Biostatistics
Week V

Ege Ülgen, M.D.

4 November 2021

Hypothesis Testing - Steps

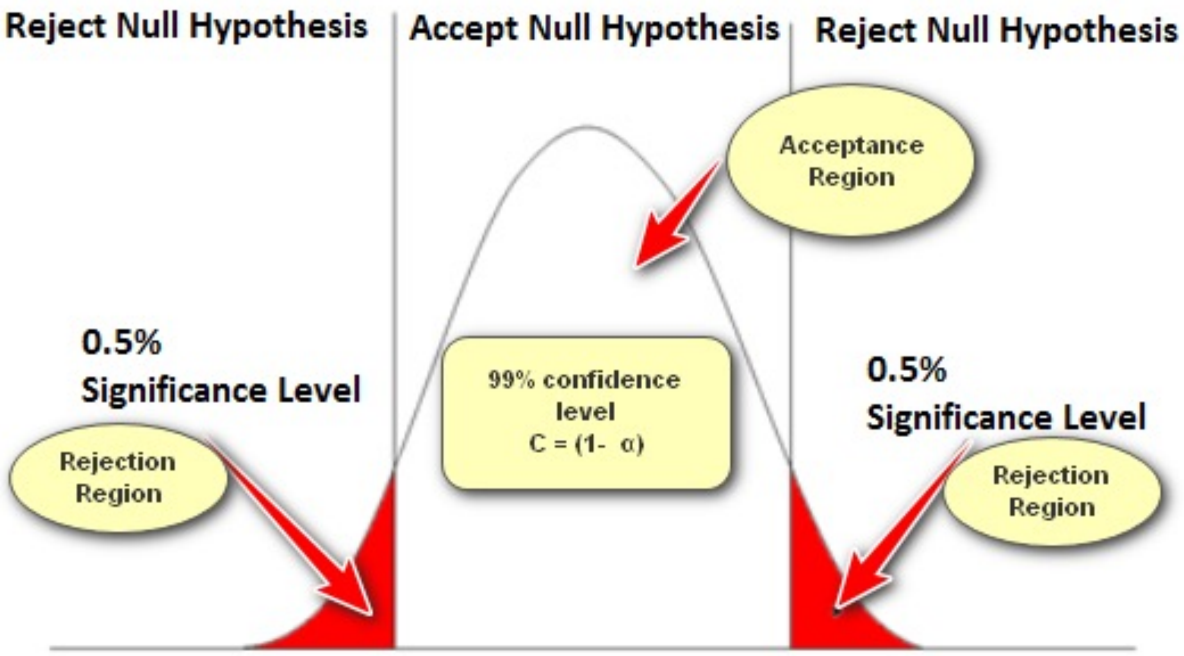
1. **Check assumptions, determine H_0 and H_a, choose α**
    - Assumptions differ based on the test
    - The null hypothesis always contains equality (=)
2. **Calculate the appropriate test statistic**
    - z, t, χ^2, …
3. **Calculate critical values/p value**
    - With the aid of precalculated tables/software
4. **Decide whether to reject/fail to reject H_0**
    - Reject if the statistic is within the critical region/$p \leq \alpha$

H_0	Decision	
	Accept H_0	Reject H_0
H_0 is True	Correct decision	**Type I Error** **α**
H_0 is False	**Type II Error** **β**	Correct decision

Barai A. Hypothesis Testing | All a beginner needs to know [Internet]. Medium. 2020 [cited 2021 Oct 4]. Available from: https://medium.com/analytics-vidhya/hypothesis-testing-all-a-beginner-needs-to-know-dd1bdeebdbf1

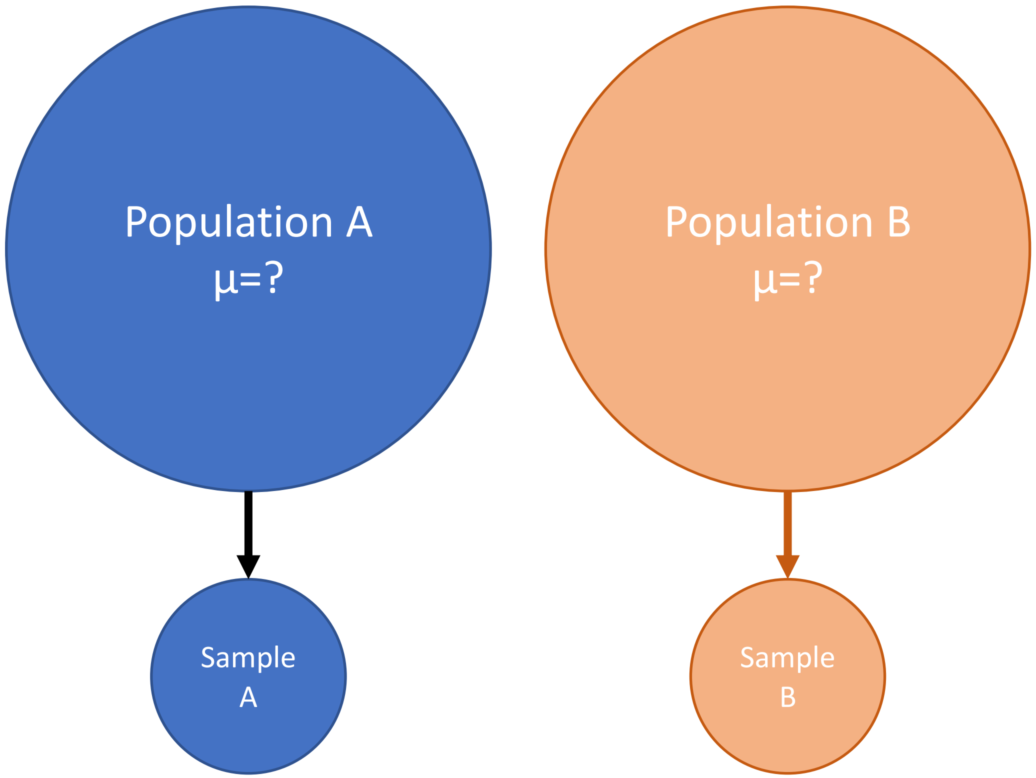
Reminder

$$\text{test statistic} = \frac{\text{estimator} - \text{null value}}{\text{standard error of estimator}}$$



Two-Sample t-Test

- The **two-sample t-test** (also known as the **independent samples t-test**) is a method used to test whether the unknown population means of two groups are equal or not



Two-sample t-Test

$H_0: \mu_X = \mu_Y$

$H_a: \mu_X \neq \mu_Y$

or

$\mathbf{H_0: \mu_X - \mu_Y = 0}$

$\mathbf{H_a: \mu_X - \mu_Y \neq 0}$

Two-sample t-Test

$$T = \frac{\bar{X} - \bar{Y}}{\sqrt{\frac{s_X^2}{n_X} + \frac{s_Y^2}{n_Y}}} \sim \mathrm{t(m)},$$

$$m = \frac{(w_X + w_Y)^2}{\left(\frac{w_X^2}{n_X - 1} + \frac{w_Y^2}{n_Y - 1}\right)}$$

$$w_X = s_X^2 / n_X, \quad w_Y = s_Y^2 / n_Y$$

Two-sample t-Test – Example I

id	treatment	perc_benefit
158	trt1	37.2549020
392	trt1	-4.3864459
457	trt1	-5.1075269
487	trt1	36.7043369
723	trt1	5.1303099
832	trt1	3.1806616
894	trt1	-3.9062500
1104	trt1	5.9443608
1283	trt1	-0.8601855
1288	trt1	-3.1674208

id	treatment	perc_benefit
15	trt2	10.0978368
143	trt2	0.5048635
470	trt2	-0.8156940
536	trt2	50.0000000
549	trt2	-3.0303030
750	trt2	-2.8977108
891	trt2	26.3872135
997	trt2	4.3651179
1000	trt2	2.3582125
1209	trt2	8.9702189

- Mean percentage benefit is 7.078674 for group 1, and 9.593976 for group 2
- Is the difference a significant one?

Two-sample t-Test – Example I (cont.)

