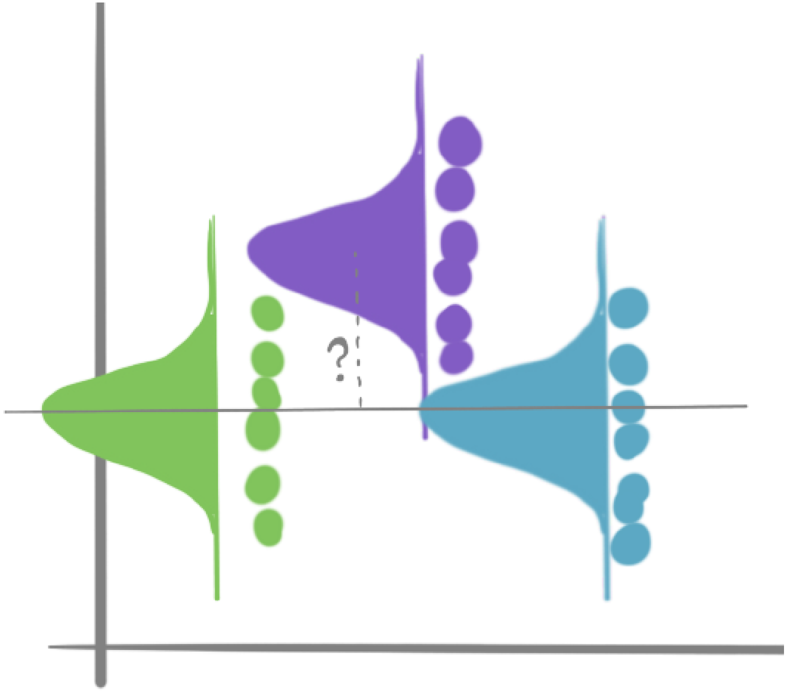
Contrasts and Multiple Comparisons



Statistical Experimental Design

Today

- Book Sections: 3.5
- Online Notes: Week 3 [3] and [4]

Limitation of ANOVA F-test

Recall the ANOVA model,

$$\begin{aligned} y_{ij} &= \mu + \tau_i + \epsilon_{ij} \\ \epsilon_{ij} &\sim \mathcal{N}\left(0, \sigma^2\right) \end{aligned}$$

and the associated hypothesis test,

$$\begin{aligned} H_0 &: \tau_1 = \cdots = \tau_a = 0 \\ H_1 &: \tau_i \neq 0 \text{ for at least one } i. \end{aligned}$$

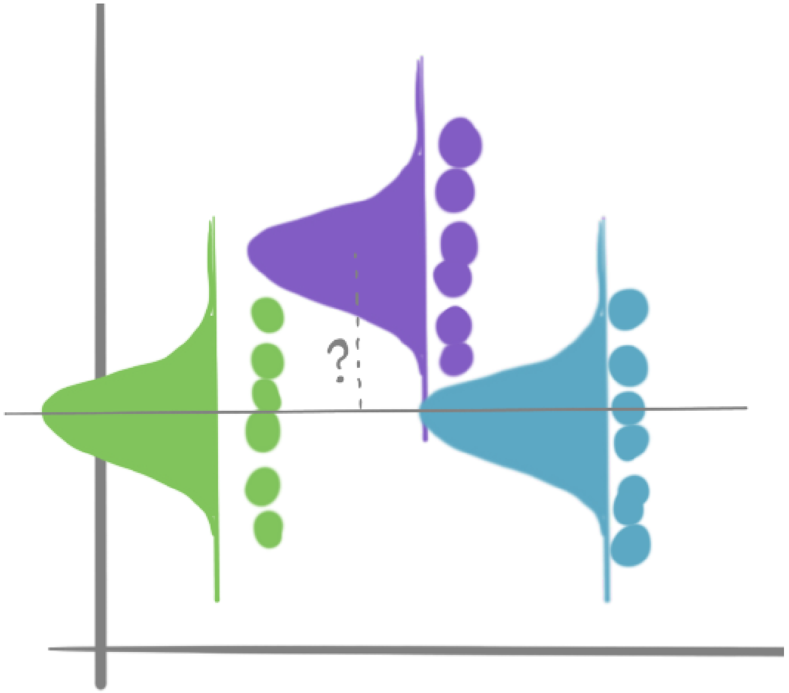
Note that it *does not* allow us to conclude which group(s) are responsible for a rejection.

