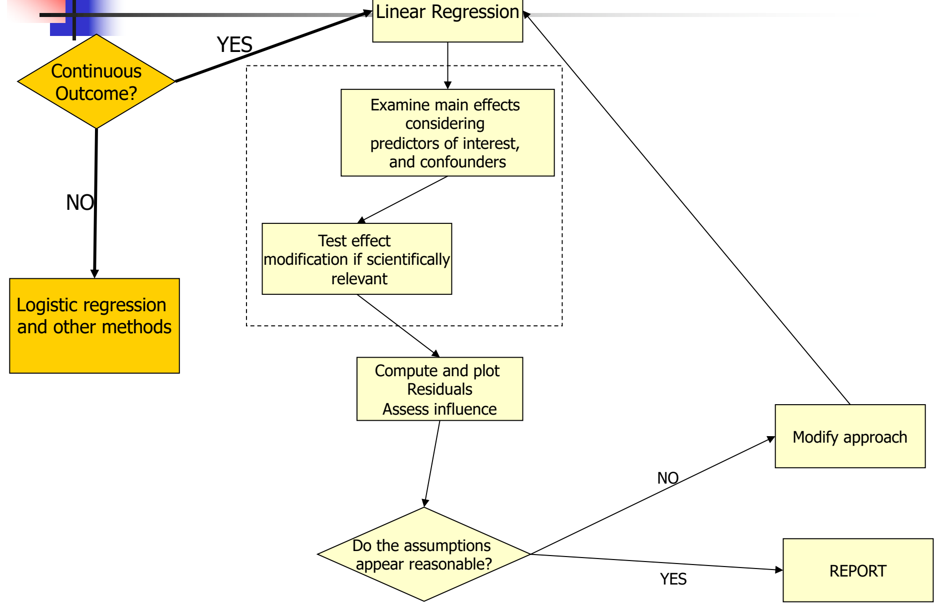
SCHOOL OF PUBLIC HEALTH · UNIVERSITY of WASHINGTON
Department of Biostatistics

REGRESSION MODELS

ANOVA

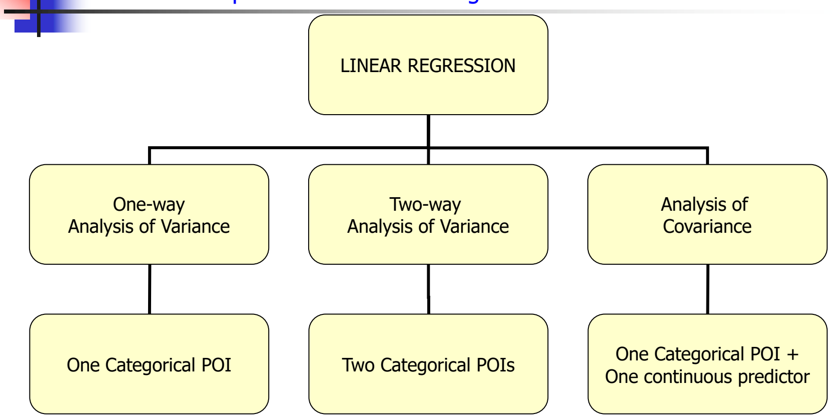
RECAP:



COMING UP NEXT: ANOVA – a special case of linear regression

- What if the independent variables of interest are categorical?
- In this case, comparing the mean of the continuous outcome in the different categories may be of interest
- This is what is called ANalysis Of VAriance
- We will show that it is just a special case of linear regression

ANOVA – a special case of linear regression



Uses dummy variables to represent categorical variables!

Outline

- Motivation: We will consider some examples of ANOVA and show that they are special cases of linear regression
- ANOVA as a regression model
  - Dummy variables
- One-way ANOVA models
  - Contrasts
  - Multiple comparisons
- Two-way ANOVA models
  - Interactions
- ANCOVA models

ANOVA/ANCOVA: Motivation

- Let's investigate if genetic factors are associated with cholesterol levels.
  - Ideally, you would have a confirmatory analysis of scientific hypotheses formulated prior to data collection
  - Alternatively, you could consider an exploratory analysis – hypotheses generation for future studies

ANOVA/ANCOVA: Motivation

- Scientific hypotheses of interest:
  - Assess the effect of rs174548 on cholesterol levels.
  - Assess the effect of rs174548 and diabetes on cholesterol levels
    - Does the effect of rs174548 on cholesterol differ between people with and without diabetes?
  - Assess the effect of rs174548 and age on cholesterol levels
    - Does the effect of rs174548 on cholesterol differ depending on subject's age?

