Parametric tests for continuous variables

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Chung Shing Rex Ha
Institute of Medical Biostatistics, Epidemiology and Informatics (IMBEI)
University Medical Center
rexha@uni-mainz.de

Agenda

- Parametric tests & continuous variables
- Test for two independent populations
- Test for two dependent populations
- Power analysis

Parametric tests & continuous variables

- Continuous variables are variables whose value is obtained by measuring and is uncountable.

- In contrast, discrete variables are countable.

- Examples of continuous variables:
  - Height & weight & BMI
  - Blood pressure
  - Tumor sizes
  - Dose intake
  - Time, e.g., hours

Parametric tests & continuous variables

- Parametric tests are those assuming that sample data comes from a population which can be adequately modeled by a probability distribution with a fixed set of parameters.

- Gaussian/normal distribution is the most common, but not necessary, assumption for population data of continuous variables.

- Normal distribution is parameterized by mean (μ) and standard deviation (σ)

$$X_1, \ldots, X_N \sim N(\mu, \sigma)$$

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Case Study

- A pharmaceutical company is testing a new drug of controlling the high blood pressure. A randomised control-case study is conducted to examine the efficacy of the new drug (drug B) compared to the standard one (drug A).

Control

Baseline blood pressure → Drug A → Blood pressure after four hours

Case

Baseline blood pressure → Drug B → Blood pressure after four hours

Two independent populations

- Research question:
  Is the drug B different from the drug A in terms of efficacy?

- We need to translate the research question into a hypothesis

- What are the dependent and independent variables?
  - Dependent variable: **blood pressure changes**
  - Independent variable: **drugs / groups (case & control)**

Two independent populations

- Null hypothesis H_0:
  The population means of the blood pressure changes of two groups are the same.
  $$\mu_A = \mu_B$$

- Alternative hypothesis H_1:
  The population means of the blood pressure changes of two groups are different.
  $$\mu_A \neq \mu_B$$

Two independent populations

- Null hypothesis H_0:
  The population means of the blood pressure changes of two groups are the same.

$$\mu_A = \mu_B$$

$$\mu_B - \mu_A = 0$$

- Alternative hypothesis H_1:
  The population means of the blood pressure changes of two groups are different.

$$\mu_A \neq \mu_B$$

$$\mu_B - \mu_A \neq 0$$

Two independent populations

- The changes of the blood pressure are continuous variables.
- We assume that the observed changes come from normally distributed populations.
- Under weak assumptions, this also follows in large samples from the central limit theorem. (e.g., $n \geq 30$ per group)

Two independent populations

- The changes of the blood pressure are continuous variables.
- We assume that the observed changes come from normally distributed populations.
- Under weak assumptions, this also follows in large samples from the central limit theorem. (e.g., $n \geq 30$ per group)

- Based on our assumption, we use a t-test to examine the null-hypothesis
- Two popular types of t-test:
  - Student's t-test (with the assumption of equal population variance)
  - Welch's t-test (allowing unequal population variance)

We focus on this t-test!

Two independent populations

- $\bar{X}_A$ and $\bar{X}_B$ are the sample means of the blood pressure changes of control and case groups
- T statistics of Welch's t-test:

$$\mathrm{T} = \frac{\bar{X}_B - \bar{X}_A}{s_\Delta} \qquad \text{where} \quad s_\Delta = \sqrt{\frac{s_A^2}{n_A} + \frac{s_B^2}{n_B}}$$

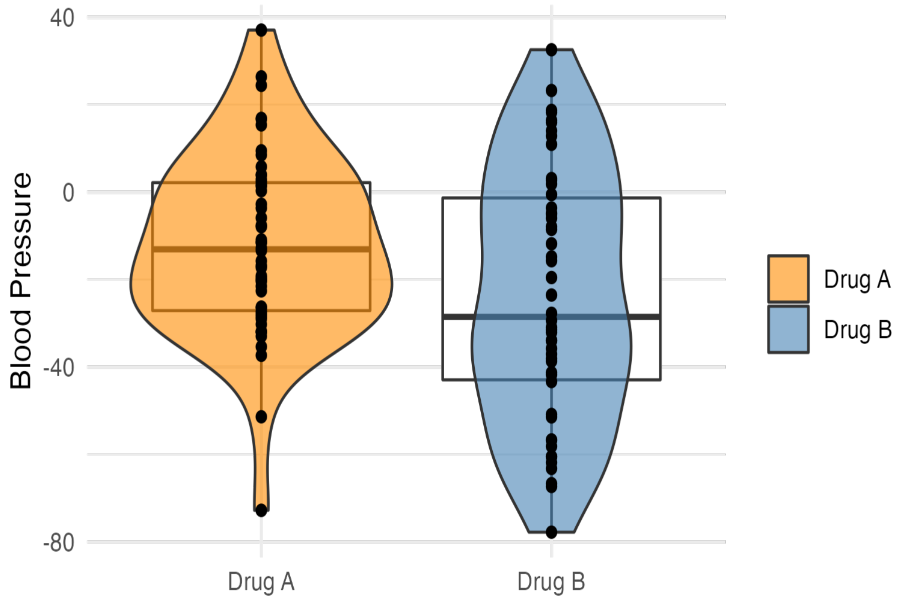
$$T \sim t_\nu \text{ with degree of freedom } \nu$$

