About OMICS Group

OMICS Group International is an amalgamation of Open Access publications and worldwide international science conferences and events. Established in the year 2007 with the sole aim of making the information on Sciences and technology 'Open Access', OMICS Group publishes 400 online open access scholarly journals in all aspects of Science, Engineering, Management and Technology journals. OMICS Group has been instrumental in taking the knowledge on Science & technology to the doorsteps of ordinary men and women. Research Scholars, Students, Libraries, Educational Institutions, Research centers and the industry are main stakeholders that benefitted greatly from this knowledge dissemination. OMICS Group also organizes 300 International conferences annually across the globe, where knowledge transfer takes place through debates, round table discussions, poster presentations, workshops, symposia and exhibitions.

About OMICS Group Conferences

OMICS Group International is a pioneer and leading science event organizer, which publishes around 400 open access journals and conducts over 300 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

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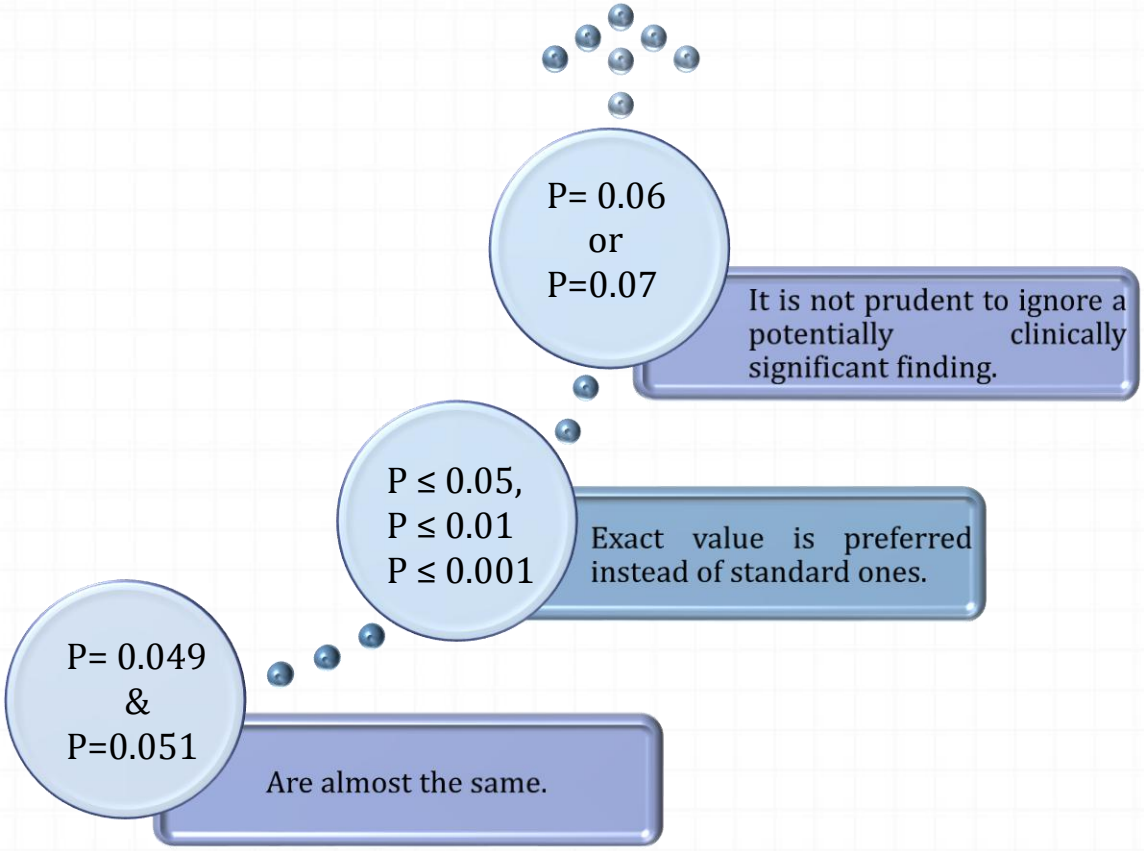
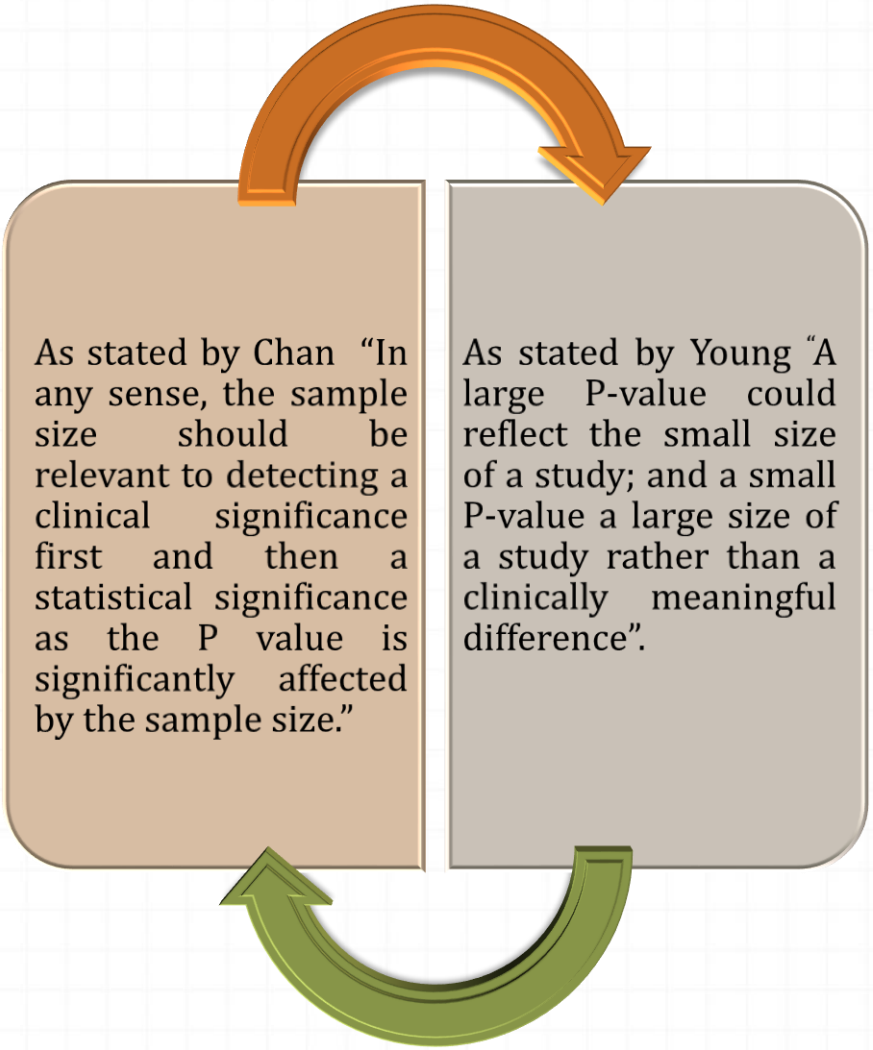
Workshop on Statistical Versus Clinical Significance.

