Pharmaceutical statistics

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One Tailed Z-Test of population mean

- **Right Tailed Z-Test of population mean**

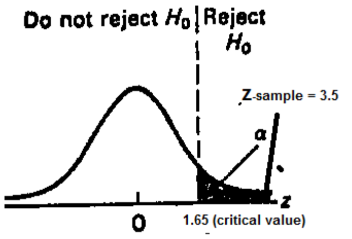
★ Example:

An antihypertensive drug is to be considered for clinical trials in human if it results in reduction of diastolic blood pressure of more than 10 mmHg <u>with at least high significance</u>. The drug was given to 16 animals after hypertension was induced. The mean reduction of BP was 17 mmHg. *σ was* estimated to be 8 mmHg. Is the drug considered a good candidate for further clinical trials at α of 0.05.

- ✓ ***H_0*: *$\mu \leq 10$*,** The null hypothesis suggests that the mean BP reduction is <u>not</u> significantly <u>higher</u> than 10.
- ✓ ***H_1*: *$\mu > 10$*,** the alternative hypothesis and the research hypothesis or what the researchers hope for are the same.
- ✓ Thus, the test is one sided with <u>one upper rejection region</u> of an area = α (0.05)
- ✓ Thus, area below $Z_{1-\alpha)}$ is 0.95 and the corresponding Z is 1.65 as critical value.
- ✓ If test statistic (Z-sample) is higher than 1.65, H_0 is rejected.
- ✓ If Z-sample was less than +1.65 we accept the null hypothesis.
- ✓ But the calculated Z of the sample (3.5) was > +1.65, thus, null hypothesis is rejected meaning that BP reduction is significantly higher than 10.

$$Z_{sample} = \frac{\bar{X} - \mu_{\bar{x}}}{\sigma / \sqrt{n}}$$

$$Z_{sample} = \frac{17 - 10}{2} = 3.5$$

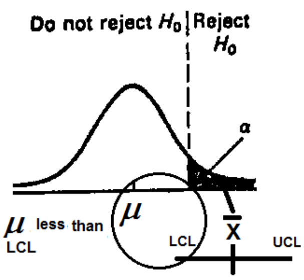


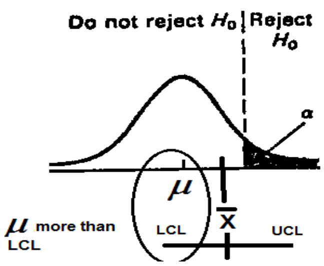
Right-tailed

- ✓ However, for the drug to considered for further clinical studies the reduction should be highly significant, which can be assessed by finding out p-value <u>(one sided)</u> equivalent to the area above 3.5: 1-0.9998 = 0.0002 from Z-table, well very highly significant making the drug a good candidate for further clinical studies.
- ✓ 95% of all possible samples would have z scores ≤1.645 (acceptance region) and 5% of all possible samples would have z scores < 1.645 (rejection region).

- **Testing H_0 by Means of a Confidence Interval: right tailed**

  - ➢ If the lower confidence limit (LCL) is higher than the hypothetical mean, H_0 is rejected.
  - ➢ If LCL is lower or equal to the hypothetical mean H_0 is accepted.





★ Example:

An antihypertensive drug is to be considered for clinical trials in humans if it results in reduction of diastolic blood pressure of more than 10 mmHg <u>with at least **high** significance</u>. The drug was given to 16 animals after hypertension was induced. The mean reduction of BP was 17 mmHg. *σ* was estimated to be 8 mmHg. Is the drug considered a good candidate for further clinical trials at α of 0.05.

- ✓ ***H_0*: *$\mu \leq 10$***
- ✓ ***H_1*: *$\mu > 10$***
- ✓ Since 13.7 (LCL) is **higher** than 10 (hypothetical mean) **we reject H_0 and conclude BP reduction is significantly higher than 10.** Hypothetical mean is not included in the confidence interval.

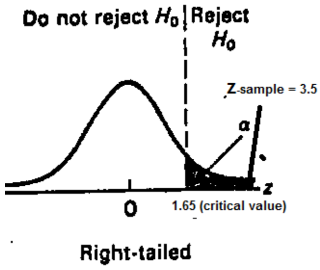
$$\bar{X} \pm Z_{1-\alpha} * \frac{\sigma}{\sqrt{n}} =$$

$$17 \pm 1.65 \times 2$$

$$13.7 to 20.3.$$

- ✓ 95% of all possible samples would have $\bar{x} \le 10 + 1.645*2$ (acceptance region) and 5% of all possible samples would have $\bar{x} > 10 + 1.645*2$ (rejection region).

