REGRESSION METHODS: CONCEPTS & APPLICATIONS

LECTURE 1: SIMPLE LINEAR REGRESSION

Motivation

- Objective: Investigate associations between two or more variables
- What tools do you already have?
  - t-test
    - Comparison of means in two populations
  - Chi-squared test
    - Comparison of proportions in two populations
- What will we cover in this module?
  - Linear Regression
    - Association of a continuous outcome with one or more predictors (categorical or continuous)
  - Analysis of Variance (as a special case of linear regression)
    - Comparison of a continuous outcome over a fixed number of groups
  - Logistic and Relative Risk Regression
    - Association of a binary outcome with one or more predictors (categorical or continuous)

Module structure

- Lectures and hands-on exercises in R over 2.5 days
- Day 1
  - Simple linear regression
  - Model checking
- Day 2
  - Multiple linear regression
  - ANOVA
- Day 3
  - Logistic regression
  - Generalized linear models

Outline: Simple Linear Regression

- Motivation
- The equation of a straight line
- Least Squares Estimation
- Inference
  - About regression coefficients
  - About predictions
- Model Checking
  - Residual analysis
  - Outliers & Influential observations

Motivation: Cholesterol Example

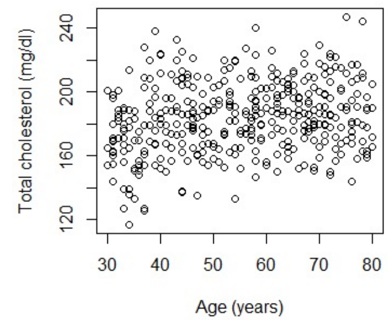
- Linear regression is concerned with a **continuous** outcome
- Data: Factors related to serum total cholesterol (continuous outcome), 400 individuals, 11 variables

```
> head(cholesterol)

  ID  DM age chol  BMI  TG APOE rs174548 rs4775401 HTN chd
  1   1  74  215 26.2 367    4        1         2   1   1
  2   1  51  204 24.7 150    4        2         1   1   1
  3   0  64  205 24.2 213    4        0         1   1   1
  4   0  34  182 23.8 111    2        1         1   1   0
  5   1  52  175 34.1 328    2        0         0   1   0
  6   1  39  176 22.7  53    4        0         2   0   0
```

- Our first goal:
  - Investigate the relationship between cholesterol (mg/dl) and age in adults

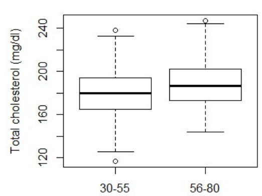
Motivation: Cholesterol Example



Motivation: Cholesterol Example

- Is cholesterol associated with age?
  - You could dichotomize age and compare cholesterol between two age groups

```
> group = 1*(age > 55)
> group=factor(group,levels=c(0,1), labels=c("30-55","56-80"))
> table(group)
group
30-55 56-80
  201   199
> boxplot(chol~group,ylab="Total cholesterol(mg/dl)")
```



Motivation: Cholesterol Example

- Is cholesterol associated with age?

  - You could compare mean cholesterol between two groups: t-test

```
> t.test(chol ~ group)

        Welch Two Sample t-test

data:  chol by group
t = -3.637, df = 393.477, p-value = 0.0003125
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 -12.200209  -3.638487
sample estimates:
mean in group 30-55 mean in group 56-80
       179.9751        187.8945
```

