Editing file

Feedback

Statistical significance using confidence intervals

Objectives:

1. To be able to understand the concept of confidence intervals.
2. To be able to apply the concepts of statistical significance using confidence intervals in a Analyzing data.
3. To be able to interpret of concept of 95% confidence intervals in making valid conclusions.

Click here for the practical

26th lecture

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MED439

Research Team

RESEARCH TEAM 438

Statistical significance using confidence intervals

Note: No need to memorize formula, No calculation in final Exam.
focus on Concepts and interpretation.
10-15 Question from these 2 lectures (P value and C.I)(5-7 marks) in final exam

Statistic and Parameter

Statistic	Parameter
✓ An observed value drawn from the **sample.**	✓ The corresponding value in a **population**

- We measure, analyze, etc **statistic** and translate them as **parameters**.
- Sample is assumed to be **representative** to the population.
- In research: measurements are **always** done in the sample, the results will be applied to population.

Hypothesis testing (p value) & Estimation (confidence interval) (both of them are statistical inference)

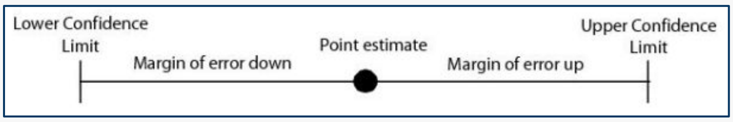
Two form of estimation

Point estimation[1] = single value,e.g.

(mean, proportion, difference of two means, difference of two proportion, odds ratio(OR), relative risk (RR), Prevalence, incidence etc,)

Interval estimation = range of value.

= **Confidence interval(CI).** A confidence interval consist of:



Confidence intervals

- **P values** give **no indication** about **clinical importance** of the observed association.
- Relying on information from a sample will always lead to some level of uncertainty.
- **Confidence interval** is a range of values that tries to quantify this uncertainty:
  - For example: 95% CI mean that under repeated sampling 95% of C.Is will contain the true population parameter.

1-Anything calculated from the sample

Statistical significance using confidence intervals

Computing confidence intervals (CI)

General formula:
(sample statistic) ± [(confidence level) x (measure of how high the sampling variability is?)].

Sample statistic: observed magnitude of effect or association (e.g.,odds ratio , risk ratio, single mean, single proportion, difference in two mean, difference in two proportions, correlation, regression coefficient, etc...).

Confidence interval: varies — 90%, 95% (we use it most of the time), 99%.
For example, to construct a 95% confidence interval $Z_{\alpha/2} = 1.96$

Sampling variability: Standard error (S.E.) of the estimate is a measure of variability. What is the measuring of the sampling variability ? Standard error

Example :

Data: X = [6, 10, 5, 4, 9, 8]
N=6

Mean: $\bar{X} = \sum x / N$ (no. Of sample) = 42/6 = 7

Variance = $S^2 = \sum(X-\bar{X})^2 / N = 28/6 = 4.67$

Standard deviation = $\sqrt{S^2} = \sqrt{4.67} = 2.16$
The standard deviation measures how each X value (6, 10,5, 4, 9, 8) on average is deviating from the mean ($\bar{X}$=7)

X	$X-\bar{X}$	$(X-\bar{X})^2$
6	-1	1
10	3	9
5	-2	4
4	-3	9
9	2	4
8	1	1
42 (total)	0 (total)	28 (total)

Statistical inference is based on sampling variability

Sample statistic

We summarize a sample into one number; e.g., could be a mean , a difference in means or proportions, an odds ratio, or a correlation coefficient
E.g.: average blood pressure of a sample of 50 Saudi men
E.g.: the difference in average blood pressure between a sample of 50 men and a sample of 50 women

Sample variability

If we could repeat an experiment many, many times with different samples on the same number of subjects, the resultant sample statistic would not always be the same (because of chance).

