

Module 1: MLR Review

Wednesday, August 23, 2023 1:33 PM



BIOS526_M
1_Multipl...

$$SE(1,2) = \text{SQR}(SE_1^2 + SE_2^2 - 2 * \text{COV}(1,2))$$

For dependent/paired

Module 1: Multiple Linear Regression Review

BIOS 526
Instructor: Benjamin Risk

From

<https://stats.stackexchange.com/questions/378684/how-to-calculate-standard-error-of-the-difference-between-two-random-variables-w>

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Reading

- Review matrix algebra. See notes on github, [M0_MatrixReview_bios526.pdf](#). For a more advanced reference, see [The Matrix Cookbook](#).
- Review notes from Applied Linear Regression (e.g., BIOS 509).
- A detailed reference: Sheather, Simon J. *A Modern Approach to Regression with R*. Springer, 2009.

Concepts

- Linear regression model in matrix notation.
- Inference for regression coefficient estimates, expected values, and predictions.
- Dummy variables.
- Effect modification and confounding.
aka interaction

Acknowledgments

- Lecture notes build upon materials from Prof. Howard Chang.

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Motivating Example

What maternal traits are associated with a child's cognitive test score at age 3?

- score: cognitive test score at age 3.
- age: maternal age at delivery.
- edu: maternal education: (1) less than high school, (2) high school, (3) some college, (4) college and above.

```
> dat = read.csv ("testscore.csv")
> str(dat)
'data.frame': 400 obs. of 3 variables:
 $ score : int 120 89 78 42 115 97 94 68 103 94 ...
 $ edu   : int 2 1 2 1 4 1 1 2 3 3 ...
 $ age   : int 21 17 19 20 26 20 20 24 19 24 ...
>
> summary (dat$score)
   Min. 1st Qu. Median  Mean 3rd Qu.  Max.
 20.00  74.00  90.00  86.93 102.00 144.00
> table (dat$edu)
 1 2 3 4 
85 212 76 27
> summary (dat$age)
   Min. 1st Qu. Median  Mean 3rd Qu.  Max.
17.00 21.00 23.00 22.79 25.00 29.00
```

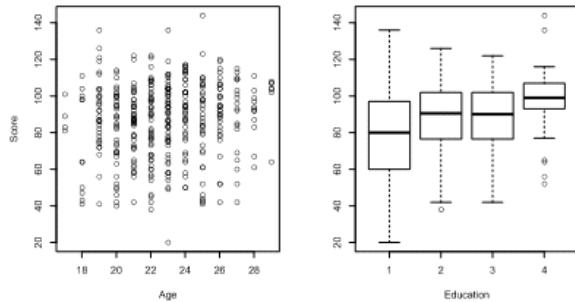
in file
Github M1-MLR.R

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Exploratory Plots

Exploratory Plots

> par(mfrow = c(1,2)) *→ makes 1 row, 2 "columns"*
 > plot(score ~ age, data = dat, xlab = "Age", ylab = "Score")
 > boxplot(score ~ edu, xlab = "Education", data = dat)



Simple Linear Regression

Let y_i denote the test score for child i , Age_i denote the corresponding maternal age at delivery, and ϵ_i denote the error term. We will consider the following linear model:

$$\begin{aligned} y_i &= \beta_0 + \beta_1 x_i + \epsilon_i & i = 1, \dots, 400 \\ &= \beta_0 + \beta_1 \text{age}_i + \epsilon_i & \text{e.g. the } 400^{\text{th}} \text{ child} \end{aligned}$$

- y_i is a linear function of Age_i .
- β_0 = the test score for a child born of a mother at age zero. (Not meaningful directly!)
- β_1 = increase in test score associated with one year increase in maternal age.
- $\mathbb{E}\epsilon_i = 0$. *each i has expected value of 0* ↗ technically we don't make this assumption yet?
- To start, we do not make assumptions regarding the ϵ_i .

Clearly, we cannot find β_0 and β_1 such that model (1) fits all of our observations perfectly.

Least Squares Estimate

We can write model (1) in matrix form by stacking observations by row:

$$\tilde{Y} = \begin{bmatrix} y_1 \\ y_2 \\ \vdots \\ y_n \end{bmatrix} = \begin{bmatrix} \beta_0 + \beta_1 \text{age}_1 \\ \vdots \\ \beta_0 + \beta_1 \text{age}_n \end{bmatrix} + \begin{bmatrix} \epsilon_1 \\ \vdots \\ \epsilon_n \end{bmatrix}$$

Now write as design matrix
Elem i gets coefficients for betas

$$= \begin{bmatrix} 1 & \text{age}_1 \\ \vdots & \vdots \\ 1 & \text{age}_n \end{bmatrix} \begin{bmatrix} \beta_0 \\ \beta_1 \end{bmatrix} + \begin{bmatrix} \epsilon_1 \\ \vdots \\ \epsilon_n \end{bmatrix}$$

$n \times 2$

$$= \tilde{X} \tilde{\beta} + \tilde{\epsilon}$$

Least Squares Estimate, cont.

$$Y = X\beta + \epsilon$$

same as \tilde{Y}

same as $\tilde{Y} = \tilde{X}\tilde{\beta} + \tilde{\epsilon}$

- Y is an $n \times 1$ response (dependent variable) vector.
- X is an $n \times p$ (design) matrix where p is the number of covariates (i.e., predictors, i.e., independent variables).
- β is a $p \times 1$ vector of regression coefficients.
- ϵ is an $n \times 1$ vector of errors.

→ in general,
pft says
p includes
intercept

- X is an $n \times p$ (design) matrix where p is the number of covariates (i.e., predictors, i.e., independent variables).
→ in general,
not says
P includes
Intercept
+ 1 to $p+1$)
 - β is a $p \times 1$ vector of regression coefficients.
 - ϵ is an $n \times 1$ vector of errors.

