Medical research

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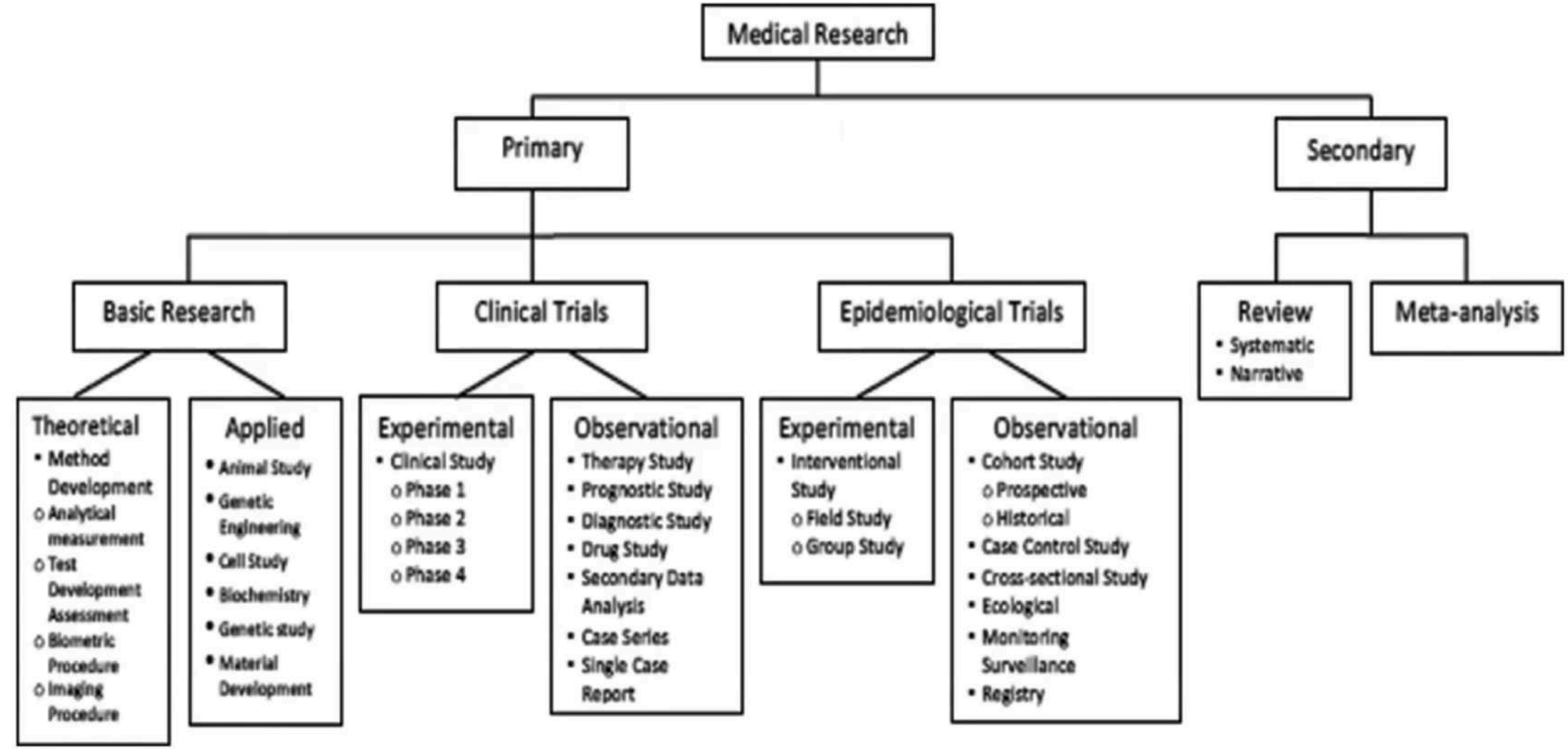
Medical research has evolved, from individual expert described opinions and techniques, to scientifically designed methodology-based studies. Research methodology is now protocol based with predefined steps. Studies were classified based on the method of collection and evaluation of data.

Medical research is classified into primary and secondary research.

Clinical/experimental studies are performed in primary research

Three main areas in primary research are basic medical research, clinical research and epidemiological research

Secondary research consolidates available studies as reviews, systematic reviews and meta-analyses.



- Basic research includes fundamental research in fields.
- Clinical studies include observational studies and interventional studies and are subclassified

- Observational clinical study is a study in which knowledge from treatment of persons with drugs is analysed using epidemiological methods.

- Here, the diagnosis, treatment and monitoring are performed exclusively according to medical practice and not according to a specified study protocol

Narrative review

An expert senior author writes about a particular field, condition or treatment, including an overview, and this information is fortified by his experience.

The article is in a narrative format.

Its limitation is that one cannot tell whether recommendations are based on author's clinical experience, available literature and why some studies were given more emphasis.

Systematic reviews

Methodically and comprehensively identify studies.

Focused on a specified topic, appraise their methodology, summate the results, identify key findings and reasons for differences across studies, and cite limitations of current knowledge.

They adhere to reproducible methods and recommended guidelines.

The methods used to compile data are explicit and transparent.

A properly conducted systematic review presents the best available research evidence for a focused clinical question.

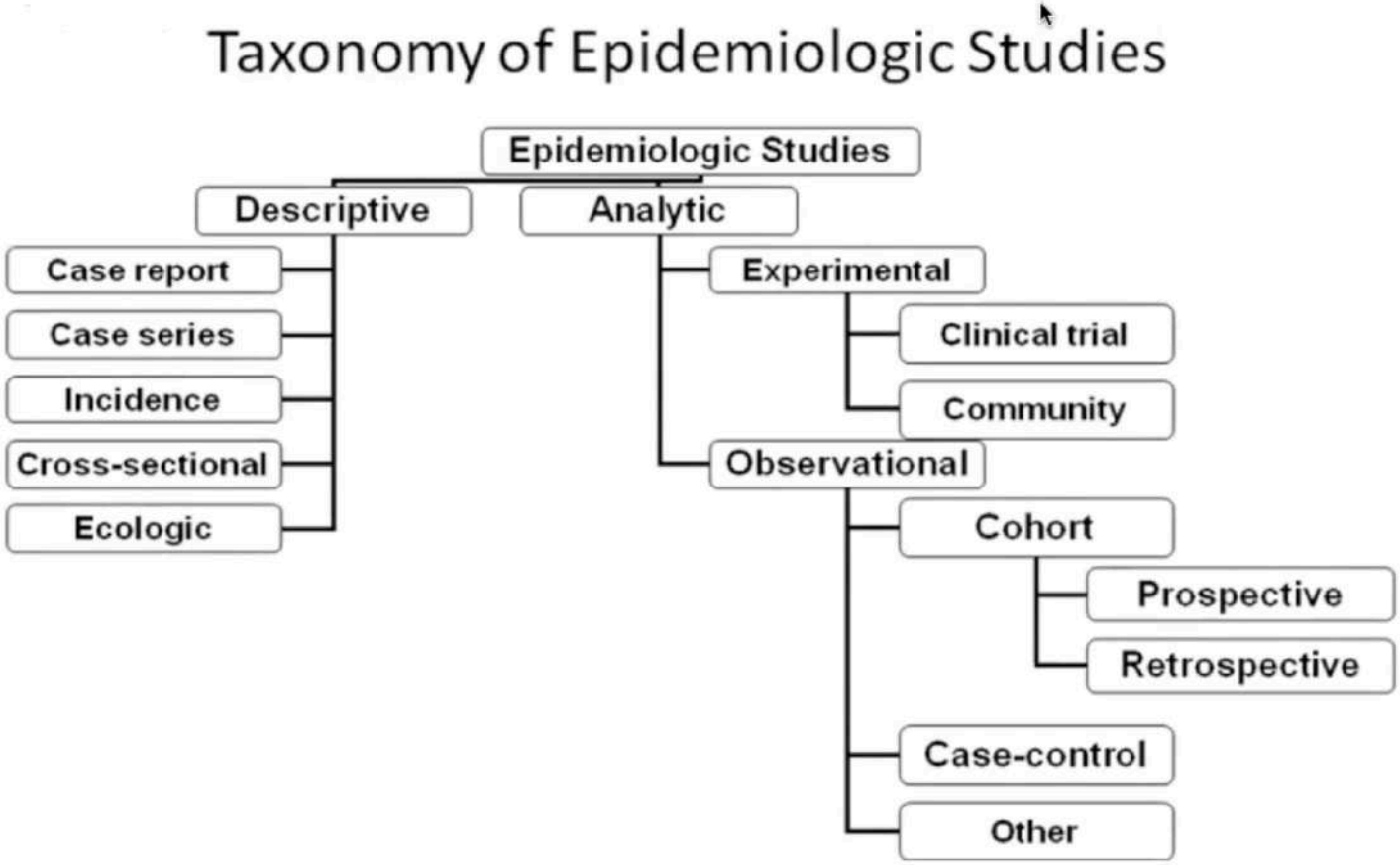
A systematic review attempts to reduce bias identification and studies selection for review, using a comprehensive search strategy and specifying inclusion criteria.

