



Statistical significance using p-value







Objectives:

1. To understand the concepts of statistical inference and statistical significance.
2. To apply the concept of statistical significance (p-value) in analyzing the data.
3. To interpret the concept of statistical significance (p-value) in making valid conclusions.

[Click here for the practical](#)

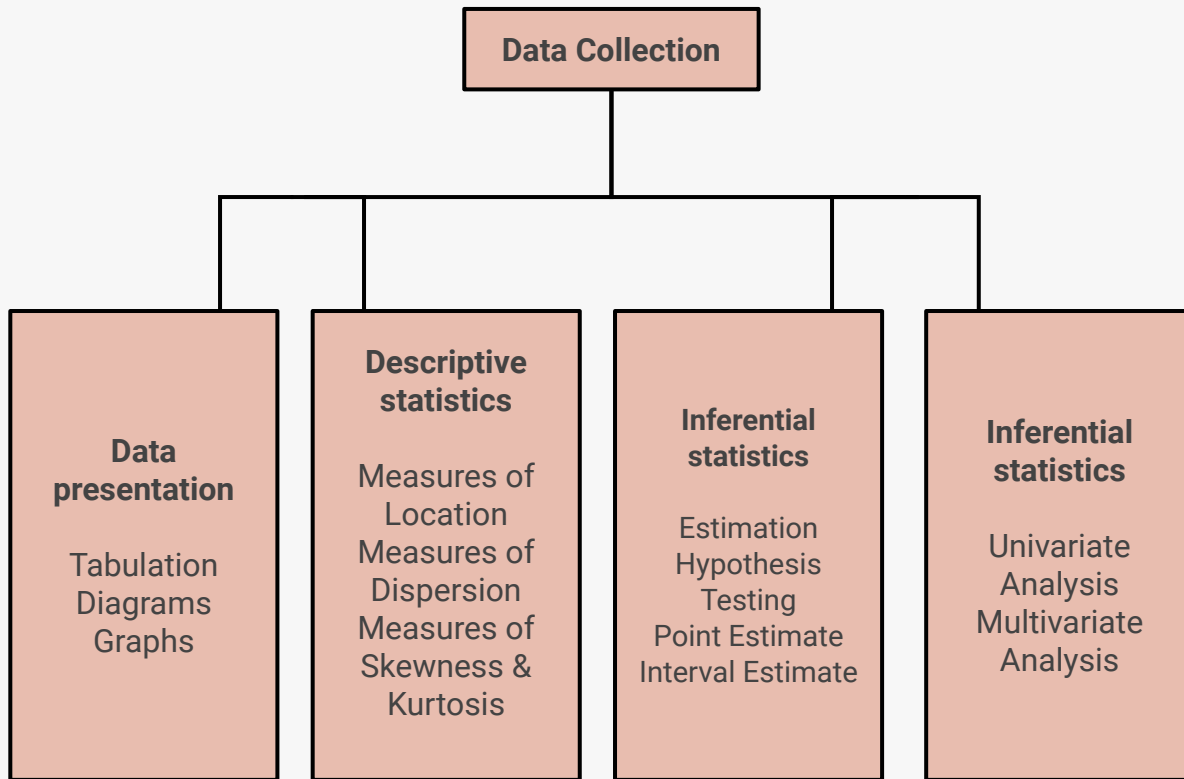
25th lecture

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Overview



Importance of inferential statistics

- Using inferential statistics¹, we make inferences about population (taken to be unobservable) based on a random **sample** taken from the **population** of interest.
- We can generate the parameter from the statistic.

Parameter:

- Numbers that summarize data for an entire population.
- E.g. Average height of all 25-year-old men (population) in KSA.
- Not always possible to measure because it needs the actual value in the population.
- What you collect from the population called parameter

Statistic:

- Numbers that summarize data from a sample.
- E.g. The height of the members of a sample of 100 such men are measured; the average of those 100 numbers is a statistic.
- Always possible to measure because it doesn't need the actual value in the population

1. inference = reaching a conclusion

Overview

Is risk factor X associated with disease Y?

