Pharmaceutical statistics

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ACADEMY

Hypothesis testing of the difference between 2 population means

- Dependent samples
  - Paired t-test
- Indepedent samples
  - Unknown σ
    - Assuming equal variances or σ
      - Pooled t-test
    - Assuming unequal variances or σ
      - Unpooled t-test
  - Known σ
    - Z-test

Hypothesis Testing: Difference Between Two Populations: Independent samples (z and t tests)

- **Assumptions**
  - Two populations are normally distributed, if not normal, requires large samples.
  - Standard deviations of populations:
    - ✓ **known**, z-stat can be calculated, and **z-test** is performed.
    - ✓ **Unknown** standard deviations
      1. Pooled t-test: assuming equal standard deviations
      2. Unpooled t-test: unequal standard deviations
  - The samples are independent: the scores of one sample do not affect those of the other as the following scenarios:
    - ✓ Random samples from different populations: Testing the difference of the means between two fixed populations we test the differences between samples from each population. When both samples are randomly selected, the samples are independent because they came from two different populations randomly.
    - ✓ Random assignment to different treatments or groups: When working with subjects, if we select a random sample and then randomly assign half of the subjects to one group and half to another, we can make inferences about the populations by z or t test.
    - ✓ If we have a drug that is tested for its effect on FBG and we take 2 samples (one took the placebo and the other took the drug), every sample has subjects that are different from the subjects in the other sample, so they are independent.
    - ❖ **Note:** The following illustrate dependent samples for which z or t-test cannot be used: If we need to compare STAT scores for your section between first and second exam (same students and thus dependent samples). Similarly, If the same sample was subjected to two different treatments (first the sample was given drug A and after washout period the same sample was given drug B). When the samples are dependent paired t-test rather than t-test is performed.
- **Z-test of Independent Samples (known σ) steps:**
  - State the null and alternative hypotheses.
    - ✓ Two tailed: H_0: $\mu_1 - \mu_2 = 0$ or $\mu_1 = \mu_2$, H_A: $\mu_1 - \mu_2 \neq 0$ or $\mu_1 \neq \mu_2$
    - ✓ Right tailed: H_0: $\mu_1 - \mu_2 \leq V$, H_A: $\mu_1 - \mu_2 > V$
    - ✓ Left tailed: H_0: $\mu_1 - \mu_2 \geq V$, H_A: $\mu_1 - \mu_2 < V$
      (V can be zero or any other value)
  - Calculate the standard error: SE = $\sqrt{\frac{\sigma 1^2}{n1} + \frac{\sigma 2^2}{n2}}$
  - Choose α and set the criterion (critical values) for rejecting the null Hypothesis as follows:

α	Z-Critical		
	Two tailed	Right tailed	Left tailed
0.1	±1.65	1.28	-1.28
0.05	±1.96	1.65	-1.65
0.01	±2.58	2.33	-2.33

  - Compute the test statistic: (The subscript 0 indicates that the difference is a hypothesized parameter).

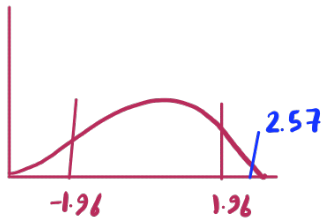
$$z = \frac{(\bar{x}1 - \bar{x}2) - (\mu_1 - \mu_2)_0}{SE}$$

  - Compare z with the critical value (s) and make a decision: reject or fail to reject the null hypothesis

★ Example 1:

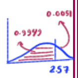
Researchers wish to know if the data they collected provide sufficient evidence to indicate a difference (two sided) in the mean uric acid levels between normal individuals and individuals with Down's syndrome. The data consist of uric acid readings on 12 individuals with Down's syndrome and 15 normal individuals. The means are: $\bar{x}_1 = 4.5 \text{ mg/100 mL}$ and $\bar{x}_2 = 3.4 \text{ mg/100 mL}$

- ✓ The data constitute two independent simple random samples each drawn from normally distributed population with **variance** equal to 1 for the Down's syndrome population and 1.5 for the normal population.
- ✓ H_0: $\mu_1 - \mu_2 = 0$, H_A: $\mu_1 - \mu_2 \neq 0$
- ✓ An alternative way of stating the hypothesis is as follows: H_0: $\mu_1 = \mu_2$, HA: $\mu_1 \neq \mu_2$
- ✓ Let α = 0.05, the critical values of z are 1.96 and -1.96. Reject H_0 unless $-1.96 \geq z \geq 1.96$
- ✓ $$SE = \sqrt{\frac{\sigma_1^2}{n_1} + \frac{\sigma_2^2}{n_2}} = \sqrt{\frac{1}{12} + \frac{1.5}{15}} = 0.4282$$