Meta-analysis

Combining data from well-conducted primary studies provide a precise estimate of the "true effect.

Pooling the samples of individual studies increases overall sample size, enhances statistical analysis power, reduces confidence interval and thereby improves statistical value.

Taxonomy of Epidemiologic Studies:



Descriptive or Analytic Studies?

Descriptive studies

- Generate hypotheses
- Answer what, who, where, and when

Analytic studies

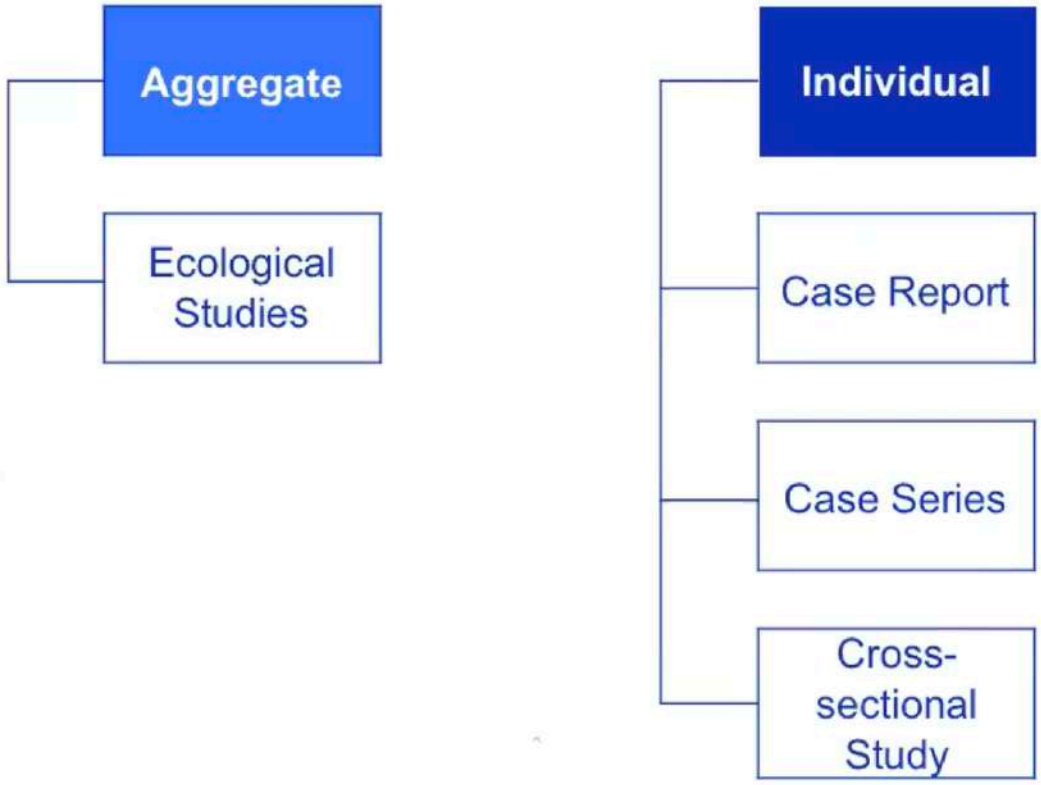
- Test hypotheses
- Answer why and how

Descriptive Studies

Characterize who, where, or when in relation to what (outcome)

- **Person**: characteristics (age, sex, occupation) of the individuals affected by the outcome
- **Place:** geography (residence, work, hospital) of the affected individuals
- **Time**: when events (diagnosis, reporting; testing) occurred

Types of Descriptive Studies



Cross-Sectional

Purpose: To learn about the characteristics of a population at one point in time (like a photo "snap shot")

Design: No comparison group

Population: All members of a small, defined group or a sample from a large group

Results: Produces estimates of the prevalence of the population characteristic of interest

When to Conduct a Cross-Sectional Study

- To estimate prevalence of a health condition or prevalence of a behavior, risk factor, or potential for disease
- To learn about characteristics such as knowledge, attitude and practices of individuals in a population
- To monitor trends over time with serial cross-sectional studies

Cross-Sectional Study Measures

Prevalence of a condition:

= number of existing cases / size of population

(or population count)

Studies to Track Trends in Newly Recognized Cases

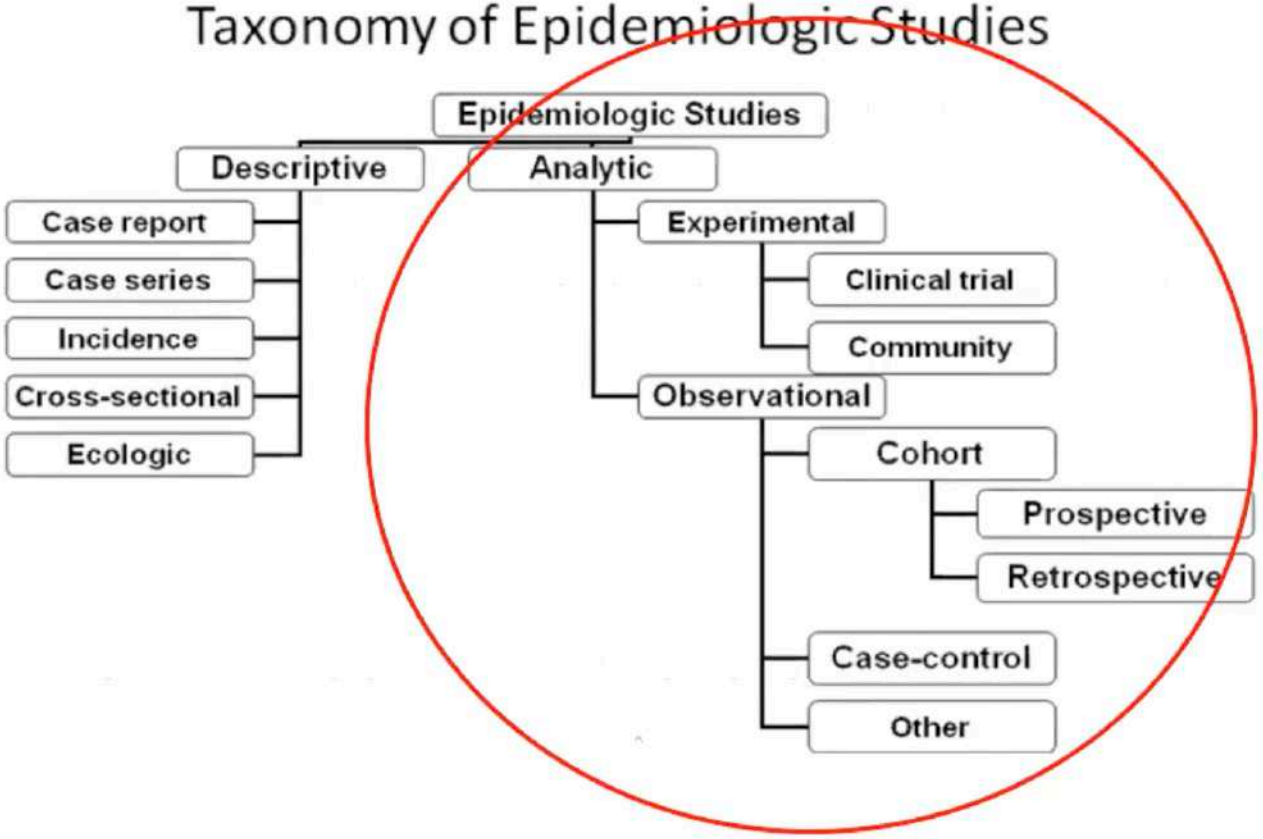
Incidence study

- Newly reported or registered disease cases compared over time, place, or person
- Population estimates or other population group totals used as denominators

Ecological study

- Rates are linked to the level of exposure to some agent for the group as a whole

Taxonomy of Epidemiologic Studies: Figure 2



Analytic Studies Definition

Analytic studies test hypotheses about exposure-outcome relationships

- Measure the association between exposure and outcome
- Include a comparison group

Developing Hypotheses

- A hypothesis is an educated guess about an association that is testable in a scientific investigation.
- Descriptive data (Who? What? Where? When?) provide information to develop hypotheses.
- Hypotheses tend to be broad initially and are then refined to have a narrower focus.