Follow-up Tests

We may instead define a follow-up hypothesis test.

Imagine we had 4 groups,

- Are the first two means different from the last two? $H_0 : \tau_1 + \tau_2 = \tau_3 + \tau_4$
- Are the first two means equal to each other? $H_0 : \tau_1 = \tau_2$
- ...



Contrasts

A single framework covers all these cases.

- Let $\mu_i = \mu + \tau_i$ be the mean of group i.
- A contrast is a linear combination of the means,

$$\Gamma(c) = \sum_{i=1}^{a} c_i \mu_i$$

- The previous examples reduce to,

$$\begin{aligned} H_0 &: \Gamma(c) = 0 \\ H_1 &: \Gamma(c) \neq 0 \end{aligned}$$

for $c = (1, 1, -1, -1)$ and $c = (1, -1, 0, 0)$, respectively.

Plug-In Approximations

Since the sample means $\bar{y}_i \approx \mu_i$, we can approximate,

$$\hat{\Gamma}(c) := \sum_i c_i \bar{y}_i \approx \sum_i c_i \mu_i = \Gamma(c)$$

Moreover, since $\hat{\sigma}^2 \approx \sigma^2$,

$$\widehat{\mathrm{Var}}\left(\hat{\Gamma}(c)\right) := \left[\sum_i c_i^2\right] \frac{\hat{\sigma}^2}{n} \approx \left[\sum_i c_i^2\right] \frac{\sigma^2}{n} = \mathrm{Var}\left(\hat{\Gamma}(c)\right)$$

Reference Distribution

If the null hypothesis is true, the statistic is close to 0, because,

$$\hat{\Gamma}(c) \approx \Gamma(c) = 0$$

In fact, under the null, it's possible to derive that

$$\frac{\hat{\Gamma}(c)}{\sqrt{\widehat{\text{Var}}\left(\hat{\Gamma}(c)\right)}}$$

is t-distributed with $N - a$ degrees of freedom (the proof is unimportant in this class). This gives the basis for a t-test for any specific contrast.

Confidence Interval

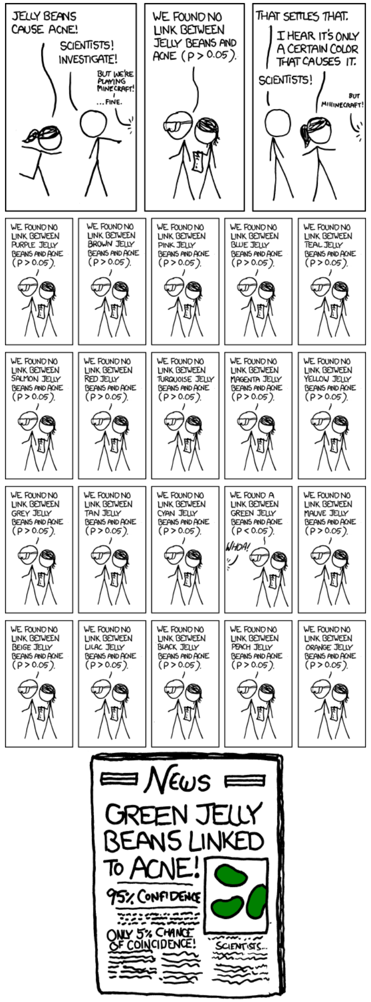
Given this reference distribution, it's also possible to derive a confidence interval,

$$\left[\hat{\Gamma}(c) - t_{\text{left}}\sqrt{\widehat{\text{Var}}(\hat{\Gamma}(c))}, \hat{\Gamma}(c) + t_{\text{left}}\sqrt{\widehat{\text{Var}}(\hat{\Gamma}(c))}\right]$$

- This quantifies the uncertainty in our estimate of $\hat{\Gamma}(c)$.
- In practice, we would never compute these statistics by hand.

Multiple Comparisons

- If we knew the interesting contrasts in advance, we will be fine
- But what if we go in search for significant results using different contrasts?