- ◉ From the sample, we compute an estimate of the effect of X (risk factor) on Y (disease or outcome) (e.g. risk ratio if cohort study):
 - Is the effect real? Did chance play a role?
 - Why worry about chance?
 - Because of sampling variability...you only get to pick **one sample!**

Interpreting the results

- ◉ Make inferences from data collected using laws of probability and statistics, **You have to use these two concepts:**
 - Tests of significance (p-value).
 - Confidence intervals.

Significance testing

- ◉ The interest is generally in comparing **two groups**:
 - Significance testing can only be done **if we have 2 comparison groups (Analytical study)** ex: cross sectional study, case control, cohort study, and RCT (it **can't be applied to purely descriptive research**)
 - (e.g., risk of outcome in the treatment and placebo group)
- ◉ The statistical test depends on the type of data and the study design.
 - (eg. odds ratio in case-control or cross-sectional studies, and relative risk in RCTs and cohort studies)

Hypothesis Testing

Null hypothesis Vs Alternative hypothesis

Null hypothesis (H_0)	Alternative hypothesis (H_A)
<ul style="list-style-type: none"> There is no association between the predictors (associated factors) and outcome variable in the population ex: the exposure and the outcome 	<ul style="list-style-type: none"> The proposition that there is an association between the predictors and outcome variable.
<ul style="list-style-type: none"> Assuming there is no association, statistical tests estimate the probability that the association is due to chance. 	<ul style="list-style-type: none"> We do not test this directly but accept it by default if the statistical test rejects the null hypothesis.
<ul style="list-style-type: none"> States the assumption (numerical) to be tested. 	<ul style="list-style-type: none"> The opposite of the null hypothesis, challenges the status quo.
<ul style="list-style-type: none"> Begin with the assumption that the null hypothesis is TRUE. 	<ul style="list-style-type: none"> Is generally the hypothesis that is believed to be true by the researcher.
<ul style="list-style-type: none"> Always contains the '=' sign. 	<ul style="list-style-type: none"> Never contains just the '=' sign.
<p>We always test the null hypothesis. if it's rejected we automatically accept the alternative hypothesis.</p>	

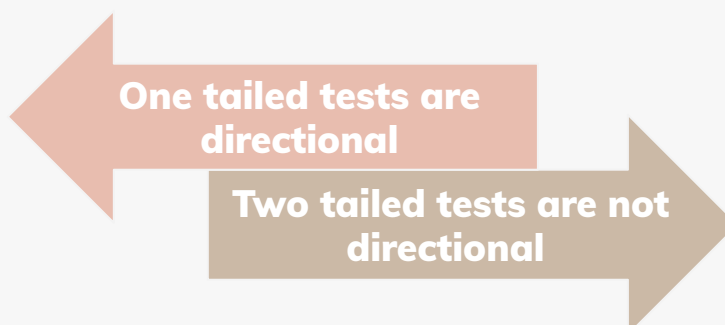
- The null hypothesis is rejected when there is a relationship between two measured variables.
- The null hypothesis is accepted when there is no relationship between two measured variables.

One and Two Sided Tests

- Hypothesis tests can be one or two sided (tailed):

- $H_0: \mu_1 - \mu_2 = 0$

- $H_A: \mu_1 - \mu_2 > 0$ or $H_A: \mu_1 - \mu_2 < 0$



- $H_0: \mu_1 - \mu_2 = 0$

- $H_A: \mu_1 - \mu_2 \neq 0$

From 437:

- One sided test:**

- A statistical hypothesis test in which alternative hypothesis has only one end. So, it will tell you if there is a relationship between variables in single direction.

- Two sided test:**

- A statistical hypothesis test in which alternative hypothesis has two end. So, it will tell you if there is a relationship between variables in both direction.