Developing Hypotheses Example

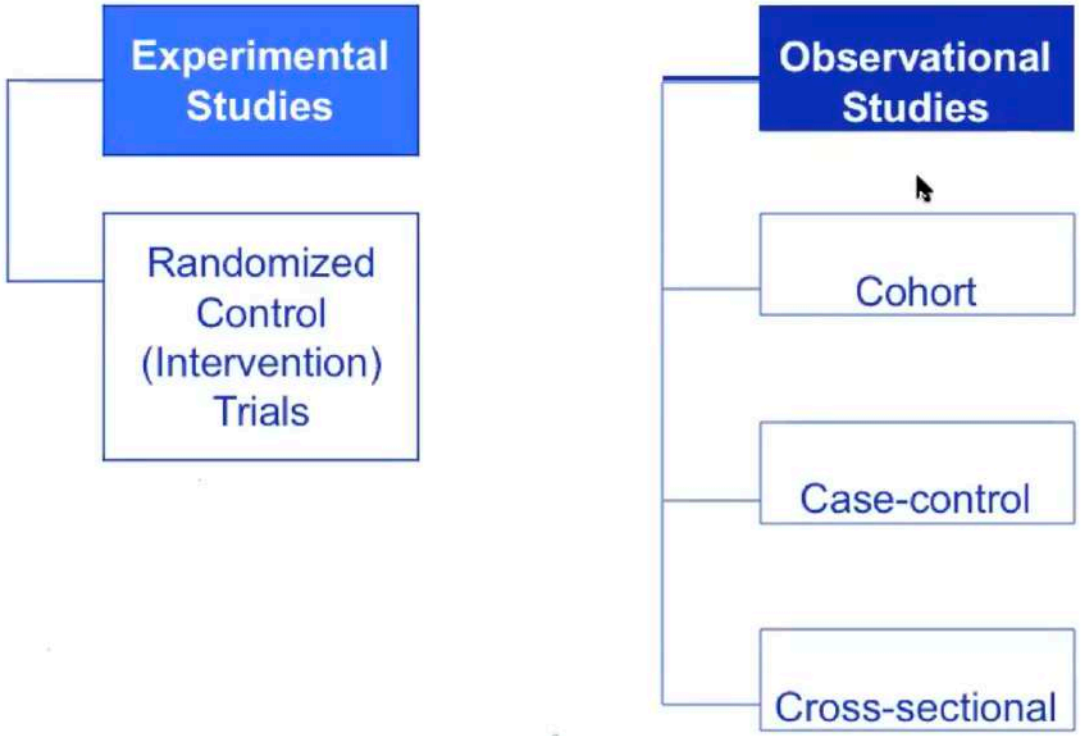
Hypothesis: visco-suplimentation leads to decrease pain in OA of knee

- Exposure: viscosuplimentation
- Outcome: pain relief

Hypothesis: ?

- Exposure: ?
- Outcome: ?

Analytic Study Types



Cohort Studies

What is a cohort?

A well-defined group of individuals who share a common characteristic or experience

- Example: Individuals born in the same year

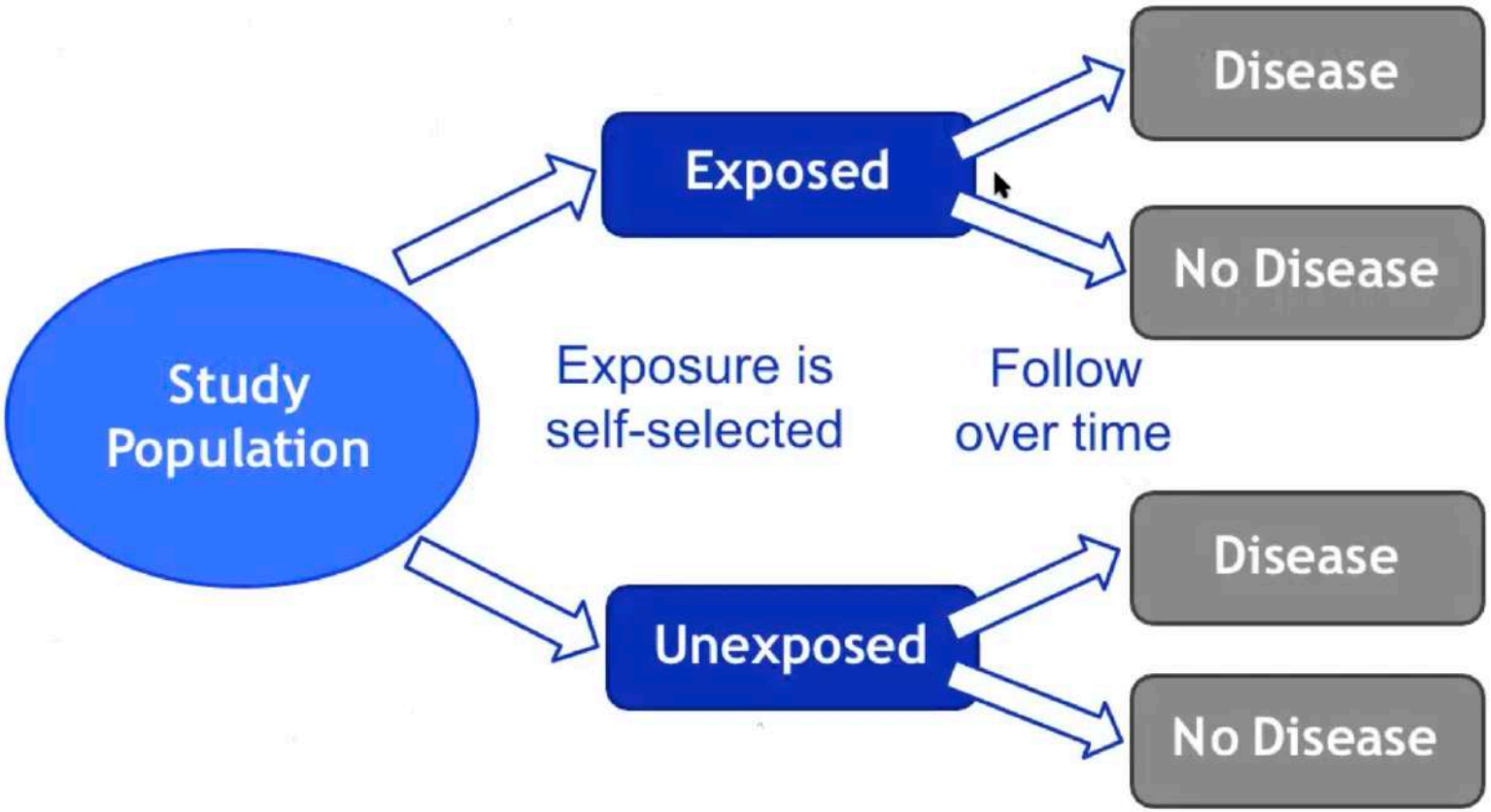
What are other examples of cohorts?

