Jumping into Statistics: Introduction to Study Design and Statistical Analysis for Medical Research Using JMP Pro Statistical Software

FALL 2022/SPRING 2023

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Meet the Instructors

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Course Objectives

- Review fundamentals of study design and research methodology
- Understand how to choose best statistical test for your research question
- Practice basic statistical analysis use JMP Pro Software

Course Topics

- Life Cycle of Research and Asking a Good Research Question
- Choosing the Right Study Design for Your Research
- Clinical Trial Design
- Populations, Samples, and Hypothesis Testing in Medical Research
- Introduction to Data Types
- Best Practices in Data Collection and Database Management: Getting Started with SAS JMP Pro
- Summarizing and Visualizing Data
- Statistical Methods and How to Choose Them
- Risk Assessment Methods
- Introduction to Regression and Correlation
- Time-to-Event (Survival) Analysis
- Methods for Clinical Diagnostic Testing

Choosing the Right Study Design for Your Research

9/21/2022

Learning Objectives

Participants will be able to:

1) Identify appropriate study designs for different type of research questions

2) Distinguish between different levels of evidence

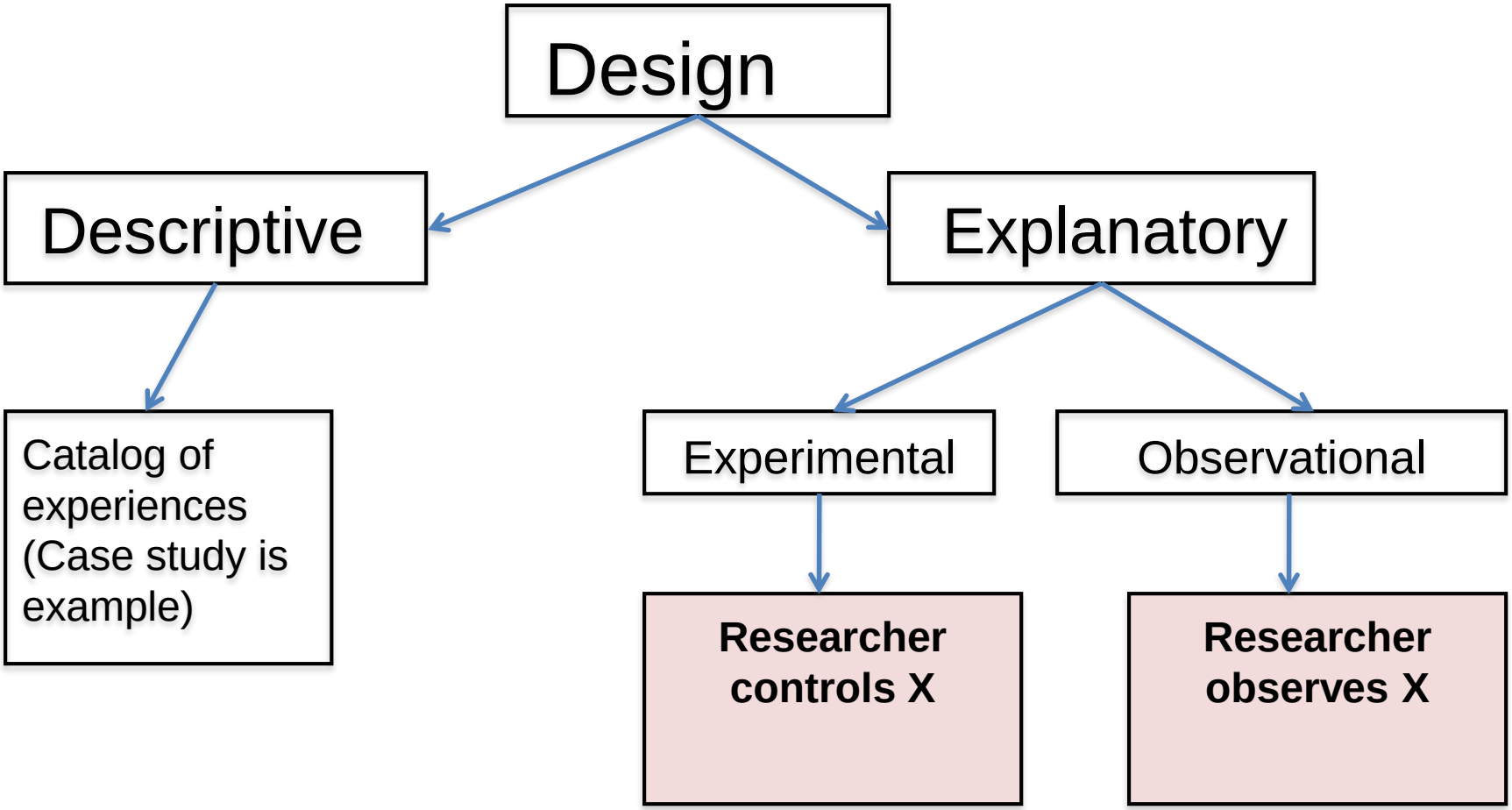
3) Recognize threats to study validity and sources of bias

Why is this topic important?

It is truth we seek.

SYDNEY AGE 14 – Soccer or Dance Team?

Research Designs



Experimental Designs

Pre-experimental

- No control group
- Example: Pre-post design (Quality Improvement)

Quasi-experimental

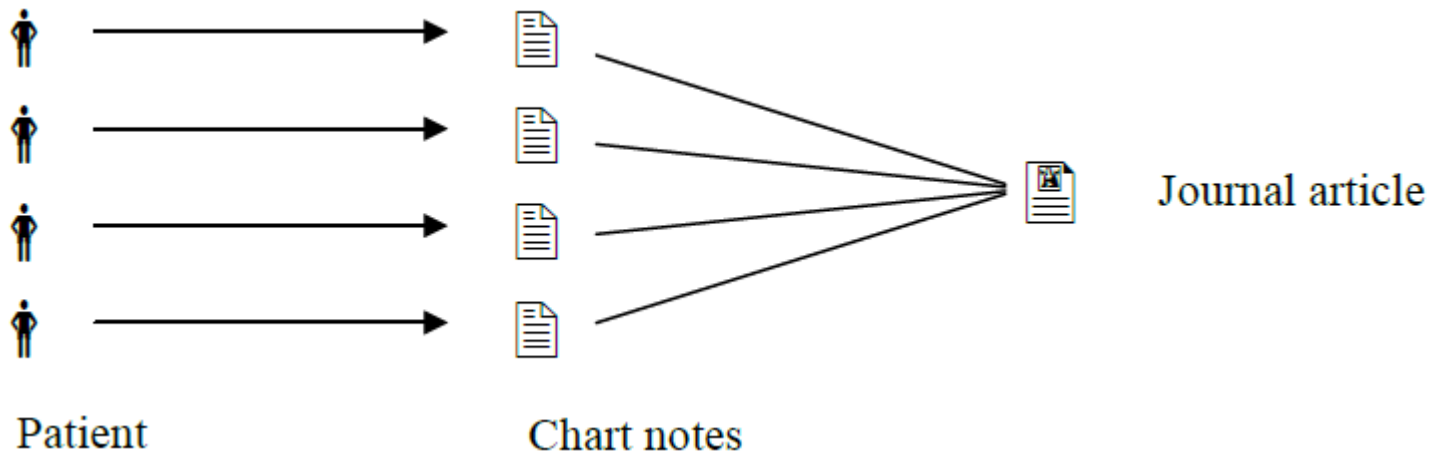
- No randomization to intervention
- Example: Groups already exist- say patients at two hospitals.

