Pharmaceutical statistics

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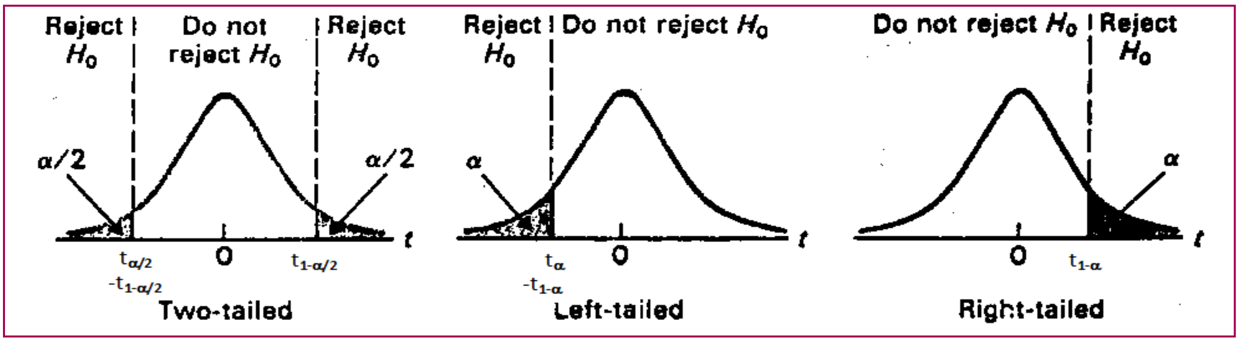
ARKAN ACADEMY

t-Test for mean of a Normally Distributed Population: σ unknown

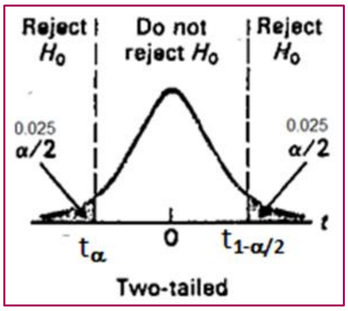
- **Assumptions:**
  - The population is normally distributed.
  - If not normal, requires large samples > 30
  - Population has unknown or no good estimate of its standard deviation (σ). The sample standard deviation (s) is used to replace σ. Thus t-statistic instead of z-statistic can be calculated.
- **Steps include:**
  - State null and the alternative hypotheses

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

  - Choose a significance level α (usually 0.05).
  - Determine the critical region.
  - Compute the test statistics (**t-stat**), Instead of using σ (population SD) for Z-score we use **s** (sample standard deviation) for t-value. This is the calculated value that you will compare with the critical value.
  - $t = \dfrac{\bar{x} - \mu}{s/\sqrt{n}} = \dfrac{\bar{x} - \mu}{SE}$
  - Reject the null hypothesis if the test statistic falls in the rejection region, otherwise do not reject null hypothesis.
  - State the appropriate conclusions.



- **Two Tailed t-Test**
  - ★ Example:
    The body mass index of a group of 14 healthy adult males has a mean of 30.5 and a standard deviation (s) of 10.6392 (<u>for the sample not the population</u>), can we conclude that the mean BMI of the population is equal to 35 at α=0.05?



    - ✓ H_0: μ = 35
    - ✓ H_A: μ ≠ 35
    - ✓ **t-stat** = $\frac{\bar{x} - \mu_0}{SE}$, SE = s / $\sqrt{n}$
    - ✓ t (1-α/2, df) or t (0.975, df 13) = 2.160.
    - ✓ Thus, critical values (t*) are -2.160 and +2.16

