Module 1: Multiple Linear Regression Review

BIOS 526
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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.

Acknowledgments

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

Motivating Example

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

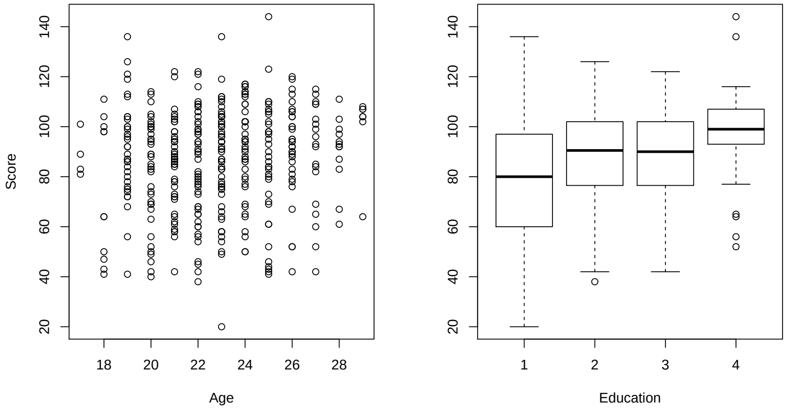
- score: cognitive test score at age 3.
- age: maternal age at delivery.
- edu: maternal education: (1) less than high school, (2) high school, (3) some college, (4) college and above.

```
> 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
```