True experiment

- Control group
- Randomization to intervention
- Example: Randomized Control Trial

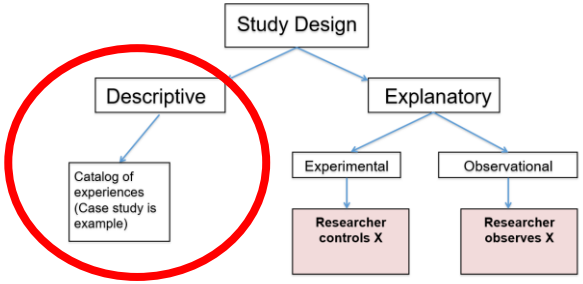
Common study design types

Case Series and Case Reports



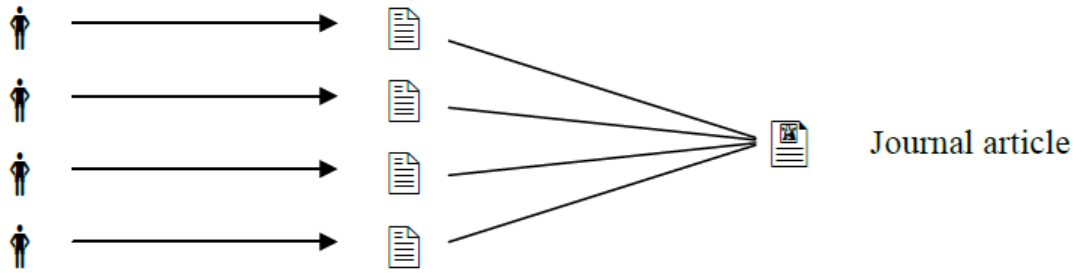
- Either collection of reports (same condition) or a report on a single patient
- Illustrate condition, treatment, reactions to treatment
- No study design

What kind of design is Case Report/Case Series?

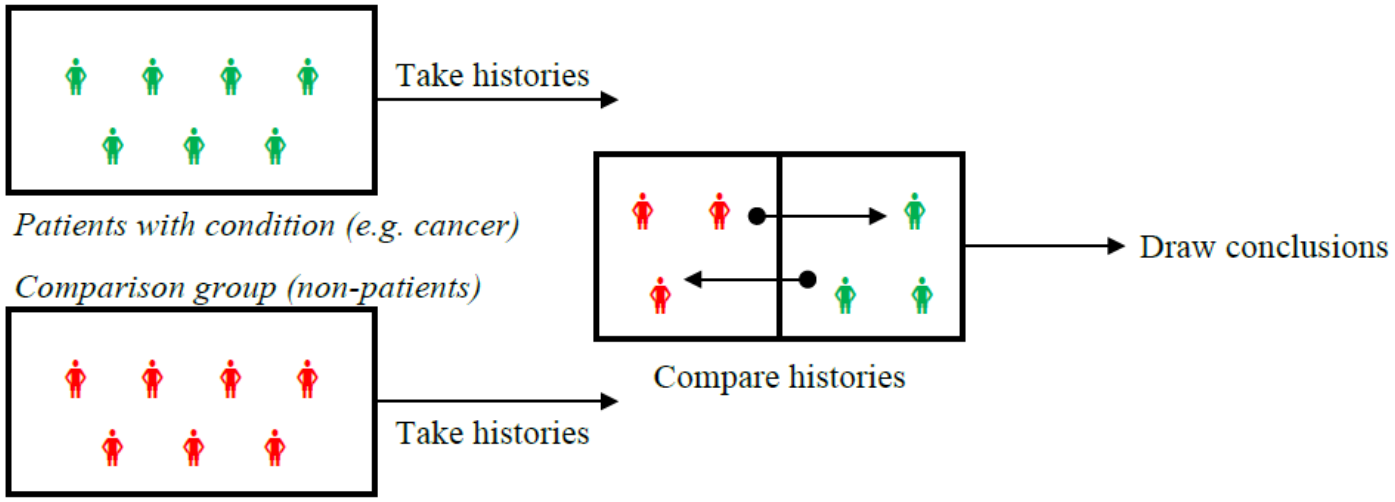


Case Study and Series

A **case study** is a descriptive analysis of a single patient with a disease. A **case series** is a descriptive analysis of a series of people with the disease (there is no comparison group in case series). Case studies illustrate a condition, a treatment, and reactions to treatment.

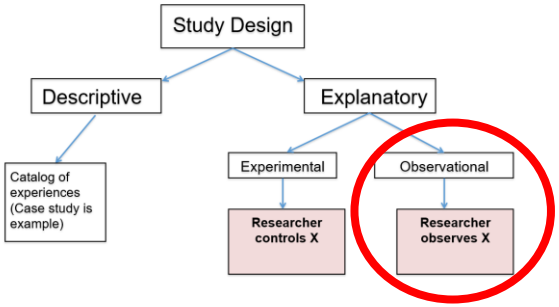


Case Control Studies



- Patients with condition compared to those without
- Retrospective
- Relationship between condition and risk factor (odds ratio)
- Quick studies and good for rare diseases
- Less reliable than cohort or RCTs
- Not a direct measure of incidence

What kind of design is Case Control Study?

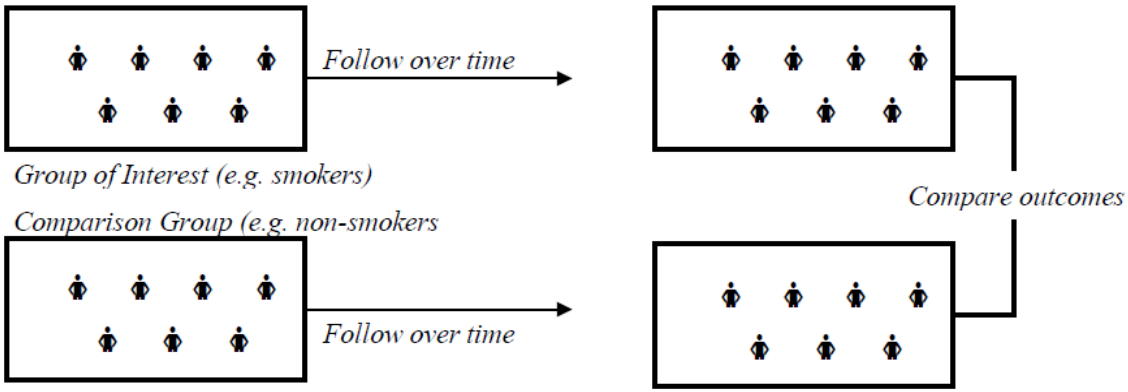


Case-control Study

A **case-control study design** is a study design that examines a group of people who have experienced an event (usually an adverse event) and a group of people who have not experienced the same event, and looks at how exposure to suspect (usually noxious) agents differed between the two groups.

https://bestpractice.bmj.com/info/us/toolkit/ebm-tools/a-glossary-of-ebm-terms

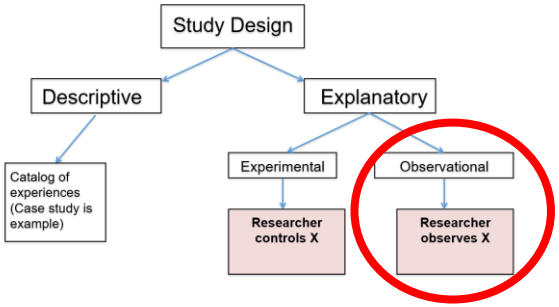
Cohort Studies



- Defined population (risk factor) followed over time
- Compared to group without risk factor
- Prospective, longitudinal, or historical retrospective

- Relationship between risk factor and incidence of condition/disease (absolute/relative risk)
- Can provide evidence for causation
- Typically need large samples and time

What kind of design is a Cohort Study?

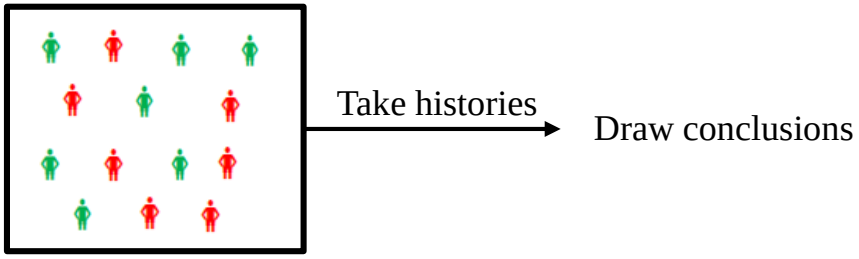


Cohort Study

A **cohort study** is a study design that follows a group of people, a cohort, prospectively in time, and then looks at how events differ among people within the group. A study that examines a cohort, which differs in respect to exposure to some suspected risk factor (e.g., smoking), is useful for trying to ascertain whether exposure is likely to cause specified events (e.g., lung cancer).