We can view the expected value of \mathbf{Y} as a **linear combination** of the two columns of \mathbf{X} . $E\mathbf{Y} = E[\mathbf{X}\beta + \varepsilon] = E[\mathbf{X}\beta] + E[\varepsilon]$

$$EY = E[X\beta + \varepsilon] = E[X\beta] + E[\varepsilon]$$

\downarrow
fixed 0 from above

$$= X\beta + 0$$

Try to find estimate of
 β_0 and β_1

Least Squares Solution

One approach is to minimize a **loss function**. A popular loss function is the sum of squared differences between the observed \mathbf{Y} and $\mathbf{X}\theta$ for some vector $\theta \in \mathbb{R}^k$.

$$\begin{aligned}
 \hat{\theta} &= \underset{\theta \in \mathbb{R}^2}{\operatorname{argmin}} \sum_{i=1}^n (\mathbf{y}_i - \theta_0 - \theta_1 \mathbf{x}_{i1})^2 \\
 &= \underset{\theta \in \mathbb{R}^2}{\operatorname{argmin}} (\mathbf{Y} - \mathbf{X}\theta)^T (\mathbf{Y} - \mathbf{X}\theta) \\
 &\quad \downarrow \\
 &= \underset{\theta \in \mathbb{R}^2}{\operatorname{argmin}} \underbrace{\mathbf{Y}^T \mathbf{Y} - \theta^T \mathbf{X}^T \mathbf{Y} - \mathbf{Y}^T \mathbf{X}\theta + \theta^T \mathbf{X}^T \mathbf{X}\theta}_{\text{linear part}} \\
 &\quad \downarrow \qquad \downarrow \\
 &\quad \text{scalar} \qquad \text{scalar} \\
 &= \mathbf{Y}^T \mathbf{Y} - 2\mathbf{Y}^T \mathbf{X}\theta + \theta^T \mathbf{X}^T \mathbf{X}\theta
 \end{aligned}$$

★ MEMORIZE ★

$$\hat{\beta}_{OLS} = (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{X}^T \mathbf{Y}$$

- For OLS, we have a nice closed-form solution. Other loss functions or models often require iterative optimization routines.

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- $H = X(X^T X)^{-1}X^T$ is the **hat matrix**. It shows that \hat{Y} can be expressed as a **linear combination** of Y .
 - $\hat{\epsilon} = Y - X\hat{\beta}$ is the **residual**.

Geometric interpretation of the least squares estimate:

- \hat{Y} and $\hat{\epsilon}$ are orthogonal. $\hat{Y}^\top \hat{\epsilon} = 0$ will talk more during PCA
 - H is a projection matrix of Y on the column space of X . Also note that $HH = H$ (definition of idempotent = projection matrix) \rightarrow Idempotent \rightarrow multiply by itself, get itself
 - $\text{tr}(H) = p = \text{number of covariates (including intercept)}$. comes up during df
 trace \rightarrow sum of diagonals

Least squares and hyperplanes

The least squares solution minimizes the sum of squared distances between \mathbf{Y} and $\hat{\mathbf{Y}}$.

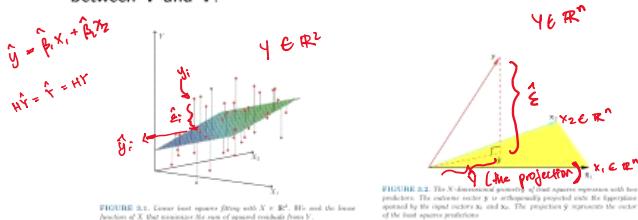
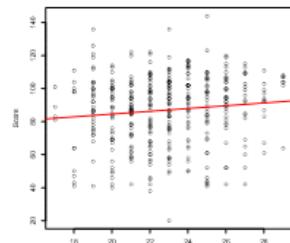


FIGURE 2.1. Linear least squares fitting with $X \in \mathbb{R}^d$. Here we find the linear function of X that minimizes the sum of squared residuals from y .

Figure: The view of OLS in \mathbb{R}^2 (left) and the view in \mathbb{R}^n (right). Note the picture on the right is an abstract view of n -dimensional vectors, which humans generally aren't able to visualize. Taken from Hastie et al ESL.

OLS calculations in R

```
> X = cbind(1, dat$age)
> Y = dat$score
> beta = solve(t(X) %*% X) %*% t(X) %*% Y = (X'X)^{-1} X'Y
> beta
[1,]
[1] 67.7826813
[2,] 0.8402729
> plot(score~age, data = dat, xlab="Age", ylab="Score")
> abline(beta, lwd = 3, col = 2)
```



(SOLVE) in R
FINDS INVERSE

Properties of the Estimator

The estimator

$$\hat{\beta} = (\mathbf{X}'\mathbf{X})^{-1}\mathbf{X}'\mathbf{Y}$$

has the following properties.

1. $\hat{\beta}$ is an unbiased estimator of β : $E\hat{\beta} = \beta$.
2. $\hat{\beta}$ is a consistent estimator of β under very general assumptions. Let $\hat{\beta}_n$ be the OLS estimator from n observations. Then $\lim_{n \rightarrow \infty} P(|\hat{\beta}_n - \beta| > \epsilon) = 0$. (Details omitted.)
3. $\hat{\beta}$ is an unbiased estimator of the mean trend $\mathbf{X}\beta$: $E\hat{Y} = \mathbf{X}\beta$.
4. Supposing $\epsilon_i \stackrel{iid}{\sim} (0, \sigma^2)$, $Cov(\hat{\beta}) = \sigma^2(\mathbf{X}'\mathbf{X})^{-1}$. $Cov((\mathbf{X}'\mathbf{X})' \mathbf{X}' \mathbf{Y}) = ((\mathbf{X}'\mathbf{X})^{-1})' \mathbf{X}' \underbrace{Cov(\mathbf{Y})}_{\sigma^2 \mathbf{I}} \mathbf{X} (\mathbf{X}'\mathbf{X})^{-1}$
5. $Cov(\hat{Y}) = \sigma^2 \mathbf{X}(\mathbf{X}'\mathbf{X})^{-1} \mathbf{X}'$.