Exploratory Plots

```
> par (mfrow =c(1,2))
> 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:

$$y_i = \beta_0 + \beta_1 Age_i + \epsilon_i, \qquad i = 1, 2, \ldots, 400. \tag{1}$$

- y_i is a linear function of Age_i.
- $\beta_0 =$ the test score for a child born of a mother at age zero. (Not meaningful directly!)
- $\beta_1 =$ increase in test score associated with one year increase in maternal age.
- $\mathbb{E}\,\epsilon_i = 0$.
- 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:

$$\begin{aligned}
\mathbf{Y} &= \begin{bmatrix} y_1 \\ y_2 \\ \vdots \\ y_n \end{bmatrix} \\
&= \begin{bmatrix} \beta_0 + \beta_1 Age_1 \\ \beta_0 + \beta_1 Age_2 \\ \vdots \\ \beta_0 + \beta_1 Age_n \end{bmatrix} + \begin{bmatrix} \epsilon_1 \\ \epsilon_2 \\ \vdots \\ \epsilon_n \end{bmatrix} \\
&= \begin{bmatrix} 1 & Age_1 \\ 1 & Age_2 \\ \vdots & \\ 1 & Age_n \end{bmatrix} \begin{bmatrix} \beta_0 \\ \beta_1 \end{bmatrix} + \begin{bmatrix} \epsilon_1 \\ \epsilon_2 \\ \vdots \\ \epsilon_n \end{bmatrix} \\
&= \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\epsilon}.
\end{aligned}$$

Least Squares Estimate, cont.

$$\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\epsilon}$$

- $\mathbf{Y}$ is an $n \times 1$ response (dependent variable) vector.
- $\mathbf{X}$ is an $n \times p$ (design) matrix where p is the number of covariates (i.e., predictors, i.e., independent variables).
- $\boldsymbol{\beta}$ is a $p \times 1$ vector of regression coefficients.
- $\boldsymbol{\epsilon}$ 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 $\mathbf{X}$.

$$\mathbb{E}\,\mathbf{Y} = \mathbf{X}\boldsymbol{\beta}$$

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 $\mathbf{X}\boldsymbol{\theta}$ for some vector $\boldsymbol{\theta} \in \mathbb{R}^2$.

$$\begin{aligned}
\hat{\beta} &= \underset{\boldsymbol{\theta}}{\text{argmin}} \sum_{i=1}^{n} (y_i - \theta_0 - \theta_1 Age_i)^2 \\
&= \underset{\boldsymbol{\theta}}{\text{argmin}} \, (\mathbf{Y} - \mathbf{X}\boldsymbol{\theta})^T (\mathbf{Y} - \mathbf{X}\boldsymbol{\theta}) \\
&= \underset{\boldsymbol{\theta}}{\text{argmin}} \, \mathbf{Y}^T\mathbf{Y} - 2\mathbf{Y}^T\mathbf{X}\boldsymbol{\theta} + \boldsymbol{\theta}^T\mathbf{X}^T\mathbf{X}\boldsymbol{\theta}
\end{aligned}$$

Differentiate the above with respect to $\boldsymbol{\theta}$ and set to zero, we get

$$-2\mathbf{X}^T\mathbf{Y} + 2\mathbf{X}^T\mathbf{X}\boldsymbol{\theta} = 0$$

If $\mathbf{X}$ is full-rank, solving this gives us the ordinary least squares estimate:

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

Properties of LS Estimate

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

- For OLS, we have a nice closed-form solution. Other loss functions or models often require iterative optimization routines.
- $\hat{\mathbf{Y}} = \mathbf{X}\hat{\beta}$ is the fitted value.
- $\mathbf{H} = \mathbf{X}(\mathbf{X}^T\mathbf{X})^{-1}\mathbf{X}^T$ is the hat matrix. It shows that $\hat{\mathbf{Y}}$ can be expressed as a linear combination of $\mathbf{Y}$.
- $\hat{\epsilon} = \mathbf{Y} - \mathbf{X}\hat{\beta}$ is the residual.

Geometric interpretation of the least squares estimate:

1. $\hat{\mathbf{Y}}$ and $\hat{\epsilon}$ are orthogonal.
2. $\mathbf{H}$ is a projection matrix of $\mathbf{Y}$ on the column space of $\mathbf{X}$. Also note that $\mathbf{HH} = \mathbf{H}$ (definition of idempotent = projection matrix)
3. tr $(\mathbf{H}) = p =$ number of covariates (including intercept).

Least squares and hyperplanes

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

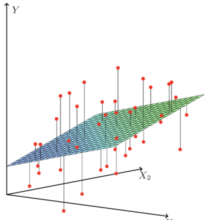


FIGURE 3.1. *Linear least squares fitting with $X \in \mathbb{R}^2$. We seek the linear function of X that minimizes the sum of squared residuals from Y.*

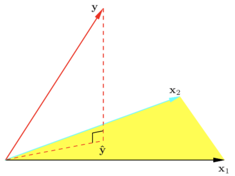
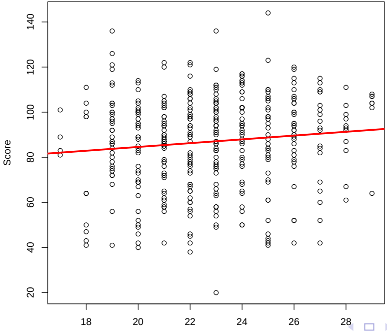


FIGURE 3.2. *The N-dimensional geometry of least squares regression with two predictors. The outcome vector $\mathbf{y}$ is orthogonally projected onto the hyperplane spanned by the input vectors $\mathbf{x}_1$ and $\mathbf{x}_2$. The projection $\hat{\mathbf{y}}$ represents the vector of the least squares predictions*

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
> beta
           [,1]
[1,] 67.7826813
[2,]  0.8402729
> plot (score~age, data = dat, xlab="Age",ylab="Score")
> abline (beta, lwd = 3, col = 2)
```



Properties of the Estimator

The estimator

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

has the following properties.

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

Statistical Linear Regression Model

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

$$y_i = \beta_0 + \beta_1 Age_i + \epsilon_i, \qquad i = 1, 2, \ldots, 400. \tag{2}$$

$$\epsilon_i \overset{iid}{\sim} N(0, \sigma^2).$$

This implies the following model:

- y_i is normally distributed:

$$y_i \overset{ind}{\sim} N(\beta_0 + \beta_1 Age_i, \sigma^2).$$

- i.e., the observed y_i is normally distributed around the linear trend $\beta_0 + \beta_1 Age_i$.

Statistical Linear Regression Model

- Note: In our data application predicting child's test score from maternal age at delivery and mother's education, this model is wrong. Why?
- Can a wrong model be useful?