Motivation: Cholesterol Example

- Question: What do the boxplot and the t-test tell us about the relationship between age and cholesterol?

```
> t.test(chol ~ group)

        Welch Two Sample t-test

data:  chol by group
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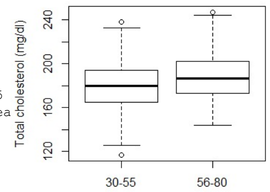
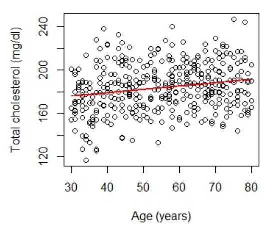


Motivation: Cholesterol Example

- Using the t-test:
  - There is a statistically significant association between cholesterol and age
  - There appears to be a positive association between cholesterol and age
    - Is there any way we could estimate the magnitude of this association without breaking the “continuous” measure of age into subgroups?
  - With the t-test, we compared mean cholesterol in two age groups, could we compare mean cholesterol across “continuous” age?

Motivation: Cholesterol Example

- We might assume that mean cholesterol changes linearly with age:



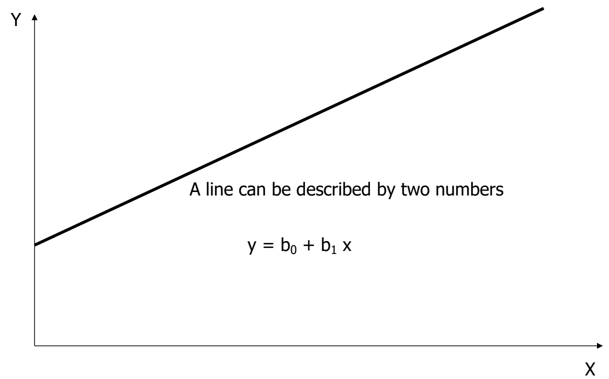
- Can we find the equation for a straight line that best fits these data?

Linear Regression

- A statistical method for modeling the relationship between a continuous variable [response/outcome/dependent] and other variables [predictors/exposure/independent]
  - Most commonly used statistical model
  - Flexible
  - Well-developed and understood properties
  - Easy interpretation
  - Building block for more general models
- Goals of analysis:
  - Estimate the association between response and predictors

  or,
  - Predict response values given the values of the predictors.
- We will start our discussion studying the relationship between a response and <u>a single predictor</u>
  - Simple linear regression model

The straight line equation



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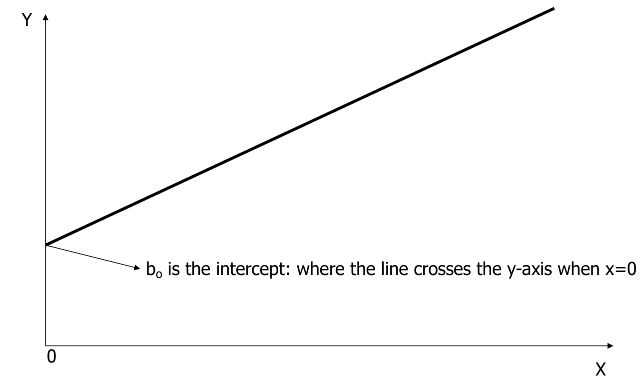

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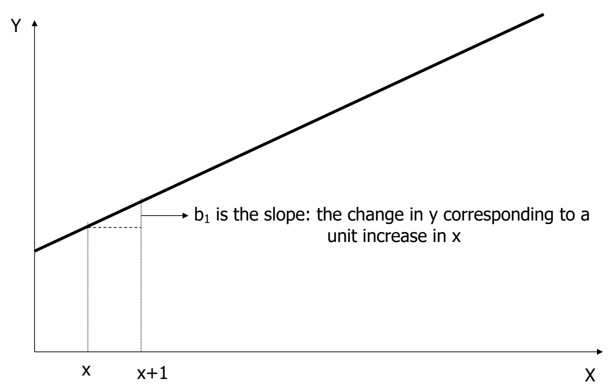

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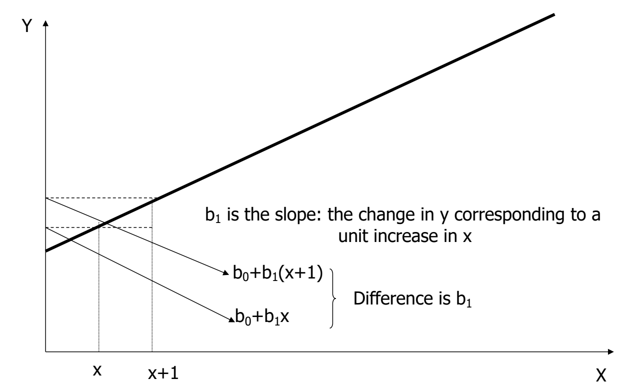

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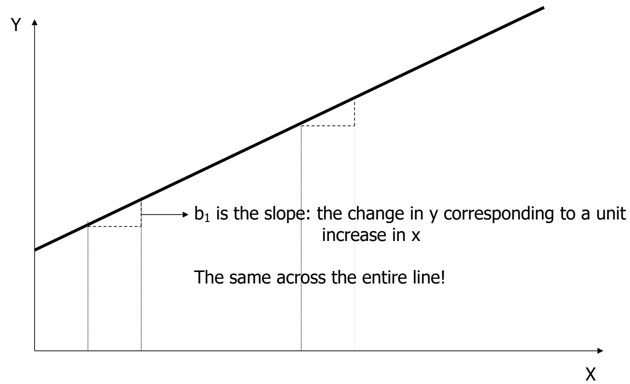

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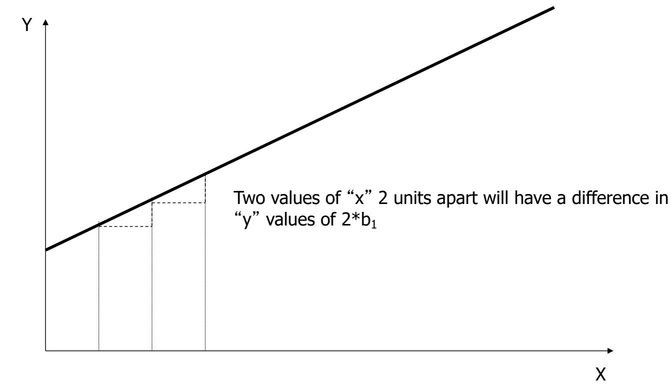
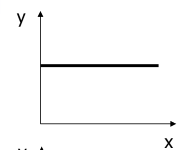