Fisher – "This fixed level was **"absurdly academic"** & should be flexible based on the evidence"

"Guideline only; not an all or none phenomenon"

Subdividing P value which is essentially a continuous scale, into **'significant' and 'non-significant'** amounts to gross oversimplification - a poor statistical practice.

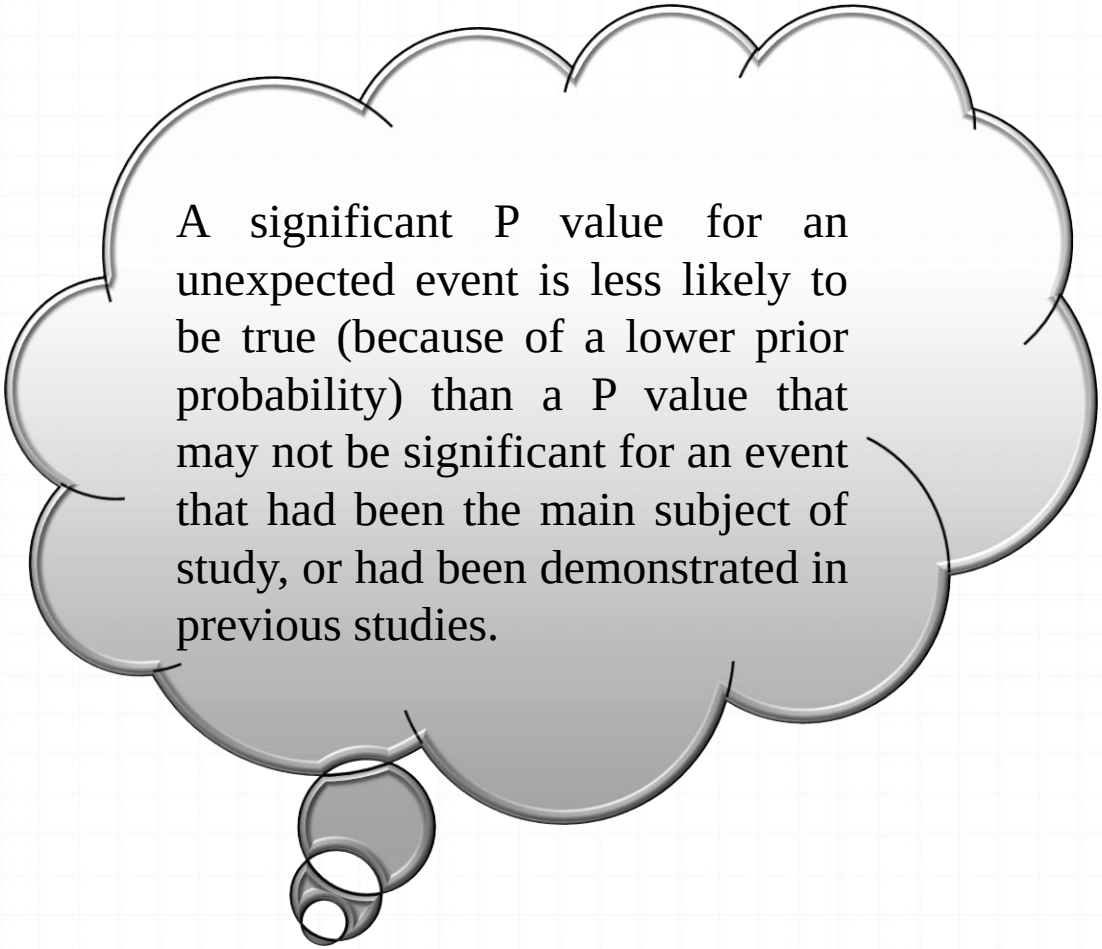




For every 20 hypotheses tests that are performed one significant finding will emerge just by chance-

Multiple hypotheses testing or data dredging or fixing expedition.

Bayesian Approach

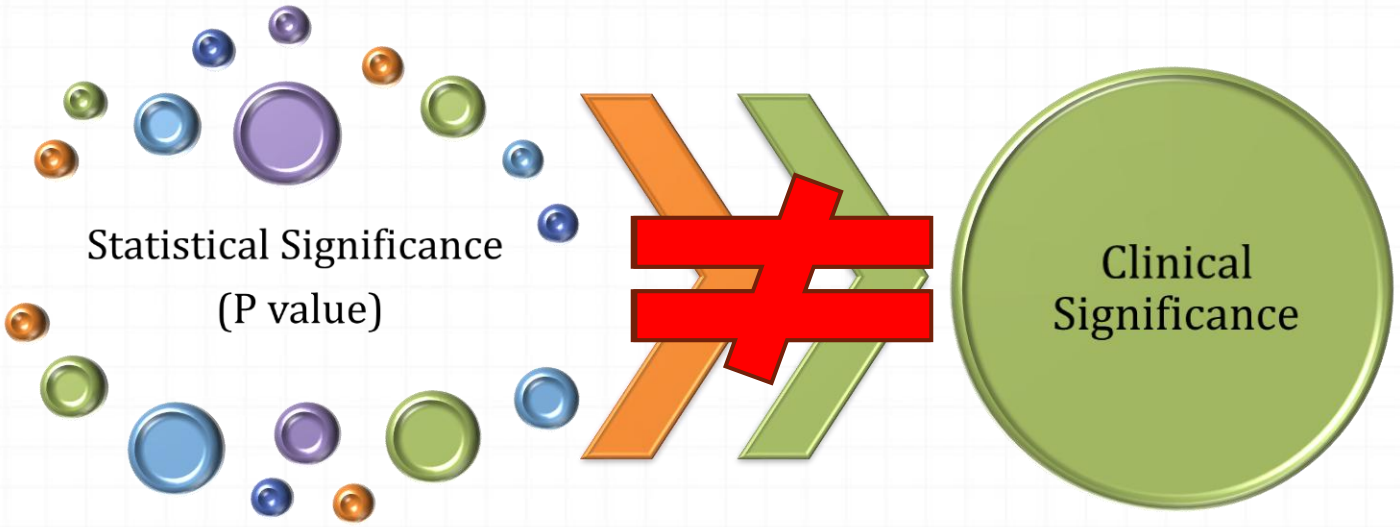


Consider the totality of knowledge

Statistical significance is a function of many factors such as……..

- The magnitude of the effect.
- The sample size.
- The reliability of the effect (i.e., is the treatment equally effective for all the patients?).
- The reliability of the measuring instrument.

Statistical Versus Clinical Significance



Measure of chance occurrence.

Measure of clinically important effect.

Manipulation of data-unethical.

But currently, there is too great a reliance on using statistical significance testing or hypothesis testing to detect a statistically significant difference between therapies, which then often is used to infer that a therapy supplied clinically meaningful result.

Burns stated in this context "If we go around manipulating the research after the event to suit our wishful thinking, there is no reason to do the experiment in the first place and we might as well believe anything we want to believe".

Serious threat to the integrity of scientific research.

