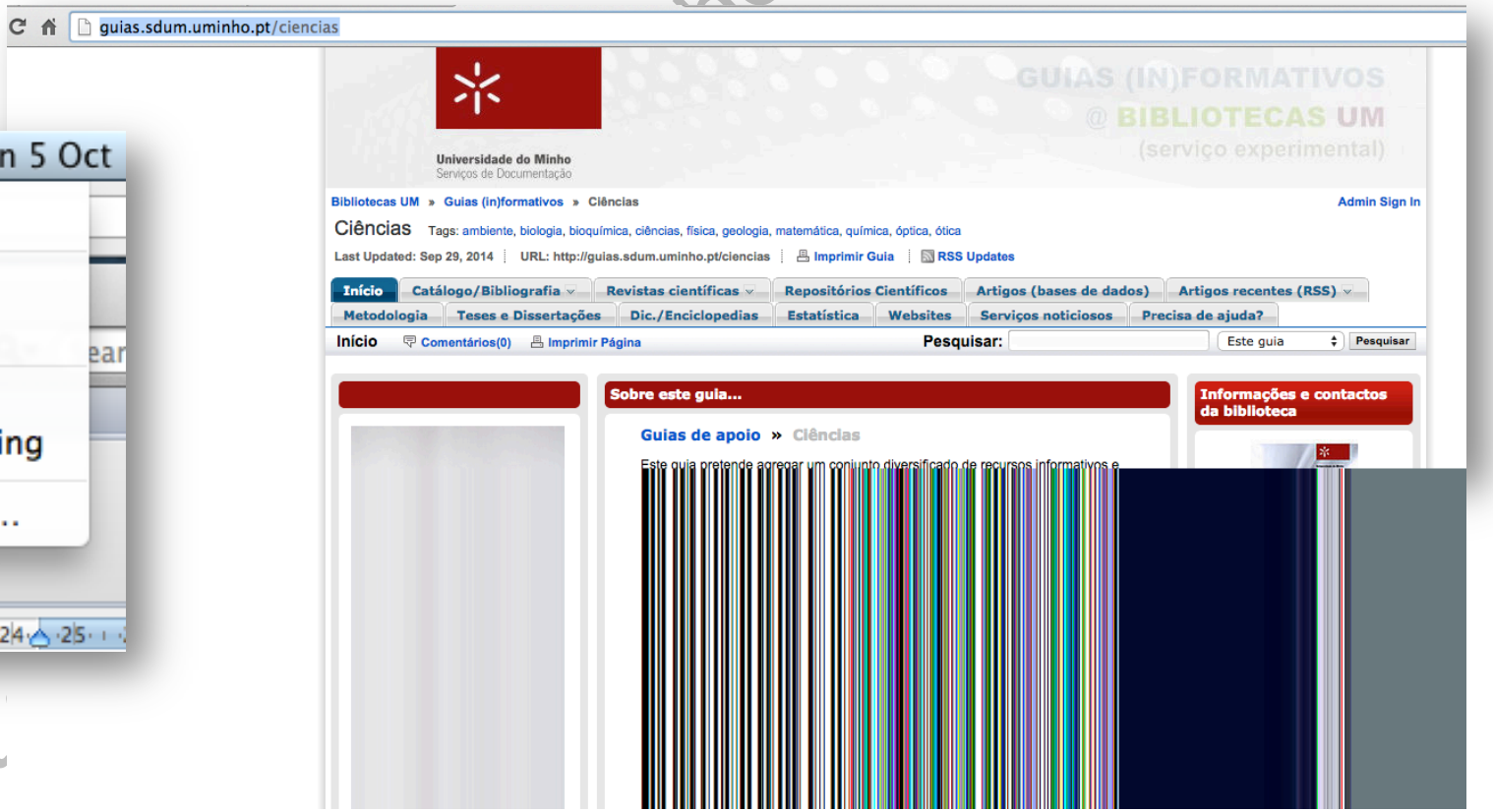
_FDA
http://www.fda.gov/

_Patent Database
www.freepatentsonline.com

www.patentstorm.us

3.4.2. For using University of Minho resources from home

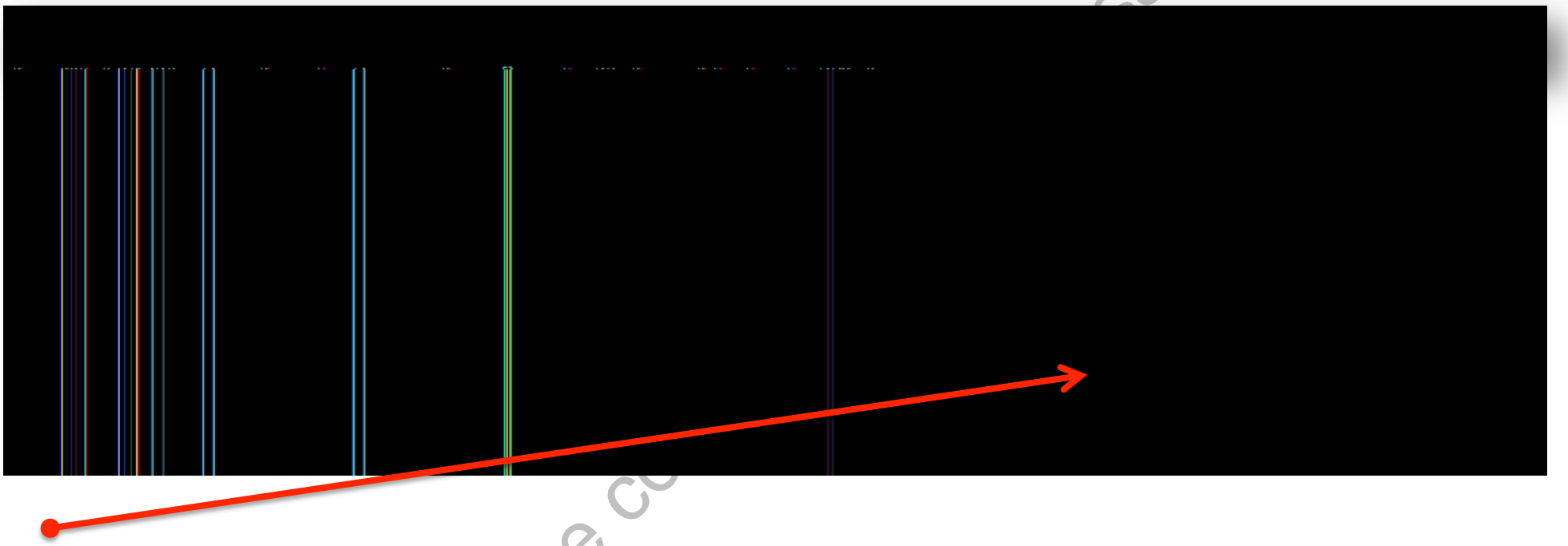




Alternative (in case you do not have VPN protocol in your computer)

https://webvpn.uminho.pt/webvpn.html?next=/http/0/www.sdum.uminho.pt/Default.aspx%3Ftabid%3D4%26pageid%3D13%26lang%3Dpt-PT
(copy and past this address to your browser)

Enter your user name and password provided by the university

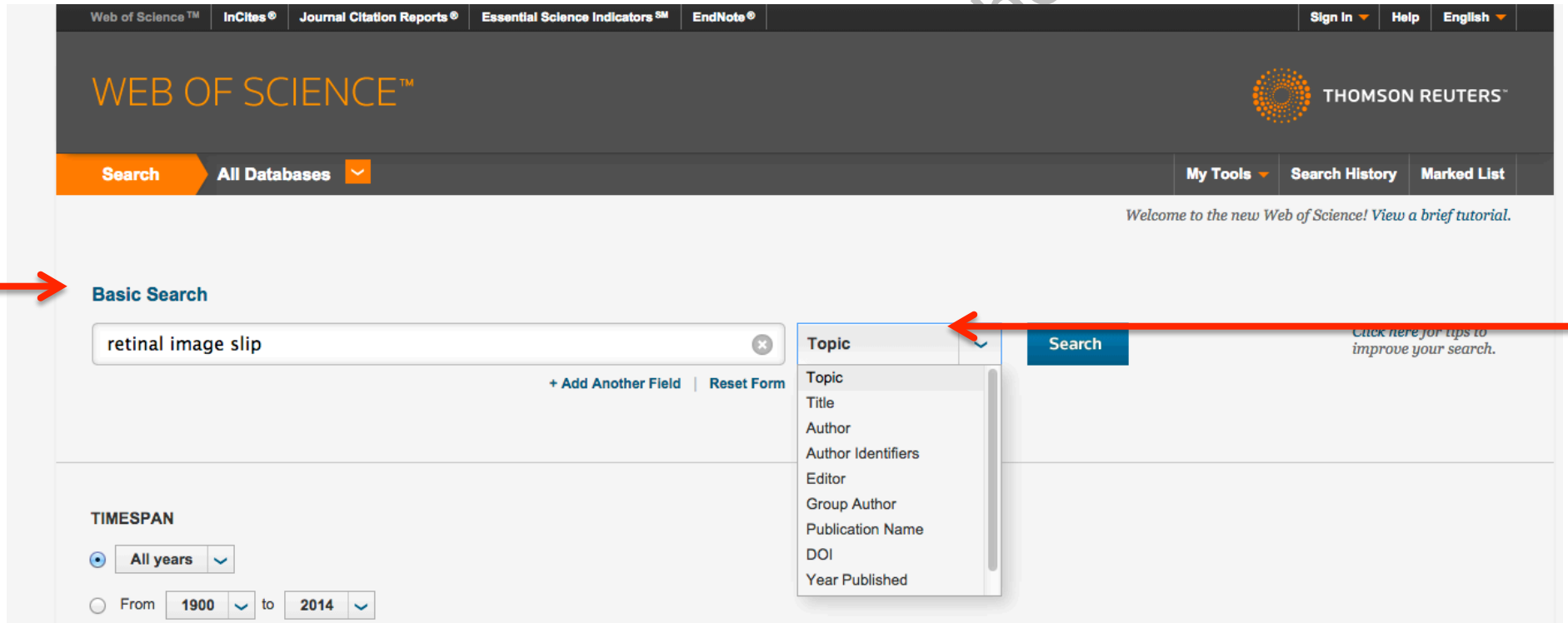


Click “ SDUM- Bases de Dados”

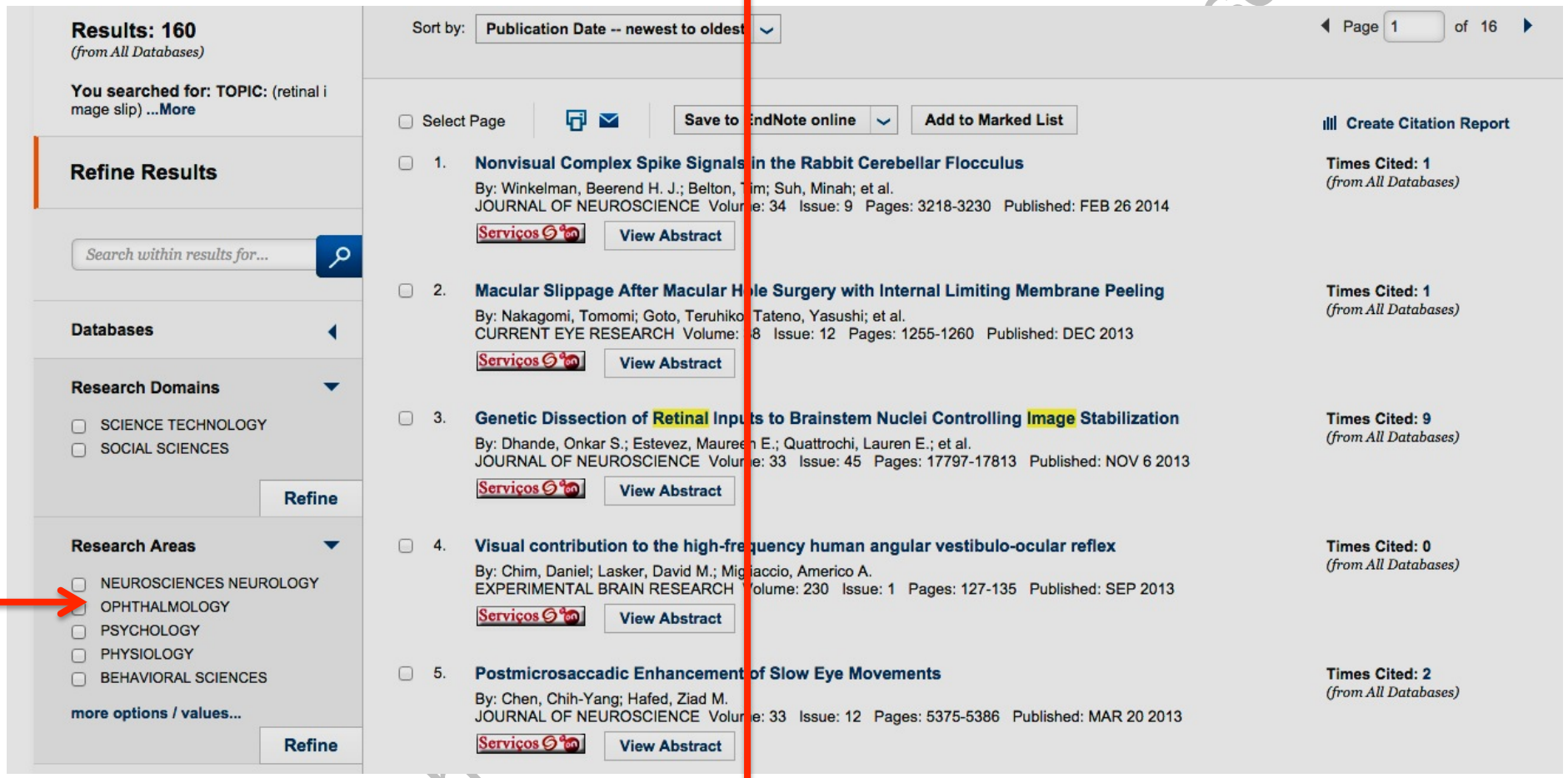
Choose the database where you want to work

Economia y Negocios	Economia, Gestão	Breve descrição b-on
ERIC - Educational Resources Information Center	Educação	Breve descrição b-on
ISI Web of Knowledge (WoK) Inclui *Cross search* em:	Multidisciplinar	Breve descrição b-on
- Current Contents Connect	Multidisciplinar	Breve descrição b-on
- Derwent Inovation Index	Multidisciplinar	Base patentes Breve descrição b-on
- Essential Science Indicators	Multidisciplinar	B.bibliométrica Breve descrição b-on
- Journal Citation Reports	Multidisciplinar	B.bibliométrica Breve descrição b-on
- Web of Science + Proceedings	Multidisciplinar	*Citation index* Breve descrição b-on
Library, Information Science & Technology Abstracts (LISTA)	Ciências da Informação	Breve descrição b-on
MathSciNet	Matemática	Breve descrição

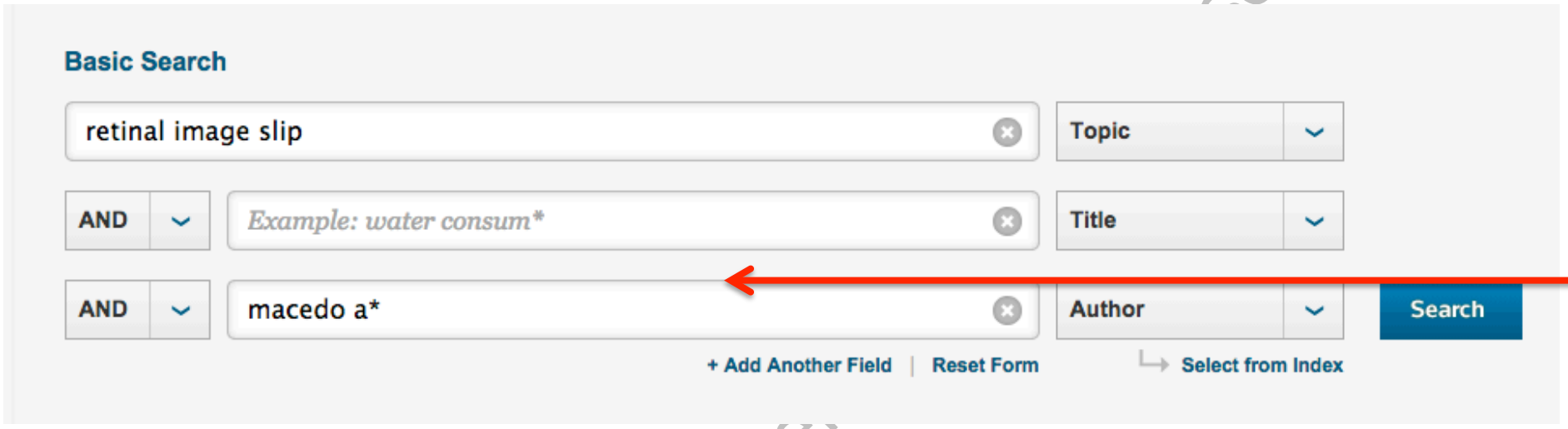
You will get the interface below, below “Basic Search” you can type keywords. In the dropdown menu you can select for what this keywords stand for (Topic or Title etc)



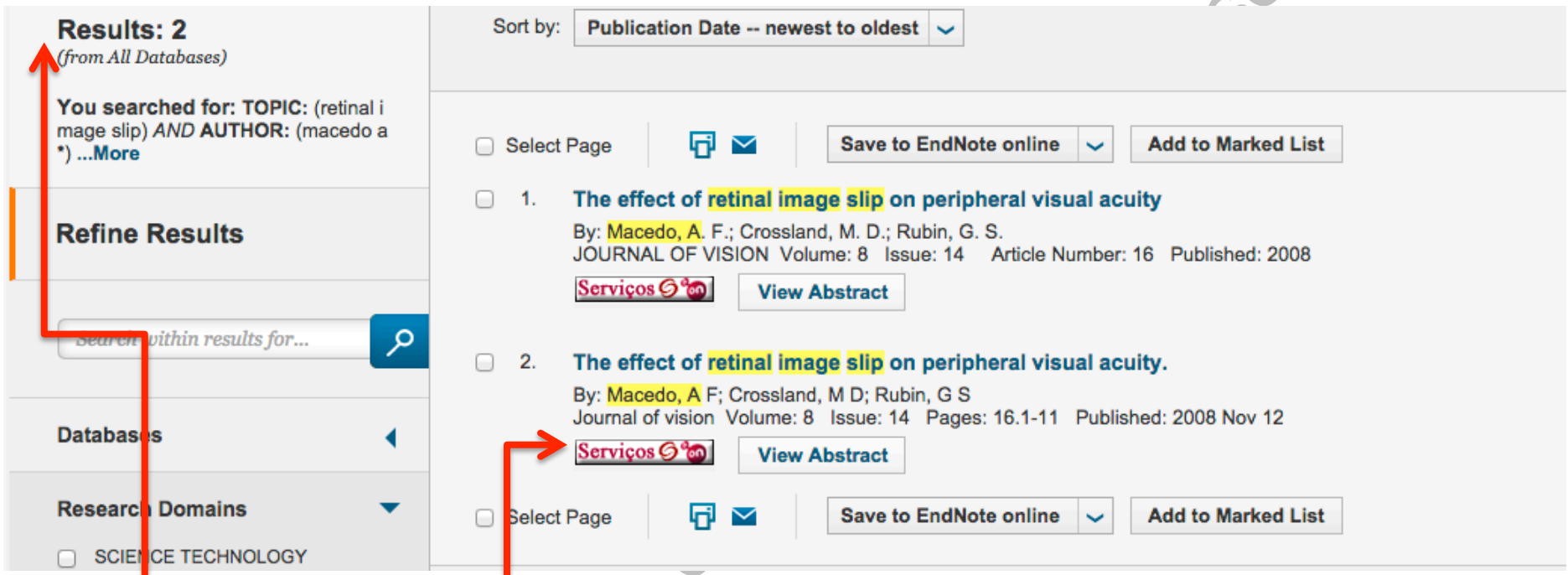
You might find it useful to add another field to narrow down your search



This is a good result with 160 papers, but you can refine your search if you look for an area

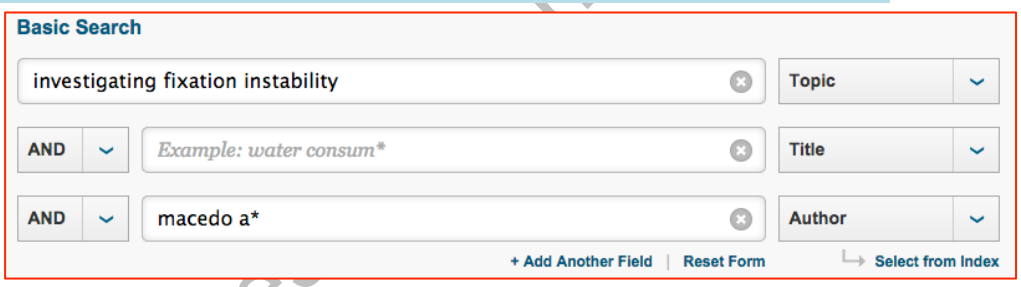


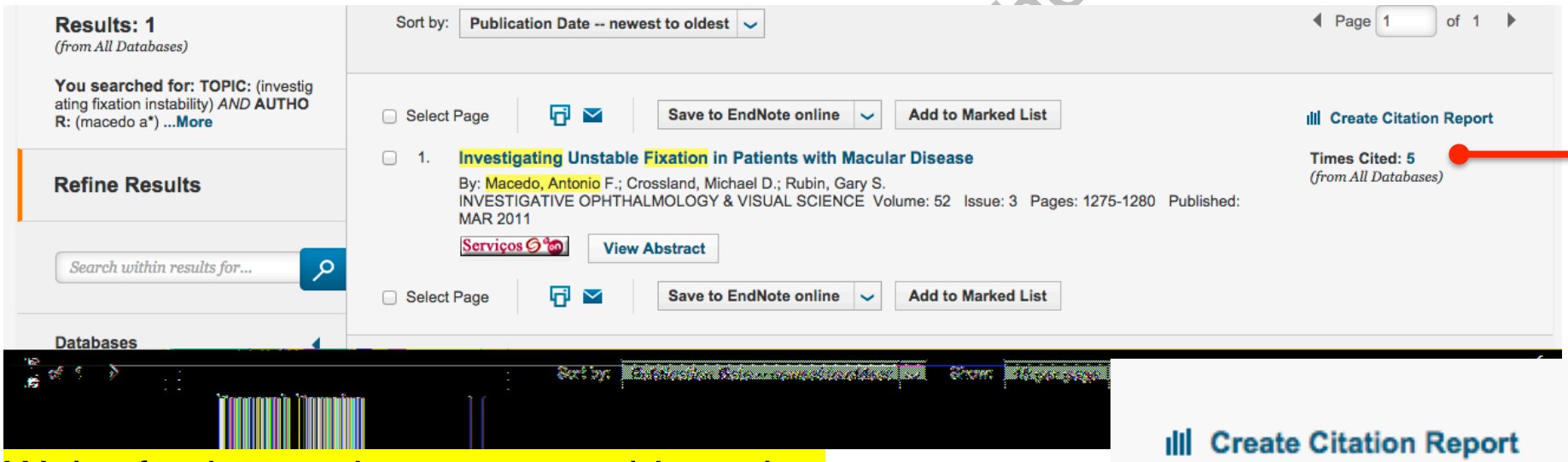
By adding an author field you can narrow down your search for 2 or 3 results

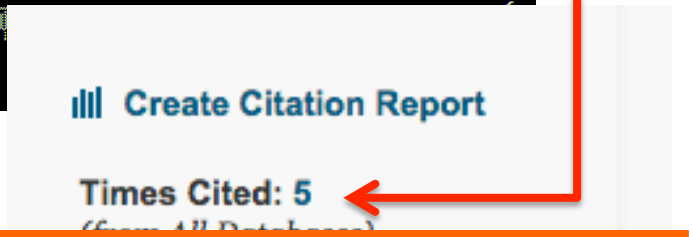


Now you have two results only and you can select what paper you want by clicking “SERVIÇOS”

3.4.3. Why Web of Science?







Web of science gives you two things that can be extremely useful when you are reading. One is the “times cited” information

Click on **“5”** and you will get a list of the papers citing that work (next page) and you can follow-up that research

Select Page | Save to EndNote online | Add to Marked List | Create Citation Report

1. **Decreased Fixation Stability of the Preferred Retinal Location in Juvenile Macular Degeneration**
   By: Bethlehem, Richard A. I.; Dumoulin, Serge O.; Dalmaijer, Edwin S.; et al.
   PLOS ONE Volume: 9 Issue: 6 Article Number: e100171 Published: JUN 17 2014
   Serviços | View Abstract
   Times Cited: 0 (from All Databases)

2. **Relationship between fixation stability measured with MP-1 and reading performance**
   By: Amore, Filippo M.; Fasciani, Romina; Silvestri, Valeria; et al.
   OPHTHALMIC AND PHYSIOLOGICAL OPTICS Volume: 33 Issue: 5 Pages: 611-617 Published: SEP 2013
   Serviços | View Abstract
   Times Cited: 1 (from All Databases)

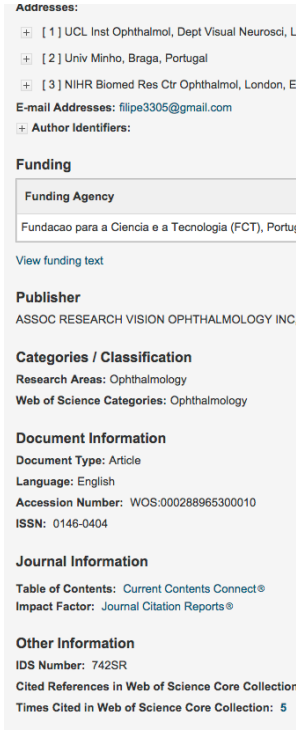
3. **Image Jitter Enhances Visual Performance When Spatial Resolution Is Impaired**
   By: Watson, Lynne M.; Strang, Niall C.; Scobie, Fraser; et al.
   INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE Volume: 53 Issue: 10 Pages: 6004-6010 Published: SEP 2012
   Serviços | View Abstract
   Times Cited: 1 (from All Databases)

4. **Fixation Patterns in Maculopathy: From Binocular to Monocular Viewing**
   By: Tarita-Nistor, Luminita; Brent, Michael H.; Steinbach, Martin J.; et al.
   OPTOMETRY AND VISION SCIENCE Volume: 89 Issue: 3 Pages: 277-287 Published: MAR 2012
   Serviços | View Abstract
   Times Cited: 4 (from All Databases)

5. **Resolution of static and dynamic stimuli in the peripheral visual field**
   By: Lewis, Peter; Rosen, Robert; Unsbo, Peter; et al.
   VISION RESEARCH Volume: 51 Issue: 16 Pages: 1829-1834 Published: AUG 15 2011
   Serviços | View Abstract
   Times Cited: 3 (from All Databases)

Investigating Unstable Fixation in Patients with Macular Disease

By: Macedo, Antonio F.; Crossland, Michael D.; Rubin, Gary S.
INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE Volume: 52 Issue: 3 Pages: 1275-1280 Published: MAR 2011


Addresses:
[1] UCL Inst Ophthalmol, Dept Visual Neurosci, L
[2] Univ Minho, Braga, Portugal
[3] NIHR Biomed Res Ctr Ophthalmol, London, E
E-mail Addresses: filipe3305@gmail.com
Author Identifiers:

Funding

Funding Agency
Fundacao para a Ciencia e a Tecnologia (FCT), Portu

View funding text

Publisher
ASSOC RESEARCH VISION OPHTHALMOLOGY INC

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Research Areas: Ophthalmology
Web of Science Categories: Ophthalmology

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ISSN: 0146-0404

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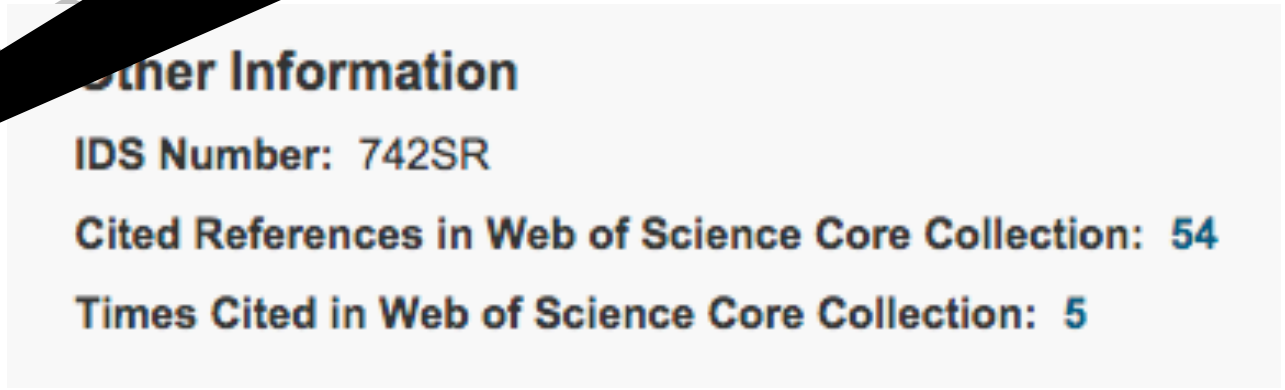
Table of Contents: Current Contents Connect®
Impact Factor: Journal Citation Reports®

Other Information
IDS Number: 742SR
Cited References in Web of Science Core Collectior
Times Cited in Web of Science Core Collection: 5

At the bottom of the page you can find a link to “cited references” and times cited link



UNIT 3 Literature review and critical analysis

Cited References: 54

(from Web of Science Core Collection)

From: Investigating Unstable Fixation in Patients with Macular Disease **...More**

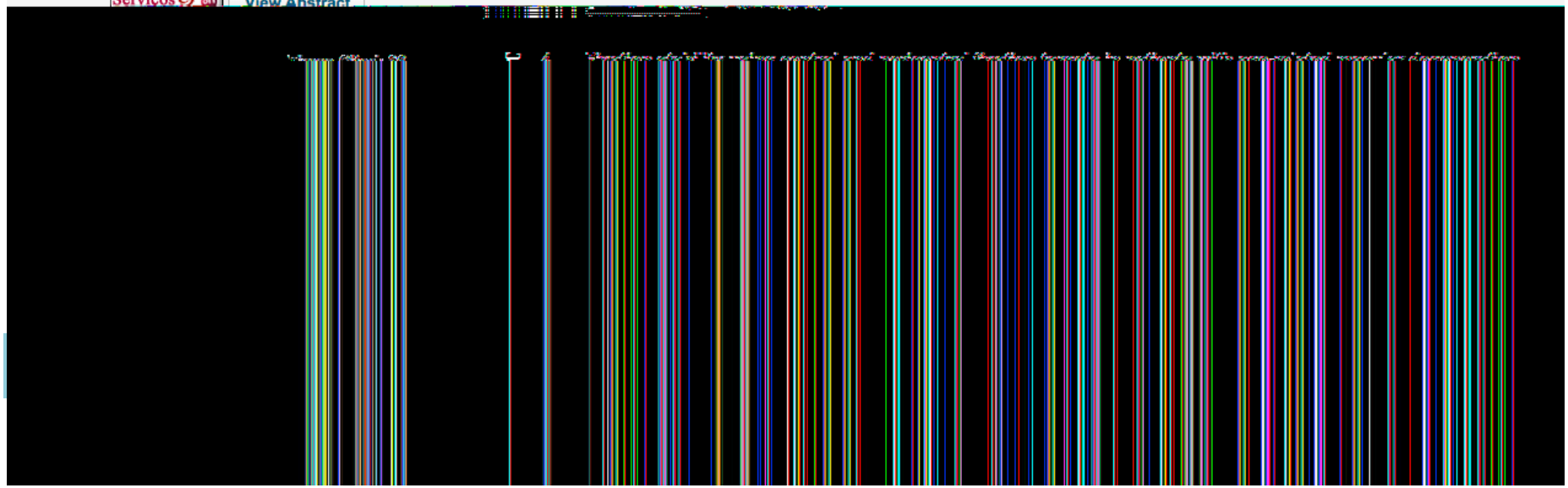
Page 1 of 2

Select Page | Save to EndNote online | Add to Marked List | Find Related Records >

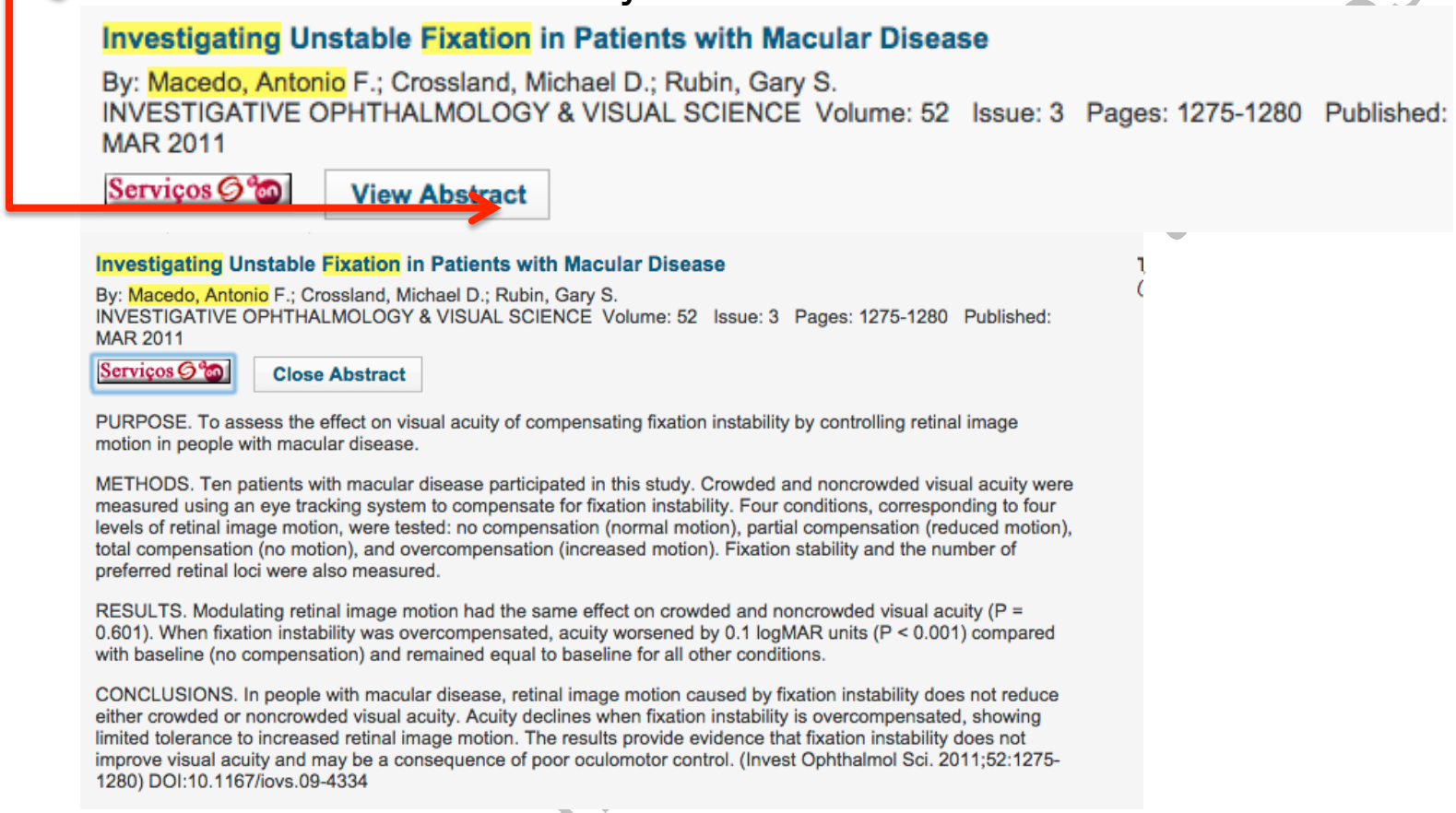
1. **HUMAN PERIPHERAL SPATIAL-RESOLUTION FOR ACHROMATIC AND CHROMATIC STIMULI - LIMITS IMPOSED BY OPTICAL AND RETINAL FACTORS**
By: ANDERSON, SJ; MULLEN, KT; HESS, RF
JOURNAL OF PHYSIOLOGY-LONDON Volume: 442 Pages: 47-64 Published: OCT 1991
Serviços | View Abstract
Times Cited: 96 *(from All Databases)*

2. **RESISTANCE TO POSITIONAL NOISE IN HUMAN VISION**
By: BADCOCK, DR; WONG, TL
NATURE Volume: 343 Issue: 6258 Pages: 554-555 Published: FEB 8 1990
Serviços
Times Cited: 14 *(from All Databases)*

3. **PERIPHERAL SPATIAL VISION - LIMITS IMPOSED BY OPTICS, PHOTORECEPTORS, AND RECEPTOR POOLING**
By: BANKS, MS; SEKULER, AB; ANDERSON, SJ
JOURNAL OF THE OPTICAL SOCIETY OF AMERICA A-OPTICS IMAGE SCIENCE AND VISION Volume: 8 Issue: 11 Pages: 1775-1787 Published: NOV 1991
Serviços | View Abstract
Times Cited: 108 *(from All Databases)*



View abstract can be very useful



Investigating Unstable Fixation in Patients with Macular Disease

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INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE Volume: 52 Issue: 3 Pages: 1275-1280 Published: MAR 2011

Serviços | View Abstract

Investigating Unstable Fixation in Patients with Macular Disease

By: Macedo, Antonio F.; Crossland, Michael D.; Rubin, Gary S.
INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE Volume: 52 Issue: 3 Pages: 1275-1280 Published: MAR 2011

Serviços | Close Abstract

PURPOSE. To assess the effect on visual acuity of compensating fixation instability by controlling retinal image motion in people with macular disease.

