T-test

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Contents

1 Basic knowledge

$\phi(x)$ and $\Phi(x)$ are pdf and cdf of standard normal distribution, respectively. We use Z to represent a random variable that follows standard normal distribution and z_α the lower α quantile of standard normal distribution. Therefore

$$P(Z \le z_\alpha) = \Phi(z_\alpha) = \alpha.$$

Theorem 1. *Let $x_1, \cdots, x_n$ be a random sample from a population with mean μ and variance $\sigma^2 < \infty$. Then*

1. $\mathrm{E}\bar{x} = \mu$.

2. $\mathrm{Var}\bar{x} = \sigma^2/n$.

3. $\mathrm{E}S^2 = \sigma^2$, *where* $S^2 = \frac{1}{n-1}\sum\limits_{i=1}^{n}(x_i - \bar{x})^2$.

Theorem 2. *Let $x_1, \cdots, x_n$ be a random sample from $N(\mu, \sigma^2)$. Then*

1. $\bar{X} \sim N(\mu, \sigma^2/n)$.

2. $\bar{X}$ *is independent of* S^2.

3. $(n-1)S^2/\sigma^2$ *follows a chi-squared distribution with* $n-1$ *degree of freedom.*

2 One-sample test

Consider a random sample $x_1, \cdots, x_n$ from $N(\mu, \sigma^2)$. The likelihood is

$$f(x_1, \cdots, x_n) = \prod_{i=1}^{n} \left(2\pi\sigma^2\right)^{-1/2} \exp\left(-\frac{(x_i - \mu)^2}{2\sigma^2}\right)$$
$$= \left(2\pi\sigma^2\right)^{-n/2} \exp\left(-\frac{\sum_{i=1}^{n}(x_i-\mu)^2}{2\sigma^2}\right).$$

We propose the test

$$H_0: \ \mu = \mu_0 \quad \textbf{v.s} \quad H_1: \ \mu \neq \mu_0$$

2.1 variance known

Construct LRT

$$LR = \frac{\max\limits_{\mu \in H_0} f(x_1, \cdots, x_n | \mu)}{\max\limits_{\mu \in H_0 \cup H_1} f(x_1, \cdots, x_n | \mu)} = \frac{f(x_1, \cdots, x_n | \mu = \mu_0)}{f(x_1, \cdots, x_n | \mu = \bar{x})} = \exp\left(-\frac{(\bar{x} - \mu_0)^2}{2\sigma^2/n}\right)$$

Therefore rejecting H_0 when LR is smaller than some constant C is equivalent to rejecting H_0 when $|\bar{x} - \mu_0|$ is larger than some other constant C. Hence

$$\text{Reject Region: } \{\bar{x} : \quad |\bar{x} - \mu_0| > C\}$$

2.2 variance unknown

When σ^2 is unknown, the MLE under H_0 is

$$\mu_{(0)} = \mu_0, \quad \sigma^2_{(0)} = \frac{1}{n}\sum_{i=1}^{n}(x_i - \mu_0)^2.$$

And the MLE under $H_0 \cup H_1$ is

$$\mu_{(0\cup 1)} = \bar{x}, \quad \sigma^2_{(0\cup 1)} = \frac{1}{n}\sum_{i=1}^{n}(x_i - \bar{x})^2.$$

Note: MLE for σ^2 offers smaller MSE than S^2, but it's biased.

Then the likelihood ratio is

$$LR = \frac{f\left(x_1, \cdots, x_n \middle| \mu = \mu_{(0)}, \sigma^2 = \sigma^2_{(0)}\right)}{f\left(x_1, \cdots, x_n \middle| \mu = \mu_{(0\cup 1)}, \sigma^2 = \sigma^2_{(0\cup 1)}\right)} = \left(\frac{\sum_{i=1}^{n}(x_i - \mu_0)^2}{\sum_{i=1}^{n}(x_i - \bar{x})^2}\right)^{-n/2} \propto \left(\frac{\sum_{i=1}^{n}(\bar{x} - \mu_0)^2}{\sum_{i=1}^{n}(x_i - \bar{x})^2}\right)^{-n/2},$$

where for the last part we mainly focus on terms related to μ_0. So to reject H_0 when LR is small is equivalent to

$$\text{Reject Region: } \left\{\bar{x} : \quad \frac{|\bar{x} - \mu_0|}{\sqrt{\sum_{i=1}^{n}(x_i - \bar{x})^2}} > C\right\}$$

The idea is similar to that in Section 2.1. But we replace σ^2 with S^2.