➢ In the question he asked (results in reduction of diastolic blood pressure of more than 10 mmHg with at least **high** significance). So, we must make sure about the significance level, so we go with the p-value.



- ✓ P-value is the area to the right of z-sample or above z-sample.
- ✓ From z table the area above (3.5) is 0.0002
- ✓ P < 0.001 results is very high significant

- **Left Tailed Z-Test of population mean**

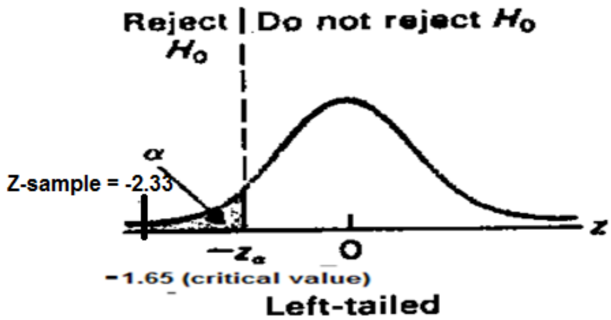
★ Example:

There are claims that the Mediterranean diet can result in lower bad cholesterol (LDL) levels in healthy subjects. A researcher decided to put this claim to the test. 100 subjects who follow this diet were randomly selected and their LDL level was measured as mean value of 93 mg/dl. σ was estimated to be 30 mg/dl. At significance level of 0.05, does mediterranean diet result in mean LDL lower than normal average LDL level of 100 mg/dl.

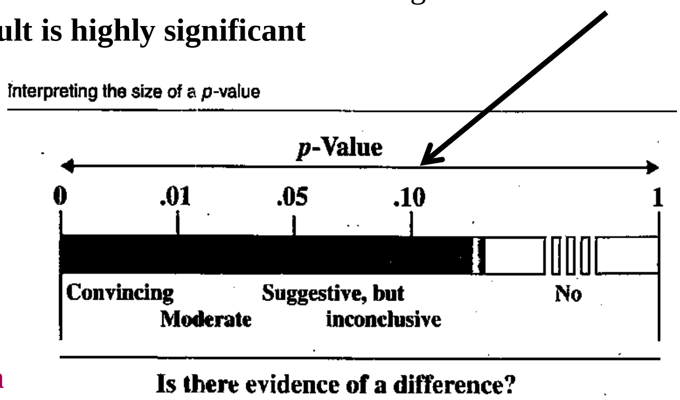
- ✓ $\boldsymbol{H_0: \mu \ge 100}$
- ✓ $\boldsymbol{H_1: \mu < 100}$
- ✓ The null hypothesis suggests that cholesterol level is not significantly lower than 100. Thus, Z-test is one sided with one lower rejection region of an area = α (0.05) Thus area below Z (α) is 0.05 and the corresponding Z is -1.65 as critical value. If test statistic (Z-sample) is lower than -1.65 H_0 is rejected.

$$Zsample = \frac{\bar{X} - \mu_{\bar{x}}}{\sigma / \sqrt{n}}$$

$$Zsample = \frac{93 - 100}{3} = -2.33$$

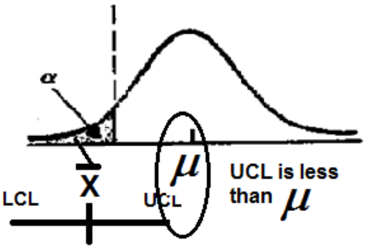


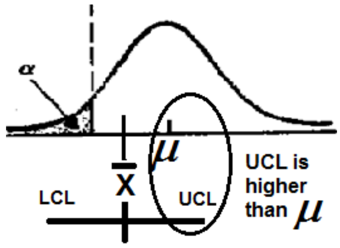
- ✓ If Z-sample was higher than -1.65 we accept the null hypothesis.
- ✓ But the calculated Z of the sample was < -1.65, thus null hypothesis is rejected meaning that LDL is significantly lower than 100.
- ✓ p-value (one sided) equivalent to the area below -2.3 is **0.0099** from Z-table, highly significant. The summary of testing can be stated as there is convincing evidence for the association between Mediterranean diet and mean LDL level as lowering effect.
- ✓ **p-value < 0.01 result is highly significant**



- **Testing H_0 by Means of a Confidence Interval**

- If the upper confidence limit (UCL) is <u>lower</u> than the hypothetical mean, H_0 is rejected.
- If UCL is <u>higher or equal</u> to the hypothetical mean, H_0 is accepted.