Standard error

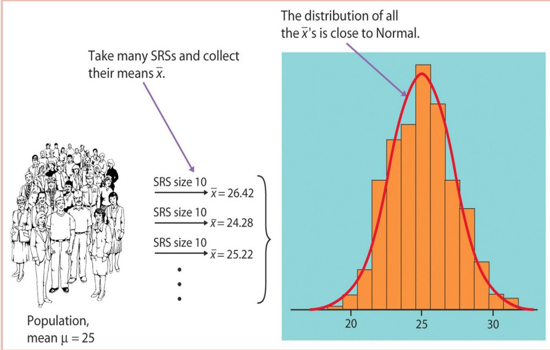
A measure of the sampling variability.
Don't get confused with the terms of **standard deviation** and **standard error**

Statistical significance using confidence intervals

Standard error of the mean[1] (sem)

$S_{\bar{x}}$ = sem = S / √N
n = sample size
s = standard deviation

- Even for large **s**, if **n** is large, we can get good precision for sem[2]
- ★ Standard error of the mean (sem) is **always smaller** than standard deviation (s).



We have different samples and different values but some are close to the population and some are away so how much the variabilities **among** the different sample means? This is nothing but standard error.

You can calculate the standard error from the standard deviation

$$SE = \frac{\sigma}{\sqrt{n}}$$

σ ← Standard deviation
n ← Number of samples

Example

In representative sample of 100 observations of heights of men, drawn at random from a large population, suppose the sample mean is found to be 175 cm (standard deviation = 10cm).
Can we make any statement about the population mean ?

- We can not say that population mean is 175 cm because we are uncertain As to how much sampling fluctuation has occurred.
- What to do instead is to determine a range of possible values for population mean, with 95% of confidence[3].
- This range is called the 95% confidence interval and can be important adjuvant to significance test.

In the example , n= 100, sample mean= 175, S.D,=10, and the S, Error = 10/√100 = 1

- Using the general format of confidence interval :
  Statistic ± confidence factor x Standard Error of statistic
- **Therefore the 95% confidence is 175 ± 1.96 * 1 = 173 to 177**
- That is, if numerous random sample of size 100 are draw. And 95% confidence interval is computed for each sample, **the population mean will be within the computed intervals in 95% of instances**[4].

1-**Standard Error** means how much is the **Variability among different samples.** while **standard Deviation** is How much the the values in one sample deviating on average from mean (**Variability in one sample)**
2-Smaller Standard Error , Deviation indicates a good precision and vice viscera
3-Instead of given point estimate, we can provide interval estimate with 95% confidence interval
4-It means,If we repeat the study 100 times on the same population, 95 of the time the mean will be between this interval

Statistical significance using confidence intervals

Confidence Intervals

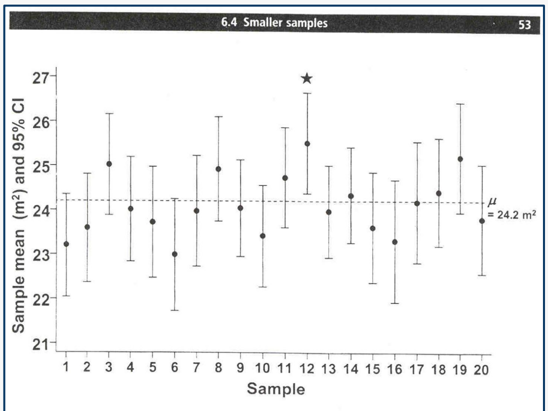


Fig. 6.2 Mean sprayable areas, with 95% confidence intervals, from 20 samples of 100 houses in a rural area. The star indicates that the CI does not contain the population mean.

- This picture shows 20 confidence interval for μ
- Each 95% confidence interval has fixed endpoints, where might be in between (or not).
- There is no probability of such an event!
- 19 out of 20 of C.I intervals include (cross) the population mean which represent 95% of whole intervals.
- If confidence is 90%, 18 out of 20 of C.I intervals will include population mean and so on.

Suppose α =0.05, we can not say with probability 0.95 the parameter μ lies within the confidence interval.

We only know that by repetition, 95% of the intervals will contain the true population parameter (μ)

In 5% of cases however it doesn't. And unfortunately we don't know in which of cases this happen.

That's why we say: with confidence level 100(1 -α)% μ lies in the confidence interval.

Different interpretation of 95% confidence interval

We are 95 % sure that the true parameter value is the 95% confidence interval.

If we repeat the experiment many many times, 95% of the time the true parameter value would be in the interval.