Cohort Study

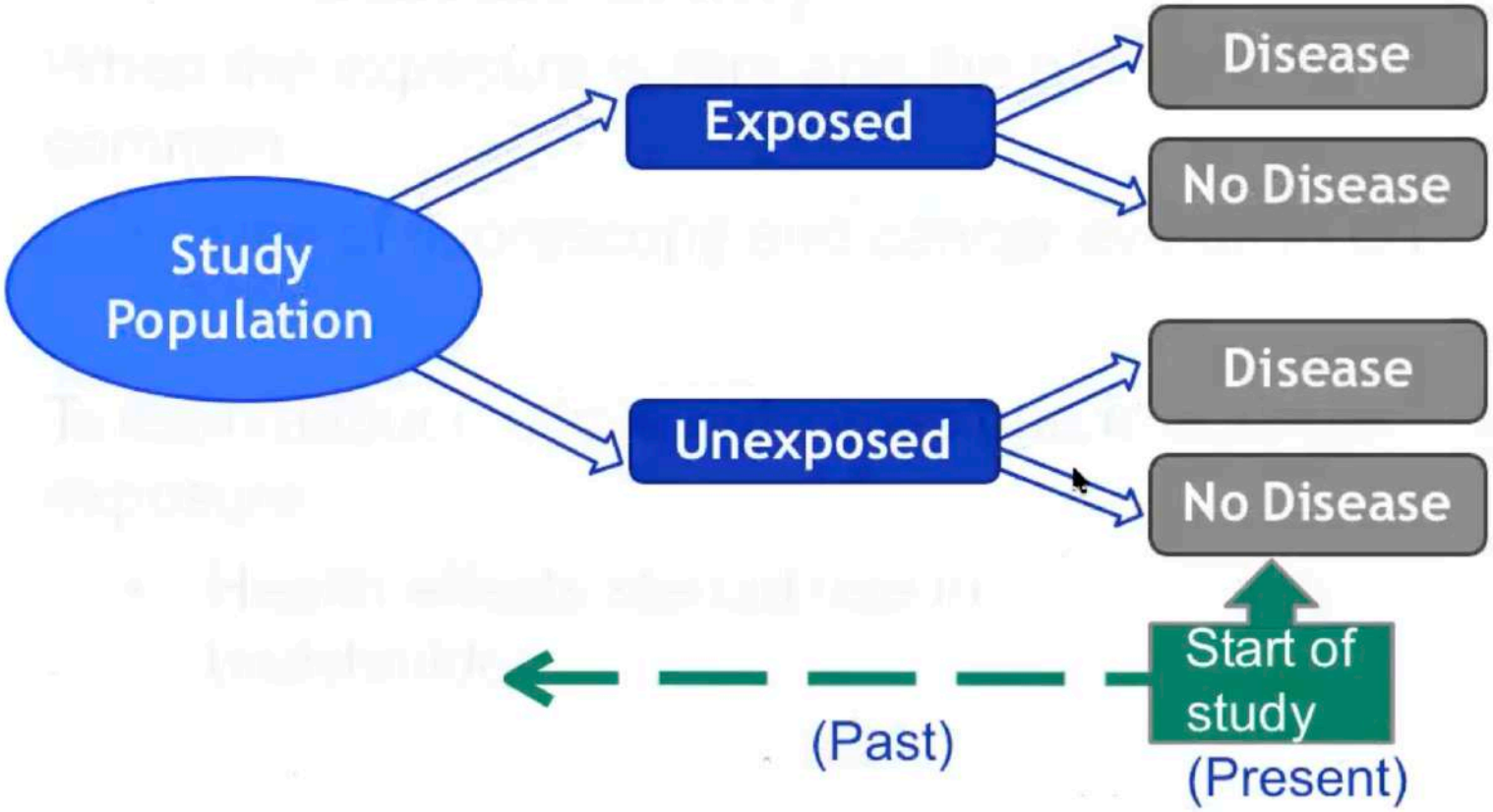
(longitudinal study, follow-up study)

- Participants classified according to exposure status and followed-up over time to ascertain outcome
- Can be used to find multiple outcomes from a single exposure
- Appropriate for rare exposures or defined cohorts
- Ensures temporality (exposure occurs before observed outcome)

Cohort Study Design



Retrospective Cohort Studies



When to Conduct a Cohort Study

When the exposure is rare and the outcome is common

- Use of fluoroscopy and cancer events in OT

To learn about multiple outcomes due to a single exposure

- Health effects steroid use in bodybuilders

Analysis of Cohort Studies

Risk:

Quantifies probability of experiencing the outcome of interest in a given population

- Calculation: Number of new occurrences of outcome/population at risk

Example:

Risk Ratio

- Can also be called Relative Risk or RR
- Quantifies a population's risk of disease from a particular exposure
- Calculation:

Risk in the exposed group /
Risk in the unexposed group

Case-Control Study

Purpose:

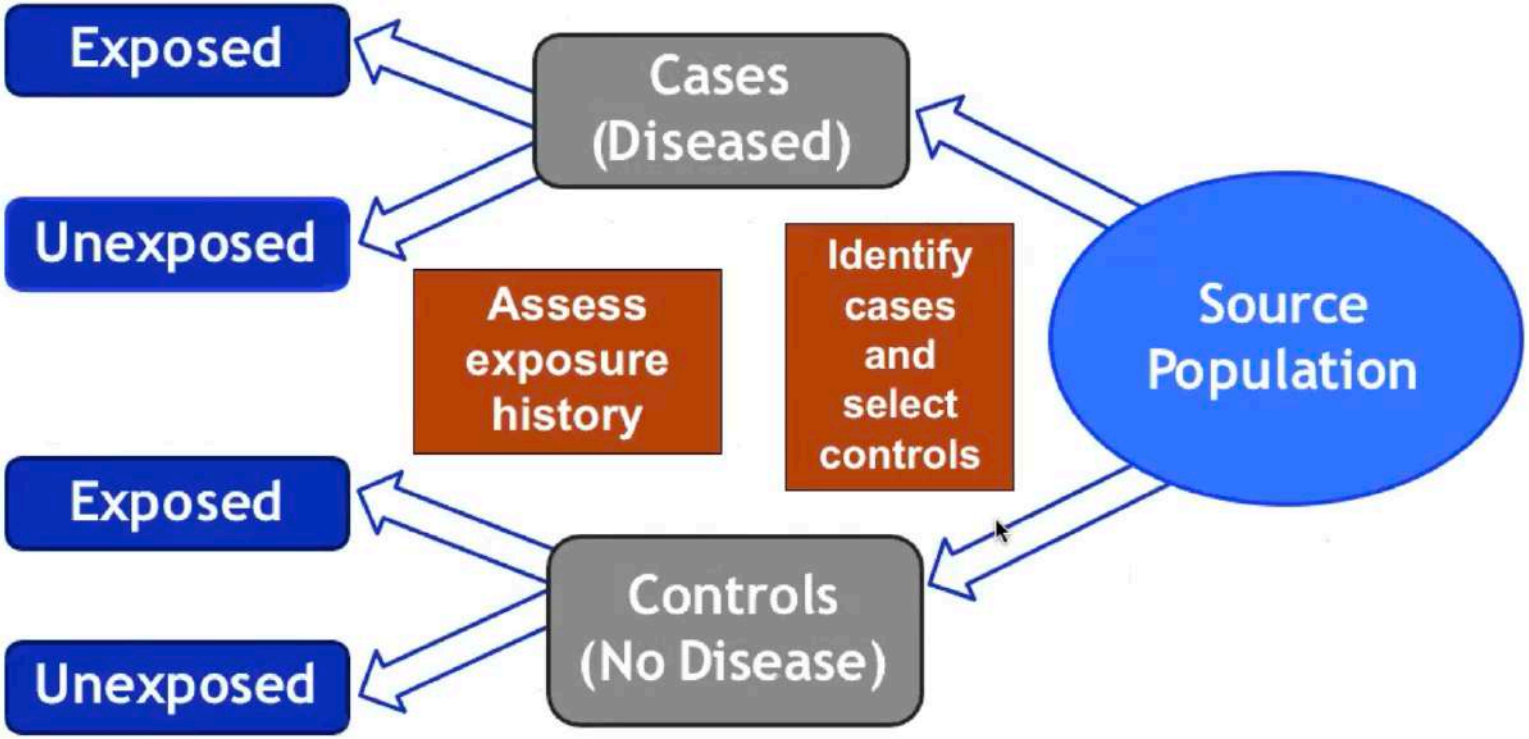
- To study rare diseases
- To study multiple exposures that may be related to a single outcome

Study Subjects

Participants selected based on outcome status:

- Case-subjects have outcome of interest
- Control-subjects do not have outcome of interest

Case-Control Study Design



When to Conduct a Case-Control Study

- The outcome of interest is rare
- Multiple exposures may be associated with a single outcome
- Funding or time is limited

Case-Control Study: Analysis Format

Exposure	Cases	Controls
Yes	a	b
No	c	d

Exposure odds ratio (OR) ≈ RR when disease is rare

Odds of being exposed among the cases = a/c
Odds of being exposed among the controls = b/d