- $(1-\alpha)\times 100\%$ confident interval:

$$(\bar{X}_B - \bar{X}_A) \pm t_{\alpha/2,\nu}\, s_\Delta$$

Two independent populations

- Example 1



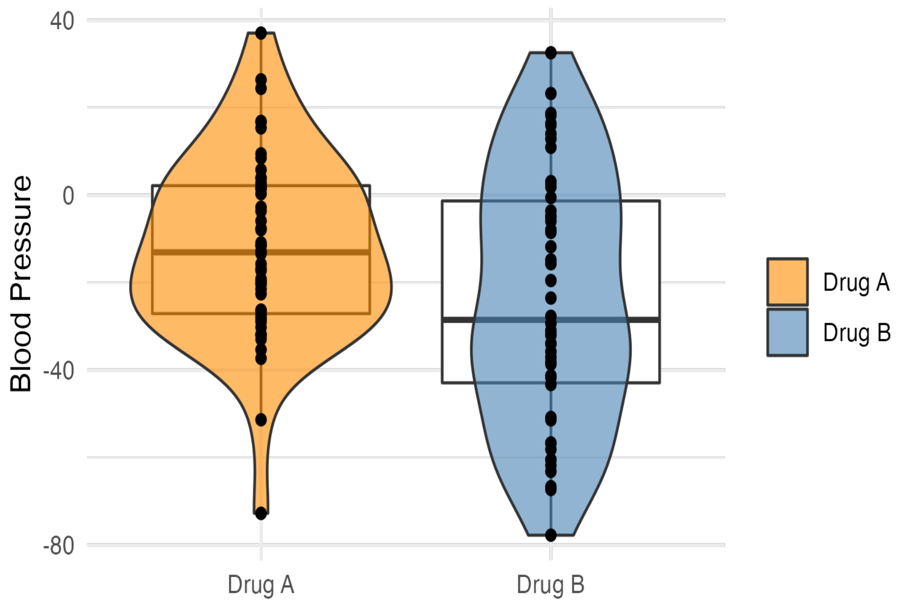
Two independent populations

- Example 1

```
# Run the t-test
t.test(bp_A1-bp_A0, bp_B1-bp_B0, alternative="two.sided")

    Welch Two Sample t-test

data:  bp_A1 - bp_A0 and bp_B1 - bp_B0
t = 2.2911, df = 88.975, p-value = 0.02432
alternative hypothesis: true difference in means is not
equal to 0
95 percent confidence interval:
  1.520065 21.381367
sample estimates:
mean of x mean of y
-12.11779 -23.56851
```



Two independent populations

- Recap for two-tailed test:
  - H_0 is rejected, when
    - $|T|$ statistics is greater than the critical value $t_{1-(\alpha/2),\nu}$, or
    - the corresponding p-value is smaller than $\alpha/2$, or
    - (1−α)×100% confident interval does not include zero
- Important reminder!

Under the principle of proof by contradiction, we can only conclude if H_0 is rejected or not,
but we cannot conclude if H_0 or H_1 is true.

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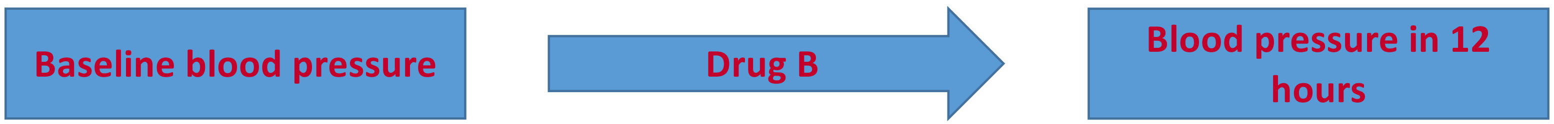
Case Study - Two dependent populations

- Now, the company wants to examine lasting effect of drug B. The blood pressure of the individuals treated with the new drug is measured in 12 hours again.