Most commonly used CI:

1 CI 90% corresponds to α 0.10

2 CI 95% corresponds to α 0.05

3 CI 99% corresponds to α 0.01

P value is only for analytical studies (Comparison group)

CI is for both descriptive and analytical studies

Statistical significance using confidence intervals

How to calculate CI

General formula: **$CI = P + Z_{\alpha} \times SE$**

- P = point of estimate, a value drawn form sample (a statistic).
- Zα = standard Normal deviate for α , if α= 0.05, Zα= 1.96 (~95% CI)

Descriptive study (no comparison)

Example 1

- 100 KKUH student 60 do daily exercise (p =0.6).
- What it the proportion of student do daily exercise in the KSU.

$$SE(p) = \sqrt{\frac{pq}{n}}$$

$$=> 95\%\ CI = 0.6 \pm 1.96 \sqrt{\frac{0.6 \times 0.4}{100}}$$

$$= 0.6 \pm 1.96 \times \frac{0.5}{10}$$

$$= 0.6 \pm 0.1 = 0.5 ; 0.7$$

Example 2: CI of the mean

- 100 newborn babies, mean BW = 3000 (SD = 400) grams, what is 95% CI?
- 95% CI = $\bar{X}$ + 1.96 (SEM)

$$SEM = \frac{SD}{\sqrt{n}}$$

$$=> 95\%\ CI = 3000 \pm 1.96\ (\frac{400}{\sqrt{100}})$$

$$= 3000 \pm 80 = (3000 - 80) ; (3000 + 80)$$

$$= 2920 ; 3080$$

Analytical study (comparison)

Example 3: CI of difference between proportions (p1- p2)

- 50 patients with drug A, 30 cured (p1=0.6)
- 50 patients with drug B, 40 cured (p2=0.8)

$$95\%\ CI\ (P1 - P2) = (P1 - P2) \pm 1.96 \times SE\ (P1 - P2)$$

$$SE(P1 - P2) = \sqrt{\frac{p1q1}{n1} + \frac{p2q2}{n2}}$$

$$= \sqrt{\frac{(0.6 \times 0.4)}{50} + \frac{(0.8 \times 0.2)}{50}} = \sqrt{0.008} = 0.09$$

$$=> 95\%\ CI\ (P1 - P2) = [0.2 - (0.09 \times 1.96)] ; [0.2 + SE\ (0.09 \times 1.96)]$$

$$= 0.024 ; 0.3764 = 2.4\%\ to\ 37.6\%$$

Example 4: CI for difference between 2 means

- **Mean systolic BP:**
  - **50 smokers = 146.4 (SD 18.5) mmHg**
  - **50 non-smokers = 140.4 (SD 16.8) mmHg**
- $\bar{X}1$-$\bar{X}2$ = 6.0 mmHg
- 95% CI($\bar{X}1$-$\bar{X}2$) = ($\bar{X}1$-$\bar{X}2$) ± 1.96 x SE ($\bar{X}1$-$\bar{X}2$)
- SE ($\bar{X}1$-$\bar{X}2$) = S x √(1/n1+1/n2)

$$S = \sqrt{\frac{(n1 - 1)s1^2 + (n2 - 1)s2^2}{(n1 + n2 - 2)}}$$

$$S = \sqrt{\frac{(49 \times 18.6) + (49 \times 16.2)}{98}} = 17.7$$

$$SE(\bar{X}1 - \bar{X}2) = 17.7 \sqrt{\frac{1}{50} + \frac{1}{50}} = 3.53$$

$$95\%\ CI = 6.0 \pm (1.96 \times 3.53) = -1.0 ; 13.0$$

Interpretation of the results

Example1	If someone repeat the study,We are 95 % confident that people who do daily exercise between 0.5(50%) to 0.7(70%). (The closer the interval the better the precision is. And vice versa)	***Example 3***	-Statically significant because the C.I doesn't include zero value -The Confidence interval is wide due to low sample size (poor precision).
Example 2	We are 95% confident that true population mean lies within 2920 to 3080	***Example 4***	The result is Not statically significant because the confidence interval include Zero value, so we accept H_0