* go back to JWB side

Statistical Linear Regression Model

So far, we have not discussed the distribution of the errors in Model (1).
For inference, let's now assume

$$(1) \quad y_i = \beta_0 + \beta_1 \text{Age}_i + \epsilon_i, \quad i = 1, 2, \dots, 400. \quad (2)$$

$\epsilon_i \stackrel{iid}{\sim} N(0, \sigma^2)$. Errors are normally distributed

This implies the following model:

- y_i is normally distributed:
$$(2) \quad y_i \stackrel{ind}{\sim} N(\beta_0 + \beta_1 \text{Age}_i, \sigma^2).$$
 ① and ② are equivalent
- i.e., the observed y_i is normally distributed around the linear trend $\beta_0 + \beta_1 \text{Age}_i$.

Statistical Linear Regression Model

$$y_i = \beta_0 + \beta_1 \text{age}_i + \epsilon_i, \quad \epsilon_i \stackrel{iid}{\sim} N(0, \sigma^2)$$

- Note: In our data application predicting child's test score from maternal age at delivery and mother's education, this model is

- Note: In our data application predicting child's test score from maternal age at delivery and mother's education, this model is wrong. Why? y_i are INTEGERS, and so is AGE
but ϵ_i is not an integer (ϵ_i are real numbers)
- Can a wrong model be useful?
We can still make useful approximations
All models are wrong, some are useful"

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Inference for Regression Coefficients

$$\mathbf{Y} = \begin{bmatrix} y_1 \\ \vdots \\ y_n \end{bmatrix}, \mathbf{Y} = \begin{bmatrix} \text{age} \\ \vdots \\ \text{age}_n \end{bmatrix}$$

Model (2) also implies that the joint distribution of \mathbf{Y} is

$$\mathbf{Y} \sim N(\mathbf{X}\beta, \sigma^2 \mathbf{I}),$$

where \mathbf{I} is an $n \times n$ identity matrix.

But we don't know σ^2 .

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lm() and Residual Error

We often estimate σ^2 with an unbiased estimator

$$\hat{\sigma}^2 = \frac{1}{n-p} \sum_{i=1}^n (y_i - \hat{y}_i)^2.$$

```
> fit = lm(score~age, data = dat)
> summary(fit)
Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept) 67.7827    8.6880   7.802 5.42e-14 ***
age          0.8403    0.3786   2.219   0.027 *
---
Signif. codes:  0 *** 0.001 ** 0.01 * 0.05 . 0.1   1

Residual standard error: 20.34 on 398 degrees of freedom
Multiple R-squared:  0.01223, Adjusted R-squared:  0.009743
F-statistic: 4.926 on 1 and 398 DF, p-value: 0.02702
```

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Confidence Interval for the Estimate of the Mean

Method 1 (manual-ish):

```
> invXtX = solve(t(X) %*% X) #aka  $(X'X)^{-1}$ 
> beta = invXtX %*% t(Y) %*% Y
> sigmahat = sum((Y - X %*% beta)^2) / (length(Y)-2)
> V = sigmahat*invXtX →  $\hat{\sigma}^2 (X'X)^{-1} = \text{Var}(\hat{\beta})$ 
> X = cbind(1, 17:30) #Design matrix with age=17, 18, ..., 30
> Est = X %*% beta
> SE = sqrt(diag(X %*% V %*% t(X))) →  $\hat{\sigma}^2 \times (X'X)^{-1} X'$ 
> Upper95 = Est + 1.96*SE → 0.975 quantile of normal dist
> Lower95 = Est - 1.96*SE
> cbind(Est, Lower95, Upper95)[1:3,]
[1,] 82.06732 77.33092 86.80372
[2,] 82.90759 78.83235 86.98283
[3,] 83.74787 80.30069 87.19504
```

Method 2:

```
> confint = predict(fit, newdata = data.frame(age=17:30), interval="conf")
> confint[1:3,]
      fit     lwr      upr
1 82.06732 77.31656 86.81808
2 82.90759 78.83235 86.98283
3 83.74787 80.30069 87.19504
```

```

> confInt = predict(fit, newdata = data.frame(age=17:30), interval="conf")
> confInt[1:3,]
   fit      lwr      upr
1 82.06732 77.31656 86.81808
2 82.90759 78.82000 86.99519
3 83.74787 80.29024 87.20549

```

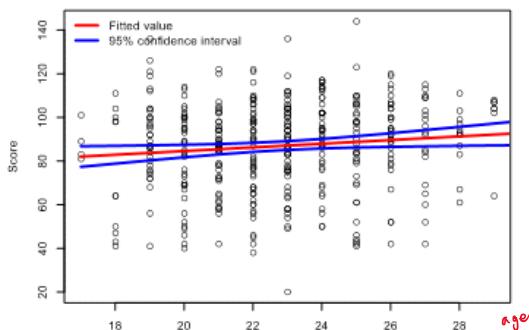
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Confidence Interval for the Estimate of the Mean, ii

```

> plot(score~age, data = dat, xlab="Age", ylab="Score")
> lines(Est~c(17:30), col = 2, lwd =3)
> lines(Upper95~c(17:30), col = 2, lwd = 3, lty = 3)
> lines(Lower95~c(17:30), col = 2, lwd = 3, lty = 3)
> legend("topleft", legend = c("Fitted value", "95% confidence interval"),
lty = c(1,3), bty="n", lwd=3)

```



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Prediction Interval for New Observation

Let y_i be a **new observation** with covariate value age_i . How do we predict its uncertainty?

We want to capture the uncertainty in our estimate of the expected value, \hat{y}_i , plus the uncertainty due to measurement error ϵ_i . Recall

$$y_i = \beta_0 + \beta_1 age_i + \epsilon_i$$

for $\epsilon_i \sim N(0, \sigma^2)$.