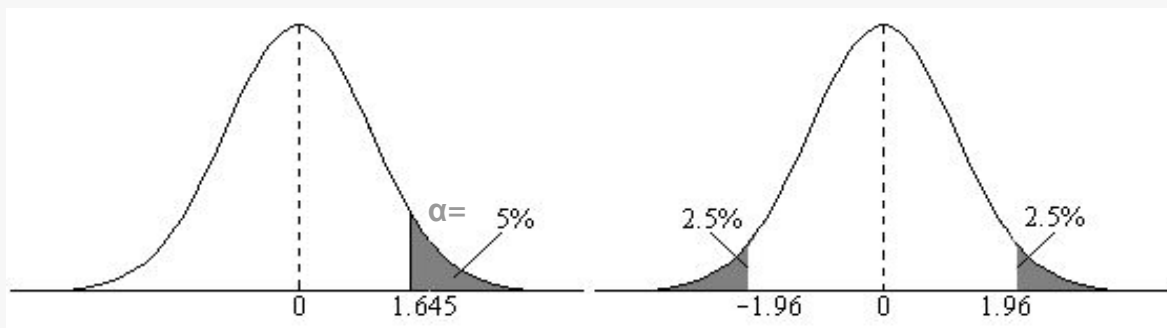
Hypothesis Testing

When To Reject H_0 ?

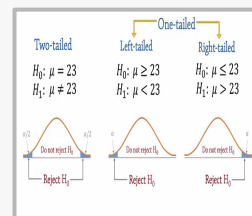
- Rejection region: set of all test statistic values for which H_0 will be rejected.
- Level of significance, α : Specified before an experiment to define rejection region.

One sided: $\alpha = 0.05$

Two sided: $\alpha/2 = 0.025$



Example:



Critical Value =

-1.64

-1.96 and +1.96

Rejection region =

Either left or right

Both left & right

Type-I and Type-II Errors

α

- Probability of rejecting H_0 when H_0 is true.
- Called **significance level** of the test.

Type 1 error :

- The **null hypothesis is rejected when it is actually true**; (false positive error)
- Significance level (type 1 error rate): the probability of a type 1 error (denoted with " α ")
- significance level α is usually set to 0.05

β

- Probability of not rejecting H_0 when H_0 is false.
- $1-\beta$ called **statistical power** of the test.

Type 2 error

- The **null hypothesis is accepted when it is actually false** and, consequently, the alternative hypothesis is rejected even though an observed effect did not occur due to chance (false negative error).
- Type 2 error rate: the probability of a type 2 error (denoted by " β ")

Diagnosis and statistical reasoning

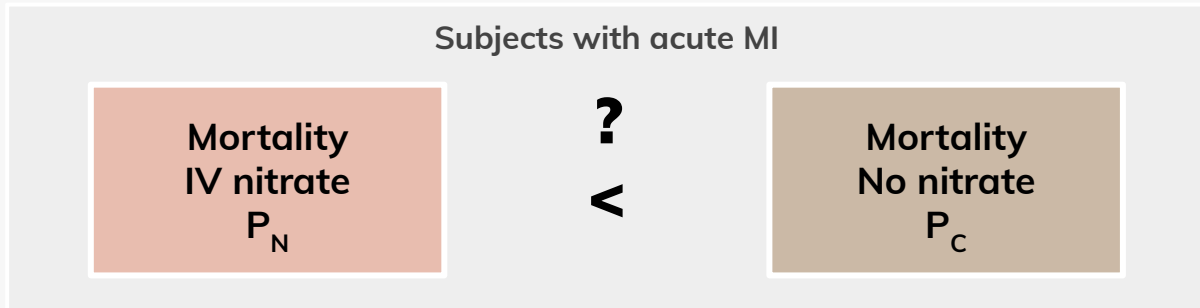
Significance Difference:

Test result	Present (H_0 not true)	Absent (H_0 is true)
Reject H_0	No error ($1-\beta$)	Type I error (α)
Accept H_0	Type II error (β)	No error ($1-\alpha$)

Disease status:

Test result	Present (H_0 not true)	Absent (H_0 is true)
+ve	True +ve (Sensitivity)	False +ve
-ve	False -ve	True -ve (specificity)

Significance testing



- Suppose we do a clinical trial to answer the above question.
- Even if IV nitrate has no effect on mortality, due to sampling variation, it is very unlikely that $P_N = P_C$
- Any observed difference between groups may be due to treatment or a coincidence (or chance).