JELLY BEANS CAUSE ACNE!
SCIENTISTS! INVESTIGATE!
BUT WE'RE PLAYING MINECRAFT!
...FINE.
WE FOUND NO LINK BETWEEN JELLY BEANS AND ACNE (P > 0.05).
THAT SETTLES THAT.
I HEAR IT'S ONLY A CERTAIN COLOR THAT CAUSES IT.
SCIENTISTS!
BUT MIIIINECRAFT!
WE FOUND NO LINK BETWEEN PURPLE JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN BROWN JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN PINK JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN BLUE JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN TEAL JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN SALMON JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN RED JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN TURQUOISE JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN MAGENTA JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN YELLOW JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN GREY JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN TAN JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN CYAN JELLY BEANS AND ACNE (P > 0.05).
WE FOUND A LINK BETWEEN GREEN JELLY BEANS AND ACNE (P < 0.05).
WHOA!
WE FOUND NO LINK BETWEEN MAUVE JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN BEIGE JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN LILAC JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN BLACK JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN PEACH JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN ORANGE JELLY BEANS AND ACNE (P > 0.05).
News
GREEN JELLY BEANS LINKED TO ACNE!
95% CONFIDENCE
ONLY 5% CHANCE OF COINCIDENCE!
SCIENTISTS...

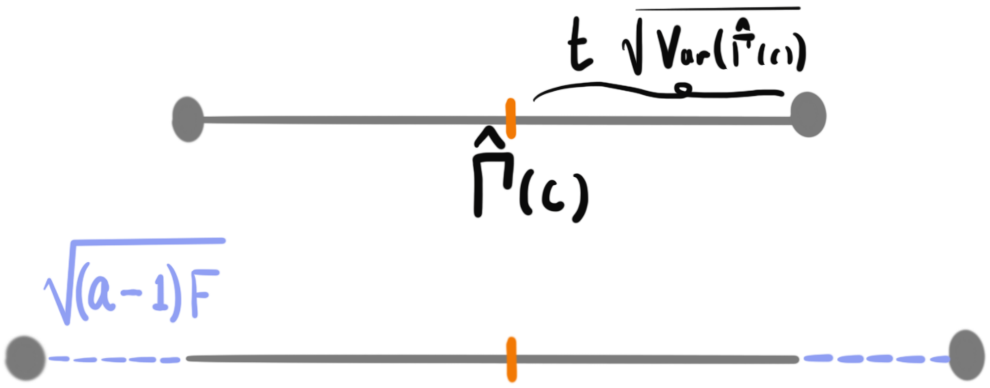
Multiple Comparisons

- We need to adapt our methodology to account for the search over contrasts
- The quantity of interest is the experimentwise error rate, the probability that we get at least one false positive across the entire experiment
- Two methods, each with different properties,
    - Scheffe's method
    - Tukey's Honest Significant Difference

Scheffe's Method

- Suppose we are interested in m contrasts $c_1, \ldots, c_m$
- We can widen the confidence intervals for each to control the experimentwise error
- It's not obvious, but the appropriate scaling factor is

$$\sqrt{(a-1)\,F_{\frac{\alpha}{2},a-1,N-a}}$$



Tukey's Honest Significant Difference

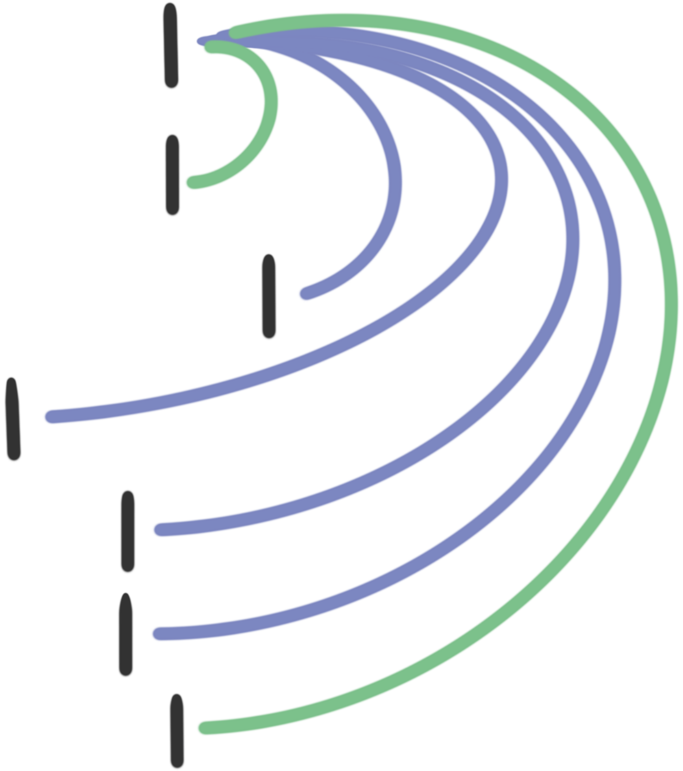
- A common special case is when we're interest in all pairwise comparisons,

$$\Gamma\left(c\right)=\mu_i-\mu_j$$

- If we want to make confidence intervals, we should center them around,

$$\hat{\Gamma}\left(c\right)=\bar{y}_i-\bar{y}_j.$$

but how wide should they be?