If we knew ϵ_i , a point estimator would be

$$\tilde{y}_i = \hat{\beta}_0 + \hat{\beta}_1 age_i + \epsilon_i.$$

Then

$$\text{Var}(\tilde{y}_i) = \text{Var}(\hat{\beta}_0 + \hat{\beta}_1 age_i) + \text{Var}(\epsilon_i)$$

$\uparrow \sigma^2 X(X'X)^{-1} X'$ $\uparrow \sigma^2$

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Prediction Interval for New Observation, ii

much wider

We have

$$\text{Var}(\tilde{y}_i) = \text{Var}(\hat{\beta}_0 + \hat{\beta}_1 age_i) + \text{Var}(\epsilon_i)$$

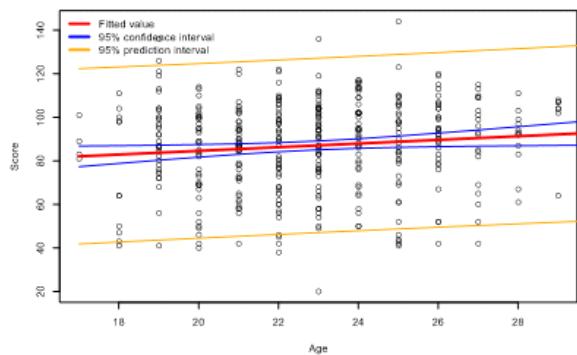
So we plug in our estimator to get the predictive variance:

$$\hat{\sigma}^2 = \text{Var}(\tilde{y}_i) = \text{Var}(\hat{\beta}_0 + \hat{\beta}_1 age_i) + \delta^2$$

and the approximate prediction interval is $\tilde{y}_i \pm 1.96\hat{\sigma}$.

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Prediction Interval for New Observation, iii



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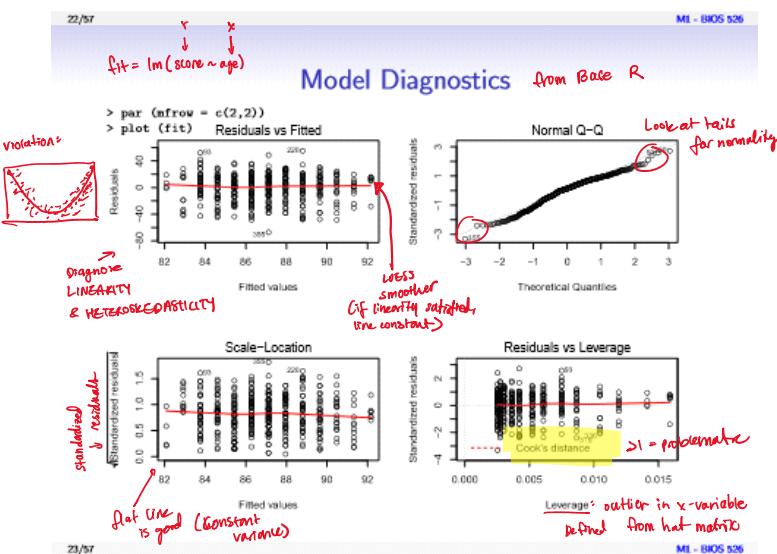
Assumptions of Linear Regression

$$Y_i = \beta_0 + \beta_1 X_i + \varepsilon_i$$

$$\varepsilon_i \sim N(0, \sigma^2)$$

HEIL GANSS

- ① homoskedasticity
- ② normally distributed errors
- ③ errors are independent
- ④ Linearity



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Model Diagnostics

Residual vs Fitted

- $\hat{\epsilon}_i$ should be independent of \hat{y}_i (no patterns): *above, red line NOT flat*
- Linearity: Red line should be flat.
- Variance constant (homoscedasticity)

Normal Q-Q Plot

- Standardized residual $\hat{\epsilon}_i/(\hat{\sigma}\sqrt{1-h_{ii}})$ should be standard normal.
- We expect the points to follow a straight line. Check non-normality, particularly skewed tails.

Scale-Location

- Similar to residual-vs-fitted, but use $\hat{\epsilon}_i/(\hat{\sigma}\sqrt{1-h_{ii}})$. Diagnose heteroscedasticity (e.g., red line increasing).

Residual vs Leverage

- Leverage h_{ii} is how far away x_i is from other x_{ij} . $h_{ii} = \frac{\partial \hat{y}_i}{\partial y_i}$.
- high leverage and outlier = problem.
- Cook's Distance: measures how much model changes when remove i th point; > 1 is problematic. (Note: when this occurs, a contour line appears in plot.)

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Model Coefficient Interpretations

```
> fit = lm(score~age, data = dat)

> summary(fit)
Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept) 67.7827    8.6880  7.802 5.42e-14 ***
age          0.8403    0.3786  2.219   0.027 *

```

Residual standard error: 20.34 on 398 degrees of freedom
Multiple R-squared: 0.01223, Adjusted R-squared: 0.009743
F-statistic: 4.926 on 1 and 398 DF, p-value: 0.02702

- A one year increase in mother's age at delivery was associated with a 0.84 ($CI_{95\%} 0.84 \pm 2*0.38$) increase in the child's average test score, where test score was measured at age 3. This association was statistically significant at a type I error rate of 0.05.
- There was considerable heterogeneity in test scores ($\hat{\sigma} = 20.34$). Therefore the regression model does not predict individual test scores well ($R^2 = 0.012$).

↳ 1.2% of variance explained by mother's age

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Hypothesis testing

```
> fit = lm(score~age, data = dat)
                y_i = \beta_0 + \beta_1 age_i + \varepsilon_i
                ↓
> summary(fit)
Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept) 67.7827    8.6880  7.802 5.42e-14 ***
age          0.8403    0.3786  2.219   0.027 *

```

Residual standard error: 20.34 on 398 degrees of freedom
Multiple R-squared: 0.01223, Adjusted R-squared: 0.009743
F-statistic: 4.926 on 1 and 398 DF, p-value: 0.02702

- (Intercept): $H_0 : \beta_0 = 0$ when age=0. In words, test scores are equal to zero for a mother at age=0. $H_A : \beta_0 \neq 0$. Conclusion: $p < 0.05$ so we reject the null hypothesis at $\alpha = 0.05$ and conclude the intercept differs from zero.
- age: $H_0 : \beta_1 = 0$. In words, the slope of age is equal to zero. Equivalently, there is no linear effect of age. $H_A : \beta_1 \neq 0$. Conclusion: $p < 0.05$, so we reject the null hypothesis and conclude there is a significant linear effect of age.

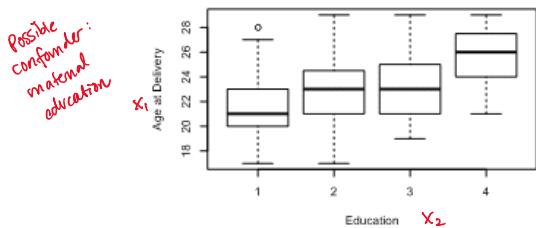
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Quiz 1

Class activity: Break-out session and quiz 1.