Null Hypothesis (H_0)

- There is no association between the independent and dependent/outcome variables.
 - Formal basis for hypothesis testing.
- In the example, H_0 : "The administration of IV nitrate has no effect on mortality in MI patients" or $P_N - P_C = 0$
- Obtaining P values:**

Trial	Number dead (randomized)		Risk Ratio	95% C.I.	P value
	IV nitrate	(control)			
Chiche	3/50	8/45	0.33	(0.09, 1.13)	0.08 <small>How did we get this p-value?</small>
Bussman	4/31	12/29	0.24	(0.08, 0.74)	0.01
Flaherty	11/56	11/48	0.83	(0.33, 2.12)	0.70
Jaffe	4/57	2/57	2.04	(0.39, 10.71)	0.40
Lis	5/64	10/76	0.56	(0.19, 1.65)	0.29
Jugdutt	24/154	44/156	0.48	(0.28, 0.82)	0.007

From 437:

- In the table, there are the 6 studies in the first column, sample size of iv nitrate patients and control in the second and third column. So in IV nitrate (in chiche study) 50 patients were randomized, yet 3 have died (people who died\ total) and we are interested to know how we got the p value and its interpretation?

Significance testing

Example of significance testing

- **In the Chiche trial:**
 - $p_N = 3/50 = 0.06$; $p_C = 8/45 = 0.178$
- **Null hypothesis:**
 - $H_0: p_N - p_C = 0$ or $p_N = p_C$
- **Statistical test:**
 - Two-sample proportion

Interpretation:

6% have died from the intervention group (IV nitrate)
 17% have died from the control group (no nitrate)
 -We need to prove that nitrate had a real effect, and it was not by chance.

Test statistic for Two Population Proportions

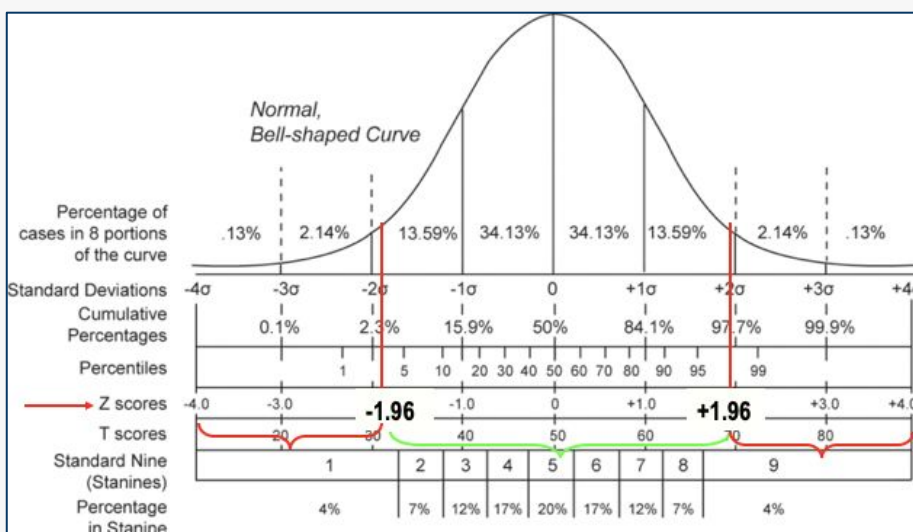
- The test statistic for $p_1 - p_2$ is a Z statistic:

$$Z = \frac{(p_N - p_C) - (P_N - P_C)_o}{\sqrt{\bar{p}(1-\bar{p})\left(\frac{1}{n_N} + \frac{1}{n_C}\right)}}$$

P_C → Observed difference
 $(P_N - P_C)_o$ → Null hypothesis
 n_N → Number of subjects in IV nitrate group
 n_C → Number of subjects in control group

- Where: $\bar{p} = \frac{X_N + X_C}{n_N + n_C}$, $p_N = \frac{X_N}{n_N}$, $p_C = \frac{X_C}{n_C}$

Testing significance at 0.05 level



$Z_{\alpha/2} = 1.96$
 Reject H_0 if $Z < -Z_{\alpha/2}$ or $Z > Z_{\alpha/2}$

Z score more than 1.96 and less than -1.96 is rejected

Rejection region Non Rejection region Rejection region

Significance testing

Two Population Proportions

$$Z = \frac{(0.06 - 0.178)}{\sqrt{0.116(1 - 0.116)\left(\frac{1}{50} + \frac{1}{45}\right)}} = -1.79$$