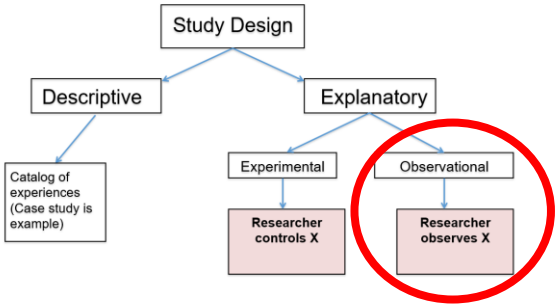
https://bestpractice.bmj.com/info/us/toolkit/ebm-tools/a-glossary-of-ebm-terms

Cross-sectional Studies



- One point in time
- Quick studies
- Good way to estimate characteristics (such as risk or disease prevalence) in a population
- Can compare patients with condition to those without
- Cannot measure of incidence

What kind of design is a Cross-sectional Study?

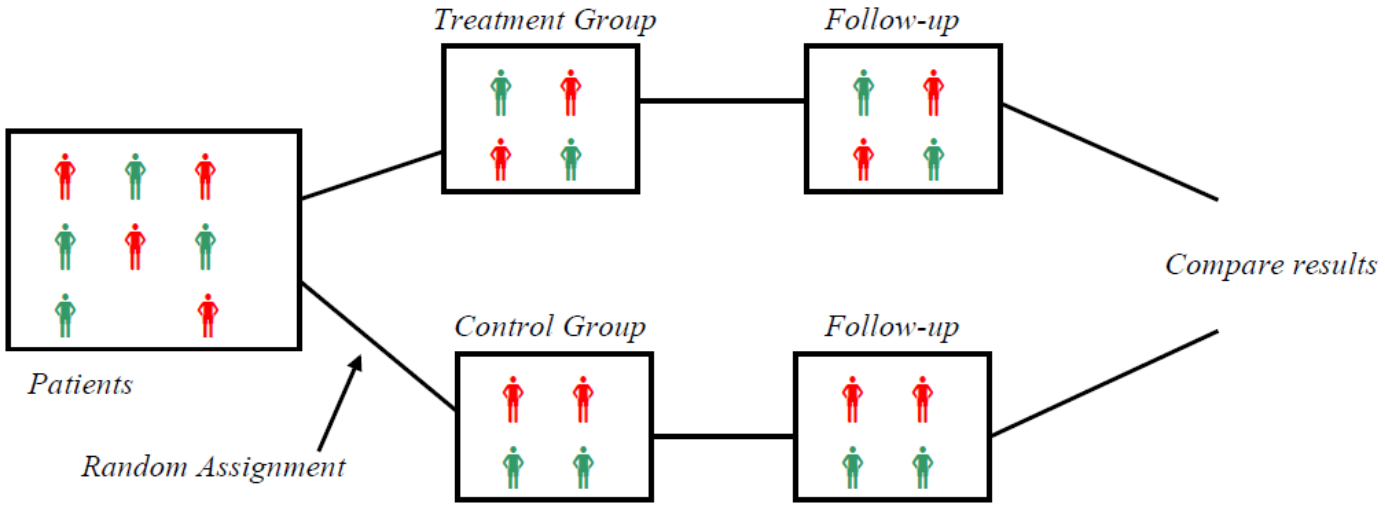


Cross-sectional Study

A **cross-sectional study** design is a study design that involves surveying a population about exposure, or condition, or both, at one point in time. It can be used for assessing the prevalence of a condition in the population. ***Cross-sectional studies should never be used for assessing causality of a treatment***.

https://bestpractice.bmj.com/info/us/toolkit/ebm-tools/a-glossary-of-ebm-terms

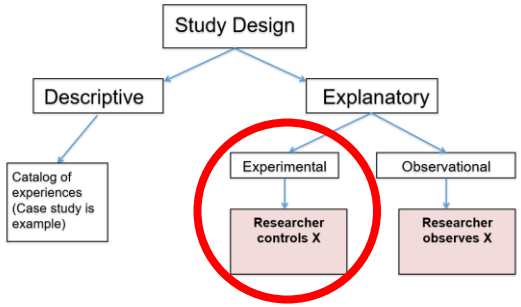
Randomized Control Trials



- Treatment group versus control groups
- Compare to placebo/standard treatment
- Patients randomly assigned to groups and followed; prospective
- Gold Standard

- Can have non-random trials (not as high level of evidence)

What kind of design is Randomized Control Trial?

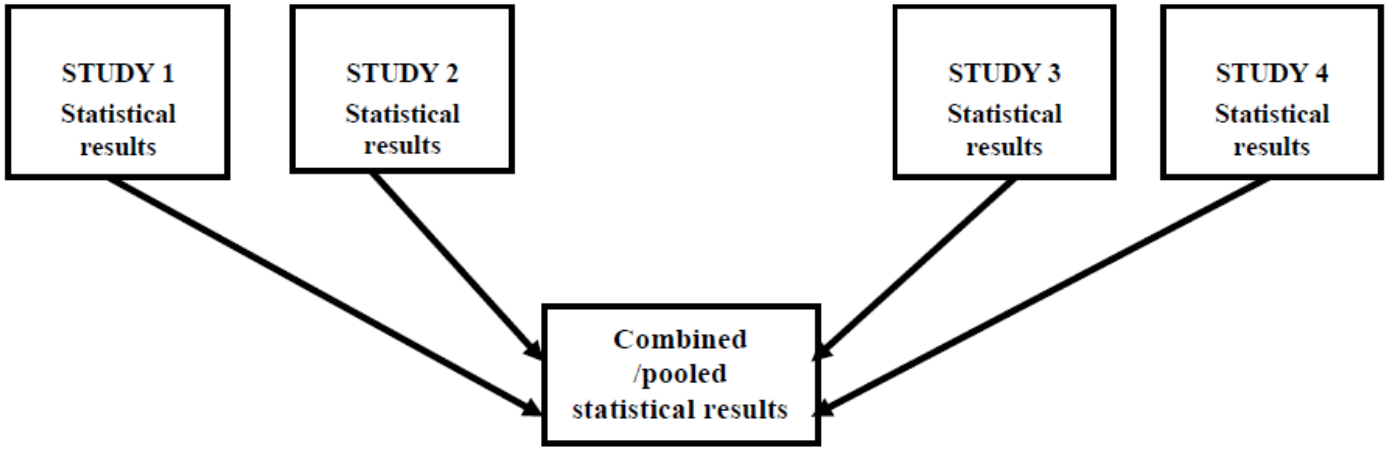


Randomized Control Trials

A randomized control trial (RCT) in an experimental study design which participants are randomly assigned to two or more groups: at least one (the experimental group) receiving an intervention that is being tested and another (the comparison or control group) receiving an alternative treatment or placebo. This design allows assessment of the relative effects of interventions.

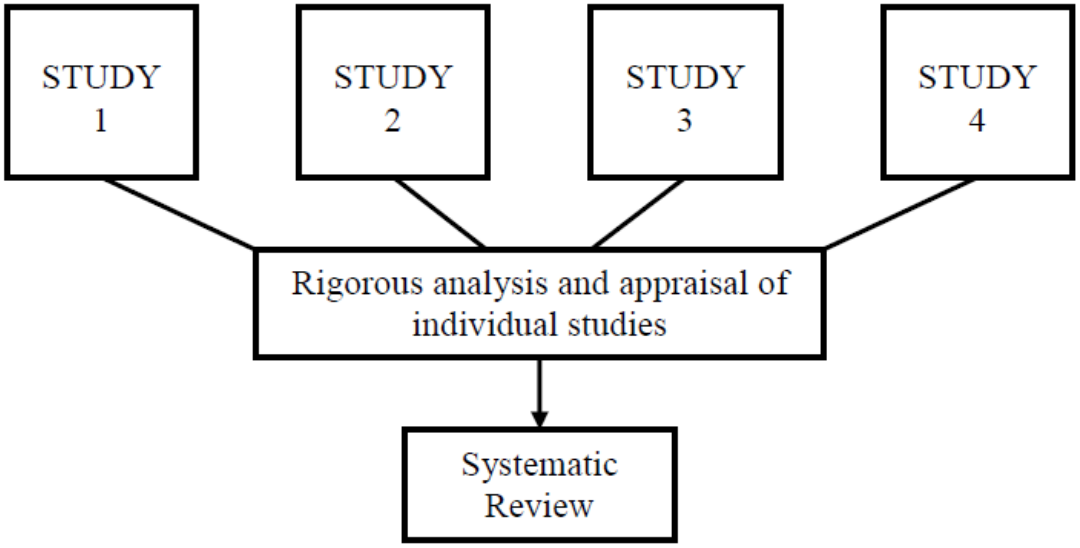
https://bestpractice.bmj.com/info/us/toolkit/ebm-tools/a-glossary-of-ebm-terms

Meta-analyses



- Combination of data from several studies
- Pooled estimate of effects
- Not a review, involves statistical analysis
- High level of evidence
- Can be affected by publication bias
  - Studies with little or no effects are often not published or less visible to the research community

Systematic Review



- Comprehensive survey of specific topic
- Unbiased synthesis of findings
- More rigorous than just a literature review
- Included published and unpublished work
- Formal process
- High level of evidence
- Systematic reviews→ qualitative

Comparing designs

Let's consider three goals that drive medical research:

1. Efficiency. Is the result obtained with minimal time, cost and resources (e.g., number of subjects required)?
2. Validity. Is the result likely to be true? (Internal validity)
3. Generalizability. Is the result widely applicable? (External validity)

	Efficient	Valid	Generalizable
Case report/Case series			
Case-control study			
Cohort study			
Randomized control trial (RCT)			

Rules of Evidence to establish causality that “X” causes “Y”

1. X is related to Y
2. X precedes Y
3. Other variables don’t explain Y

Validity and threats*

*Threats come from bias – there are many sources of bias!