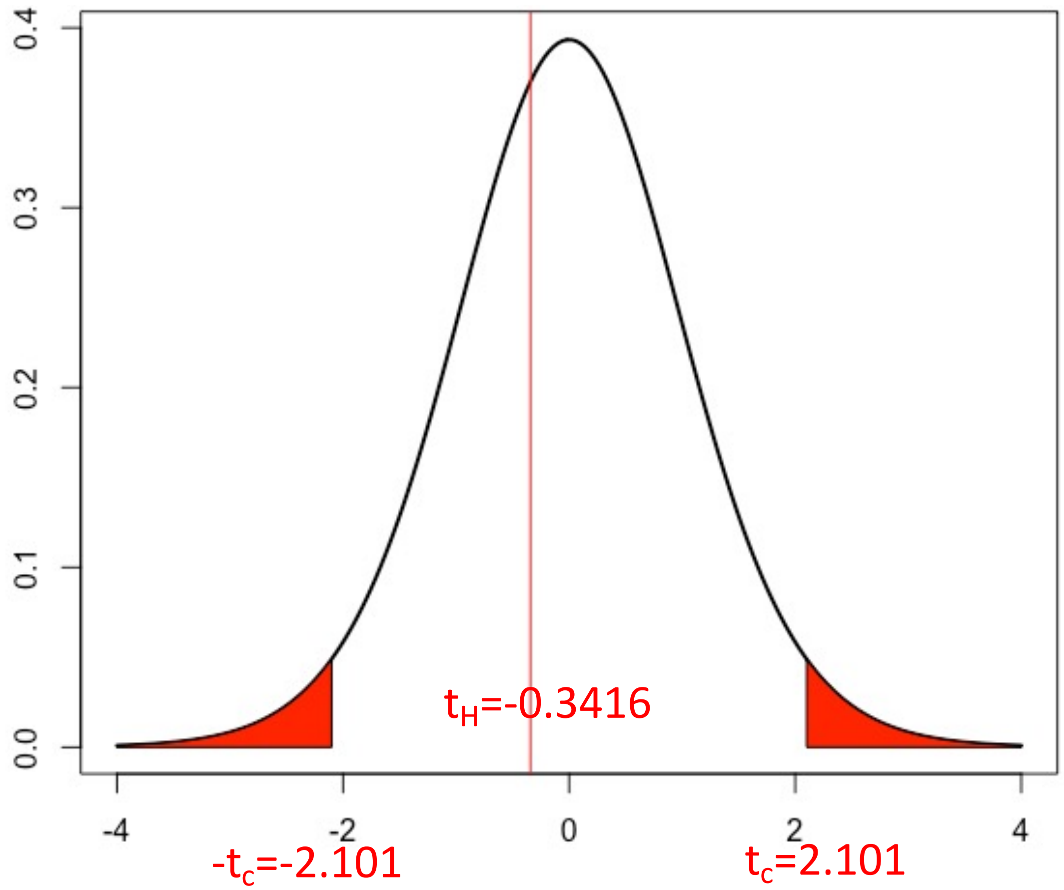
1. Check assumptions, determine H_0 and Ha, choose α
   - We check that the variables are normally distributed
   - H_0: $\mu_1 = \mu_2$ H_a: $\mu_1 \neq \mu_2$
   - $\alpha = 0.05$

2. Calculate the appropriate test statistic

$$t = -0.3416(\sim t_{17.98834})$$

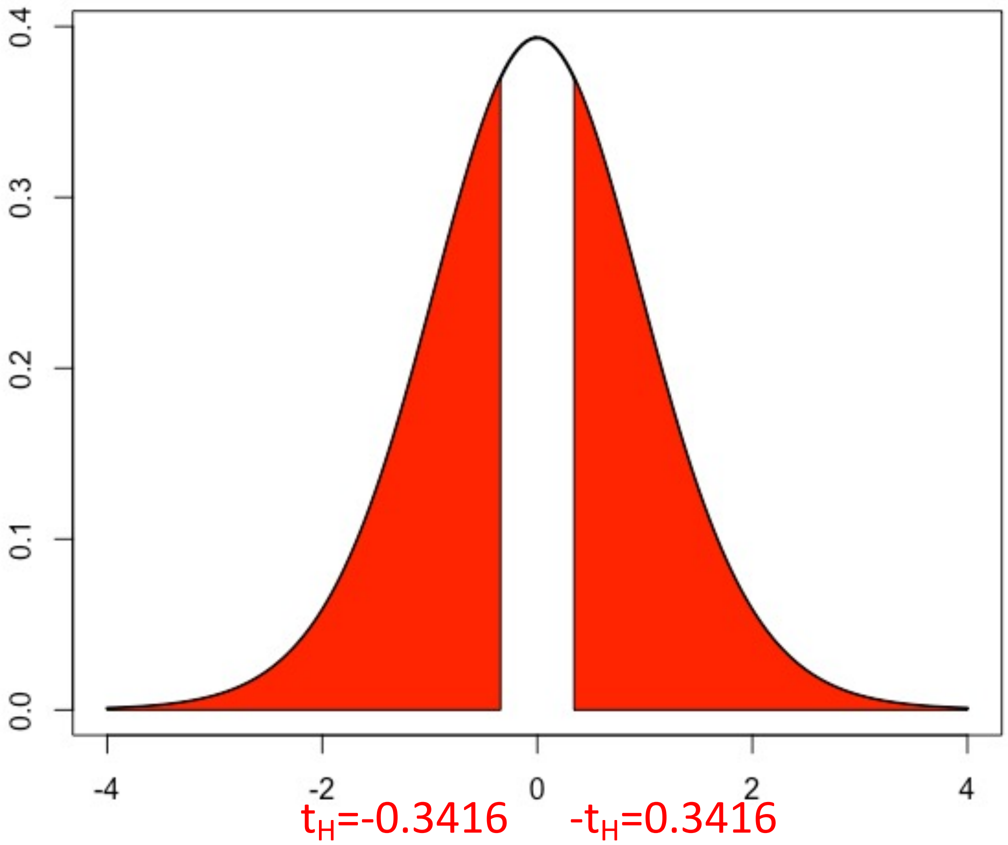
Two-sample t-Test – Example I (cont.)

3. Calculate **critical values**/p value
4. Decide whether to reject/fail to reject H_0

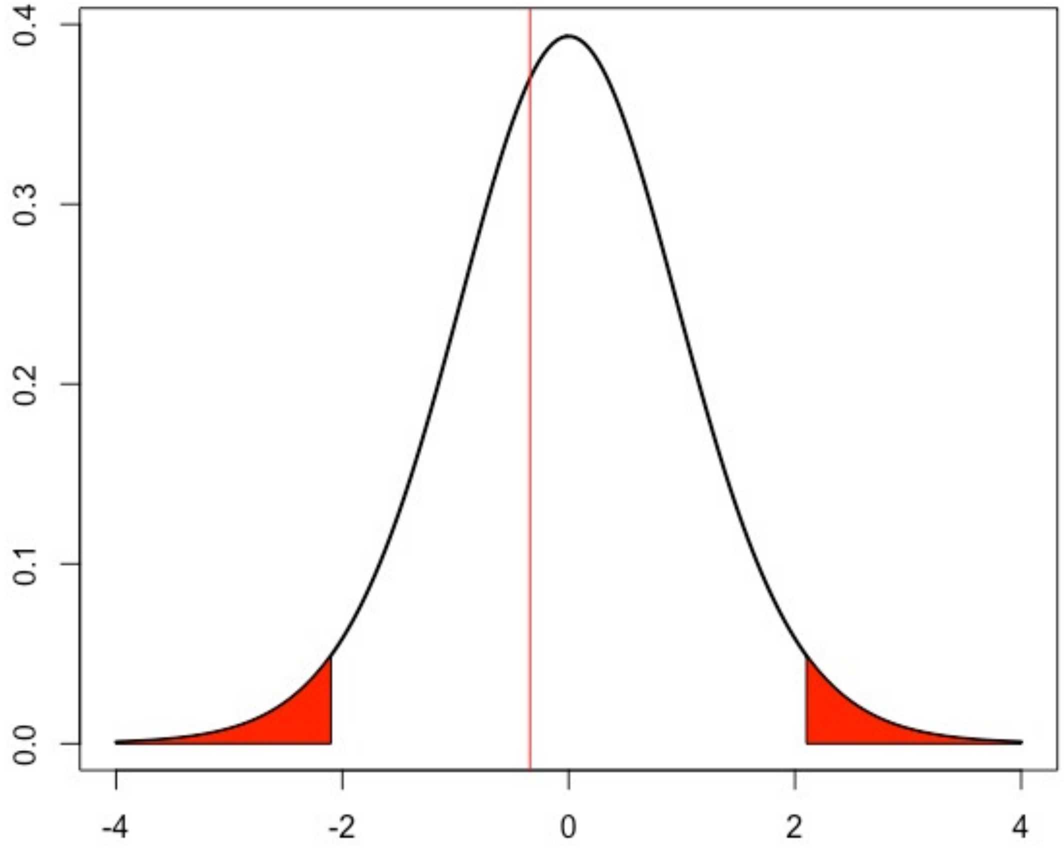


Two-sample t-Test – Example I (cont.)

3. Calculate critical values/**p value**
4. Decide whether to reject/fail to reject H_0



Two-sample t-Test – Example I (cont.)



95% confidence interval for $\mu_1 - \mu_2$ = [-17.98 , 12.95]

Two-sample t-Test – Example I (cont.)

- there is not enough evidence to say mean percentage benefit for treatment 1 and treatment 2 are significantly different

Two-sample t-Test – Example II

- In a study,
  - The sedimentation rate of 12 arthritis patients was measured:

    $\bar{X}_1 = 82.79$ mm and $s_1 = 18.4$ mm
  - The sedimentation rate of 15 healthy controls was measured

    $\bar{X}_2 = 69.03$ mm and $s_2 = 21.4$ mm
- Is there a difference between the mean sedimentation rates of the two groups?

Two-sample t-Test – Example II (cont.)