d.f.	.75	.80	.85	.90	.95	.975	.98
						Probability p	
1	1.000	1.376	1.963	3.078	6.314	12.71	15.89
2	0.816	1.061	1.386	1.886	2.920	4.303	4.849
3	0.765	0.978	1.250	1.638	2.353	3.182	3.482
4	0.741	0.941	1.190	1.533	2.132	2.776	2.999
5	0.727	0.920	1.156	1.476	2.015	2.571	2.757
6	0.718	0.906	1.134	1.440	1.943	2.447	2.612
7	0.711	0.896	1.119	1.415	1.895	2.365	2.517
8	0.706	0.889	1.108	1.397	1.860	2.306	2.449
9	0.703	0.883	1.100	1.383	1.833	2.262	2.398
10	0.700	0.879	1.093	1.372	1.812	2.228	2.359
11	0.697	0.876	1.088	1.363	1.796	2.201	2.328
12	0.695	0.873	1.083	1.356	1.782	[illegible]	2.303
13	0.694	0.870	1.079	1.350	1.771	2.160	2.282
14	0.692	0.868	1.076	1.345	1.761	[illegible]	2.264

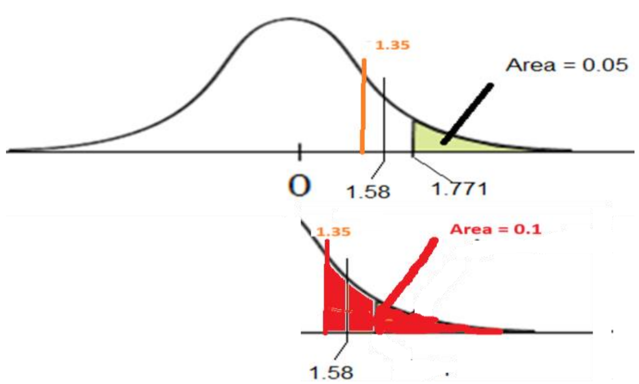
- ✓ Decision rule: this is a two-sided test and so we put α/2 (0.025) in each tail. The t values (t-critical) to the right and left of which 0.025 of the area are 2.1604 and -2.1604.
- ✓ Calculation of the test statistic:

$$t-stat = \frac{\bar{x}-\mu_0}{SE} = \frac{\bar{x}-\mu_0}{s/\sqrt{n}} = \frac{30.5-35}{10.6392/\sqrt{14}} = \frac{-4.5}{2.8434} = -1.58$$

- ✓ We do not reject H_0 since -1.58 falls in the nonrejection region. $-t^* < t\text{-stat} < t^*$ or -2.16<-1.58<+2.16
- ✓ We can conclude that the mean of the population from which the sample is not significantly different from 35 at significance level (α) of 0.05.

➢ P-value:

- ✓ Finding p-value for t-stat is not direct as for z-stat. The table below can be used to find p-value by comparing t-stat to the closest t-values from the t-distribution table at df =13 as follows:
- ✓ t-stat (1.58) is larger than 1.35 and smaller than 1.771 at df=13. Thus p-value (**two sided**) is smaller than 0.2 and larger than 0.1 (in the range 0.1 to 0.2, not inclusive), which is larger than alpha (0.05), suggesting insufficient evidence to reject the H0.



d.f.	.75	.80	.85	.90	.95	.975
1	1.000	1.376	1.963	3.078	6.314	12.71
2	0.816	1.061	1.386	1.886	2.920	4.303
3	0.765	0.978	1.250	1.638	2.353	3.182
4	0.741	0.941	1.190	1.533	2.132	2.776
5	0.727	0.920	1.156	1.476	2.015	2.571
6	0.718	0.906	1.134	1.440	1.943	2.447
7	0.711	0.896	1.119	1.415	1.895	2.365
8	0.706	0.889	1.108	1.397	1.860	2.306
9	0.703	0.883	1.100	1.383	1.833	2.262
10	0.700	0.879	1.093	1.372	1.812	2.228
11	0.697	0.876	1.088	1.363	1.796	2.201
12	0.695	0.873	1.083	1.356	1.782	2.179
13	0.694	0.870	1.079	1.350	1.771	2.160
14	0.692	0.868	1.076	1.345	1.761	2.145

➢ We can also find the confidence interval using the t value:

- ✓ CI = $\bar{x} \pm t_{(1-\alpha/2,\ df=13)} \times SE$ = 30.5 ± 2.16 × 2.8434
- ✓ CI: 24.4 to 36.6, capturing the hypothetical mean (35) and suggesting insignificant difference at significance level of 0.05

• Right Tailed t-Test

★ Example:

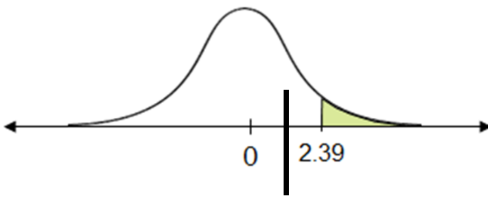
A new antihypertensive drug is being tested. It is supposed to lower blood pressure more than other drugs. Other drugs have been found to lower the pressure by 10 mmHg on average, so we suspect (or hope) that our drug will lower blood pressure by more than 10 mmHg. We would like to know whether the new drug shows result different from the other drugs at α=0.01, in particular whether it is better than the old drugs, i.e. does the new drug lower blood pressure more than other drugs?
To collect evidence, we select a random sample of size n = 61, which was found to have a sample mean of 11.3 and a sample standard deviation of 5.1

- ✓ H_0: μ ≤ 10
- ✓ H_A: μ > 10
- ✓ From t-distribution table t(1-α, df) or t (0.99, df=60) = 2.39 as t-critical

	Probability p							
d.f.	.75	.80	.85	.90	.95	.975	.98	.99
40	0.681	0.851	1.050	1.303	1.684	2.021	2.123	2.423
50	0.679	0.849	1.047	1.299	1.676	2.009	2.109	2.403
60	0.679	0.848	1.045	1.296	1.671	2.000	2.099	2.390
70	0.678	0.847	1.044	1.294	1.667	1.994	2.093	2.381
80	0.678	0.846	1.043	1.292	1.664	1.990	2.088	2.374
90	0.677	0.846	1.042	1.291	1.662	1.987	2.084	2.368

- ✓ $t-stat = \dfrac{\overline{X}-\mu_0}{SE} = \dfrac{11.3-10}{5.1/\sqrt{61}} = \dfrac{1.3}{0.653} = 1.98$

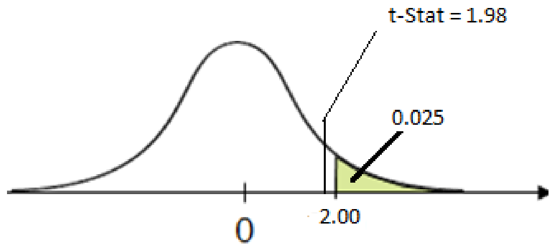
- ✓ t-stat (1.94) < t* (2.39) Thus, there is **NOT** enough evidence to reject H_0, thus the drug does not significantly reduce mean blood pressure by more than 10 mmHg at α=0.01.

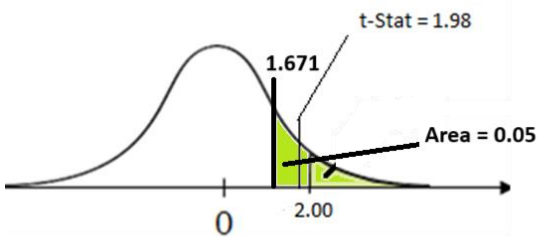


➢ **P-value:**

- ✓ t-stat (1.94) is larger than 1.671 and smaller than 2.0 at df=60. Thus p-value (one sided) is smaller than 0.05 and larger than 0.025 (in the range 0.025 to 0.05, not inclusive), larger than alpha (0.01), suggesting insufficient evidence to reject the H_0.