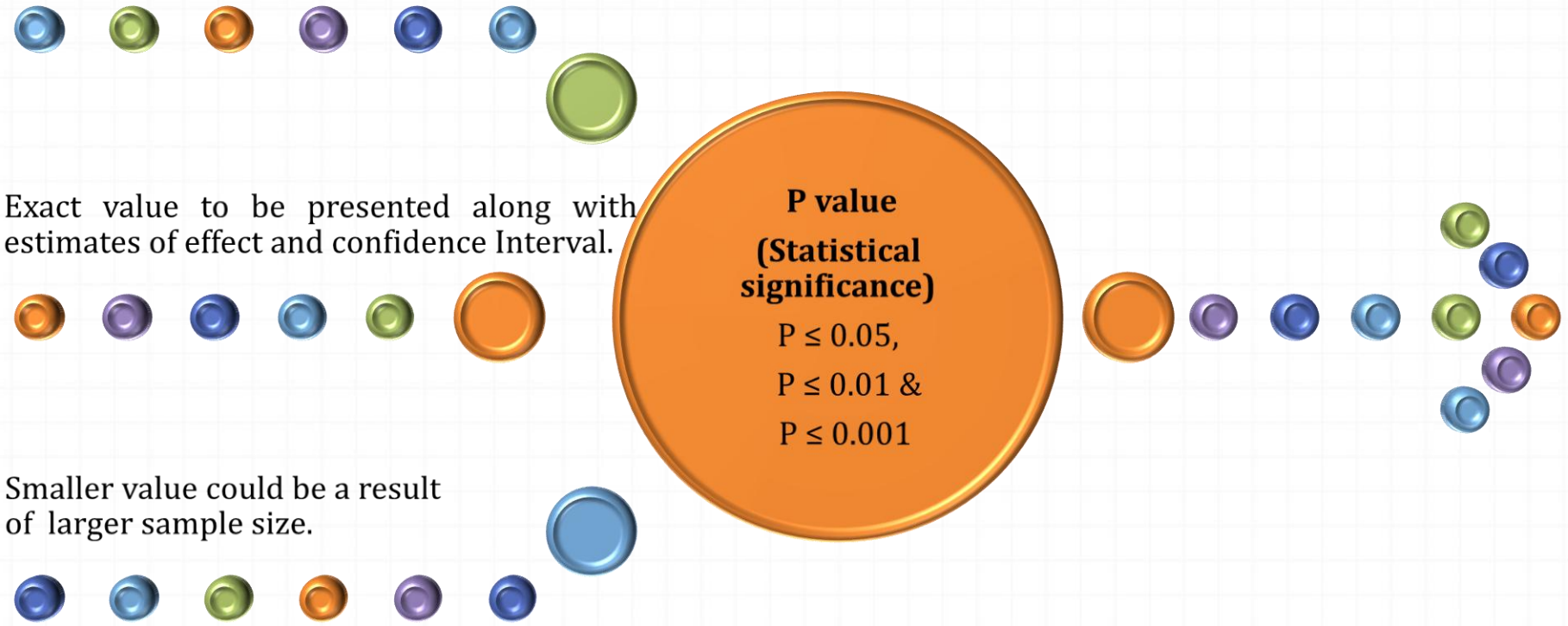
Concerns from the proponents of meta-analysis.

How to compare treatment effects across different studies when the traditionally reported statistical significance tests were contaminated by all those other factors ????

Larger value could be a result of smaller sample size.

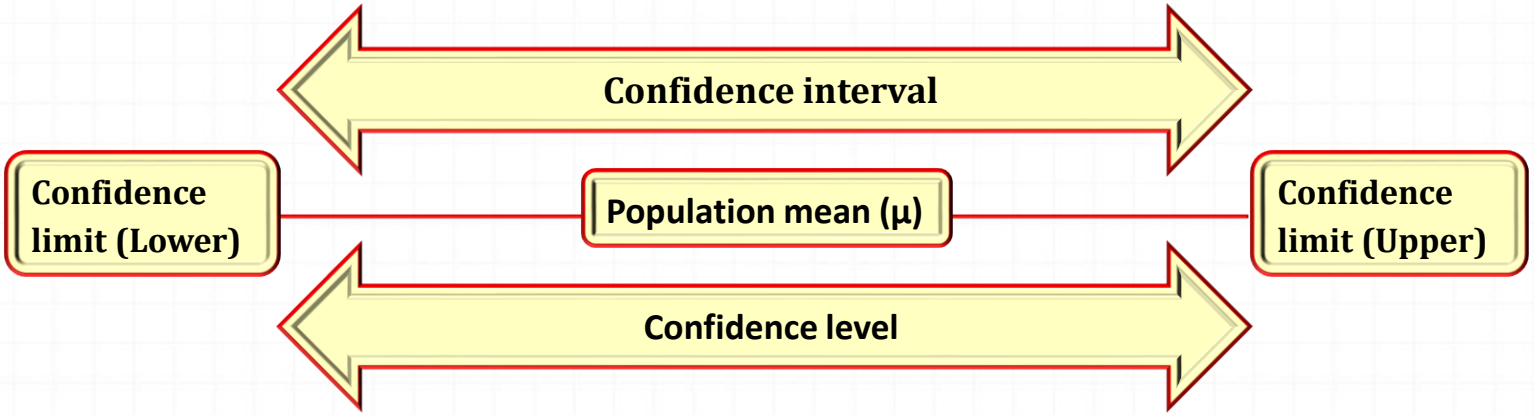
Exact value to be presented along with estimates of effect and confidence Interval.

Smaller value could be a result of larger sample size.



Confidence Interval

Range of values within which we are willing to assert with a specified level of confidence that an unknown population mean or any other parameter lies.