Assessing Research Quality: Validity

- Validity is the soundness or rigor of a study.
- Research quality is the degree to which study measures and evaluates what it intended to.
- Internal validity is the extent to which a piece of evidence supports a claim about cause and effect, within the context of a particular study.
- External validity is the validity of applying the conclusions of a scientific study outside the context of that study. If a study has external validity it is said to be generalizable.

What are potential sources of bias in doing a valid history and physical on a patient undergoing elective surgery?

Linking to what you know

Potential sources of bias in doing a valid history and physical on a patient undergoing elective surgery

- If the surgeon is doing the history and physical he would inherently concentrate only on his area of expertise. And he will often miss other physical signs and symptoms.
- The patient may lie about smoking history to appear more “socially acceptable.”
- Incomplete or inaccurate blood work may miss a diagnosis of diabetes in a patient.
- Incomplete or inaccurate self-report information due to a patient’s low literacy level.
- And many more

Major Types of Validity

Internal validity

- Can we infer that differences in the outcome can be attributed to the exposure/intervention?

External validity

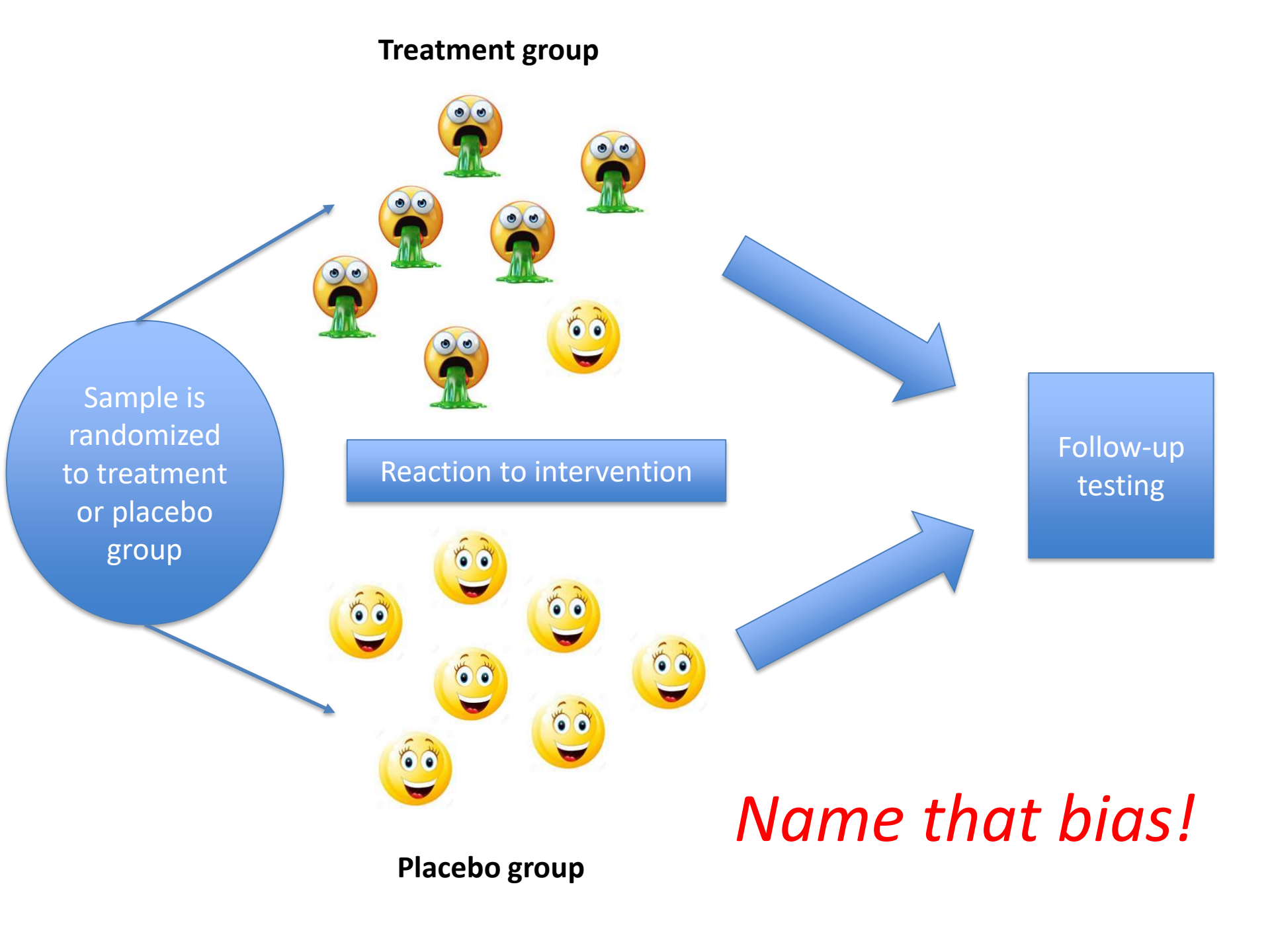
- Can we infer that the relationship observed between variables is similar across different settings (generalizability)?

Statistical conclusion validity

- Are conclusions from the research study founded in adequate/sound analysis of the data and interpretation of results?

Threats to Validity

Name	***X is the focus variable – Y is the outcome***
History	Spurious event causes change in Y, not X
Testing	Taking pre-test alters result of post-test
Maturation	Changes occur in subjects not due to X
Instrumentation	Measuring instrument changes during study or is unreliable
Selection	•Study sample does not fairly represent population of interest •Change in Y due to group differences at baseline
Regression to mean	Subjects with extreme scores tend to score less extremely in subsequent testing
Mortality	Loss of subjects from study connected to X