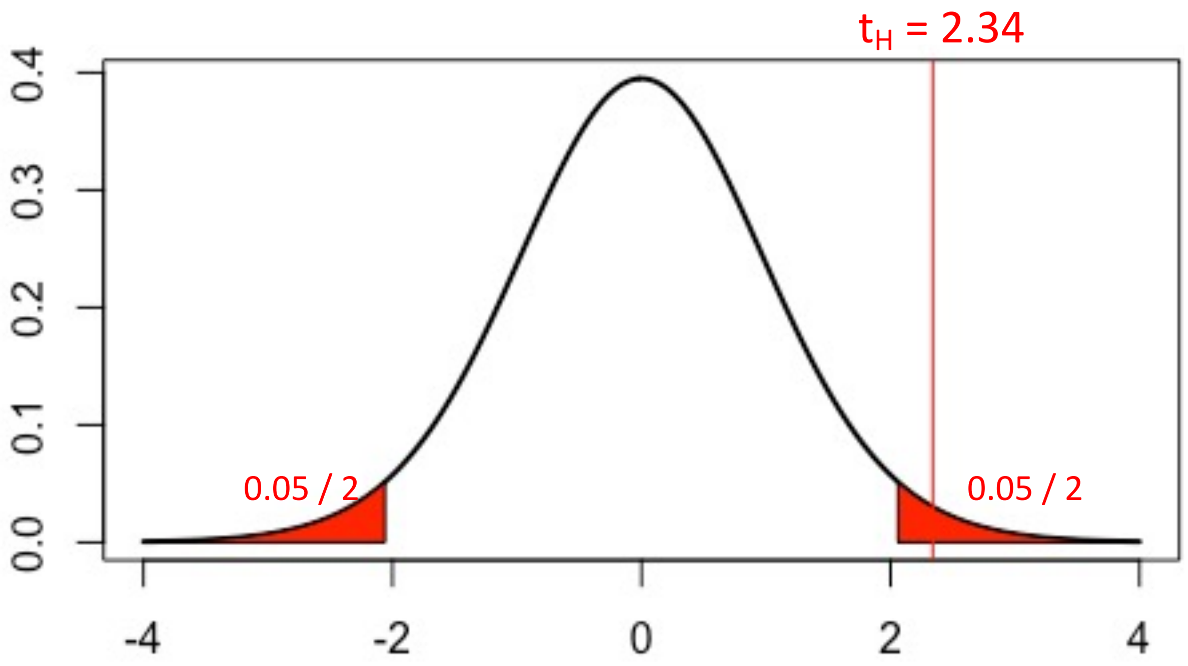
1. Check assumptions, determine H_0 and Ha, choose α
   - We check that the variables are normally distributed
   - H_0: $\mu_1 = \mu_2$ H_a: $\mu_1 \neq \mu_2$
   - $\alpha = 0.05$

2. Calculate the appropriate test statistic

$$t = 2.34 \qquad (\sim t_{25})$$

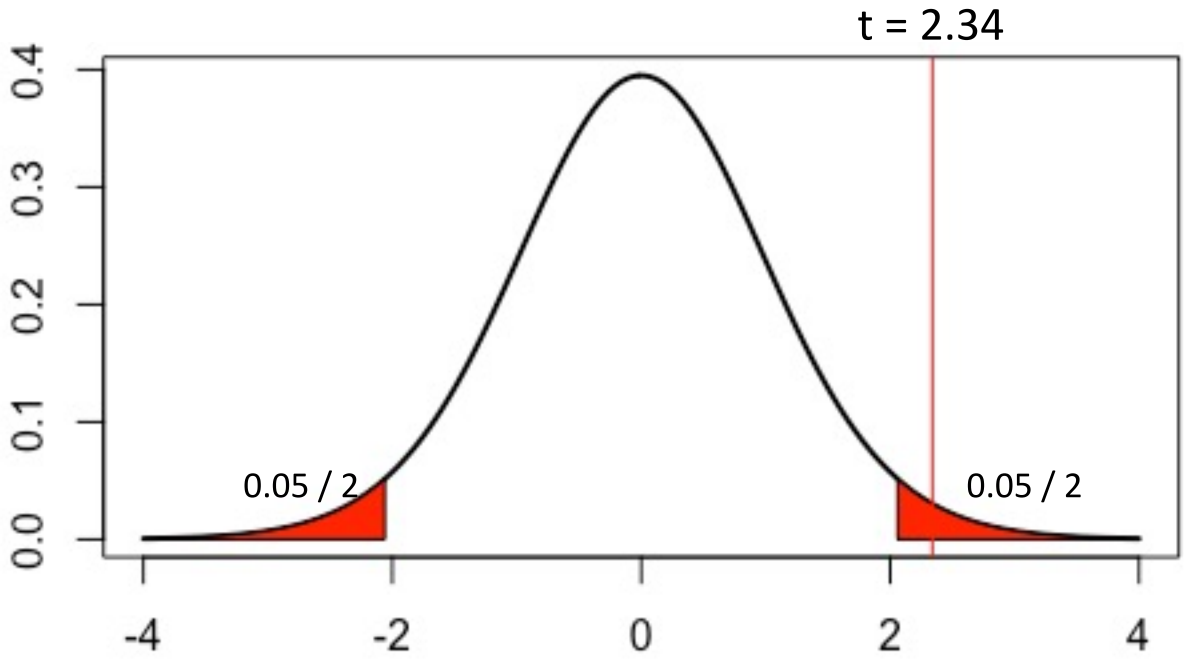
Two-sample t-Test – Example II (cont.)

3. Calculate critical values/p value
4. Decide whether to reject/fail to reject H_0



p = 0.027568

Two-sample t-Test – Example II (cont.)



p = 0.027568

95% confidence interval for $\mu_1 - \mu_2$ = [3.52, 33]

Two-sample t-Test – Example II (cont.)

- With 95% confidence, there is enough evidence to say that there is a difference between the mean sedimentation rates of the two groups

Two-sample t-Test – Example III

- “Morbidly obese patients undergoing general anesthesia are at risk of hypoxemia during anesthesia induction”
- A randomized controlled trial investigating:
- Does high-flow nasal oxygenation provide longer safe apnea time compared to conventional facemask oxygenation during anesthesia induction in morbidly obese surgical patients?

Wong DT, Dallaire A, Singh KP, Madhusudan P, Jackson T, Singh M, et al. High-flow nasal oxygen improves safe apnea time in morbidly obese patients undergoing general anesthesia: a randomized controlled trial. Anesth Analg. 2019 Oct;129(4):1130–6.

Two-sample t-Test – Example III (cont.)

- Safe Apnea time in Control Group (n = 20)
  - $\overline{X_c} = 185.5$
  - $s_c = 53$
- Safe Apnea time in High-Flow Nasal Oxygenation Group (n = 20)
  - $\overline{X_T} = 261.4$
  - $s_T = 77.7$

Two-sample t-Test – Example III (cont.)

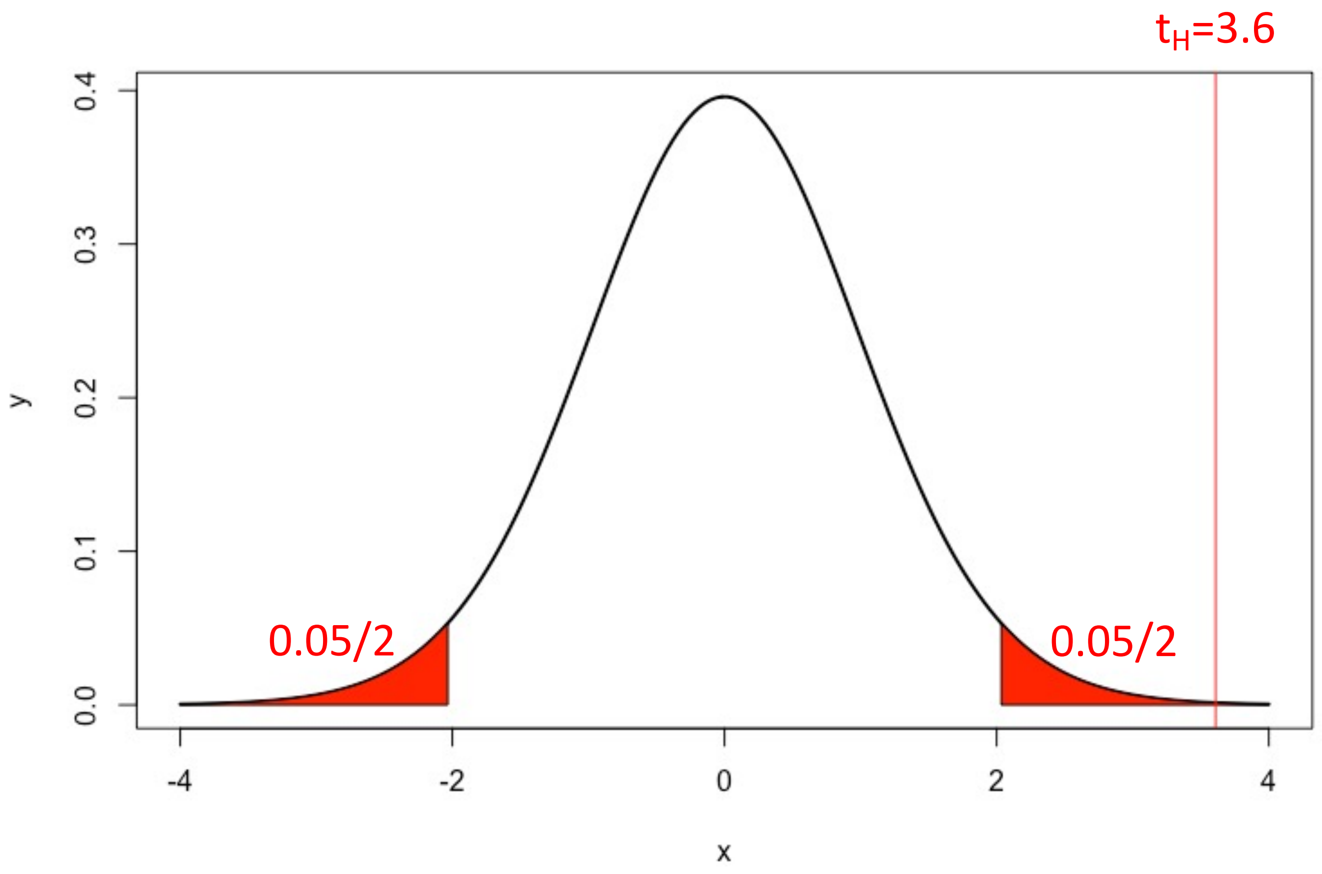
1. Check assumptions, determine H_0 and Ha, choose α
   - We check that the variables are normally distributed
   - H_0: $\mu_c = \mu_T$ H_a: $\mu_c \neq \mu_T$
   - $\alpha = 0.05$