METHODS. Ten patients with macular disease participated in this study. Crowded and noncrowded visual acuity were measured using an eye tracking system to compensate for fixation instability. Four conditions, corresponding to four levels of retinal image motion, were tested: no compensation (normal motion), partial compensation (reduced motion), total compensation (no motion), and overcompensation (increased motion). Fixation stability and the number of preferred retinal loci were also measured.

RESULTS. Modulating retinal image motion had the same effect on crowded and noncrowded visual acuity ($P = 0.601$). When fixation instability was overcompensated, acuity worsened by 0.1 logMAR units ($P < 0.001$) compared with baseline (no compensation) and remained equal to baseline for all other conditions.

CONCLUSIONS. In people with macular disease, retinal image motion caused by fixation instability does not reduce either crowded or noncrowded visual acuity. Acuity declines when fixation instability is overcompensated, showing limited tolerance to increased retinal image motion. The results provide evidence that fixation instability does not improve visual acuity and may be a consequence of poor oculomotor control. (Invest Ophthalmol Sci. 2011;52:1275-1280) DOI:10.1167/iovs.09-4334

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Investigating Unstable Fixation in Patients with Macular Disease

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This Article

Published online before print October 6, 2010, doi: 10.1167/iovs.09-4334

Invest. Ophthalmol. Vis. Sci. March 9, 2011 vol. 52 no. 3 1275-1280

Abstract *Free*

» Full Text

Antonio F. Macedo[1,2], Michael D. Crossland[1,3] and Gary S. Rubin[1,3]

Author Affiliations

Corresponding author: Antonio F. Macedo, Department of Visual Neuroscience, UCL Institute of Ophthalmology, London EC1V 9EL, UK; filipe3305@gmail.com.

3.4.4. Limitations of Web of Science

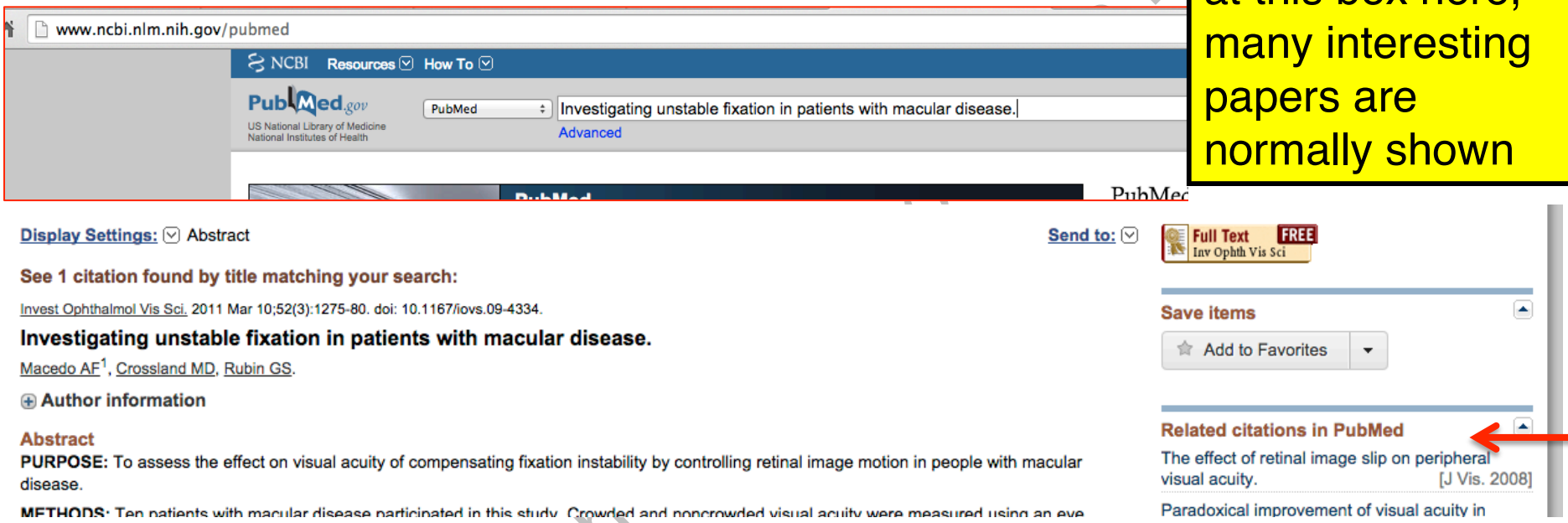
- ✓ You need to be in an institutional network
- ✓ Sometimes, due to information confirmations, it takes to much to update citations etc

3.4.5. Other sources not requiring institutional login (but that might help)

- ❖ Pubmed: http://www.ncbi.nlm.nih.gov/pubmed
- ❖ Google Scholar http://scholar.google.pt/

Why be logged at UMinho? see section 3.4.5.3

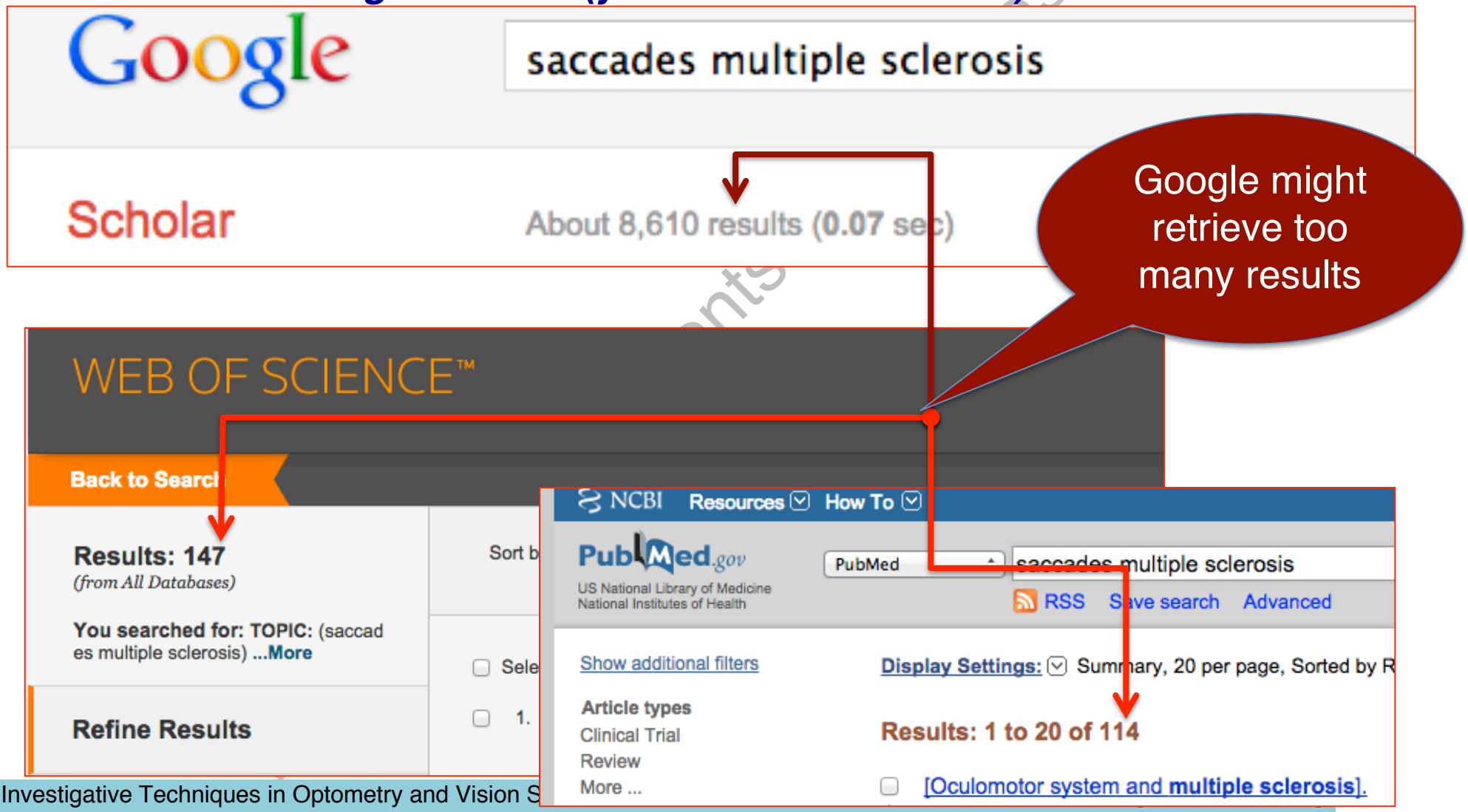
3.4.5.1. Pubmed



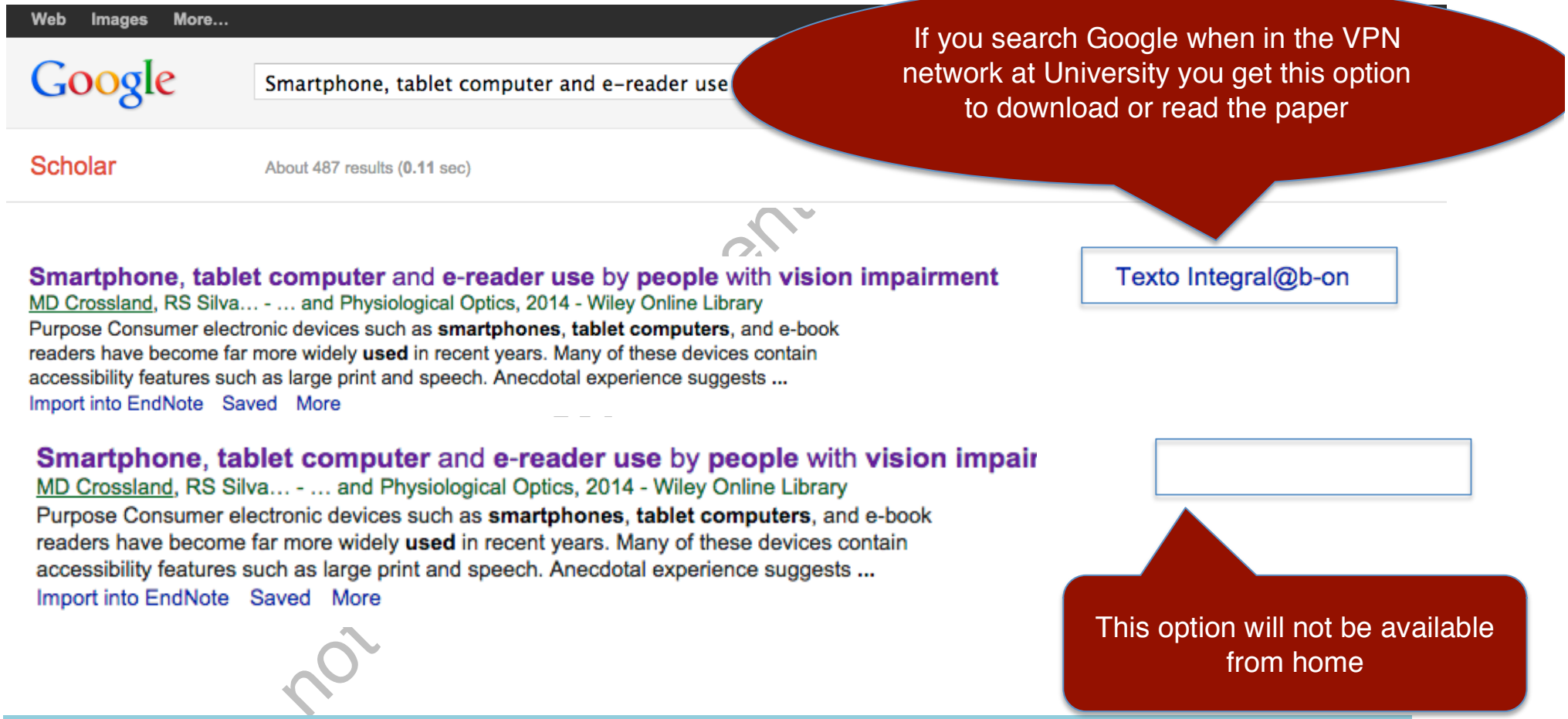
Always give a look at this box here, many interesting papers are normally shown

Pubmed is a free (you can use it from home) searching engine for science but it can be annoying because (sometimes) it does not provide a link to the journal (or if provides, you might not have access…)

3.4.5.2. Google scholar (you need to be careful)

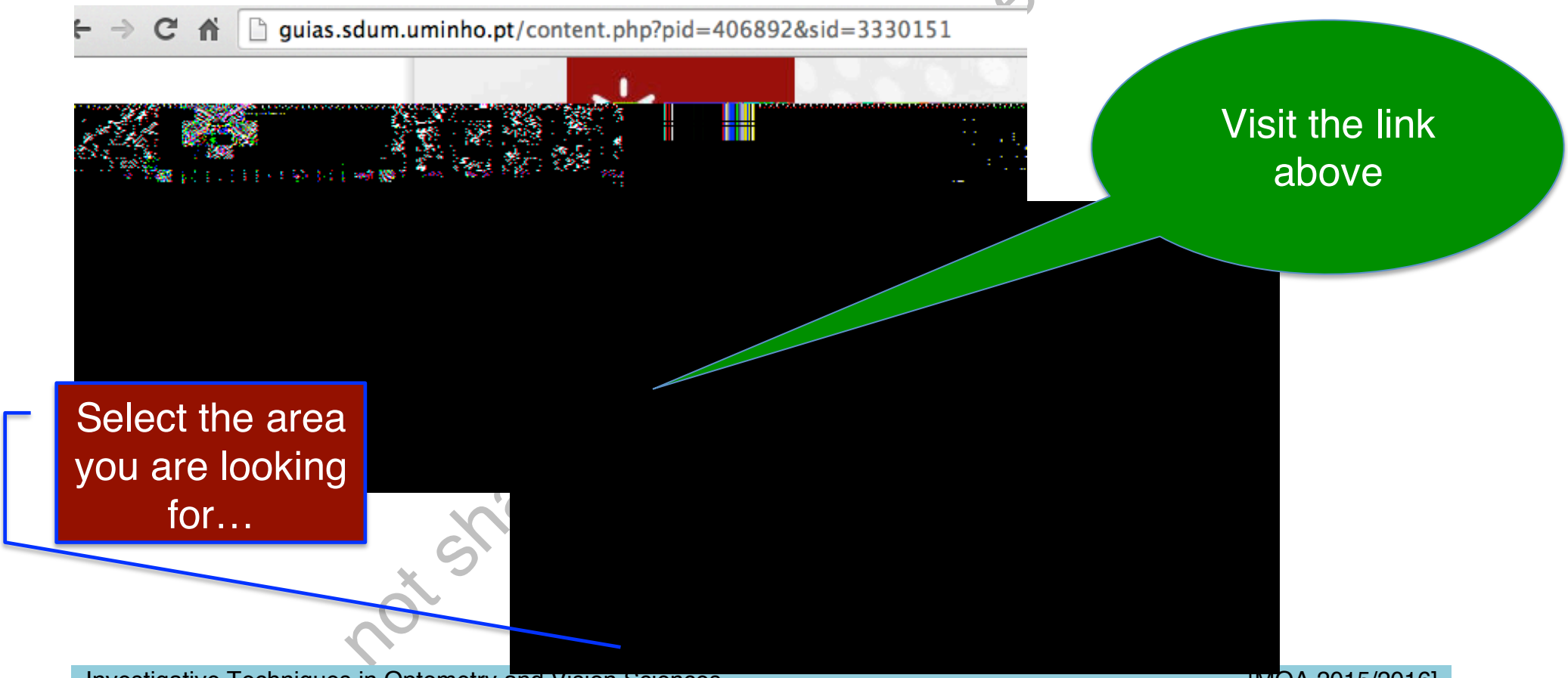


3.4.5.3. Why login in Google scholar



3.4.6. Where to find previous thesis?

http://guias.sdum.uminho.pt/content.php?pid=406892&sid=3330151



3.4.7. Want to know more about sources?

The Literature Review: A Step-by-Step Guide for Students
by Ridley, Diana

(You can get this from the library)

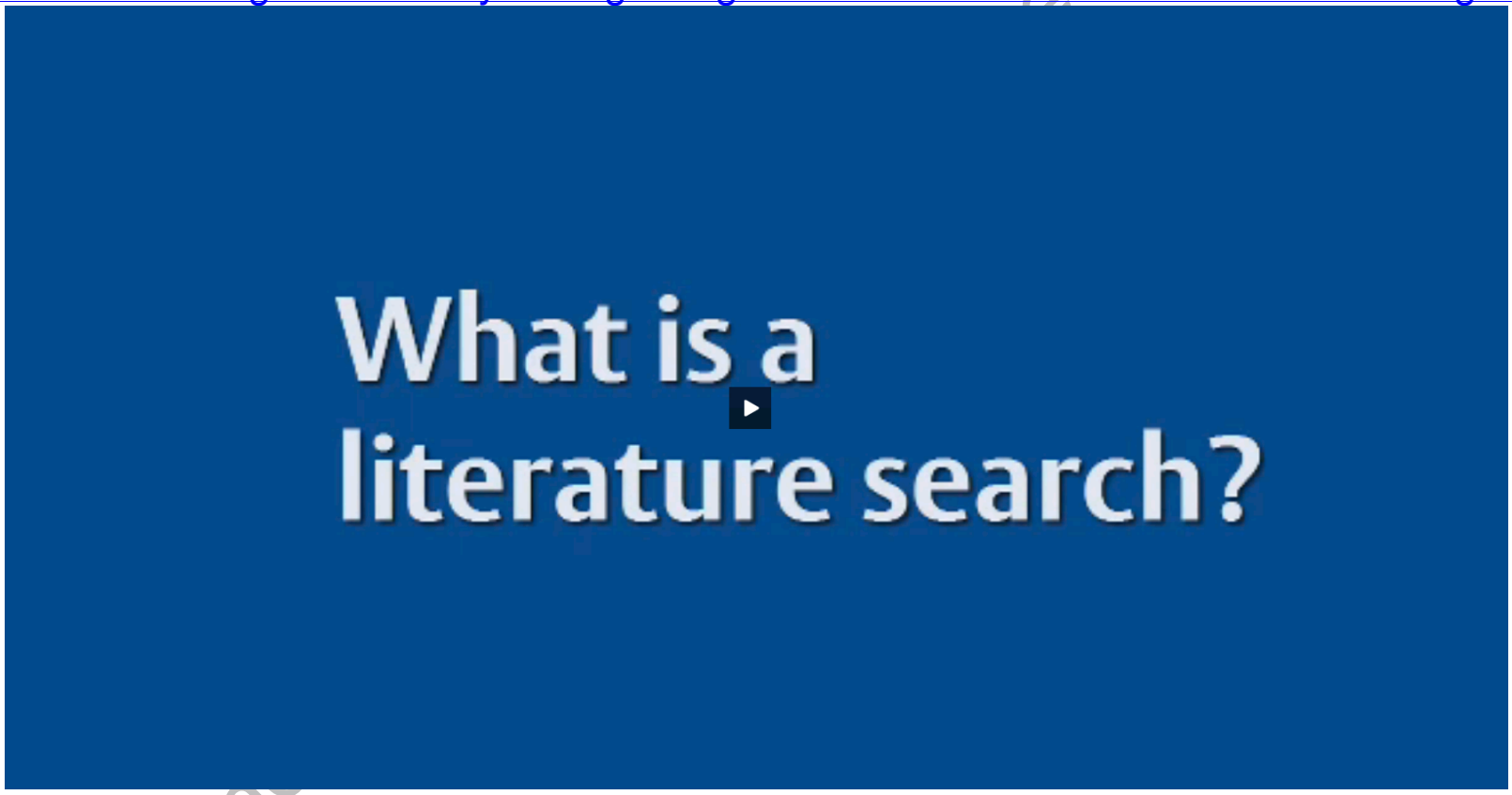
Escolha o Formato: Standard | Ficha do Catálogo | Referência Bibliográfica | Etiquetas UNIMARC

ID	000314906
Autor	Ridley, Diana
Título	The literature review : a step-by-step guide for students / Diana Ridley
Edição	2nd ed
Local	Los Angeles
Editor	Sage
Ano	imp. 2013
Descrição	[XI], 214 p. : il. ; 25 cm
Colecção	Sage study skills
CDU	001.8
ISBN	978-1-4462-0143-5

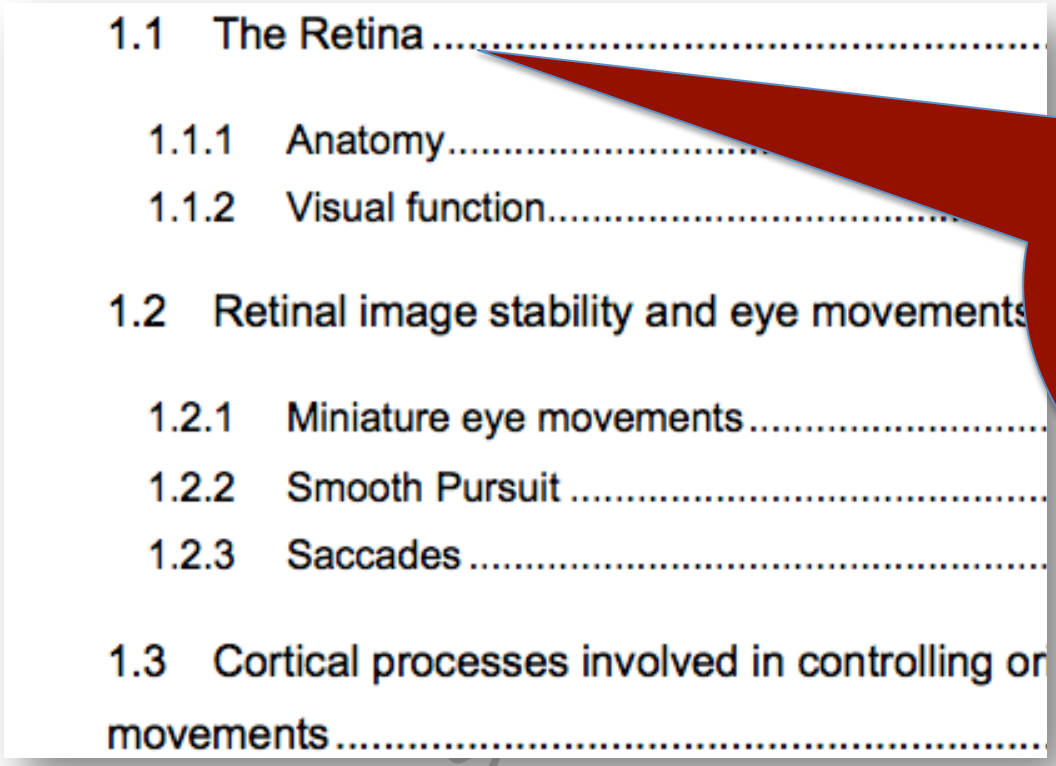
http://www.syndetics.com/index.php?isbn=9781446201435/toc.html&client=udminho&type=

3.4.8. Video guide for web of science

To know more about how to search, for example, web of science see this video
http://www.reading.ac.uk/library/finding-info/guides/videos/lib-video-literature-searching.aspx



3.5. Structuring your reading



If you have thought about the areas you need to research and have conducted some searches for literature, you should be ready to set down some draft topic headings to structure your literature review

3.5.1. Reading, note-taking and referencing

Always write the details of the text at the top of your page of notes, and add page numbers against your notes as you write them, so you can find your place again if necessary

Select one of your headings and choose a few key texts to read first - three is ideal to start with

Remember that you may eventually be writing about the same text under different headings, so bear that in mind when you are reading and making notes

More: www.reading.ac.uk/internal/studyadvice/Studyresources/sta-reading.aspx (University of Reading)

3.5.1.1. Passive note-taking (poor habit) includes

- underlining words
- cutting and pasting from online documents
- trying to write everything you hear in a lecture
- copying slides from the screen
- copying lots of direct quotes rather than putting the ideas in your own words
- writing notes on everything you read, because you're not sure what will turn out to be important
- not evaluating or criticising the sources you use, but just accepting them as suitable evidence

3.5.1.2. Active note-taking means:

- thinking about what you want to get out of your research before you start
- looking for answers to any questions you may have about the topic
- looking for connections within the topic you're studying, and to other topics on your course
- writing notes mostly in your own words - your own explanation of what something says or means
- recording direct quotes only when it's important to have the exact words that someone else has used (i.e. when how they say something is as significant as what they say)

3.5.1.3. Making your notes user-friendly

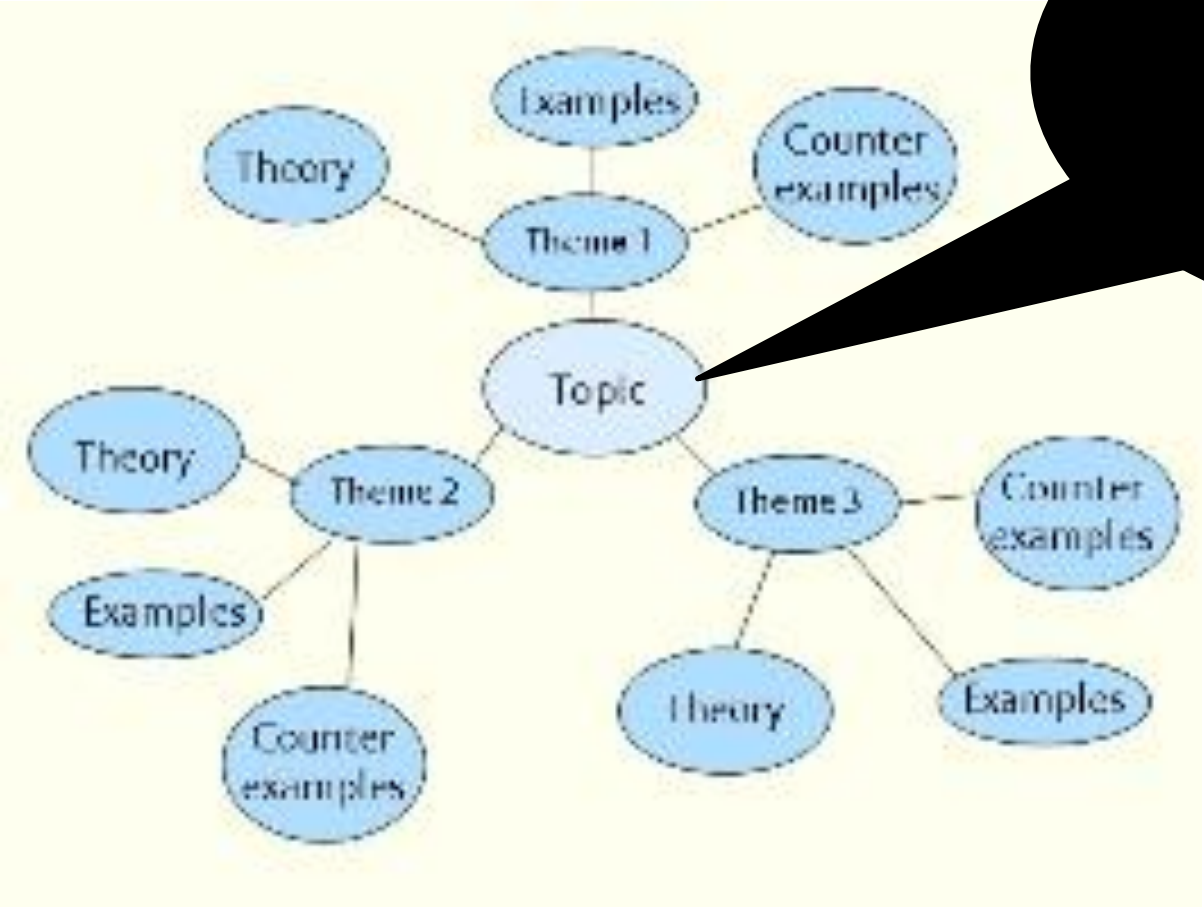
- Make your notes brief and be selective
- Keep them well-spaced so you can see individual points and add more details later if necessary
- Show the relationships between the main points (link with a line along which you write how they relate to each other, for instance)
- Use your own words to summarise - imagine someone has asked you "so what did x say about this?" and write down your reply
- Illustrations, examples and diagrams can help to put ideas in a practical context
- Make them memorable using: colour, pattern, highlighting and underlining
- Read through to make sure they're clear - will you still understand them when you come to revise?
- File with care! - use a logical system so you can find them when you need them, but keep it simple or you won't use it

3.5.1.4. Linear notes

Linear notes are what most people are used to doing. They are written down a page with headings and subheadings. They should have plenty of room for detail. Some suggestions:

- Use loads of HEADINGS for main ideas and concepts
- Use subheadings for points within those ideas
- Stick to one point per line
- Underline key words
- You can use numbering to keep yourself organised
- Use abbreviations - and don't worry about using full sentences
- Leave plenty of SPACE - for adding detail and for easy reading

3.5.1.5. Spidergrams



Spider diagrams are on one page and are good for showing structure and organising your ideas. They are sometimes called mindmaps, which indicates how they are good for making connections clear and visual

3.5.1.6. To make a spidergram

- Use whole side of paper - A4 at least!
- Put the subject in the centre
- Use one branch per main point - radiating outwards
- Don't start by making your points too big - you will need more space than you think
- You can add how the points are connected on the joining spokes
- Make it large enough - enough space to add detail
- Add smaller branches for detail & examples
- Summarise just enough to remind you of point - details and definitions can be added as footnotes
- Label with the source

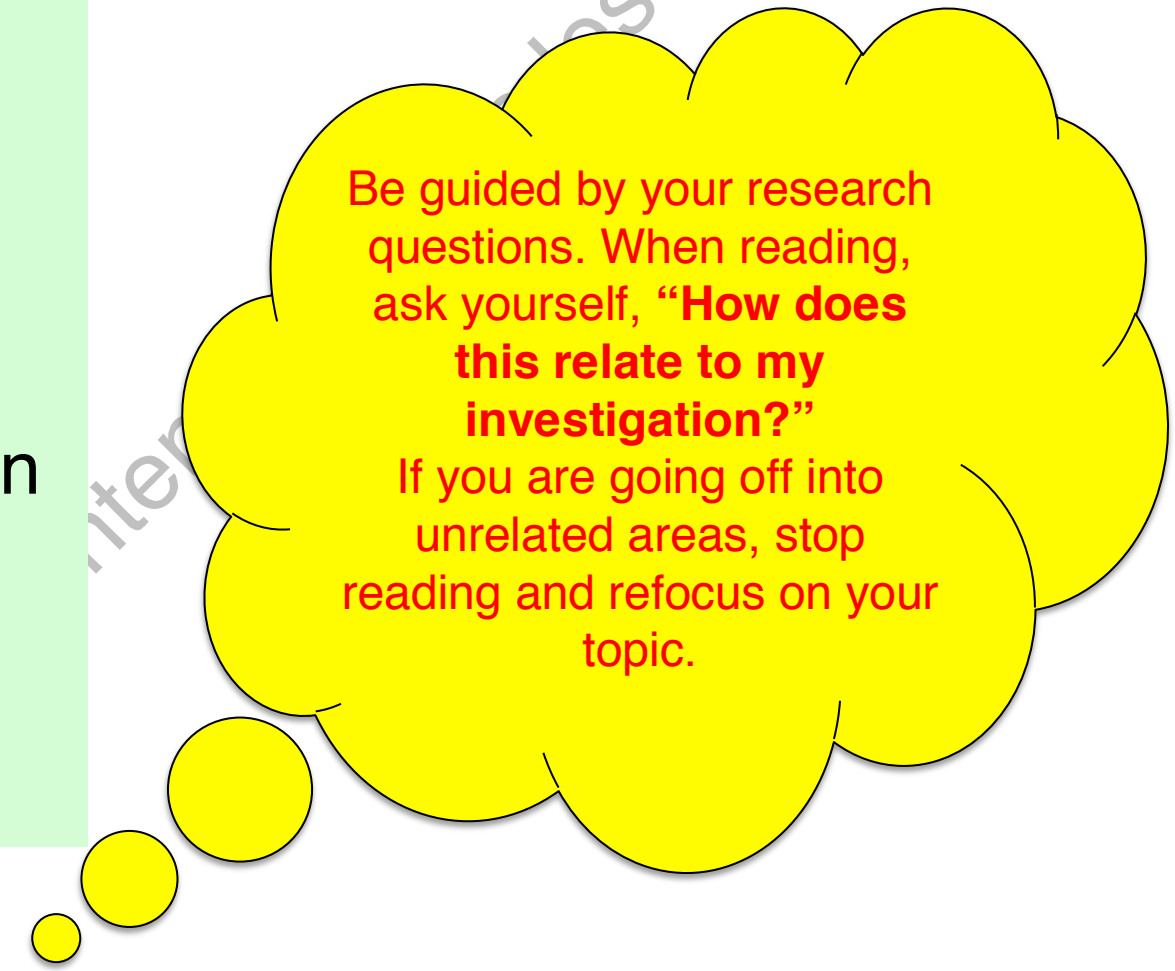
3.6. When should I stop reading?

Set limits on how long you will spend reading. Plan backwards from your deadline and decide when you need to move on to other parts of your investigation e.g. gathering the data

You need to show you have read the major and important texts in your topic, and that you have also explored the most up-to-date research. If you have demonstrated both of these, you are on the right lines.

An easy way to identify the major standard texts in your field is to check reference lists to see which texts are frequently cited

If you keep coming across very similar viewpoints and your reading is no longer providing new information, this is a sign you have reached saturation point and should probably stop!



3.6.1. I have too much information – how can I organise it all?

Keep in mind that you are not the unique person in the world with that problem, we all have that!

Go back to section 3.5.1.5 and read how to organize your ideas

- Group topics together
- Be selective
- Don't refer everything

3.7. Writing your literature review

3.7.1. Introduction

This explains the broad context of your research area and the main topics you are investigating

It briefly highlights the relevant issues or debates that have characterised your field of research

3.7.2. Main body

An analysis of the literature according to a number of themes or topics that overlap with your research, it may have headings

You can write your literature review one section at a time, but make sure you read through them all to check they link together and tell a coherent “story”.

This should show how your research builds on what has been done before. Based on previous research, you provide justifications for what you are doing, why you are doing it, and how you are going to do it.

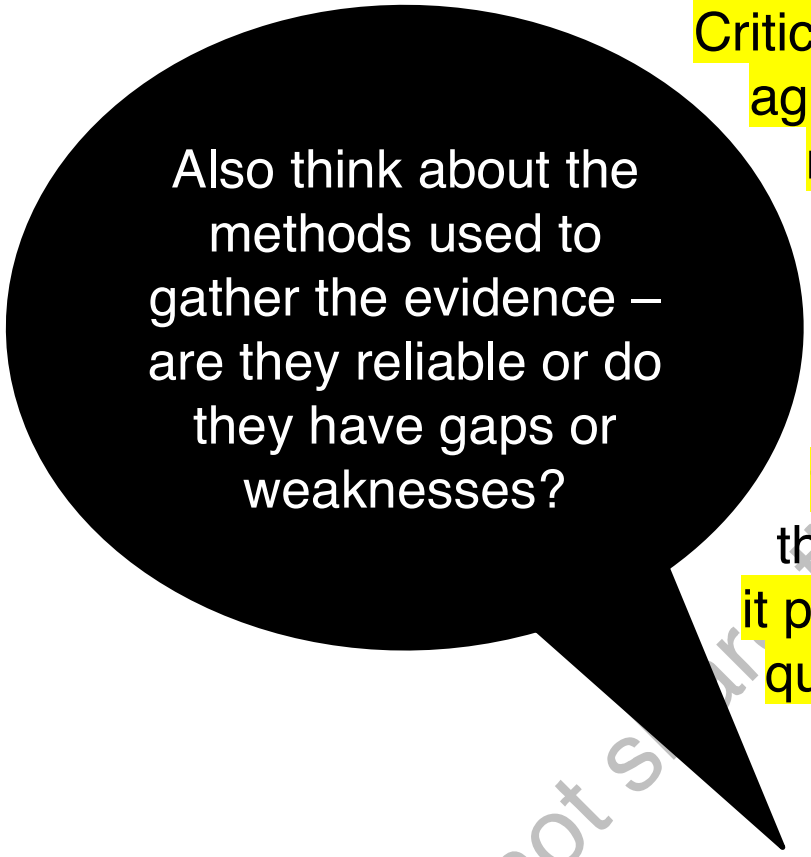
3.7.3. Conclusion

This should summarise the current state of the research in your field as analysed in the main body. It should identify any gaps or problems with the existing research, and explain how your investigation is going to address these gaps or build on the existing research.

3.8. Developing your literature review

Analysing the literature critically
Referring back to your literature review in the discussion section

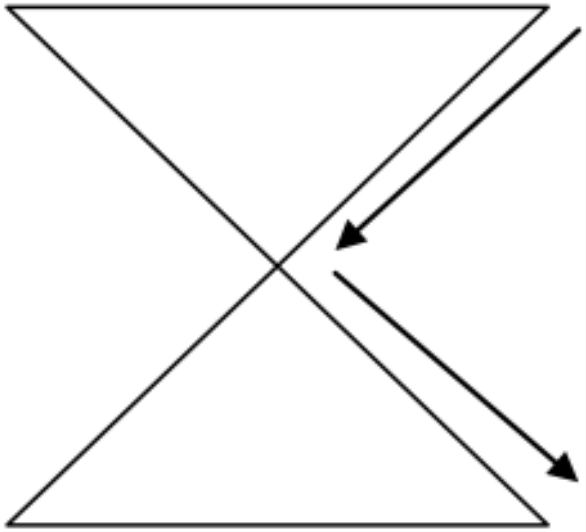
3.8.1. How can I analyse critically and not just be descriptive?



Critical analysis means asking yourself whether you agree with a viewpoint and if so, why? What is it that makes you agree or disagree?

You can ensure you are analysing critically by testing out your own views against those you are reading about: What do you think about the topic? Then as you read each new study, does the evidence presented confirm your view, or does it provide a counter-argument that causes you to question your view?