27/57 Confounding, i

We found that older mothers had children on average with higher test scores. However, higher maternal education was associated with higher age as shown in the boxplots below.



How do we estimate the age association accounting for the effect of education?

28/57 Confounding, ii

- confounding causes spurious correlation aka "omitted variable bias"
- "adjusting for" [mother's education]
- "controlling for"
- "accounting for"
- classical DAG:
$$\begin{array}{c} z \\ \downarrow \quad \downarrow \\ x \rightarrow y \end{array}$$

Bios 761 / Epi 760
- we will fit $y \sim x + z$

29/57

Assumptions of Linear Regression (plus omitted variables assumption)

1. Residuals are independent.
2. Linearity.
3. Residuals are normal.
4. Homoscedasticity (variance of residuals is constant).
5. All variables that are not included in the model have coefficient equal to zero (omitted variables bias = 0).

30/57 Categorical Variables

First, examine the effects of education on scores.

edu is coded as 1, 2, 3, 4 – don't want to code as a continuous variable.

Approach 1: an indicator (dummy) for each group

$$X_{1i} = 1_{\{edu_i=1\}}, X_{2i} = 1_{\{edu_i=2\}}, X_{3i} = 1_{\{edu_i=3\}}, X_{4i} = 1_{\{edu_i=4\}}$$

If we have $edu_i = [1, 1, 2, 2, 3, 3, 4, 4]$, the design matrix is

$$X = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} \beta_1 \\ \beta_2 \\ \beta_3 \\ \beta_4 \end{bmatrix}$$

What does each element of the corresponding β vector mean?

31/57 Average Score by Maternal Education, i

```
> E1 = as.numeric(dat$edu == 1)
> E2 = as.numeric(dat$edu == 2)
> E3 = as.numeric(dat$edu == 3)
> E4 = as.numeric(dat$edu == 4)

> fit = lm (dat$score ~ E1 + E2 + E3 + E4 - 1) #use "-1" to remove intercept
> summary (fit)
```

Coefficients:

	Estimate	Std. Error	t value	Pr(> t)
E1	78.447	2.159	36.33	<2e-16 ***
E2	88.703	1.367	64.88	<2e-16 ***
E3	87.789	2.284	38.44	<2e-16 ***
E4	97.333	3.831	25.41	<2e-16 ***

Residual standard error: 19.91 on 396 degrees of freedom
Multiple R-squared: 0.9508, Adjusted R-squared: 0.9503
F-statistic: 1913 on 4 and 396 DF, p-value: < 2.2e-16

This is equivalent to calculating the mean IQ for each education group:
calculate score for each unique value of index variable

```
> tapply(dat$score, INDEX = dat$edu, FUN = mean)
1      2      3      4
78.44706 88.70283 87.78947 97.33333
```

Equivalent to taking avg of scores for kids with edu = 1, 2, 3, 4
means

supporting R code

Why do we need to do this?
If we tried to include an intercept, we'd get linear dependence.

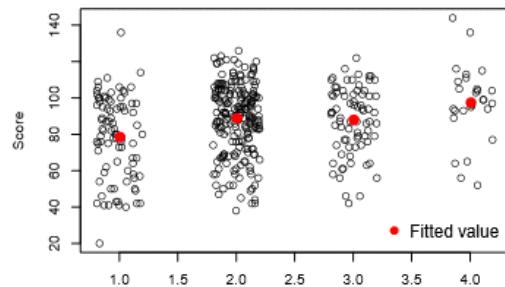
The intercept would be a linear combination of the other columns.
So there would be no unique solution.

E.g. $\hat{\beta}_0 = 2$, $\hat{\beta}_1 = 78.447 - 2$, $\hat{\beta}_2 = 88.703 - 2$, etc.

Average Score by Maternal Education, ii

What is the estimated difference in average score between mothers without high school and mothers with college and above?

```
> plot(score~jitter(edu), data = dat, xlab="Education Group",ylab="Score")
> lines(coef(fit)*c(1,2,3,4), col = 2, cex=1.5, pch=16, type = "p")
> legend ("bottomright", legend=c("Fitted value"),pch=16,col=2,cex=1.2,bty="n")
```



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Categorical Variables, Approach 2

Approach 2: an intercept + three indicators for group 2, 3, and 4.

$$X_{1i} = 1, X_{2i} = 1_{\{edu_i=2\}}, X_{3i} = 1_{\{edu_i=3\}}, X_{4i} = 1_{\{edu_i=4\}}$$

Similarly, if we have $edu_i = [1, 1, 2, 2, 3, 3, 4, 4]$, the design matrix is

$$X = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 \\ 1 & 1 & 0 & 0 \\ 1 & 0 & 1 & 0 \\ 1 & 0 & 1 & 0 \\ 1 & 0 & 0 & 1 \\ 1 & 0 & 0 & 1 \end{bmatrix}$$

What does each element of the corresponding β vector mean?

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Difference in Average Score w.r.t. Edu = 1

```
> fit = lm (dat$score ~ E2 + E3 + E4 )
> summary (fit)
Coefficients:
            Estimate Std. Error t value Pr(>|t|)    
(Intercept) 78.447     2.159   36.330 < 2e-16 ***
E2          10.256     2.556   4.013 7.18e-05 ***
E3          9.342      3.143   2.973  0.00313 **  
E4         18.886     4.398   4.294 2.21e-05 ***
```

```
## R can automatically create dummy variables with "factor"
> fit = lm (dat$score ~ factor(dat$edu))
> summary(fit)
Coefficients:
            Estimate Std. Error t value Pr(>|t|)    
(Intercept) 78.447     2.159   36.330 < 2e-16 ***
factor(dat$edu)2 10.256     2.556   4.013 7.18e-05 ***
factor(dat$edu)3  9.342      3.143   2.973  0.00313 **  
factor(dat$edu)4 18.886     4.398   4.294 2.21e-05 ***
```

Residual standard error: 19.91 on 396 degrees of freedom
Multiple R-squared: 0.05856, Adjusted R-squared: 0.05142
F-statistic: 8.21 on 3 and 396 DF, p-value: 2.59e-05

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MI - BIOS 526

Adjusting for Confounding

Now consider the following model:

$$y_i = \beta_0 + \beta_1 E2_i + \beta_2 E3_i + \beta_3 E4_i + \beta_4 \text{age}_i + \epsilon_i. \quad (3)$$

- Each education group has their own intercept.
- The effect (slope) of maternal age is constant across groups (parallel lines).
- β_4 is the association between score and age, **accounting for different averages in score** in different education groups.