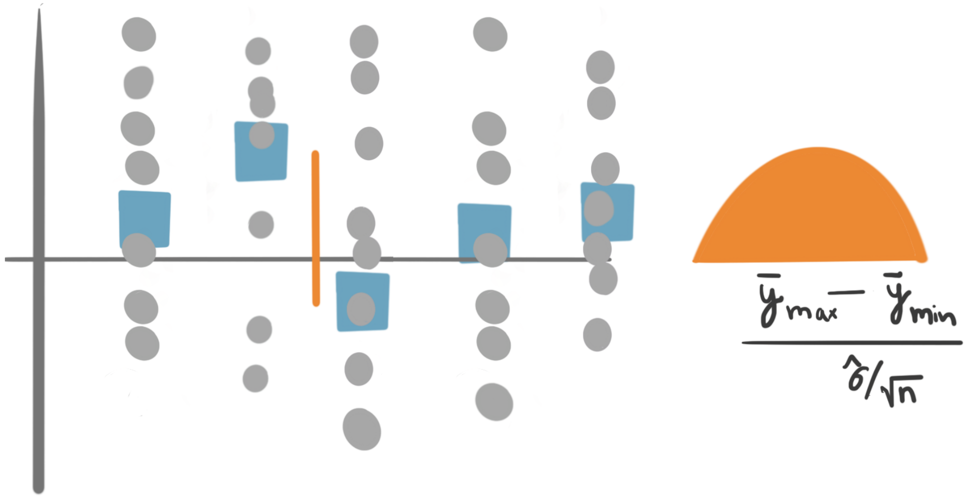


Tukey's Honest Significant Difference

- Let $\bar{y}_{\max}$ and $\bar{y}_{\min}$ be the largest and smallest of the group means
- Notice that

$$\left|\bar{y}_i - \bar{y}_j\right| \leq \bar{y}_{\max} - \bar{y}_{\min}$$

- Therefore, we can rescale our confidence intervals based on the reference distribution for the difference $\bar{y}_{\max} - \bar{y}_{\min}$


$\frac{\bar{y}_{max} - \bar{y}_{min}}{\hat{\sigma}/\sqrt{n}}$

Fisher's Least Significant Difference

- A final method, closely related to Tukey's HSD is Fisher's LSD
- It also tests for all pairwise differences, but does not control experimentwise error rate
- Notice that the variance of the differences between two group's means is,

$$\begin{aligned}
\mathrm{Var}\left(\bar{y}_i - \bar{y}_j\right) &= \mathrm{Var}(\bar{y}_i) + \mathrm{Var}\left(\bar{y}_j\right) \\
&= \frac{\sigma^2}{n_i} + \frac{\sigma^2}{n_j} \\
&\approx \hat{\sigma}^2 \left(\frac{1}{n_i} + \frac{1}{n_j}\right)
\end{aligned}$$

Fisher's LSD

Fisher’s LSD compares each difference $\left|y_i - y_j\right|$ to the cutoff,

$$t_{\text{right}} \sqrt{\hat{\sigma}^2 \left(\frac{1}{n_i} + \frac{1}{n_j}\right)}$$

and rejects the null that the pairs have equal means if the difference is larger.

Unlike the two-sample t-test, it accounts for the total number of samples in each group.

Code Implementation

ANOVA Estimates

Before we construct any contrasts, we need to have an underlying ANOVA fit.

```r
library(readr)
etch_rate <- read_csv("https://uwmadison.box.com/shared/static/vw3ldbgvgn7rupt4tz3ditl1mpupw
etch_rate$power <- as.factor(etch_rate$power)
fit <- lm(rate ~ power, data = etch_rate)
aov_fit <- aov(fit)
```

Defining and Testing a Contrast

- To fit a contrast, we can use the `fit.contrast` function from the `gmodels` package.
- Which power levels are we comparing with this contrast?

```r
library(gmodels)
contrast <- c(1, -1, 0, 0)
fit.contrast(aov_fit, "power", contrast)
```

```
##                         Estimate Std. Error   t value    Pr(>|t|)
## power c=( 1 -1 0 0 )    -36.2   11.55335 -3.133289 0.006416224
## attr(,"class")
## [1] "fit_contrast"
```