Exposure odds ratio = (a/c)/(b/d) = (a*d)/(b*c)
(Cross-product ratio)

Example
Odds Ratio

Meniscus tear

contact sports?	Cases	Controls
Yes	17	13
No	83	87

Odds Ratio = 17/83 ÷ 13/87 = 17x87 / 13x83= 1.37

Level of Evidence

Level of Evidence

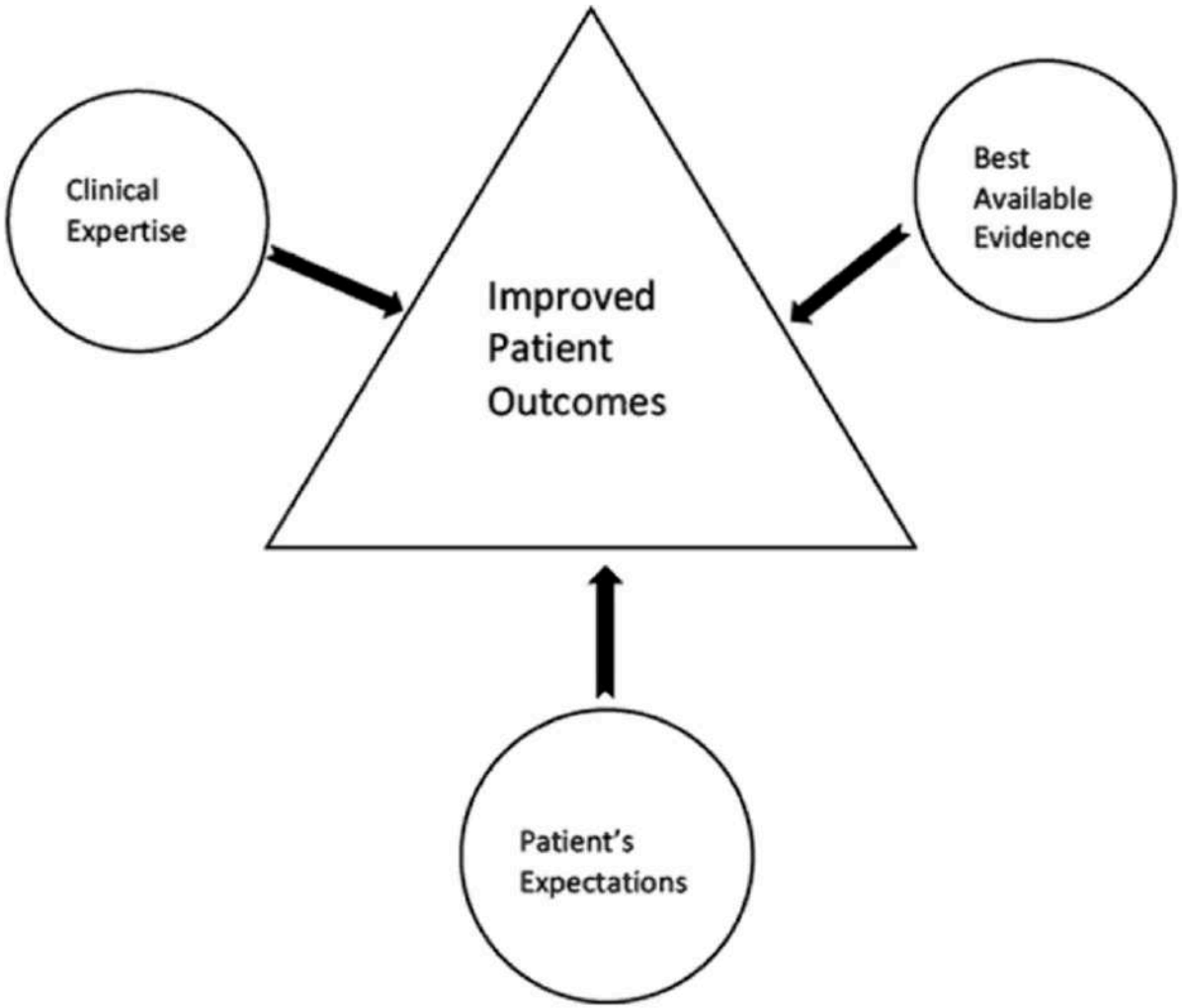
- A method utilized in the 3rd step of evidence based medicine (EBM) to determine the clinical value of a study

Evidence-based medicine (EBM) defined as 'the conscientious, explicit and judicious use of the current best evidence in making decisions about the care of individual patients.

*five steps of EBM

1. formulate an answerable question
2. gather the evidence
3. appraise the evidence
4. Implement the evidence
5. evaluate the process

Triad of evidence-based medicine



Level 1.

1.Randomized controlled trial (RCT)

- a study in which patients are randomly assigned to the treatment or control group and are followed prospectively

2.Meta-analysis of randomized trials with homogeneous results

Level 2

1.Poorly designed RCT

- •follow up less than 80%

2.Prospective cohort study (therapeutic)

- •a study in which patient groups are separated non-randomly by exposure or treatment, with exposure occurring after the initiation of the study

3.Meta-analysis of Level 2 studies

Level 3

1.Retrospective cohort study

- a study in which patient groups are separated non-randomly by exposure or treatment, with exposure occurring before the initiation of the study

2.Case-control study

- a study in which patient groups are separated by the current presence or absence of disease and examined for the prior exposure of interest

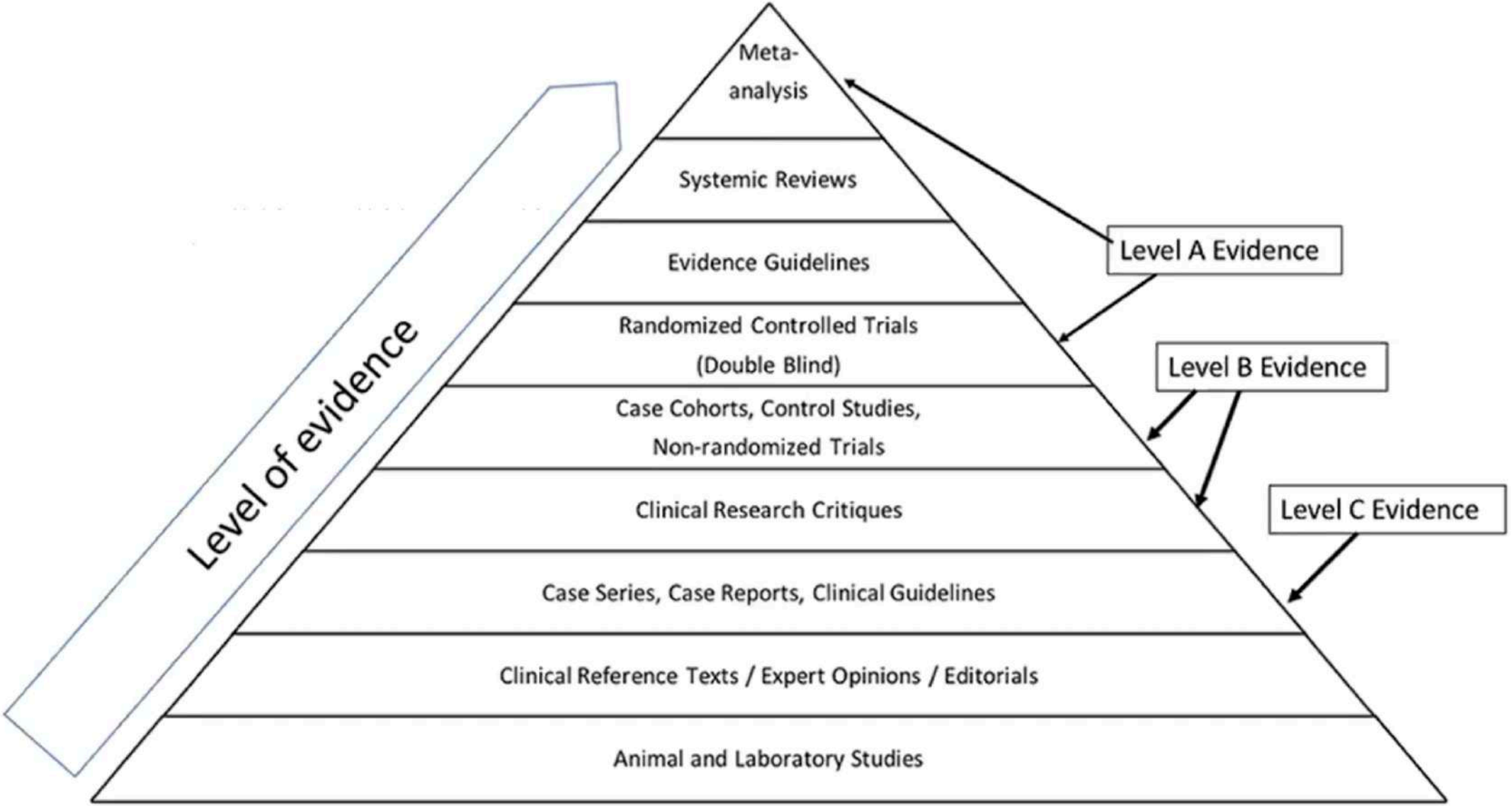
3.Meta-analysis of Level 3 studies

Level 4

Case series
a report of multiple patients with the same treatment, but no control group or comparison group

Level 5.