Case



Case Study - Two dependent populations

- The populations of two measurements are no longer independent, because they are measured from the same group of individuals
  - Also called paired/matched samples
  - Individual effects may affect the measurements

- To ”eliminate” the dependence between the measurements,
  1. Calculate the differences individually, i.e. $d_j = X_{jt_0} - X_{jt_{12}}$
  2. Use one-sample t-test to examine $\bar{d} = \frac{1}{n_B} \sum d_j$

Two dependent populations (paired samples)

- Null hypothesis H_0:

  The population means of the blood pressure difference (μ_d) in 12 hours are equal to zero ($\mu_0 = 0$).

  $$\mu_d = \mu_0 = 0$$

- Alternative hypothesis H_1:

  The population means of the blood pressure difference (μ_d) in 12 hours are not equal to zero ($\mu_0 = 0$).

  $$\mu_d \neq \mu_0 = 0$$

Two dependent populations (paired samples)

- Null hypothesis H_0:
  The population means of the blood pressure difference in 12 hours are equal to zero.
  $$\mu_d = \mu_0 = 0$$
- Alternative hypothesis H_1:
  The population means of the blood pressure difference in 12 hours are not equal to zero.
  $$\mu_d \neq \mu_0 = 0$$

- T statistic: $T = \dfrac{\bar{d} - \mu_0}{s_d/\sqrt{n}}$; $T \sim t_{n-1}$
- $(1-\alpha)\times 100\%$ confident interval: $\bar{d} \pm t_{\alpha/2,n-1}\, s_d$

Two dependent populations

- ## Example 2 (R codes)

Using paired/matched t-test

```
t.test(bp_B0, bp_B12, alternative="two.sided",
paired=TRUE)


     Paired t-test


data:  bp_B0 and bp_B12
t = 2.18, df = 49, p-value = 0.03409
alternative hypothesis: true mean difference is not equal
to 0
95 percent confidence interval:
  0.4234831 10.4087044
sample estimates:
mean difference
       5.416094
```

Two dependent populations

- Example 2 (R codes)

Using paired/matched t-test

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t.test(bp_B0, bp_B12, alternative="two.sided",
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t = 2.18, df = 49, p-value = 0.03409
alternative hypothesis: true mean difference is not equal
to 0
95 percent confidence interval:
  0.4234831 10.4087044
sample estimates:
mean difference
       5.416094
```

Results can be quite different!!

Using (unpaired) Welch t-test

```
t.test(bp_B0, bp_B12, alternative="two.sided",
paired=FALSE)

    Welch Two Sample t-test

data:  bp_B0 and bp_B12
t = 1.9072, df = 84.72, p-value = 0.05988
alternative hypothesis: true difference in means is not
equal to 0
95 percent confidence interval:
 -0.2303989 11.0625864
sample estimates:
mean of x mean of y
 130.0550  124.6389
```

More than two independent/dependent populations

- What if the company wants to compare the efficacy of more than two drugs at the same time?

  $\Longrightarrow$ more than two independent populations

  $\Longrightarrow$ analysis of variance (ANOVA) - This will be taught in the course IV.

- What if the company wants to investigate the lasting effect of drug B via measuring the blood pressure at multiple time points?

  $\Longrightarrow$ more than two dependent populations

  $\Longrightarrow$ repeated measures ANOVA (rANOVA)

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Power analysis

- Power of a hypothesis test is the probability that the test correctly rejects the null hypothesis H_0 when a specific alternative hypothesis H_1 is true.

$$power = P(reject\ H_0 \mid H_1\ is\ true)$$

- Power $(1-\beta)$ depends mainly on
  - statistical significance level (α)
  - magnitude of the effect of interest (effect size) in the population, e.g., μ, σ
  - sample size (N)

- Sample size estimation for two-tailed t-test (for each group)

$$N_i = \frac{\sigma_\Delta^2 \left(Z_{\alpha/2} + Z_\beta\right)^2}{\mu_0 - \mu_a}$$

Sample size determination

- Statistically speaking, sample size depends mainly on
  - statistical significance level (α)
  - magnitude of the effect of interest (effect size) in the population, e.g., μ, σ
  - expected power $(1 - \beta)$

- Practically, however, we should also consider
  - the financial budget
  - the capacity for patient recruitment

Questions?