2. Calculate the appropriate test statistic

$$t = 3.6 \qquad (\sim t_{33.53})$$

Two-sample t-Test – Example III (cont.)

3. Calculate **critical values**/p value
4. Decide whether to reject/fail to reject H_0



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Two-sample t-Test – Example III (cont.)

Table 2. Study Outcomes: Safe Apnea Time, Minimum SpO_2, Plateau $ETCO_2$, and Time to Regain Baseline SpO_2

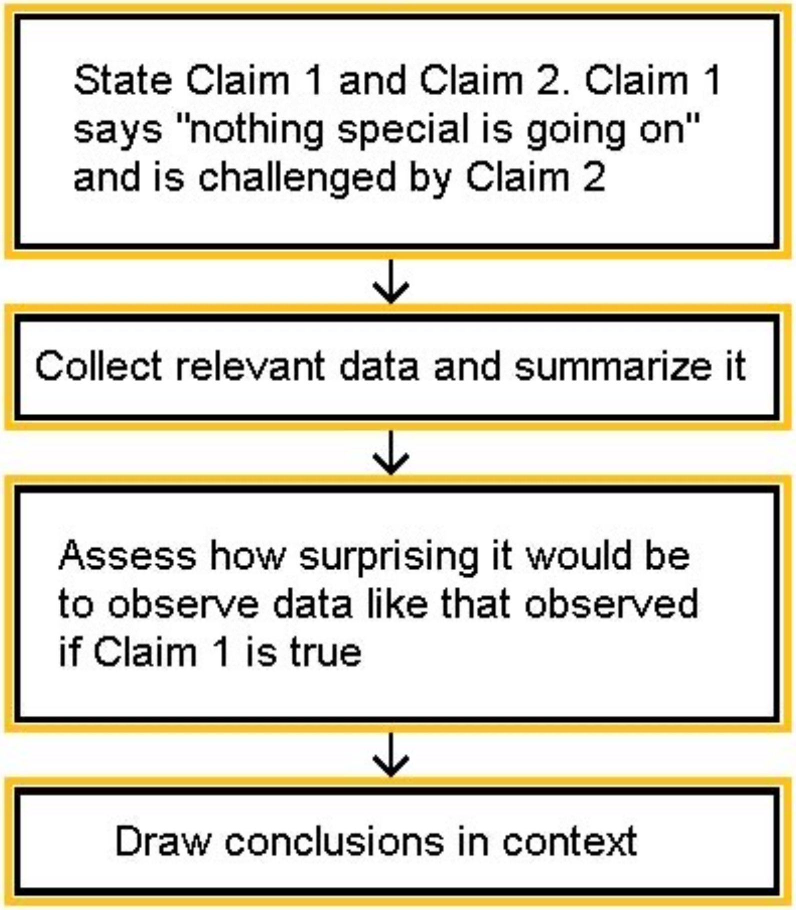
	Control Group (n = 20)	High-Flow Nasal Oxygenation Group (n = 20)	Mean Difference (95% CI)	*P* Value
Safe apnea time (s)	185.5 ± 53.0	261.4 ± 77.7	75.9 (33.3–118.5)	.001
Minimum SpO_2 (%)	87.9 ± 4.7	90.9 ± 3.5	3.1 (0.4–5.7)	.026
Plateau $ETCO_2$ (mm Hg)	38.8 ± 2.5	37.9 ± 3.0	–0.8 (–2.6 to 0.9)	.33
Time to regain baseline SpO_2 (s)	49.6 ± 20.8	37.3 ± 6.8	–12.3 (–22.2 to –2.4)	.016

Values represent mean ± SD.
Control group: facemask oxygenation.
Abbreviations: CI, confidence interval; $ETCO_2$, end-tidal carbon dioxide; SpO_2, oxygen saturation measured by pulse oximetry.

"Safe apnea time was significantly longer (261.4 ± 77.7 vs 185.5 ± 52.9 seconds; mean difference [95% CI], 75.9 [33.3–118.5]; *P* = .001)…"

Barai A. Hypothesis Testing | All a beginner needs to know [Internet]. Medium. 2020 [cited 2021 Oct 4]. Available from: https://medium.com/analytics-vidhya/hypothesis-testing-all-a-beginner-needs-to-know-dd1bdeebdbf1

Brief Summary



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    - z, t, χ^2, …
3. **Calculate critical values/p value**
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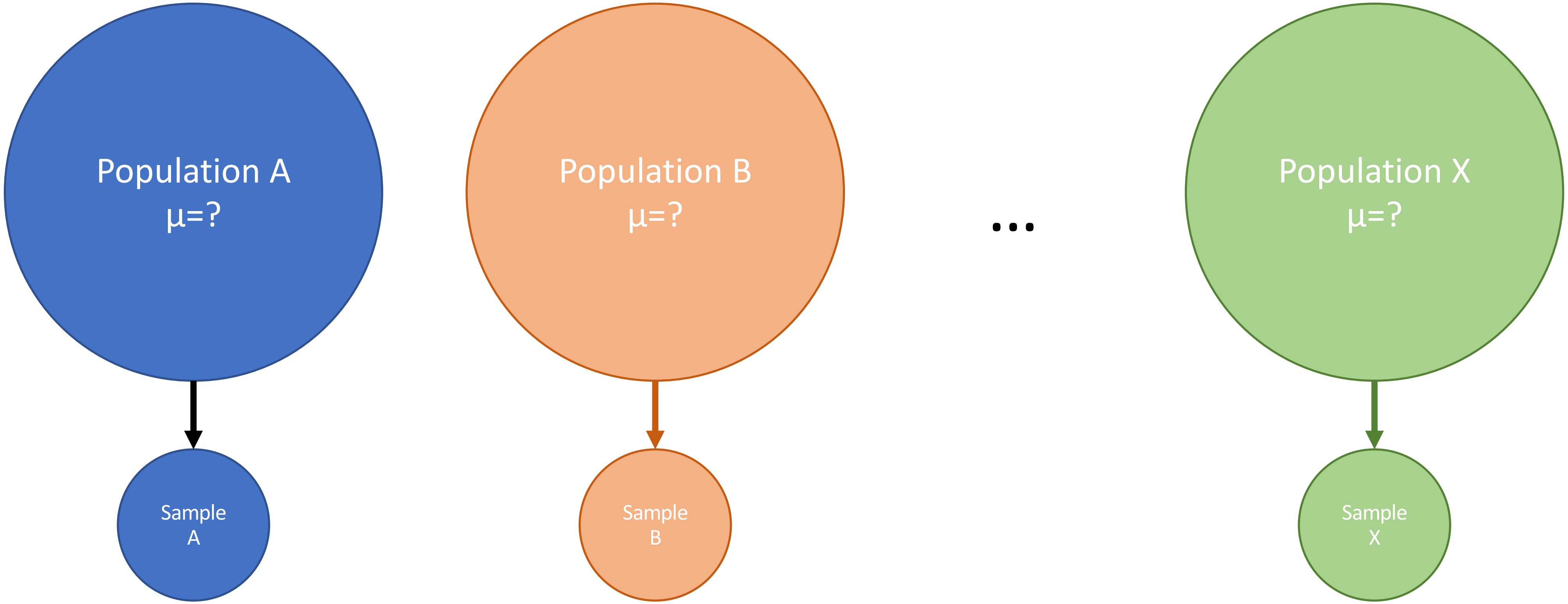
4. **Decide whether to reject/fail to reject H_0**
    - Reject if the statistic is within the critical region/$p \leq \alpha$