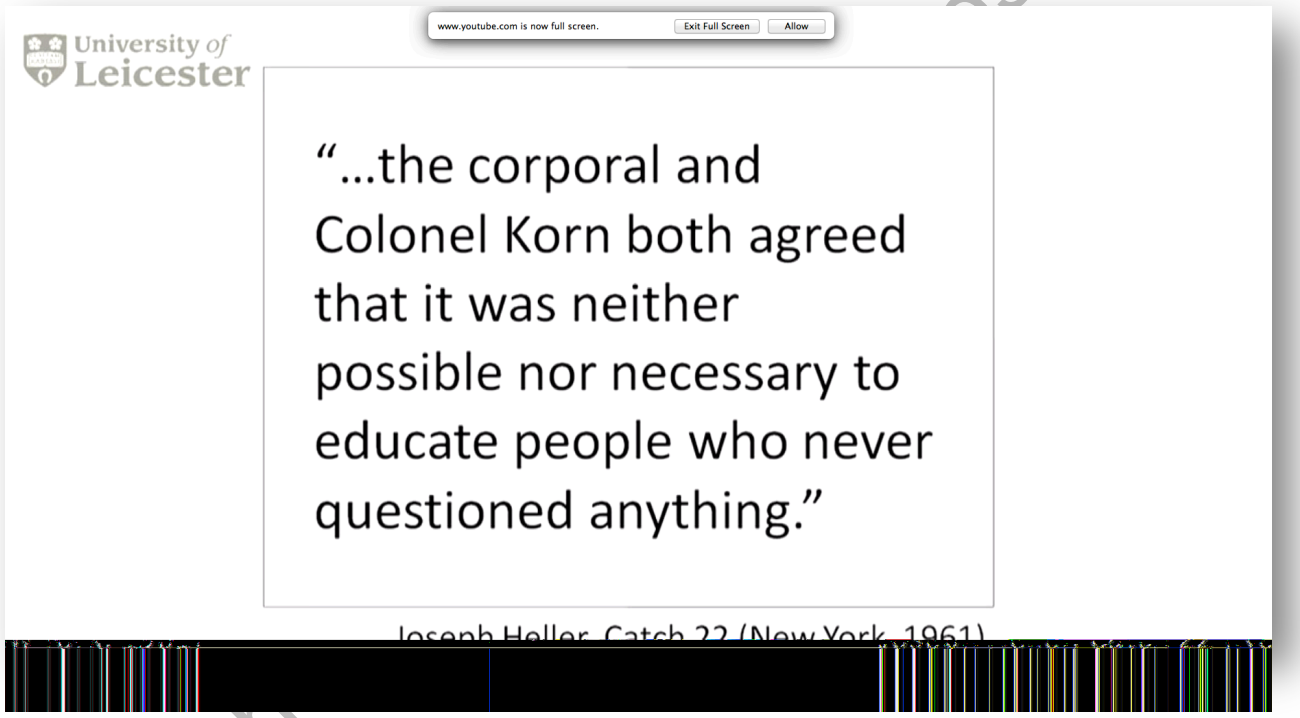
3.8.2. Literature review and discussion of my results, how are they related?



Literature Review: Starts broad and narrows to show how past research relates to your project.

Discussion: Starts specific by explaining what your results show in relation to your project, then widens out to say what this may mean for the field of research as a whole.

3.9. Critical, what does that mean?



https://www.youtube.com/watch?v=YVLjziA5U2o

Examples taken from University of Queensland: Writing the literature review www.uq.edu.au/student-services/phdwriting/phlink18.html

Descriptive	Analytical
• Summarises what other people have found without saying what these findings mean for your investigation. • Usually a chronological list of who discovered what, and when.	• Synthesises the work and succinctly passes judgement on the relative merits of research conducted in your field. • Reveals limitations or recognises the possibility of taking research further, allowing you to formulate and justify your aims for your investigation.
For example: "Green (1975) discovered …."; "In 1978, Black conducted experiments and discovered that …."; "Later Brown (1980) illustrated this in …	**For example:** There seems to be general agreement on x, (see White 1987, Brown 1980, Black 1978, Green 1975). However, Green (1975) sees x as a consequence of y, while Black (1978) sees x and … while Green's work has some …

3.9.1. Referring back to your literature review in the discussion section

Taken from LearnHigher report writing webpages: www.learnhigher.ac.u

Finding	95% of the students you surveyed have problems managing their time at university.
What do you think about this?	I expected it to be less than that.
What makes you think that?	Research I read for my literature survey was putting the figure at 60-70%.
What conclusions can you draw from this?	There must be reasons why the figures are so different. The sample I surveyed included a large number of mature students, unlike the samples in the previous research. That was because the brief was to look at time management in a particular department which had a high intake of post-experience students.
Final paragraph for Discussion section	The percentage of students surveyed who experienced problems with time management was much higher at 95% than the 60% reported in Jones (2006: 33) or the 70% reported in Smith (2007a: 17). This may be due to the large number of mature students recruited to this post-experience course. Taylor (2004: 16-21) has described the additional time commitments reported by students with young families, and the impact these may have on effective management of study time. The department recognises this, offering flexible seminar times. However it may be that students would benefit from more advice in this area.

3.10. Further resources

https://www.youtube.com/watch?v=6wWeeCBBlk4
http://www.citewrite.qut.edu.au/write/litreview.jsp
https://www.youtube.com/watch?v=dncRQ1cobdc&feature=relmfu

web of science and Google collaboration
https://www.youtube.com/watch?v=q4v5j96SKHc

Técnicas de Investigação em Optometria e Ciências da Visão

UNIT 4 Conceiving the research question and hypothesis

Aula 4
09 Nov 2015

Mestrado em Optometria Avançada
António Filipe Macedo

4.1. Origins of a research question

The challenge in searching for a research question is not a shortage of uncertainties; it is the difficulty of finding an important question that can be transformed into a feasible and valid study plan

For an established investigator the best research questions usually emerge from the findings and problems she /he has observed in her own prior studies and in those of others in the same field

4.1.1. Mastering de literature

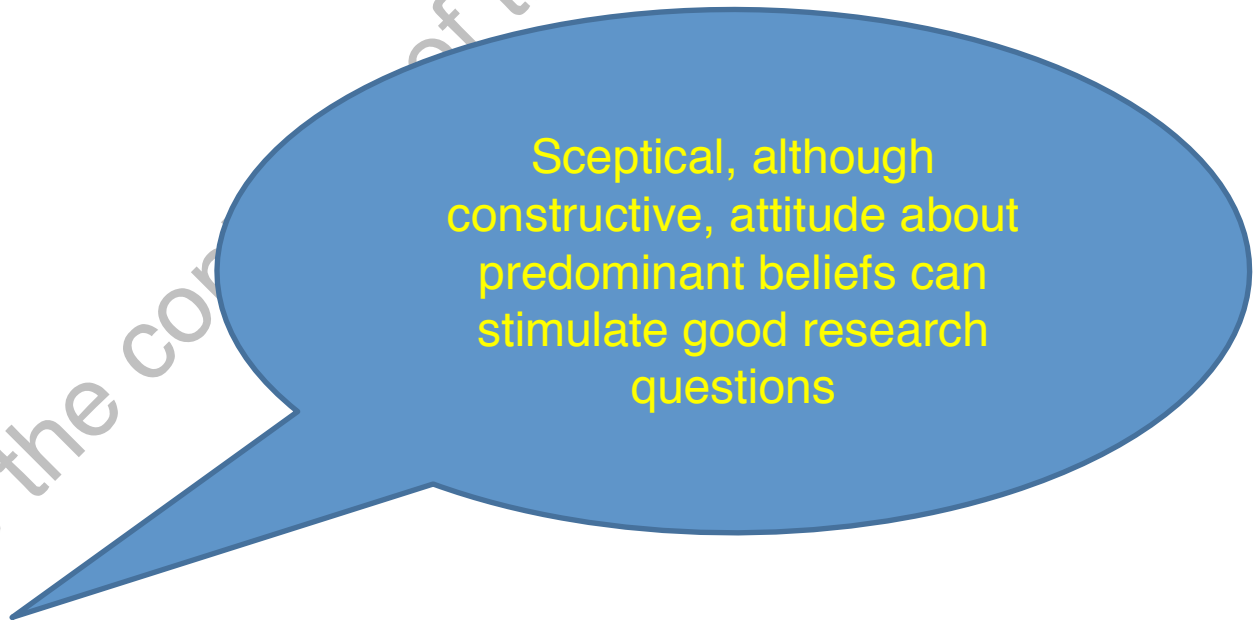
You must master the published literature in your area of study

Reading is not all, you should try to attend meeting and have constructive conversations with colleagues and experts about your research

4.1.2. Being alert to new ideas and techniques

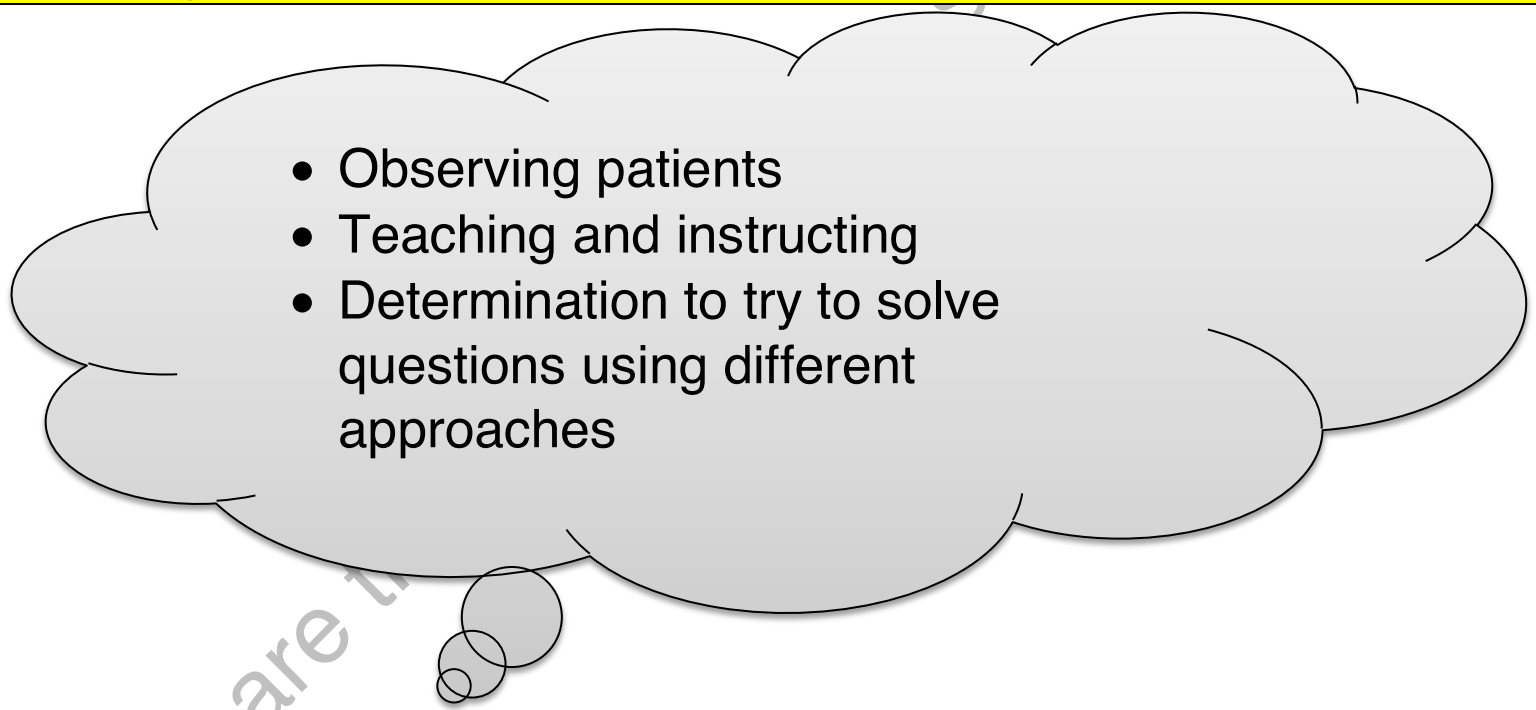
Attending conferences is a good way to get updated about the latest methodology

Junior research must overcome their shyness and engage a speaker during the coffee break, you normally will that experience richly rewarding



4.1.3. Keep the imagination roaming

From where can you get your inspirations for new studies?



4.2. Characteristics of a good research question

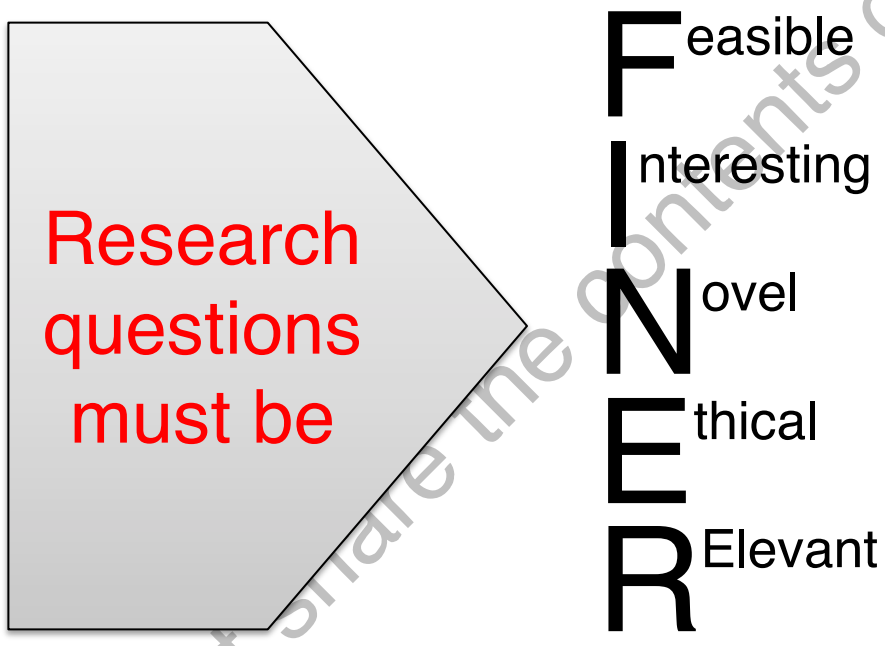
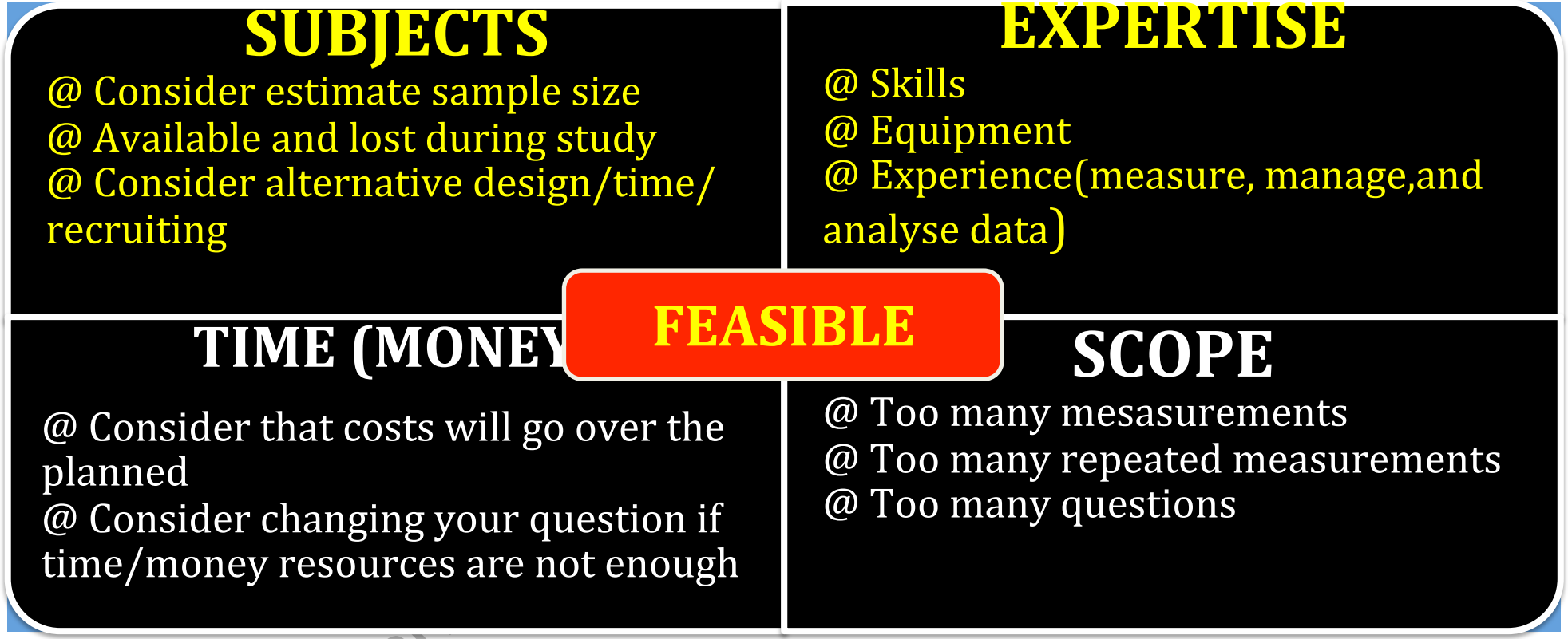


Table 4.1: FINER Criteria for a Good Research Question

FEASIBLE	Adequate number of subjects Adequate technical expertise Affordable in the time and money Manageable in scope
INTERESTING	To the investigator
NOVEL	Confirms or refutes previous findings Extends previous findings Provides new findings
ETHICAL	---
RELEVANT	To scientific knowledge To clinical and health policy To future research directions

4.2.1. What does that mean, FEASIBLE?

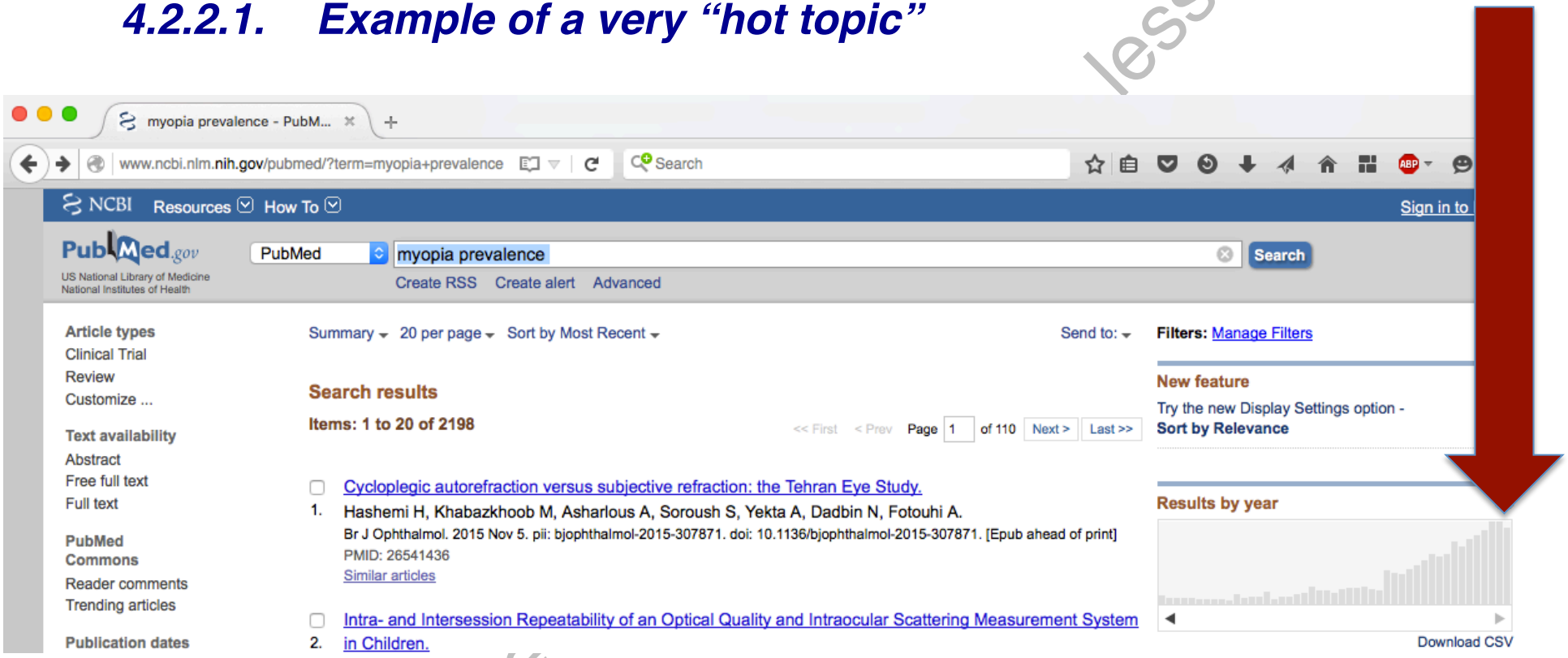


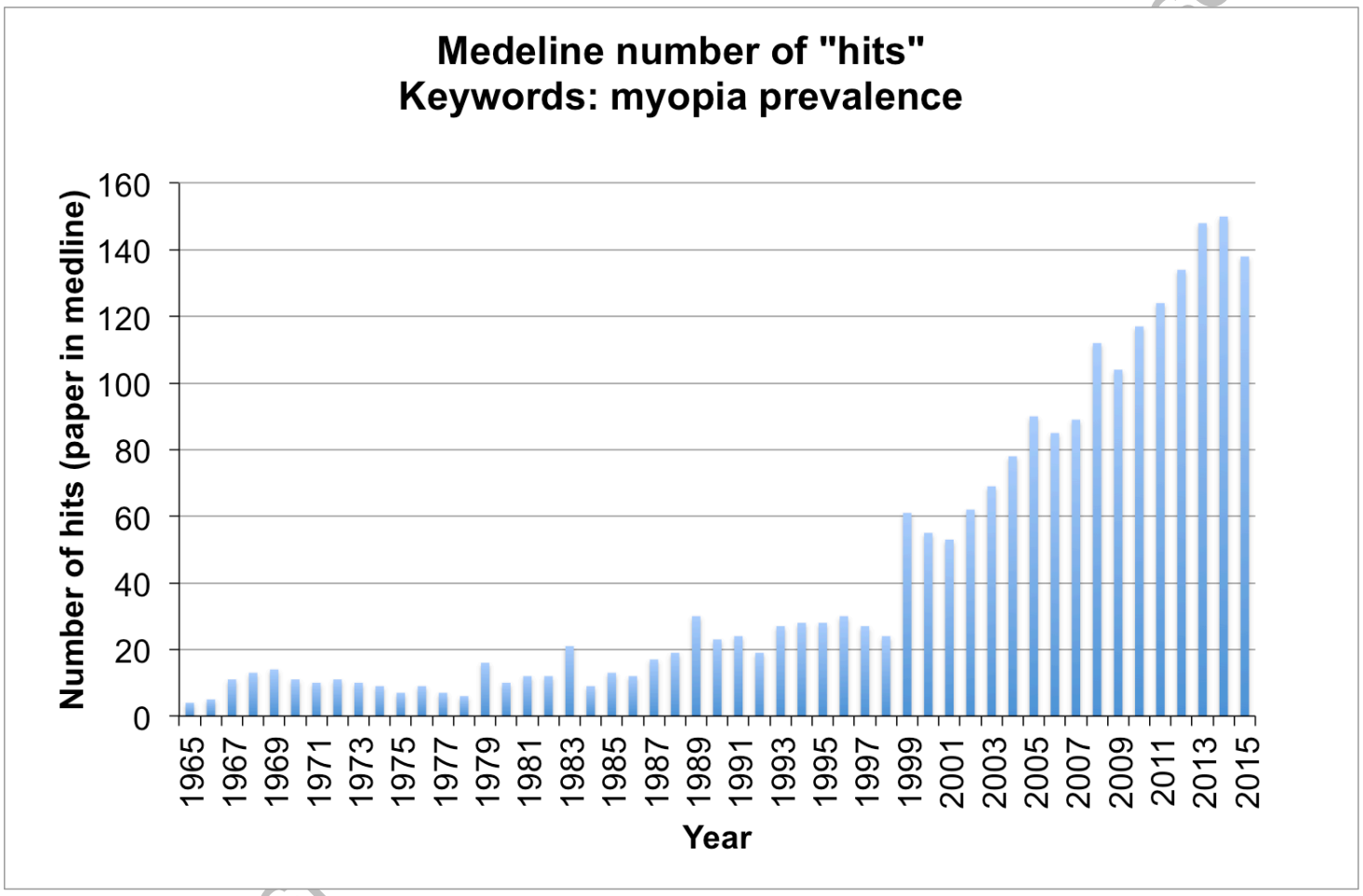
4.2.2. What does it mean, NOVEL?

A study that only reiterates what is already established is not worth the effort and cost

- Good research contributes with new information
- Literature review, talking with experts, projects search should give you an idea of how novel your research is
- Studies that investigate whether a previous research can be replicated, whether findings from one population apply to other or uses improved measurement techniques are worth doing

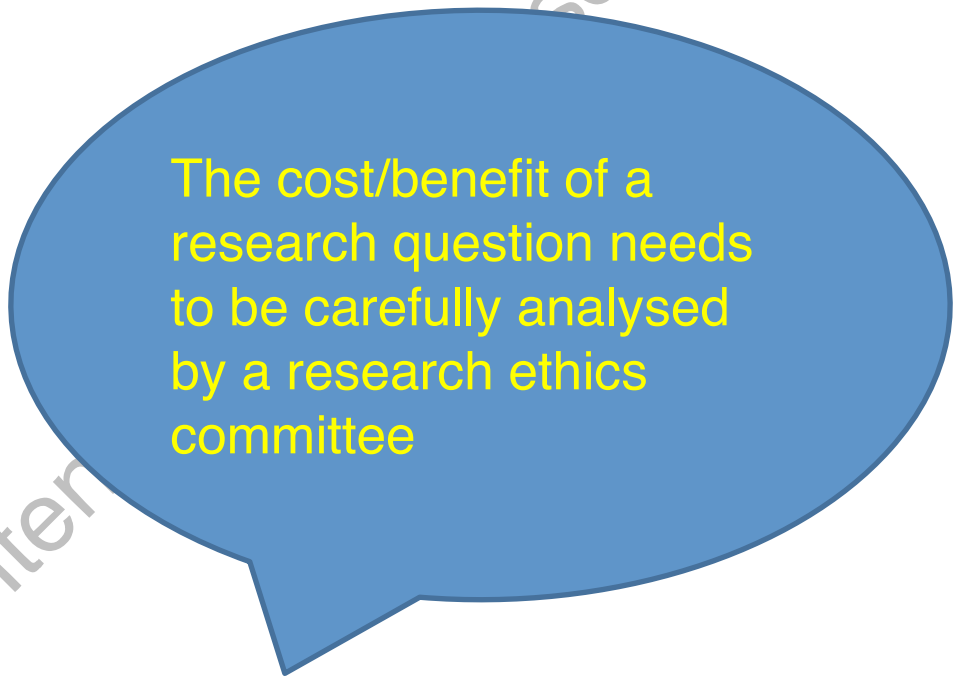
4.2.2.1. Example of a very "hot topic"




Medeline number of "hits"
Keywords: myopia prevalence
Number of hits (paper in medline)
160
140
120
100
80
60
40
20
0
1965
1967
1969
1971
1973
1975
1977
1979
1981
1983
1985
1987
1989
1991
1993
1995
1997
1999
2001
2003
2005
2007
2009
2011
2013
2015
Year

4.2.3. What does it mean, ETHICAL?

Researchers should avoid studies that might impose disproportioned physical risks or invasion of privacy

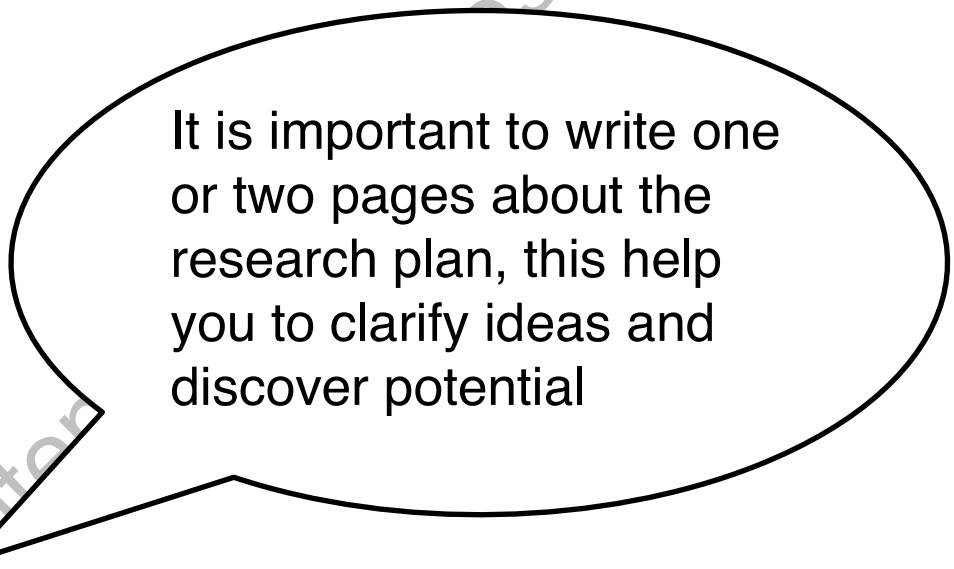


More about this topic will be discussed in chapter/section **Error! Reference source not found.**

4.2.4. What does it mean RELEVANT?

A good way to decide about the relevance of your research question is to imagine the various outcomes that are likely to occur and consider how each possible might advance scientific knowledge, influence clinical management and practices policies or guide future research

4.3. Developing the research question and study plan



4.3.1. Problems and solutions Table 4.2

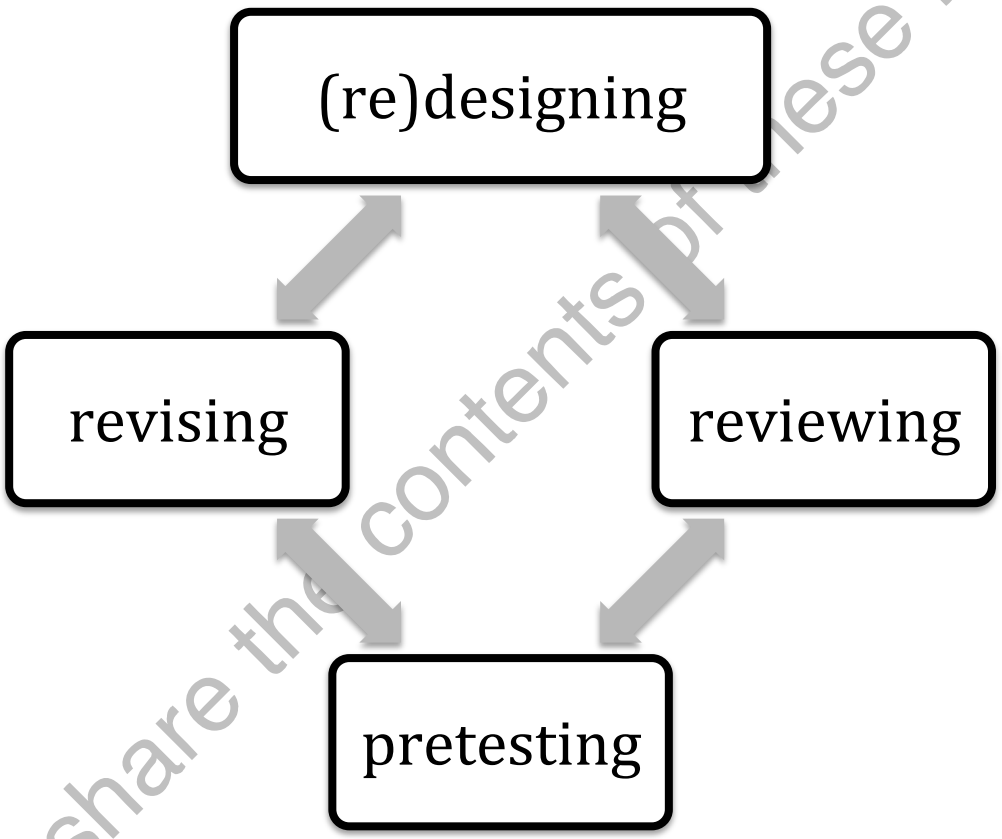


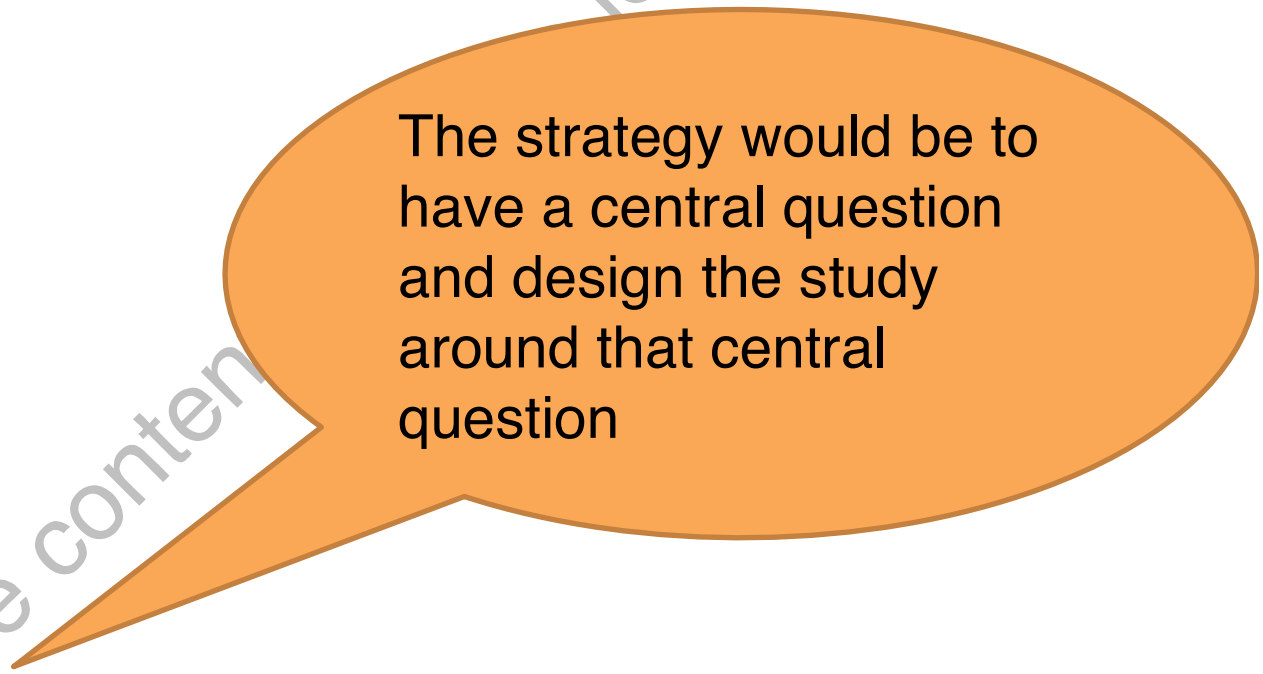
Table 4.2: The research question and study plan: problems and solutions

Problem	Solution
A. Research question is not FINER	
1. Not feasible	
• Too broad	➢ Specify a smaller set of variables ➢ Narrow the question
• Not enough subjects available	✓ Expand the inclusion criteria ✓ Eliminate or modify exclusion criteria ✓ Add other sources of subjects ✓ Extend the recruitment period ✓ Use strategies to decrease sample
• Methods beyond the skills of the investigator	➢ Collaborate with colleagues who have the skills ➢ Consult experts and review the literature for alternative methods ➢ Learn the skills

Problem	Solution
• Too expensive	✓ Consider less costly study designs ✓ *Fewer subjects and measurements* ✓ *Less extensive measurements* ✓ *Fewer follow-up visits*
2. Not interesting, novel or relevant	➢ Consult with mentor ➢ Modify the research question
3. Uncertain ethical suitability	✓ Consult with institutional review board ✓ Modify the research question
B. The study plan is vague	✓ Write the research question at an early stage ✓ Get specific in the one or two page study plan (example) ***How the subjects will be sampled?*** ***How the variables will be measured?***

4.3.2. Primary and secondary questions

Many studies have more than one research question that might lead to increased complexity not only during the designing process but also for data analysis



Técnica de Investigação em Optometria e Ciências da Visão

UNIT 5 Designing a study

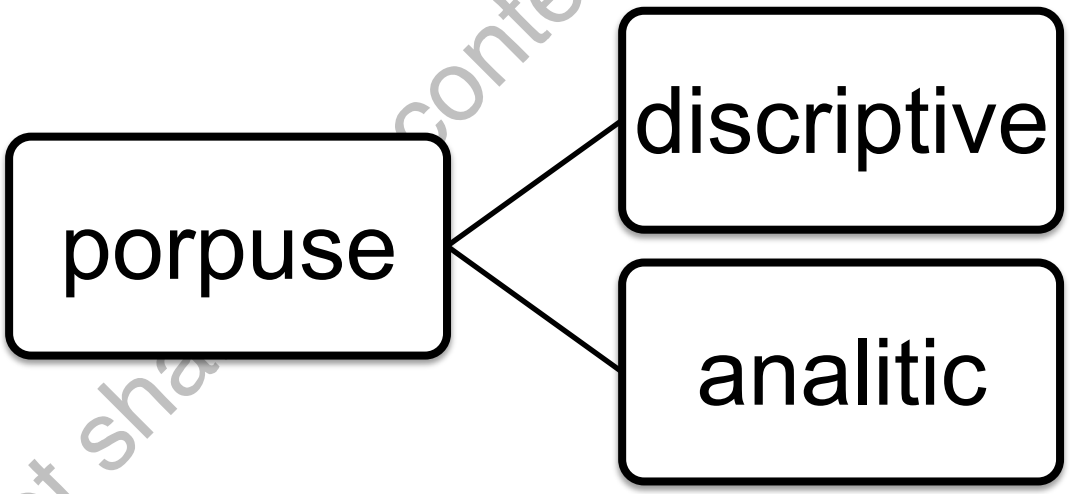
Most contents of this chapter are from: Hulley, S. B., Cummings, S. R., Browner, W. S., Grady, D., Hearst, N., & Newman, T. B. (2001). Designing Clinical Research: an epidemiologic approach (Second edition ed.). Philadelphia: Lippincott Williams & Wilkins.