ANOVA: One-Way Model Motivation:

- Scientific question:
  - Assess the effect of rs174548 on cholesterol levels.

Motivation: Example

Here are some descriptive summaries:

```
> tapply(chol, factor(rs174548), mean)
       0        1        2
181.0617 187.8639 186.5000

> tapply(chol, factor(rs174548), sd)
       0        1        2
21.13998 23.74541 17.38333
```


Motivation: Example

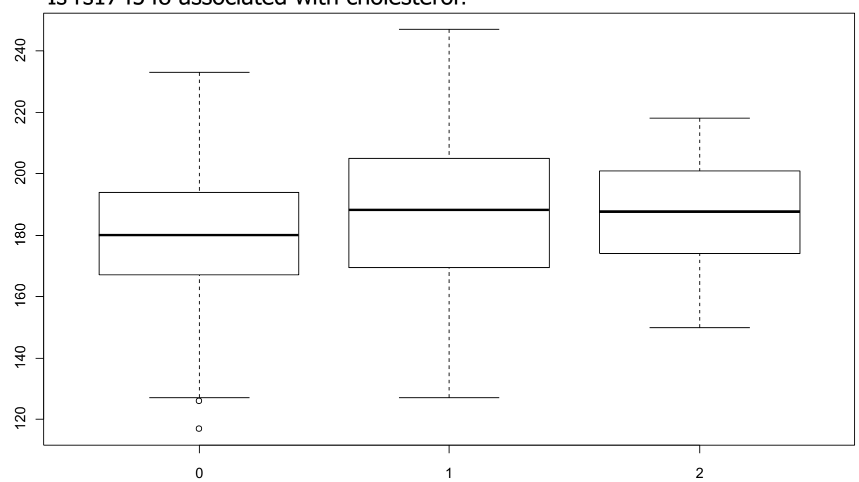
Another way of getting the same results:

```
> by(chol, factor(rs174548), mean)
   factor(rs174548): 0
[1] 181.0617
-------------------------------------------------------------------
   factor(rs174548): 1
[1] 187.8639
-------------------------------------------------------------------
   factor(rs174548): 2
[1] 186.5

> by(chol, factor(rs174548), sd)
   factor(rs174548): 0
[1] 21.13998
-------------------------------------------------------------------
   factor(rs174548): 1
[1] 23.74541
-------------------------------------------------------------------
   factor(rs174548): 2
[1] 17.38333
```


Motivation: Example

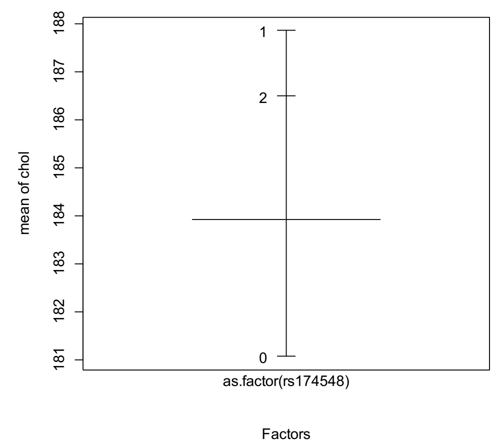
Is rs174548 associated with cholesterol?