- Where: $\bar{p} = \frac{3+8}{45+50} = 0.116$, $p_N = \frac{3}{45} = 0.06$, $p_C = \frac{8}{50} = 0.178$

Statistical test for $p_1 - p_2$

- Two Population Proportions, Independent Samples:

Two-tail test:

$$H_0: p_N - p_C = 0$$

$$H_1: p_N - p_C \neq 0$$

$$Z = \frac{(0.06 - 0.178)}{\sqrt{0.116(1 - 0.116)\left(\frac{1}{50} + \frac{1}{45}\right)}} = -1.79$$

- $Z_{\alpha/2} = 1.96$
 - Reject H_0 if $Z < -Z_{\alpha/2}$ or $Z > Z_{\alpha/2}$
 - Since -1.79 is $>$ than -1.96, we **fail to reject the null hypothesis**.
 - The actual p-value = $P(Z < -1.79) + P(Z > 1.79) = 0.08$

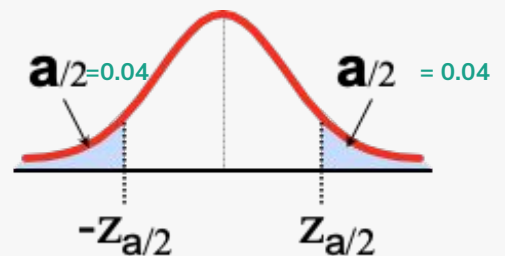


Table 1: Table of the Standard Normal Cumulative Distribution Function $\Phi(z)$

z	0.00	0.01	0.02	0.03	0.04	0.05	0.06	0.07	0.08	0.09
-3.4	0.0003	0.0003	0.0003	0.0003	0.0003	0.0003	0.0003	0.0003	0.0003	0.0002
-3.3	0.0005	0.0005	0.0005	0.0004	0.0004	0.0004	0.0004	0.0004	0.0004	0.0003
-3.2	0.0007	0.0007	0.0006	0.0006	0.0006	0.0006	0.0006	0.0005	0.0005	0.0005
-3.1	0.0010	0.0009	0.0009	0.0009	0.0008	0.0008	0.0008	0.0008	0.0007	0.0007
-3.0	0.0013	0.0013	0.0013	0.0012	0.0012	0.0011	0.0011	0.0011	0.0010	0.0010
-2.9	0.0019	0.0018	0.0018	0.0017	0.0016	0.0016	0.0015	0.0015	0.0014	0.0014
-2.8	0.0026	0.0025	0.0024	0.0023	0.0023	0.0022	0.0021	0.0021	0.0020	0.0019
-2.7	0.0035	0.0034	0.0033	0.0032	0.0031	0.0030	0.0029	0.0028	0.0027	0.0026
-2.6	0.0047	0.0045	0.0044	0.0043	0.0041	0.0040	0.0039	0.0038	0.0037	0.0036
-2.5	0.0062	0.0060	0.0059	0.0057	0.0055	0.0054	0.0052	0.0051	0.0049	0.0048
-2.4	0.0082	0.0080	0.0078	0.0075	0.0073	0.0071	0.0069	0.0068	0.0066	0.0064
-2.3	0.0107	0.0104	0.0102	0.0099	0.0096	0.0094	0.0091	0.0089	0.0087	0.0084
-2.2	0.0139	0.0136	0.0132	0.0129	0.0125	0.0122	0.0119	0.0116	0.0113	0.0110
-2.1	0.0179	0.0174	0.0170	0.0166	0.0162	0.0158	0.0154	0.0150	0.0146	0.0143
-2.0	0.0228	0.0222	0.0217	0.0212	0.0207	0.0202	0.0197	0.0192	0.0188	0.0183
-1.9	0.0287	0.0281	0.0274	0.0268	0.0262	0.0256	0.0250	0.0244	0.0239	0.0233
-1.8	0.0359	0.0351	0.0344	0.0336	0.0329	0.0322	0.0314	0.0307	0.0301	0.0294
-1.7	0.0446	0.0436	0.0427	0.0418	0.0409	0.0401	0.0392	0.0384	0.0375	0.0367
-1.6	0.0548	0.0537	0.0526	0.0516	0.0505	0.0495	0.0485	0.0475	0.0465	0.0455
-1.5	0.0668	0.0655	0.0643	0.0630	0.0618	0.0606	0.0594	0.0582	0.0571	0.0559
-1.4	0.0808	0.0793	0.0778	0.0764	0.0749	0.0735	0.0721	0.0708	0.0694	0.0681
-1.3	0.0968	0.0951	0.0934	0.0918	0.0901	0.0885	0.0869	0.0853	0.0838	0.0823
-1.2	0.1151	0.1131	0.1112	0.1093	0.1075	0.1056	0.1038	0.1020	0.1003	0.0985
-1.1	0.1357	0.1335	0.1314	0.1292	0.1271	0.1251	0.1230	0.1210	0.1190	0.1170
-1.0	0.1587	0.1562	0.1539	0.1515	0.1492	0.1469	0.1446	0.1423	0.1401	0.1379
-0.9	0.1841	0.1814	0.1788	0.1762	0.1736	0.1711	0.1685	0.1660	0.1635	0.1611
-0.8	0.2119	0.2090	0.2061	0.2033	0.2005	0.1977	0.1949	0.1922	0.1894	0.1867
-0.7	0.2420	0.2389	0.2358	0.2327	0.2296	0.2266	0.2236	0.2206	0.2177	0.2148
-0.6	0.2743	0.2709	0.2676	0.2643	0.2611	0.2578	0.2546	0.2514	0.2483	0.2451
-0.5	0.3085	0.3050	0.3015	0.2981	0.2946	0.2912	0.2877	0.2843	0.2810	0.2776