Analysis of Variance (ANOVA)

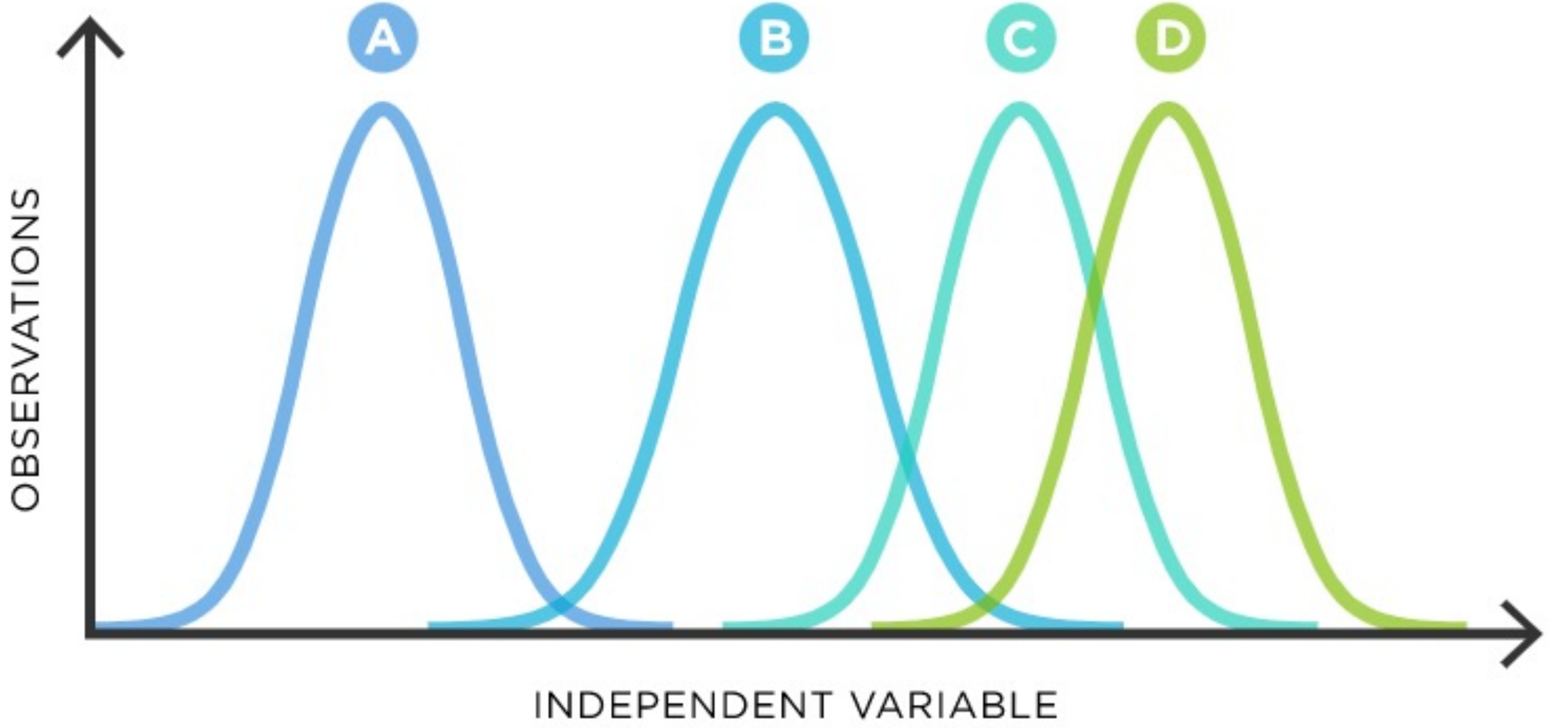
- Analysis of variance (ANOVA) is a statistical technique that is used to check if the means of **two or more groups** are significantly different from each other



ANOVA

$$H_0: \mu_1 = \mu_2 = \ldots = \mu_n$$

H_a: at least one μ_i is different



One-way ANOVA

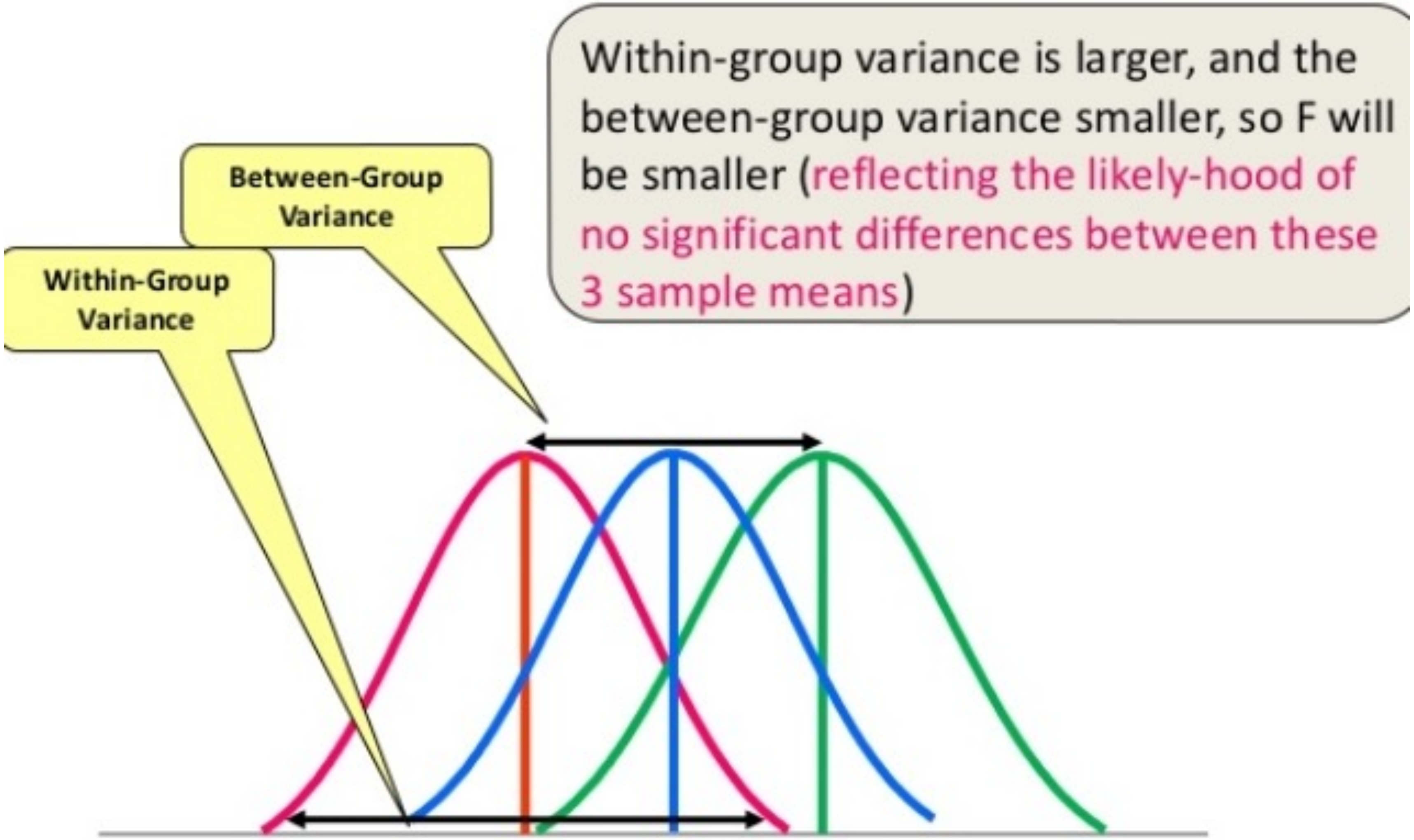
Analysis of Variance(ANOVA)

Source of Variation	Sum of Squares	Degrees of Freedom	Mean Squares (MS)	F
Within	$SS_w = \sum_{j=1}^{k}\sum_{j=1}^{l}(X-\bar{X}_j)^2$	$df_w = k-1$	$MS_w = \frac{SS_w}{df_w}$	$F = \frac{MS_b}{MS_w}$
Between	$SS_b = \sum_{j=1}^{k}(\bar{X}_j - \bar{X})^2$	$df_b = n-k$	$MS_b = \frac{SS_b}{df_b}$	
Total	$SS_t = \sum_{j=1}^{n}(\bar{X}_j - \bar{X})^2$	$df_t = n-1$		

How to perform analysis of variance (Anova) - step by step procedure [Internet]. The Genius Blog. 2018 [cited 2021 Oct 6]. Available from: https://kindsonthegenius.com/blog/how-to-perform-analysis-of-variance-anova-step-by-step-procedure/

Analysis of variance (Anova) | introduction, types & techniques [Internet]. Analytics Vidhya. 2018 [cited 2021 Oct 6]. Available from: https://www.analyticsvidhya.com/blog/2018/01/anova-analysis-of-variance/

ANOVA



One-way ANOVA – Example I

Table 1: Percentage benefits for 5 patients from each treatment groups.