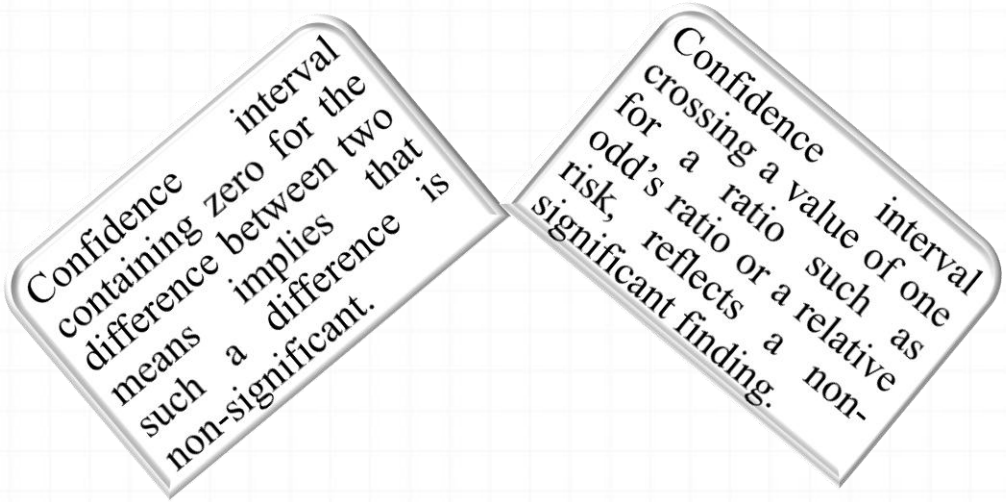


Confidence interval (CI) = $\bar{X} \pm 1.96$ SE (corresponding to 95% confidence level).

Corresponding values for multiplication with SE for 90% & 99% are 1.645 & 2.58.

Multiplication factors for confidence intervals based on the t-distribution

Sample size	10	20	30	40	50	200
Multiplication factor	2.26	2.09	2.05	2.02	2.01	1.97



The smallest amount of change in the outcome (effect size) that could be considered clinically important or relevant to clinical practice by most of the clinicians.

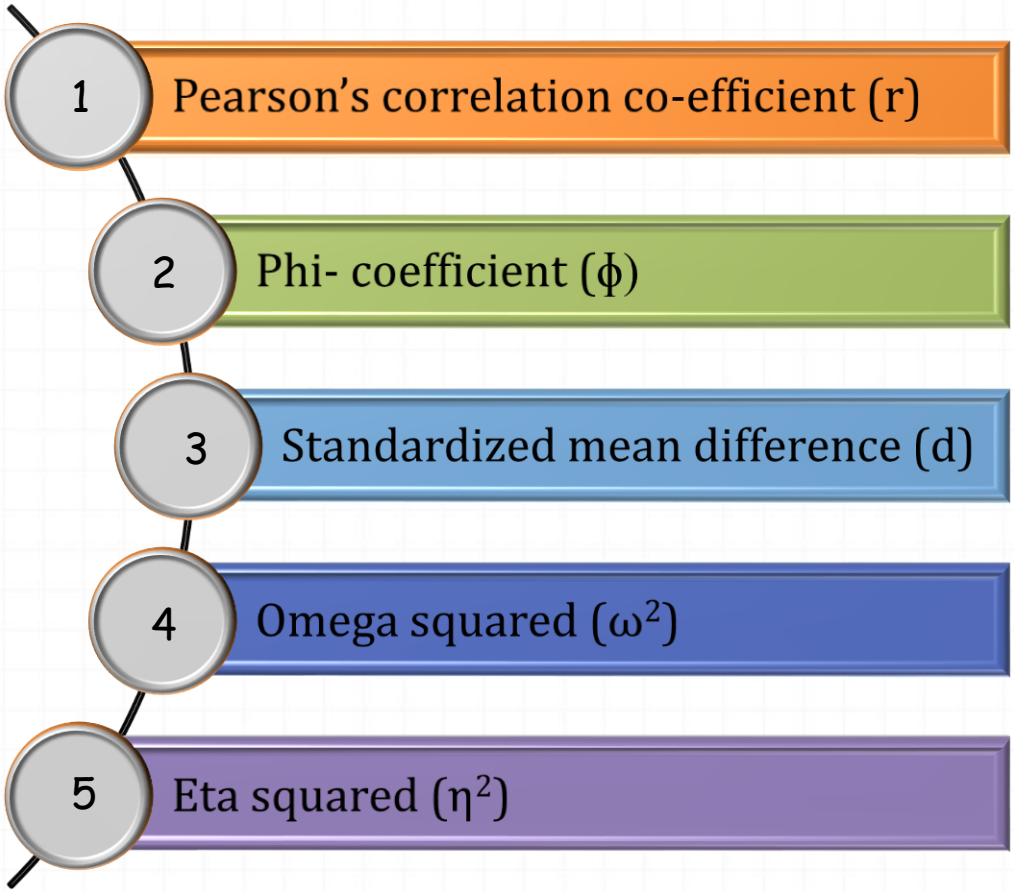
Effect size is a standard and hence an objective measure of the magnitude of an observed difference in an experimental manipulation or the strength of the relationship between variables.