Confidence Intervals

Other commonly supplied CI

- Number needed to treat (NNT)
- Relative risk (RR)
- Relative risk reduction (RRR)
- Odds ratio (OR)
- Likelihood ratio (LR)
- Sensitivity, specificity (Se,Sp)

CHARACTERISTICS OF CI'S

- The (im) precision of the estimate is indicated by the width of the confidence interval.
- The wider the interval the less precision, The narrower interval more precision

★ The **width of C.I.** depends on:[1]
  - Sample size[2]
  - Variability
  - Degree of confidence

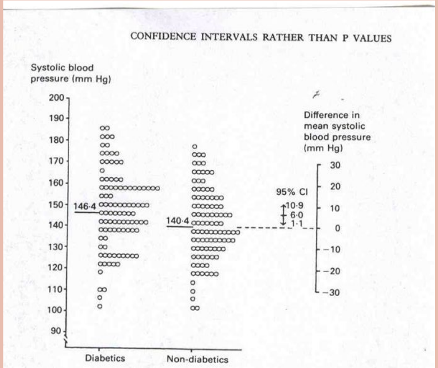


FIG 2.1—Systolic blood pressures in 100 diabetics and 100 non-diabetics with mean levels of 146·4 and 140·4 mm Hg respectively. The difference between the sample means of 6·0 mm Hg is shown to the right together with the 95% confidence interval from 1·1 to 10·9 mm Hg.

Normal distribution bell shaped curve. Is it statically significant ? Yes because it does not include 0.
Upper limit: 10.9
difference: 6
lower limit: 1.1

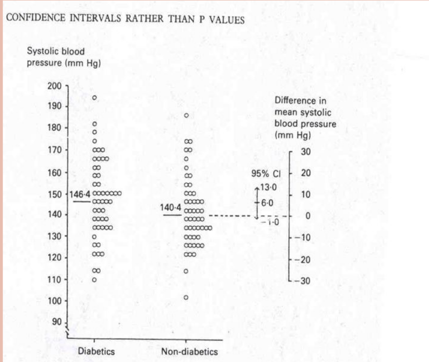


FIG 2.2—As fig 2.1 but showing results from two samples of half the size—that is, 50 subjects each. The means and standard deviations are as in fig 2.1, but the 95% confidence interval is wider, from −1·0 to 13·0 mm Hg, owing to the smaller sample sizes.

By reducing the sample size to half the bell shape is gone, high variability even though the accurate mean difference is same, statistical significance disappeared and the CI increase width n= 50. So when we decrease the sample size the width will increase.0

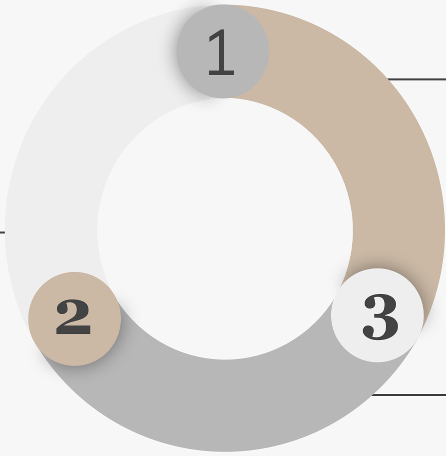
1- Increasing the sample size will increase precision and narrow C.I
2-By reducing sample size 1-Bell shape converted to skewed 2-increase variability 3- widen C.I

Confidence Intervals

EFFECT OF VARIABILITY

- **Properties of Standard error (SE)**

SE increases with larger standard Deviation As variation among the individuals in the population increases, so does the error of our estimate



SE increases with smaller sample size. for any confidence level, large samples reduce the margin.

SE increases with larger z values Tradeoff between confidence level and margin of error

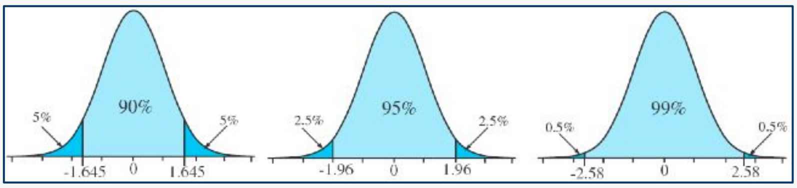
NOT ONLY 95%....