We round up the value into 0.04

- After calculating a test statistic we convert this to a p-value by comparing its value to distribution of test statistic under the null hypothesis.
- Measure of how likely the test statistic value is under the null hypothesis:

- $p\text{-value} \leq \alpha \Rightarrow$ Reject H_0 at level α
- $p\text{-value} > \alpha \Rightarrow$ Do not reject H_0 at level α

P-Value

What is a P-value?

- 'p' stands for probability.
 - Tail area probability based on the observed effect.
 - Calculated as the probability of an effect as large as or larger than the observed effect (more extreme in the tails of the distribution), assuming null hypothesis is true.
- **Size of the P-value is related to:** the sample size and the outcome
 - **The sample size.**
 - The effect size or the observed association or difference.
- **Measures the strength of the evidence against the null hypothesis**
 - **Smaller p- values indicate stronger evidence against the null hypothesis**

→ Stating the Conclusions of our Results

p-value is small

- we reject the null hypothesis or, equivalently, we accept the alternative hypothesis.
- **"Small" is defined as a p-value $\leq \alpha$, where α = acceptable false (+) rate (usually 0.05).**

p-value is not small

- we conclude that we cannot reject the null hypothesis or, equivalently, there is not enough evidence to reject the null hypothesis.
- **"Not small" is defined as a p-value $> \alpha$, where α = acceptable false (+) rate (usually 0.05).**
- Large p value indicate weak evidence against the null hypothesis

- **$p \leq 0.05$ is an arbitrary cut-point**
 - Does it make sense to adopt a therapeutic agent because p-value obtained in a RCT was 0.049, and at the same time ignore results of another therapeutic agent because p-value was 0.051?
- **Hence important to report the exact p-value and not 0.05 or >0.05**
- P values give **no indication about the clinical importance of the observed association.**
- A very large study may result in very small p-value based on a small difference of effect that may not be important when translated into clinical practice.
- Therefore, important to look at the effect size and confidence intervals.

- If the p-value is equal to or less than a predetermined significance level (usually set at 0.05), the association is considered **statistically significant** (i.e., the probability that the result was obtained by chance is $< 5\%$)
 - It is not possible to prove H1 is true, but having a p-value that is lower than the significance level indicates that it is very unlikely that the H0 is correct.