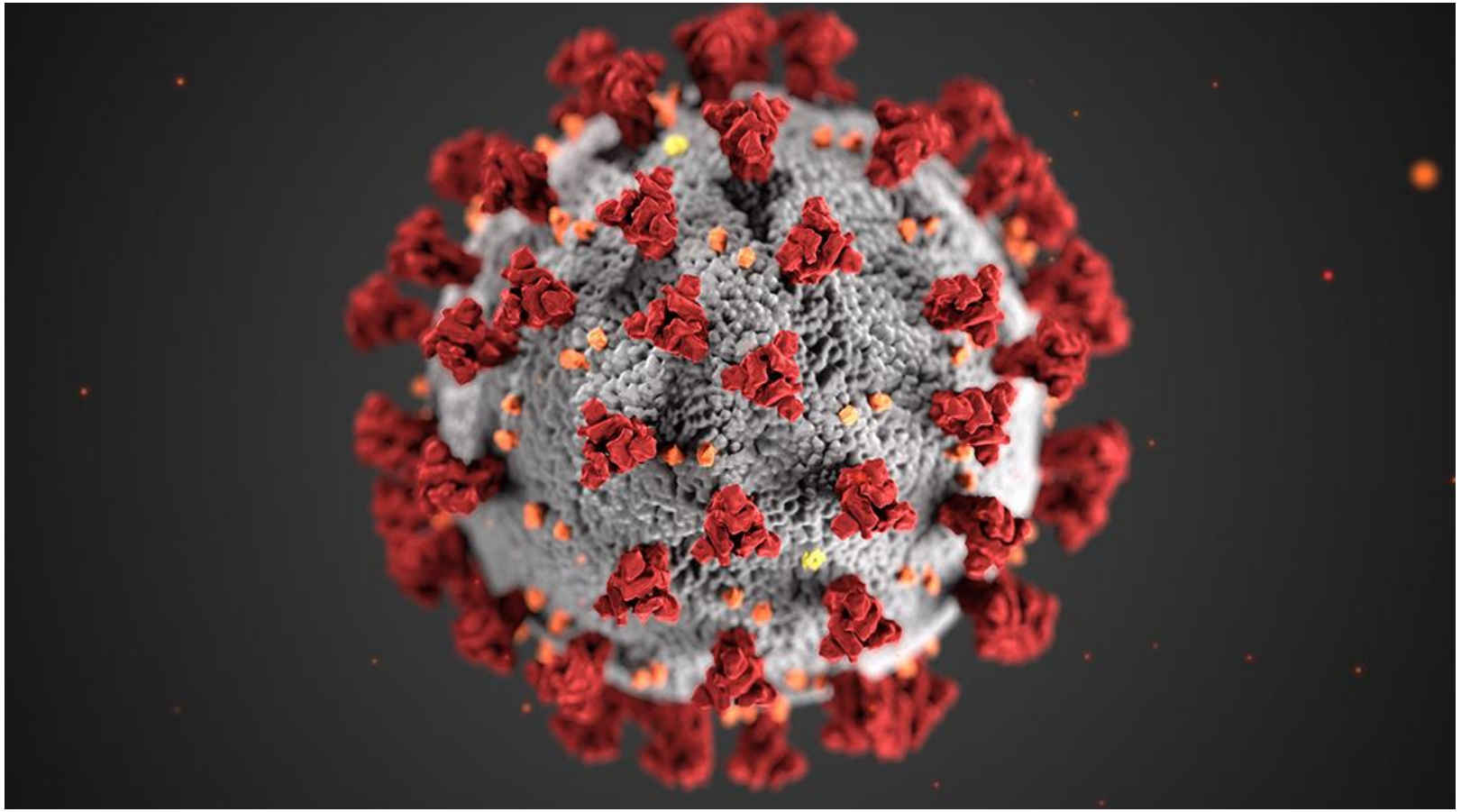

Treatment group
Sample is randomized to treatment or placebo group
Reaction to intervention
Follow-up testing
Placebo group
Name that bias!

Math education study

- High school kids meet every Saturday during the school year for study session and pizza.
- Test scores significantly improve by the end of the year.

Is the Saturday Math Social an effective intervention?

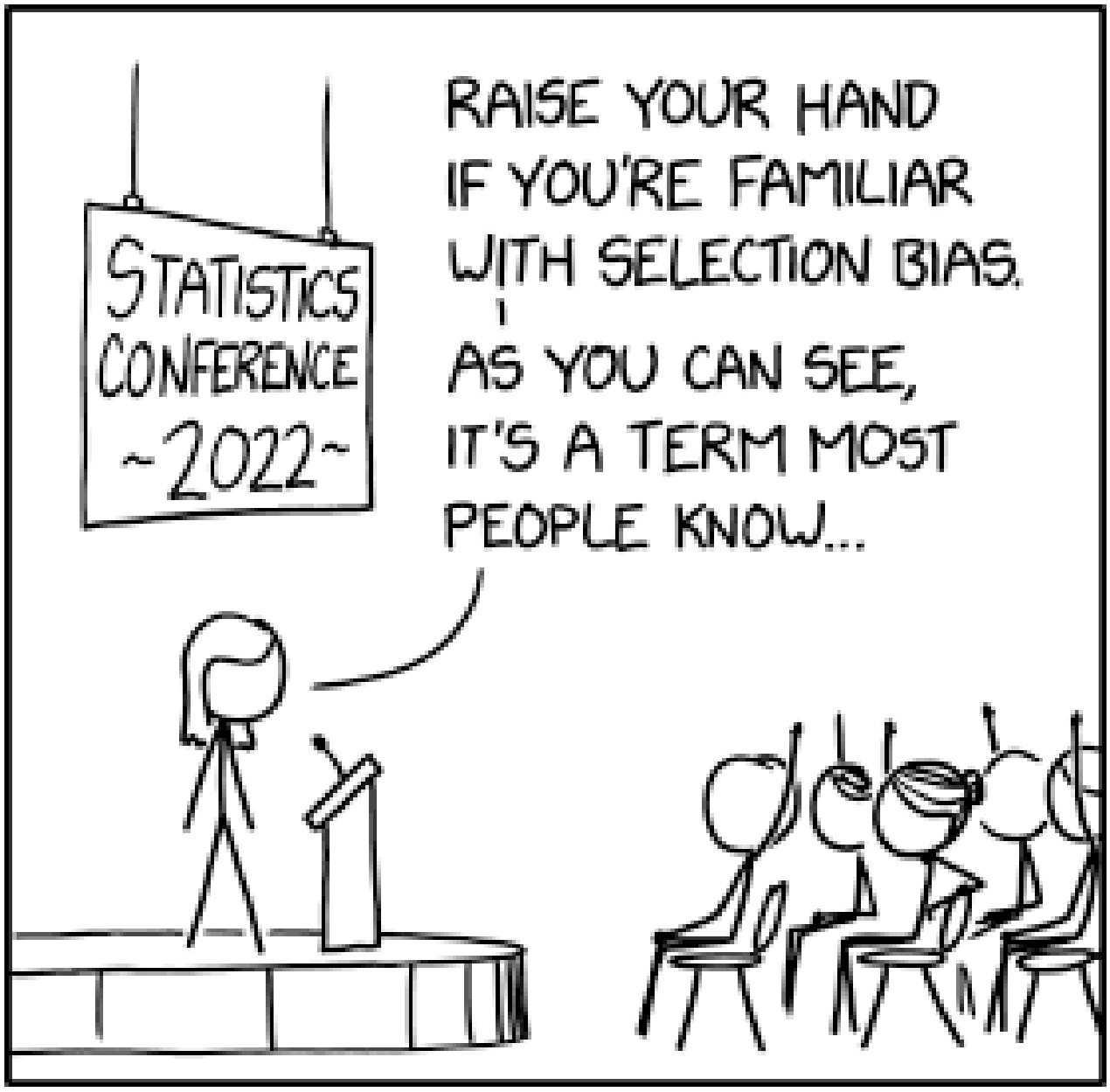
Name that bias!



Name that bias!

A RESEARCHER IS HAVING RECRUITMENT PROBLEMS WITH AN ANXIETY STUDY OF CHILDREN WHICH REQUIRES TAKING BLOOD SAMPLES. WHICH TYPE OF BIAS MAY BE AFFECTING THIS STUDY?

Name that bias!


STATISTICS CONFERENCE ~2022~
RAISE YOUR HAND IF YOU'RE FAMILIAR WITH SELECTION BIAS.
AS YOU CAN SEE, IT'S A TERM MOST PEOPLE KNOW...