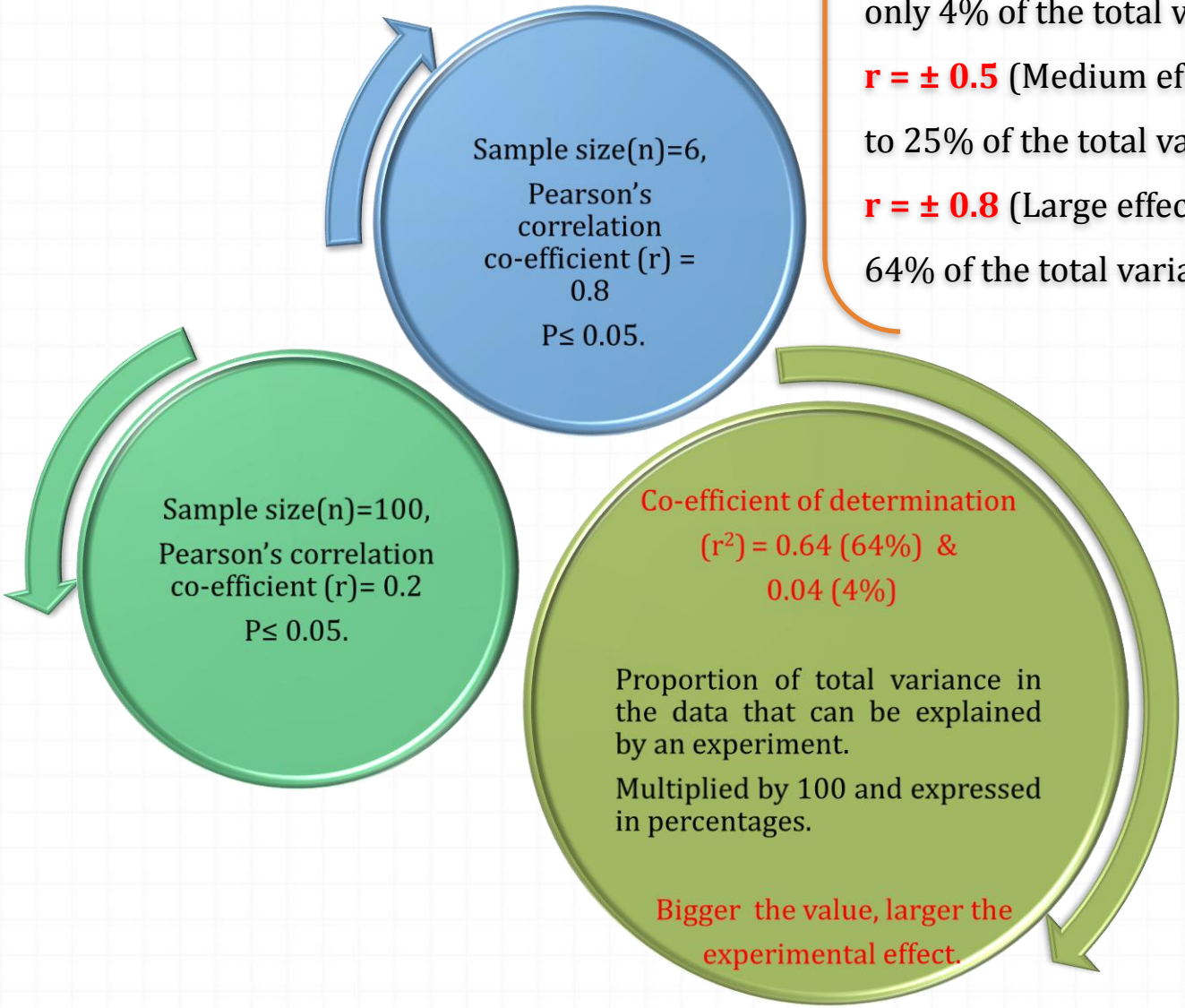
Clinical significance - a change that may alter, how a clinician will treat a patient.

There is however, no precise way to define clinical relevance regarding how small an improvement is meaningful in every situation and this value judgment varies depending upon the situation.

Since the measurement is standardized it is comparable across studies that have used different scales of measurements for the quantification of same variable or different variables.

Measures of effect size





r = ± 0.2 (Small effect accounting to only 4% of the total variance)

r = ± 0.5 (Medium effect accounting to 25% of the total variance)

r = ± 0.8 (Large effect accounting to 64% of the total variance)

Standardized mean difference (d)

0

$$d = \frac{\text{Experimental group mean} - \text{Control group mean}}{\text{Pooled within group standard deviation}}$$

$$\text{Pooled within group standard deviation} = \sqrt{\frac{(n_1-1)s_1^2 + (n_2-1)\,s_2^2}{n_1+n_2-2}}$$

n_1 and s_1 represent sample size and standard deviation of 1^{st} group respectively.

n_2 and s_2 represent sample size and standard deviation of 2^{nd} group respectively.