3 Two sample test

Consider two random samples $x_1, \cdots, x_{n_1} \sim N(\mu_1, \sigma_1^2)$ and $y_1, \cdots, y_{n_2} \sim N(\mu_2, \sigma_2^2)$. Then the likelihood of the data is

$$
\begin{aligned}
& f\left(x_1, \cdots, x_{n_1}, y_1, \cdots, y_{n_2} \middle| \mu_1, \mu_2, \sigma_1^2, \sigma_2^2\right) \\
= & \left(2\pi\sigma_1^2\right)^{-n_1/2} \left(2\pi\sigma_2^2\right)^{-n_2/2} \exp\left(-\frac{\sum_{i=1}^{n_1} (x_i - \mu_1)^2}{2\sigma_1^2} - \frac{\sum_{i=1}^{n_2} (y_i - \mu_2)^2}{2\sigma_2^2}\right) \\
=
\end{aligned}
$$

We propose the test

$$H_0: \ \mu_1 = \mu_2 \quad \textbf{v.s.} \quad H_1: \ \mu_1 \neq \mu_2.$$

3.1 Two-sample, variance known

When σ_1^2 and σ_2^2 are known, the likelihood satisfies

$$f(x_1, \cdots, x_{n_1}, y_1, \cdots, y_{n_2} | \mu_1, \mu_2) \propto \exp\left(-\frac{n_1 (\bar{x} - \mu_1)^2}{2\sigma_1^2} - \frac{n_2 (\bar{y} - \mu_2)^2}{2\sigma_2^2}\right).$$

Therefore under H_0, the MLE for μ_1 and μ_2 is

$$\mu_{1(0)} = \mu_{2(0)} = \mu_{(0)} = \frac{\sigma_2^2 n_1 \bar{x} + \sigma_1^2 n_2 \bar{y}}{\sigma_2^2 n_1 + \sigma_1^2 n_2}.$$

And under $H_0 \cup H_1$, the MLE for μ_1 and μ_2 is

$$\mu_{1(0\cup 1)} = \bar{x}, \quad \mu_{2(0\cup 1)} = \bar{y}.$$

Then the likelihood ratio is

$$
\begin{aligned}
LR = & \frac{\max_{H_0} f(\boldsymbol{x}, \boldsymbol{y} | \mu_1, \mu_2)}{\max_{H_0 \cup H_1} f(\boldsymbol{x}, \boldsymbol{y} | \mu_1, \mu_2)} \\
= & \frac{f\left(\boldsymbol{x}, \boldsymbol{y} \middle| \mu_1 = \mu_2 = \mu_{(0)}\right)}{f\left(\boldsymbol{x}, \boldsymbol{y} \middle| \mu_1 = \mu_{1(0\cup 1)}, \mu_2 = \mu_{2(0\cup 1)}\right)} \\
\propto & \exp\left(-\frac{1}{2}\left(\frac{n_1 \left(\bar{x} - \mu_{(0)}\right)^2}{\sigma_1^2} + \frac{n_2 \left(\bar{y} - \mu_{(0)}\right)^2}{\sigma_2^2}\right)\right) \\
= & \exp\left(-\frac{1}{2} \frac{n_1 n_2}{\sigma_2^2 n_1 + \sigma_1^2 n_2} (\bar{x} - \bar{y})^2\right).
\end{aligned}
$$