Aula 5
09 Nov 2015

Mestrado em Optometria Avançada
António Filipe Macedo

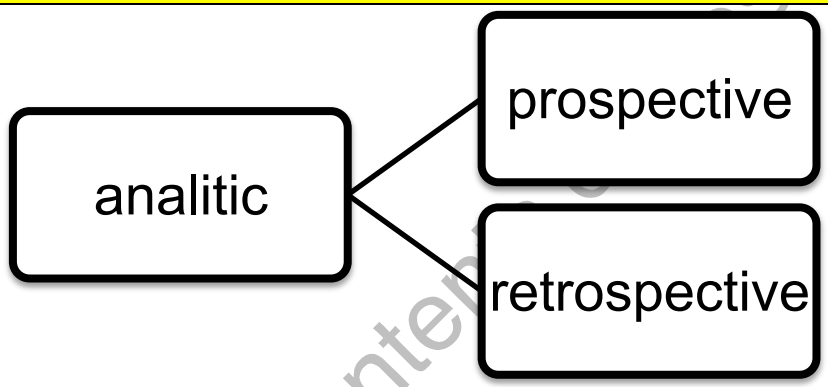
5.1. Designing observational studies: Cohort studies

Definition: Cohort studies involve following groups overtime



Descriptive: to describe the incidence of certain outcomes over time

Analytic: to analyse the associations between predictors and those outcomes



Retrospective
The investigator defines the sample and collects data about predictor variables after the outcomes have occurred;
Prospective
The investigator defines the sample and measures predictor variables before any outcomes have occurred;

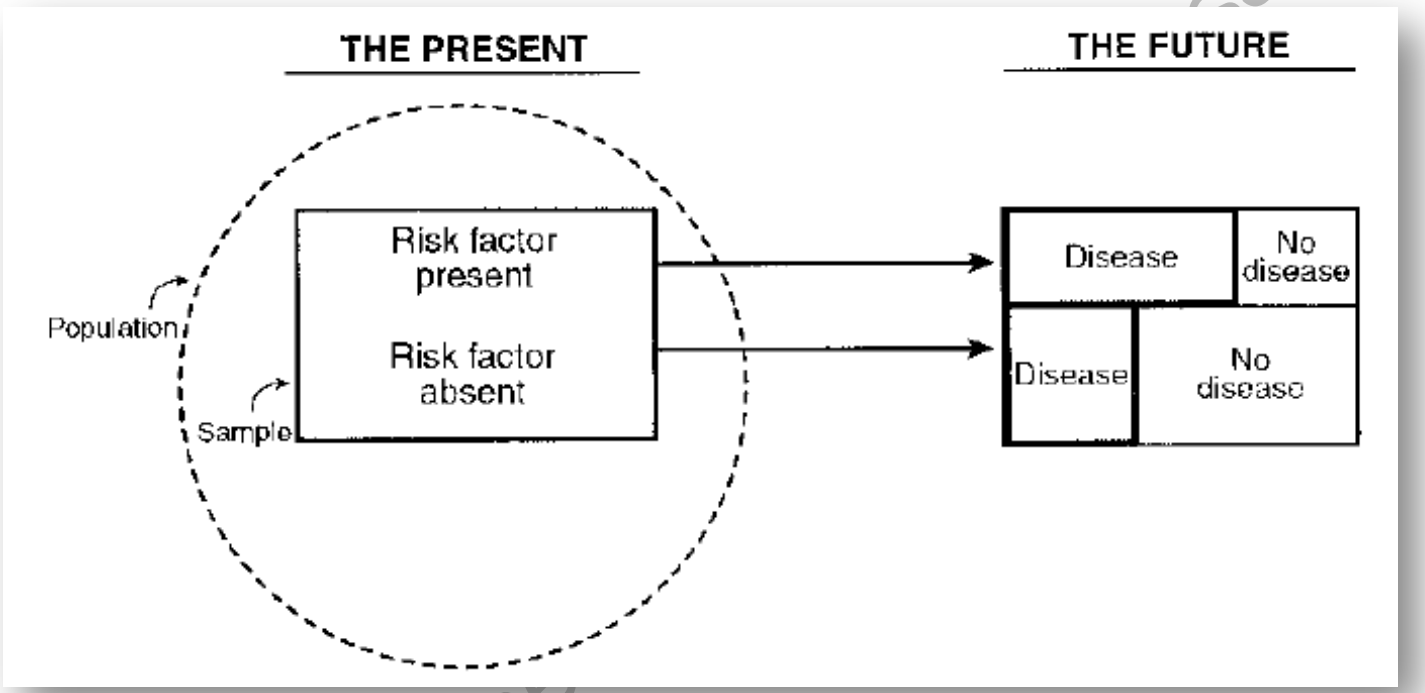


Figure 5.1: in a prospective cohort study the investigator: a) selects a sample from a population (the dotted line signifies its large and undefined size); b) measures the predictor variable (in the case whether a dichotomous risk factor is present); c) measures the outcome during follow-up (in this case a disease -- outlined in bold -- that developed in a higher proportion of subjects who had the risk factor)

5.1.1. Prospective cohort studies

(the myopia study)

- Step 1: assembly the cohort
- Step 2: measuring predictor variables and potential confounders
- Step 3: follow-up the cohort and measure outcomes

5.1.1.1. Strengths

These studies are a powerful strategy for:

1. *Defining the incidence*
2. *Investigating the potential causes of a condition because potential causative factors are measured before the outcome occurs*

5.1.1.2. Weakness

1. *These studies are an expensive and inefficient way to study a rare outcome*
2. *A prospective cohort study to study a condition normally excludes subjects diagnosed with the condition but can often include those in pre-clinical stages of the disease. Correcting this limitation can be extremely expensive.*

Exercise this question: does any of your studies is a prospective cohort study?

5.1.2. Retrospective cohort study

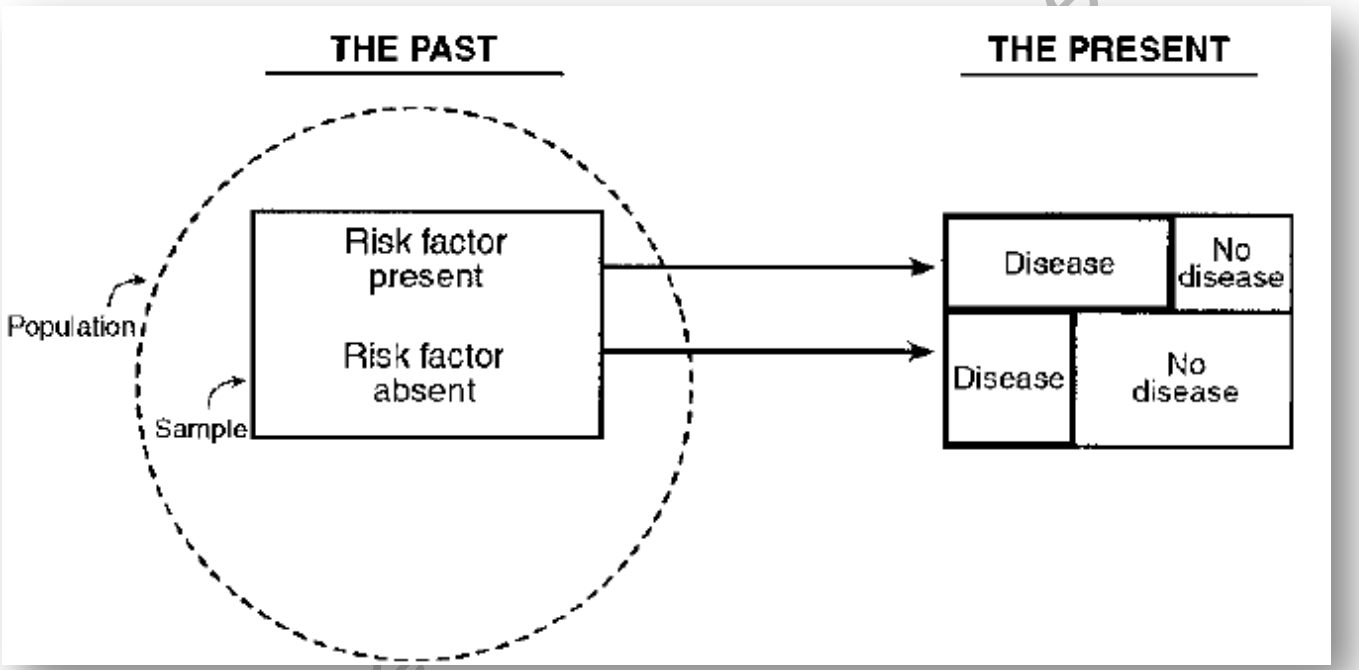


Figure 5.2: In a retrospective cohort study the investigator: a) identifies a cohort that has been assembled in the past; b) collects data on predictor variables (measured in the past); c) collects data on outcomes variables (measured in the past or present)

The design of a prospective cohort study is similar to a prospective. A group of subjects is followed over time with measurements of potential predictor variables

5.1.2.1. Strengths

This retrospective design has the same strengths of the prospective design.

1. Can establish that predictor variables precede outcomes

2. Because measurements are all collected before the outcome in known, the measurements of predictor variables cannot be biased by knowledge of which subjects have the outcome of interest

3. Retrospective as cheaper than prospective studies

4. Less time consuming that prospective studies

5.1.2.2. Weakness

1. Limited control over the design approach the population and over the nature and quality of the predictor variables

2. Existing data may not include the subjects and information that are important to answering the research question

5.1.3. Nested case-control and case-cohort studies

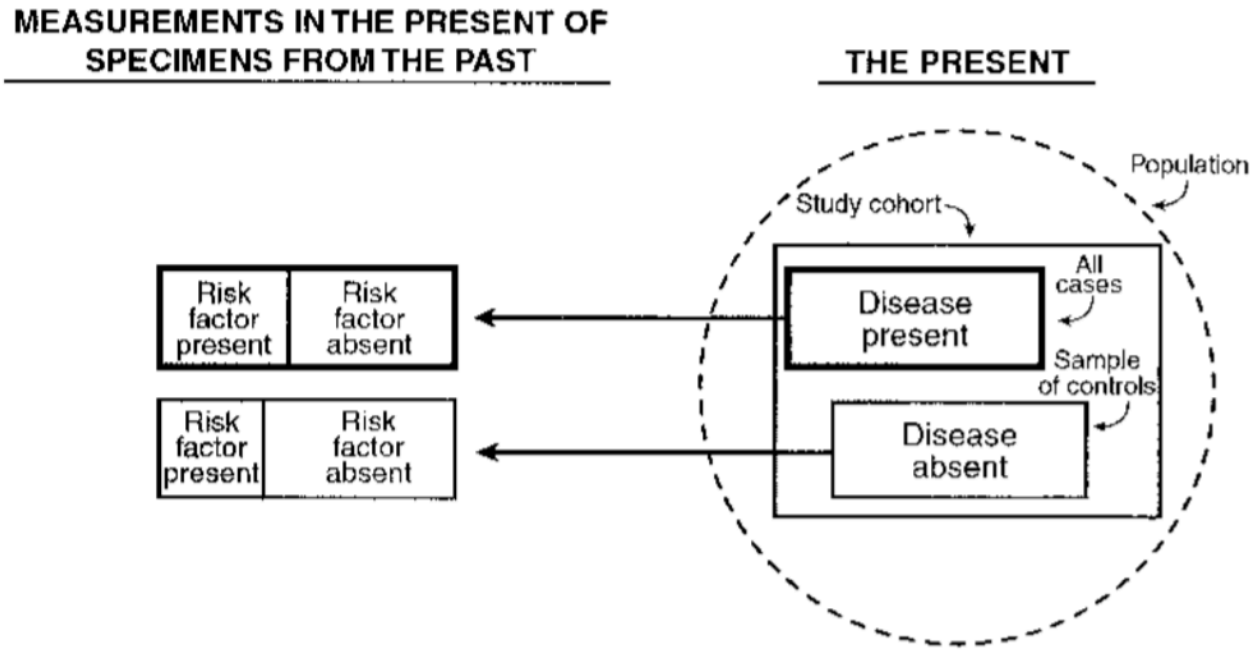


Figure 5.3: In a nested case-control study the investigator: a) identifies a cohort with banked specimens or information, b) identifies those participants who developed the outcome during the follow-up (the cases), c) selects a sample from the rest of the cohort (the controls), d) measures predictor variables in cases and controls

Visual Field Defects and the Risk of Motor Vehicle Collisions among Patients with Glaucoma

Gerald McGwin, Jr,[1,2] *Aiyuan Xie,*[1] *Andrew Mays,*[1] *Wade Joiner,*[1] *Dawn K. DeCarlo,*[3] *Tyler Andrew Hall,*[1] *and Cynthia Owsley*[1]

Purpose. To evaluate the association between visual field defects in the central 24° field and the risk of motor vehicle collisions (MVCs) among patients with glaucoma.

Methods. A nested case–control study was conducted in patients with glaucoma aged 55 or more. Cases were patients who were involved in a police-reported motor vehicle collision (MVC) between January 1994 and June 2000; controls were those who had not experienced an MVC at the time of their selection. For each patient, an Advanced Glaucoma Intervention Study (AGIS) score was calculated on automated visual fields collected with the 24-2 or 3-2 programs.

Results. With respect to the better-eye AGIS score, compared with patients with no visual field defect, those with severe defects (scores 12–20) had an increased risk of an MVC (odds ratio [OR] 3.2, 95% CI 0.9–10.4), although the association was not statistically significant. Moderate (6–11) or minor field defects (1–5) in the better eye were not associated with the risk of involvement in a crash. In the worse eye, patients with moderate or severe field defects were at significantly increased risk of an MVC (OR 3.6, 95% CI 1.4–9.4 and OR 4.4, 95% CI 1.6–12.4, respectively) compared with those with no defects. Minor field defects in the worse eye did not increase risk of MVC (OR 1.3, 95% CI 0.5–3.4).

Conclusions. Patients with glaucoma who have moderate or severe visual field impairment in the central 24° radius field in the worse-functioning eye are at increased risk of involvement in a vehicle crash. (*Invest Ophthalmol Vis Sci.* 2005;46: 4437–4441) DOI:10.1167/iovs.05-0750

Methods

Study Cohort

The study cohort consisted of individuals aged 55 or more who had been seen at least once between January 1994 and December 1995 in any of three university-affiliated ophthalmology and optometry practices specializing in the diagnosis and treatment of glaucoma. The *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes 365.1 and 365.2 were used to identify all potentially eligible patients with glaucoma seen at each of these locations. The medical records of each potentially eligible patient were abstracted to verify the diagnosis of glaucoma though information regarding the basis for that diagnosis was not obtained. Patients were excluded if (1) their primary cause of visual impairment was an ocular disorder other than glaucoma (e.g., macular degeneration, diabetic retinopathy, or clinically significant cataract for which surgery was recommended). Persons with diagnoses of refractive error, dry eye, and early cataract were eligible for the study. (2) Automated visual field data (either a 30-2 or 24-2 test) for both eyes were not in the medical record during the study period; and (3) patients were not legally licensed to drive by the State of Alabama. Information on licensure status was obtained by cross-referencing each subject's demographic and residential information obtained from the medical record with the Alabama Department of Public Safety (ADPS) database.

5.1.3.1. Multiple cohort studies and external controls

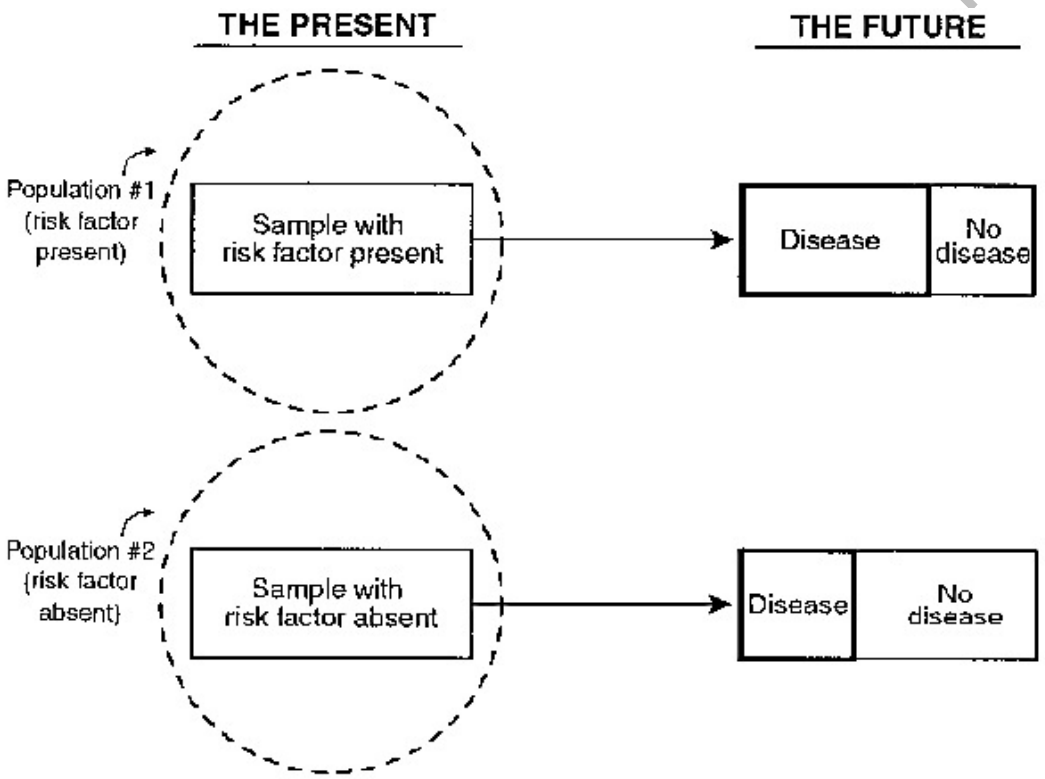


Figure 5.4: In a prospective double-cohort study the investigator: a) selects the samples from a population with different levels of the predictor, b) measures outcome variables during follow-up (double-cohort studies can also be conducted retrospectively).

Example 7.4. Multiple Cohort Design

To determine whether physicians who were exposed to radiation had higher mortality rates, Matanoski and colleagues (5) undertook a retrospective triple cohort study. The basic steps in performing the study were to

1. *Identify cohorts with different exposures.* The investigators obtained the membership lists for the Radiological Society of North America, the American College of Physicians, and the American Academy of Ophthalmology and Otolaryngology; the lists included all who had joined since 1920.
2. *Determine outcomes.* The investigators determined the vital status for all members of these societies, including year and cause of death for those who had died.

Radiologists had a higher mortality rate from cancer than the members of the other two societies, supporting the hypothesis that exposure to radiation increased cancer mortality rates.

5.1.4. Planning a cohort study

Table 5.1: Strategies to minimizing losses during studies requiring follow-up: during enrolment

1. Exclude those likely to be lost
a) Planning to move
b) Unwilling to return
2. Obtain information to allow future tracking
a) Address, telephone and email of the participant
b) Social security number etc (if you are allowed)
c) Name, address, telephone and email of the one or two persons related with the participant but who do not live with him/her

Table 5.2: Strategies to minimizing losses during studies requiring follow-up: during follow-up

1. Periodic contact with subjects
a) By telephone: might require calls during weekends and evenings
b) By mail: repeated mailings by email or with stamped, self-addressed return-cards
c) Other: newsletters, gifts with the study logo ☺
2. For those who are not reached by phone or mail
a) Contact friends, relatives etc
b) Request forwarding services form postal services (if they moved)
c) Seek for new address in other sources of public information
d) Determine vital status if possible

5.1.5. Summary of cohort studies design

I. In cohort studies subjects are followed over time to describe the incidence or natural history of a condition and to analyse predictors (risk factors) for various outcomes. Measuring the predictor before the outcome occurs establishes the sequence of events and helps control bias in that measurement

II. Prospective cohort studies may require large number of subjects followed for long periods of time. This disadvantage can sometimes be overcome by analysing records or samples that have already been collected, using a retrospective cohort design

III. An efficient variant is the nested case-control design. A bank of images, measurements and other records is collected at baseline and stored until the end of the study; measurements are made on stored materials for all subjects who have developed a disease and in a subset of those who have not developed de condition. In the nested case-control strategy a single random sample of the cohort can provide controls for several case-control studies

IV. The multiple-cohort design, which compares the incidence of outcomes in cohorts that differs in level of a predictor variable, is useful for studying the effects of rare and occupational exposures. A census registry can provide efficient external control group

V. Inferences about an effect are strengthened by measuring all important potential confounding variables at baseline. Bias in the assessment of outcomes is prevented by standardizing the measurements

5.2. Designing observational studies: cross-sectional

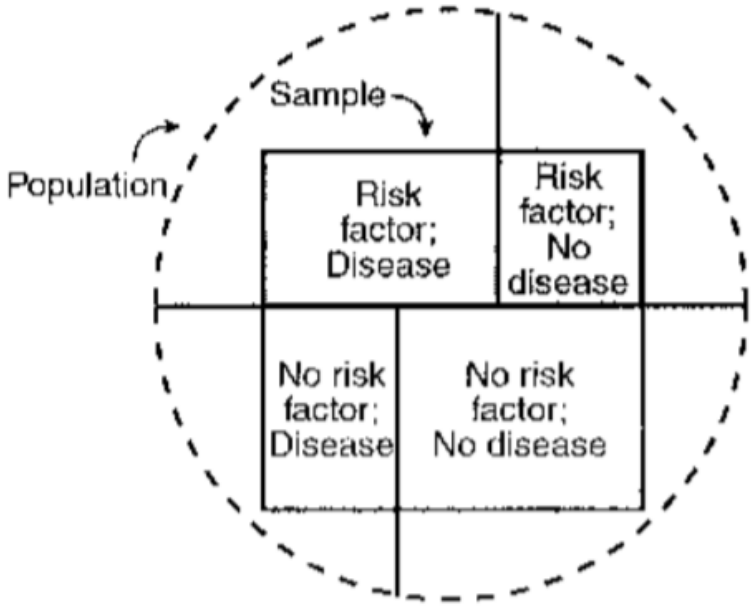
- In a cross-sectional study, the investigator makes all his/her measurements on a single occasion

- The investigator draws a sample from the population

- In cross-sectional studies the investigator looks at distributions of variables within the sample. Researchers may the infer cause and effect from associations between variables she/he decides (using information from various sources) to designate as predictor and outcome

- In case-control studies the investigator works backward. Investigators start by choosing one sample from a population of patients with the outcome (the cases) and another from a population without the outcome (the controls); then compares the levels of the predictor variables in the two samples to see which ones are associated with the outcome

5.2.1. Structure of a Cross-sectional study



Measurements are made at once with no follow-up

Figure 5.5: In a cross-sectional study the investigator: a) selects a sample from the population and b) measures predictor and outcome variables (e.g. presence or absence of a risk factor and disease)

5.2.2. Key epidemiologic concepts

Type of Study	Statistic	Definition
Cross-sectional	Prevalence	$\frac{\text{Number of people who } \textit{have} \text{ the disease at one point in time}}{\text{Number of people at risk at that point}}$
Cohort	Incidence	$\frac{\text{Number who } \textit{get} \text{ disease over a period of time}}{\text{Number of people at risk during that period}}$

- Cross-sectional studies provide typically useful information about prevalence of conditions. Prevalence and incidence concepts can also apply to variables not only to diseases
- Cross-sectional studies can also be used to examining associations, although the choice of which **variable to label as predictors** and which **as outcomes** depends on the cause-and-effect hypothesis of the investigator rather than on the study design

Factors such age and gender are typically analysed as predictors because they cannot be altered. However, choosing predictor and outcome is not always easy, consider the example below:

A cross sectional finding of the NHANES III study is the association between childhood obesity and hours spent watching TV

1. What variable is the predictor?

2. Is it straight forward for you to identify the predictor vs outcome?

5.2.3. Strengths and weakness of cross-sectional studies

5.2.3.1. Strengths

1. The major advantage of cross-sectional studies (and experimental studies) is that there is no waiting time for the outcome to occur

2. A cross-sectional study can be included as the first step of a cohort or experimental study at little or no added cost

5.2.3.2. Weakness

1. *A weakness of cross-sectional studies is the difficulty of establishing causal relationships from data collected*

This is way many studies only establish associations between predictors and outcomes, they are not able to establish causal relationship

2. *Cross-sectional studies are also impractical for the study of rare diseases if the design involves collecting data from a sample of individuals from a general population*

A cross-sectional study of stomach cancer in a general population would take 10 000 subjects to find 1 case

To avoid this weakness **number 2)** is common to use samples from a population of diseased patients

i. This will be useful to analyse the characteristics of the disease rather than analysing differences between patients and healthy people

ii. However sometimes some strong risk effects can be associated. Example below.

The first study about AIDS enrolled 1000 participants with the disease: 727 were homosexual or bisexual males and 236 were injecting drug users -> it did not required a control group to verify that these groups were at increased risk

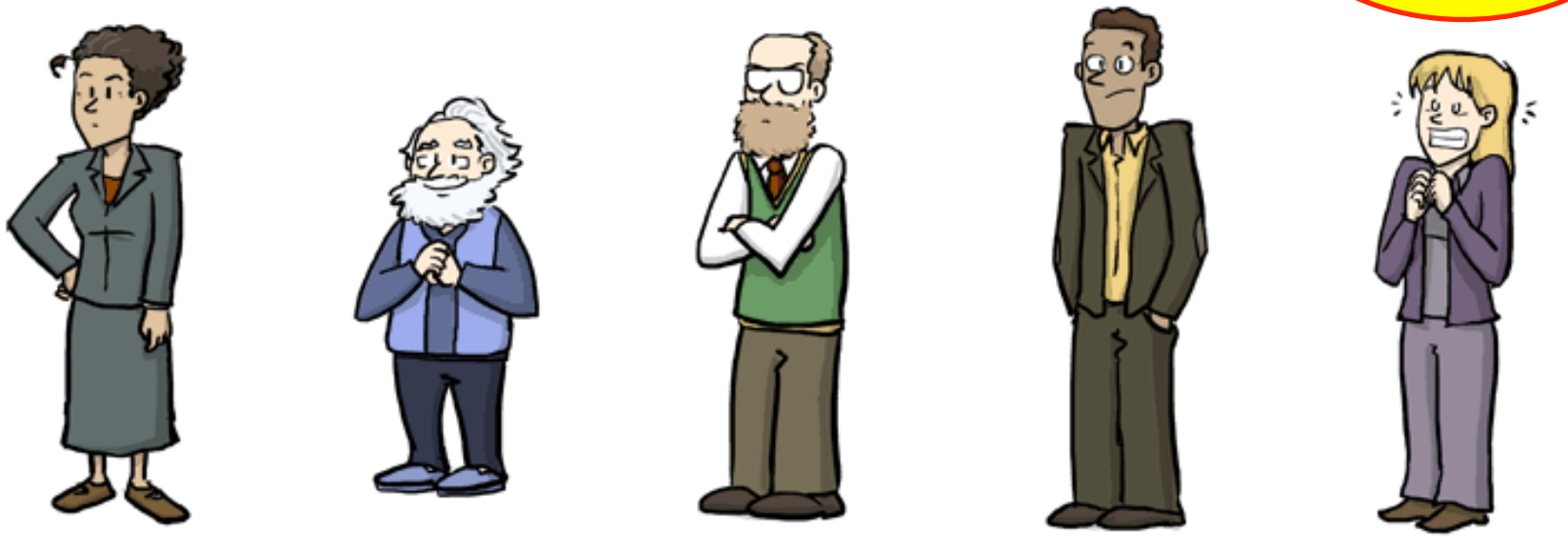
3. Cross-sectional studies can only measure prevalence, not incidence, that limits the information they can produce on prognosis, natural history and disease causation

To show causation investigators need to demonstrate that the incidence of the outcome (often – the disease) differs in those exposed to a risk factor. Cross-sectional studies can only show effects on prevalence, which is the product of disease incidence and disease duration

YOUR THESIS COMMITTEE

Thesis project 31-Oct

Also known as: an impossibly difficult group to get together in one room but who nevertheless hold your future in their hands depending on their ability to reach a civilized consensus.



Your Professor

Simultaneously your biggest ally and your worst enemy. Will be the first to suggest you do more work.

The Guru

Only here for the free cookies. Don't forget to bring cookies.

The Adversary

Has bitter rivalry with your Professor and will argue the exact opposite view. Work this to your advantage.

The Strawman/woman

Nice guy. No opinions.

The Assistant Professor

Still doesn't believe just a few months ago they were on the other side just like you. Pretends to be an adult.

NONE OF THEM WILL ACTUALLY READ YOUR ENTIRE THESIS.

5.2.4. Structure of Case-control studies

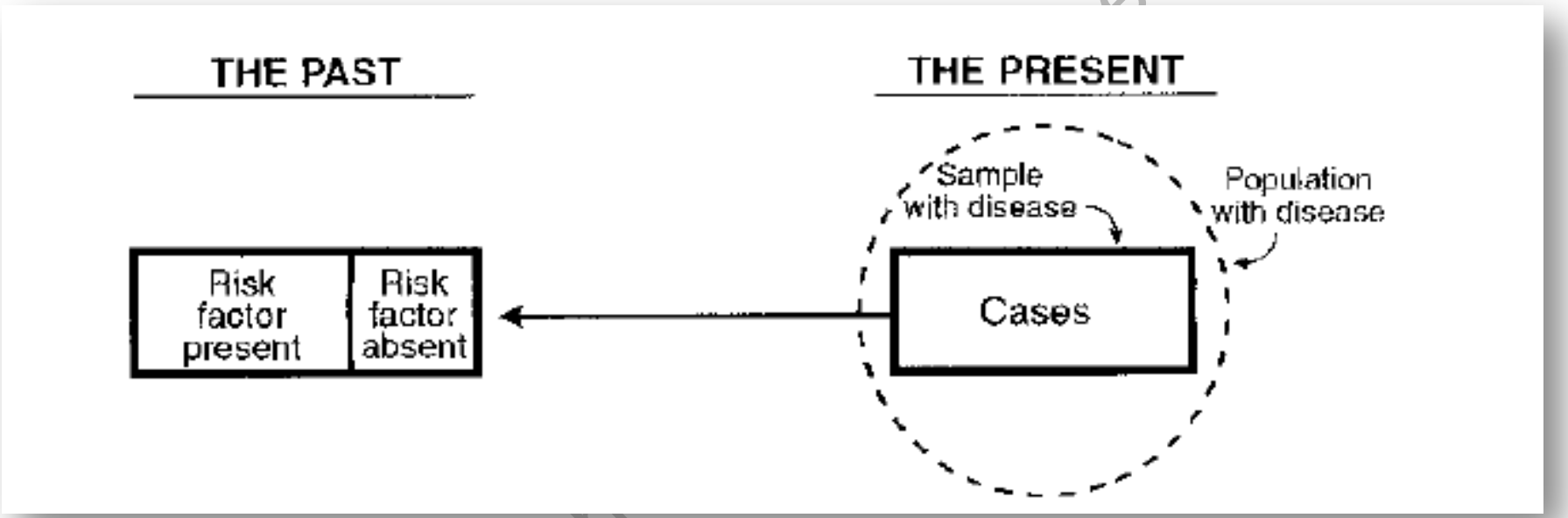


Figure 5.6: STEP 1 of a case-control - the investigator selects a random sample from a population of people with the disease (cases)

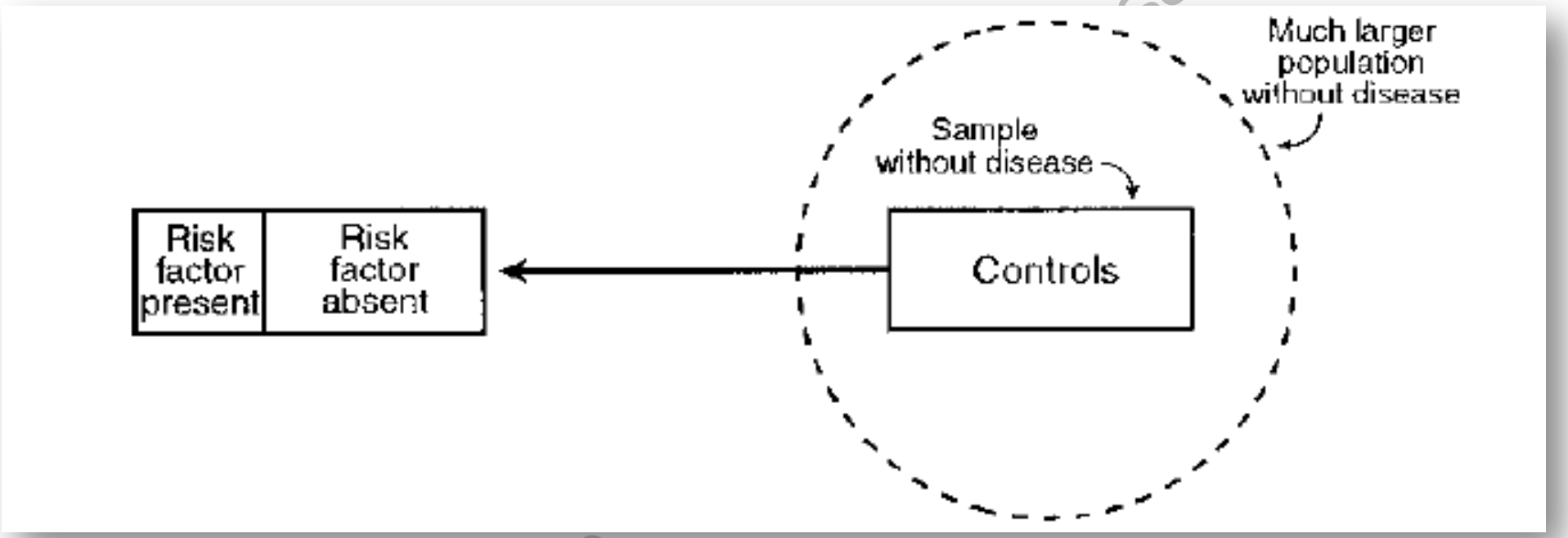


Figure 5.7: STEP 2 of a case-control – the investigator also selects a sample from a population at risk that is free of the disease (controls) and then measures predictor variables

Bacterial Infection and Trachoma in The Gambia: A Case–Control Study

Matthew J. Burton [1,2], **Richard A. Adegbola** [2], **Fabakary Kinteh** [3], **Usman N. Ikumapayi** [2], **Allen Foster** [1], **David C. W. Mabey** [1] and **Robin L. Bailey** [1,2]

[+] Author Affiliations

Abstract

PURPOSE. Trachoma is the leading infectious cause of blindness worldwide. Conjunctival scarring is initiated by recurrent *Chlamydia trachomatis* infection. However, disease progression to trichiasis occurs even in regions where chlamydial prevalence is currently low, which suggests that other factors, for example other bacterial infection, may also drive inflammation and scarring, particularly in the late stages of trachoma. This study was undertaken to investigate whether trachomatous trichiasis or conjunctival scarring are associated with increased prevalence of bacterial infection.

METHODS. Within a case-control study design, individuals with trichiasis or conjunctival scarring (without trichiasis) were compared with normal matched control subjects. Subjects were examined for signs of trachoma. Conjunctival swab samples were collected for bacteriologic culture and *C. trachomatis* PCR.

RESULTS. Recruited for the study were 121 trichiasis case-control pairs and 117 conjunctival scarring case-control pairs. Eyes with trichiasis were more frequently infected with bacteria (37%) than were normal control eyes (7%) (OR: 8.2; $P < 0.001$; 95% CI: 3.24–20.8). Bacterial infection was more common with increased trichiasis severity. In the conjunctival scarring case-control group, scarred eyes had slightly more bacterial infection (11%) than did normal control eyes (6%), although this was not significantly different (OR: 2.2; $P = 0.144$; 95% CI: 0.79–6.33).

CONCLUSIONS. Trichiasis is associated with increased risk of bacterial infection, and there may be a similar trend in eyes with conjunctival scarring. Bacterial infection of the conjunctiva is associated with inflammation, which may result in progressive scarring. Prospective studies are needed to determine the contribution of bacterial infection to disease progression. Bacterial infection probably also contributes to the development of corneal opacification.