Treatment 1	Treatment 2	Treatment 3	Treatment 4
-7.2	-13.0	-3.8	7.0
2.5	-0.4	-2.7	1.5
1.4	-1.6	5.3	9.4
-0.7	4.9	-5.9	9.5
-0.9	-0.7	3.7	9.9

The hypothesis of interest is

$H_0 : \mu_1 = \mu_2 = \mu_3 = \mu_4$
$H_1 :$ at least one is different from the others

One-way ANOVA – Example I (cont.)

1. Check assumptions, determine H_0 and H_a, choose α
    - Check that data is normally distributed
    - H_0: $\mu_1 = \mu_2 = \mu_3 = \mu_4$ H_a: at least one mean is different
    - $\alpha = 0.05$

One-way ANOVA – Example I (cont.)

2. Calculate the appropriate test statistic

Sources of variation	Sum of squares	degrees-of-freedom	Mean squared error	F	p-value
Between treatment					
Within treatment					
Total					

One-way ANOVA – Example I (cont.)

2. Calculate the appropriate test statistic

Step 1: Calculate the treatment means and grand mean:

$$\bar{x}_1 = \frac{-7.2+2.5+1.4+(-0.7)+(-0.9)}{5} = -0.98$$
$$\bar{x}_2 = \frac{-13.0+(-0.4)+(-1.6)+4.9+(-0.7)}{5} = -2.16$$
$$\bar{x}_3 = \frac{-3.8+(-2.7)+(5.3)+(-5.9)+3.7}{5} = 0.68$$
$$\bar{x}_4 = \frac{7.0+1.5+9.4+9.5+9.9}{5} = 7.46$$
$$\bar{x} = \frac{-7.2+...+(-0.9)+(-13.0)+...(-0.7)+(-3.8)+...+3.7+7.0+...+9.9}{20} = 0.91$$

One-way ANOVA – Example I (cont.)

2. Calculate the appropriate test statistic

Step 3: Calculate between treatment sum of squared error:

$$5\ (\text{-}0.98\ \text{-}\ 0.91\ )^2 + 5(-2.16 - 0.91)^2 + 5(0.68 - 0.91)^2 + 5(7.46 - 0.91)^2 = 292.138$$

Step 4: Calculate the total sum of squared error:

$$(-7.2 - 0.91)^2 + \ldots + (-0.9 - 0.91)^2 + (-13.0 - 0.91)^2 + \ldots (-0.7 - 0.91)^2 + (-3.8 - 0.91)^2 + \ldots + (3.7 - 0.91)^2 + (7.0 - 0.91)^2 + \ldots + (9.9 - 0.91)^2 = 667.198$$

Step 5: Calculate the within-group sum of squared error as $667.198 - 292.138 = 375.06$

One-way ANOVA – Example I (cont.)

2. Calculate the appropriate test statistic

Step 6: Total d.o.f.: 20 - 1, 19; between treatment d.o.f: 4-1=3; within treatment d.o.f.: 19-3=16

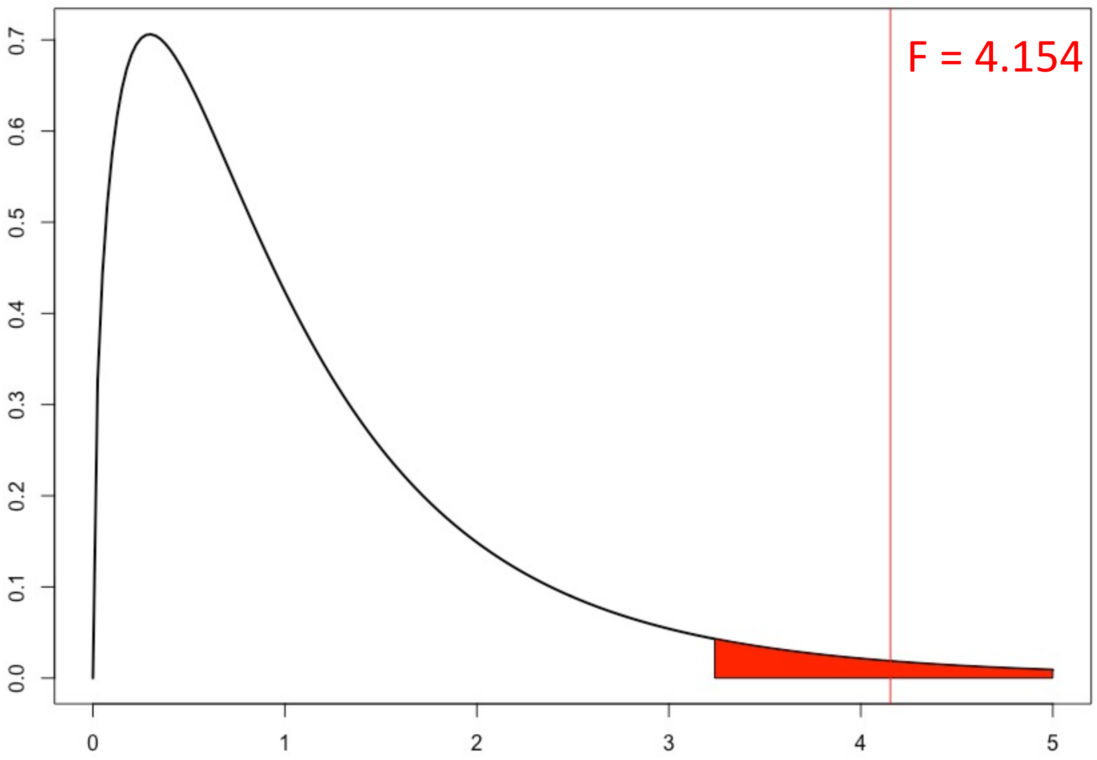
Step 7: Calculate mean suqared error for between treatment as 292.138/3=97.38

Step 8: Calculate mean squared error for within treatment as 375.06.198/16=23.44

Step 9: Calculate F value as 97.38/23.44=4.154

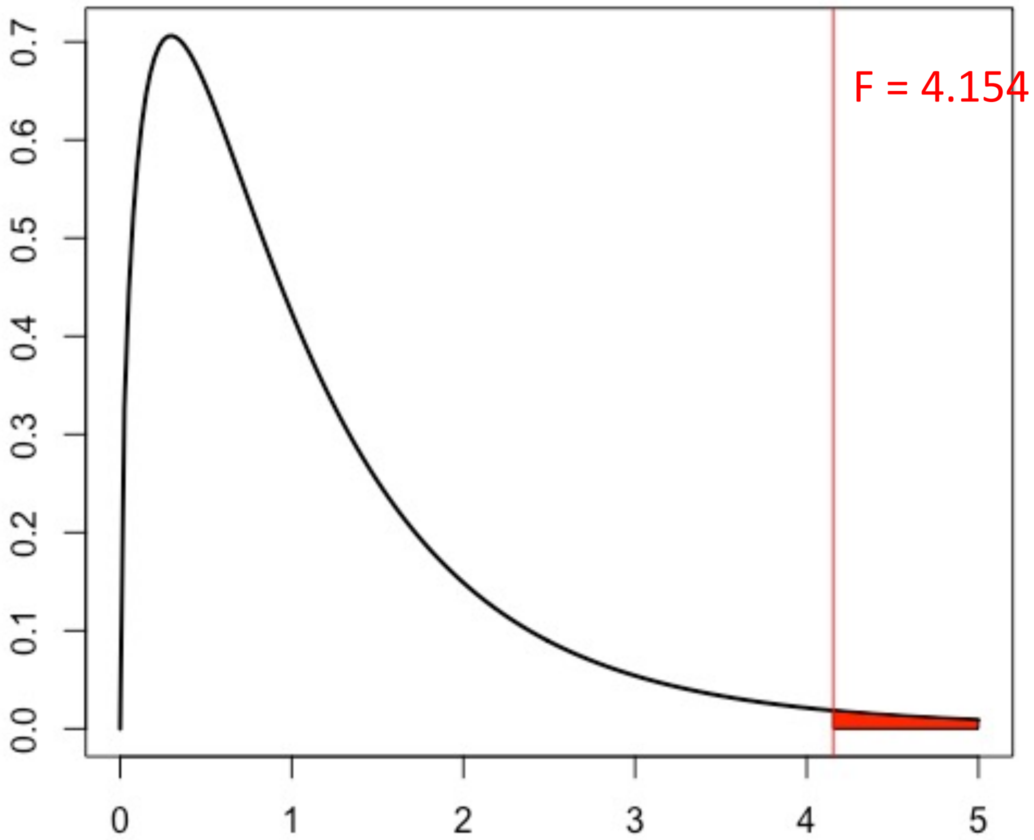
One-way ANOVA – Example II (cont.)

3. Calculate **rejection zone**/p value
4. Decide whether to reject/fail to reject H_0



One-way ANOVA – Example II (cont.)

