JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

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Section C

Two Sample t-test, Approach with Smaller Samples

Sampling Distribution

- What is sampling distribution of the difference in sample means?
  - If either (or both) sample sizes are less than 60, a t-distribution is used with $n_1 + n_2 - 2$ degrees of freedom: this is the degrees of freedom for the total sample size from both groups minus two

Two Sample t-test

- Example
  - In a randomized design, 23 patients with hyperlipidemia were randomized to either take Treatment A or Treatment B for 12 weeks
  - 12 patients assigned to Treatment A
  - 11 patients assigned to Treatment B

Two Sample t-test

- Example
  - LDL cholesterol levels (mmol/L) measured on each subject at baseline, and 12 weeks after start of study
  - The 12-week change in LDL cholesterol was computed for each subject

Two Sample t-test

- Summary of results:

	Treatment Group	
	A	B
Number of subjects (n)	12	11
Mean LDL change (mmol/L) Post-trt less pre-trt	-1.41	-0.32
Standard deviation of LDL changes (mmol/L)	0.55	0.65

Two Sample t-test

- Scientific question
  - Is there a difference in LDL change between the two treatment groups?

- Methods of inference
  - Confidence interval for the difference in mean LDL cholesterol will change between the two groups
  - Statistical hypothesis test

95% Confidence Interval for Difference in Means

- The general formula (large samples):

$$(\bar{x}_1 - \bar{x}_2) \pm 2 \times S\hat{E}(\bar{x}_1 - \bar{x}_2)$$

- The general formula ("smaller" samples):

$$(\bar{x}_1 - \bar{x}_2) \pm t_{.95, n_1 + n_2 - 2} \times S\hat{E}(\bar{x}_1 - \bar{x}_2)$$

Two Sample t-test

- Sample mean difference and estimated standard error:

	Treatment Group	
	A	B
Number of subjects (n)	12	11
Mean LDL change (mmol/L) Post-trt less pre-trt	-1.41	-0.32
Standard deviation of LDL changes (mmol/L)	0.55	0.65

$$\bar{x}_1 - \bar{x}_2 = 1.41 - (-0.32) = -1.09\, mmol/L$$

$$S\hat{E}\,(\overline{X}_1 - \overline{X}_2) = \sqrt{\frac{0.55^2}{12} + \frac{0.65^2}{11}} \approx 0.25$$

95% CI for Difference in Means: Hyperlipidemia Ex

- How many standard errors to add and subtract?
  - Since sample sizes are small we will have to add slightly more than two standard errors

- Number we need to add and subtract for 95% confidence comes from a t-distribution with (12 + 11 - 2 = 21) degrees of freedom
  - From t-table this value is 2.08

- So, 95% CI for true mean difference in change in LDL cholesterol, drug A to drug B

$$-1.09 \pm 2.08 \times .25 \rightarrow$$

$$-1.61\, mmol/L to \text{ -0.57 } mmol/L$$

Hypothesis Test to Compare Two Independent Groups

- Two-sample (unpaired) t-test: getting a p-value

- Is the change in LDL cholesterol the same in the two treatment groups?
  - H_o: $\mu_1 = \mu_2$ → H_o: $\mu_1 - \mu_2 = 0$
  - H_A: $\mu_1 \neq \mu_2$ → H_A: $\mu_1 - \mu_2 \neq 0$

Hypothesis Test to Compare Two Independent Groups

- Recall, general "recipe" for hypothesis testing . . .
  1. Start by assuming H_o true
  2. Measure distance of sample result from μ_o (here again its 0)
  3. Compare test statistic (distance) to appropriate distribution to get p-value

$$t = \frac{(observed\ diff) - (null\ diff)}{SE\ of\ observed\ difference}$$

$$t = \frac{\vec{x}_1 - \bar{x}_2}{\hat{SE}(\vec{x}_1 - \bar{x}_2)} = \frac{\vec{x}_1 - \bar{x}_2}{\sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}}$$

Diet Type and Weight Loss Study

- In the diet types and weight loss study, recall:

$$\bar{x}_1 - \bar{x}_2 = -1.09\ mmol/L$$

$$S\hat{E}(\bar{x}_1 - \bar{x}_2) = 0.25\ mmol/L$$

- So in this study:

$$t = \frac{-1.09}{.25} \approx -4.4$$

  - So this study result was 4.4 standard errors below the null mean of 0 (i.e., 4.4 standard errors from the less expected mean difference in cholesterol change between the two treatments if null was true)

How Are p-values Calculated?