Cross-sectional studies are generally “retrospective” because they identify one group of subject with the disease and another without it, and look back in time to look for differences in predictor variables that might explain why the cases got the disease and the controls did not

5.2.5. Strengths and weaknesses of case-control studies

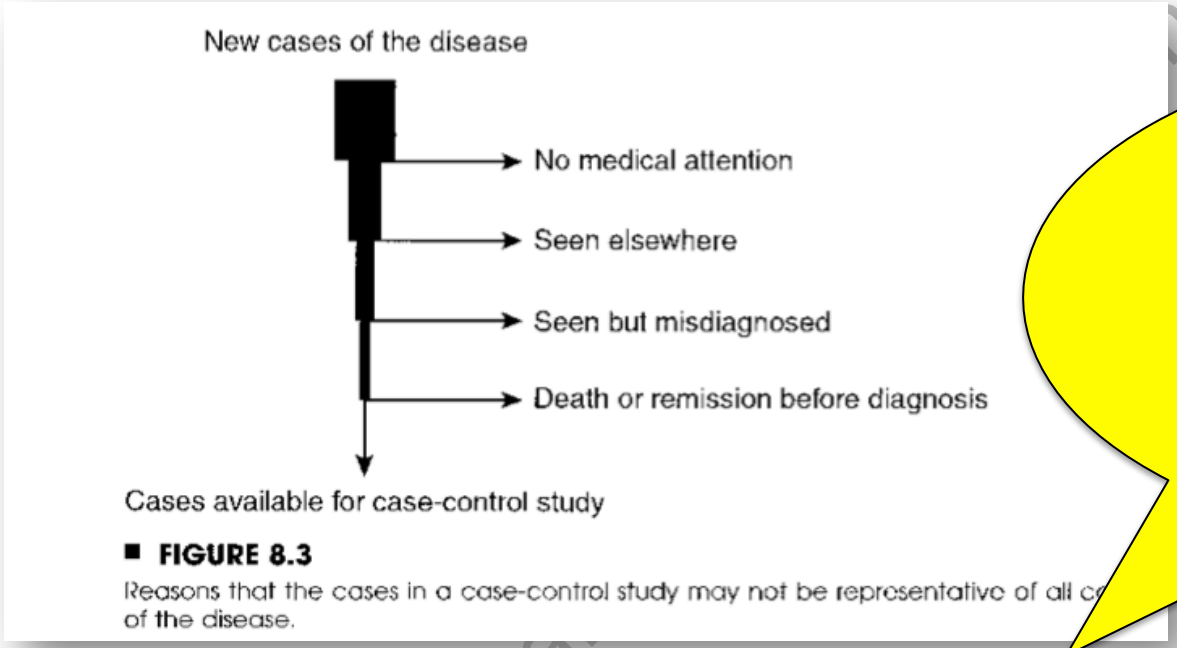
Strengths

- Efficient for rare outcomes
- Usefulness for generating Hypotheses

Weakness

- There is no direct way to estimate the prevalence or incidence, nor the attributable or excess risk
- Increased susceptibility to bias

5.2.6. Sampling bias in case-control studies, how to control it!



■ **FIGURE 8.3**
Reasons that the cases in a case-control study may not be representative of all c
of the disease.

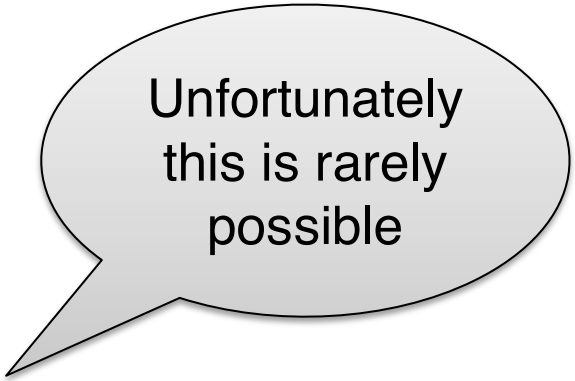
More difficult is to select controls! Controls must be at the same risk of having an outcome (disease) as our cases.

Figure 5.8: Case-control cases selection can be affected by bias due to the reasons in this figure.

How to select a good group of controls?

1. If the study is taking place in a hospital, select controls form the same facilities and service but not with the disease (problem)

For example: “ideally” in a multiple sclerosis study using cases from a neurology department should select controls from the same department looking for care for a complete unrelated problem



2. Matching: at least for age and gender
3. Using a population-based sample
4. Using two or more control groups

5.2.7. Differential measurements bias, how to control it?

Example: You are interested to know life style habits of people with a certain condition (cases) vs controls.

The responses to such a study might be biased because the accuracy of the information recalled by people with the disease is probably better than people without it

Possible reasons include the fact that your **cases** already though and are looking in life style for causes of their problem whilst controls do not care

1. Whenever possible use recorded data for both groups

2. Use blinding (to avoid bias more during measures)
    - Blind subjects: don't tell then why they are included and the purpose of the study (ethical implications)
    - Blind researchers: to avoid bias toward/against the hypothesis of the study during measurements, interviews etc

You can learn a lot more than we are covering in this chapter visiting:
http://www.fda.gov/drugs/developmentapproval process/conductingclinicaltrials/default.htm

5.3. Designing an experiment: studies for clinical trials

1. In clinical trials the investigator applies a treatment (intervention) and observes the effect on an outcome. The major advantage of this type of design over observational studies is the ability to show causality

2. In particular when the intervention is randomly assigned to participants and the investigator is blinded to the type of intervention he/she is doing

3. Clinical trials are expensive and time consuming and address very narrow clinical questions and sometimes expose participants to harm. Because of this clinical trials are reserved to investigate very mature questions

5.3.1. Randomized blind trial

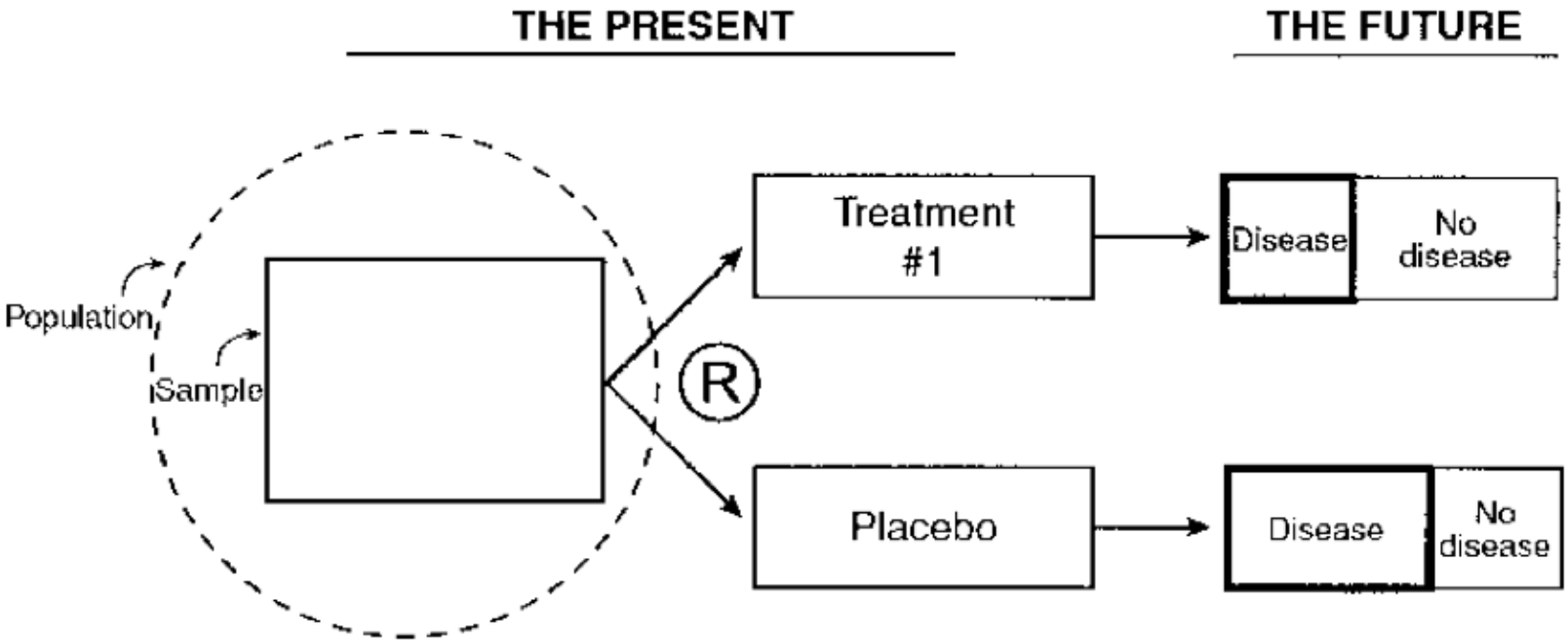
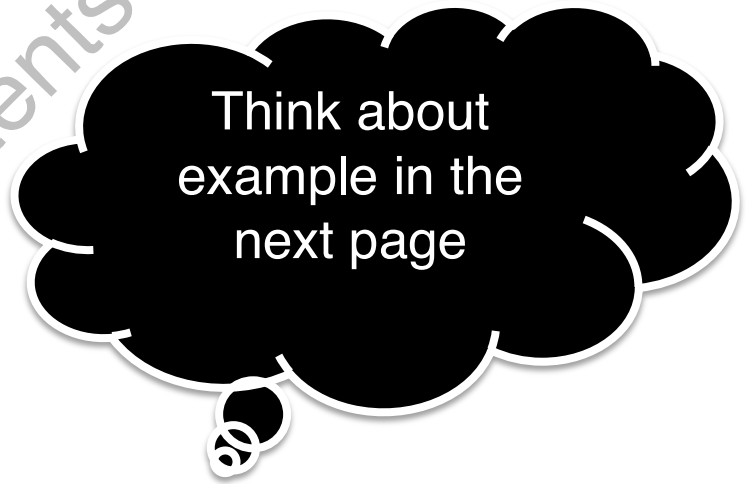


Figure 5.9: In a randomized trial the investigator a) selects a sample from a population, b) measures the baseline variables, c) randomizes the participants, d) applies interventions (one should be a blinded placebo, if possible), e) follows the cohort, f) measures outcome variables (blindly, if possible) and analyses the results

5.3.2. Define entry criteria

In a clinical trial inclusion and exclusion criteria have the joint goal of identifying important population for whom a statistically significant impact of the intervention on the outcome is feasible and likely!



Retardation of Myopia in Orthokeratology (ROMIO) Study: A 2-Year Randomized Clinical Trial

Pauline Cho and Sin-Wan Cheung

[+] Author Affiliations

Corresponding author: Sin-Wan Cheung, School of Optometry, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong, China; sopeggy@polyu.edu.hk.

Abstract

Purpose. This single-masked randomized clinical trial aimed to evaluate the effectiveness of orthokeratology (ortho-k) for myopic control.

Methods. A total of 102 eligible subjects, ranging in age from 6 to 10 years, with myopia between 0.50 and 4.00 diopters (D) and astigmatism not more than 1.25D, were randomly assigned to wear ortho-k lenses or single-vision glasses for a period of 2 years. Axial length was measured by intraocular lens calculation by a masked examiner and was performed at the baseline and every 6 months. This study was registered at ClinicalTrials.gov, number NCT00962208.

Results. In all, 78 subjects (37 in ortho-k group and 41 in control group) completed the study. The average axial elongation, at the end of 2 years, were 0.36 ± 0.24 and 0.63 ± 0.26 mm in the ortho-k and control groups, respectively, and were significantly slower in the ortho-k group ($P < 0.01$). Axial elongation was not correlated with the initial myopia ($P > 0.54$) but was correlated with the initial age of the subjects ($P < 0.001$). The percentages of subjects with fast myopic progression (>1.00D per year) were 65% and 13% in younger (age range: 7–8 years) and older (age range: 9–10 years) children, respectively, in the control group and were 20% and 9%, respectively, in the ortho-k group. Five subjects discontinued ortho-k treatment due to adverse events.

Conclusions. On average, subjects wearing ortho-k lenses had a slower increase in axial elongation by 43% compared with that of subjects wearing single-vision glasses. Younger children tended to have faster axial elongation and may benefit from early ortho-k treatment. (ClinicalTrials.gov

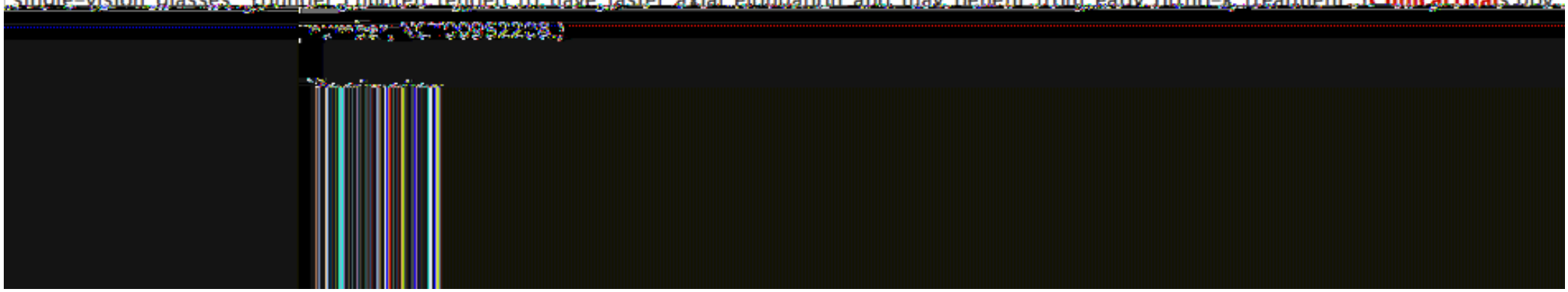


Table 5.3: Reasons for excluding people from a clinical trial

Reason	Examples
1. A study treatment would be harmful	
a. Unacceptable risk of adverse reaction to active treatment	Prior zoster virus in the cornea with scars (orthokeratology trial)
b. **Unacceptable risk of assignment to placebo**	Receiving placebo in cancer treatment trial

Table 5.3 continued

2. Active treatment cannot or is unlikely to be affective **a. Not a risk for the outcome** **b. Has a type of disease that is not likely to respond to treatment** **c. Taking a treatment that is likely to interfere with the intervention**	
3. Unlikely to adhere to the intervention	Poor adherence during the process of recruiting
4. Unlikely to complete follow-up	Plans to move Short life expectancy Unreliable participation in initial visits
5. Practical problems with participating in the protocol	Impaired mental state

5.3.3. Measuring baseline variables

Table 5.4: Check list of aspects to consider during baseline measurements

1. Collect tracking information
2. Describe the participants
3. Measure variables that are risk factors for the outcome or that can be used to define subgroups
4. Establish banks of materials (if applicable)
5. Measure the outcome variable
6. Be tight (few measurements to control costs)

5.3.4. Randomizing

1. Do a good job of random assignment
2. Consider special randomization techniques
    a. Blocked randomization

Example: allocate participants to groups 3 by 3, first 3 to group 1, second 3 to group 2… in a 30 participants study it would be 15:15, whilst in a 33 participants study would be 18:15

    b. Stratified blocked randomization

Here you want to make sure that the number of people with predictor variable is equality distributed between groups. Example (imaginary): In the orthokeratology study corneal thickness is one predictor of the outcome – make sure subject with thin/tick corneas are evenly distributed between the two study groups

5.3.5. Applying the interventions

Table 5.5: Randomization eliminates confounding by baseline variables and blinding eliminates confounding by co-interventions

Explanation for Association		Strategy to Rule Out Rival Explanation
1. Chance		Same as in observational studies
2. Bias		Same as in observational studies
3. Effect-Cause		(Not a possible explanation in an experiment)
4. Confounding	Prerandomization confounding variables	**Randomization**
	Postrandomization confounding variables (unintended interventions)	**Blinding**
5. Cause-Effect		

5.3.6. Alternatives to the randomized blinded trial

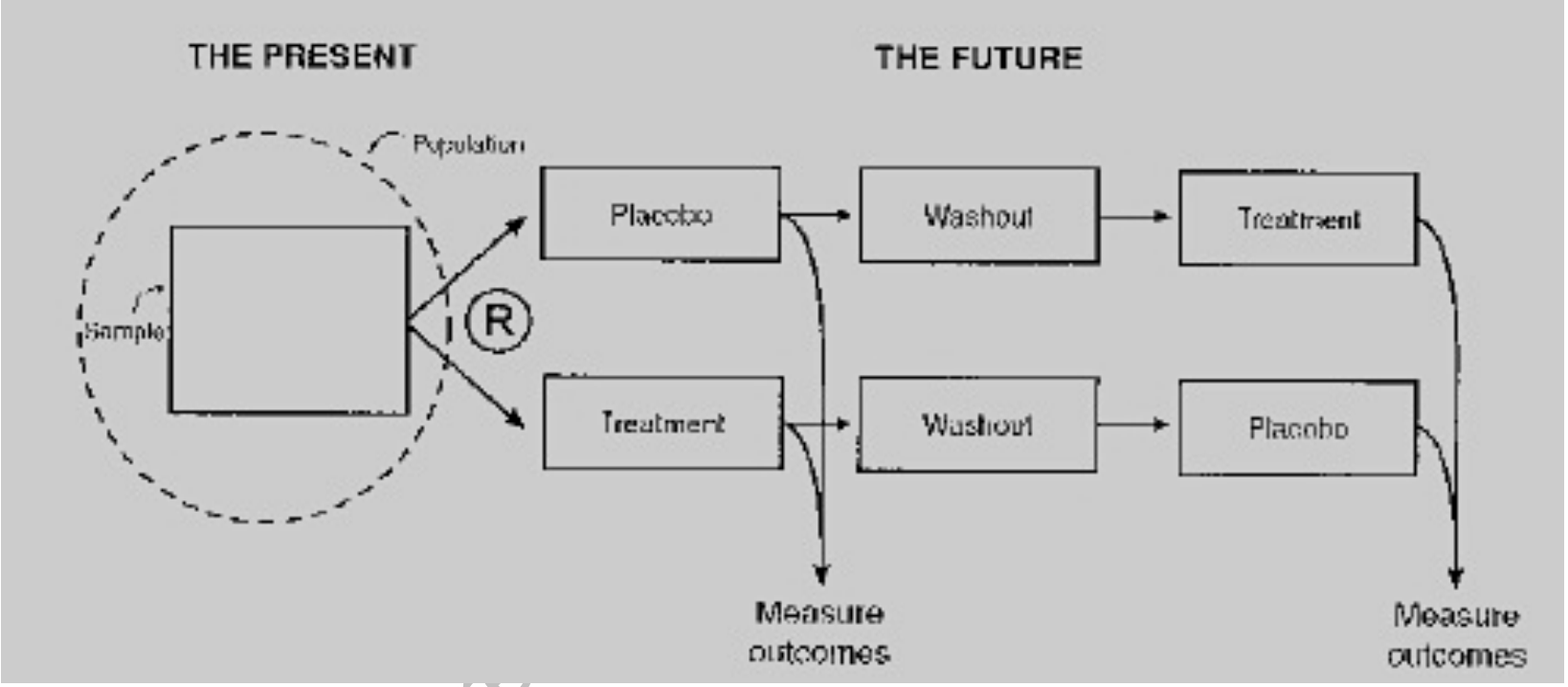


Figure 5.10: In the cross-over randomized trial the investigator a) selects a sample from the population; b) measures baseline variables; c) randomizes the participants; d) applies interventions; e) measures outcomes variables; f) allows washout period to reduce carryover effect; g) applies intervention to former placebo group; h) measures outcome variables again.

5.3.7. Trial for new therapies: US Food and Drug Administration (FDA)

Table 5.6: Stages in testing new therapies

Preclinical	Studies in cell culture and Animals
Phase I	Unblended, uncontrolled studies in a few volunteers to test safety
Phase II	Relatively smart randomized controlled blinded trails to test tolerability and different intensity or "dose" of the intervention on surrogate outcomes
Phase III	Relatively large randomized, controlled blinded trials to test the effect of the therapy on clinical outcomes
Phase IV	Large trials or observations studies conducted after the therapy has been approved by FDA to assess the rate of serious side effects and evaluate additional therapeutic uses

5.4. Researching using existing data

An efficient way to answer a question is to use data that have already been collected. There are 3 general approaches to this type of studies:

1. Secondary data analysis: use of existing data to investigate research questions other than the initial for which the data were originally gathered
2. Ancillary studies: add measurements of small number of variable to the study, often in a subset of the participants, to answer a separate research question
3. Systematic reviews: combine the results of multiple previous studies that have addressed a given research question to calculate a summary estimate of effect

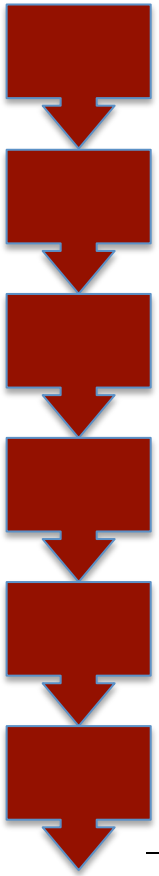
5.4.1. Secondary data analysis

Secondary data analysis studies use two types of data: individual and aggregate.

1. Individual data arrives normally form previous research studies, data were collected at institutions and after the principal study the principal investigator is happy to let other try an analysis of other variables etc

2. Large regional datasets that are publicly available ad do not have a principal investigator (Example: INE, Instituto Ricardo Jorge, etc)

Table 5.7: Steps in finding "Research Questions" to fit an existing database



1. Choose a database
2. Become fully familiar with the database
3. Identity pairs or groups of variables whose association may be of interest
4. Review the literature and consult experts to determine if these questions would be novel and important
5. Formulate specific hypotheses and settle on the statistical methods
6. Analyse the data

5.4.2. Ancillary studies

1. A clever ancillary study can answer a question at little or no cost and effort. As with secondary data analysis, the investigator cannot control the design, including the population and many off the variables measured, but he is able to specify a few key additional measurements
2. Good opportunities for ancillary studies may be found in cohort studies or clinical trials that include the predictor or the outcome variable for the research question of interest
3. Most studies have written procedures that allow investigators (including outside scientists) to propose and carry out ancillary studies

Macular Pigment Imaging in AREDS2 Participants: An Ancillary Study of AREDS2 Subjects Enrolled at the Moran Eye Center

Paul S. Bernstein[1], Faisal Ahmed[1], Aihua Liu[1], Susan Allman[1], Xiaoming Sheng[2], Mohsen Sharifzadeh[3], Igor Ermakov[3] and Werner Gellermann[3]

[+] Author Affiliations

Corresponding author: Paul S. Bernstein, Moran Eye Center, University of Utah School of Medicine, 65 Mario Capecchi Drive, Salt Lake City, UT 84132; paul.bernstein@hsc.utah.edu.

Abstract

Purpose. Age-Related Eye Disease Study 2 (AREDS2) is a randomized, placebo-controlled study designed to determine whether supplementation with 10 mg of lutein and 2 mg of zeaxanthin per day can slow the rate of progression of age-related macular degeneration (AMD). Although some biomarkers of response to carotenoid supplementation such as serum concentrations are part of the AREDS2 protocol, measurement of carotenoid concentrations in the eye and other tissues is not. In this approved ancillary study, macular pigment optical density (MPOD), macular pigment distributions, and skin carotenoid levels at enrollment and at each annual visit were measured to assess baseline carotenoid status and to monitor response to assigned interventions.

Methods. All subjects enrolled at the Moran Eye Center had MPOD and macular pigment spatial distributions measured by dual-wavelength autofluorescence imaging and total skin carotenoids measured by resonance Raman spectroscopy.

Results. Baseline MPOD in enrolled subjects was unusually high relative to an age-matched control group that did not consume carotenoid supplements regularly, consistent with the high rate of habitual lutein and zeaxanthin consumption in Utah AREDS2 subjects prior to enrollment. MPOD did not correlate with serum or skin carotenoid measurements.

Conclusions. Useful information is provided through this ancillary study on the ocular carotenoid status of AREDS2 participants in the target tissue of lutein and zeaxanthin supplementation: The macula. When treatment assignments are unmasked at the conclusion of the study, unique tissue-based insights will be provided on the progression of AMD in response to long-term, high-dose carotenoid supplementation versus diet alone. (ClinicalTrials.gov number, NCT00345176.)

5.4.3. Systematic reviews

You can get a lot more Information by visiting this website at University of Edinburgh (copy-and-past to your browser)

http://www.ccace.ed.ac.uk/research/software-resources/systematic-reviews-and-meta-analyses

1. A good systematic review, like any other study, requires a complete written protocol before the study begins. The protocol should include the research question, methods for identifying all eligible studies, methods for abstracting data from the studies, and statistical methods

2. The statistical aspects of a systematic review, termed meta-analysis, include the summary effect estimate and confidence interval, tests for evaluation heterogeneity and potential publication bias, and planned subgroup and sensitivity analysis

Screening Tests for Detecting Open-Angle Glaucoma: Systematic Review and Meta-analysis

Graham Mowatt [1], Jennifer M. Burr [1,2], Jonathan A. Cook [1], M. A. Rehman Siddiqui [2], Craig Ramsay [1], Cynthia Fraser [1], Augusto Azuara-Blanco [2], Jonathan J. Deeks [3] and for the OAG Screening Project

[+] Author Affiliations

Abstract

PURPOSE. To assess the comparative accuracy of potential screening tests for open angle glaucoma (OAG).

METHODS. Medline, Embase, Biosis (to November 2005), Science Citation Index (to December 2005), and The Cochrane Library (Issue 4, 2005) were searched. Studies assessing candidate screening tests for detecting OAG in persons older than 40 years that reported true and false positives and negatives were included. Meta-analysis was undertaken using the hierarchical summary receiver operating characteristic model.

RESULTS. Forty studies enrolling over 48,000 people reported nine tests. Most tests were reported by only a few studies. Frequency-doubling technology (FDT; C-20-1) was significantly more sensitive than ophthalmoscopy (30, 95% credible interval [CrI] 0-62) and Goldmann applanation tonometry (GAT; 45, 95% CrI 17-68), whereas threshold standard automated perimetry (SAP) and Heidelberg Retinal Tomograph (HRT II) were both more sensitive than GAT (41, 95% CrI 14-64 and 39, 95% CrI 3-64, respectively). GAT was more specific than both FDT C-20-5 (19, 95% CrI 0-53) and threshold SAP (14, 95% CrI 1-37). Judging performance by diagnostic odds ratio, FDT, oculokinetic perimetry, and HRT II are promising tests. Ophthalmoscopy, SAP, retinal photography, and GAT had relatively poor performance as single tests. These findings are based on heterogeneous data of limited quality and as such are associated with considerable uncertainty.

CONCLUSIONS. No test or group of tests was clearly superior for glaucoma screening. Further research is needed to evaluate the comparative accuracy of the most promising tests.

3. The characteristics and findings of individual studies should be displayed clearly in table and figures so that the reader can form opinions that do not depend solely on the statistical summary estimates

4. The biggest drawback to a systematic review is that the results can be no more reliable that the quality of the underlying studies upon which it is based

Does Cigarette Smoking Alter the Risk of Pterygium? A Systematic Review and Meta-Analysis

Shi Song Rong[1], Yi Peng[1], Yuan Bo Liang[2], Di Cao[1] and Vishal Jhanji[1,3,4]

Author Affiliations

Correspondence: Vishal Jhanji, Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong; vishaljhanji@gmail.com.

Abstract

Purpose. To determine the association of cigarette smoking with pterygium.

Methods. Potentially eligible studies published from the year 1946 to December 28, 2013 were identified from MEDLINE, EMBASE, and Cochrane Library databases, and reference lists. All studies that evaluated smoking as an independent factor for pterygium were identified. Study-specific odds ratios (ORs) were combined using the random-effects model when $P < 0.1$ in the test for heterogeneity, or otherwise the fixed-effects model was used. Meta-regression, sensitivity **analysis**, and evaluation of potential biases were undertaken. The ORs with 95% confidence intervals (CIs) of smoking as an associated factor for pterygium were analyzed.

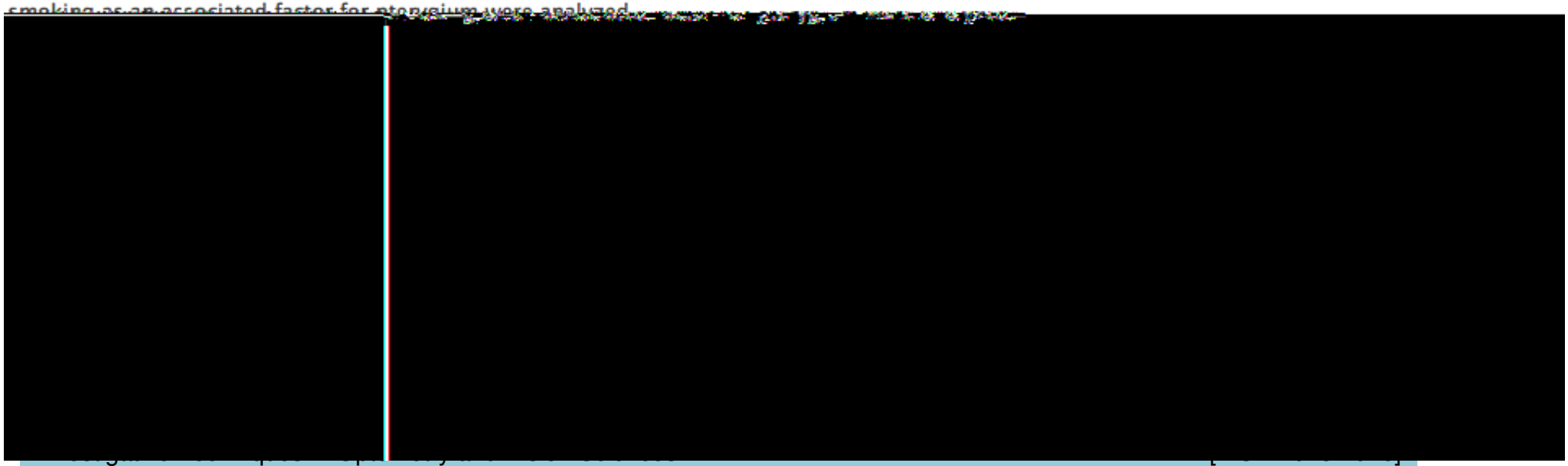


Table 5.8: elements of a good systematic review

1. Clear research question
2. Comprehensive and unbiased identification of completed studies
3. Definition of inclusion and exclusion criteria
4. Uniform and unbiased abstraction of the characteristics and findings of each study
5. Clear and uniform presentation of data from individual studies
6. Calculation of a summary estimate of effect and confidence interval based on the findings of all eligible studies when appropriate
7. Assessment of the heterogeneity of the findings of the individual studies
8. Assessment of potential publication bias
9. Subgroup and sensitivity analyses

5.5. Choosing the study subjects

5.6. Estimate sample size

[These topics will be studied in UNIT 6]

Técnica de Investigação em Optometria e Ciências da Visão

UNIT 6 Planning your measurements

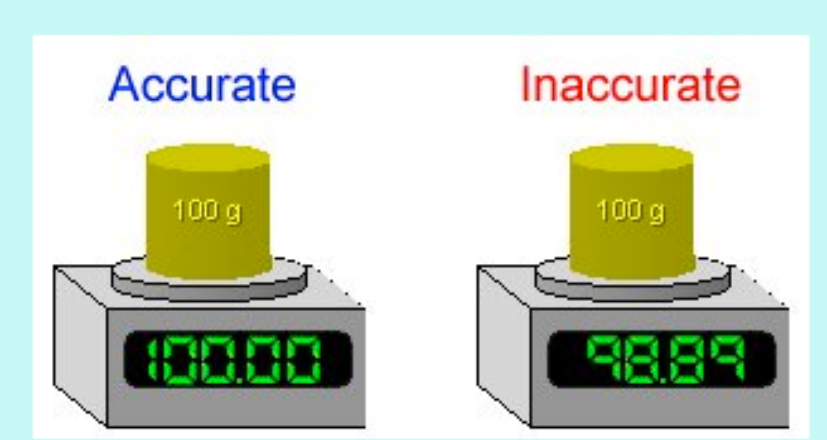
Aula 6
16 Nov 2015

Mestrado em Optometria Avançada
António Filipe Macedo

6.1. Measurements scale

Measurements should be

precise (free of random error)
and
accurate (free of systematic error)



More precise		Less precise	
Trial #	**Mass (g)**	**Trial #**	**Mass (g)**
1	100.00	1	100.10
2	100.01	2	100.00
3	99.99	3	99.88
4	99.99	4	100.02
Average	**100.00**	**Average**	**100.00**
Range	**± 0.01**	**Range**	**± 0.11**

Table 6.1: Measurements scales. This table is a simplified classification of measurements scales and the information that results.

Type of measurement	Characteristics of Variance	Example	Descriptive statistics	Information content
Categorical*: Nominal	Unordered categories	Gender, blood type, vital status	Counts, proportions	Lower

*Categorical measurements that contain only two classes (e.g. gender) are termed dichotomous

Type of measurement	Characteristics of Variance	Example	Descriptive statistics	Information content
Categorical: Ordinal	Ordered categories with intervals that are not quantifiable	Degree of pain	In addition to the above: medians	Intermediate

Type of measurement	Characteristics of Variance	Example	Descriptive statistics	Information content
Continuous** or ordered discrete	Ranked spectrum with quantifiable intervals	Weight; number of cigarettes-a-day	In addition to the above: means, standard deviations	Higher

**Continuous variables have an infinite number of values (e.g. Weight) whereas discrete variables have a finite scale (e.g. number of cigarettes/day). Discrete variables that are ordered (i.e., arranged in sequences from few to many) and that have large number of possible values resemble continuous variables for practical purposes of measurements and analysis.

Categorical variables

Are used for phenomena that are not suitable for quantification can often be measured by classifying them in categories

Dichotomous = 2 categories (dead or alive)

Polychotomous = more than two categories

Nominal = categories that are not ordered (e.g. blood type)

Ordinal = categories that do have an order such as: moderate, severe or moderate pain

Choosing a measurement scale

A good rule is prefer continuous variables because they contain the maximum amount of information

Example

When measuring IOP pressure you should express your results in a continuous scale and not as: high-IOP vs normal-IOP

The use of continuous variables normally reduces the number of subjects necessary to the study (sample size – next unit)

6.2. Precision

6.2.1. Advantages of good precision

A very precise measurement is one that is reproducible, that is, it has nearly the same value each time it is measured

The greater the precision of the measurements the smaller the sample size required to test the hypothesis

Precision is also known by: reproducibility, reliability or consistency is affected by random error (chance). The greater the error the less precise the measurement

6.2.2. Main sources of random error

Observer variability

Variability in measurements that is due to the observer

Instrument variability

Variability in the measurement caused due changing environmental factors such as temperature or any components of the instrument

Subject variability

Intrinsic biologic variations caused by changing in mood, etc etc

6.2.3. Assessment of precision

Within-observer reproducibility

A single observer performs repeated measurements

Between-observer reproducibility

Different observers perform measurements

Within-instrument reproducibility

A single instruments is used for repeated measurements on a set of subjects

Between-instruments reproducibility

Different instruments are used for measurements on a set of subjects

6.2.4. Strategies for enhancing precision

Standardizing the measurement methods

Specific instructions for making the measurements, even if you perform all data collection (example next page)

Training and certifying the observers

Refine the instrument

Automating the instruments

Repetition of measurements

Table 6.2: Examples from a study of antihypertensive treatment

Strategy to reduce random error	Source of Random error	Example of random error	Example of strategy to prevent random error
1. Standardizing the measurement methods in an operations manual	Observer	Variation of blood pressure (BP) measurement due to variable rate of deflation (sometimes faster than 2mm/Hg and other times slower)	Specify that the cuff need to be deflated at 2mm Hg/sec
	Subject	Variation in BP due to variable length of quiet sitting	Specify that the subject sit in a quiet room for 5 min before BP measurement
2. Training and certifying the observer	Observer	Variation in BP due to variable observer technique	Train observers in standard techniques

3. Refining the instrument	Instrument or observer	Variation in BP due to digit preference (e.g. the tendency to round numbers to a multiple of 5)	Use random zero sphygmomanometry to conceal BP reading until after it has been recorded
4. Automating the instrument	Observer	Variation in BP due to variable observer technique	Use automatic BP measurement device
5. Repeating the measurement	Observer, subject and instrument	All measurements and all sources of variation	Use mean of two or more BP measurements

Example of step-by-step data collection

1ºDIA
participante não dilatado

1. MICROPERIMETRIA

1.1. Coloque o participante aproximadamente 5 minutos nas condições de iluminação da sala (baixa iluminação);

1.2. Introduza a identificação do participante de acordo com o que estabeleceu no **campo [6]** deste formulário;

1.3. Código: **CVS** / Utilizador: **YYTF;**

1.4. No menu do canto inferior esquerdo -- certifique-se de que o protocolo correto **"*FMCVS*"** está selecionado!

1.5. Coloque o queixo do participante no encaixe oposto ao olho que vai testar. Comece pelo OD;

1.6. Coloque o oclusor no olho que não vai testar (OE);

1.7. Dê instruções ao participante:

- *"fixe a cruz vermelha"*
- *"manter cabeça e queixo encostados"*
- *"carregue cada vez que vir um ponto brilhante dentro da máquina, mesmo que o ponto seja pouco brilhante"*

1.8. Interrompa o teste a meio (2 ou 3 minutos depois de ter começado) -- este primeiro teste serviu para treino;
1.9. Inicie novo teste no mesmo olho em que fez o treino;

1.10. Repita o teste para o OE

6.3. Accuracy

The accuracy of a variable is the degree to which it actually represents what it is intended to represent. Accuracy is different from precision in the ways shown in Figure 6.1

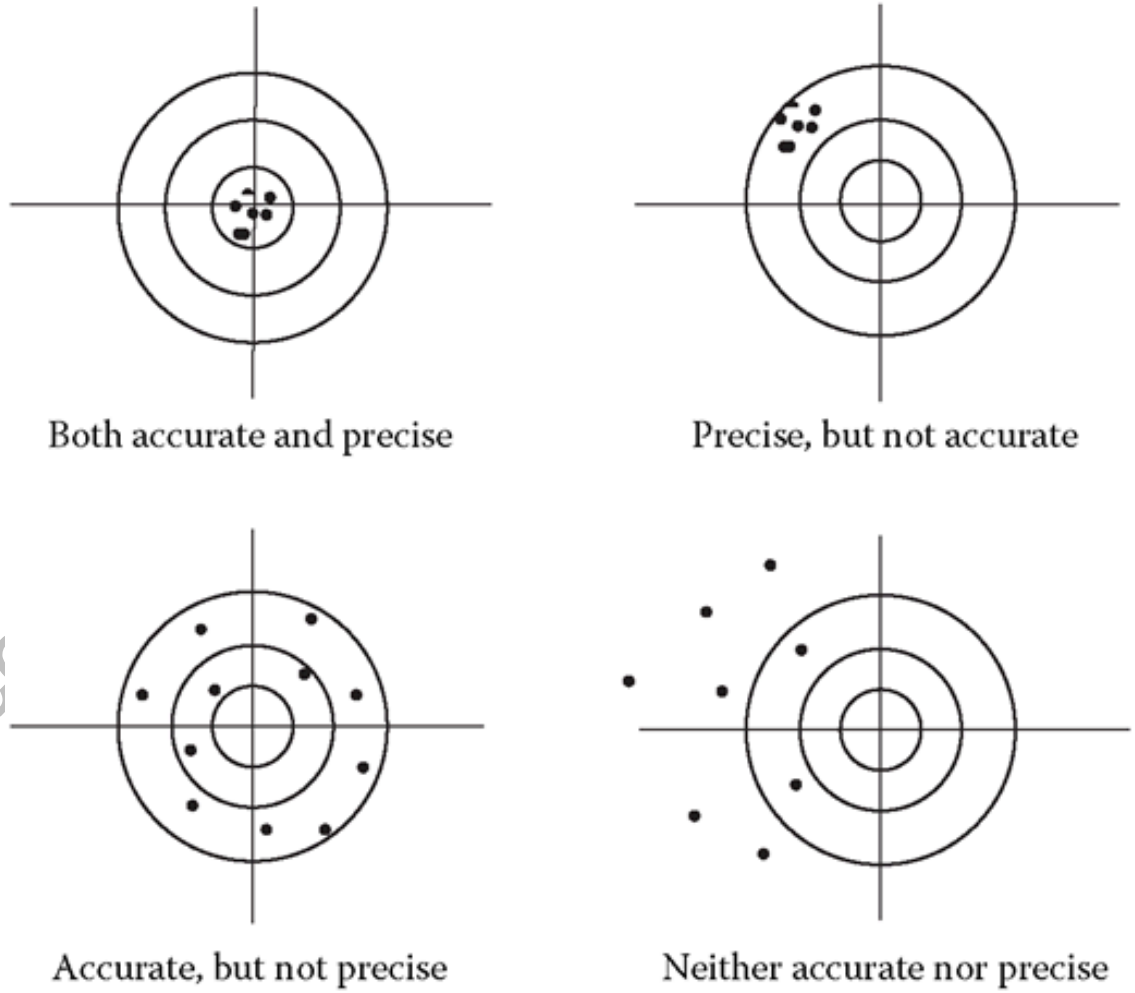


Figure 6.1: The difference between precision and accuracy

6.3.1. Accuracy is a function of systematic error

Observer bias

The observer might introduce systematic measurement bias by for example rounding obtained values in a random way

Subject bias

Subjects that do not follow instructions can introduce errors. For example, if you ask them to take the contact lens off 3 hours before the measurements and they take it 15min in one day, 3 hours in another day e 30 min in another day

Instrument bias

Instruments that are not properly calibrated can give the wrong measurement readings. For example the auto-refractometer

6.3.2. Assess and increase accuracy

The accuracy of a measurement is best assessed by comparing it to a **"gold standart". That is, a reference technique that is considered accurate**

1. Standardizing the measurement methods
2. Training and certifying the observers
3. Refining the instruments
4. Automating the instruments
5. Making unobtrusive measures (subjects do not know the purpose/variable)
6. Binding
7. Calibrating the instruments

Table 6.3: Reducing systematic error in order to increase accuracy. Illustrations from a study of antihypertensive treatment.