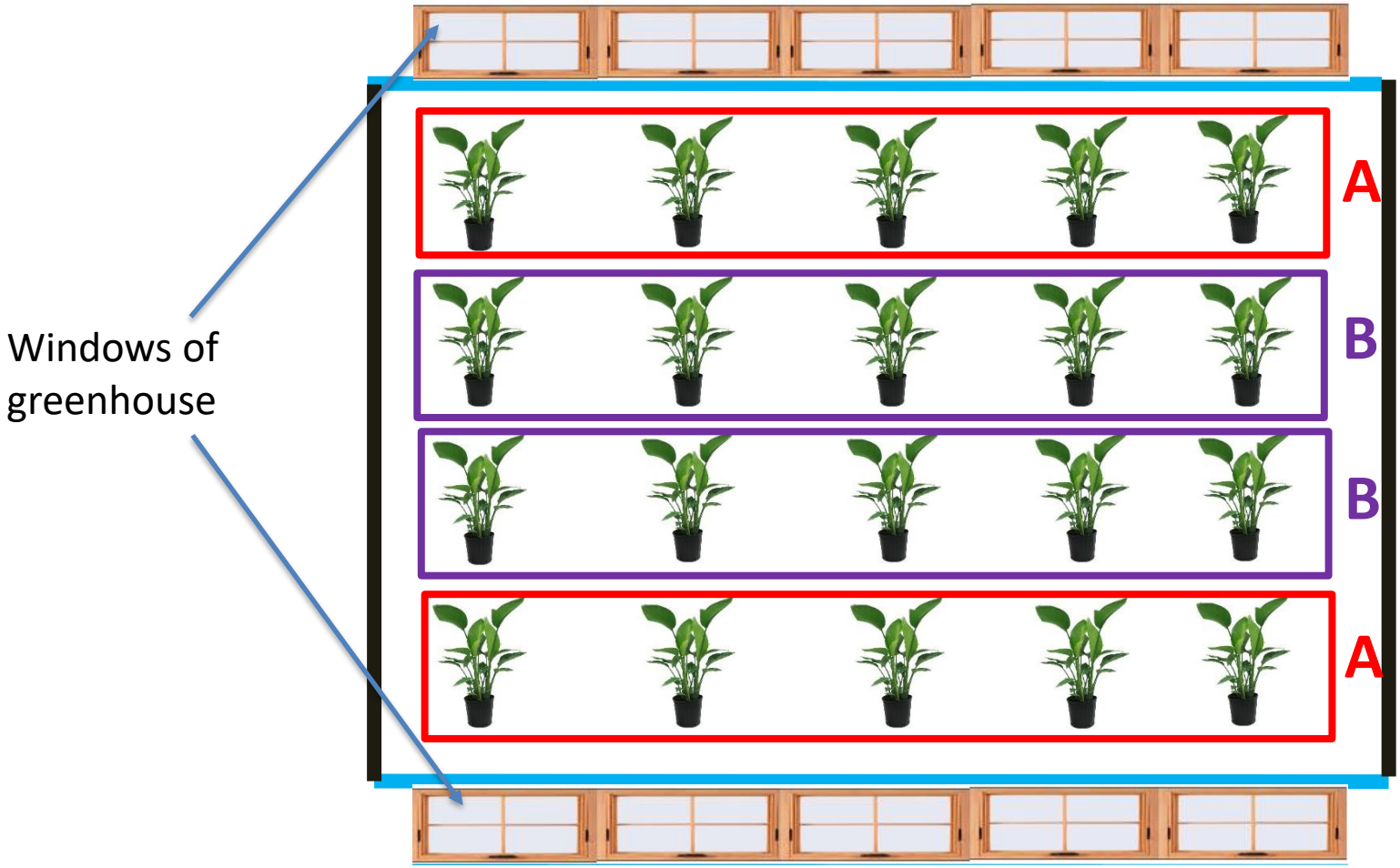
Confounding

Confounding obscures the 'real' effect of an exposure on outcome.

To be a potential confounder of a “focus” variable X, a confounding variable Z must:

1) have an association with the outcome Y
2) have an association with X
3) not be an effect of X

Can you identify a problem in this design?



A is one type of fertilizer, **B** is another type of fertilizer.

Which one is better?

True experimental design (e.g., RCT) controls for most, but not all, threats.

KEY POINT

A few basic ways to reduce bias

Sampling: Ensure your sample is representative of the population you are interested in studying.

Randomization: Ensure a rigorous randomization scheme.

Blinding: A technique which reduces sources of participant and research bias.

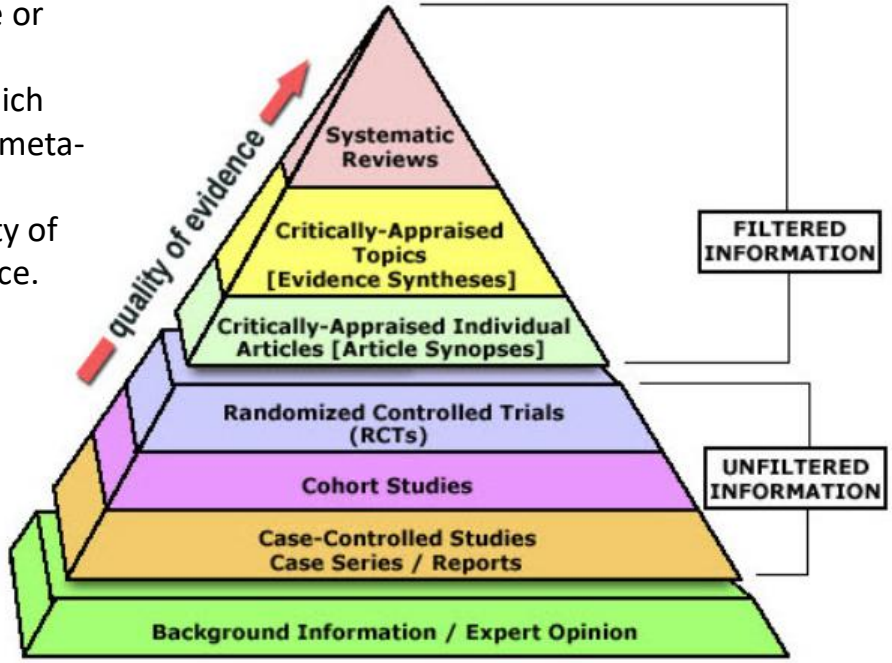
1. **Single blinded**: participant cannot figure out his assignment
2. **Double blinded**: neither participant nor research observer can figure out participant assignment
3. **Triple blinded**: participant, research observer, and data analyst can not figure out participant assignment

For more detail, please see: Pannucci, C.J. and Wilkins, E.G., 2010. Identifying and avoiding bias in research. Plastic and reconstructive surgery, 126(2), p.619.

Levels of evidence

The notion of quality of evidence or level of evidence is based on the premise that multiple studies which are rigorously reviewed through meta-analysis and systematic reviews provide the highest overall quality of evidence to inform clinical practice.

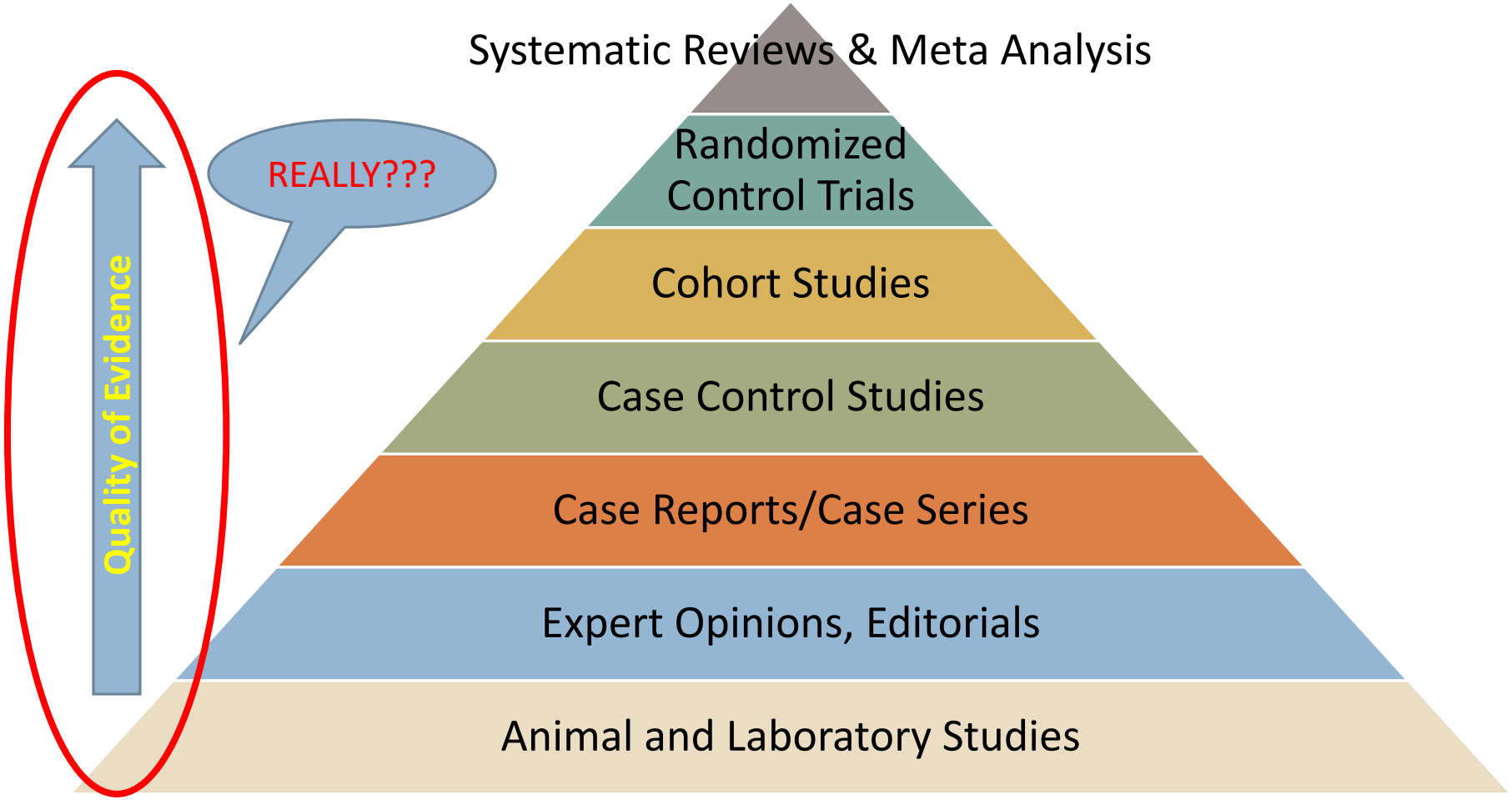
At each level, quality depends on the quality of the levels below.