R command: `boxplot(chol ~ factor(rs174548))`

Motivation: Example

Another graphical display:



R command:
`plot.design(chol ~ factor(rs174548))`

Motivation: Example

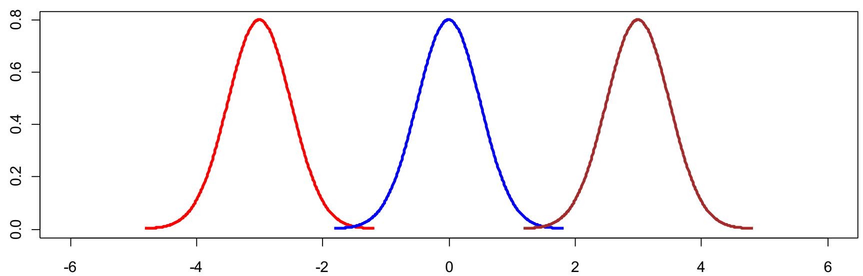
- Feature:
  - How do the mean responses compare across different groups?
    - Categorical/qualitative predictor

REGRESSION MODELS

One-way ANOVA as a regression model

ANalysis Of VAriance Models (ANOVA)

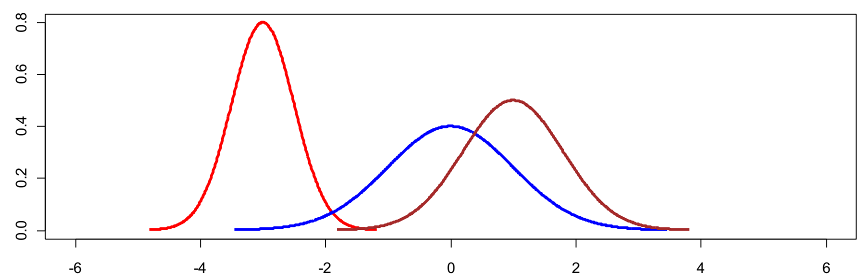
- Compares the means of several populations



Assumptions for Classical ANOVA Framework: Independence
Normality
Equal variances

ANalysis Of VAriance Models (ANOVA)

- Compares the means of several populations



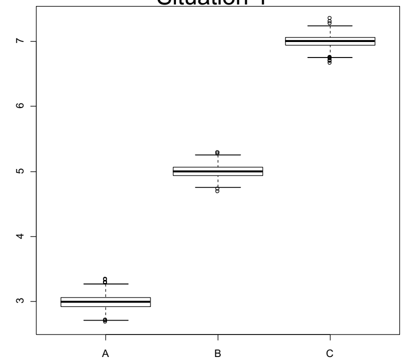
ANalysis Of VAriance Models (ANOVA)

- Compares the means of several populations
  - Counter-intuitive name!

ANalysis Of VAriance Models (ANOVA)

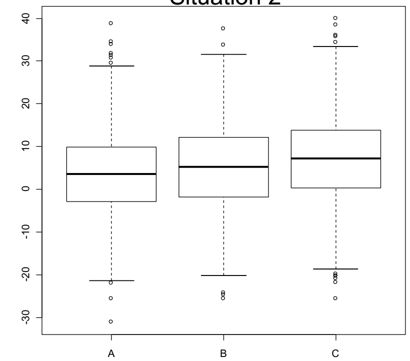
In both data sets, the true population means are: 3 (A), 5 (B), 7(C)

Situation 1



Low variance within groups

Situation 2



High variance within groups

Where do you expect to detect difference between population means?

ANalysis Of VAriance Models (ANOVA)

- Compares the means of several populations
  - Counter-intuitive name!
    - Underlying concept:
      - To assess whether the population means are equal, compares:
        - Variation between the sample means (MSR) to
        - Natural variation of the observations within the samples (MSE).
      - The larger the MSR compared to MSE the more support that there is a difference in the population means!
      - The ratio MSR/MSE is the F-statistic.

- We can make these comparisons with multiple linear regression: the different groups are represented with "dummy" variables

ANOVA as a multiple regression model

- Dummy Variables:
  - Suppose you have a categorical variable C with k categories 0,1, 2, …, k-1. To represent that variable we can construct k-1 dummy variables of the form

$$x_1 = \begin{cases} 1, & \text{if subject is in category } 1 \\ 0, & \text{otherwise} \end{cases}$$

$$x_2 = \begin{cases} 1, & \text{if subject is in category } 2 \\ 0, & \text{otherwise} \end{cases}$$

…

$$x_{k-1} = \begin{cases} 1, & \text{if subject is in category } k\text{-}1 \\ 0, & \text{otherwise} \end{cases}$$

The omitted category (here category 0) is the **reference group**.