Inference for Regression Coefficients

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

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

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

But we don't know σ^2.

lm() and Residual Error

We often estimate σ^2 with an unbiased estimator

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

```
> 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
```

Confidence Interval for the Estimate of the Mean

Method 1 (manual-ish):

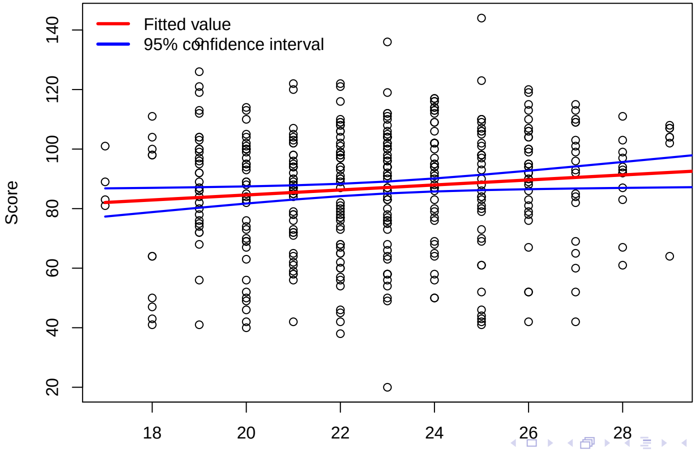
```
> invXtX = solve(t(X)%*%X)
> beta = invXtX %*% t(X) %*% Y
> sigmahat = sum((Y - X%*%beta)^2) / (length(Y)-2)
> V = sigmahat*invXtX
> X = cbind (1, 17:30)  #Design matrix with age=17, 18, ..., 30
> Est = X %*% beta
> SE = sqrt( diag(X%*%V%*%t(X)) )
> Upper95 = Est + 1.96*SE
> Lower95 = Est - 1.96*SE
> cbind(Est, Lower95, Upper95)[1:3,]
         [,1]     [,2]     [,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 78.82000 86.99519
3 83.74787 80.29024 87.20549
```

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)
```



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 uncertainy 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

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

Prediction Interval for New Observation, ii

We have

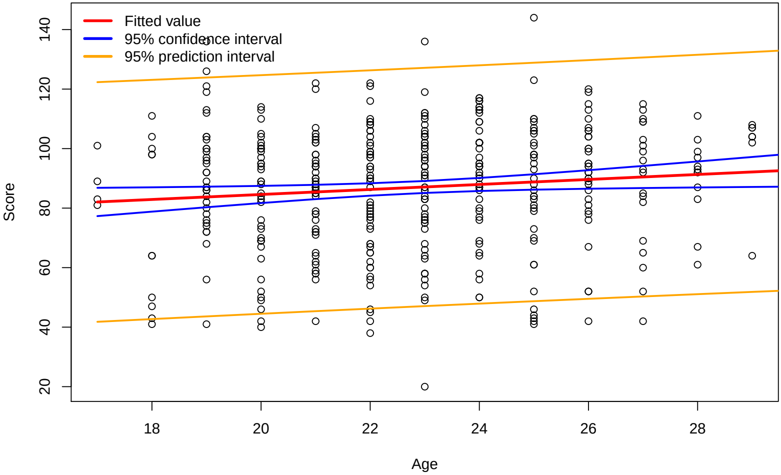
$$\text{Var}(\tilde{y}_i) = \text{Var}(\hat{\beta}_0 + \hat{\beta}_1 age_i) + \text{Var}(\epsilon_i)$$

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

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

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

Prediction Interval for New Observation, iii

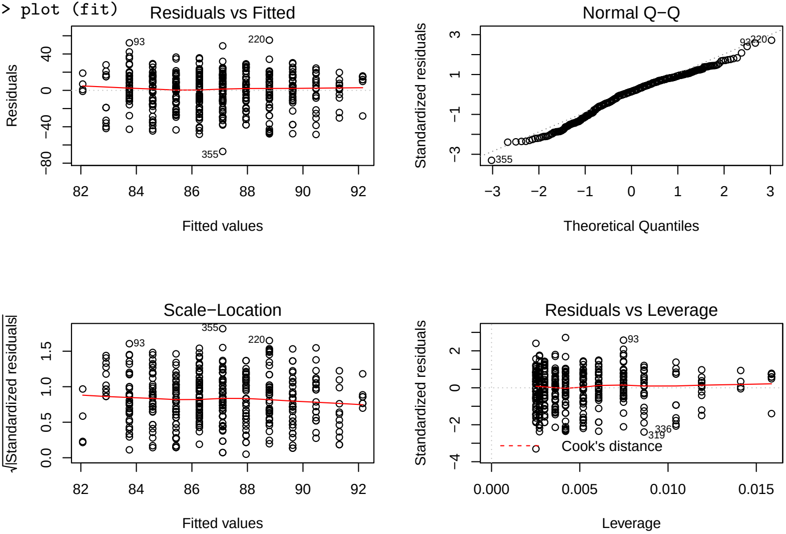


Assumptions of Linear Regression

1. Residuals are independent.
2. Linearity.
3. Residuals are normal.
4. Homoscedasticity (variance of residuals is constant).

Model Diagnostics