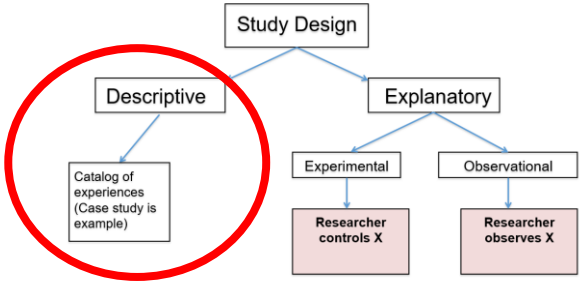
Produced by Jan Glover, David Izzo, Karen Odato and Lei Wang.

https://ncu.libguides.com/researchprocess/systematicreviews

Levels of Evidence for Study Designs



How was AIDS discovered?



The HIV/AIDS epidemic was revealed through a case series published in the Lancet in 1981 (and other such studies).

Lancet. 1981 Sep 19;2(8247):598-600.

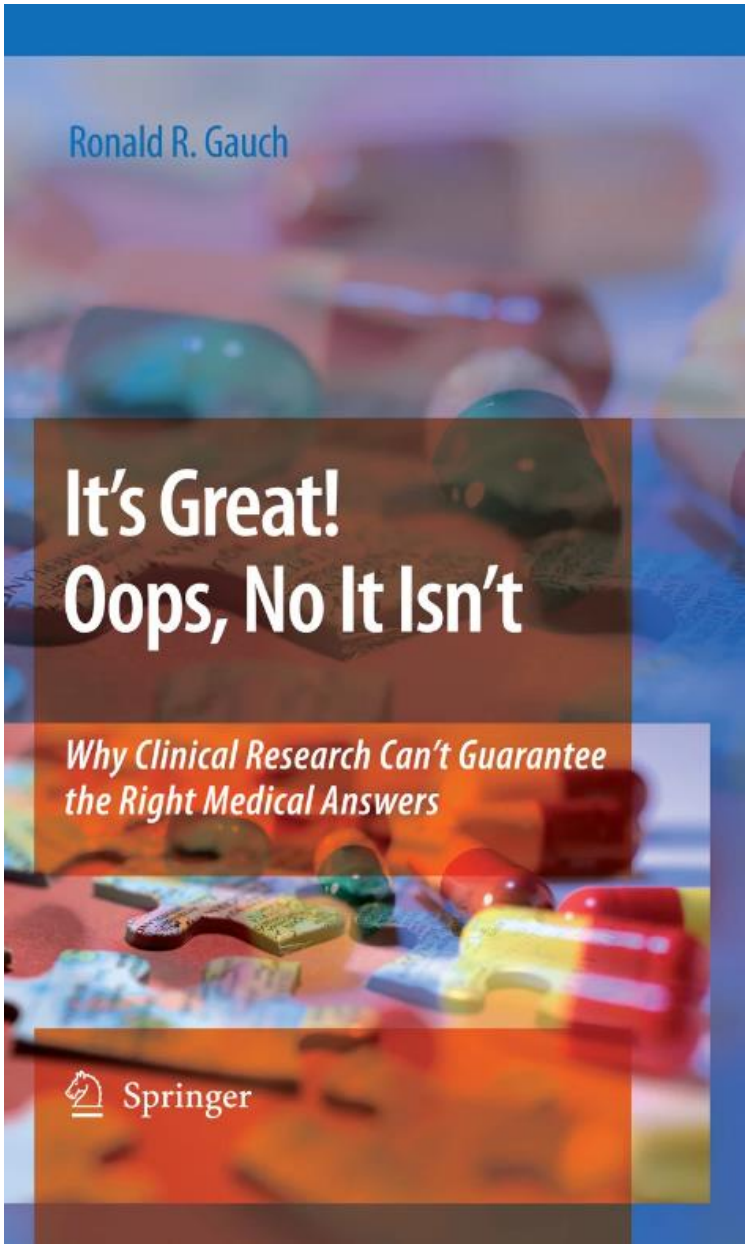
Kaposi's sarcoma in homosexual men-a report of eight cases.

Hymes KB, Cheung T, Greene JB, Prose NS, Marcus A, Ballard H, William DC, Laubenstein LJ.

Abstract

The clinical findings in eight young homosexual men in New York with Kaposi's sarcoma showed some unusual features. Unlike the form usually seen in North America and Europe, it affected younger men (4th decade rather than 7th decade); the skin lesions wee generalised rather than being predominantly in the lower limbs, and the disease was more aggressive (survival of less than 20 months rather 8-13 years). All eight had had a variety of sexually transmitted diseases. All those tested for cytomegalovirus antibodies and hepatitis B surface antigen of anti-hepatitis B antibody gave positive results. This unusual occurrence of Kaposi's sarcoma in a population much exposed to sexually transmissible diseases suggests that such exposure may play a role in its pathogenesis.

Bottom line: CASE STUDIES AND CASE SERIES ARE IMPORTANT!


Ronald R. Gauch
It's Great!
Oops, No It Isn't
Why Clinical Research Can't Guarantee
the Right Medical Answers
Springer

Seven Deadly Flaws – The Clinical Trials' Achilles' Heel

Wrong results from clinical trials occur because of (1) mistakes by researchers in the planning and execution of clinical trials, (2) the complex and inexact nature of information researchers require and (3) factors that are beyond the control of the researcher. Chapter 7 in “It’s Great, Oops, No It Isn’t” examines the last element and identifies seven fatal flaws that are inherent in the methodology of clinical trial.

Factors that are beyond the control of the researcher

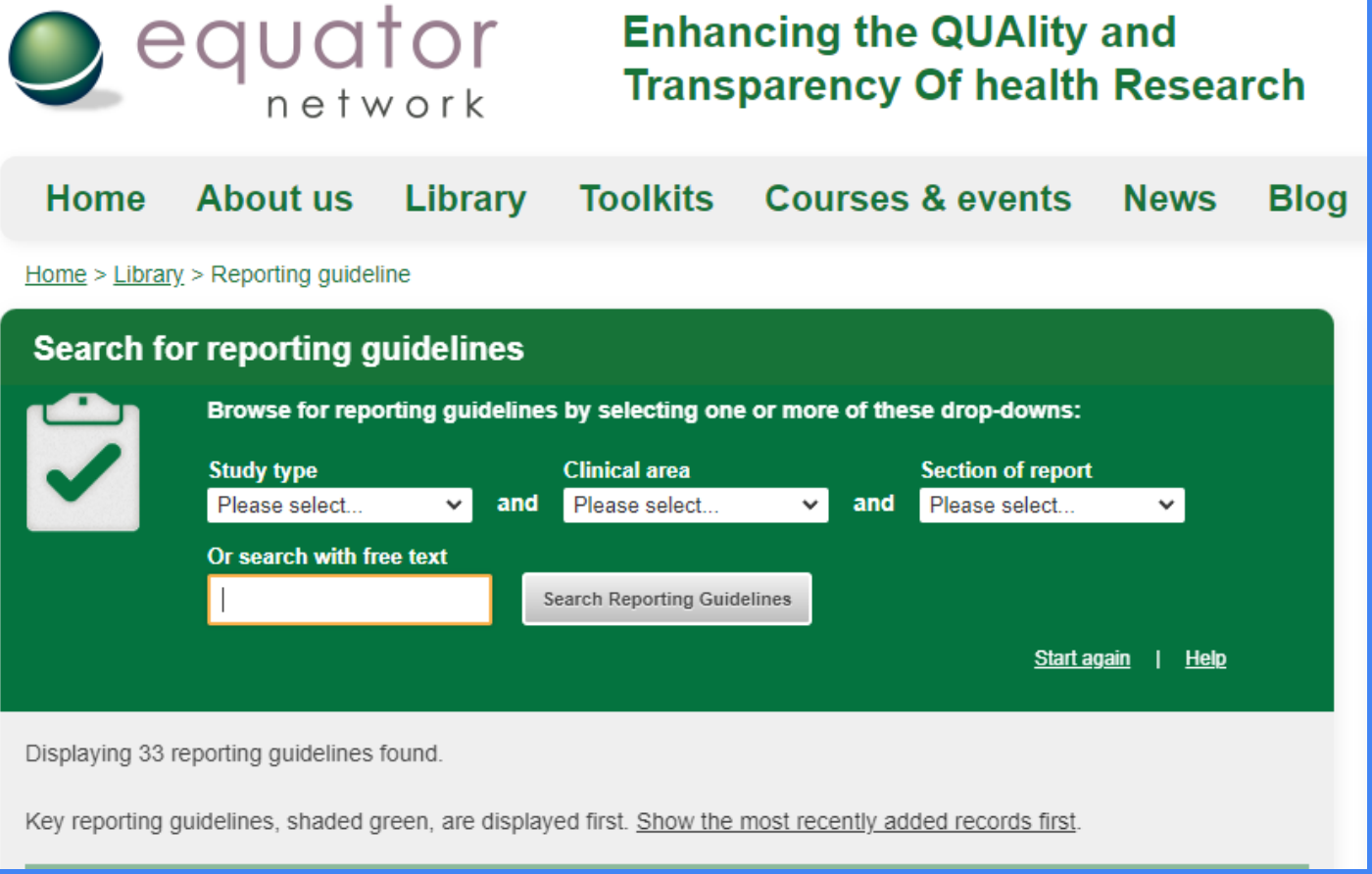
1. The unknown population
2. The imperfect sample
3. The unequal treatment groups
4. The uncontrolled experimental setting
5. The breakdown of blinding
6. The impractical result
7. The insufficient sample size