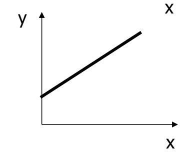
The straight line equation

- Slope b_1 is the change in y corresponding to a one unit increase in x
- Slope gives information about magnitude and direction of the association between x and y

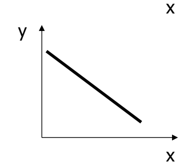
The straight line equation



(b_1=0) No association between x and y
(values of y are the same regardless of x)



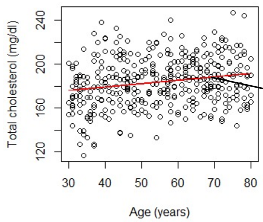
(b_1 > 0) Positive association between x and y
(values of y increase as values of x increase)



(b_1 < 0) Negative association between x and y
(values of y decrease as values of x increase)

Simple Linear Regression

- We can use linear regression to model how the mean of an outcome Y changes with the level of a predictor, X
- The individual Y observations will be scattered about the mean



We estimate a straight line describing trend in the **mean** of an outcome Y as a function of predictor X

Simple Linear Regression

- In **regression:**
  - *X* is used to predict or explain outcome *Y*.
- **Response** or **dependent** variable (Y):
  - continuous variable we want to predict or explain
- **Explanatory** or **independent** or **predictor** variable (X):
  - attempts to explain the response
- **Simple Linear Regression Model**:

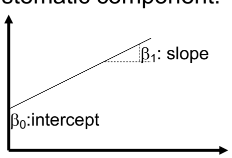
$$y = \beta_0 + \beta_1 x + \varepsilon, \quad \varepsilon \sim N(0, \sigma^2)$$

Simple Linear Regression

$$y = \beta_0 + \beta_1 x + \varepsilon, \quad \varepsilon \sim N(0, \sigma^2)$$

The model consists of two components:

- Systematic component: $E[Y \mid X = x] = \beta_0 + \beta_1 x$



Mean population value of Y at X=x

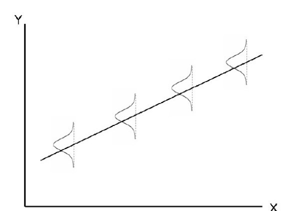
- Random component: $Var[Y \mid X = x] = \sigma^2$

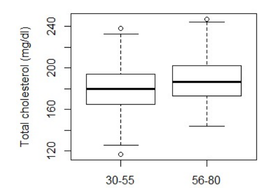
Variance does not depend on x

Simple Linear Regression: Assumptions

MODEL: $E[Y \mid X = x] = \beta_0 + \beta_1 x \qquad Var[Y \mid X = x] = \sigma^2$

Distribution of Y at different x values:





Compare with the boxplots for two age groups

Simple Linear Regression: Interpreting model coefficients

- Model: $E[Y|x] = \beta_0+\beta_1 x$ $\quad Var[Y|x] = \sigma^2$
- Question: How do you interpret β_0?
- Answer:

  $\beta_0 = E[Y|x=0]$, that is, the mean response when x=0

Your turn: interpret β_1!