★ Example:

There are claims that the Mediterranean diet can result in lower bad cholesterol (LDL) levels in healthy subjects. A researcher decided to put this claim to the test. 100 subjects who follow this diet were randomly selected and their LDL level was measured as mean value of 93 mg/dl. σ was estimated to be 30 mg/dl. At significance level of 0.05, does mediterranean diet result in mean LDL lower than normal average LDL level of 100 mg/dl.

- ✓ H_0: $\mu \geq 100$
- ✓ H_1: $\mu < 100$
- ✓ Since 97.3 (UCL) is higher than 100 (hypothetical mean)
  We reject the H_0 and conclude LDL is significantly lower than 100.

$$\overline{X} \pm Z_{1-\alpha} * \frac{\sigma}{\sqrt{n}} =$$

$$93 \pm 1.65 \times 3$$

$$88.05 to 97.95.$$

- **Summary notes on hypothesis testing**

- Steps of testing:

1. State null and the alternative hypotheses

$$H_0 : \mu = \mu_0 \; versus \; H_1 : \mu \neq \mu_0$$
$$H_0 : \mu \geq \mu_0 \; versus \; H_1 : \mu < \mu_0$$
$$H_0 : \mu \leq \mu_0 \; versus \; H_1 : \mu > \mu_0$$

2. Choose a significance level α (usually .05)
3. Determine the critical value, acceptance and rejection region.
4. Compute the test statistic (Z-stat or z-sample). This is the calculated value that you will compare with the critical value.
5. Reject the null hypothesis if the test statistic falls in the rejection region, otherwise do not reject null hypo. But no conclusion on how much difference or the evidence can be made.
6. Calculate p-value which can provide the amount of difference or evidence.
7. Construct confidence interval
8. State the appropriate conclusions

- **Approaches of hypothesis testing**

Approach	Criteria
Critical value approach	Two sided: Accept H_0 if −Z-critical≤ Z-sample≤ +Z-critical, otherwise reject H_0). E.g. for α =0.05 accept H_0 if -1.96≤ Z-sample≤ +1.96 and reject if Z-sample> +1.96 or Z-sample< -1.96 . Right sided: Accept H_0 if Z-sample≤ +Z-critical, otherwise reject H_0. E.g. for α =0.05 accept H_0 if -Z-sample≤ +1.65 and reject if Z-sample> +1.65 Left sided: Accept H_0 if Z-sample ≥-Z-critical otherwise reject H_0. E.g. for α =0.05 accept H0 if Z-sample ≥-1.65 ; Reject if Z-sample<-1.65 .

- **Decision making approaches of hypothesis testing**

Approach	Criteria
Confidence interval approach	Two sided: if hypothetical value is not contained in the CI of the sample mean reject H_0, otherwise accept Right sided: If the lower limit of CI is higher than the hypothetical mean reject H_0 otherwise accept Left sided: If the upper limit of CI is lower than the hypothetical mean reject H_0 otherwise accept
P-value approach	If $P < \alpha$ reject H_0 and $P \geq \alpha$ accept. When reject, the lower the p-value the higher the significant difference or evidence against H_0.

- **Summary notes on hypothesis testing**
  - An indication of equality (=, ≥, ≤) must appear in the null hypothesis. Conversely ≠, < and > must a pear for the alternative hypothesis.
  - The null hypothesis is the hypothesis to be tested.
  - The null and alternative hypothesis are complementary. The two together exhaust all possibilities regarding the value that the hypothesized parameter can assume
  - If H_0 is rejected, we conclude that H_A is true, but usually we state our conclusion as reject or accept H_0 without referring to H_A.
  - Accepting or rejecting a hypothesis is not 100% proof of the hypothesis because of possible type I and type II errors.
  - Common encountered α values are 0.01, 0.05 and 0.1, but the most used one is 0.05.
  - The level of significance α is the probability of rejecting a true null hypothesis (type error). This probability or chance of type I error for α of 0.1 is 0.1 and for 0.05 is 0.05.
  - The decision of which values go into the rejection region and which ones go into the nonrejection region is based on the desired level of significance α. Higher α means higher area of rejection area (s) with higher chance of rejecting H_0 when it is true (Type I error).
  - Since rejection of a true null hypothesis is an error, we should make the level of significance small (usually 0.05), otherwise the probability of choosing samples from the rejection area (s) is quite higher

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