Interpretation:

- $d < 0.2$ (Small effect)
- $d = 0.2 - 0.5$ (Medium effect)
- $d < 0.5$ (Large effect)

Hands on : Statistical Versus Clinical Significance

Example–1. Comparative evaluation of two different salivary stimulants for their effectiveness to improve unstimulated whole salivary flow rate in two groups of elderly patients (different patients in each group) undergoing radiation therapy for head and neck cancer, given the following details;

Sample size in each group (n_1 & n_2) –10.

Group means – 0.2 & 0.1 mL/min respectively.

Standard deviations – 0.15 & 0.06 respectively.

'α' fixed at 5% ($P \leq 0.05$) and 'β' at 20% (0.2) or power at 80%.

Hands on : Statistical Versus Clinical Significance

Example–2. Comparative evaluation of two different drugs for their effectiveness in reducing the diastolic blood pressure among two groups of elderly patients (different patients in each group) given the following details;

Sample size in each group (n_1 & n_2)–215.

Group means – 97 & 95 mm Hg respectively.

Standard deviations – 11 & 10 respectively.

'α' fixed at 5% ($P \leq 0.05$) and 'β' at 20% (0.2) or power at 80%.

A small sample size can only detect a very strong effect. Hence, if a study with small sample size manages to be significant, that significance must be due to a large effect size. Whereas a study with a large sample size that is statistically significant may or may not have a large effect size.

Number Needed to Treat (NNT)

An attractive means of summarizing the results of a clinical trial in a single figure.

A measure of the effectiveness of a treatment/therapy or a preventive measure in achieving a dichotomous outcome.

Reciprocal of Absolute Risk Reduction(ARR)/ risk difference.

Estimates the number of patients who need to be treated in order to obtain one more success in the experimental group than that obtained in the control group.

Conversely, it refers to the number of patients who need to be treated in order to prevent one additional adverse outcome in the experimental group as compared with the control group.

"Difference between the proportion of adverse events in the control group and the intervention group".

Hands on : Number Needed to Treat (NNT)

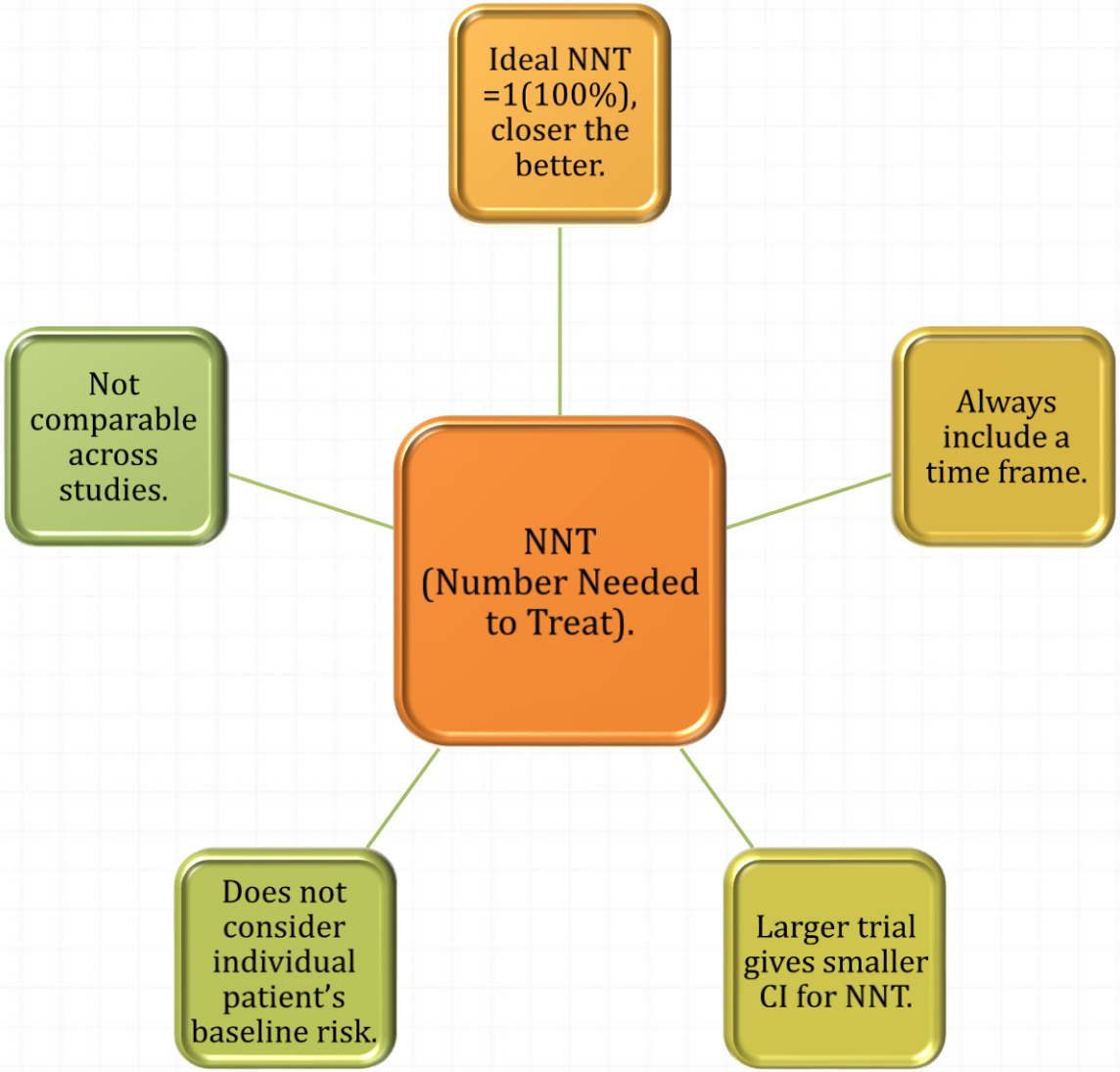
Example–1. Estimation of number needed to treat(NNT) for the two different treatment modalities (R_{X1} & R_{X2}) aimed at 5–year survival rates for carcinoma of tongue.