ANOVA as a multiple regression model

- Dummy Variables:
  - Back to our motivating example:
    - Predictor: rs174548 (coded 0=C/C, 1=C/G, 2=G/G)
    - Outcome (Y): cholesterol

Let's take C/C as the reference group.

$$x_1 = \begin{cases} 1, & \text{if code 1 (C/G)} \\ 0, & \text{otherwise} \end{cases}$$

$$x_2 = \begin{cases} 1, & \text{if code 2 (G/G)} \\ 0, & \text{otherwise} \end{cases}$$

ANOVA as a multiple regression model

rs174548	Mean cholesterol	X_1	X_2
C/C	μ_0	0	0
C/G	μ_1	1	0
G/G	μ_2	0	1

ANOVA as a multiple regression model

- Regression with Dummy Variables:
  - Example:

  Model: $E[Y|x_1, x_2] = \beta_0 + \beta_1 x_1 + \beta_2 x_2$

- Interpretation of model parameters?

ANOVA as a multiple regression model

Mean	Regression Model
μ_0	β_0
μ_1	$\beta_0 + \beta_1$
μ_2	$\beta_0 + \beta_2$

ANOVA as a multiple regression model

- Regression with Dummy Variables:
  - Example:

    Model: $E[Y|x_1, x_2] = \beta_0 + \beta_1 x_1 + \beta_2 x_2$

- Interpretation of model parameters?
  - $\mu_0 = \beta_0$: mean cholesterol when rs174548 is C/C
  - $\mu_1 = \beta_0+\beta_1$: mean cholesterol when rs174548 is C/G
  - $\mu_2 = \beta_0+\beta_2$: mean cholesterol when rs174548 is G/G

ANOVA as a multiple regression model

- Regression with Dummy Variables:
  - Example:

    Model: $E[Y|x_1, x_2] = \beta_0 + \beta_1 x_1 + \beta_2 x_2$

- Interpretation of model parameters?
  - $\mu_0 = \beta_0$: mean cholesterol when rs174548 is C/C
  - $\mu_1 = \beta_0+\beta_1$: mean cholesterol when rs174548 is C/G
  - $\mu_2 = \beta_0+\beta_2$: mean cholesterol when rs174548 is G/G
  - Alternatively
    - β_1: difference in mean cholesterol levels between groups with rs174548 equal to C/G and C/C ($\mu_1 - \mu_0$).
    - β_2: difference in mean cholesterol levels between groups with rs174548 equal to G/G and C/C ($\mu_2 - \mu_0$).

ANOVA: One-Way Model

- Goal:
  - Compare the means of K independent groups (defined by a categorical predictor)
    - Statistical Hypotheses:
      - (Global) Null Hypothesis:

        H_0: $\mu_0 = \mu_1 = \ldots = \mu_{K-1}$ or, equivalently,

        H_0: $\beta_1 = \beta_2 = \ldots = \beta_{K-1} = 0$
      - Alternative Hypothesis:

        H_1: not all means are equal
  - If the means of the groups are not all equal (i.e. you rejected the above H_0), determine which ones are different (multiple comparisons)

Estimation and Inference

- Global Hypotheses

  H_0: $\mu_1 = \mu_2 = \ldots = \mu_K$ vs. H_1: not all means are equal

  H_0: $\beta_1 = \beta_2 = \ldots = \beta_{K-1} = 0$

- Analysis of variance table

Source	df	SS	MS	F
Regression	K-1	SSR= $\sum_i (\bar{y}_i - \bar{y})^2$	MSR= SSR/(K-1)	MSR/ MSE
Residual	n-K	SSE= $\sum_{i,j} (y_{ij} - \bar{y}_i)^2$	MSE= SSE/n-K	
Total	n-1	SST= $\sum_{i,j} (y_{ij} - \bar{y})^2$		

ANOVA: One-Way Model

- How to fit a one-way model as a regression problem?
  - Need to use "dummy" variables
    - Create on your own (can be tedious!)
    - Most software packages will do this for you
      - R creates dummy variables in the background as long as you state you have a categorical variable (may need to use: factor)