3. Calculate rejection zone/**p value**
4. Decide whether to reject/fail to reject H_0



p=0.023516

One-way ANOVA – Example II

THE LANCET, AUGUST 12, 1978

MEGALOBLASTIC HÆMOPOIESIS IN PATIENTS RECEIVING NITROUS OXIDE

J. A. L. AMESS   J. F. BURMAN
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D. L. MOLLIN

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- 22 patients who underwent coronary artery bypass graft surgery (CABG) are separated into 3 different treatment groups (different ventilation strategies)
- Is there a difference in red blood cell folic acid measurements at 24 hours between the 3 treatment groups?

One-way ANOVA – Example II (cont.)

Group I.—8 patients received approximately 50% nitrous oxide and 50% oxygen mixture continuously for 24 h. 1 patient received 2000 μg of hydroxocobalamin intramuscularly immediately before and after the operation.

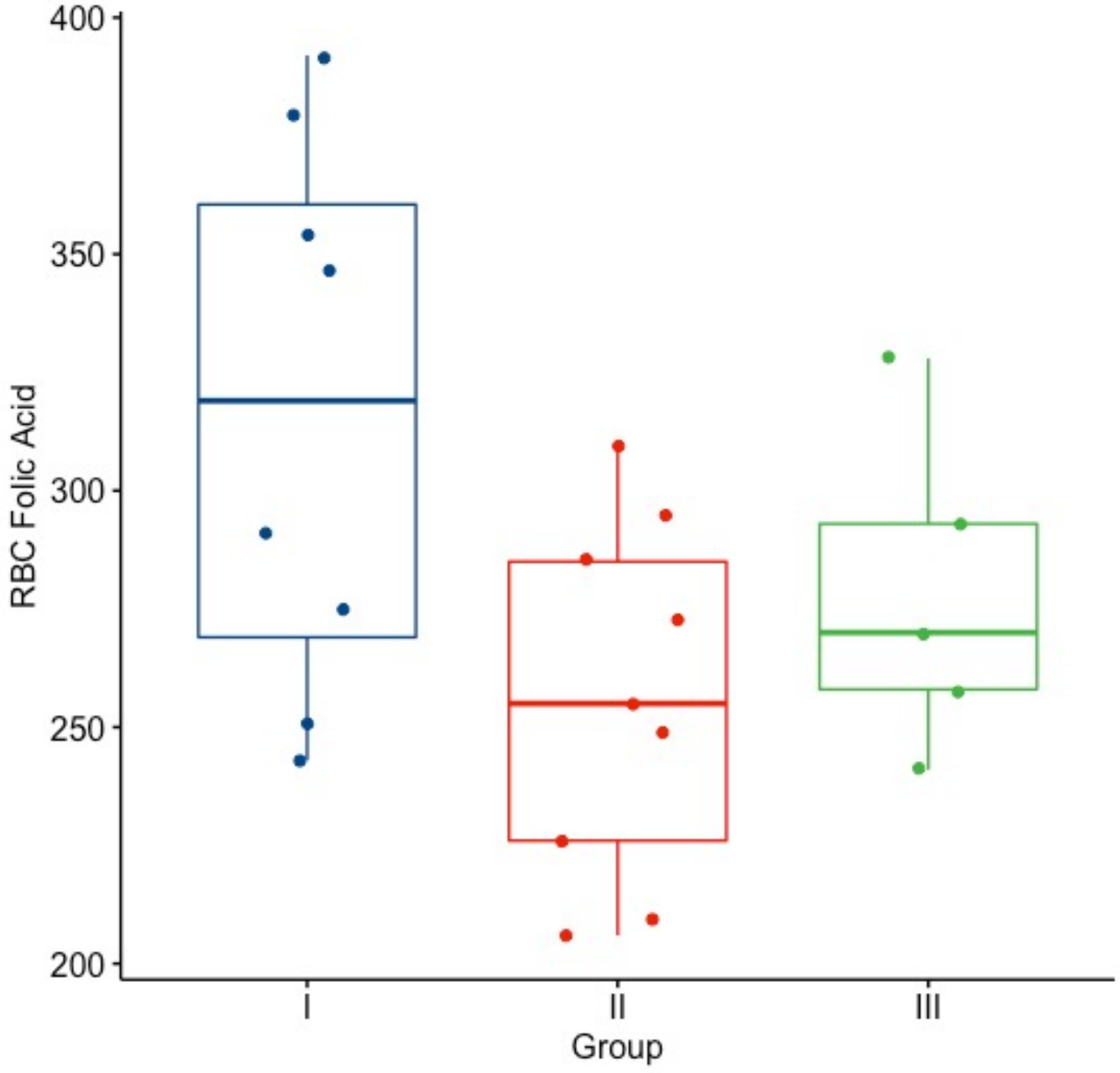
Group II.—9 patients received approximately 50% nitrous oxide and 50% oxygen mixture only during the operation (5–12 h) and thereafter 35–50% oxygen for the remainder of the 24 h period.

Group III.—5 patients received no nitrous oxide but were ventilated with 35–50% oxygen for 24 h.

Group I	Group II	Group III
243	206	241
251	210	258
275	226	270
291	249	293
347	255	328
354	273	
380	285	
392	295	
	309	

Amess JA, Burman JF, Rees GM, Nancekievill DG, Mollin DL. Megaloblastic haemopoiesis in patients receiving nitrous oxide. Lancet. 1978 Aug 12;2(8085):339–42.

One-way ANOVA – Example II (cont.)



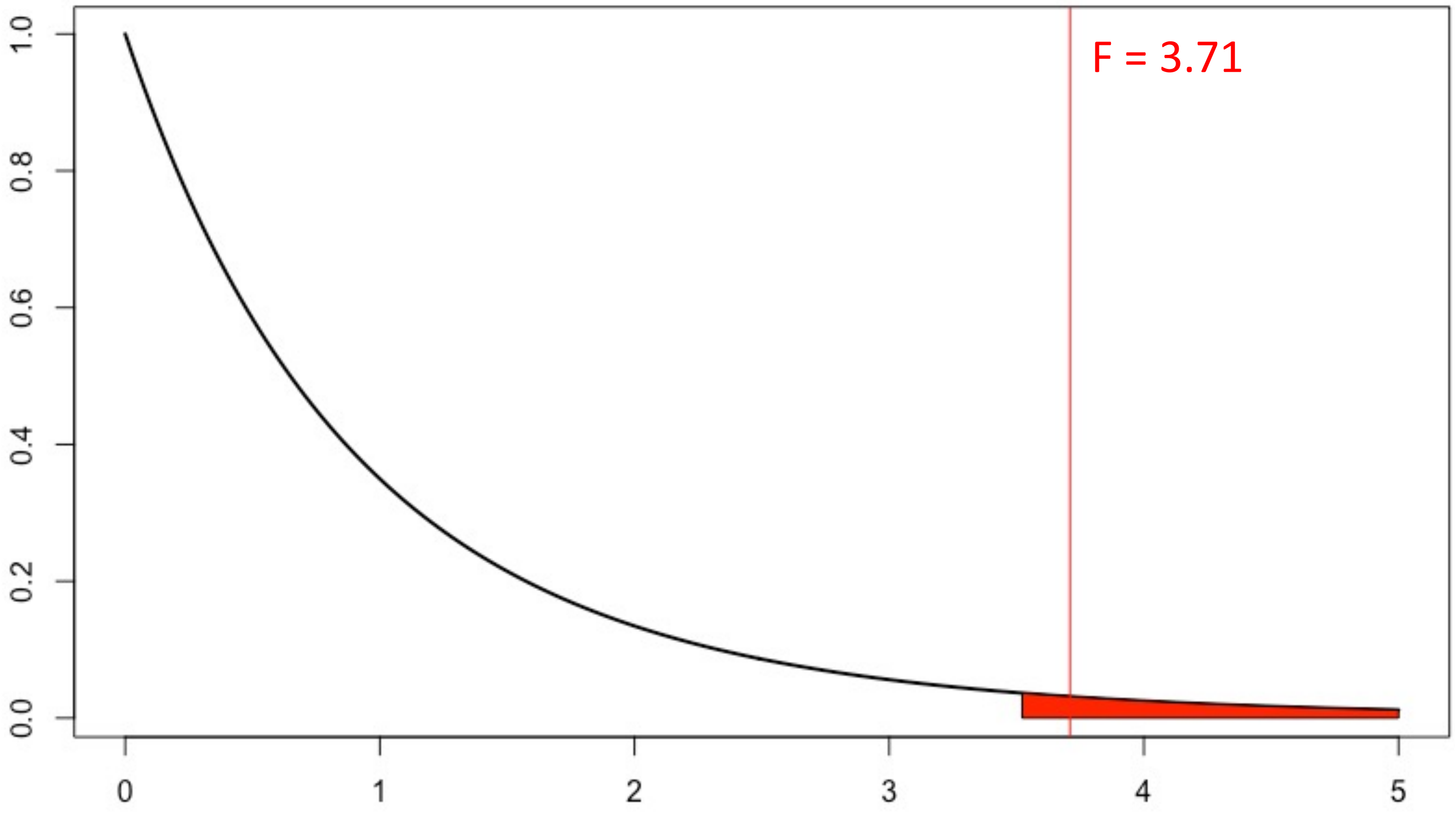
One-way ANOVA – Example II (cont.)