Reporting Guidelines

Background of Equator Network

Enhancing the QUAlity and Transparency Of health Research

The EQUATOR Network is an “umbrella” organisation that brings together researchers, medical journal editors, peer reviewers, developers of reporting guidelines, research funding bodies and other collaborators with mutual interest in improving the quality of research publications and of research itself.


equator network
Enhancing the QUAlity and Transparency Of health Research
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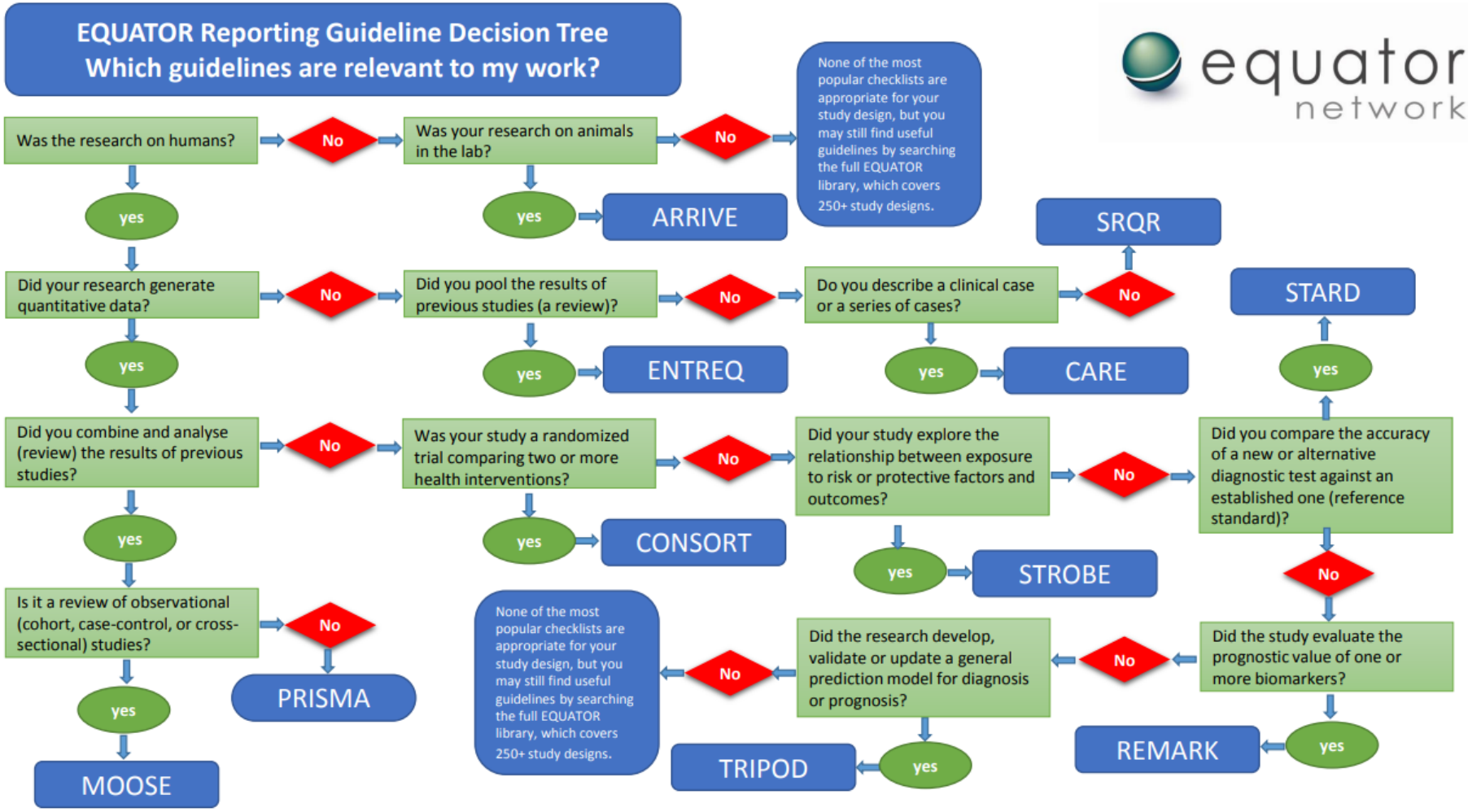
Search for reporting guidelines
Browse for reporting guidelines by selecting one or more of these drop-downs:
Study type
Please select...
and
Clinical area
Please select...
and
Section of report
Please select...
Or search with free text
Search Reporting Guidelines
Start again | Help
Displaying 33 reporting guidelines found.
Key reporting guidelines, shaded green, are displayed first. Show the most recently added records first.


EQUATOR Reporting Guideline Decision Tree
Which guidelines are relevant to my work?
equator network
Was the research on humans?
No
Was your research on animals in the lab?
No
None of the most popular checklists are appropriate for your study design, but you may still find useful guidelines by searching the full EQUATOR library, which covers 250+ study designs.
yes
yes
ARRIVE
Did your research generate quantitative data?
No
Did you pool the results of previous studies (a review)?
No
Do you describe a clinical case or a series of cases?
No
SRQR
yes
yes
ENTREQ
yes
CARE
STARD
yes
Did you combine and analyse (review) the results of previous studies?
No
Was your study a randomized trial comparing two or more health interventions?
No
Did your study explore the relationship between exposure to risk or protective factors and outcomes?
No
Did you compare the accuracy of a new or alternative diagnostic test against an established one (reference standard)?
yes
yes
CONSORT
yes
STROBE
No
Is it a review of observational (cohort, case-control, or cross-sectional) studies?
No
None of the most popular checklists are appropriate for your study design, but you may still find useful guidelines by searching the full EQUATOR library, which covers 250+ study designs.
Did the research develop, validate or update a general prediction model for diagnosis or prognosis?
No
Did the study evaluate the prognostic value of one or more biomarkers?
yes
PRISMA
No
TRIPOD
yes
REMARK
yes
MOOSE
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Summary Tips

- Understand study types
- Be aware of threats to validity
- Familiarize yourself with reporting guidelines (https://www.equator-network.org/reporting-guidelines)

QUESTIONS?

References

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Jager KJ, Zoccali C, Macleod A, Dekker FW. Confounding: what it is and how to deal with it. Kidney international. 2008 Feb 1;73(3):256-60.

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Pannucci, C.J. and Wilkins, E.G., 2010. Identifying and avoiding bias in research. Plastic and reconstructive surgery, 126(2), p.619.