Simple Linear Regression: Interpreting model coefficients

- Model: $E[Y|x] = \beta_0+\beta_1 x$ $\quad Var[Y|x] = \sigma^2$
- Question: How do you interpret β_1?
- Answer:

$$E[Y|x] = \beta_0 + \beta_1 x$$
$$E[Y|x+1] = \beta_0 + \beta_1(x+1) = \beta_0 + \beta_1 x + \beta_1$$

$E[Y|x+1] - E[Y|x] = \beta_1$ independent of x (linearity)

i.e. β_1 is the difference in the mean response associated with a one unit positive difference in x

Example: Cholesterol and age

- Recall: Our motivating example was to determine if there is an association between age (a continuous predictor) and cholesterol (a continuous outcome)
- Suppose: We believe they are associated via the linear relationship $E[Y|x] = \beta_0+\beta_1 x$
- Question: How would you interpret β_1?
- Answer:

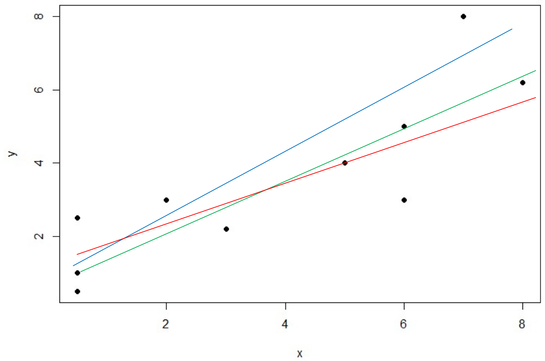
Example: Cholesterol and age

- Recall: Our motivating example was to determine if there is an association between age (a continuous predictor) and cholesterol (a continuous outcome)
- Suppose: We believe they are associated via the linear relationship $E[Y|x] = \beta_0+\beta_1 x$
- Question: How do you interpret β_1?
- Answer:

  β_1 is the difference in mean cholesterol associated with a one year increase in age

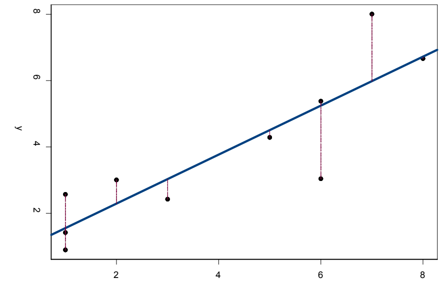
Least Squares Estimation

- Question: How to find a "best-fitting" line?



Least Squares Estimation

- Question: How to find a "best-fitting" line?



- Method: Least Squares Estimation

Idea: chooses the line that minimizes the sum of squares of the vertical distances from the observed points to the line.

Least Squares Estimation

- The least squares regression line is given by

$$\hat{y} = \hat{\beta}_0 + \hat{\beta}_1 x$$

- So the (squared) distance between the data (y) and the least squares regression line is

$$D = \sum_i (y_i - \hat{y}_i)^2$$

- We estimate β_0 and β_1 by finding the values that minimize D

- We can use these estimates to get an estimate of the variance about the line (σ^2)

Least Squares Estimation

- These values are:

$$\hat{\beta}_0 = \bar{y} - \hat{\beta}_1 \bar{x}$$

$$\hat{\beta}_1 = \frac{\sum (x_i - \bar{x})(y_i - \bar{y})}{\sum (x_i - \bar{x})^2}$$

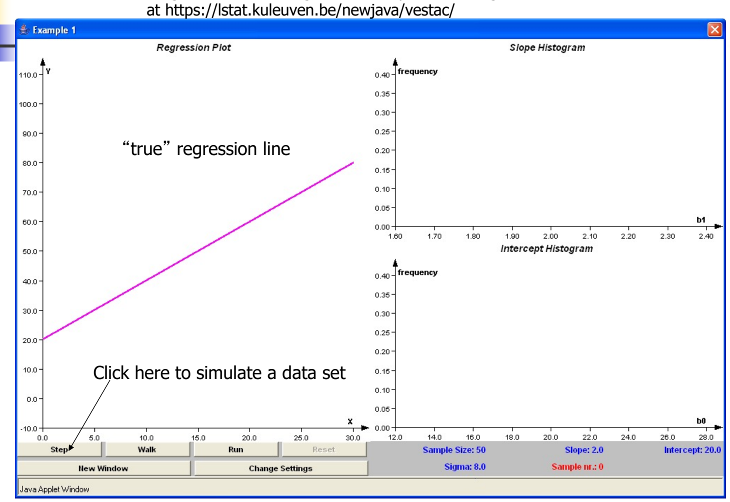
- We estimate the variance as:

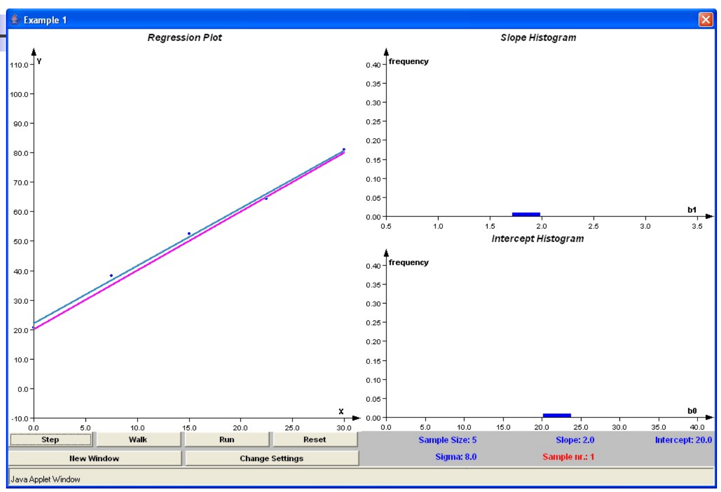
$$\hat{\sigma}^2 = \frac{\sum_{i=1}^{n} r_i^2}{n-2} = \frac{\sum_{i=1}^{n} (y_i - \hat{y}_i)^2}{n-2} = \frac{\sum_{i=1}^{n} (y_i - \hat{\beta}_0 - \hat{\beta}_1 x_i)^2}{n-2}$$

Estimated Standard Errors

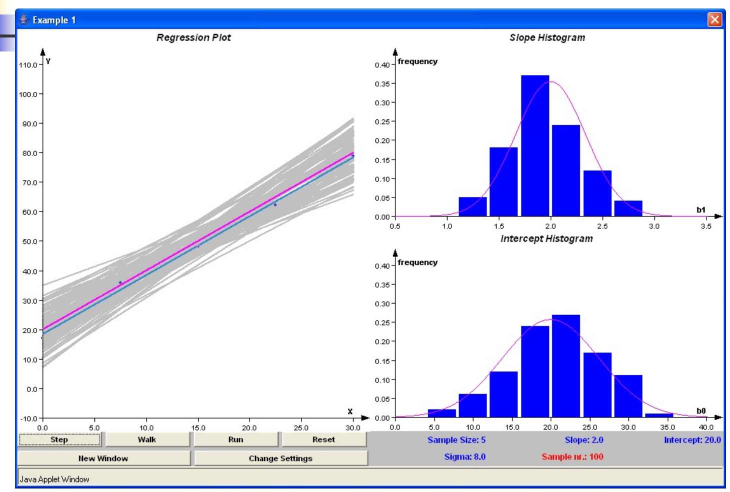
- Recall that, when estimating parameters from a sample, there will be sampling variability in the estimates
- This is true for regression parameter estimates
- Looking at the formulas for $\hat{\beta}_0$ and $\hat{\beta}_1$, we can see that they are just complicated means
- In repeated sampling we would get different estimates
- Knowledge of the sampling distribution of parameter estimates can help us make inference about the line
- Statistical theory shows that the sampling distributions are Normal and provides expressions for the mean and standard error of the estimates over repeated samples

“Regression” -> “Histograms on Simple Linear Regression” at https://lstat.kuleuven.be/newjava/vestac/





Sampling Distribution



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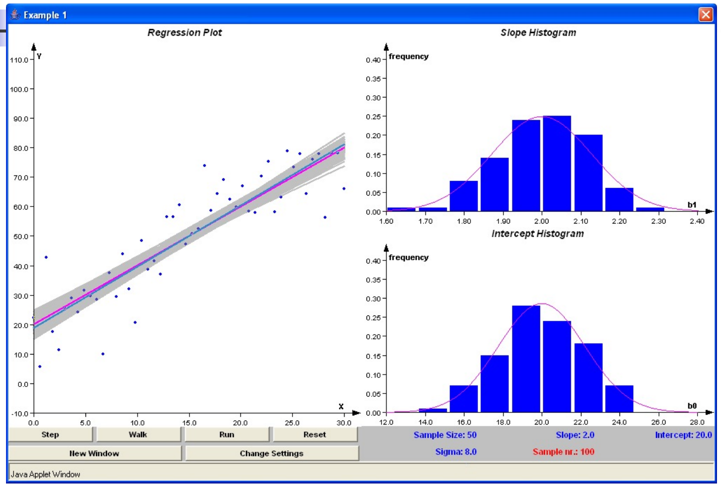


Inference

- About regression model parameters
  - Hypothesis testing: H_0: β_j=0 (j=0,1)
    - Test Statistic:
      - Large Samples: $\dfrac{\hat{\beta}_j - (null\ hyp)}{se(\hat{\beta}_j)} \sim N(0,1)$
      - Small Samples: $\dfrac{\hat{\beta}_j - (null\ hyp)}{se(\hat{\beta}_j)} \sim t_{n-2}$
  - Confidence Intervals:

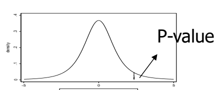
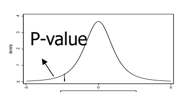
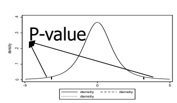
$$\hat{\beta}_j \pm (critical\ value) \times se(\hat{\beta}_j)$$

[Don't worry about these formulae: we will use R to fit the models!]

Inference: Hypothesis Testing

Null Hypothesis: β_j = 0

T=test statistic

Alternative	**P-Value**	
$\beta_j > 0$	$P(t_{n-2} > T)$	
$\beta_j < 0$	$P(t_{n-2} < T)$	
$\beta_j \neq 0$	$2P(t_{n-2} > \lvert T \rvert)$	

Inference: Confidence Intervals

100 (1-α)% Confidence Interval for β_j (j=0,1)

$$\hat{\beta}_j \pm t_{n-2,\alpha/2} SE(\hat{\beta}_j)$$

Gives intervals that (1- α)100% of the time will cover the true parameter value (β_0 or β_1).

We say we are "(1- α)100% confident" the interval covers β_j.

Example:
Scientific Question: Is cholesterol associated with age?