ANOVA: One-Way Model

By hand:
Creating "dummy" variables:

```
> dummy1 = 1*(rs174548==1)
> dummy2 = 1*(rs174548==2)
```

```
> fit0 = lm(chol ~ dummy1 + dummy2)
> summary(fit0)
Call:
lm(formula = chol ~ dummy1 + dummy2)

Residuals:
      Min        1Q    Median        3Q       Max
-64.06167 -15.91338  -0.06167  14.93833  59.13605

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  181.062      1.455 124.411  < 2e-16 ***
dummy1         6.802      2.321   2.930  0.00358 **
dummy2         5.438      4.540   1.198  0.23167
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 21.93 on 397 degrees of freedom
Multiple R-squared: 0.0221,     Adjusted R-squared: 0.01718
F-statistic: 4.487 on 2 and 397 DF,  p-value: 0.01184
```

Fitting the ANOVA model:

```
> anova(fit0)
Analysis of Variance Table

Response: chol
           Df Sum Sq Mean Sq F value   Pr(>F)
dummy1      1   3624    3624  7.5381 0.006315 **
dummy2      1    690     690  1.4350 0.231665
Residuals 397 190875     481
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```


ANOVA: One-Way Model

Better:
Let R do it for you!

```
> fit1 = lm(chol ~ factor(rs174548))
> summary(fit1)
Call:
lm(formula = chol ~ factor(rs174548))

Residuals:
      Min        1Q    Median        3Q       Max
-64.06167 -15.91338  -0.06167  14.93833  59.13605

Coefficients:
                  Estimate  Std. Error t value Pr(>|t|)
(Intercept)        181.062       1.455 124.411  < 2e-16 ***
factor(rs174548)1    6.802       2.321 2.930    0.00358 **
factor(rs174548)2    5.438       4.540 1.198    0.23167
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 21.93 on 397 degrees of freedom
Multiple R-squared: 0.0221,     Adjusted R-squared: 0.01718
F-statistic: 4.487 on 2 and 397 DF,  p-value: 0.01184

> anova(fit1)
Analysis of Variance Table

Response: chol
                  Df Sum Sq Mean Sq F value  Pr(>F)
factor(rs174548)   2   4314    2157 4.4865 0.01184 *
Residuals        397 190875     481
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```


ANOVA: One-Way Model

- Your turn!
  - Compare model fit results (fit0 & fit1)
    What do you conclude?

ANOVA: One-Way Model

```
> fit0 = lm(chol ~ dummy1 + dummy2)
> summary(fit0)
Call:
lm(formula = chol ~ dummy1 + dummy2)

Residuals:
     Min       1Q   Median       3Q      Max
-64.06167 -15.91338  -0.06167  14.93833  59.13605

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dummy1      1   3624    3624  7.5381 0.006315 **
dummy2      1    690     690  1.4350 0.231665
Residuals 397 190875     481
---
```

```
> fit1 = lm(chol ~ factor(rs174548))
> summary(fit1)
Call:
lm(formula = chol ~ factor(rs174548))

Residuals:
     Min       1Q   Median       3Q      Max
-64.06167 -15.91338  -0.06167  14.93833  59.13605

Coefficients:
                  Estimate Std. Error t value Pr(>|t|)
(Intercept)        181.062      1.455 124.411  < 2e-16 ***
factor(rs174548)1    6.802      2.321   2.930  0.00358 **
factor(rs174548)2    5.438      4.540   1.198  0.23167
---

Residual standard error: 21.93 on 397 degrees of freedom
Multiple R-squared: 0.0221,  Adjusted R-squared: 0.01718
F-statistic: 4.487 on 2 and 397 DF,  p-value: 0.01184

> anova(fit1)
Analysis of Variance Table

Response: chol
                  Df Sum Sq Mean Sq F value  Pr(>F)
factor(rs174548)   2   4314    2157  4.4865 0.01184 *
Residuals        397 190875     481
---
```