1. **Case report** (a report of a single case)
2. **Expert opinion**
3. **Personal observation**



Level 3

1.Retrospective cohort study

- a study in which patient groups are separated non-randomly by exposure or treatment, with exposure occurring before the initiation of the study

2.Case-control study

- a study in which patient groups are separated by the current presence or absence of disease and examined for the prior exposure of interest

3.Meta-analysis of Level 3 studies

It is naturally neither practical nor feasible to study the whole population in any study.

Hence, a set of participants is selected from the population, which is less in number (size) but adequately represents the population from which it is drawn.

Hence, true inferences about the population can be made from the results obtained.

This set of individuals is known as the “sample.”

Sample size calculation

It is naturally neither practical nor feasible to study the whole population in any study.

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•Principal of sample size

•Every individual in the chosen population should have an equal chance to be included in the sample.
•Ideally, choice of one participant should not affect the chance of another's selection

•If we include very few subjects in a study, the results cannot be generalized to the population as this sample will not represent the size of the target population. Further, the study then may not be able to detect the difference between test groups, making the study unethical.

•If we study more subjects than required, we put more individuals to the risk of the intervention, also making the study unethical, and waste precious resources, including the researchers' time.

The sample size for any study depends on the:

- Acceptable level of significance
- Power of the study
- Expected effect size
- Underlying event rate in the population
- Standard deviation in the population.

LEVEL OF SIGNIFICANCE

Alpha error/ type 1 error

"*p*" value is level of significance.

prior to starting a study we set an acceptable value for this "*p*."

Example

If we will accept a $p<0.05$ as significant, we mean that we are ready to accept that the probability that the result is observed due to chance (and NOT due to our intervention) is 5%.

Or
we are willing to accept the detection of a difference 5 out of 100 times when actually no difference exists (i.e., get a "false positive" result).

Conventionally, the *p* value of 5% ($p = 0.05$) or 1% ($p = 0.01$), which means 5% (or 1%) chance of erroneously reporting a significant effect is accepted.

POWER

Beta error/ type 2 error

another type of error where we fail to detect a difference when actually there is a difference.

detects a false negative difference

We must decide what is the false negative rate we are willing to accept to make our study adequately powered to accept or reject our null hypothesis accurately.

Power of the study = $(1 - \beta)$

The power of a study increases as the chances of committing a Type II error decrease.

Usually most studies accept a power of 80%. This means that we are accepting that one in five times (that is 20%) we will miss a real difference. Sometimes for pivotal or large studies, the power is occasionally set at 90% to reduce to 10% the possibility of a "false negative" result.

EXPECTED EFFECT SIZE

The difference between the value of the variable in the control group and that in the test drug group is known as effect size.

This difference can be expressed as the absolute difference or the relative difference.

We can estimate the effect size based on previously reported or preclinical studies

Example
If the average weight loss following one diet program is 20 kg and following another is 10 kg, the absolute effect size would be 10 kg and the relative reduction with the test intervention is 10/20, or 50%.

if the effect size is large between the study groups then the sample size required for the study is less and if the effect size between the study groups is small, the sample size required is large

UNDERLYING EVENT RATE IN THE POPULATION (prevalence rate)

This unlike the level of significance and power is not selected by convention. Rather, it is estimated from previously reported studies.

STANDARD DEVIATION (SD OR Σ)

Standard deviation is the measure of dispersion or variability in the data.

We would require a smaller sample if the population is more homogenous and therefore has a smaller variance or standard deviation

The sample size is calculated using the following formula:

$$n = \frac{2(Z\alpha + Z1-\beta)^2\sigma^2}{\Delta^2}$$

where n is the required sample size.

For Z_{α}, Z is a constant (set by convention according to the accepted α error and whether it is a one-sided or two-sided effect).

For Z1-β, Z is a constant set by convention according to power of the study as shown.

σ is the standard deviation (estimated)

Δ the difference in effect of two interventions which is required (estimated effect size).

Statistical tests

For a statistical test to be valid sample size needs to be large enough to approximate the true distribution of the population being studied.

To determine which statistical test to use, we need to know:

•whether data meets certain assumptions.

•the types of variables that we are dealing with.

Statistical assumptions

Statistical tests make some common assumptions about the data they are testing:

1.Independence of observations (a.k.a. no autocorrelation): The observations/variables you include in your test are not related
(for example, multiple measurements of a single test subject are not independent, while measurements of multiple different test subjects are independent).

2. Homogeneity of variance: the variance within each group being compared is similar among all groups. If one group has much more variation than others, it will limit the test's effectiveness.

3. Normality of data: the data follows a normal distribution (a.k.a. a bell curve). This assumption applies only to quantitative data.

Types of variables

The types of variables usually determine what type of statistical test can be used.

Quantitative variables represent amounts of things (e.g. the number of trees in a forest).

Types of quantitative variables include:

- **Continuous** (a.k.a ratio variables): represent measures and can usually be divided into units smaller than one (e.g. 0.75 grams).
- **Discrete** (a.k.a integer variables): represent counts and usually can't be divided into units smaller than one (e.g. 1 tree).

If data do not meet the assumptions of normality or homogeneity of variance, then perform **nonparametric statistical test**

Allows to make comparisons without any assumptions about the data distribution.

Categorical variables represent groupings of things (e.g. the different tree species in a forest). Types of categorical variables include:

- **Ordinal**: represent data with an order (e.g. rankings).
- **Nominal**: represent group names (e.g. brands or species names).
- **Binary**: represent data with a yes/no or 1/0 outcome (e.g. win or lose).

Choosing a parametric test: regression, comparison, or correlation

Parametric tests usually have stricter requirements than nonparametric tests.

make stronger inferences from the data.

can only be conducted with data that adheres to the common assumptions of statistical tests.

The most common types of parametric test include regression tests, comparison tests, and correlation tests.

Regression tests

Regression tests are used to **test cause-and-effect relationships**.

They look for the effect of one or more continuous variables on another variable.

	Predictor variable	Outcome variable	Research question example
Simple linear regression	•Continuous •1 predictor	•Continuous •1 outcome	What is the effect of income on longevity?
Multiple linear regression	•Continuous •2 or more predictors	•Continuous •1 outcome	What is the effect of income and minutes of exercise per day on longevity?
Logistic regression	•Continuous	•Binary	What is the effect of drug dosageon the survival of a test subject?

Comparison tests

Comparison tests look for **differences among group means**.

They can be used to test the effect of a categorical variable on the mean value of some other characteristic.

T-tests are used when comparing the means of precisely two groups (e.g. the average heights of men and women).

ANOVA and MANOVA tests are used when comparing the means of more than two groups (e.g. the average heights of children, teenagers, and adults).

	Predictor variable	Outcome variable	Research question example
Paired t-test	•Categorical •1 predictor	•Quantitative •groups come from the same population	What is the effect of two different test prep programs on the average exam scores for students from the same class?
Independent t-test	•Categorical •1 predictor	•Quantitative •groups come from different populations	What is the difference in average exam scores for students from two different schools?
ANOVA	•Categorical •1 or more predictor	•Quantitative •1 outcome	What is the difference in average pain levels among post-surgical patients given three different painkillers?
MANOVA	•Categorical •1 or more predictor	•Quantitative •2 or more outcome	What is the effect of flower specieson petal length, petal width, and stem length?