```
> fit = lm(chol ~ age)
> summary(fit)

Call:
lm(formula = chol ~ age)

Residuals:
      Min        1Q    Median        3Q       Max 
-60.45306 -14.64250  -0.02191  14.65925  58.99527 

Coefficients:
             Estimate Std. Error t value Pr(>|t|)    
(Intercept) 166.90168    4.26488  39.134  < 2e-16 ***
age           0.31033    0.07524   4.125 4.52e-05 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1 

Residual standard error: 21.69 on 398 degrees of freedom
Multiple R-squared: 0.04099,	Adjusted R-squared: 0.03858 
F-statistic: 17.01 on 1 and 398 DF,  p-value: 4.522e-05
```

```
> confint(fit)
                  2.5 %      97.5 %
(Intercept) 158.5171656 175.2861949
age           0.1624211   0.4582481
```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Estimates of the model parameters and standard errors

$\hat{\beta}_0 = 166.90$; $se(\hat{\beta}_0) = 4.26$

$\hat{\beta}_1 = 0.31$; $se(\hat{\beta}_1) = 0.08$

```
> confint(fit)
                  2.5 %      97.5 %
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95% Confidence intervals

```
> confint(fit)
                  2.5 %      97.5 %
(Intercept) 158.5171656 175.2861949
age           0.1624211   0.4582481
```


Example:
Scientific Question: Is cholesterol associated with age?