ANOVA: One-Way Model

```
> fit0 = lm(chol ~ dummy1 + dummy2)
> summary(fit0)
Call:
lm(formula = chol ~ dummy1 + dummy2)

Residuals:
     Min       1Q   Median       3Q      Max
-64.06167 -15.91338  -0.06167  14.93833  59.13605

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  181.062      1.455 124.411  < 2e-16 ***
dummy1         6.802      2.321   2.930  0.00358 **
dummy2         5.438      4.540   1.198  0.23167
---

Residual standard error: 21.93 on 397 degrees of freedom
Multiple R-squared: 0.0221, Adjusted R-squared: 0.01718
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> anova(fit0)
Analysis of Variance Table

Response: chol
           Df Sum Sq Mean Sq F value   Pr(>F)
dummy1      1   3624    3624  7.5381 0.006315 **
dummy2      1    690     690  1.4350 0.231665
Residuals 397 190875     481
---
```

```
> fit1 = lm(chol ~ factor(rs174548))
> summary(fit1)
Call:
lm(formula = chol ~ factor(rs174548))

Residuals:
     Min       1Q   Median       3Q      Max
-64.06167 -15.91338  -0.06167  14.93833  59.13605

Coefficients:
                  Estimate Std. Error t value Pr(>|t|)
(Intercept)        181.062      1.455 124.411  < 2e-16 ***
factor(rs174548)1    6.802      2.321   2.930  0.00358 **
factor(rs174548)2    5.438      4.540   1.198  0.23167
---

Residual standard error: 21.93 on 397 degrees of freedom
Multiple R-squared: 0.0221,  Adjusted R-squared: 0.01718
F-statistic: 4.487 on 2 and 397 DF,  p-value: 0.01184

> anova(fit1)
Analysis of Variance Table

Response: chol
                  Df Sum Sq Mean Sq F value  Pr(>F)
factor(rs174548)   2   4314    2157  4.4865 0.01184 *
Residuals        397 190875     481
---
```


```
> 1-pf(4.4865,2,397)
[1] 0.01183671
> 1-pf(((3624+690)/2)/481,2,397)
[1] 0.01186096
```


ANOVA: One-Way Model

```
> fit1 = lm(chol ~ factor(rs174548))
> summary(fit1)
Call:
lm(formula = chol ~ factor(rs174548))

Residuals:
     Min       1Q   Median       3Q      Max
-64.06167 -15.91338  -0.06167  14.93833  59.13605

Coefficients:
                  Estimate Std. Error t value Pr(>|t|)
(Intercept)        181.062      1.455 124.411  < 2e-16
factor(rs174548)1    6.802      2.321   2.930  0.00358
factor(rs174548)2    5.438      4.540   1.198  0.23167
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Residual standard error: 21.93 on 397 degrees of freedom
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> anova(fit1)
Analysis of Variance Table

Response: chol
                  Df Sum Sq Mean Sq F value  Pr(>F)
factor(rs174548)   2   4314    2157  4.4865 0.01184 *
Residuals        397 190875     481
---
```

- Let's interpret the regression model results!
  - What is the interpretation of the regression model coefficients?

ANOVA: One-Way Model

```
> fit1 = lm(chol ~ factor(rs174548))
> summary(fit1)
Call:
lm(formula = chol ~ factor(rs174548))

Residuals:
     Min       1Q   Median       3Q      Max
-64.06167 -15.91338  -0.06167  14.93833  59.13605

Coefficients:
                  Estimate Std. Error t value Pr(>|t|)
(Intercept)        181.062      1.455 124.411  < 2e-16
factor(rs174548)1    6.802      2.321   2.930  0.00358
factor(rs174548)2    5.438      4.540   1.198  0.23167
---

Residual standard error: 21.93 on 397 degrees of freedom
Multiple R-squared: 0.0221,  Adjusted R-squared: 0.01718
F-statistic: 4.487 on 2 and 397 DF,  p-value: 0.01184

> anova(fit1)
Analysis of Variance Table

Response: chol
                  Df Sum Sq Mean Sq F value  Pr(>F)
factor(rs174548)   2   4314    2157  4.4865 0.01184 *
Residuals        397 190875     481
---
```

- Interpretation:
  - Estimated mean cholesterol for C/C group: 181.062 mg/dl
  - Estimated difference in mean cholesterol levels between C/G and C/C groups: 6.802 mg/dl
  - Estimated difference in mean cholesterol levels between G/G and C/C groups: 5.438 mg/dl