Correlation tests

Correlation tests **check whether two variables are related** without assuming cause-and-effect relationships.

	Predictor variable	Outcome variable	Research question example
Pearson	Continuous	Continuous	How are latitude and temperature related?
Chi-Square	Categorical	Categorical	How is membership in a sports team related to membership in drama club among high school students?

Nonparametric test

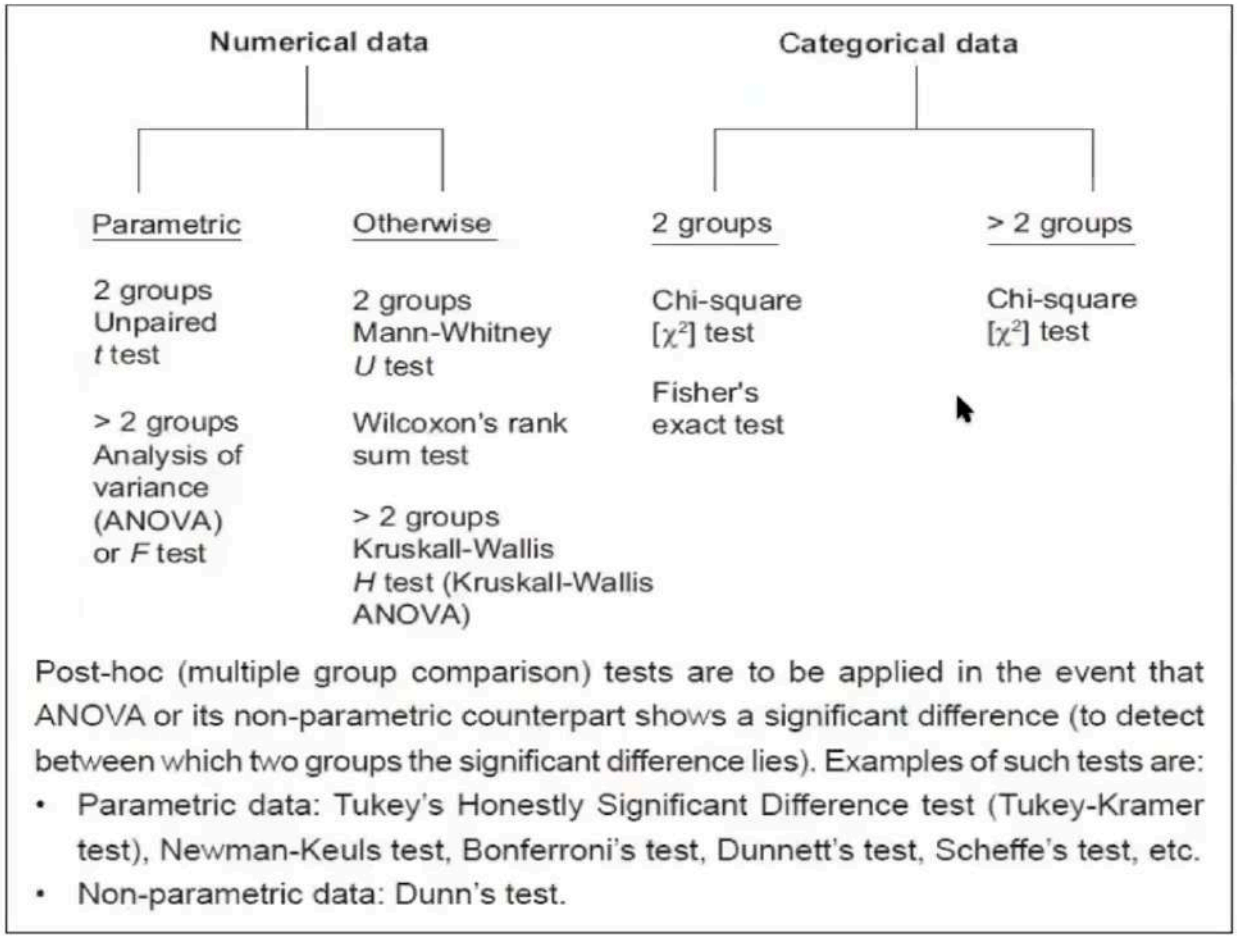
Non-parametric tests don't make as many assumptions about the data, and are useful when one or more of the common statistical assumptions are violated.

However, the inferences they make aren't as strong as with parametric tests.

	Predictor variable	Outcome variable	Use in place of...
Spearman	•Ordinal	•Ordinal	Regression and correlation tests
Sign test	•Categorical	•Quantitative	T-test
Kruskal–Wallis	•Categorical •3 or more groups	•Quantitative	ANOVA
ANOSIM	•Categorical •3 or more groups	•Quantitative •2 or more outcome variables	MANOVA
Wilcoxon Rank-Sum test	•Categorical •2 groups	•Quantitative •groups come from different populations	Independent t-test
Wilcoxon Signed-rank test	•Categorical •2 groups	•Quantitative •groups come from the same population	Paired t-test

Tests to address the question: Is there a difference between groups – unpaired (parallel and independent groups) situation?

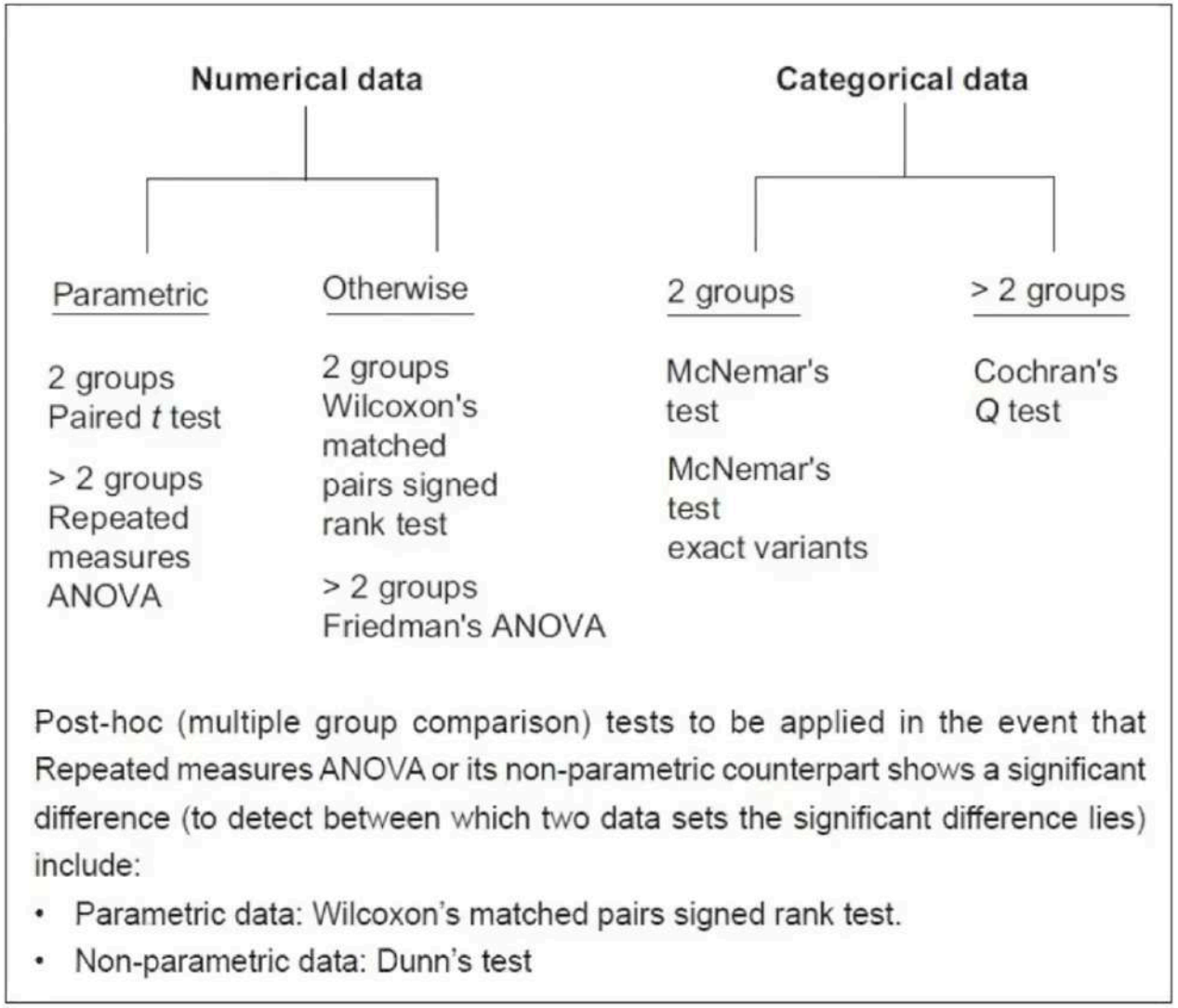
*Groups or data sets are regarded as unpaired if there is no possibility of the values in one data set being related to or being influenced by the values in the other data sets.