- What do these model results mean in terms of our scientific question?
  - Parameter estimates and confidence intervals:

$\hat{\beta}_0 = 166.90$ 95% CI: (158.5, 175.3)

$\hat{\beta}_1 = 0.31$ 95% CI: (0.16, 0.46)

$\hat{\beta}_0$: The estimated average serum cholesterol for someone of age = 0 is 166.9 !?

Your turn: What about $\hat{\beta}_1$?

Example:

Scientific Question: Is cholesterol associated with age?

- What do these models results mean in terms of our scientific question?
  - Parameter estimates and confidence intervals:

$$\hat{\beta}_0 = 166.90 \quad \text{95\% CI: (158.5, 175.3)}$$

$$\hat{\beta}_1 = 0.31 \quad \text{95\% CI: (0.16, 0.46)}$$

  - Answer: $\hat{\beta}_1$: mean cholesterol is estimated to be 0.31 mg/dl higher for each additional year of age.
  - Question: What about the confidence intervals?

Example:

Scientific Question: Is cholesterol associated with age?

- What do these models results mean in terms of our scientific question?
  - Parameter estimates and confidence intervals:

$$\hat{\beta}_0 = 166.90 \quad \text{95\% CI: (158.5, 175.3)}$$

$$\hat{\beta}_1 = 0.31 \quad \text{95\% CI: (0.16, 0.46)}$$

  - Answer: 95% CIs give us a range of values that will cover the true intercept and slope 95% of the time
    - For instance, we can be 95% confident that the true difference in mean cholesterol associated with a one year difference in age lies between 0.16 and 0.46 mg/dl

Example:

Scientific Question: Is cholesterol associated with age?

- Presentation of the results?
  - The mean serum total cholesterol is significantly higher in older individuals ($p < 0.001$).
  - For each additional year of age, we estimate that the mean total cholesterol differs by approximately 0.31 mg/dl (95% CI: 0.16, 0.46). Or:
  - For each additional 10 years of age, we estimate that the mean total cholesterol differs by approximately 3.10 mg/dl (95% CI: 1.62, 4.58).
    - Note:
      - Emphasis on slope parameter (sign and magnitude)
      - Confidence interval
      - Units for predictor and response. Scale matters!

Inference for predictions

- Given estimates $\hat{\beta}_0$, $\hat{\beta}_1$ we can find the **predicted** $\hat{y}_i$ **value**, for any value of x_i as

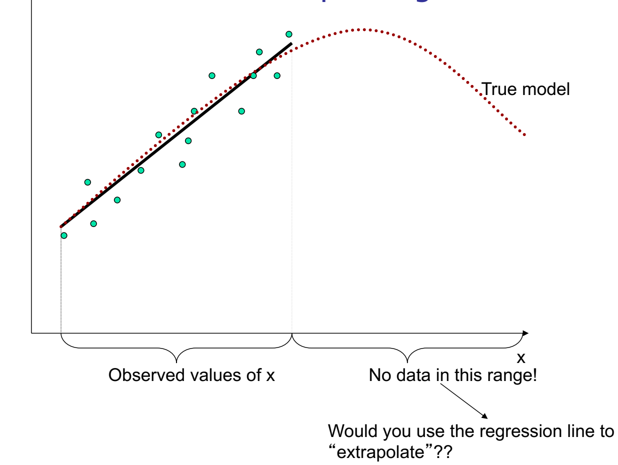
$$\hat{y}_i = \hat{\beta}_0 + \hat{\beta}_1 x_i$$

- Interpretation of $\hat{y}_i$:
  - Estimated mean value of Y at $X = x_i$

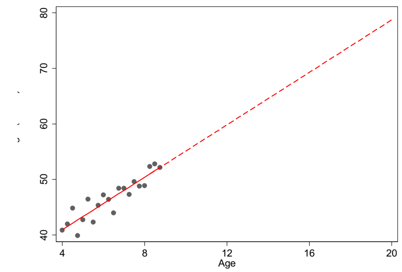
Be Cautious: This assumes the model is true.