From the idea of LRT, H_0 is rejected when LR is small enough, which means the reject rule is

$$\text{Reject Region: } \{(\bar{x}, \bar{y}) || \bar{x} - \bar{y}| > C\}$$

3.2 Two-sample, variance unknown but equal

When σ_1 and σ_2 are both unknown but equal, denoted by σ. The likelihood of the data becomes

$$\begin{aligned}
&f\left(x_1,\cdots,x_{n_1},y_1,\cdots,y_{n_2}\middle|\mu_1,\mu_2,\sigma^2\right)\\
=&\left(2\pi\sigma^2\right)^{-n_1/2-n_2/2}\exp\left(-\frac{\sum\limits_{i=1}^{n_1}\left(x_i-\mu_1\right)^2+\sum\limits_{i=1}^{n_2}\left(y_i-\mu_2\right)^2}{2\sigma^2}\right).
\end{aligned}$$

So the MLE under H_0 is

$$\mu_{1(0)}=\mu_{2(0)}=\mu_{(0)}=\frac{n_1\bar{x}+n_2\bar{y}}{n_1+n_2},\quad \sigma^2_{(0)}=\frac{\sum\limits_{i=1}^{n_1}\left(x_i-\mu_{(0)}\right)^2+\sum\limits_{i=1}^{n_2}\left(y_i-\mu_{(0)}\right)^2}{n_1+n_2}$$

And the MLE under $H_0\cup H_1$ is

$$\mu_{1(0\cup1)}=\bar{x},\quad \mu_{2(0\cup1)}=\bar{y},\quad \sigma^2_{(0\cup1)}=\frac{\sum\limits_{i=1}^{n_1}\left(x_i-\bar{x}\right)^2+\sum\limits_{i=1}^{n_2}\left(y_i-\bar{y}\right)^2}{n_1+n_2}.$$

Then the likelihood ratio is

$$\begin{aligned}
LR=&\frac{f\left(\boldsymbol{x},\boldsymbol{y}\middle|\mu_1=\mu_2=\mu_{(0)},\sigma^2=\sigma^2_{(0)}\right)}{f\left(\boldsymbol{x},\boldsymbol{y}\middle|\mu_1=\mu_{1(0\cup1)},\mu_2=\mu_{2(0\cup1)},\sigma^2=\sigma^2_{(0\cup1)}\right)}\\
=&\left(\frac{\sigma^2_{(0)}}{\sigma^2_{(0\cup1)}}\right)^{-n_1/2-n_2/2}\\
=&\left(\frac{\sum\limits_{i=1}^{n_1}\left(x_i-\bar{x}+\bar{x}-\mu_{(0)}\right)+\sum\limits_{i=1}^{n_2}\left(y_i-\bar{y}+\bar{y}-\mu_{(0)}\right)}{\sum\limits_{i=1}^{n_1}\left(x_i-\bar{x}\right)^2+\sum\limits_{i=1}^{n_2}\left(y_i-\bar{y}\right)^2}\right)^{-n_1/2-n_2/2}\\
=&\left(1+\frac{n_1\left(\bar{x}-\mu_{(0)}\right)^2+n_2\left(\bar{y}-\mu_{(0)}\right)^2}{\sum\limits_{i=1}^{n_1}\left(x_i-\bar{x}\right)^2+\sum\limits_{i=1}^{n_2}\left(y_i-\bar{y}\right)^2}\right)^{-n_1/2-n_2/2}\\
=&\left(1+\frac{n_1n_2}{n_1+n_2}\cdot\frac{\left(\bar{x}-\bar{y}\right)^2}{\sum\limits_{i=1}^{n_1}\left(x_i-\bar{x}\right)^2+\sum\limits_{i=1}^{n_2}\left(y_i-\bar{y}\right)^2}\right)^{-n_1/2-n_2/2}.
\end{aligned}$$

So to reject H_0 when the likelihood ratio is small enough implies that the reject region is

$$\text{Reject region: }\left\{(\boldsymbol{x},\boldsymbol{y})\middle|\frac{|\bar{x}-\bar{y}|}{\sqrt{\sum\limits_{i=1}^{n_1}\left(x_i-\bar{x}\right)^2+\sum\limits_{i=1}^{n_2}\left(y_i-\bar{y}\right)^2}}>C\right\}.$$