ANOVA: One-Way Model

```
> fit1 = lm(chol ~ factor(rs174548))
> summary(fit1)
Call:
lm(formula = chol ~ factor(rs174548))

Residuals:
      Min        1Q    Median        3Q       Max
-64.06167 -15.91338  -0.06167  14.93833  59.13605

Coefficients:
                     Estimate Std. Error t value Pr(>|t|)
(Intercept)           181.062      1.455 124.411  < 2e-16
factor(rs174548)1       6.802      2.321   2.930  0.00358
factor(rs174548)2          5.438       4.540   1.198
0.23167
---

Residual standard error: 21.93 on 397 degrees of freedom
Multiple R-squared: 0.0221,  Adjusted R-squared: 0.01718
F-statistic: 4.487 on 2 and 397 DF,  p-value: 0.01184

> anova(fit1)
Analysis of Variance Table

Response: chol
                     Df Sum Sq Mean Sq F value  Pr(>F)
factor(rs174548)      2   4314    2157  4.4865 0.01184 *
Residuals           397 190875     481
---
```

- Overall F-test shows a significant p-value. We reject the null hypothesis that the mean cholesterol levels are the same across groups defined by rs174548 ($p=0.01184$).
  - This does not tell us which groups are different!

    (Need to perform multiple comparisons! More soon…)

ANOVA: One-Way Model

Alternative form: (better if you will perform multiple comparisons)

```
> fit2 = lm(chol ~ -1 + factor(rs174548))
> summary(fit2)
Call:
lm(formula = chol ~ -1 + factor(rs174548))

Residuals:
      Min        1Q    Median        3Q       Max
-64.06167 -15.91338  -0.06167  14.93833  59.13605

Coefficients:
                  Estimate Std. Error t value Pr(>|t|)
factor(rs174548)0   181.062      1.455  124.41   <2e-16 ***
factor(rs174548)1   187.864      1.809  103.88   <2e-16 ***
factor(rs174548)2   186.500      4.300   43.37   <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 21.93 on 397 degrees of freedom
Multiple R-squared: 0.9861,     Adjusted R-squared: 0.986
F-statistic:  9383 on 3 and 397 DF,  p-value: < 2.2e-16

> anova(fit2)
Analysis of Variance Table
Response: chol
                  Df   Sum Sq Mean Sq F value    Pr(>F)
factor(rs174548)   3 13534205 4511402  9383.2 < 2.2e-16 ***
Residuals        397   190875     481
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```


ANOVA: One-Way Model

How about this one? How is rs174548 being treated now?

Compare model fit results from (fit1 & fit1.1).

```
> fit1.1 = lm(chol ~ rs174548)
> summary(fit1.1)

Call:
lm(formula = chol ~ rs174548)

Residuals:
    Min      1Q  Median      3Q     Max
-64.575 -16.278  -0.575  15.120  60.722

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  181.575      1.411 128.723  < 2e-16 ***
rs174548       4.703      1.781   2.641  0.00858 **
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 21.95 on 398 degrees of freedom
Multiple R-squared: 0.01723,    Adjusted R-squared: 0.01476
F-statistic: 6.977 on 1 and 398 DF,  p-value: 0.008583

> anova(fit1.1)
Analysis of Variance Table

Response: chol
           Df Sum Sq Mean Sq F value   Pr(>F)
rs174548    1   3363    3363  6.9766 0.008583 **
Residuals 398 191827     482
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```


ANOVA: One-Way Model


```
> fit1.1 = lm(chol ~ rs174548)
> summary(fit1.1)

Call:
lm(formula = chol ~ rs174548)

Residuals:
    Min      1Q  Median      3Q     Max
-64.575 -16.278  -0.575  15.120  60.722

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  181.575      1.411 128.723  < 2e-16 ***
rs174548       4.703      1.781   2.641  0.00858 **

Residual standard error: 21.95 on 398 degrees of freedom
Multiple R-squared: 0.01723, Adjusted R-squared: 0.01476
F-statistic: 6.977 on 1 and 398 DF,  p-value: 0.008583

> anova(fit1.1)
Analysis of Variance Table

Response: chol
           Df Sum Sq Mean Sq F value   Pr(>F)
rs174548    1   3363    3363  6.9766 0.008583 **
Residuals 398 191827     482
```


