



Basics of statistics in clinical trials

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Learning outcomes

- The student explains the null hypothesis.
- The student identifies error I. and II. type.
- The student interprets the magnitude of the p value and the confidence interval.
- The student recognizes the valid results of clinical studies.

Content of the lecture

- Confidence interval
- Null hypothesis
- P-value

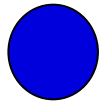
Confidence interval

- Population
- Sample
- Variation due to sampling
- Error of sampling
- Confidence interval - range, in which the true value of the mean of the quantity for the entire population is found with a predetermined (high) probability.



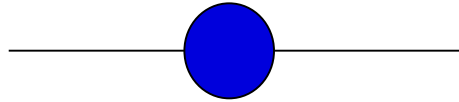
Interval estimate of the mean

– Point mean

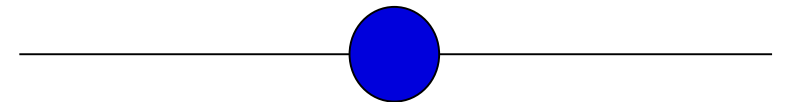


80 kg

Interval estimate of the mean



70 - 90 kg



65 - 120 kg

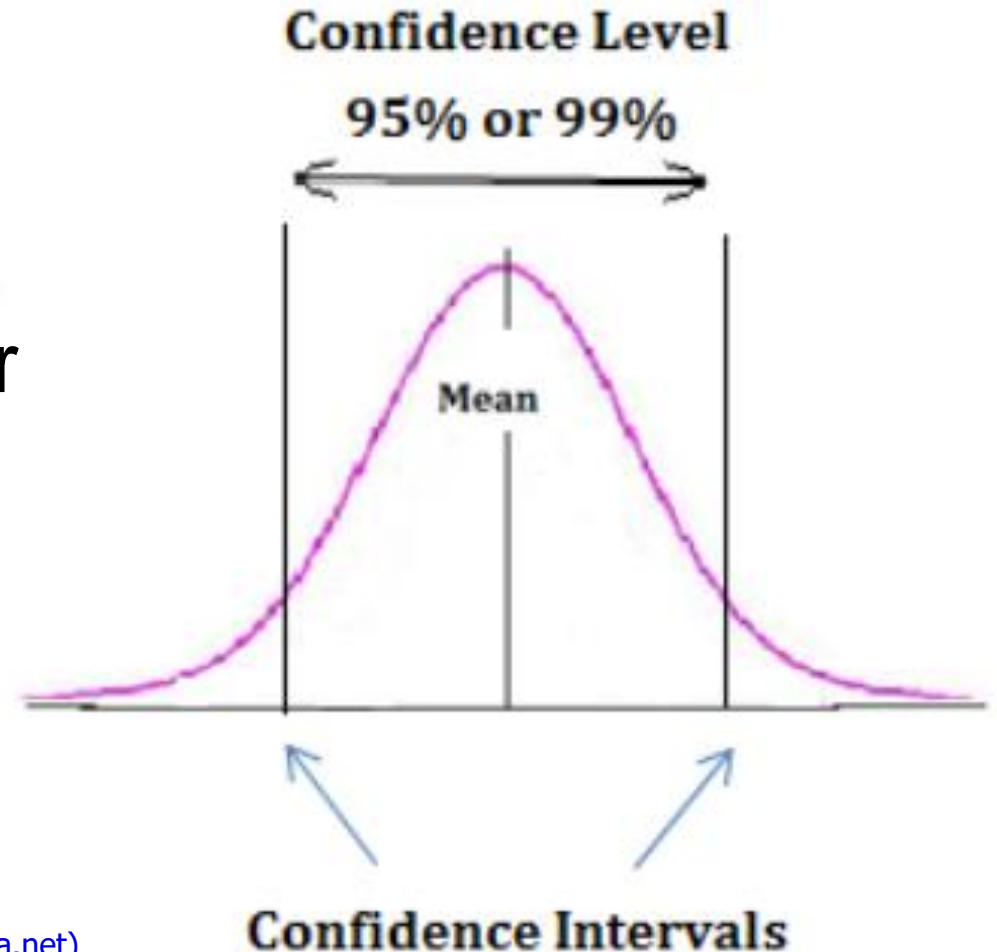
The higher the confidence coefficient, the longer and less accurate the resulting interval.

A trade-off between the required reliability and accuracy of the estimate - the length of the interval.

Width of confidence interval

relies on:



- size of selected population
- variability of selected parameter in tested population
- confidence level



[Difference between Confidence Level and Confidence Interval \(whatissixsigma.net\)](http://whatissixsigma.net)

Null hypothesis

- Comparison: study drug vs. comparator (e.g. another drug, placebo)
- Direct question or open question

drug A  vs.  drug B

- Null hypothesis

- is basis for test decision

accepted

rejected in favor of alternative hypothesis

Null hypothesis

Results of our test (test decision)	Reality	
	Null hypothesis is true	Alternative hypothesis is true
We accept the null hypothesis	Correct decision	Error of II. type – beta - FN
We reject the null hypothesis	Error I. type – alpha - FP	Correct decision