P-Value

Statistically significant Vs not statistically significant

Statistically significant	Not statistically significant
<ul style="list-style-type: none">• Reject Ho	<ul style="list-style-type: none">• Do not reject Ho
<ul style="list-style-type: none">• Sample value not compatible with Ho.	<ul style="list-style-type: none">• Sample value compatible with Ho.
<ul style="list-style-type: none">• Sampling variation is an unlikely explanation of discrepancy between Ho and sample value.	<ul style="list-style-type: none">• Sampling variation is a likely explanation of discrepancy between Ho and sample value.

Clinical importance vs. statistical significance

From 437:

Clinical importance	Statistically significant
<ul style="list-style-type: none">• The practical importance of the treatment effect, whether it has a real, palpable, noticeable effect on daily life.	<ul style="list-style-type: none">• Ruled by the p-value (and C.I).• When $p < 0.05$, we call this 'statistically significant'.• It simply means it was unlikely to have occurred by chance.• It doesn't necessarily tell us about the importance of this difference or how meaningful it is for patients.
<ul style="list-style-type: none">• Dependent on its implications on existing practice-treatment effect size being one of the most important factors that drives treatment decisions.	<ul style="list-style-type: none">• Heavily dependent on the study's sample size; with large sample sizes, even small treatment effects (which are clinically inconsequential) can appear statistically significant; therefore, the reader has to interpret carefully whether this "significance" is clinically meaningful.

Statistical significance vs. clinical significance :

- Significance (epidemiology): the statistical probability that a result did not occur by chance alone
- Statistical significance: describes a true statistical outcome (i.e., that is determined by statistical tests) that has not occurred by chance
- Clinical significance (epidemiology): describes an important change in a patient's clinical condition, which may or may not be due to an intervention introduced during a clinical study

-Statistical and clinical significance do not necessarily correlate.

-“Statistical significance” does not mean “clinical significance.”

P-Value

Interpretation

From 437:

- **Statistically significant & clinically important.**
 - This is where there is an important, meaningful difference between the groups and the statistics support this.
 - The flip side of this is where a difference is neither clinically nor statistically significant.
- **Not statistically significant BUT clinically important.**
 - This is most likely to occur if your study is underpowered and you do not have a large enough sample size to detect a difference between groups.
- **Statistically significant BUT NOT clinically important.**
 - If you have enough participants, even the smallest differences can become statistically significant.
 - just because a treatment is statistically significantly better than an alternative treatment, does not necessarily mean that these differences are clinically important.

Example

	Yes	No
Standard	0	10
New	3	7

- **Clinical** → Absolute risk reduction = 30%
- **Statistical** → Fischer exact test: $p = 0.211$
- **In this example**, you have only 10 cases in each group:
 - In the standard treatment there is no improvement.
 - In the new treatment there are 3 cases that improved.
 - clinically GOOD but statistically NOT GOOD. why? sample size is small.

Reaction of investigator to results of a statistical significance test

		Statistical Significance	
		Not significant	significant
Practical importance of observed effect	Not important	0	Annoyed
	important	Very Sad	Elated

Examples

Interpreting P values

Trial	Number dead (randomized)		Risk Ratio	95% C.I.	P value
	IV nitrate (control)				
Chiche	3/50	8/45	0.33	(0.09, 1.13)	0.08

Some evidence against the null hypothesis.

If the null hypothesis were true:

8 out of 100 such trials would show a risk reduction of 67% or more extreme just by chance.

Bussman	4/31	12/29	0.24	(0.08, 0.74)	0.01
Flaherty	11/56	11/48	0.83	(0.33, 2.12)	0.70

Very weak evidence against the null hypothesis...very likely a chance finding.

If the null hypothesis were true:

70 out of 100 such trials would show a risk reduction of 17% or more extreme just by chance (very likely a chance finding).

Jaffe	4/57	2/57	2.04	(0.39, 10.71)	0.40
Lis	5/64	10/76	0.56	(0.19, 1.65)	0.29
Jugdutt	24/154	44/156	0.48	(0.28, 0.82)	0.007

Very strong evidence against the null hypothesis...very unlikely to be a chance finding.

If the null hypothesis were true:

very unlikely to be a chance finding.