```
> par (mfrow = c(2,2))
> plot (fit)
```



Model Diagnostics

Residual vs Fitted

- $\hat{\epsilon}_i$ should be independent of $\hat{y}_i$ (no patterns):
- 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 $\boldsymbol{x}_i$ is from other $\boldsymbol{x}_{i'}$. $h_{ii} = \frac{\partial \hat{y}_i}{\partial y_i}$.
- high leverage and outlier = problem.
- Cook's Distance: measures how much model changes when remove ith point; > 1 is problematic. (Note: when this occurs, a contour line appears in plot.)

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 ($\text{CI}_{95\%}$ $0.84 \pm 2{*}0.38$) 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 ($R^2 = 0.012$).

Hypothesis testing

```
> 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
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```

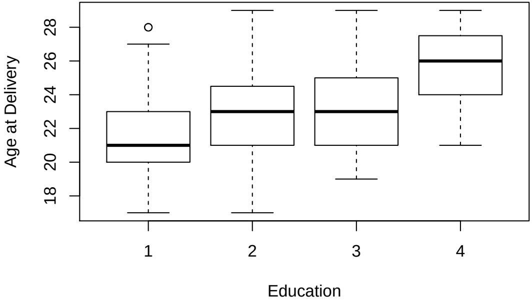
- (Intercept): $H_0 : \beta_0 = 0$ when age=0. In words, test scores are equal to zero for a mother at age=0. $H_A : \beta_0 \neq 0$.
  Conclusion: $p < 0.05$ so we reject the null hypothesis at $\alpha = 0.05$ and conclude the intercept differs from zero.
- age: $H_0 : \beta_1 = 0$. In words, the slope 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.

Quiz 1

Class activity: Break-out session and quiz 1.

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?

Confounding, ii

- Confounding causes spurious correlation.
- This is also called "omitted variables bias."
- We can use multiple regression to account for possible confounding factors.
- Other words meaning the same thing: "adjusting for" mother's education, "accounting for" mother's education.
- "controlling for" mother's education.
- Note: Causal inference provides a formal treatment for confounding; EPI 760 / BIOS 761. For X, Y, Z, if $Z \to X$ and $Z \to Y$, then Z is a confounding variable for $X \to Y$.
- This course: we model $E[Y|X, Z]$, such that the effect of X is adjusted for Z, whereas $E[Y|X]$ is unadjusted.
- In this class, if a coefficient for a predictor of interest changes greatly when accounting for a new predictor, then this may be due to confounding.

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 $= 0$).

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

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

What does each element of the corresponding β vector mean?

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
```

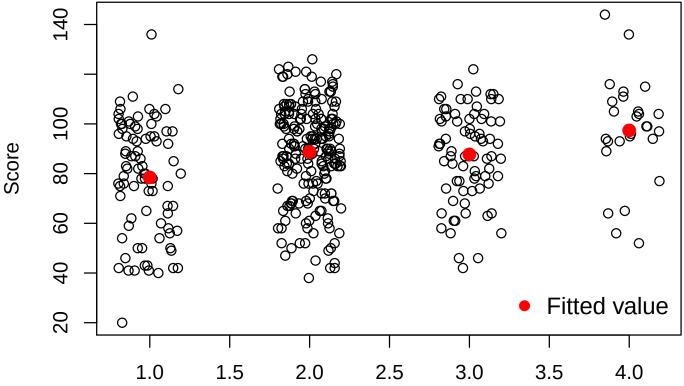
This is equivalent to calculating the mean IQ for each education group:

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

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")
```



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

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

What does each element of the corresponding $\boldsymbol{\beta}$ vector mean?