- Is a result 4.4 standard errors below 0 unusual?
  - It depends on what kind of distribution we are dealing with

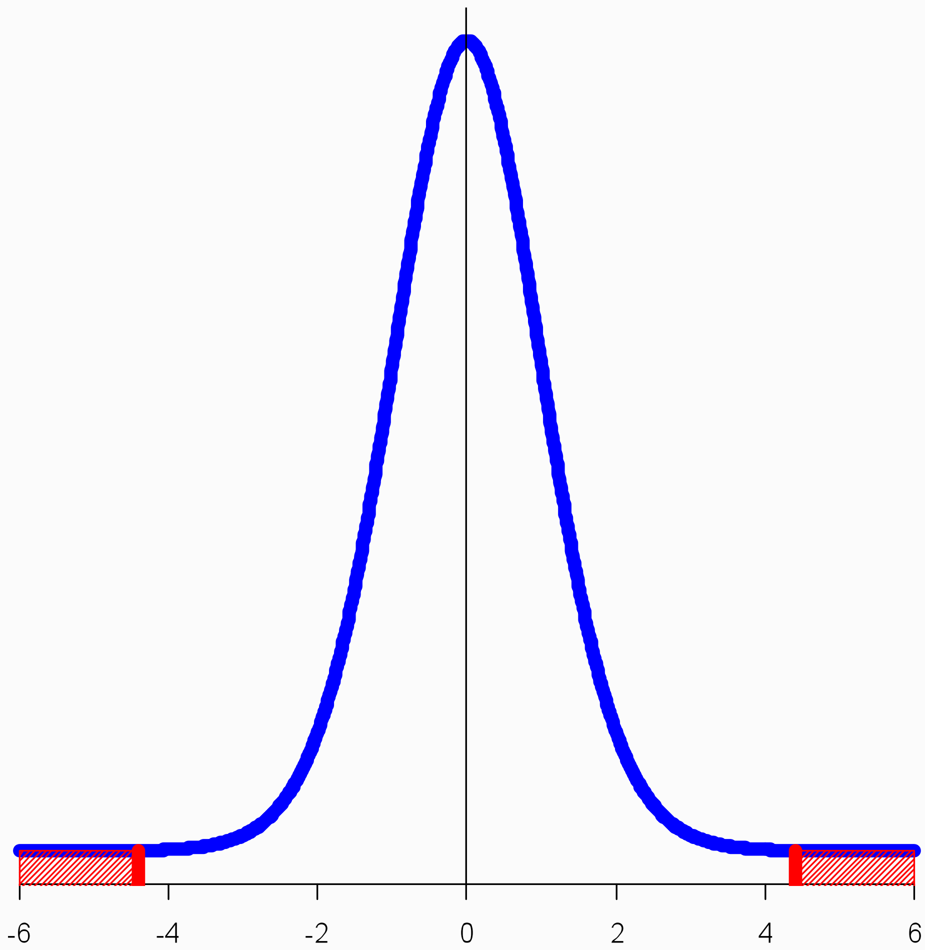
- The p-value is the probability of getting a test statistic (distance) as or more extreme than what you observed (-4.4) by chance if it was true

- The p-value comes from the sampling distribution of the difference in two sample means

- What is the sampling distribution of the difference in sample means?
  - t-distribution with 12 + 1 – 2 = 21 degrees of freedom

Hyperlipidemia Example

- To compute a p-value, we would need to compute the probability of being 4.4 or more standard errors away from 0 on a t-distribution with 21 degrees of freedom



Using Stata

- Command syntax:
  - ttesti $n_1\ \bar{x}_1\ s_1\ n_2\ \bar{x}_2\ s_2$, unequal

```
. ttesti 11 -1.41 .55 12 -.32 .65, unequal

Two-sample t test with unequal variances
------------------------------------------------------------------------------
         |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Interval]
---------+--------------------------------------------------------------------
       x |      11       -1.41    .1658312         .55   -1.779495   -1.040505
       y |      12        -.32    .1876388         .65   -.7329903    .0929903
---------+--------------------------------------------------------------------
combined |      23   -.8413043    .1692296    .8115967   -1.192265   -.4903436
---------+--------------------------------------------------------------------
    diff |               -1.09    .2504163                -1.61095   -.5690505
------------------------------------------------------------------------------
    diff = mean(x) - mean(y)                                      t =  -4.3528
Ho: diff = 0                     Satterthwaite's degrees of freedom =  20.8813

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0.0001         Pr(|T| > |t|) = 0.0003          Pr(T > t) = 0.9999
```

Using Stata

- Command syntax:
  - ttesti n_1 $\bar{x}_1$ s_1 n_2 $\bar{x}_2$ s_2 , unequal

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 Pr(T < t) = 0.0001         Pr(|T| > |t|) = 0.0003          Pr(T > t) = 0.9999
```

Summary: Weight Loss Example

- **Statistical method**
  - Twenty-three patients with hyperlipidemia were randomly assigned to one of two treatment groups: Treatment A or Treatment B
  - 12 patients were assigned to receive Treatment A
  - 11 patients were assigned to receive Treatment B

Summary: Weight Loss Example

- **Statistical method**
  - Baseline LDL cholesterol measurements were taken on each subject, and LDL was again measured after 12 weeks of treatment
  - The change in LDL cholesterol was computed for each subject
  - The mean LDL changes in the two treatment groups were compared using an unpaired t-test and a 95% confidence interval was constructed for the difference in mean LDL changes

Summary: Weight Loss Example

- **Result**
  - Patients on treatment A showed a decrease in LDL cholesterol of 1.41 mmol/L and subjects on treatment B showed a decrease of .32 mmol/L (a difference of 1.09 mmol/L, 95% CI .57 to 1.61 mmol/L)
  - The difference in LDL changes was statistically significant ($p < .001$)