- ✓ $$z = \frac{(\bar{x}1 - \bar{x}2) - (\mu_1 - \mu_2)_0}{SE} \qquad z = \frac{(4.5 - 3.4) - 0}{0.4282} = \frac{1.1}{0.4282} = 2.57$$
- ✓ Statistical decision to reject H_0 since 2.57 > 1.96 Conclude that on the basis of the data, there is an indication that the two-population means are not equal.
- ✓ p value: 0.0102 (total area to the right of 2.57 and the left of -2.57), p < α so we reject H_0
- ✓ Confidence Interval:
- ✓ $$(\bar{x}1 - \bar{x}2) \pm z_{(1-\alpha/2)} * SE =$$
  $$1.1 \pm 1.96 * 0.4282$$
  $$\text{From } 0.26 \text{ to } 1.94$$

z	0.00	0.01	0.02	0.03	0.04	0.05	0.06	0.07
0.00	.5000	.5040	.5080	.5120	.5160	.5199	.5239	.5279
0.10	.5398	.5438	.5478	.5517	.5557	.5596	.5636	.5675
0.20	.5793	.5832	.5871	.5910	.5948	.5987	.6026	.6064
0.30	.6179	.6217	.6255	.6293	.6331	.6368	.6406	.6443
0.40	.6554	.6591	.6628	.6664	.6700	.6736	.6772	.6808
0.50	.6915	.6950	.6985	.7019	.7054	.7088	.7123	.7157
0.60	.7257	.7291	.7324	.7357	.7389	.7422	.7454	.7486
0.70	.7580	.7611	.7642	.7673	.7704	.7734	.7764	.7794
0.80	.7881	.7910	.7939	.7967	.7995	.8023	.8051	.8078
0.90	.8159	.8186	.8212	.8238	.8264	.8289	.8315	.8340
1.00	.8413	.8438	.8461	.8485	.8508	.8531	.8554	.8577
1.10	.8643	.8665	.8686	.8708	.8729	.8749	.8770	.8790
1.20	.8849	.8869	.8888	.8907	.8925	.8944	.8962	.8980
1.30	.9032	.9049	.9066	.9082	.9099	.9115	.9131	.9147
1.40	.9192	.9207	.9222	.9236	.9251	.9265	.9279	.9292
1.50	.9332	.9345	.9357	.9370	.9382	.9394	.9406	.9418
1.60	.9452	.9463	.9474	.9484	.9495	.9505	.9515	.9525
1.70	.9554	.9564	.9573	.9582	.9591	.9599	.9608	.9616
1.80	.9641	.9649	.9656	.9664	.9671	.9678	.9686	.9693
1.90	.9713	.9719	.9726	.9732	.9738	.9744	.9750	.9756
2.00	.9772	.9778	.9783	.9788	.9793	.9798	.9803	.9808
2.10	.9821	.9826	.9830	.9834	.9838	.9842	.9846	.9850
2.20	.9861	.9864	.9868	.9871	.9875	.9878	.9881	.9884
2.30	.9893	.9896	.9898	.9901	.9904	.9906	.9909	.9911
2.40	.9918	.9920	.9922	.9925	.9927	.9929	.9931	.9932
2.50	.9938	.9940	.9941	.9943	.9945	.9946	.9948	.9949
2.60	.9953	.9955	.9956	.9957	.9959	.9960	.9961	.9962
2.70	.9965	.9966	.9967	.9968	.9969	.9970	.9971	.9972
2.80	.9974	.9975	.9976	.9977	.9977	.9978	.9979	.9979



- ✓ Since the confidence interval does not capture the hypothetical mean difference (0), It is suggested that the two populations (normal and downs syndrome) means (uric acid) are significantly different at α = 0.05

★ Example 2:

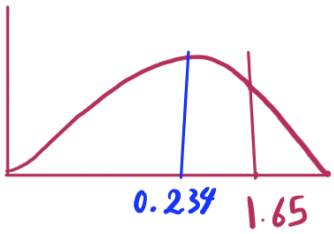
Suppose in the previous example the question of interest was is mean uric acid is higher in the population of downs syndrome than in that of normal subjects:

- ✓ The z-test becomes right sided with single critical value of 1.65.
- ✓ H_0: $\mu_1 - \mu_2 \leq 0$, H_A: $\mu_1 - \mu_2 > 0$
- ✓ Or H_0: $\mu_1 \leq \mu_2$, H_A: $\mu_1 > \mu_2$
- ✓ Because the hypothesized difference is still zero Z-stat is not changed and still calculated as 2.57, well higher than the critical value and thus H_0 is rejected.
- ✓ Confidence Interval: $$\bar{x}1 - \bar{x}2 \pm z_{(1-\alpha)} * SE =$$
  $$1.1 \pm 1.65 * 0.4282$$
  $$\text{From } 0.39 \text{ to } 1.81$$
- ✓ LCL is higher than the hypothesized difference of 0, Thus consistent with above conclusion that H0 is rejected.
- ✓ P-value = 0.0051 which is < α

★ Example 3:

Suppose in the previous example the question of interest was is mean uric acid is 1 mg% higher in the population of downs syndrome than in that of normal subjects:

- ✓ The z-test is right sided with a single critical value of 1.65.
- ✓ H_0: $\mu_1 - \mu_2 \leq 1$, H_A: $\mu_1 - \mu_2 > 1$
- ✓ Because the hypothesized difference is 1.
- ✓ $z = \frac{(4.5-3.4)-1}{0.4282} = \frac{0.1}{0.4282} = 0.234$



- ✓ z-stat is lower than the critical value, H_0 is not rejected.
- ✓ P-value = 0.591 which is > α = 0.05 so H_0 is not rejected.
- ✓ Confidence Interval is the same as in the previous slide: 0.39 to 1.81.
- ✓ LCL is lower than the hypothesized difference of 1, thus consistent with the above conclusion that H_0 is not rejected.

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