1. Check assumptions, determine H_0 and H_a, choose α
   - Check that data is normally distributed
   - H_0: $\mu_1 = \mu_2 = \mu_3$ H_a: at least one mean is different
   - $\alpha = 0.05$

2. Calculate the appropriate test statistic
   - F = 3.71 $\sim F_{2,19}$

One-way ANOVA – Example II (cont.)

3. Calculate **critical values**/p value
4. Decide whether to reject/fail to reject H_0



One-way ANOVA – Example II (cont.)

3. Calculate critical values/**p value**
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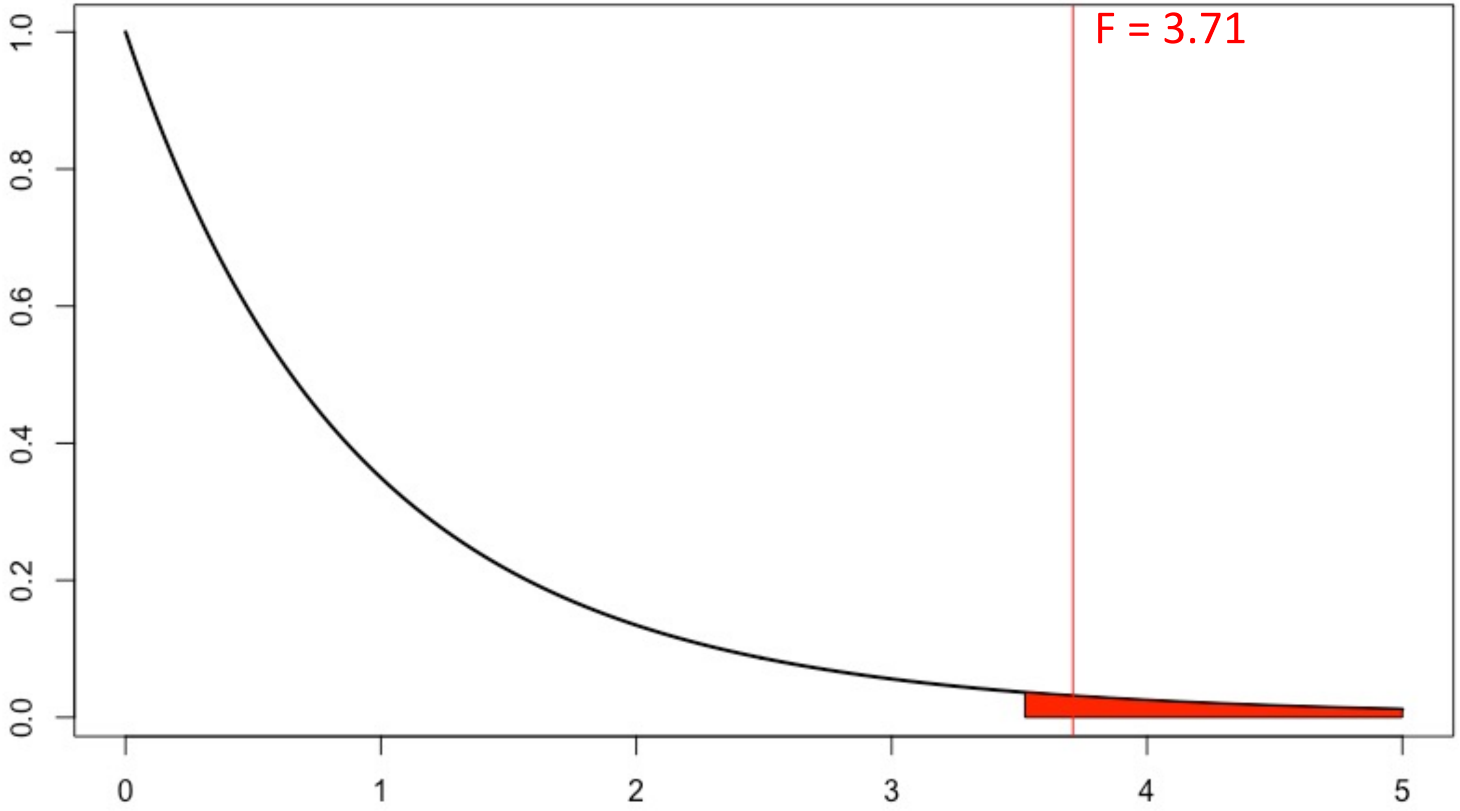
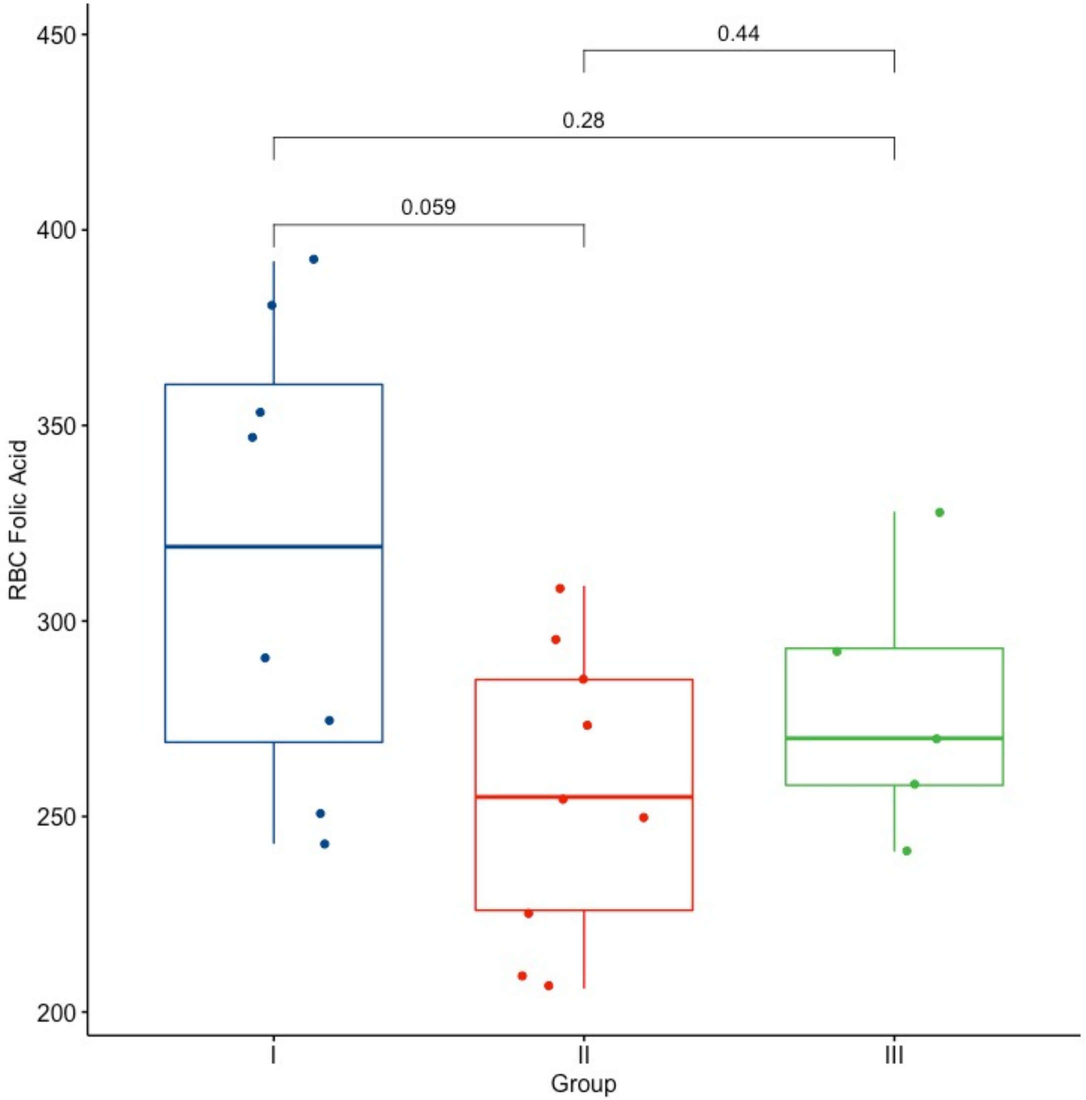


p = 0.043631

One-way ANOVA – Example II (cont.)

- With 95% confidence, we can conclude that the mean RBC folic acid level of at least one group is significantly different than the others
- Next, we perform 2-sample t-tests between all pairs of groups

One-way ANOVA – Example II (cont.)



Brief Summary

- Analysis of variance (ANOVA) is a statistical technique that is used to check if the means of **two or more groups** are significantly different from each other
    - ANOVA checks **the impact** of one or more factors by comparing the means of different samples
    - One-way ANOVA checks the impact of one factor
- Pairwise two-sample t-tests can then be used to determine which group(s) is different