3.2.1 Regional consistency

We asume there's no difference in regional and global efficacy, which means

$$\begin{aligned} x_{r,1}, \cdots, x_{r,n_{r,1}} &\sim N\left(\mu_1, \sigma^2\right) \\ x_{o,1}, \cdots, x_{o,n_{o,1}} &\sim N\left(\mu_1, \sigma^2\right) \\ y_{r,1}, \cdots, y_{r,n_{r,2}} &\sim N\left(\mu_2, \sigma^2\right) \\ y_{o,1}, \cdots, y_{o,n_{o,2}} &\sim N\left(\mu_2, \sigma^2\right) \end{aligned}$$

where r and o stand for 'region' and 'other' and clearly we have

$$n_{r,1} + n_{o,1} = n_1, \quad n_{r,2} + n_{o,2} = n_2$$

For regional and global summary, we have

$$\begin{aligned} \bar{x}_r &\sim N\left(\mu_1, \sigma^2/n_{r,1}\right) \\ \bar{x}_o &\sim N\left(\mu_1, \sigma^2/n_{o,1}\right) \\ \bar{y}_r &\sim N\left(\mu_2, \sigma^2/n_{r,2}\right) \\ \bar{y}_o &\sim N\left(\mu_2, \sigma^2/n_{o,2}\right) \end{aligned}$$

and

$$\begin{aligned} \bar{x} &= \frac{n_{r,1}}{n_{r,1}+n_{o,1}}\bar{x}_r + \frac{n_{o,1}}{n_{r,1}+n_{o,1}}\bar{x}_o \sim N\left(\mu_1, \sigma^2/n_1\right) \\ \bar{y} &= \frac{n_{r,2}}{n_{r,2}+n_{o,2}}\bar{y}_r + \frac{n_{o,2}}{n_{r,2}+n_{o,2}}\bar{y}_o \sim N\left(\mu_2, \sigma^2/n_2\right) \end{aligned}$$

And the treatment effect summary follows

$$\begin{aligned} \Delta_r = \bar{x}_r - \bar{y}_r &\sim N\left(\mu_1 - \mu_2, \left(\frac{1}{n_{r,1}} + \frac{1}{n_{r,2}}\right)\sigma^2\right) \\ \Delta_o = \bar{x}_o - \bar{y}_o &\sim N\left(\mu_1 - \mu_2, \left(\frac{1}{n_{o,1}} + \frac{1}{n_{o,2}}\right)\sigma^2\right) \end{aligned}$$

And

$$\begin{aligned} \Delta =& \bar{x} - \bar{y} \sim N\left(\mu_1 - \mu_2, \left(\frac{1}{n_1} + \frac{1}{n_2}\right)\sigma^2\right) \\ =& \frac{n_{r,1}}{n_{r,1}+n_{o,1}}\bar{x}_r + \frac{n_{o,1}}{n_{r,1}+n_{o,1}}\bar{x}_o - \left(\frac{n_{r,2}}{n_{r,2}+n_{o,2}}\bar{y}_r + \frac{n_{o,2}}{n_{r,2}+n_{o,2}}\bar{y}_o\right) \end{aligned}$$

But unfortunately, Δ can NOT be easily break into Δ_r and Δ_o. Now, let's first assume there's a fixed ratio between the two arms, both in region and other areas, which means

$$n_{r,1} = kn_{r,2}, \quad n_{o,1} = kn_{o,2}$$

Then

$$\begin{aligned} \Delta_r &\sim N\left(\mu_1 - \mu_2, \frac{1+k}{n_{r,1}}\sigma^2\right) \\ \Delta_o &\sim N\left(\mu_1 - \mu_2, \frac{1+k}{n_{o,1}}\sigma^2\right) \\ \Delta &= \frac{n_{r,1}}{n_{r,1}+n_{o,1}}\Delta_r + \frac{n_{o,1}}{n_{r,1}+n_{o,1}}\Delta_o \sim N\left(\mu_1 - \mu_2, \frac{1+k}{n_1}\sigma^2\right) \end{aligned}$$

Considering the show trend crieteria 'Method 1', which is regional treatment improvement keeps certain percentage of global treatment improvement, that is to say for some fixed POSITIVE ρ, it's required that

$$\Delta_r \geq \rho\Delta$$

as a 'show trend criteria'.