Intervention	No of patients survived	No of patients died	Total
R_{X1} (New therapy)	60	40	100
R_{X2} (Conventional therapy)	40	60	100

$$NNT = \frac{1}{ARR} = \frac{1}{(0.6-0.4)} = \frac{1}{0.2} = 5$$

(one in every 5 patients will benefit from the treatment).

Smaller the NNT, the more successful the intervention.



"We need to remember the absolute risk reduction(ARR)scale when trying to interpret the number needed to treat (NNT) and its confidence interval."

Hands on : Number Needed to Treat (NNT)

Example–2. Estimation of number needed to treat (NNT) for antiretroviral Pre-Exposure prophylaxis (PrEP) for contracting HIV infection in high-risk individuals compared to Placebo in 2 years.

Intervention	No of individuals contracting HIV infection	No of individuals prevented from contracting HIV infection	Total
PrEP	50	50	100
Placebo	52	48	100

$$NNT = \frac{1}{ARR} = \frac{1}{(0.52-0.5)} = \frac{1}{0.02} = 50$$

(one in every 50 patients will be prevented from contracting HIV infection).

The 95% confidence interval for the NNT ranges from -8.4 to 6.3.

Number Needed to Harm (NNH)

A negative NNT - indicates that the intervention has a higher proportion of adverse outcomes (harmful) than the control treatment.	A useful measure for assessing the relative benefits of a treatment with known side effects.

NNTB (Benefit) / NNTH (Harm)

Drug A prevents heart attack(Myocardial Infraction)but also increases the risk of lung cancer. A placebo-controlled randomized trial in 200 individuals(100 in each arm) found that 15 and 30 heart attacks were observed in the treated and placebo groups respectively over a period of 5 years. Also the corresponding numbers for lung cancer in the two groups were 10 and 1.

NNT 7 vs NNH12 ✓

NNT34 vs NNH12 ✘

If a clinical end point is devastating enough without the drug (e.g. death, heart attack) drugs with a low NNH may still be indicated in such situations as long as the NNT < NNH. However, for a drug with high NNT a small NNH may overweigh the benefits.

When is the difference between two therapies large enough for you to alter your practice?

Magnitude of benefit of each treatment.

The respective profiles of side effects of the two treatments.

Their relative costs (e.g. Drug A-$2 each, Drug B-$1 each ARR -20% in favour of drug A and NNT =5).

Your comfort with prescribing a new therapy.

The patient's preferences and so on….

Take home message……..

Statistical and clinical significances are not mutually exclusive; instead complementary in reporting the results of a clinical research. Henceforth, researchers should abandon the only use of the p-value interpretation.

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THANK
YOU!


Welcome


PROBLEM SOLVING

A study comparing the Body Mass Index(BMI) of two groups of men and women (15 each) found a mean difference of 1.5 Kg/m^2 and a standard error (SE) of 1kg/m^2. Calculate, interpret and comment on the confidence interval(CI) for the mean difference (Note: Multiplication factor for CI based on t distribution is 2.05 for the sample size of 30).

$$CI = 1.5 \pm (2.05 \times 1)$$

$$CI = 1.5 \pm 2.05$$

$$CI = -0.55 \text{ to } 3.55$$

Non-significant – Probably because of the inadequate sample size.

Pearson's correlation coefficient (r) for the effect of a specific calcium supplement on serum calcium levels in a sample of 500 patients before and after its supplementation has a value of 0.14 which is significant at p=0.046. Calculate the Co-efficient of determination (i.e., r^2 - expressed in percentage).

$$r^2 = 0.14 \times 0.14$$

$$r^2 = 0.0196$$

$$r^2(\%) = 0.0196 \times 100$$

Co-efficient of determination (r^2)= $1.96 \approx 2\%$

Calculate and interpret Number Needed to Treat (NNT) for the following :

Intervention	No of individuals with xerostomia	No of individuals without xerostomia	Total
Radiation therapy	24	76	100
Control	22	78	100

$$NNT = \frac{1}{ARR} = \frac{1}{(0.22-0.24)} = \frac{1}{-0.02} = -50$$

(one in every 50 patients will be harmed by the therapy).


Thank you
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