1. Standardizing the measurement methods in the operations manual	Observer	Consistently high diastolic BP readings due to using the point at which sound become inaudible	Specify the operational definition of diastolic BP as the point at which sounds cease to be heard
	Subject	Consistently high readings due to measuring BP right after walking upstairs to clinic	Specify that the subject sit in quiet room for 5 minutes before measuring
2. Training and certifying the	Observer	Consistently high BP blood	Trainer checks accuracy of

observer		pressure readings due to failure to follow procedures specified in operations manual	observer's reading with a double-headed stethoscope
3. Refining the instrument	Instrument	Consistently high BP readings with standard cuff in subjects with very large arms	Use extra-wide BP cuff in obese patients
4. Automating the instrument	Observer	Conscious or unconscious tendency for observer to read BP lower in	Use automatic BP measurement device

		treatment group	
	Subject	BP increase due to proximity of attractive technician	Use automatic – autonomous measurement device
5. Making unobstructive measurements	Subject	Tendency of subject to overestimate compliance with study drug	Measure study drug level in urine
6. Blinding	Observer	Conscious or unconscious tendency for observer to read BP lower in active treatment group	Use double-blind placebo to conceal study group assignment

	Subject	Tendency of subject to over-report side effects if he knew he was on active drug	Use double-blind placebo to conceal study group assignment
7. Calibrating the instrument	Instrument	Consistently high BP readings due to anaeroid manometer being out of adjustment	Calibrate against mercury manometer each month

6.3.3. Validity

A difficult decision is to know whether a variable represents what is to quantify, for example, pain or quality of life. This issue is termed validity.

Assessment of validity

Content validity

- Face validity

Is a subjective judgment about whether a measurement makes sense intuitively - whether it is reasonable

- Sampling validity

Refers to whether the measurement incorporates all or most of the aspects of the phenomenon under study

For example: a valid measure of quality of life includes questions on social, physical, emotional and intellectual functioning

Construct validity

Refers to how well a measurement conforms to theoretical concepts (constructs) concerning the entity under study. For example, if a particular trait is theoretically believed to differ between two groups of individuals a measurement with construct validity would show this difference

Criterion-related validity

Is the degree to which the measurement correlates with an external criterion of the phenomenon under investigation. A variation is predictive validity – the ability of the measurement to predict the future occurrence of that criterion. For example, an investigator could validate a measurement of depression by examining its ability to predict suicide.

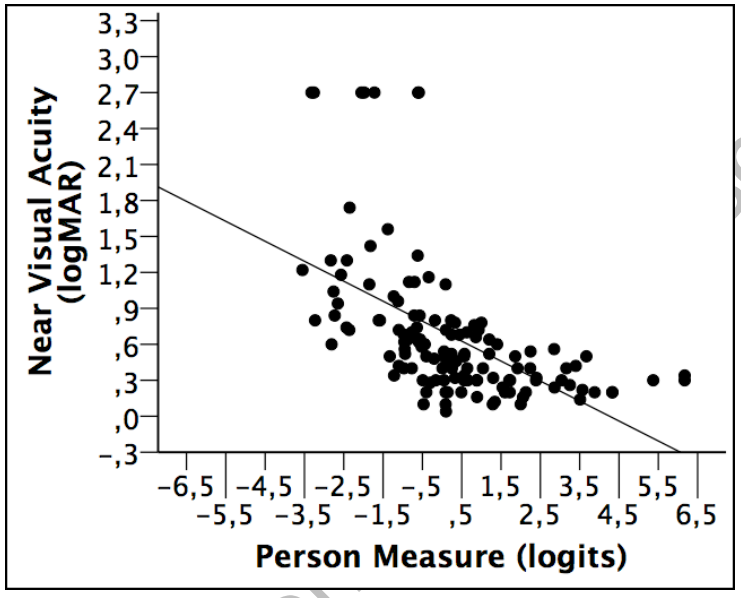


Figure 6.2: Example of how "person measure" a measure of visual ability obtained via activity inventory questionnaire and its relationship with near acuity

The Portuguese version of the activity inventory
L Hernández-Moreno, RW Massof, S Sousa, J Cima, JPM Costa, ...
Investigative Ophthalmology & Visual Science 56 (7), 1368-1368

2015

UNIT 7 Research Hypothesis

Aula 6
23 Nov 2015

Mestrado em Optometria Avançada
António Filipe Macedo

The research hypothesis summarizes the elements of the study: sample, design, predictor and outcome variables

The primary purpose of the hypothesis is to establish the basis for tests of statistical significance

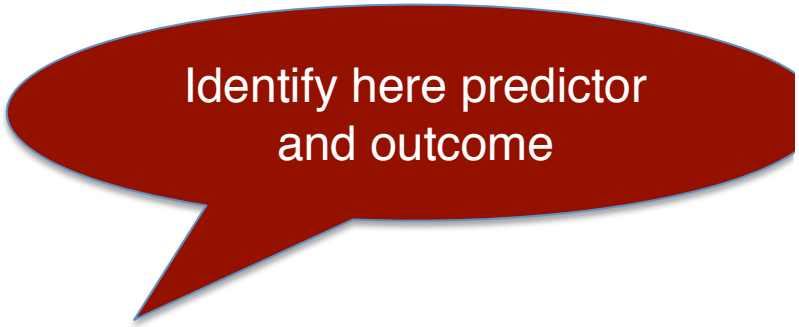
Examples of “key words” that tell you that you need to define a clear research hypothesis

greater than, less than, causes, leads to, compared with, more likely than, associated with, related to, similar to, correlated with

7.1.1. Characteristics of a good research hypothesis

First you need to start with a good research question. With that you must state a hypothesis: **simple, specific and stated in advance**

7.1.1.1. Simple vs complex hypothesis



Simple hypothesis

[contains one predictor and one outcome variable]

Example: Poor contrast sensitivity is associated with a reduced reading speed in patients with low vision

Complex hypothesis are not readily to be tested with a single statistical test

A complex hypothesis contains more than one predictor variable

Poor contrast sensitivity and reduced visual field are associated with poor reading speed in patients with low vision

or contains more than one outcome

Poor contrast sensitivity is associated with poor reading speed and increase risk of falls in patients with low vision

Complex hypothesis can be more easily approached as two simple hypotheses

7.1.1.2. Specific vs vague hypothesis

- A specific hypothesis leaves no ambiguity about the subjects and variables or about the test of statistical significance that will be applied
- When necessary the hypothesis can specify if the variables (predictors and outcomes) will be dichotomous, continuous or categorical

e.g. caffeine consumption in mg/day is associated with an increased risk of high IOP (>21 mmHg) In patients at risk of glaucoma

if the statement of the hypothesis gets to difficult to read the definitions must be left out but must be specified clearly in another part of the protocol

Hormonal changes associated with pregnancy may influence a woman's cornea. Corneal thickness, corneal curvature, and corneal biomechanical parameters have been found to be affected by variations in sex hormones.[1–5] Corneal thickness has been found to increase during pregnancy, resolving postpartum.[2] A possible cause of increased corneal thickness is fluid retention related to pregnancy. The corneal curvature is also found to increase by an average of 1.00 diopter (D) in the second half of pregnancy, resolving postpartum or after cessation of breastfeeding.[1] Hormonal changes during pregnancy may affect corneal biomechanics because pregnancy has been described as a potential risk factor for the progression of keratoconus.[6] Women taking contraceptives report problems with hard contact lenses, and pregnant women frequently report contact lens intolerance.[7,8] These changes are probably driven by direct interaction of sex hormones with sex hormone receptors located in the human cornea.[9,10]

The ability to assess and predict these corneal changes during pregnancy might have clinical implications, such as need to change spectacles, intolerance

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(delay in performing) refractive eye surgery. For that reason, the aim of our study was to evaluate the changes in the biomechanical properties of the cornea, anterior segment anatomy, and intraocular pressure (IOP) in pregnant women.

SUBJECTS AND METHODS

This prospective case-control study enrolled healthy pregnant women and a control group of healthy nonpregnant women visiting the Assaf Harofeh Medical Center

Table [illegible] measured using the dynamic bidirectional applanation device.

Parameter	Mean (mm Hg) ± SD		P Value
	Pregnant	Control	
CH	11.39 ± 1.5	11.00 ± 1.3	.14
CRF	9.89 ± 1.7	10.17 ± 1.6	.37
IOPg	10.96 ± 3.1	12.97 ± 2.7	<.001
IOPcc	10.97 ± 2.8	13.16 ± 2.2	<.001

Consider the study from previous page and perform analysis

Classify the hypothesis of the study below in terms of:

- Simple vs complex
- Predictor(s) and outcome(s)
- Specifc vs Vague

For that reason, the aim of our study was to evaluate the changes in the biomechanical properties of the cornea, anterior segment anatomy, and intraocular pressure (IOP) in pregnant women.

Ref: Goldich, Y et al.; J Cataract Refract Surg 2014; -:-–- Q 2014 ASCRS and ESCRS (in press)

7.1.1.3. Hypothesis in advance vs after the fact

- The hypothesis must be clear before the beginning of the study, this will keep your research focused

A clear hypothesis also creates a strong basis for interpreting / analysing the study results

- Hypothesis formulated after the results often lead to a lot of dispersion when analysing your data and lead to over-interpreting the importance of your findings

7.1.2. Types of hypothesis

For the purpose of testing statistical significance, the research hypothesis must be restated in forms that categorize the expected difference between the study groups

7.1.2.1. Null and alternative hypotheses

Null hypotheses

states that there is no association between predictor and outcome variables:

e.g. caffeine consumption does not increase IOP

Alternative hypotheses:

e.g. caffeine consumption increase IOP

You need to perform a statistical test to know which hypotheses was confirmed by your study

One and two-sided alternative hypotheses

A one-sided hypothesis specifies the direction of the association between the predictor and the outcome variable

e.g. caffeine consumption influences IOP

- ☐ one-sided
- ☐ two-sided

e.g. caffeine consumption increase IOP

- ☐ one-sided
- ☐ two-sided

One and two-sided alternative hypotheses

A one-sided hypothesis specifies the direction of the association between the predictor and the outcome variable

e.g. caffeine consumption influences IOP

☐ one-sided

☒ two-sided

e.g. caffeine consumption increase IOP

☒ one-sided

☐ two-sided

7.1.3. Underlying statistical principles

7.1.3.1. Type I and type II errors

When an investigator performs a statistical test **and gets the level of statistical significance** he/she must decide if they accept the null or the alternative hypotheses

Type I error: (false-positive): occurs if an investigator rejects a null hypothesis (**accepts a false alternative**) that is actually true in the population

Type II error: (false-negative): occurs if an investigator fails to reject a null hypothesis (**rejects a true alternative**) that is actually not true

7.1.3.2. Effect size

The likelihood that a study will be able to detect and association between a predictor and an outcome variable depends on the actual magnitude of that association in the target population

If it is large (*e.g. IOP increase by 5mmHg in individuals that consume 10mg caffeine a day- compared with no consumption*) it will be easy to detected in a sample of the population

If the effect is small (*e.g. a 0.5 increase in IOP is expected*) it will be difficult to detect in a sample of the population

- Unfortunately how large the effect of the predictor on the outcome is not n known (that is normally why we conduct the studies)

The investigator must decide the expected size and that is normally know as the effect size

- Estimating the effect size is normally a difficult exercise and needs to be decided, typically, form previous results reported in the literature

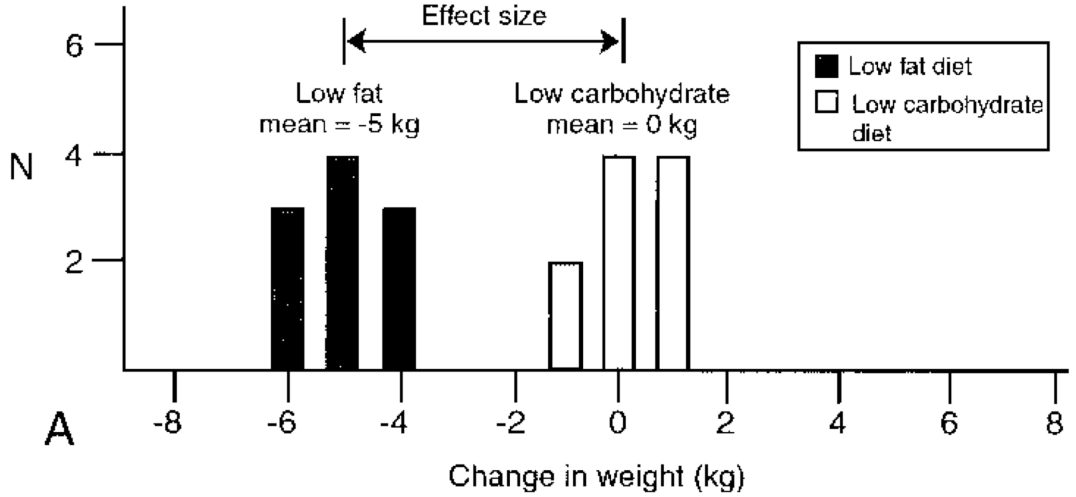


Figure 7.1: Weight loss achieved by two diets the effect size is 5Kg

7.1.3.3. Example

SAMPLE SIZE – BEFORE THE STUDY

A study to whether middle-aged men are more like more likely to have impaired vision than middle-aged woman.

Suppose an investigator finds that 20% of woman and 30% of men 50-65 years of age are hard of seeing.

These results could be interpreted as showing that men are 10% more likely to have impaired vision than women (30%-20%, the absolute difference) or 50% more likely ([30% - 20%]/20%, the relative difference. For sample size planning, both of the proportions matter.

Most of the time here we will consider the smaller proportion (in this case, 20%) and the absolute difference (10%) between the groups being compared.

7.1.3.4. Alpha, beta and power

With statistical tests we try to reject the null hypothesis. With sample size calculations we try to avoid errors type I and Type II

Table 7.1: Truth in the population vs Results in the Study Sample - The four possibilities.

	TRUTH IN THE POPULATION	
Results in the study sample	**Association between Predictor and Outcome**	**No Association Between Predictor and Outcome**
Reject null	Correct	Type I error
Fail to reject null	Type II error	Correct

Table 7.2: The analogy between a court (judge decisions) and statistical tests

Innocence The defendant did not counterfeit money	*Null hypothesis* There is no association between time spent in activities outdoors and the incidence of myopia in the population
Guilt The defendant did counterfeit money	*Alternative hypothesis* There is an association between time spent in outdoor activities and the incidence of myopia in the population
Standard for rejecting innocence Beyond a reasonable doubt	*Standard for rejecting null hypothesis* Level of statistical significance (alfa)
Correct judgment Convict a counterfeiter of money	*Correct inference* Conclude that there **is an** association between time spend in outdoors activities and the incidence of myopia in the population

Correct judgment Acquit and innocent person	*Correct inference* Conclude that there **is no** association between time spent in outdoor activities and the incidence of myopia in the population
Incorrect judgment Convict an innocent person	*Incorrect inference (type I error)* Conclude that there is an association between time spent in outdoor activities and the incidence of myopia in the population **when there is actually none**
Incorrect judgment Acquit a counterfeiter	*Incorrect inference (type II error)* Conclude that there is not an association between time spent in outdoor activities and the incidence of myopia in the population **when there actually is one**

Example

A study of the effect of caffeine on IOP is designed with an alpha of 0.05, that means that the investigator has set 5% as the maximum chance of incorrectly rejecting the null hypothesis (and inferring that caffeine as no effect on IOP).

This is a level of reasonable doubt that the investigator will be willing to accept when she/he uses statistical tests to analyse the data after the study is completed.

The maximum chance of Type I error (rejecting the null hypothesis when it is actually true) in called alpha. Another name – level of statistical significance

The probability of making a type II error (failing to reject the null hypothesis when it is actually false) is called beta

The quantity [1-beta] is called **POWER** an is the probability of rejecting the null hypothesis in the sample if the actual effect in the population equals the effect size

A *beta* of 0.1, means the investigator accepts a chance of 10% of missing an association of a effect size, this represents a power of 0.9, that is, a 90% chance of finding an association of that size.

If you set *alpha* and *beta* @ ZERO (0) you will reduce the chance of *FALSE-POSITIVE* (alpha) and FALSE-NEGATIVE (beta)

7.1.3.5. How is it normally?

Typically they assume:

- alpha = 0.05
- beta = 0.2 (Power=0.8)

7.1.3.6. P-value

The null hypothesis is assumed to be true until it is knocked-down as false by a statistical test;

p-Value is the probability of seeing an effect as big or bigger than that in the study by chance if the null hypothesis is actually true;

7.1.3.7. Type of statistical test

The formulas used to calculate sample size are based on mathematical assumptions, which differ for each statistical test;

Because of the above, before the study the investigator must decide on the statistical tests that will be used to analyse the data;

7.1.3.8. Data variability

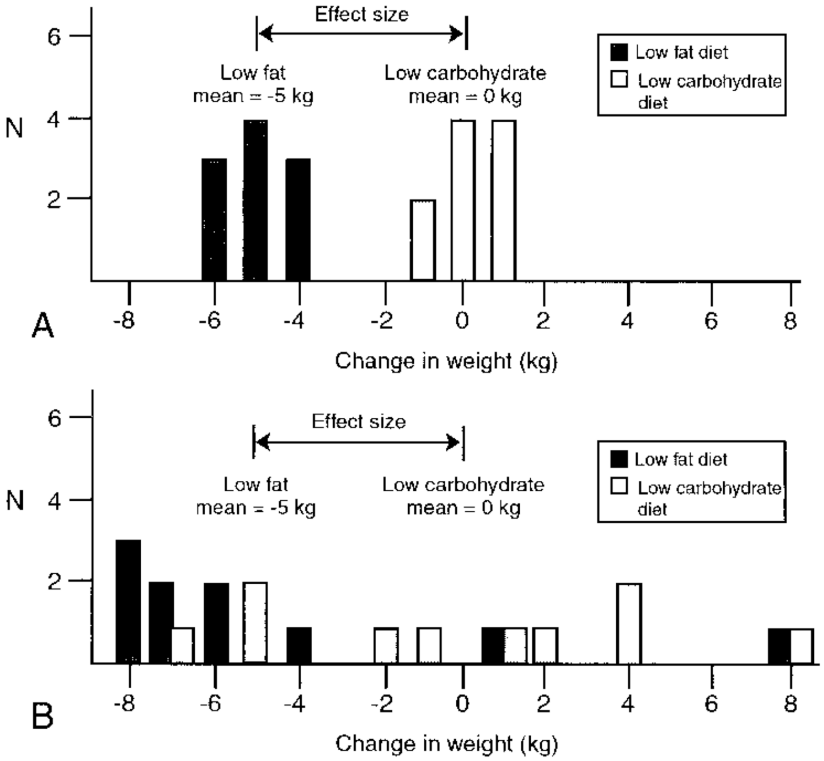


Figure 7.2: Weight loss achieved by two diets.

It is not simply the size of one effect that is important; it also matters the variability;

The greater the variability in the outcome variable among the subjects, the more likely it is that the values in the groups will overlap;

In Figure 7.2 you can see the effect size is the same in both A and B. In a there is no overlap between groups whilst in B there is a great deal of overlap. In A the effect of diet would be sig. but not in B

7.1.4. Sample size calculation: check list

- ☐ State the null hypothesis
- ☐ Select the appropriate statistical test
- ☐ Choose a reasonable effect size (and variability, if necessary)
- ☐ Set alfa and beta
- ☐ Use table or formula (or software) to calculate sample size

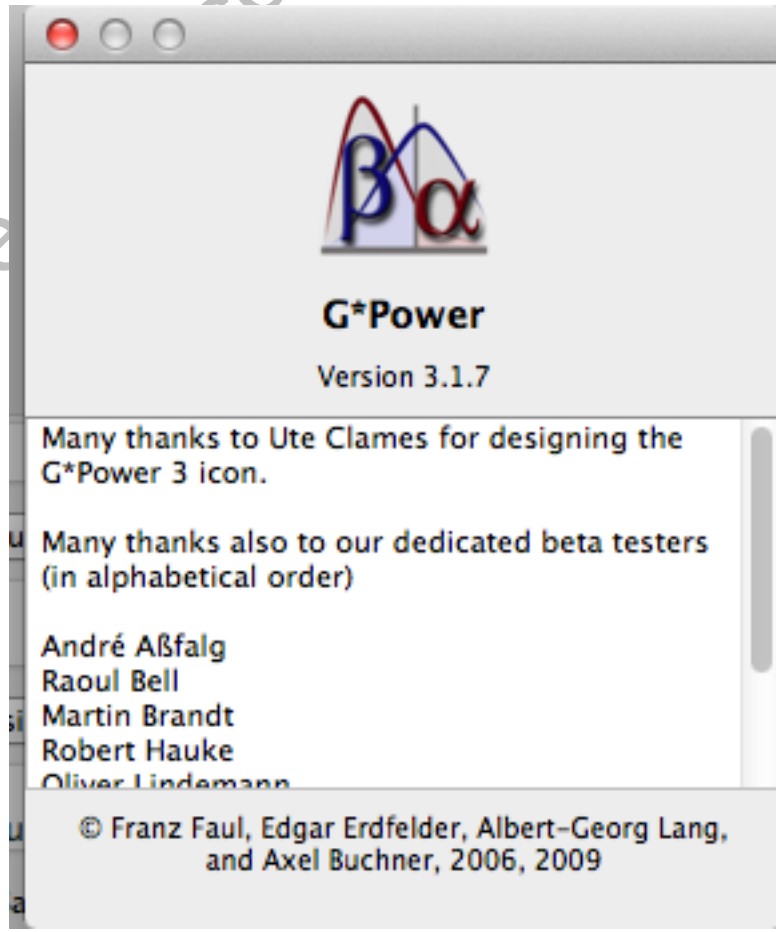
Problem

Chi-squared test

Problem: The research question is whether elderly smokers have a greater incidence of age-related macular degeneration (AMD) than non-smokers.

A review of previous literature suggests that the 5-year incidence of is about 0.20 in the elderly non-smokers.

At an *alpha = 0.05 (two-sided)* and *power 0.80*, how many smokers and non-smokers will need to be studied to determine whether the 5-year AMD incidence is at least **0.30** in smokers?



Solution

1. Null hypothesis: the incidence of AMD is the same in the elderly smokers and non-smokers;
   Alternative Hypothesis: The incidence of AMD is different in elderly smokers and nonsmokers;
2. P2 (incidence in non-smokers) = 0.2; P1 (incidence in smokers) = 0.3. The smaller of these values is 0.2 and the difference between them (P1-P2) is 0.10;
3. Alfa (two-sided) = 0.05; beta = 1-0.80 = 0.20;
4.

Look at the G-power outputs. But please think about the check list in section 7.1.4

[6] -- Monday, November 24, 2014 -- 07:39:27

Exact - Proportions: Inequality, two independent groups (unconditional)

Options: z-test pooled

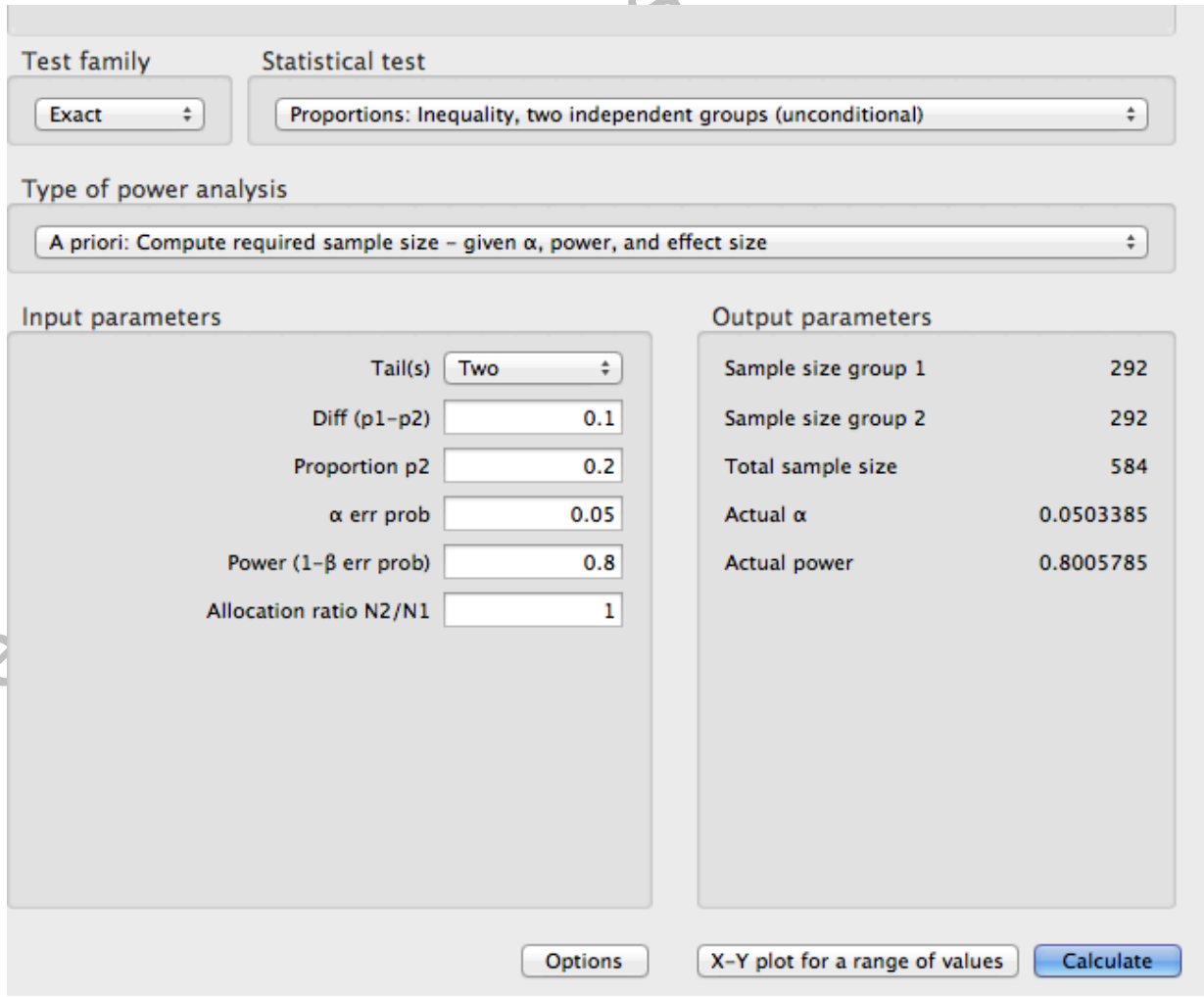
Analysis: A priori: Compute required sample size

Input:

Tail(s)	=	Two
Diff (p1-p2)	=	0.1
Proportion p2	=	0.2
α err prob	=	0.05
Power (1-β err prob)	=	0.8
Allocation ratio N2/N1	=	1

Output:

Sample size group 1	=	292
Sample size group 2	=	292
Total sample size	=	584
Actual α	=	0.0503385
Actual power	=	0.8005785



[7] -- Monday, November 24, 2014 -- 07:42:50

Exact - Proportions: Inequality, two independent groups (unconditional)

Options: z-test pooled

Analysis: A priori: Compute required sample size

Input:

Tail(s)	=	**One**
Diff (p1-p2)	=	0.1
Proportion p2	=	0.2
α err prob	=	0.05
Power (1-β err prob)	=	0.8
Allocation ratio N2/N1	=	1

Output:

Sample size group 1	=	231
Sample size group 2	=	231
Total sample size	=	462
Actual α	=	0.0495550
Actual power	=	0.8011904

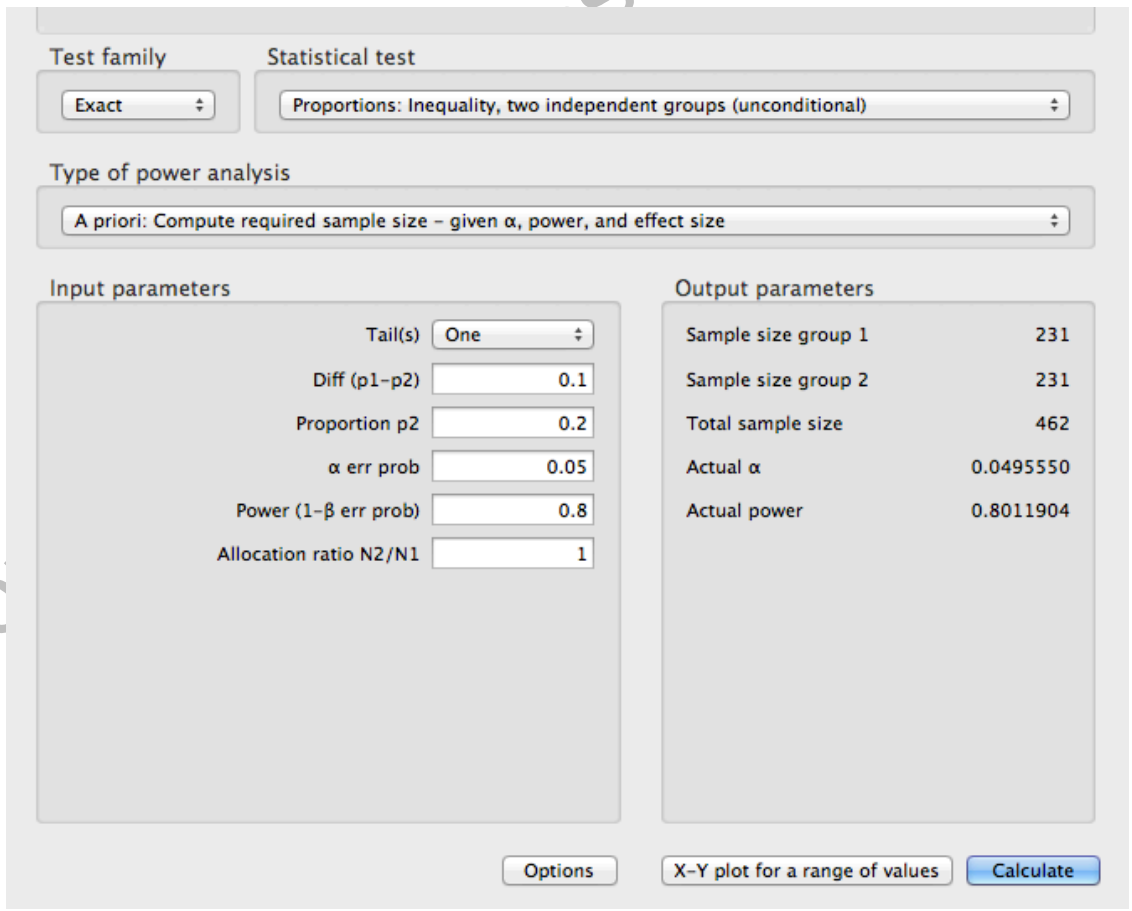


Table 7.3

ONE-SIDED α =	0.005			0.025			0.05		
TWO-SIDED α =	0.01			0.05			0.10		
*E/S** β =	0.05	0.10	0.20	0.05	0.10	0.20	0.05	0.10	0.20
0.10	3,565	2,978	2,338	2,600	2,103	1,571	2,166	1,714	1,238
0.15	1,586	1,325	1,040	1,157	935	699	963	762	551
0.20	893	746	586	651	527	394	542	429	310
0.25	572	478	376	417	338	253	347	275	199
0.30	398	333	262	290	235	176	242	191	139
0.40	225	188	148	164	133	100	136	108	78
0.50	145	121	96	105	86	64	88	70	51
0.60	101	85	67	74	60	45	61	49	36
0.70	75	63	50	55	44	34	45	36	26
0.80	58	49	39	42	34	26	35	28	21
0.90	46	39	32	34	27	21	28	22	16
1.00	38	32	26	27	23	17	23	18	14

Table 7.4

UPPER NUMBER: $\alpha = 0.05$ (ONE-SIDED) OR $\alpha = 0.10$ (TWO-SIDED); $\beta = 0.20$
MIDDLE NUMBER: $\alpha = 0.025$ (ONE-SIDED) OR $\alpha = 0.05$ (TWO-SIDED); $\beta = 0.20$
LOWER NUMBER: $\alpha = 0.025$ (ONE-SIDED) OR $\alpha = 0.05$ (TWO-SIDED); $\beta = 0.10$

SMALLER OF P_1 AND P_2	EXPECTED DIFFERENCE BETWEEN P_1 AND P_2									
	0.01	0.02	0.03	0.04	0.05	0.06	0.07	0.08	0.09	0.10
0.01	2,019	700	396	271	204	162	134	114	98	87
	2,512	864	487	332	249	197	163	138	120	106
	3,300	1,125	631	428	320	254	209	178	154	135
0.02	3,205	994	526	343	249	193	157	131	113	97
	4,018	1,237	651	423	306	238	192	161	137	120
	5,320	1,625	852	550	397	307	248	207	177	154
0.03	4,367	1,283	653	414	294	224	179	148	126	109
	5,493	1,602	813	512	363	276	220	182	154	133
	7,296	2,114	1,067	671	474	359	286	236	199	172
0.04	5,505	1,564	777	482	337	254	201	165	139	119
	6,935	1,959	969	600	419	314	248	203	170	146
	9,230	2,593	1,277	788	548	410	323	264	221	189
0.05	6,616	1,838	898	549	380	283	222	181	151	129
	8,347	2,308	1,123	686	473	351	275	223	186	159
	11,123	3,061	1,482	902	620	460	360	291	242	206
0.06	7,703	2,107	1,016	615	422	312	243	197	163	139
	9,726	2,650	1,272	769	526	388	301	243	202	171
	12,973	3,518	1,684	1,014	691	508	395	318	263	223
0.07	8,765	2,369	1,131	680	463	340	263	212	175	148
	11,076	2,983	1,419	850	577	423	327	263	217	183
	14,780	3,965	1,880	1,123	760	555	429	343	283	239
0.08	9,803	2,627	1,244	743	502	367	282	227	187	158
	12,393	3,308	1,562	930	627	457	352	282	232	195
	16,546	4,401	2,072	1,229	827	602	463	369	303	255
0.09	10,816	2,877	1,354	804	541	393	302	241	198	167
	13,679	3,626	1,702	1,007	676	491	377	300	246	207
	18,270	4,827	2,259	1,333	893	647	495	393	322	270
0.10	11,804	3,121	1,461	863	578	419	320	255	209	175
	14,933	3,936	1,838	1,083	724	523	401	318	260	218
	19,952	5,242	2,441	1,434	957	690	527	417	341	285

The one-sided estimates use the *Z* statistic.

7.2. Extra info – sample size matters!

Table 7.5: Example of table when thinking about the type of analysis you are going to do

Predictor	Dichotomous	Continuous
Dichotomous	Chi-square family	t-test family
Continuous	t-test family	Correlation

In addition to the check-list in section 7.1.4 you might need to perform other calculations in order to determine the sample size

Calculate the standardized effect size (sEs): defined as the effect size (E) divided by the standard deviation (S) of the outcome variable

$$sEs = E/S$$

Consider the study

An investigator is interested in studying the efficacy of two artificial tears: tA and tB, for treating dry eye.