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Activity and Quiz ii

- Breakout session with activity and quiz 2

37/57 M1 - BIOS 526

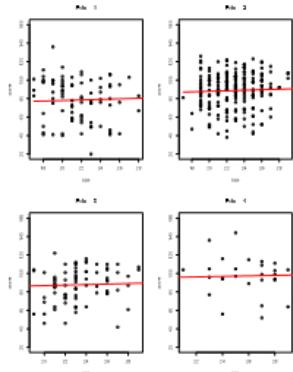
Adjusting for confounding, ii

```
> fit = lm(score~factor(edu) + age, data = dat)
> summary(fit)
Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept) 72.2360    8.8700   8.144 5.07e-15 ***
factor(edu)2  9.9365   2.5953   3.829 0.000150 ***
factor(edu)3  8.8416   3.2203   2.746 0.006316 **
factor(edu)4 17.6809   4.7065   3.757 0.000198 ***
age          0.2877   0.3985   0.722 0.470736
```

Age effect is no longer statistically significant!

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Adjusting for Confounding



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ML - BIOS 526

Variance Inflation Factors

One must always be on the look out for issues with **multicollinearity**.

The general issue is that when two variables are highly correlated, it is hard to disentangle their effects.

Mathematically, the standard errors are inflated. Suppose we have a design matrix $\mathbf{X} = [x_1, \dots, x_p]$, and we want to calculate the variance inflation factor for x_1 . We regress $x_1 \in \mathbb{R}^n$ against $[x_2, \dots, x_p]$.

Let R_1^2 be the associated R-squared. Then $VIF_1 = \frac{1}{1-R_1^2}$.

It can be shown $\text{Var } \hat{\beta}_j = VIF_j \frac{\sigma^2}{(n-1)S_{\hat{\beta}_j}^2}$.

$$\text{for } x_1 \quad \begin{aligned} x_1 &\sim x_2 + \dots + x_p \\ &\text{Extract } R^2 \end{aligned}$$

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ML - BIOS 526

VIFs

- There are different rules of thumb: $VIFs > 10$ or 5 or 3 are cause for concern, but this is only a rough guide!
- Sheather (2008) uses 5 .
- For large sample sizes, we can tolerate more multicollinearity.
- The GVIF is a generalization of VIF for factors. For $DF=1$, $GVIF^{1/2/DF}$ is the square root of the usual VIF, so one approach is to square it in order to apply the rules of thumb.

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ML - BIOS 526

VIF

```
> library(car)
> vif(fit)
      GVIF Df GVIF^(1/(2*Df))
FactorEdu 1.15514 3      1.024328
age        1.15514 1      1.074774
>
> temp = vif(fit)
>
> temp[,3]^2
FactorEdu      age
1.049248  1.155140
>
> temp[,3]^2<5
FactorEdu      age
TRUE          TRUE
```

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Interaction Effects: Effect Modification

How does age modify the effect of education?

Model (3) assumes an identical effect of age across all education groups.
We can relax this by including interaction terms.

$$y_i = \beta_0 + \beta_1 E2_i + \beta_2 E3_i + \beta_3 E4_i + \beta_4 age_i + \beta_5 E2_i age_i + \beta_6 E3_i age_i + \beta_7 E4_i age_i + \epsilon_i. \quad (4)$$

For each edu group: Reference level: EDU=1

$$y_i = \begin{cases} \beta_0 + \beta_4 age_i & Edu = 1 \rightarrow \text{slope of age if } Edu = 1 \\ \beta_0 + \beta_1 + (\beta_4 + \beta_5) age_i & Edu = 2 \rightarrow " " " \text{ if } Edu = 2 \\ \beta_0 + \beta_2 + (\beta_4 + \beta_6) age_i & Edu = 3 \\ \beta_0 + \beta_3 + (\beta_4 + \beta_7) age_i & Edu = 4 \end{cases}$$

By examining whether β_5 , β_6 , and β_7 are zero, we can determine if the effect of maternal age is modified by education.

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Interaction Effects: Effect Modification

```
> fit = lm(score~FactorEdu*age, data = dat)
> summary(fit)

Call:
lm(formula = score ~ FactorEdu * age, data = dat)

Residuals:
    Min     1Q Median     3Q    Max 
-56.70 -11.80   2.07  14.58  54.34 

Coefficients:
            Estimate Std. Error t value Pr(>|t|)    
(Intercept) 105.2202   17.6127   5.974 5.2e-09 ***
FactorEdu2 -33.0929   21.5732  -1.534 0.1258    
FactorEdu3 -53.4970   27.9460  -1.914 0.0563 .  
FactorEdu4  36.4537   49.5065   0.736 0.4620    
age        -1.2402    0.8097  -1.532 0.1264    
FactorEdu2:age  1.9704    0.9764   2.018 0.0443 *  
FactorEdu3:age  2.7862   1.2293   2.266 0.0240 *  
FactorEdu4:age -0.4799    1.9635  -0.244 0.8070    