Confidence Intervals

We can get a confidence interval for the contrast using the `confi.int` parameter.

```r
fit.contrast(aov_fit, "power", contrast, conf.int = 0.95)
```

```
##                        Estimate Std. Error   t value    Pr(>|t|)  lower CI  upper CI
## power c=( 1 -1 0 0 )    -36.2   11.55335 -3.133289 0.006416224 -60.69202 -11.70798
## attr(,"class")
## [1] "fit_contrast"
```

Defining Many Contrasts

In a multiple testing setting, we can specify each contrast as a separate row in a matrix.

```
contrasts <- matrix(
    c(1, -1, 0, 0,
      1, 1, -1, -1,
      0, 0, 1, -1),
    nrow = 3, byrow = TRUE
  )

fit.contrast(aov_fit, "power", contrasts, conf.int = 0.95)
```

```
##                         Estimate Std. Error     t value     Pr(>|t|)   lower CI    upper CI
## power c=( 1 -1 0 0 )      -36.2   11.55335   -3.133289 6.416224e-03  -60.69202  -11.70798
## power c=( 1 1 -1 -1 )    -193.8   16.33891 -11.861256 2.434581e-09 -228.43694 -159.16306
## power c=( 0 0 1 -1 )      -81.6   11.55335   -7.062884 2.683834e-06 -106.09202  -57.10798
## attr(,"class")
## [1] "fit_contrast"
```

Scheffe's Method

- The Scheffe adjusted confidence intervals can be found using `PostHocTest` from the `DescTools` package
- Make sure to set `method = "scheffe"`

```r
library(DescTools)
PostHocTest(aov_fit, method = "scheffe", contrast = t(contrasts))
```

```
##
##   Posthoc multiple comparisons of means: Scheffe Test
##     95% family-wise confidence level
##
## $power
##                    diff     lwr.ci       upr.ci    pval    
## 160-180           -36.2  -72.21352   -0.1864788  0.0486 *  
## 160,180-200,220  -193.8 -244.73081 -142.8691899 3.8e-08 ***
## 200-220           -81.6 -117.61352  -45.5864788 3.6e-05 ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Tukey's Method

- All the intervals for Tukey's method can be found using the TukeyHSD function.
- Each row gives an interval for a $\mu_i - \mu_j$.

```
TukeyHSD(aov_fit)
```

```
##   Tukey multiple comparisons of means
##     95% family-wise confidence level
##
## Fit: aov(formula = fit)
##
## $power
##          diff        lwr       upr     p adj
## 180-160  36.2   3.145624  69.25438 0.0294279
## 200-160  74.2  41.145624 107.25438 0.0000455
## 220-160 155.8 122.745624 188.85438 0.0000000
## 200-180  38.0   4.945624  71.05438 0.0215995
## 220-180 119.6  86.545624 152.65438 0.0000001
## 220-200  81.6  48.545624 114.65438 0.0000146
```

Fisher's Method

- The PostHocTest function can also be used for Fisher's method
- Notice that the intervals are all narrower: we are not controlling the experimentwise error

```r
PostHocTest(aov_fit, method = "lsd")
```

```
##
##   Posthoc multiple comparisons of means : Fisher LSD
##     95% family-wise confidence level
##
## $power
##          diff    lwr.ci    upr.ci    pval
## 180-160  36.2  11.70798  60.69202  0.0064 **
## 200-160  74.2  49.70798  98.69202 8.4e-06 ***
## 220-160 155.8 131.30798 180.29202 3.7e-10 ***
## 200-180  38.0  13.50798  62.49202  0.0046 **
## 220-180 119.6  95.10798 144.09202 1.7e-08 ***
## 220-200  81.6  57.10798 106.09202 2.7e-06 ***
##
```

Exercise

This walks through parts of problem 3.9.

The tensile strength of Portland cement is being studied. Four different mixing techniques can be used economically. An experiment was conducted and the following data were collected.