The investigator prepares a randomized control trial to assess the effect of these two tears, tA and tB, on BUT after 1 week of treatment

A previous study has reported that BUT for people with treated dry eye to be 10seconds, standard deviation 5seconds.

You would like to be able to detect a difference of 20% or more between the mean BUT between the 2 treatment groups. How many patients are required in each group (A and B) at alfa(2-sided)=0.05 and power = 0.80.

a) State H0 and H1
b) Determine effect size (E)
c) Determine sEs
d) Determine sample size using G-power or Table 7.3

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UNIT 8 Study protocol development

Aula 08
14 Dez 2015

Mestrado em Optometria Avançada
António Filipe Macedo

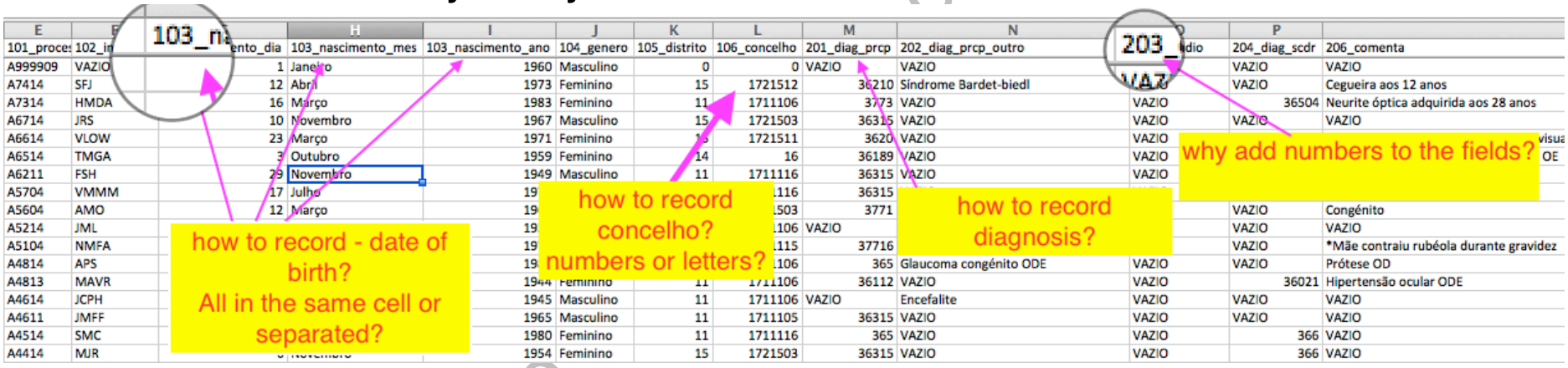
8.1. Addressing ethical issues

Principle of respect for persons
Principle of beneficence
Principle of justice

Further information – see blackboard – UNIT 8-extra

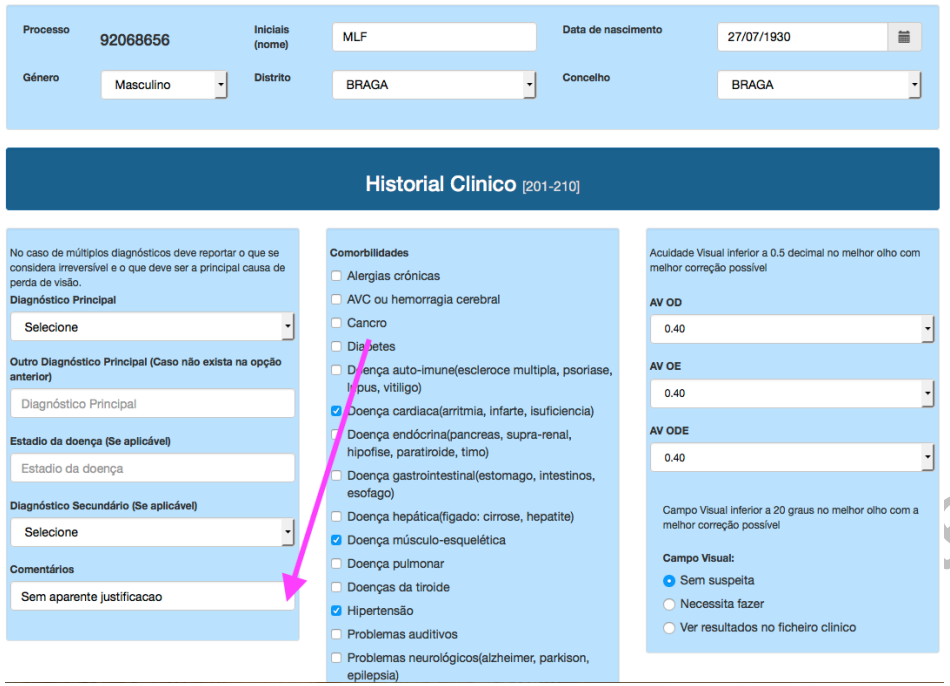
8.2. Planning measurements

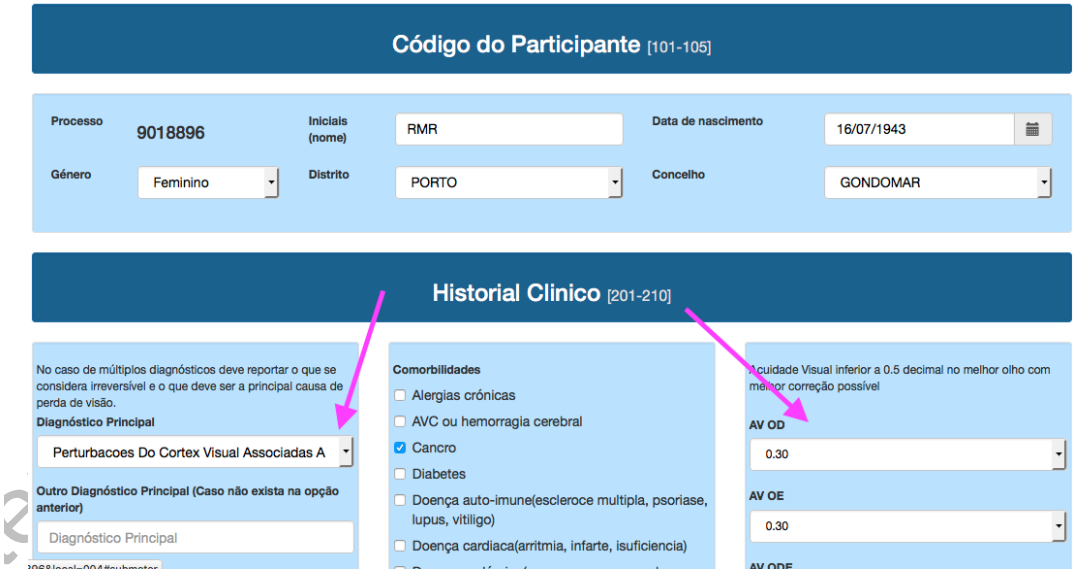
- Collect pilot data
- Organize data
- Perform an actually analysis



101_proces	102_in	103_nascimento_dia	103_nascimento_mes	103_nascimento_ano	104_genero	105_distrito	106_concelho	201_diag_prcp	202_diag_prcp_outro	203_	204_diag_scdr	206_comenta
A999909	VAZIO	1	Janeiro	1960	Masculino	0	0	VAZIO	VAZIO		VAZIO	VAZIO
A7414	SFJ	12	Abril	1973	Feminino	15	1721512	36210	Síndrome Bardet-biedl		VAZIO	Cegueira aos 12 anos
A7314	HMDA	16	Março	1983	Feminino	11	1711106	3773	VAZIO	VAZIO	36504	Neurite óptica adquirida aos 28 anos
A6714	JRS	10	Novembro	1967	Masculino	15	1721503	36315	VAZIO	VAZIO	VAZIO	VAZIO
A6614	VLOW	23	Março	1971	Feminino	15	1721511	3620	VAZIO	VAZIO		
A6514	TMGA	3	Outubro	1959	Feminino	14	16	36189	VAZIO	VAZIO		OE
A6211	FSH	29	Novembro	1949	Masculino	11	1711116	36315	VAZIO	VAZIO		
A5704	VMMM	17	Julho	19			116	36315				
A5604	AMO	12	Março	19			503	3771			VAZIO	Congénito
A5214	JML			19			106	VAZIO			VAZIO	VAZIO
A5104	NMFA			19			115	37716			VAZIO	*Mãe contraiu rubéola durante gravidez
A4814	APS			19			106	365	Glaucoma congénito ODE	VAZIO	VAZIO	Prótese OD
A4813	MAVR			1944	Feminino	11	1711106	36112	VAZIO	VAZIO	36021	Hipertensão ocular ODE
A4614	JCPH			1945	Masculino	11	1711106	VAZIO	Encefalite	VAZIO	VAZIO	VAZIO
A4611	JMFF			1965	Masculino	11	1711105	36315	VAZIO	VAZIO	VAZIO	VAZIO
A4514	SMC			1980	Feminino	11	1711116	365	VAZIO	VAZIO	366	VAZIO
A4414	MJR			1954	Feminino	15	1721503	36315	VAZIO	VAZIO	366	VAZIO

UNIT 8 Study protocol development

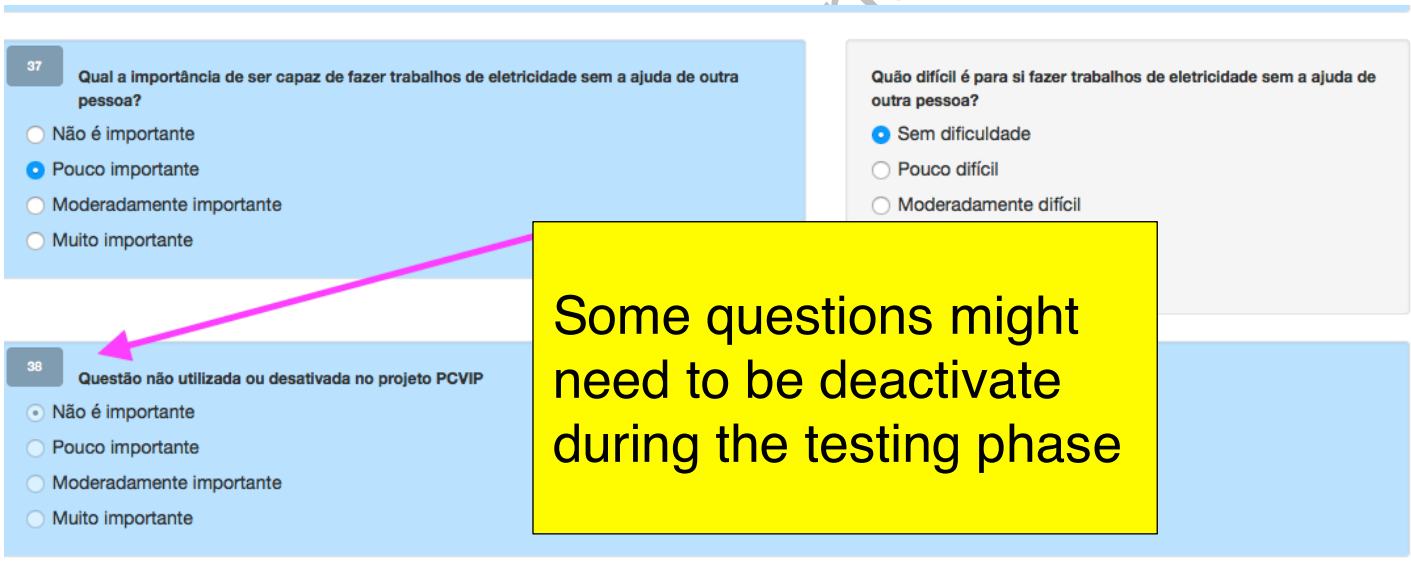




Sometimes basic information is not available and is frustrating to try to figure out the missing bits. Left form – main diagnosis is missing, that is a problem! Right form – all the vital information is there including acuity for both eyes!

8.3. Pre-testing

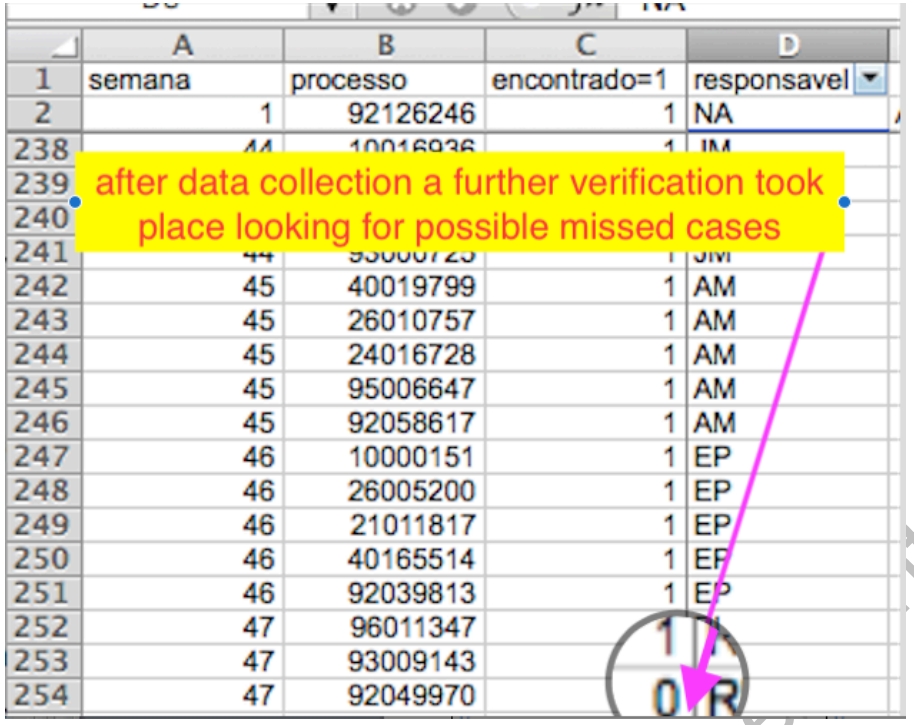
- Small pilot studies with questionnaires looking for potential problems
- Small studies to ensure that the information you want collect is really available
- Ensure the information stored (if you need to use it) is of good quality



8.4. Quality control

QC in Clinical procedures

Steps that proceed the study
• Develop a manual of operations • Operational definitions or recruitment and measurement procedures • Standardized instruments and forms • Approach to data managing and analysing the data • Quality control systems • Systems for blinding subjects and investigators • Train the research team • Certify the research team



	A	B	C	D
1	semana	processo	encontrado=1	responsavel
2	1	92126246	1	NA
238	44	10016936	1	JM
239				
240				
241	44	95000725	1	JM
242	45	40019799	1	AM
243	45	26010757	1	AM
244	45	24016728	1	AM
245	45	95006647	1	AM
246	45	92058617	1	AM
247	46	10000151	1	EP
248	46	26005200	1	EP
249	46	21011817	1	EP
250	46	40165514	1	EP
251	46	92039813	1	EP
252	47	96011347	1	
253	47	93009143		
254	47	92049970	0	R

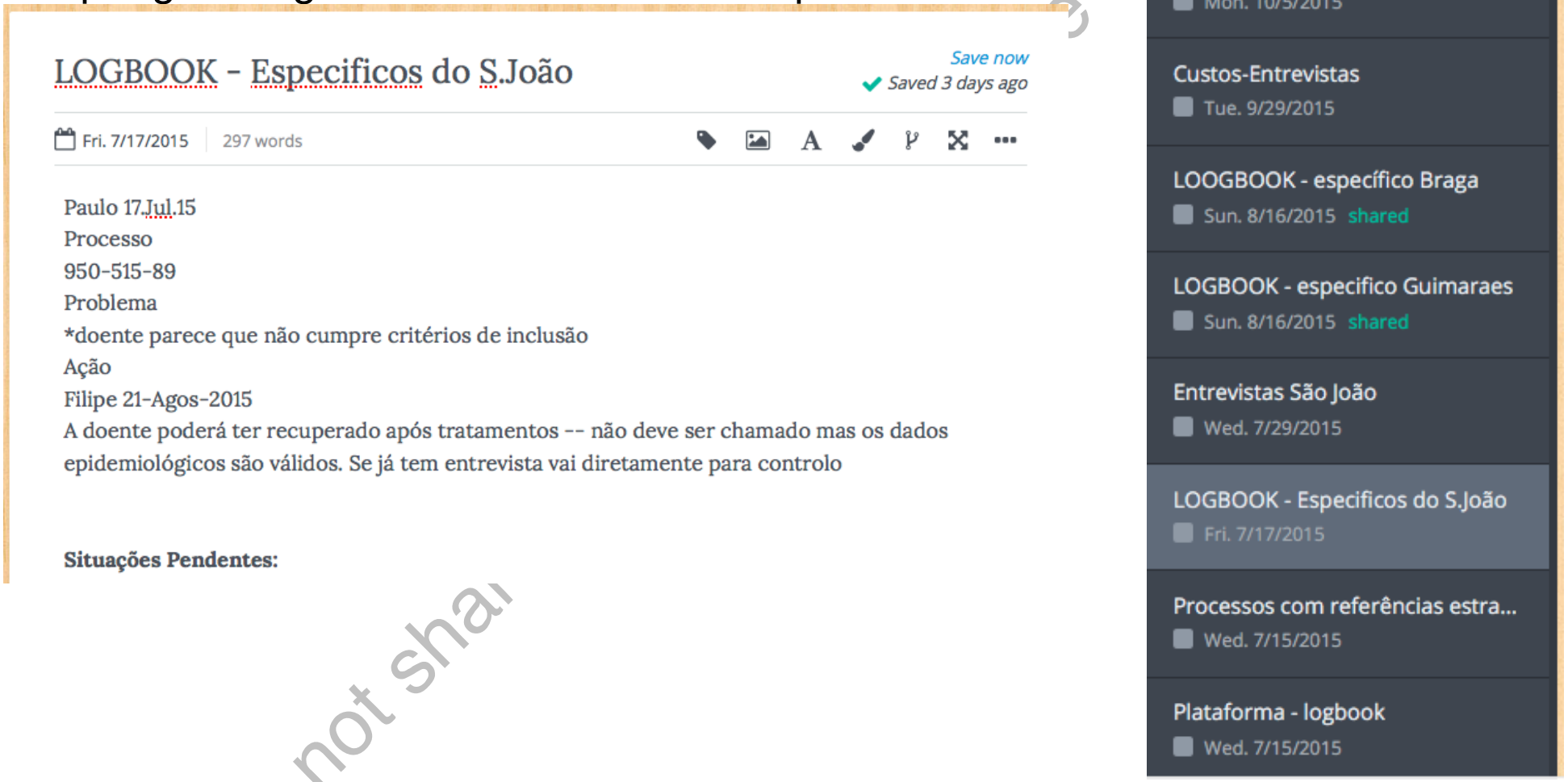
QC in Clinical procedures

Steps during the study

- Provide steady and caring leadership
- Hols regular staff meetings
- Recertify the research team
- Periodically review performance
- Periodically compare measurements across technicians

When working in a (big) team

Keep a good logbook- in our case we keep it online



LOGBOOK - Especificos do S.João

Save now
Saved 3 days ago

Fri. 7/17/2015 | 297 words

Paulo 17.Jul.15
Processo
950-515-89
Problema
*doente parece que não cumpre critérios de inclusão
Ação
Filipe 21-Agos-2015
A doente poderá ter recuperado após tratamentos -- não deve ser chamado mas os dados epidemiológicos são válidos. Se já tem entrevista vai diretamente para controlo

Situações Pendentes:

icd9 codes Diabetic Retinopathy
Mon. 10/5/2015

icd9 codes age related macular ...
Mon. 10/5/2015

Custos-Entrevistas
Tue. 9/29/2015

LOOGBOOK - específico Braga
Sun. 8/16/2015 shared

LOGBOOK - especifico Guimaraes
Sun. 8/16/2015 shared

Entrevistas São João
Wed. 7/29/2015

LOGBOOK - Especificos do S.João
Fri. 7/17/2015

Processos com referências estra...
Wed. 7/15/2015

Plataforma - logbook
Wed. 7/15/2015

Técnica de Investigação em Optometria e Ciências da Visão

UNIT 9 Data management

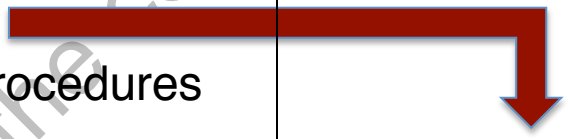
Aula 9
14 Dezembro 2015

Mestrado em Optometria Avançada
António Filipe Macedo

9.1. Defining variables

Steps in data management

- Define each variable
- Set up the study database and data dictionary
- Test data management procedures before the study begins
- Enter the data: identify and correct errors
- Document changes in the original data



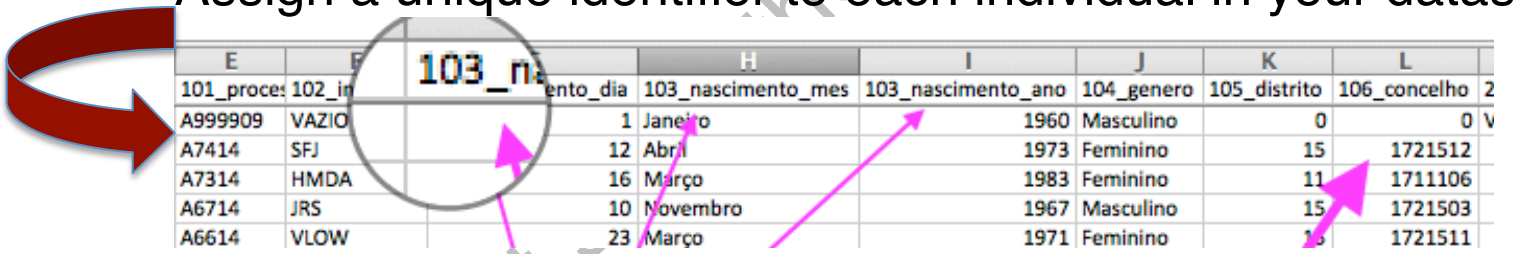
B	C
headings	**meaning**
exclu	exclude after your analysis
inc_val	included VALID after your analysis
inc_inval	included INVALID after your analysis
amp_l	amplitude of ALL included LEFT
amp_r	amplitude of ALL included RIGHT
pv_val_l	peak velocity VALID trial LEFT
pv_val_r	peak velocity VALID trial RIGHT
pv_inv_l	peak velocity (IN)VALID trial LEFT
pv_inv_r	peak velocity (IN)VALID trial RIGHT
total_anali	trials accepted for YOUR personal inspection
not_anali	trials rejected without YOUR personal inspection
lat_inv	latency INVALID and correct
lat_val	latency VALID and correct
first_in_trial	if the trial included was the FIRST detected = 1, else = 2. This is expected to allow recalculation of latency

Example of a data "dictionary"
you need to record the meaning of your columns to yourself in the future and for others if that is the case

- Back up the dataset regularly
- Create a dataset for analysis
- Achieve and store the original data, the final database, and the study analysis

9.2. Creating the study database

- Assign a unique identifier to each individual in your dataset



E	F	G	H	I	J	K	L	
101_proces	102_in	103_n	ento_dia	103_nascimento_mes	103_nascimento_ano	104_genero	105_distrito	106_concelho	2
A999909	VAZIO		1	Janeiro	1960	Masculino	0	0	V
A7414	SFJ		12	Abril	1973	Feminino	15	1721512	
A7314	HMDA		16	Março	1983	Feminino	11	1711106	
A6714	JRS		10	Novembro	1967	Masculino	15	1721503	
A6614	VLOW		23	Março	1971	Feminino	15	1721511	

- Include all information about an individual in one row of your database, rather than having the same person appear in multiple places
- Limit responses so that incorrect information cannot be entered (such as not allowing numbers that fall outside of your response choices)
- Code text responses into numerical form so that they are easier to analyze (e.g., 1=yes, 2 =no).
- Enter data in a consistent format, such as always using a “1” to reflect female gender, rather than using various labels (e.g., “F,” “female,” “girl,” etc.).

9.3. Thinking about your data analysis

The best time to start thinking about your analysis plan is when you are first identifying your key evaluation questions and determining how you will collect the needed information

It's important to match the analysis strategy to the type of information that you have and the kinds of evaluation questions that you are trying to answer

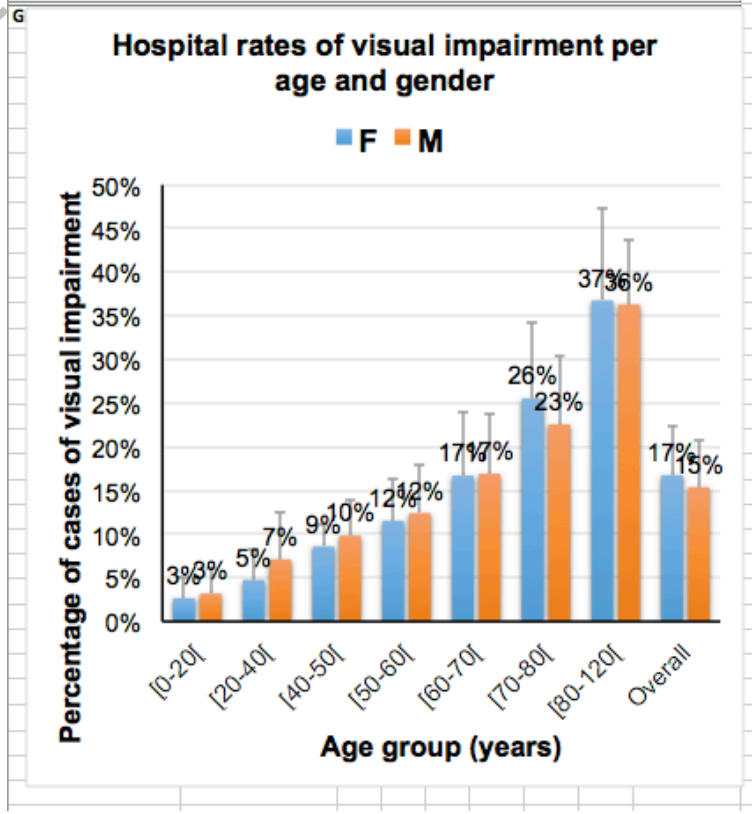
9.3.1. Analyzing quantitative data

While statistical analysis of quantitative information can be quite complex, some relatively simple techniques can provide useful information. Descriptive analysis is used to reduce your raw data down to an understandable level.

Common methods include:

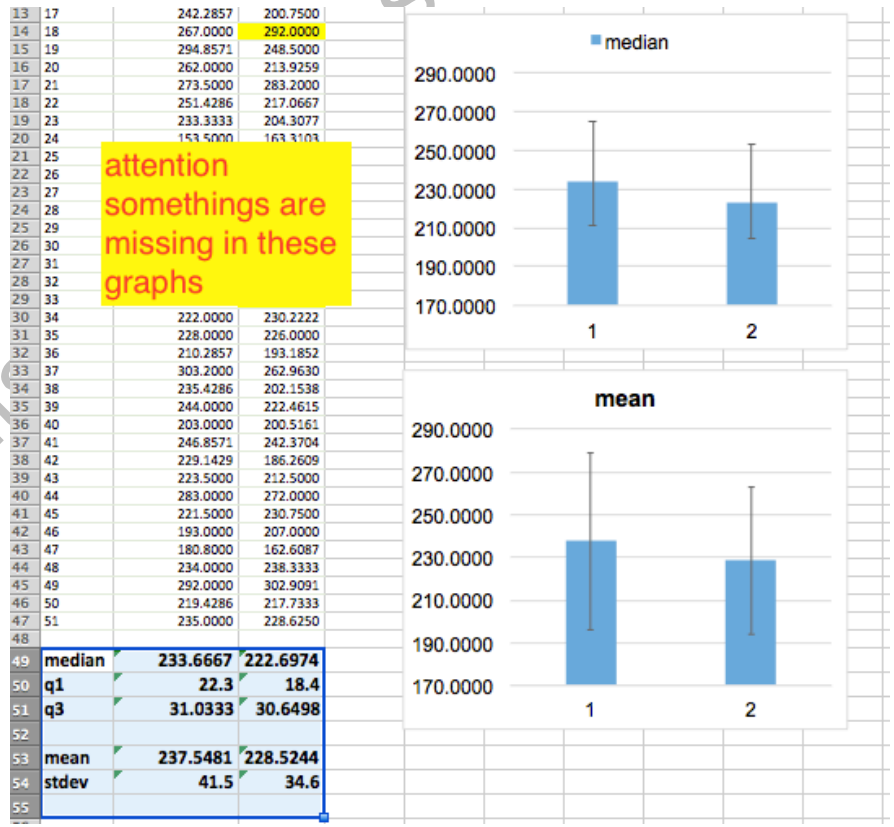
- Frequency distributions – tables or charts that show how many of your participants fall into various categories.

Count of age_group	Column Labels							
Row Labels	1	2	3	4	5	6	7	Grand Total
1	13	7	41	106	191	296	203	857
F	6	3	23	58	104	187	116	497
M	7	4	18	48	87	109	87	360
2	55	104	116	228	430	693	791	2417
F	26	50	66	124	217	415	492	1390
M	29	54	50	104	213	278	299	1027
3		9	17	21	50	134	166	397
F		2	11	12	24	85	111	245
M		7	6	9	26	49	55	152
4	162	162	157	372	761	1002	1077	3693
F	72	73	77	201	409	589	703	2124
M	90	89	80	171	352	413	374	1569



Central tendency – the number that best represents the "typical score," such as the mode (number or category that appears most frequently), median (number in the exact middle of the data set), and mean (arithmetic average of your numbers).

Variability – amount of variation or disagreement in your results, including the range (difference between the highest and lowest scores) and the standard deviation (a more complicated calculation based on a comparison of each score to the average).



13	17	242.2857	200.7500
14	18	267.0000	292.0000
15	19	294.8571	248.5000
16	20	262.0000	213.9259
17	21	273.5000	283.2000
18	22	251.4286	217.0667
19	23	233.3333	204.3077
20	24	153.5000	163.3103
21	25		
22	26		
23	27		
24	28		
25	29		
26	30		
27	31		
28	32		
29	33		
30	34	222.0000	230.2222
31	35	228.0000	226.0000
32	36	210.2857	193.1852
33	37	303.2000	262.9630
34	38	235.4286	202.1538
35	39	244.0000	222.4615
36	40	203.0000	200.5161
37	41	246.8571	242.3704
38	42	229.1429	186.2609
39	43	223.5000	212.5000
40	44	283.0000	272.0000
41	45	221.5000	230.7500
42	46	193.0000	207.0000
43	47	180.8000	162.6087
44	48	234.0000	238.3333
45	49	292.0000	302.9091
46	50	219.4286	217.7333
47	51	235.0000	228.6250
48			
49	median	233.6667	222.6974
50	q1	22.3	18.4
51	q3	31.0333	30.6498
52			
53	mean	237.5481	228.5244
54	stdev	41.5	34.6
55			

Inferential analysis is used to help you draw conclusions about your results

The goal is to determine whether results are meaningful.

For example:

- Did participants change in important ways over time?
- Were participants different from people who did not receive treatment?

The meaningfulness of findings is typically described in terms of “significance.” There are two common forms of significance.

Using probability theory, **statistical significance** indicates whether a result is stronger than what would have occurred due to random error. To be considered significant, there must be high probability that the results were not due to chance. When this occurs, we can infer that a relationship between two variables is strong and reliable. Several factors influence the likelihood of significance, including the strength of the relationship, the amount of variability in the data, and the number of people in the sample.

9.3.2. Quantitative data: further advice!

Statistical significance can be difficult to obtain, especially when data are available for a small number of people. As a result, some evaluations focus instead on **clinical significance**. Clinical significance compares results to a pre-established standard that has been determined to be meaningful (such as, average functioning of a non-problematic peer group, cultural norms, or goals set by staff or participants). Clinical significance is sometimes seen as having more practical value, but only when there is a clear and rationale for establishing the underlying standards.

Many statistical tests can be used to explore the relationships found in your data. Common statistical tests include chi-squares, correlations, t-tests, and analyses of variance. If these statistics are not familiar to you, seek consultation to ensure that you select the right type of analysis for your data and interpret the findings appropriately.

9.3.3. Analyzing qualitative data

On its own, or in combination with quantitative information, qualitative data can provide rich information about your study. The first step in analyzing qualitative information is to reduce or simplify it.

You must make important choices about which information should be emphasized, minimized, or even left out of the analysis. It is important to remain focused on the questions that you are trying to answer and the relevance of the information to these questions.

9.4. Interpreting your results and drawing conclusions

While analysis can help you identify key findings, you still need to interpret the results

Drawing conclusions involves stepping back to consider what the results mean and to assess their implications.

Consider the following types of questions:

- What patterns and themes emerged?
- Are there any deviations from these patterns? If yes, are there factors that might explain these deviations?
- Do the results make sense?
- Are there findings that are surprising? If so, how do you explain these results?
- Are the results significant from a clinical or statistical standpoint? Are they meaningful in a practical way?
- Do any interesting stories emerge from the responses?

Consider practical value, not just statistical significance

- Do not be discouraged if you do not obtain statistically significant results
- You may have chosen an outcome measure that was too ambitious
- In interpreting your results, consider alternate explanations (It is also important to consider the practical significance of the findings)
- Watch for, and resolve, inconsistencies (in some cases, you may obtain contradictory information)

Review and correct data before beginning your analysis

- Leave enough time for analysis
- Identify the appropriate statistics for each key question
- Do not use the word “significant” to describe your findings unless it has been tested and found to be true either statistically or clinically
- Keep the analysis simple

Técnica de Investigação em Optometria e Ciências da Visão

UNIT 10 Areas of study in Optometry and Vision Science

Ao longo do semestre

Mestrado em Optometria Avançada
António Filipe Macedo

10.1. Visual psychophysics (SN)

10.2. Ophthalmic instrumentation (SF)

10.3. Cataracts and refractive surgery (JMM)

10.4. Ocular surface (MML)

10.5. Low vision (AFM)

10.6. Colour Vision (JL)

10.7. Emetropization (JJ)

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UNIT 11 Reporting results and conclusions

Aula 9
14 Dezembro 2015

Mestrado em Optometria Avançada
António Filipe Macedo

11.1. Writing up your thesis

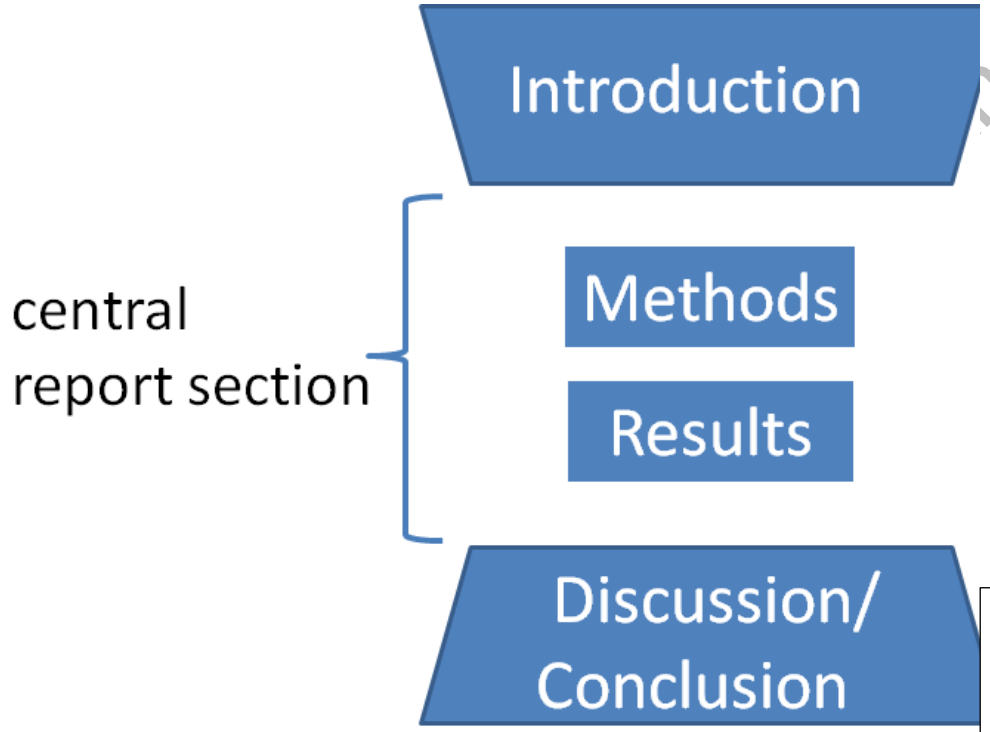


Figure 11.1: https://en.wikipedia.org/wiki/IMRAD

Most of these tips were taken form the Birkbeck website http://www.bbk.ac.uk/mybirkbeck/services/facilities/support

11.1.1. General information

- At the end of the whole work there should be a full bibliography or reference list
- Any appendices should come after the full bibliography/references
- The longest chapters will be the Literature review and Methodology
- The Introduction and Conclusion chapters will be short
- Some students find that they need to include additional chapters
- You may also be asked to include an Abstract
- You will probably want to acknowledge those who helped you or participated in your research
- And do not forget to address ethical issues

11.1.2. Chapter - Introduction (please check with your supervisor if you need this chapter)

Make sure that the readers of your work will be able to find the answers to these questions in Introduction (Chapter 1):

1 What was the purpose of the research? [this information can be put in a separated chapter]
2 **How was the topic chosen?**
3 What were the main aims and objectives of the research? [this information can be put in a separated chapter]
4 What is the scope of the research project? (If your dissertation/project is focused on one particular group, industry or technology you might include introductory remarks here.)
5 What were the limitations of the work? [this information can be put in a separated chapter]

Chapter 1 (cont.)

- How is the text arranged in the dissertation/project?
- Is there anything particular to note that will make it easier for the person reading your dissertation/project to follow the work (e.g. about the format of referencing, layout of charts/tables)?