- Model: $E[Y|x] = \beta_0 + \beta_1 x$

  where Y: cholesterol, x: rs174548
- Interpretation of model parameters?
  - β_0: mean cholesterol in the C/C group [estimate: 181.575 mg/dl]
  - β_1: mean cholesterol difference between C/G and C/C – or – between G/G and C/G groups [estimate: 4.703 mg/dl]
- This model presumes differences between "consecutive" groups are the same (in this example, linear dose effect of allele) – more restrictive than the ANOVA model!

Back to the ANOVA model…

ANOVA: One-Way Model

```
> fit1 = lm(chol ~ factor(rs174548))
> summary(fit1)
Call:
lm(formula = chol ~ factor(rs174548))

Residuals:
      Min        1Q    Median        3Q       Max
-64.06167 -15.91338  -0.06167  14.93833  59.13605

Coefficients:
                    Estimate Std. Error t value Pr(>|t|)
(Intercept)          181.062      1.455 124.411  < 2e-16
factor(rs174548)1      6.802      2.321   2.930  0.00358
factor(rs174548)2      5.438      4.540   1.198  0.23167
---

Residual standard error: 21.93 on 397 degrees of freedom
Multiple R-squared: 0.0221,  Adjusted R-squared: 0.01718
F-statistic: 4.487 on 2 and 397 DF,  p-value: 0.01184

> anova(fit1)
Analysis of Variance Table

Response: chol
                    Df Sum Sq Mean Sq F value  Pr(>F)
factor(rs174548)     2   4314    2157  4.4865 0.01184 *
Residuals          397 190875     481
---
```

- We rejected the null hypothesis that the mean cholesterol levels are the same across groups defined by rs174548 (p=0.01184).
  - What are the groups with differences in means?

MULTIPLE COMPARISONS (coming up)

One-Way ANOVA allowing for unequal variances

We can also perform one-way ANOVA allowing for unequal variances (Welch's ANOVA):

```
> oneway.test(chol ~ factor(rs174548))

        One-way analysis of means (not assuming equal variances)

data:  chol and factor(rs174548)
F = 4.3258, num df = 2.000, denom df = 73.284, p-value = 0.01676
```

- We reject the null hypothesis that the mean cholesterol levels are the same across groups defined by rs174548 (p=0.01676).
  - What are the groups with differences in means?

MULTIPLE COMPARISONS (coming up)

One-Way ANOVA with robust standard errors

We can also use robust standard errors to get correct variance estimates:

```
>  fit1 = lm(chol ~ factor(rs174548))
> summary(fit1)
Call:
lm(formula = chol ~ factor(rs174548))

Residuals:
      Min        1Q    Median        3Q       Max
-64.06167 -15.91338  -0.06167  14.93833  59.13605

Coefficients:
                    Estimate Std. Error t value Pr(>|t|)
(Intercept)          181.062      1.455 124.411  < 2e-16
factor(rs174548)1      6.802      2.321   2.930  0.00358
factor(rs174548)2      5.438      4.540   1.198  0.23167

> lmtest::coeftest(fit1, vcov = sandwich::sandwich)
t test of coefficients:

                    Estimate Std. Error  t value  Pr(>|t|)
(Intercept)         181.0617     1.4000 129.3283 < 2.2e-16 ***
factor(rs174548)1     6.8023     2.4020   2.8319  0.004863 **
factor(rs174548)2     5.4383     3.6243   1.5005  0.134272
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```


Kruskal-Wallis Test

- Non-parametric analogue to the one-way ANOVA
  - Based on ranks; does not require normality
- In our example:

```
> kruskal.test(chol ~ factor(rs174548))

        Kruskal-Wallis rank sum test

data:  chol by factor(rs174548)
Kruskal-Wallis chi-squared = 7.4719, df = 2, p-value = 0.02385
```

  - Conclusion:
    - Evidence that the cholesterol distribution is not the same across all groups.
    - With the global null rejected, you can also perform pairwise comparisons [Wilcoxon rank sum], but adjust for multiplicities!