3.2.2 Marginal show trend probability

Then marginally, we have the show trend probability

$$\begin{aligned} P\left(\Delta_r \geq \rho\Delta\right) =& P\left(\Delta_r \geq \rho\left(\frac{n_{r,1}}{n_{r,1}+n_{o,1}}\Delta_r + \frac{n_{o,1}}{n_{r,1}+n_{o,1}}\Delta_o\right)\right) \\ =& P\left(\frac{n_{r,1}-\rho n_{r,1}+n_{o,1}}{n_{r,1}+n_{o,1}}\Delta_r \geq \frac{\rho n_{o,1}}{n_{r,1}+n_{o,1}}\Delta_o\right) \end{aligned}$$

which can be easily calculated since Δ_r and Δ_o are independent with known normal distribution.

3.2.3 Show trend probability conditional on global significance (Z-statistics)

The Z-statistics version is actually **assuming σ^2 is known**. Hence the global test is constructed as to reject H_0 when

$$\frac{|\bar{x}-\bar{y}|}{\sqrt{\left(\frac{1}{n_1}+\frac{1}{n_2}\right)\sigma^2}} = \frac{|\bar{x}-\bar{y}|}{\sqrt{\frac{1+k}{n_1}\cdot\sigma^2}} > z_{1-\alpha/2}$$

where we follow the assumption that $n_1 = kn_2$. Therefore the show trend probability given global significance is given by

$$\begin{aligned} & P\left(\Delta_r \geq \rho\Delta \middle| |\Delta| > z_{1-\alpha/2}\sqrt{\frac{1+k}{n_1}\cdot\sigma^2}\right) \\ =& P\left(\Delta_r \geq \rho\Delta \middle| \left\{\Delta > z_{1-\alpha/2}\sqrt{\frac{1+k}{n_1}\cdot\sigma^2}\right\} \cup \left\{\Delta < z_{\alpha/2}\sqrt{\frac{1+k}{n_1}\cdot\sigma^2}\right\}\right) \end{aligned}$$

3.2.4 Show trend probability conditional on global significance (T-statistic)

From Section 3.2, we know the test is constructed as to reject H_0 when

$$\frac{|\bar{x}-\bar{y}|}{\sqrt{\left(\frac{1}{n_1}+\frac{1}{n_2}\right)S_p^2}} > t_{1-\alpha/2}\left(n_1+n_2-2\right)$$

3.3 Two-sample, variance unknown and unequal

For this we refer to the "Welch's unequal variance t-test"[WELCH, 1947]. The test statistic is

$$t = \frac{\bar{x}-\bar{y}}{s_{\bar{\Delta}}},$$

where

$$s_{\bar{\Delta}} = \sqrt{\frac{s_x^2}{n_1} + \frac{s_y^2}{n_2}}.$$

Here $s_x^2 = \frac{1}{n_1 - 1} \sum_{i=1}^{n_1} (x_i - \bar{x})^2$ and $s_y^2 = \frac{1}{n_2 - 1} \sum_{i=1}^{n_2} (y_i - \bar{y})^2$ are the unbiased estimator for σ_1^2 and σ_2^2. The test statistic approximately follows a t-distribution with degree of freedom being

$$\mathbf{d.f.} = \frac{\left(\frac{s_x^2}{n_1} + \frac{s_y^2}{n_2}\right)^2}{\frac{(s_x^2/n_1)^2}{n_1 - 1} + \frac{\left(s_y^2/n_2\right)^2}{n_2 - 1}}.$$

References

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