					Probability p		
d.f.	.75	.80	.85	.90	.95	.975	.98
40	0.681	0.851	1.050	1.303	1.684	2.021	2.123
50	0.679	0.849	1.047	1.299	1.676	2.009	2.109
60	0.679	0.848	1.045	1.296	1.671	2.000	2.099
70	0.678	0.847	1.044	1.294	1.667	1.994	2.093
80	0.678	0.846	1.043	1.292	1.664	1.990	2.088





➢ We can also find the confidence interval using the t value:

- ✓ CI = $\bar{x} \pm t_{(1-\alpha\ ,\ df=13)} \times SE = 11.3 \pm 2.39 \times 0.653$
- ✓ CI: 9.7 to 12.9
- ✓ LCL is less than μ_0 or 10 suggesting B.P reduction is not significantly higher than 10 at α= 0.01

- **Left Tailed t-Test**

★ Example:

A pharmaceutical company put a specification for a dissolution parameter of a drug formulated as tablet, which is time for 80% drug release (T80%), as less than 31 min. 8 tablets of a batch were tested, and their results are given below. Perform t-test at α = 0.05

T80%: 30 28 32 26 33 25 28 30

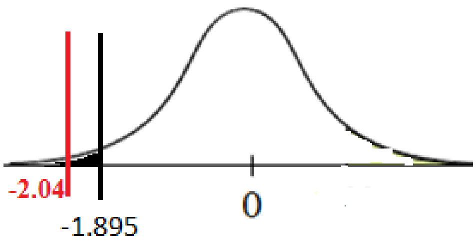
- ✓ H_0: $\mu \geq 31$,
- ✓ H_A: $\mu < 31$
- ✓ Find out critical value t (α) the degrees of freedom (df) for the test is equal to n–1 or 8 –1 = 7.
- ✓ t (0.95, df=7) = +1.895. But because the test is left-sided the critical value is – t (0.95, df=7) = -1.895.
- ✓ **Compute test statistic**: The mean is equal to 29.00 and the standard deviation is equal to 2.775. Now, we can compute *t* -statistic:

d.f.	.75	.80	.85	.90	.95
1	1.000	1.376	1.963	3.078	6.314
2	0.816	1.061	1.386	1.886	2.920
3	0.765	0.978	1.250	1.638	2.353
4	0.741	0.941	1.190	1.533	2.132
5	0.727	0.920	1.156	1.476	2.015
6	0.718	0.906	1.134	1.440	1.943
7	0.711	0.896	1.119	1.415	1.895
8	0.706	0.889	1.108	1.397	1.860

$$t = \frac{\overline{X}-\mu}{S_X/\sqrt{n}} \qquad df = n-1$$

$$t = \frac{29.00-31.00}{2.775/\sqrt{8}} = -2.04$$

- ✓ Because t-stat (-2.04) is less than the critical value (-1.895), H_0 is rejected at $\alpha = 0.05$ and we can conclude that T80% is significantly less than 31 min., in compliance with specification. Thus, the batch meets the dissolution specification.



- ➢ **p-value:** p value < 0.05
  - ✓ t-stat (-2.04) is larger than -1.895 and smaller than -2.365 at df =7. Working on areas above symmetrical values of +2.04, +1.895 and +2.365, one sided p-value is smaller than 0.05 and larger than 0.025, smaller than alpha, suggesting T80% is significantly lower than 31 min., and comply with the specification of dissolution.

d.f.	.75	.80	.85	.90	.95	.975
1	1.000	1.376	1.963	3.078	6.314	12.71
2	0.816	1.061	1.386	1.886	2.920	4.303
3	0.765	0.978	1.250	1.638	2.353	3.182
4	0.741	0.941	1.190	1.533	2.132	2.776
5	0.727	0.920	1.156	1.476	2.015	2.571
6	0.718	0.906	1.134	1.440	1.943	2.447
7	0.711	0.896	1.119	1.415	1.895	2.365
8	0.706	0.889	1.108	1.397	1.860	2.306

- ➢ We can also find the confidence interval using the t value:
  - ✓ $CI = \bar{x} \pm t_{(1-\alpha, df=13)} \times SE = 29 \pm 1.895 \times 0.981$
  - ✓ CI: 27.1 to 30.9, UCL is lower than the hypothetical mean, thus H_0 is rejected.

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