- **90% confidence interval:**
  NARROWER than 95%
  (X̄ ± 1.65sem)

- **99% confidence interval:**
  WIDER than 95%
  (X̄ ± 2.58sem)

Common Levels of confidence

Confidence level 1 - α	Alpha level α	Z value $z_{1-(\alpha/2)}$
90	10	1.645
95	05	1.960
99	01	2.576



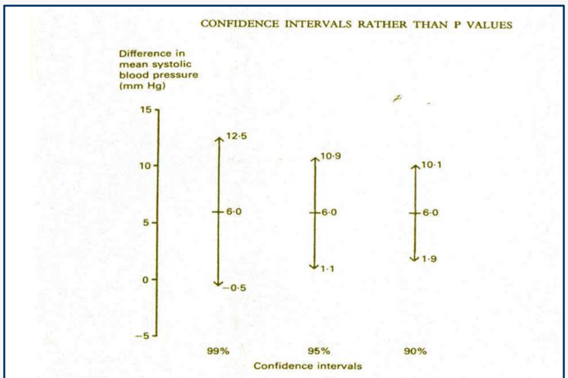


FIG 2.3—Confidence intervals associated with differing degrees of "confidence" using the same data as in fig 2.1.

Confidence Intervals

APPLICATION OF CONFIDENCE INTERVALS

- **Example:**
  The following finding of non-significance in a clinical trial on 178 patients:

Treatment	Success	Failure	Total
A	76 (75%)	25	101
B	51 (66%)	26	77
Total	127	51	178

- Chi-square value = 1.74 (p > 0.1) (non –significant)

  i.e. there is no difference in efficacy between the two treatments.
- The observed difference is:

  75% - 66% = 9%

  and the 95% confidence interval for the difference is:

  -4% to 22%
- This indicates that compared to treatment B, treatment A has at best an appreciable advantage (22%) and at worst a slight disadvantage (-4%).
- This inference is more informative than just saying that the difference is non significant.

Interpretation of Confidence intervals

- **Width of the confidence interval (CI)**
  - A narrow CI implies high precision.
  - A wide CI implies poor precision (usually due to inadequate sample size).

★ **Does the interval contain a value that implies no change or no effect or no association?**
  - CI for a difference between two means: Does the interval include 0 (zero)? If yes = no difference
  - CI for a ratio (e.g, OR, RR): Does the interval include 1? If yes = No risk, no association

Interpretation of Confidence intervals	
	No statistically significant change
	Statistically significant (increase)[1]
	Statistically significant (decrease)[2]

Null value | CI 

1-the right side of point estimate increase (statically significant)
2- On the left side of point estimate decrease (statically significant)

Confidence Intervals

Duality between P-value and CIs

- If a 95% CI includes the null effect, the P-value is > 0.05 (and we would fail to reject the null hypothesis)
- If the 95% CI excludes the null effect, the P-value is < 0.05 (and we would reject the null hypothesis)

Interpreting confidence intervals

Trial	Number dead / Randomized		Risk Ratio	95% C.I.	P value
	Intravenous nitrate	Control			
Chiche	3/50	8/45	0.33	(0.09,1.13)	0.08
Wide interval: suggests reduction in mortality of 91%(1-0.09) and an increase of 13%(1-0.13)					
Flaherty	11/56	11/48	0.83	(0.33,2.12)	0.70
Jaffe	4/57	2/57	2.04	(0.33,10.71)	0.40
Reduction in mortality as little as 18%(1-0.82), but little evidence to suggest that IV nitrate is harmful					
Jugdutt	24/154	44/156	0.48	(0.28,0.82)	0.007

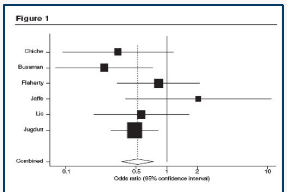


Figure 1

Individual and combined odds ratios and 95% confidence intervals for six intravenous nitrate trials.

The figer name is Forest plot
-The size of square indicates effect size.
- Diamond shape indicate sum of confidence intervals.