- **Lis and Jugdutt** trials are similar in effect (~ 50% reduction in risk)...but Jugdutt trial has a large sample size
- **Chiche and Flaherty** trials approximately same size, but observed difference greater in the Chiche trial
- **Example:**

1

If a new antihypertensive therapy reduced the SBP by 1 mmHg as compared to standard therapy we are not interested in swapping to the new therapy.

2

However, if the decrease was as large as 10 mmHg, then you would be interested in the new therapy.

3

Thus, it is important to not only consider whether the difference is statistically significant by the possible magnitude of the difference should also be considered.

Lecture Summary

Null Hypothesis (H ₀)	Alternative Hypothesis (H _A)
<ul style="list-style-type: none"> - No association between the predictors and outcome. - Probably the association is due to chance. - Always contains the '=' sign. 	<ul style="list-style-type: none"> - There is an association between the predictors and outcome. - Believed to be true by the researcher. - Never contains just the '=' sign.
One sided test	Two sided test
<ul style="list-style-type: none"> - H₀: $\mu_1 - \mu_2 = 0$ - H_A: $\mu_1 - \mu_2 > 0$ or H_A: $\mu_1 - \mu_2 < 0$ - Rejection region is on either left or right. - $\alpha = 0.05$ 	<ul style="list-style-type: none"> - H₀: $\mu_1 - \mu_2 = 0$ - H_A: $\mu_1 - \mu_2 \neq 0$ - Rejection region is on both left and right. - $\alpha/2 = 0.025$
Type I error (α)	Type II error (β)
<ul style="list-style-type: none"> - Probability of rejecting H₀ when H₀ is true. - Called significance level of the test. 	<ul style="list-style-type: none"> - Probability of not rejecting H₀ when H₀ is false. - Called statistical power of the test.
Small P-value	Not small P-value
<p>P-value is: Tail area probability based on the observed effect. Calculated as the probability of an effect as large as or larger than the observed effect assuming null hypothesis is true.</p> <ul style="list-style-type: none"> - not an indication about the clinical importance of the observed association. 	
<ul style="list-style-type: none"> - We reject the null hypothesis or, equivalently, we accept the alternative hypothesis. - $p\text{-value} \leq \alpha$ 	<ul style="list-style-type: none"> - We cannot reject the null hypothesis or, equivalently, there is not enough evidence to reject it. - $p\text{-value} > \alpha$
Statistically significant	Not Statistically significant
<ul style="list-style-type: none"> - Reject H₀ - Sample value not compatible with H₀. 	<ul style="list-style-type: none"> - Do not reject H₀ - Sample value compatible with H₀.
Statistically significant	Clinically Important
<ul style="list-style-type: none"> - When $p < 0.05$. - Heavily dependent on the study's sample size. - Simply means it was unlikely to have occurred by chance. 	<ul style="list-style-type: none"> - Importance of the treatment effect, whether it has a real, palpable, noticeable effect on daily life. - Dependent on its implications on existing practice-treatment effect size.

Questions

(1) Which of the following is believed to be true by the researcher?

- A) P value
- B) Alternative Hypothesis
- C) Null Hypothesis
- D) Statistical significance

(2) Which of the following is the rejection region of a one tailed test?

- A) Left
- B) Right
- C) Both left and right
- D) Either left or right

(3) Which of the following indicate stronger evidence against the null hypothesis?

- A) $p\text{-value} \leq \alpha$
- B) $p\text{-value} \geq \alpha$,
- C) $p\text{-value} = \alpha$,
- D) $p\text{-value} > \alpha$,

(4) If $Z_{\alpha/2} = 1.96$, when to reject H_0 ?

- A) $Z < -Z_{\alpha/2}$
- B) $Z > Z_{\alpha/2}$
- C) $Z < Z_{\alpha/2}$
- D) Both a and b

(5) When do we consider the study as statistically significant?

- A) When it rejects H_A
- B) When the Sample value is compatible with H_0 .
- C) When it rejects H_0
- D) When the Sample value is not compatible with H_A .

(6) When the P value is not small:

- A) We reject the null hypothesis
- B) We can not reject the null hypothesis.
- C) We accept the alternative hypothesis.
- D) Both a and c

Answers:

1: B, 2: D 3: A, 4: D 5: C, 6: B



Thank you for checking our work!

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