```
cement <- data.frame(
  method = c("1", "2", "3", "4"),
  rep1 = c(3129, 3200, 2800, 2600),
  rep2 = c(3000, 3300, 2900, 2700),
  rep3 = c(2865, 2975, 2985, 2600),
  rep4 = c(2890, 3150, 3050, 2765)
)
cement
```

```
##   method rep1 rep2 rep3 rep4
## 1      1 3129 3000 2865 2890
## 2      2 3200 3300 2975 3150
## 3      3 2800 2900 2985 3050
## 4      4 2600 2700 2600 2765
```

(1) Use `pivot_longer` to reshape the data so that the outcome is in a single column.

(2) Use `lm` and `aov` to make an ANOVA table. Does the method detect any difference in the means across the four groups?

(3) Use `PostHocTest` to compare between all pairs of means using Fisher's LSD.

(4) Make QQ plot of the residuals. What can you conclude about the validity of the ANOVA assumptions?

Solution

(1) The `pivot_longer` method reshapes the data, creating a new column for the replicate indicator.

```r
cement <- pivot_longer(cement, -method, names_to = "replicate")
head(cement)
```

```
## # A tibble: 6 × 3
##   method replicate value
##   <chr>  <chr>     <dbl>
## 1 1      rep1       3129
## 2 1      rep2       3000
## 3 1      rep3       2865
## 4 1      rep4       2890
## 5 2      rep1       3200
## 6 2      rep2       3300
```

Solution

(2) Yes, since the F-statistic has a very small p-value, we can conclude that there is a difference between the cement types.

```
aov_table <- aov(lm(value ~ method, data = cement))
summary(aov_table)
```

```
##             Df Sum Sq Mean Sq F value   Pr(>F)    
## method       3 489740  163247   12.73 0.000489 ***
## Residuals   12 153908   12826                     
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Solution

(3) We find 5 significant pairwise differences using Fisher's method, but these should be interpreted with a grain of salt, since the method does not control for multiple comparisons.

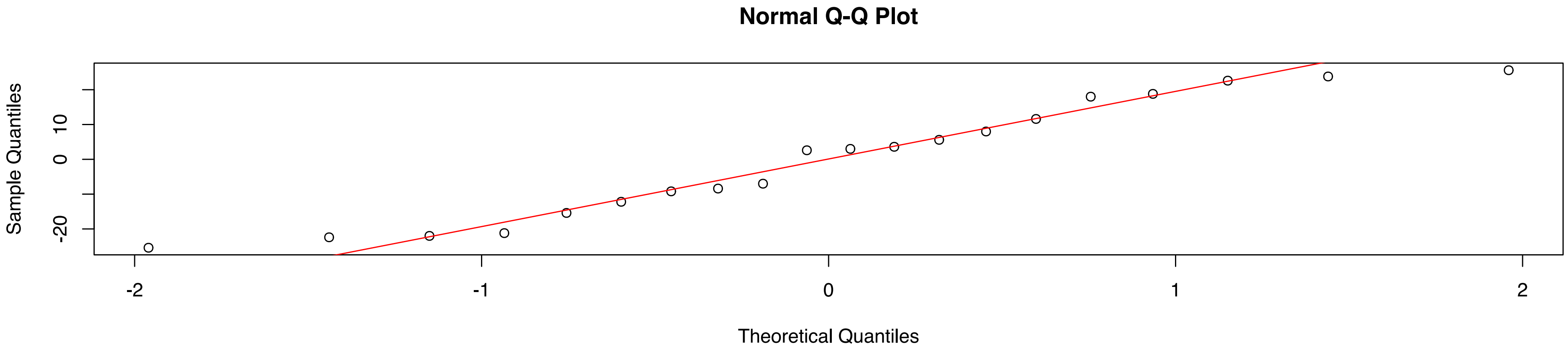
```r
library(DescTools)
PostHocTest(aov_table, method = "lsd")
```

```
##
##   Posthoc multiple comparisons of means : Fisher LSD
##     95% family-wise confidence level
##
## $method
##        diff     lwr.ci     upr.ci    pval
## 2-1  185.25   10.77016  359.72984  0.0392 *
## 3-1  -37.25 -211.72984  137.22984  0.6501
## 4-1 -304.75 -479.22984 -130.27016  0.0025 **
## 3-2 -222.50 -396.97984  -48.02016  0.0167 *
## 4-2 -490.00 -664.47984 -315.52016 5.2e-05 ***
## 4-3 -267.50 -441.97984  -93.02016  0.0059 **
```

Solution

(4) There is an unusual jump in the residuals, possibly due to a difference in the variance of the residuals across groups. This plot should be followed-up by a direct plot of the residuals to see whether any transformations might help.

```
qqnorm(resid(fit))
qqline(resid(fit), col = "red")
```


Normal Q-Q Plot
Sample Quantiles
Theoretical Quantiles