```

You lose statistical power
Generally need bigger n
This is because VIFs are higher since interaction terms are directly unrelated w/ other terms

confused to

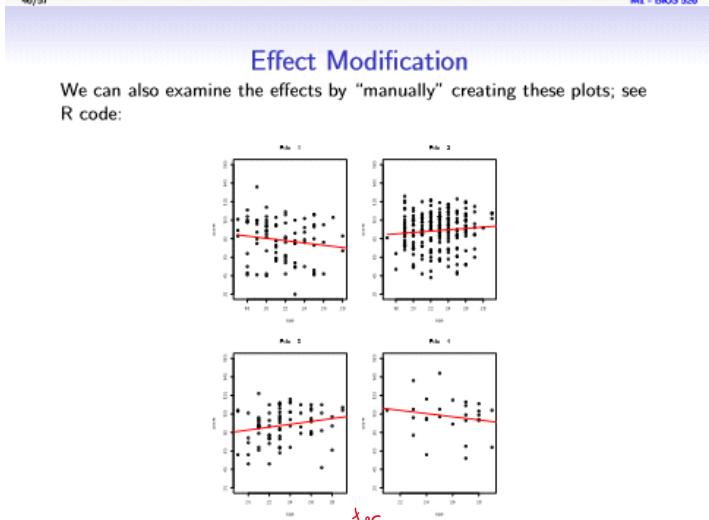
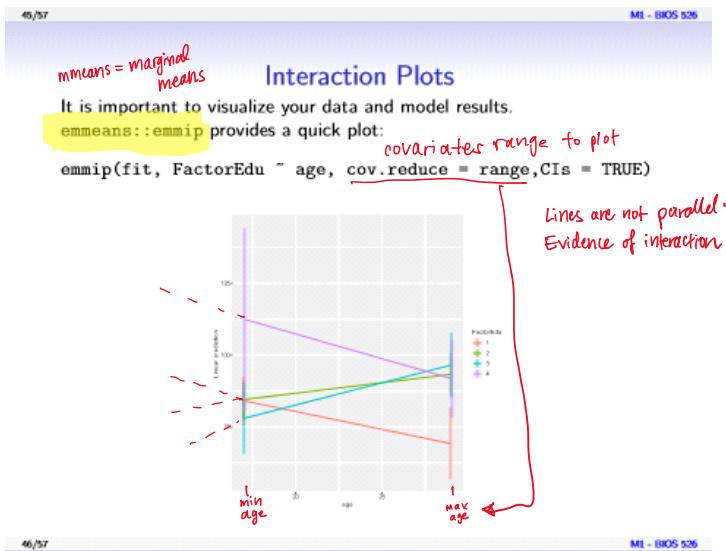
Effect Modification, continued

```
> vif(fit)
      GVIF Df GVIF^(1/(2*Df))
FactorEdu    9.093097e+05  3     9.842800
age          4.821946e+00  1     2.195893
FactorEdu:age 1.039839e+06  3    10.065322
```

Note how the variance is inflated.

This is common with interaction variables since by construction there is dependence between an interaction variable and the main effects. It is often an issue we have to live with.

In general, it means we need larger sample sizes to examine interactions.



ANCOVA just means we also have covariates that interact w/ a factor
F-test of interaction

To test whether the interaction was significant, look at whether the inclusion of the interaction significantly improved model fit.

H_0 : The interaction between education and age does not improve model fit.

H_A : The interaction improves model fit.

```
> fit_nointer = lm(score~FactorEdu+age,data=dat) Reduced model
> anova(fit_nointer,fit)
Analysis of Variance Table
```

```
Model 1: score ~ FactorEdu + age Redundant
```

go back
to working
interaction plot

```
> fit_nointer = lm(score~FactorEdu+age,data=dat) Reduced model
> anova(fit_nointer,fit)
Analysis of Variance Table
```

```
Model 1: score ~ FactorEdu + age
Model 2: score ~ FactorEdu * age
  Res.Df   RSS Df Sum of Sq    F Pr(>F)
1     395 156733
2     392 153857  3   2876.5 2.4429 0.06376 .
```

Interestingly, it is not significant. Overall, there is only limited statistical evidence of an interaction.



Interactions: compare slopes

When significant, we often conduct post-hoc tests to determine which slopes differed. Let's compare the slopes here for educational purposes.

First, ignore corrections for multiple comparisons.

```
> library(emmeans)
> emtrends(fit,pairwise="age",adjust='none')
$emtrends
FactorEdu age.trend   SE df lower.CL upper.CL
1      -1.24 0.810 392  -2.832  0.352
2       0.73 0.546 392  -0.342  1.803
3       1.55 0.925 392  -0.272  3.364
4      -1.72 1.789 392  -5.237  1.797
```

Confidence level used: 0.95

```
$contrasts
contrast estimate   SE df t.ratio p.value
1 - 2      -1.970 0.976 392 -2.018 0.0443
1 - 3      -2.786 1.229 392 -2.266 0.0240
1 - 4       0.480 1.964 392  0.244 0.8070
2 - 3      -0.816 1.074 392 -0.760 0.4479
2 - 4      2.450 1.870 392  1.310 0.1909
3 - 4      3.266 2.014 392  1.622 0.1056
```

Interactions: compare slopes

Now let's use a Bonferroni correction for the pairwise comparisons: multiply p-values by number of tests (or use Holm correction, see R code, a little more powerful). This will be discussed later in the course.

```
> emtrends(fit,pairwise="age",var="age",adjust='bonferroni')
$emtrends
FactorEdu age.trend   SE df lower.CL upper.CL
1      -1.24 0.810 392  -2.832  0.352
2       0.73 0.546 392  -0.342  1.803
3       1.55 0.925 392  -0.272  3.364
4      -1.72 1.789 392  -5.237  1.797
```

Confidence level used: 0.95

```
$contrasts
contrast estimate   SE df t.ratio p.value
1 - 2      -1.970 0.976 392 -2.018 0.2656
1 - 3      -2.786 1.229 392 -2.266 0.1438
1 - 4       0.480 1.964 392  0.244 1.0000
2 - 3      -0.816 1.074 392 -0.760 1.0000
2 - 4      2.450 1.870 392  1.310 1.0000
3 - 4      3.266 2.014 392  1.622 0.6338
```

Linear Combination of Coefficients

Let's take a closer look at the individual slopes.