11.1.3. Chapter - Literature review

- Provide an introductory paragraph which explains what is discussed in the chapter and why it is necessary to include this as part of the dissertation/project
- Demonstrate that you conducted a *thorough* literature search and have read *widely*
- Demonstrate that you have read *up to date* material
- Summarise what you have read *thematically* (and not author by author)
- Highlight *trends* in the discussion of your topic; for example over time, by geography, by sector
- Comment on the *value* of what you have read (without discussing the actual topic)
- Organise your findings from the literature review to fit in with the *main themes* of your research project
- Identify *gaps* or *anomalies* in the literature
- Demonstrate that you *assimilated and understood* what you have read and what you have written

11.1.4. Chapter - Hypothesis and aims of the thesis

Already discussed

11.1.5. Chapter - Methodology or Methods

- The Methodology chapter is used to justify the choice of methods employed during the research project
- You need to demonstrate that you understand that there are various options for conducting research
- For this reason you will need to refer back to the notes you took in any research methods classes that you have attended, as well as textbooks and/or articles on research methods
- Although much of the methodology chapter focuses on data collection, it is also worth acknowledging (not always) the techniques used for the other activities related to the research project: literature searching, sampling or case study selection, data analysis

11.1.6. Chapter - Results

Provide an introductory paragraph, which explains what is discussed in the chapter

Results tips[1]

Remember that "a figure is worth a thousand words". Hence, illustrations, including figures and tables, are the most efficient way to present your results. Your data are the driving force of the paper or thesis, so your illustrations are critical!

How do you decide between presenting your data as tables or figures?

Generally, tables give the actual experimental results, while figures are often used for comparisons of experimental results with those of previous works, or with calculated/theoretical values (Figure 11.2 – right hand side)

Whatever your choice is, no illustrations should duplicate the information described elsewhere in the manuscript or thesis

Should you use a table or chart?

	ECOLOGICAL GROUP				
Station	I	II	III	IV	V
75U	91.3	5.3	3.2	0.2	0.0
75R	89.8	6.1	3.6	0.5	0.0
200R	69.3	14.2	8.6	6.8	1.1
500R	63.0	29.5	3.4	4.2	0.0
1000R	86.7	8.5	4.5	0.2	0.0

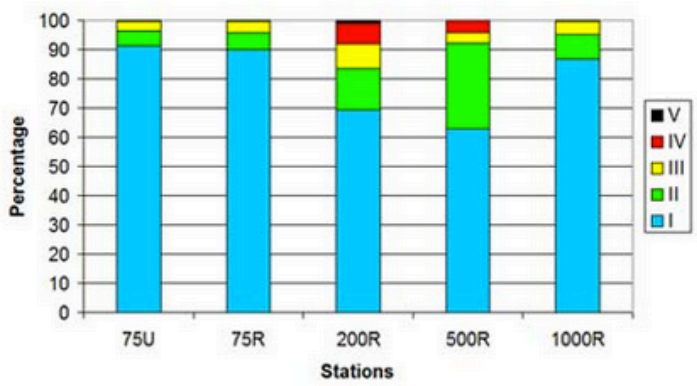


Figure 1. An example of the same data presented as table or as figure. Depending in your objectives, you can show your data either as table (if you wish to stress numbers) or as figure (if you wish to compare gradients). Note: Never include vertical lines in a table.

[1] https://www.elsevier.com/connect/11-steps-to-structuring-a-science-paper-editors-will-take-seriously#step4

Figure 11.2

Figures must be self-explanatory

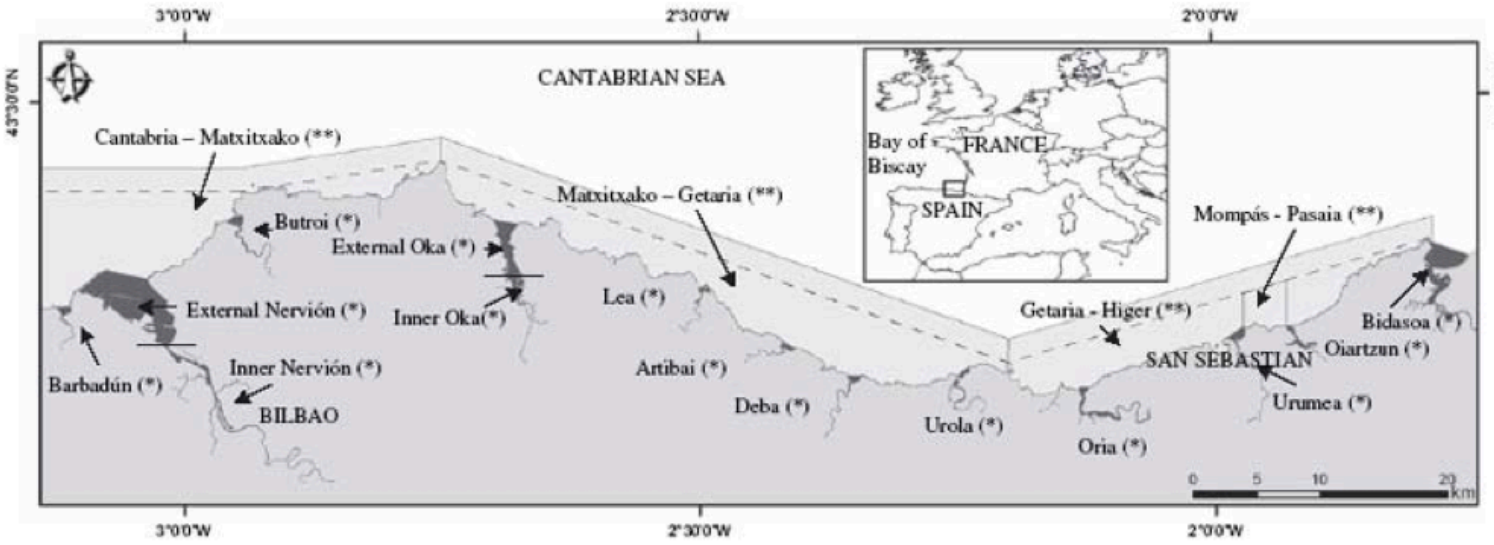


Fig. 1. Location of each of estuarine (*, black colour) and coastal (**, grey colour) water bodies, within the Basque Country. Note: dotted line shows the Basque coastal baseline. Inner and external parts of the Nervión and Oka estuaries are separated by a straight line.

Figure 2. In a figure or table, all the information must be there to understand the contents, including the spelling out of each abbreviation, the locations mentioned in the text and coordinates.

Figure 11.3

Another important factor: figure and table legends must be self-explanatory (Figure 11.3 above)

When presenting your tables and figures, appearances count!

To this end:

- Avoid crowded plots (Figure 11.4: Example of a crowded), using only three or four data sets per figure; use well-selected scales
- Think about appropriate axis label size
- Include clear symbols and data sets that are easy to distinguish.
- Never include long boring tables - You can include them as supplementary material or appendix

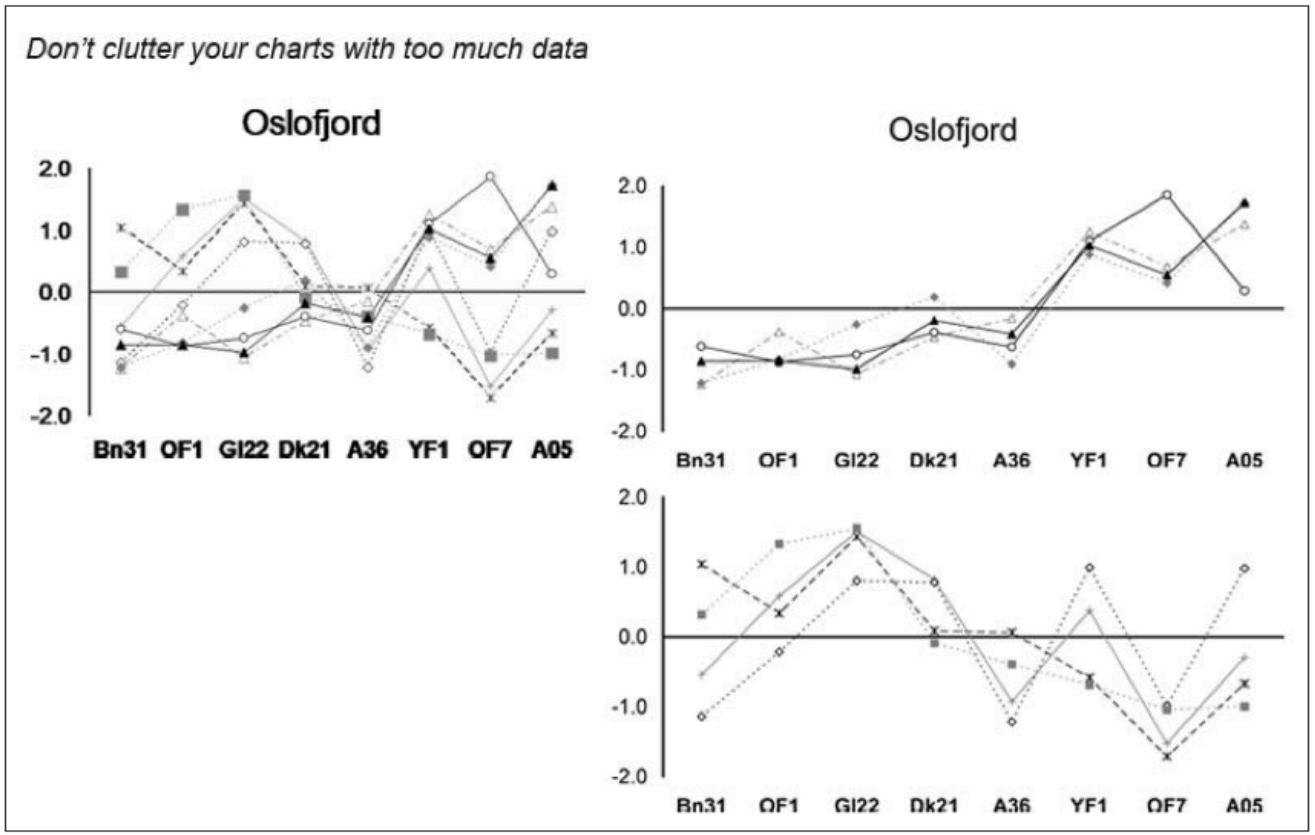


Figure 3. This is an example of how to best present your data. In the first figure (left), data are crowded with too many plots. In the second figure (right), data are separated into two datasets, and plots show gradients, which can be useful for discussion.

Figure 11.4: Example of a crowded plot

Sometimes, fonts are too small

Figures are not eye charts — make them large enough to read

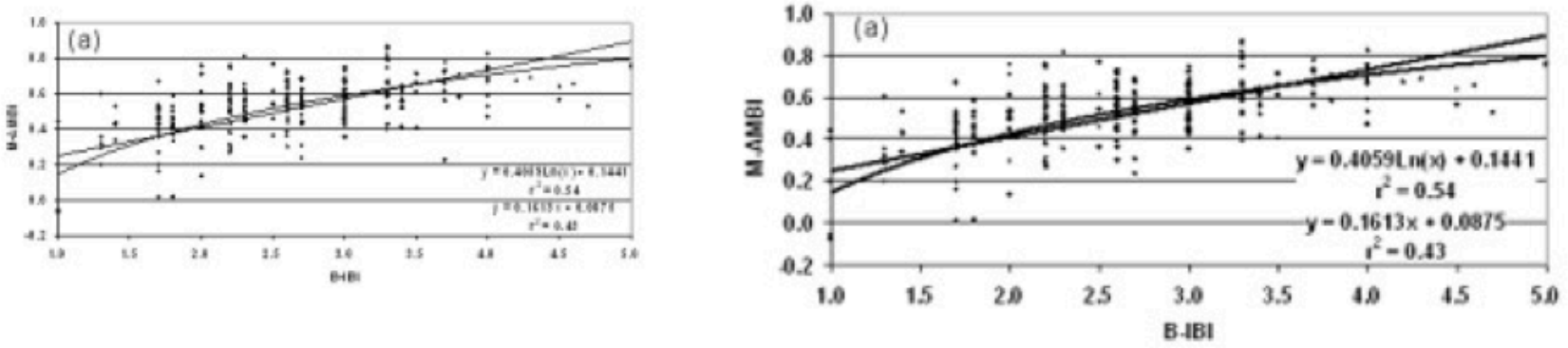


Figure 6. Example of the small fonts used when preparing a draft. The first figure shows charts where the numbers are illegible, compared to the second figure, where they are large enough to read.

You must pay attention to the use of decimals

Form should follow function

Depth	Gravel	Sand	Mud
5 m	3,42%	81.41%	15,17%
50 m	2,5%	58.42%	39.08%
100 m	0,0%	32.5%	67.5%

Water depth (m)	Gravel (%)	Sand (%)	Mud (%)
5	3.4	81.4	15.2
50	2.5	58.4	39.1
100	0.0	32.5	67.5

Figure 7. Inadequate use of lines, number of decimals, decimal separators (use always dots, not commas) and position of units (above) and its adequate use (below) for a more clear table.

11.1.7. Chapter - Discussion

Discuss your results with reference to the findings of the literature review. This will necessitate a degree of repetition, which can be minimised by good cross-referencing. The reader expects you to match your own results against what was established in the literature review. From this you should make comments and draw conclusions.

Write thematically

In the majority of cases this means following a structure determined by the arrangement of themes in the literature review and the basic questions given in hypothesis chapter

Here you must respond to what the results mean. Probably it is the easiest section to write, but the hardest section to get right. This is because it is the most important section of your article or thesis. Here you get the chance to sell your data. Take into account that a huge numbers of manuscripts or thesis are rejected (poorly evaluated) because the Discussion is weak.

You need to make the Discussion corresponding to the Results, but do not reiterate the results. Here you need to compare the published results by your colleagues with yours (using some of the references included in the Introduction). Never ignore work in disagreement with yours, in turn, you must confront it and convince the reader that you are correct or better.

Take into account the following tips:

1. Avoid statements that go beyond what the results can support

2. Avoid unspecific expressions such as "higher temperature", "at a lower rate", "highly significant". Quantitative descriptions are always preferred (35ºC, 0.5%, p<0.001, respectively).

3. Avoid sudden introduction of new terms or ideas; you must present everything in the introduction, to be confronted with your results here.

4. Speculations on possible interpretations are allowed, but these should be rooted in fact, rather than imagination. To achieve good interpretations think about:

- How do these results relate to the original question or objectives outlined in previous sections or chapters?
- Do the data support your hypothesis?
- Are your results consistent with what other investigators have reported?
- Discuss weaknesses and discrepancies. If your results were unexpected, try to explain why
- Is there another way to interpret your results?
- What further research would be necessary to answer the questions raised by your results?
- Explain what is new without exaggerating

5. Revision of Results and Discussion is not just paper work. You may do further experiments, derivations, or simulations. Sometimes you cannot clarify your idea in words because some critical items have not been studied substantially.

11.1.8. Writing tips for discussion (paraphrase and summary)[2]

Paraphrasing

Paraphrasing refers to rewriting a given sentence using your own words. When we need to use a sentence in our writing that someone else wrote, we paraphrase it. That is, we use the same idea(s) in that sentence and write it differently. In addition to using different words, we use different grammar. The main purpose of paraphrasing has to do with being able to use someone else's ideas while we write our own texts. Of course, it is required that any writer acknowledges the original source using the proper citation format.

Further information
https://owl.english.purdue.edu/exercises/32/41/77/
https://owl.english.purdue.edu/exercises/32/41/

[2] This is also important for the introduction and review of the literature section

Example

Original sentence:

PayLess is closed because of the bad weather conditions.

Inappropriate paraphrase:

PayLess is closed because of the bad weather.

This paraphrase has too many words, such as “PayLess is closed because of” are repeated. It is important to use different words and grammatical structure, while keeping the same meaning of the original sentence.

Appropriate paraphrase:

Since the weather is terrible, the grocery store is not open

In addition to using different words, the grammatical structure of the sentence was changed by starting with the second part (dependent clause) of the original sentence.

Summarizing

A summary should be a short version of a longer original source. Its main goal is to present a large amount of information in a short and concise text that includes only the most important ideas of the original text

Example

Original sentence:

"*The movement toward education by computer is developing fast. Massive Open Online Courses, called MOOCs, are changing how people learn in many places. For years, people could receive study materials from colleges or universities and take part in online classes. But such classes were not designed for many thousands of students at one time, as MOOCs are*."

(MOOCS Are Moving Forward , Voice of America, learningenglish.voanews.com)

Inappropriate summary:

Voice of America website:

"*Computer education is growing fast. MOOCs are influencing how we study. People received materials from universities for a long time to be able to take classes online. MOOCs are the only ones thousands can take at a time*."

The inappropriate summary is almost as long as the original text, which is a characteristic of a paraphrase. A summary needs to be concise.

Appropriate summary:

According to a Voice of America article, a fast-growing MOOCs movement allows thousands to take online classes at once, changing how we learn.

The appropriate summary keeps the original main idea and it is much shorter than the original text.

Paraphrasing

Source Material

Some argue that the approximately 11 million undocumented immigrants in the United States ought to receive a path to US citizenship, while others claim that these immigrants need to be deported back to their home countries.

Inappropriate paraphrase

Some say that the 11 million undocumented immigrants in the United States ought to receive a way for citizenship, while other people say that the immigrants should go back to their countries.

The inappropriate paraphrase is too close to the original sentence. Several words are the same and the complex structure of the sentence is the same. Deleting some words from the original sentence is not enough to write an appropriate paraphrase.

Appropriate paraphrase

Although some individuals maintain that undocumented immigrants should go back to their countries, others defend these immigrants' right for a path to citizenship.

The appropriate paraphrase uses a different structure for the sentence, and most words are different from the original.

11.1.9. Chapter - Conclusion

This should be a conclusion to the whole project (and not just the research findings). Check that your work answers the following questions:

- Did the research project meet its aims (check back to introduction for stated aims)?
- What are the main findings of the research?
- Are there any recommendations?
- Do you have any conclusions on the research process itself?
- Where should further research be focused?

11.1.10. Bibliography/References

Your bibliography or reference list should be set out following a recognised standard such as “Harvard”, “APA” or “numerical footnoting”. If you have not yet learned how to use EndNote (or similar software), now is the time!

11.1.11. Appendices

Appendices generally follow after the bibliography, but again check with your supervisor. They should be used for genuine purposes; for example, to provide a copy of the research instrument. Appendices should not be used as a dumping ground for material that you have not managed to incorporate into the main text. You may also be required to adhere to a word count.

11.2. Writing to a journal

Information based on the course below
http://ocw.jhsph.edu/courses/QualitativeDataAnalysis/PDFs/Session9.pdf

Options for disseminating study results include

- Journals
- Books
- Newsletters
- Conference presentations
- Others

11.2.1. What is a Peer-Reviewed Journal?

A journal that publishes papers only after they have been reviewed by (typically) 3 experts in the field.

Reviews are either single or double blinded:

- Single blinded means the reviewer knows who wrote the paper but the author of the paper doesn't know who the reviewers are.
- Double blinded means neither the reviewers nor the authors know each other's identity.

Reviewers recommend if the paper should be published and whether revisions are necessary before publication (revisions are commonly required).

11.2.2. Example of Review Criteria

Social Science and Medicine

Referees are asked to evaluate a manuscript for:

- Originality and significance of contribution
- Interest to social scientists and/or practitioners
- International relevance
- Coverage of appropriate existing literature
- Adequacy of methodology, analysis and interpretation
- Clear, concise and jargon-free writing style
- Organisation

Things to think about when choosing a journal

- What audience will your paper appeal to?
- What journals publish papers on topics similar to yours?
- What journal will provide a good opportunity to disseminate your study results to a wide audience?
- Is the journal indexed so that people will find your paper easily?
- What is the journal's "impact" score?

Vision Research

An International Journal for Functional Aspects of Vision

Chairman and Editor in Chief: D.H. Foster

View full editorial board

Supports Open Access

ISSN: 0042-6989

Guide for Authors

Submit Your Paper

Track Your Paper

Order Journal

View Articles

Journal Metrics

1. *Vision Research* is a journal devoted to the functional aspects of **human, vertebrate and invertebrate vision** and publishes experimental and observational studies, reviews, and theoretical and computational analyses. *Vision Research* also publishes clinical studies relevant to normal visual function and basic research relevant to visual dysfunction or its clinical investigation. **Functional aspects of vision** is interpreted broadly, ranging from molecular and cellular function to perception and behavior. Detailed descriptions are encouraged but enough introductory background should be included for non-specialists. Theoretical and computational papers should give a sense of order to the facts or point to new verifiable observations. Papers dealing with questions in the history of vision science should stress the development of ideas in the field.

Guide for Authors

Submit Your Paper

Track Your Paper

Order Journal

View Articles

Journal Metrics

Source Normalized Impact per Paper (SNIP): **1.289**

SCImago Journal Rank (SJR): **1.246**

Impact Factor: **1.815**

5-Year Impact Factor: **2.472**

Optics in the Investigation of Vision and Visual Function

Call for Papers for Special Issue on Adaptive Optics in the Investigation of Vision and Visual Function

Adaptive Optics is having a growing impact as an enabling technology for studying vision and visual function. By allowing the precise control of light, adaptive optics can improve retinal imaging and overcome optical blurring in presentation of the visual stimulus. This level of control is being exploited in technologies ranging from microscopy and neurophysiology to psychophysics. This special issue brings together this

Frequently Asked Questions

- Can I submit a paper to more than one journal at a time?
- Can I publish something after presenting it at a conference?
- Can I present something at a conference that I've already published?
- How do I prepare my paper for submission?
- What happens after I submit my paper?
- What happens after my paper has been accepted for publication?
- What happens if my paper is rejected?

11.2.3. Getting it Done: Some General Tips

1. Read a lot of papers! Good writers are avid readers
2. Don't wait until you have all of your thoughts clearly formulated before you start to write. Thinking and writing happen together. Your thoughts will become more developed and more clearly articulated as you write and re-write
3. Make a 2 to 3 hour writing session a regular part of your schedule (daily or weekly). The most productive writers are those who tackle writing projects in frequent short sessions rather than infrequent long sessions

Getting it Done: Tips con't

4. Share your writing with others at regular intervals to get constructive criticism
5. Create a writing schedule with small, specific and measurable targets

Example of an overly general and non-specific target:
July 15—complete the introduction of my paper / thesis

Example of a specific target:
July 15—spend 3 hours searching the PubMed database and compiling a list of literature for review and possible inclusion in my introduction.

What characterizes successful writing?

- Good writing is clear and concise. Get to the point and avoid jargon. Limit the scope of your paper. Focus on a few key points and hammer them home
- Organize your thoughts down to the last detail and keep everything focused around the key points of your paper
- Your objective is to communicate to your reader (not to prove your expertise)
- Be honest

Objectives of the Introduction

1. Define the problem, why is it important?
2. Review what is currently known about the problem, include abundant references to problem, published literature.
3. Point out what information or knowledge is missing about the problem...where are the missing about the problem...where are the gaps?
4. Indicate how your data can fill the gaps and make us more informed about the problem

Define the Problem

"Although smoking prevalence in Australia has fallen substantially across the population in the past three decades, the rates for women have declined less than those for men (refs).... Moreover, the prevalence of smoking among teenage girls (aged 12 to 17) is no longer declining (refs)....These figures represent a significant cost to women's short- and longer term health"

(Lennon 2005)

What is already known?

"Cross-sectional and longitudinal studies have identified sociodemographic, environmental, behavioral, and personal factors associated with smoking (refs). Differences in correlates of smoking for young women from those for young men have also been found (refs). This is particularly the case for behavioral and personal factors such as stress (refs), self esteem and depression (refs), self-concept (refs), concerns about body weight or shape (refs), dieting behavior (refs), and social factors such as peer influence (refs)."

(Lennon 2005)

What information is missing?

"Given the possibility that young women might derive such perceived benefits from choosing to smoke, there is a need to understand more fully why young women begin to smoke and why they continue. Previous studies have focused primarily on the initiation of smoking among adolescents, typically school children under the age of 16. However, very little is known about young adults or the identities associated with the maintenance or cessation of smoking."

(Lennon 2005)

How can your data make us more informed?

"We used a social identity perspective to explore "We used a social identity perspective to explore personal and social factors that influence the personal and social factors that influence the likelihood of smoking among young women between the ages of 16 and 28 years."

11.2.4. Guidelines for Reviewing and Citing Literature

1. Don't cite a reference unless you've read it
2. If you quote a reference, quote precisely, word-for-word, as in the original
3. Use quotation marks
4. Record complete bibliographic information for each reference source
5. You may want to learn each reference source
6. You may want to learn how to use a software program such as EndNote to make this cataloguing process easier

Guidelines for Reviewing and Citing Literature (cont)

1. Focus on the literature that relates to your paper topic most closely, is most significant, and is up-to-date
2. Make sure you include “landmark” studies
3. Take notes on the sources you read, summarize them for yourself and note the key points. This will help you build arguments for your introduction and conclusion
4. Include literature that represents conflicting sides of a contentious issue in order to be fair

11.2.5. Writing the Methods Section

What are the basic components of most methods sections?

Description of sites
Sampling and recruitment
Data collection
Data processing
Data analysis approach
Statement about ethical review and informed consent

Statement about ethical review and informed consent

Ethical clearance

Often in the beginning or end of a methods section authors include a statement about the ethical clearance.

"The study protocol was approved by the institutional review boards at X and X."

Authors may also include a statement about informed consent

"Written informed consent was obtained from all study participants prior to data collection."

Should you include a table with demographic data on the sample?

It may make sense for qualitative datasets with relatively large sample sizes (i.e over 50, 100?) But for small datasets (under 30) may not make sense to use a table to describe the sample

What you may want to say about your sample, may not best be displayed in a tabular form. You may want to describe more than the socio-demographic profile.

11.3. Further writing advice

Most materials taken from this online course
https://lagunita.stanford.edu/courses/Medicine/HRP214/Winter2014/f7c5387515db4d3d89f14c3144ad76ad/

11.3.1. What makes a good writer?

- Inborn talent?
- Years of English and humanities classes?
- An artistic nature?
- The influence of alcohol and drugs?
- Divine inspiration?

What makes a good writer:

Having something to say

Logical thinking

A few simple, learnable rules of style (the tools you'll learn in this class)

Take-home message: Good writing can be learned!

In addition to taking this class, other things you can do to become a better writer:

- Read, pay attention, and imitate
- Write in a journal.Let go of “academic” writing habits (deprogramming step!)
- Talk about your research before trying to write about it
- Write to engage your readers—try not to bore them!
- Stop waiting for “inspiration” -- Accept that writing is hard for everyone
- Revise -- Nobody gets it perfect on the first try
- Learn how to cut ruthlessly -- Never become too attached to your words.
- Find a good editor!
- Take risks

11.3.2. Examples of what not to do

This was the first sentence of an article in the Journal of Clinical Oncology (Introduction section)[3]:

"Adoptive cell transfer (ACT) immunotherapy is based on the ex vivo selection of tumor-reactive lymphocytes, and their activation and numerical expression before reinfusion to the autologous tumor-bearing host."

Ask Yourself:
Is this sentence easy to understand?
Is this sentence enjoyable and interesting to read?

[3] https://lagunita.stanford.edu/courses/Medicine/HRP214/Winter2014/f7c5387515db4d3d89f14c3144ad76ad/

"These findings imply that the rates of ascorbate radical production and its recycling via dehydroascorbate reductatse to replenish the ascorbate pool are equivalent at the lower irradiance, but not equivalent at higher irradiance with the rate of ascorbate radical production exceeding its recycling back to ascorbate." (from Photochemistry and Photobiology...)

Ask Yourself:
Is this sentence readable?
Is it written to inform or to obscure?

11.3.3. Classic hallmark of "academic writing": spunky verbs become clunky nouns...

- "These findings imply that the rates of ascorbate radical **production** and its **recycling** via dehydroascorbate reductatse to replenish the ascorbate pool are equivalent at the lower irradiance, but not equivalent at higher irradiance with the rate of ascorbate radical **production** exceeding its **recycling** back to ascorbate."

After much **work** can be translated to...

- "These findings imply that, at low irradiation, ascorbate radicals are produced and recycled at the same rate, but at high irradiation, they are produced faster than they can be recycled back to ascorbate."

-Complex ideas don't require complex language

-Scientific writing should be easy and even enjoyable to read!

"My professor friend told me that in his academic world, 'publish or perish' is really true. He doesn't care if nobody reads it or understands it as long as it's published."

There's a hint of truth here, n'est-ce pas?

From: Anne Ku. "The joys and pains of writing and editing," *Le Bon Journal, 2003 http://www.bonjournal.com/volume2/issue1writing.pdf*

"The secret of good writing is to strip every sentence to its cleanest components. Every word that serves no function, every long word that could be a short word, every adverb that carries the same meaning that's already in the verb, every passive construction that leaves the reader unsure of who is doing what—these are the thousand and one adulterants that weaken the strength of a sentence. And they usually occur in proportion to the education and rank."

-- William Zinsser in On Writing Well, 1976

11.3.4. Principles of effective writing

- 1. Cut unnecessary words and phrases; learn to part with your words!
- 2. Use the active voice (subject + verb + object)
- 3. Write with verbs: use strong verbs, avoid turning verbs into nouns, and don't bury the main verb!

Version to avoid

"This paper provides lverb a review lverb convert to noun of the basic tenets of cancer biology study design, using as examples studies that illustrate the methodologic challenges or that demonstrate successful solutions to the difficulties inherent in biological research."

Better version

This paper reviews cancer biology study design, using examples that illustrate specific challenges and solutions.

Version to avoid

"As it is well known, increased athletic activity has been related to a profile of lower cardiovascular risk, lower blood pressure levels, and improved muscular and cardio-respiratory performance."

Better version

Increased athletic activity is associated with lower cardiovascular risk, lower blood pressure, and improved fitness.

Version with stronger level of evidence

Increased athletic activity lowers cardiovascular risk and blood pressure, and improves fitness.

Version to avoid

"The experimental demonstration is the first of its kind and is a proof of principle for the concept of laser driven particle acceleration in a structure loaded vacuum."

Better version

The experiment provides the first proof of principle of laser-driven particle acceleration in a structure-loaded vacuum.

11.3.4.1. Cut unnecessary words

Example:

"Brain injury incidence shows two peak periods in almost all reports: rates are the highest in young people and the elderly."

More punch

"Brain injury incidence peaks in the young and the elderly."

Be vigilant and ruthless

After investing much effort to put words on a page, we often find it hard to part with them. But fight their seductive pull...

Try the sentence without the extra words and see how it's better—conveys the same idea with more power

11.3.4.2. Common clutter

1. Dead weight words and phrases

- As it is well known
- As it has been shown
- It can be regarded that
- It should be emphasized that

"Some words and phrases are blobs." -- William Zinsser in On Writing Well, 1976

2. Empty words and phrases

- Basic tenets of
- Methodological
- Important

3. Long words or phrases that could be short

- muscular and cardiorespiratory performance

4. Unnecessary jargon and acronyms

- Muscular and cardiorespiratory performance
- Gliomagenesis
- miR

5. Repetitive words or phrases

- Studies/examples
- Illustrate/demonstrate
- Challenges/difficulties
- Successful solutions

6. Adverbs

- very, really, quite, basically, generally, etc.

11.3.4.3. Long words and phrases that could be short...

Wordy version	Crisp version
• A majority of	most
• A number of	many
• Are of the same opinion	agree
• Less frequently occurring	rare
• All three of the	the three
• Give rise to	cause
• Due to the fact that	because
• Have an effect on	affect

11.3.4.4. Long words or phrases that could be short...

× The expected prevalence of mental retardation, based on the assumption that intelligence is normally distributed, is about 2.5%.
✓ The expected prevalence of mental retardation, if intelligence is normally distributed, is 2.5%.

11.3.4.5. Repetitive words or clauses

× A robust cell-mediated immune response is necessary, and deficiency in this response predisposes an individual towards active TB
✓ Deficiency in T-cell-mediated immune response predisposes an individual to active TB.

11.3.4.6. Blaise Pascal on the elegance in brevity:

"I have only made this letter rather long because I have not had time to make it shorter."

("Je n'ai fait celle-ci plus longue que parce que je n'ai pas eu le loisir de la faire plus courte.") -- Lettres provinciales, 16, Dec.14,1656 (though reference also attributed to St. Augustine, and Cicero....)

11.3.4.7. A few other small tricks...

Eliminate negatives

She was not often right *replace with* She was usually wrong
She did not want to perform the experiment incorrectly *replace with* She wanted to perform the experiment correctly
They did not believe the drug was harmful replace *replace with* They believed the drug was safe.

Not honest -> dishonest
Not harmful -> safe
Not important -> unimportant
Does not have -> lacks
Did not remember -> forgot
Did not pay attention to -> ignored
Did not succeed -> failed

Eliminate there are/there is

× There are many ways in which we can arrange the pulleys.
✓ We can arrange the pulleys in many ways.

× There was a long line of bacteria on the plate.
✓ Bacteria lined the plate.

× There are many physicists who like to write.
✓ Many physicists like to write.

× The data confirm that there is an association between vegetables and cancer.
✓ The data confirm an association between vegetables and cancer.

Omit needless prepositions

For example, “that” and “on” are often superfluous:

× The meeting happened on Monday
✓ The meeting happened Monday

× They agreed that it was true.
✓ They agreed it was true.

11.3.4.8. Practice: cut the clutter!

× Anti-inflammatory drugs may be protective for the occurrence of Alzheimer's Disease

Possible rewrite

✓ Anti-inflammatory drugs may protect against Alzheimer's Disease

× Injuries to the brain and spinal cord have long been known to be among the most devastating and expensive of all injuries to treat medically.

Possible rewrite

✓ Injuries to the brain and spinal cord are among the most devastating and expensive.

11.3.4.9. Use active voice

“Subject verb object”
“Subject verb object”
“Subject verb object”
“Subject verb object”

or just...
“Subject verb”

11.3.4.10. What is the passive voice?

- Object-Verb-Subject or just Object-Verb
- Classic example: “Mistakes were made.”
- Passive verb = a form of the verb “to be” + the past participle of the main verb
- The main verb must be a transitive verb (that is, take an object).

11.3.4.11. What is the passive voice?

Object-Verb-Subject or just Object-Verb
Classic example: “Mistakes were made.”
Passive verb = a form of the verb “to be” + the past participle of the main verb
The main verb must be a transitive verb (that is, take an object).

11.3.4.12. "to be" verbs

"Is"	
"Are"	could be
"Was"	should be / shall be
"Were"	will be / would be
"Be"	may be / might be
"Been"	must be
"Am"	has been

11.3.4.13. The passive voice

How do you recognize the passive voice?

Object-Verb-Subject

OR just...

Object-Verb

My first visit to Boston[object] will always be remembered[verb] by me[subject]

Active voice version

I will always remember my first visit to Boston[4]

[4] From: Strunk and White, The Elements of Style

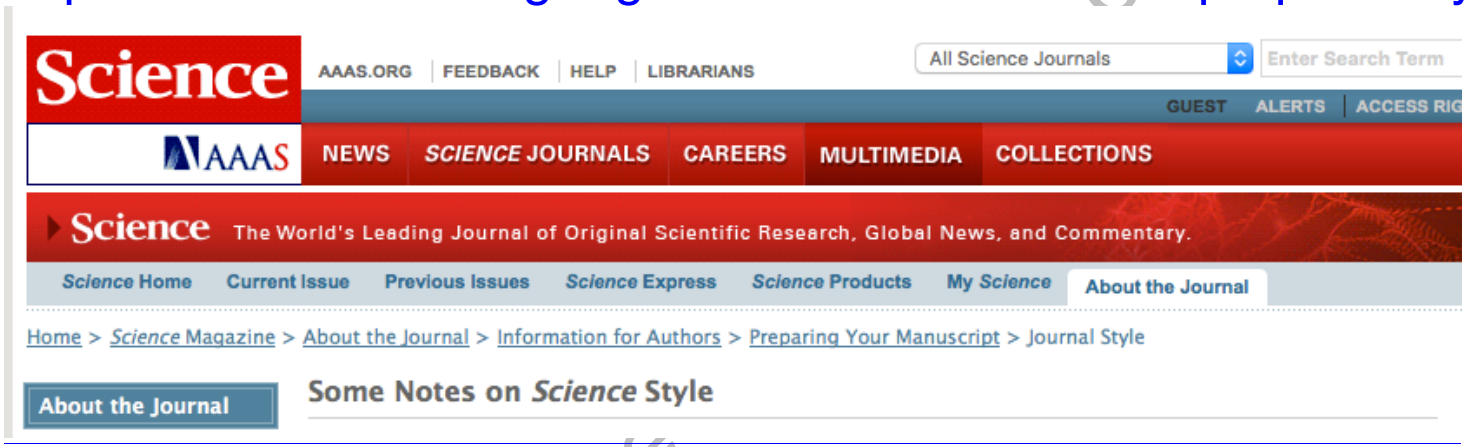
11.3.5. Is it really OK to use “We” and “I”?

Yes, it’s OK!

1. The active voice is livelier and easier to read
2. It is a myth that avoiding first-person pronouns lends objectivity to the paper.

- You (or your team) ran the experiments and interpreted the data. To imply otherwise is misleading.
- The experiments and analysis did not materialize out of thin air! (e.g., “the data were interpreted to show”).

3. By agreeing to be an author on the paper, you are taking responsibility for its content. Thus, you should also claim responsibility for the assertions in the text by using “we” or “I.”
to know more bout this:
http://www.sciencemag.org/site/feature/contribinfo/prep/res/style.xhtml



11.3.6. When is it OK to use the passive voice?

The methods section

- What was done is more important than who did it!
- Readers tend to skim the methods section for key words rather than reading it as prose.
- May be more effort than it's worth to avoid using "we" and "I" in every sentence.

11.3.7. Use strong verbs

Pick the right verb!

The WHO reports that approximately two-thirds of the world's blinds are found in developing countries, and estimates that the number of blinds in these countries will double in the next 25 year.

The WHO estimates that two-thirds of the world's diabetics are found in developing countries, and projects that the number of diabetics in these countries will double in the next 25 years.