- Predefining of errors I. type α – a significance level (usually 5 %)
- Comparing with p-value:
 - P-value $>$ α null hypothesis is not rejected, is accepted
 - P-value \leq α null hypothesis is rejected in favor of an alternative hypothesis
- 3 % $<$ 5 % - the test was in favor of the alternative hypothesis, the null hypothesis rejected
Statistically significant result BUT clinical relevance must be evaluated separately

Null hypothesis and power of test

Results of our test (test decision)	Reality	
	Null hypothesis is true	Alternative hypothesis is true
We accept the null hypothesis	Correct decision	Error of II. type – beta - FN
We reject the null hypothesis	Error I. type – alpha - FP	Correct decision

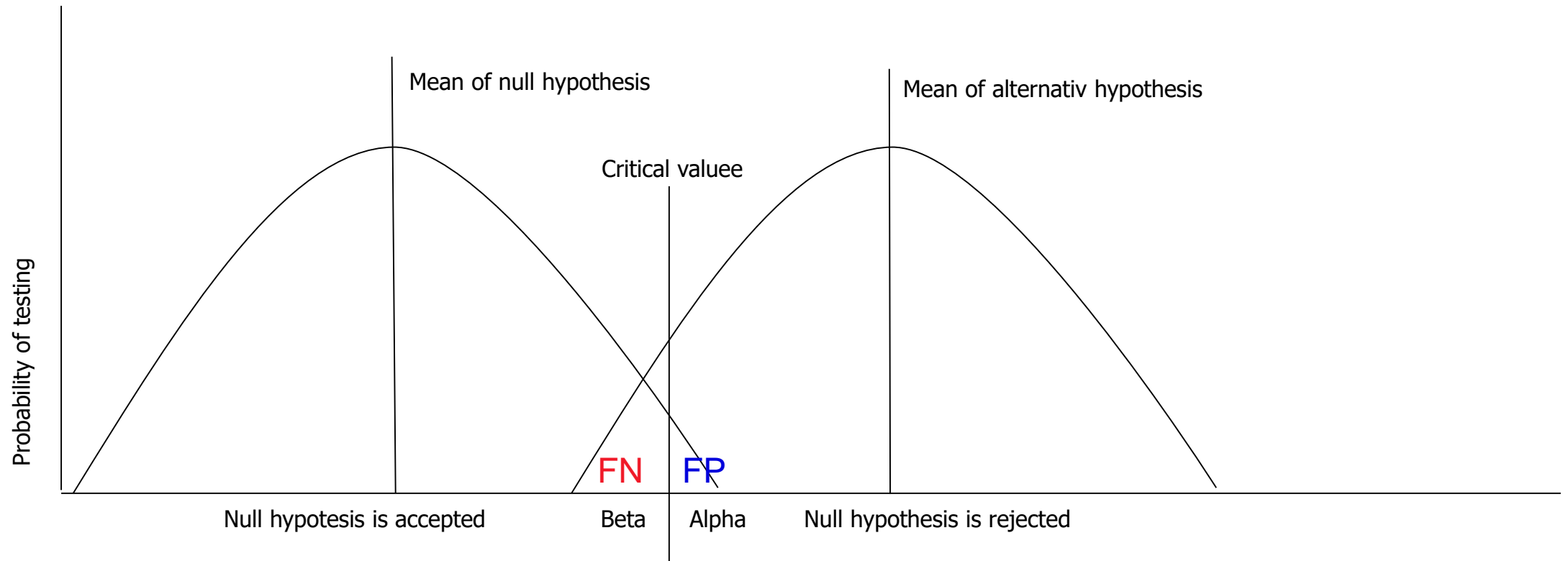
– Power of test

- 100 % - power = error II. type (beta)
- 100 % - 95 % = 5 %

90 % - 95 % - 99 %

= Probability of receiving true positive test results

Null hypothesis and p-value



- P-value is only a measure for the null hypothesis
- P-value doesn't show the probability of the null hypothesis being true

Case 1: Efficacy of tested drugs



vs.



cured	uncured	cured	uncured
1043	3	2	1432

99,7 % cured

0,1 % cured

$p = 0,05$

Case 2: Efficacy of tested drugs



cured	uncured	cured	uncured
73	125	71	127

36,8 % cured

35,8 % uncured

$P = 0,9$

Case 3: Efficacy of tested drug

False positivity



cured	uncured	cured	uncured
30	70	45	55

30 % cured

45 % cured

$P = 0,01$

Case 4: Efficacy of tested drugs

Sample size in the relation to the p-value



cured	uncured	cured	uncured
41	59	47	53

41 % cured

47 % cured

$P = 0,25$

cured	uncured	cured	uncured
4093	5805	4204	5278

41 % cured

42 % cured

$P = 0,04$

P- value

- Defines the probability of wrongly rejecting the null hypothesis
- Cannot distinguish:
 - The null hypothesis is actually true, but the random sample was not representative.
 - The null hypothesis is wrong.
- Doesn't reflect the error I. type – false positivity – case 3
 - Alpha doesn't change, independent of p-value
- Low p-value helps decide, if drug A is different from drug B, but it doesn't say how different they are - case 4

Take home message

- A null hypothesis is set up to test a certain statement, it can be confirmed or, on the contrary, rejected in favor of an alternative hypothesis.
- The p-value defines the probability of falsely rejecting the null hypothesis that is actually correct.
- A confidence interval is a range in which a given parameter lies with a given (high) degree of probability.

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2023



Funded by
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