Post-hoc (multiple group comparison) tests are to be applied in the event that ANOVA or its non-parametric counterpart shows a significant difference (to detect between which two groups the significant difference lies). Examples of such tests are:

- Parametric data: Tukey's Honestly Significant Difference test (Tukey-Kramer test), Newman-Keuls test, Bonferroni's test, Dunnett's test, Scheffe's test, etc.
- Non-parametric data: Dunn's test.

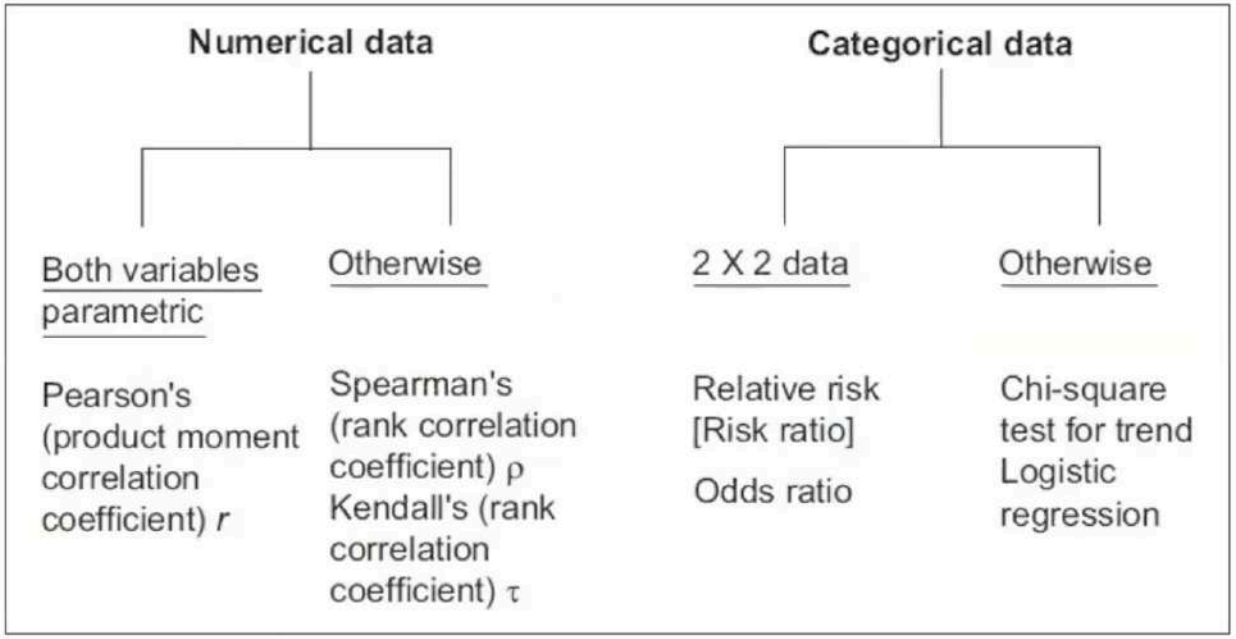
Tests to address the question: Is there a difference between groups – paired situation?



Post-hoc (multiple group comparison) tests to be applied in the event that Repeated measures ANOVA or its non-parametric counterpart shows a significant difference (to detect between which two data sets the significant difference lies) include:

- Parametric data: Wilcoxon's matched pairs signed rank test.
- Non-parametric data: Dunn's test

Tests to address the question: Is there an association between variables?



Journal Impact Factor

Frequently used as an indicator of the importance of a journal to its field

widespread misconception ????

The IF of a journal is not associated to the factors like quality of peer review process and quality of content of the journal.

It is a measure that reflects the average number of citations to articles published in journals, books, thesis, project reports.

Commonly used to evaluate the relative importance of a journal within its field and to measure the frequency with which the "average article" in a journal has been cited in a particular time period

Journal which publishes more review articles will get highest IFs.

Journals with higher IFs believed to be more important than those with lower ones

Impact factor can be calculated after completing the minimum of 3 years of publication.

IF cannot be calculated for new journals.

The journal with the highest IF is the one that published the most commonly cited articles over a 2-year period.

The IF applies only to journals, not to individual articles.

The relative number of citations an individual article receives is better evaluated as “citation impact.”

In a given year, the IF of a journal is the average number of citations received per article published in that journal during the 2 preceding years.

IFs are calculated each year by Thomson scientific for those journals that it indexes, and are published in Journal Citation Reports

Example

If a journal has an IF of 3 in 2008, then its papers published in 2006 and 2007 received three citations each on average in 2008.

The 2008 IFs are actually published in 2009; they cannot be calculated until all of the 2008 publications have been processed by the indexing agency (Thomson Reuters).

Formula of IF

2012 impact factor = A / B

Where A is the number of times articles published in 2010 and 2011 were cited by indexed journals during 2012. B is the total number of citable items like articles and reviews published by that journal in 2010 and 2011.

Limitation

- IF does not accurately reflect the quality of individual articles published in a journal.
- Journals with more issues and articles can have higher Impact Factors which could be misleading as it does not really reflect the quality of articles
- Review articles (which tend to receive more citations), editorials, letters, and news items are not counted in article total but if cited are counted as citations for the journal.
-
- Clinical journals usually have low citation counts. This puts such journals at a disadvantage with research journals in the field that have higher citation counts.

TRAUMA SYSTEM DESIGN

Trauma Centre is a healthcare institution that has

- Resources
- capabilities necessary to provide trauma services at a particular level to injured patients

criteria

strict requirements for staffing, specialist availability, response times, training, quality improvement and community education.

Trauma Care Facilities have been categorized into four levels:

Level IV trauma care:

This would be provided by appropriately equipped and manned mobile hospital / ambulances.

Level III Trauma Care Facility

Provides initial evaluation and stabilization (surgically if appropriate) to the trauma patient.

Comprehensive medical and surgical inpatient services.

Emergency doctors and nurses are available round the clock.

Physicians, surgeons, Orthopaedic surgeon and Anaesthetist would be available round the clock to assess, resuscitate, stabilize and initiate transfer as necessary to a higher-level Trauma Care Service.

Limited intensive care facility, diagnostic capability, blood bank and other supportive services.

The district/ tehsil hospitals with a bed capacity of 100 to 200 beds would be selected for level III care.

Level II Trauma Care Facility

Provides definitive care for severe trauma patients.

Emergency physicians, surgeons, Orthopaedicians and Anaesthetists are in-house.

On-call facility for neurosurgeons, pediatricians.

Emergency department, intensive care unit, blood bank, rehabilitation services, broad range of comprehensive diagnostic capabilities, and supportive services.

The existing medical college hospitals or hospitals with bed strength of 300 to 500 identified as Level II Trauma Center.

Level I Trauma Care Facility

Provide the highest level of definitive and comprehensive care for patient with complex injuries.

Emergency physicians, nurses and surgeons would be in-house and available to the trauma patient immediately on their arrival.

The services of all major super specialties associated with trauma care would be available 24*7.

Situated at essentially at a distance of less than 750 to 800 kms apart.

Level I Trauma Centres need not necessarily be along with the Highways corridor.

Level I Trauma Centres should be only in medical college hospitals.

TRAUMA CENTER vs EMERGENCY DEPARTMENT

The difference between an emergency department and a trauma center is both a **matter of law and a matter of degree.**

As a matter of law,

all hospitals are required to promptly attend to all medical emergencies and hence must have emergency services.

As a matter of degree,

emergency departments are designed for a broad scope of minor to severe medical emergencies while a trauma center has a focused scope of practice and strict requirements for staffing, specialist availability and response times to cater specifically to the critically injured.