We wish to estimate the slope of age_i among Edu_i = 3. The point estimate is $\hat{\beta}_4 + \hat{\beta}_6$. Also,

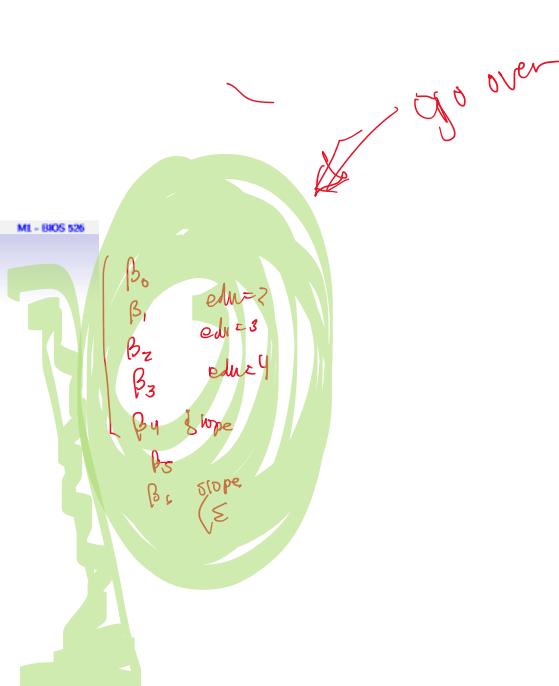
$$\text{Var}(\hat{\beta}_4 + \hat{\beta}_6) = \text{Var}(\hat{\beta}_4) + \text{Var}(\hat{\beta}_6) + 2\text{Cov}(\hat{\beta}_4, \hat{\beta}_6).$$

```
> fit = lm(score~factor(edu)*age, data = dat)
> Est = coef(fit)[5] + coef(fit)[7]
> SE = sqrt( vcov(fit)[5,5] + vcov(fit)[7,7] + 2*vcov(fit)[5,7])
> Est
  age
1.545989
> SE
[1] 0.9249421
```

So a 95% confidence interval for $\hat{\beta}_4 + \hat{\beta}_6$ is

$$1.54 \pm 1.96 \times 0.92 = (-0.27, 3.36).$$

and thus is not statistically different from 0 at $\alpha = 0.05$.



Effect of centering with interactions

Now let's fit the linear model with age centered.

```
> dat$ageC = scale(dat$age, center=TRUE, scale=FALSE)
> fit_inter_ageC = lm(score~FactorEdu*ageC, data=dat)
```

Coefficients:

	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	76.9567	2.3589	32.624	< 2e-16 ***
FactorEdu2	11.8133	2.7237	4.337	1.84e-05 ***
FactorEdu3	9.9996	3.3132	3.018	0.002710 **
FactorEdu4	25.5160	6.9760	3.658	0.000289 ***
ageC	-1.2402	0.8097	-1.532	0.126440
FactorEdu2:ageC	1.9704	0.9764	2.018	0.044263 *
FactorEdu3:ageC	2.7862	1.2293	2.266	0.023969 *
FactorEdu4:ageC	-0.4799	1.9635	-0.244	0.807027

Residual standard error: 19.81 on 392 degrees of freedom
Multiple R-squared: 0.07705, Adjusted R-squared: 0.06057
F-statistic: 4.675 on 7 and 392 DF, p-value: 4.756e-05

Effect of centering, cont.

What changed?
 $\hat{\beta}_0$ $\hat{\beta}_1$ $\hat{\beta}_2$ $\hat{\beta}_3$



Why?

Change location at which we test if the effect of edu differ
edu at age=0
vs. educ at age=22.8

Effect Modification

with centering (\star), we have no parameterization (e.g. letting age makes sense)

We now have the following model:

$$y_i = \beta_0^* + \beta_1^* E2_i + \beta_2^* E3_i + \beta_3^* E4_i + \beta_4^*(age_i - \bar{age}) + \\ \beta_5^* E2_i (age_i - \bar{age}) + \beta_6^* E3_i (age_i - \bar{age}) + \beta_7^* E4_i (age_i - \bar{age}) + \epsilon_i$$

Compare this to the previous model:

$$y_i = \beta_0 + \beta_1 E2_i + \beta_2 E3_i + \beta_3 E4_i + \beta_4 age_i + \\ \beta_5 E2_i age_i + \beta_6 E3_i age_i + \beta_7 E4_i age_i + \epsilon_i.$$

Then

$$\beta_1 = \beta_1^* - \beta_5 \bar{age}$$

In our estimates, $-33.09 = 11.81 - 1.97(22.79)$

More on centering

Compare the VIF before and after centering age:

```
> vif(fit) #not centered
          GVIF Df GVIF^(1/(2*Df))
FactorEdu  9.093097e+05  3      9.842800
age        4.821946e+00  1      2.195893
FactorEdu:age 1.039839e+06  3     10.065322
> vif(fit_inter_ageC) #centering tends to improve VIFs
          GVIF Df GVIF^(1/(2*Df))
```

```

age      4.821946e+00  1      2.195893
FactorEdu:age 1.039839e+06  3     10.065322
> vif(fit_inter_ageC) #centering tends to improve VIFs
          GVIF Df GVIF^(1/(2*Df))
FactorEdu    3.411158  3     1.226922
ageC        4.821946  1      2.195893
FactorEdu:ageC 12.285804  3     1.519033

```

F-tests and location invariance

We can test the overall effect of education using F-tests. Invariant to centering.

```

> fit_ageC = lm(score~ageC,data=dat)
> anova(fit_ageC,fit_inter_ageC)
Analysis of Variance Table

Model 1: score ~ ageC
Model 2: score ~ FactorEdu * ageC
  Res.Df   RSS Df Sum of Sq   F   Pr(>F)
1   398 164663
2   392 153857  6     10807 4.5889 0.0001617 ***
---
```

```

>
> fit_age = lm(score~age,data=dat)
> anova(fit_age,fit)
Analysis of Variance Table

Model 1: score ~ age
Model 2: score ~ FactorEdu * age
  Res.Df   RSS Df Sum of Sq   F   Pr(>F)
1   398 164663
2   392 153857  6     10807 4.5889 0.0001617 ***
---
```

Interactions, Factor Levels, and Centering

These are important

- Centering a covariate affects the location of the main effects of the terms it interacts with.
- Main effects of Education now describe education at the average age instead of Age=0. *Reduced model: no education in model*
- F-test of overall effect of Education is invariant to location of Age.
- Additionally, the reference levels of a factor will impact the p-values in `summary()`.
- Always write out the model you are fitting.
- Include main effects whenever interactions are included.
- Examine overall effects using `anova(modelreduced,modelfull)`.