Interpreting confidence intervals

Which of the following odds ratios for the relationship between various risk factors and heart disease are statistically significant at the 0.05-significance level? Which are likely to be clinically significant?

Odds ratios	Statistically significant	Clinically significant	Reason
Odds ratio for every 1-year increase in age: 1.10 (95% CI: 1.01-1.19)	✔	✔	C.I does not include 1 Significant effect size
Odds ratio for regular exercise (yes vs no): 0.50 (95% CI: 0.30-0.82)	✔	✔	C.I does not include 1 Significant effect size
Odds ratio for high blood pressure (high vs normal): 3.0 (95% CI: 0.90-5.30)		✔	C.I include 1 Significant effect size
Odds ratio for every 50-pound increase in weight: 1.05 (95% CI: 1.01-1.20)	✔		C.I does not include 1 Insignificant effect size

Confidence Intervals

Important notes:
The result considered statically significant:
1-When P value less than or equal to alpha(α) but because we mostly use 95% C.I (α=0.05)
2- In **descriptive** study when the Confidence interval **does not** include Zero value (there is difference).
3- In **analytical** study,when the Confidence interval in Odds ratio Or Relative risk (risk ratio) do not include one.(there is difference between 2 groups).
The Result considered *clinically significant* when it has *significant effect size.*

Comparison of p values and confidence interval

P values (hypothesis testing) VS Confidence interval (estimating)

P values (hypothesis testing)

- Gives you the probability that the result is merely caused by chance or not by chance, **it does not give the magnitude and direction of the difference.**
- It answers the question :

  "Is there a statistically significant difference between the two treatments?“ (or two groups). (you can not make blind conclusion depend on P value only)

Confidence interval (estimating)

- Indicates estimate of value in the population given one result in the sample, **it gives the magnitude and direction of the difference.** (C.I gives you magnitude, direction of difference and population estimation)
- The point estimate and its confidence interval answers the question :

  "What is the size of that treatment difference?", and "How precisely did this trial determine or estimate the treatment difference?"

Summary of key points (from Dr. slides)

- A P-value is a probability of obtaining an effect as large as or larger than the observed effect, assuming null hypothesis is true
  - Provides a measure of strength of evidence against the H_o
  - Does not provide information on magnitude of the effect.
  - Affected by sample size and magnitude of effect: interpret with caution!
- Confidence interval quantifies:
  - How confident are we about the true value in the source population
  - Better precision with large sample size
  - Much more informative than P-value
- Keep in mind clinical importance when interpreting statistical significance!

Questions

(1) Confidence Interval can be used in which type of study**?**

A)Analytical study

B)both of them

C) Descriptive study

D) none of them

(2) Variability among different samples is **?**

A) Standard deviation

B) Standard Error

C) P value

D) precision

(3) The result is considered statically significant when P value **?**

A)P value >0.05(α)

B) P value = 1

C)P value ≤ 0.05(α)

D) None of them

(4) The Confidence interval of students at KSU who do daily exercise range from -0.5 to 0.7 compared to students at KFUPM what is the interpretation of the result**?**

A) Statically significant

B) there is a difference

C) not statically significant

D) none of them

(5) Effect of Drug A in reducing blood pressure is 1.15 higher than Drug B, (Drug A reduce blood pressure by 20 mmHg) (95% C.I: 0.9-4.5).
The result is significant **?**

A) Statically and clinically

B) Statically, but not clinically

C)Clinically, but not statically

D)Neither clinically or statically

(6) Odd ratio of coronary heart disease in 50 pound increase in weight is 1.05(95% C.I: 1.02 -1.2) the result is significant **?**

A)statically and clinically

B)Statically, but not clinically

C) Clinically, but not statically

D) Neither clinically or statically

Answers:
1: B, 2: B 3: C, 4: C 5: C, 6: B

Research Team

RESEARCH TEAM
438
Keep it simple, Keep it focused

Thank you for checking our work!

Leaders:

Shuaa Khdary
Sarah AlQuwayz
Abdulrhman Alsuhaibany

Member:

Osama Alharbi

Note Taker:

Mohamed Alquhidan
Fatimah Alhelal

Contact us:

Research4390@gmail.com