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
```

Adjusting for Confounding

Now consider the following model:

$$y_i = \beta_0 + \beta_1 E2_i + \beta_2 E3_i + \beta_3 E4_i + \beta_4 age_i + \epsilon_i. \tag{3}$$

- 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.

Activity and Quiz ii

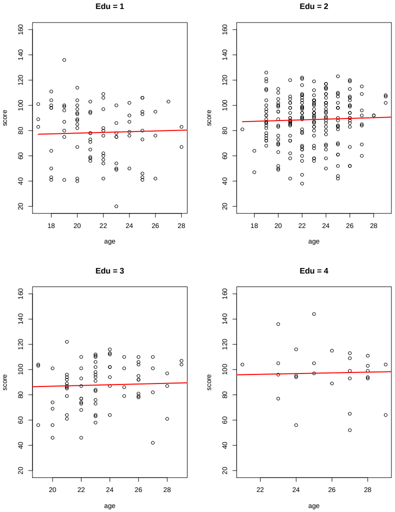
- Breakout session with activity and quiz 2

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!

Adjusting for Confounding



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 $\mathbf{X} = [\boldsymbol{x}_1, \ldots, \boldsymbol{x}_p]$, and we want to calculate the variance inflation factor for x_1. We regress $\boldsymbol{x}_1 \in \mathbb{R}^n$ against $[\boldsymbol{x}_2, \ldots, \boldsymbol{x}_p]$.

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

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

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.

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
```

Interaction Effects: Effect Modification

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:

$$y_i = \begin{cases} \beta_0 + \beta_4 age_i & Edu = 1 \\ \beta_0 + \beta_1 + (\beta_4 + \beta_5) age_i & Edu = 2 \\ \beta_0 + \beta_2 + (\beta_4 + \beta_6) age_i & Edu = 3 \\ \beta_0 + \beta_3 + (\beta_4 + \beta_7) age_i & Edu = 4 \end{cases}$$

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

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    
```

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.

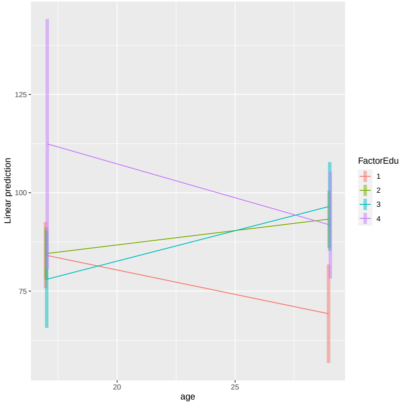
This is common with interaction variables since by construction there is dependence between an interaction variable and the main effects. It is often an issue we have to live with.

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

Interaction Plots

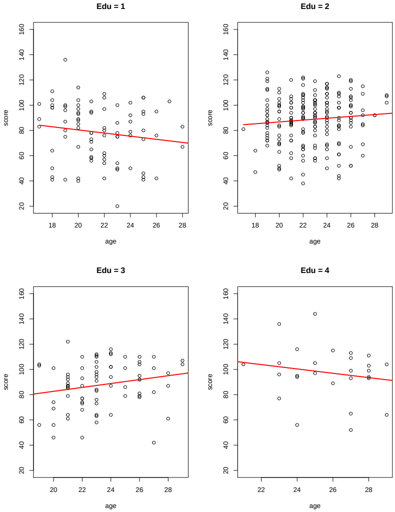
It is important to visualize your data and model results.
`emmeans::emmip` provides a quick plot:

```
emmip(fit, FactorEdu ~ age, cov.reduce = range,CIs = TRUE)
```



Effect Modification

We can also examine the effects by "manually" creating these plots; see R code:



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)
> 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~FactorEdu,var="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~FactorEdu,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,

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

```
> 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?

Why?

Effect Modification

We now have the following model:

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

Compare this to the previous model:

$$
\begin{aligned}
y_i = \beta_0 + &\beta_1 E2_i + \beta_2 E3_i + \beta_3 E4_i + \beta_4 age_i + \\
&\beta_5 E2_i age_i + \beta_6 E3_i age_i + \beta_7 E4_i age_i + \epsilon_i.
\end{aligned}
$$

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))
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.
- 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)`.