- May be a reasonable assumption within the range of your data.
- It may not be true outside the range of your data!

Be careful of extrapolating



Be careful of extrapolating



- It would not make sense to extrapolate height at age 20 from a study of girls aged 4-9 years!

Prediction

- Prediction of the mean E[Y|X=x]:
  - Point Estimate: $\hat{y} = \hat{\beta}_0 + \hat{\beta}_1 x$
  - Standard Error: $se(\hat{y}) = \hat{\sigma}\sqrt{\frac{1}{n} + \frac{(x-\bar{x})^2}{\sum_{i=1}^{n}(x_i - \bar{x})^2}}$

  Note that as x gets further from $\bar{x}$, variance increases!

  - 100 (1-α)% confidence interval for E[Y|X=x]:

$$\hat{y} \pm t_{n-2,1-\alpha/2}\, se(\hat{y})$$

Prediction

- Prediction of a new future observation, y*, at X=x:
  - Point Estimate: $\hat{y}^* = \hat{\beta}_0 + \hat{\beta}_1 x$
  - Standard Error: $se(\hat{y}^*) = \hat{\sigma}\sqrt{1 + \frac{1}{n} + \frac{(x-\bar{x})^2}{\sum_{i=1}^{n}(x_i - \bar{x})^2}}$
  - 100 (1-α)% prediction interval for a new future observation:

$$\hat{y}^* \pm t_{n-2,1-\alpha/2}\, se(\hat{y}^*)$$

Standard error for the prediction of a future observation is bigger:

It depends not only on the precision of the estimated mean, but also on the amount of variability in Y around the line.

Cholesterol Example: Prediction

Prediction of the mean

```
> predict.lm(fit, newdata=data.frame(age=c(46,47,48)), interval="confidence")
       fit      lwr      upr
1 181.1771 178.6776 183.6765
2 181.4874 179.0619 183.9129
3 181.7977 179.4392 184.1563
```

```
> predict.lm(fit, newdata=data.frame(age=c(46,47,48)), interval="prediction")
       fit      lwr      upr
1 181.1771 138.4687 223.8854
2 181.4874 138.7833 224.1915
3 181.7977 139.0974 224.4981
```

Prediction of a new observation

Example:

Scientific Question: Is cholesterol associated with age?

- Let's interpret these predictions
  - For $x = 46$

    $\hat{y} = 181.2$ 95% CI: (178.7, 183.7)

    $\hat{y}^* = 181.2$ 95% CI: (138.5, 223.9)
  - Question: How do our interpretations for $\hat{y}$ and $\hat{y}^*$ differ?

Example:

Scientific Question: Is cholesterol associated with age?

- Let's interpret these predictions
  - For $x = 46$

    $\hat{y} = 181.2$ 95% CI: (178.7, 183.7)

    $\hat{y}^* = 181.2$ 95% CI: (138.5, 223.9)
  - Question: How do our interpretations for $\hat{y}$ and $\hat{y}^*$ differ?
  - Answer: The point estimates represent our predictions for the mean serum cholesterol for individuals age 46 ($\hat{y}$) and for a single new individual of age 46 ($\hat{y}^*$)

Example:

Scientific Question: Is cholesterol associated with age?

- Let's interpret these predictions
  - For $x = 46$

    $\hat{y} = 181.2$ 95% CI: (178.7, 183.7)

    $\hat{y}^* = 181.2$ 95% CI: (138.5, 223.9)
  - Question: Why are the confidence intervals for $\hat{y}$ and $\hat{y}^*$ of differing widths?

Example:
Scientific Question: Is cholesterol associated with age?

- Let's interpret these predictions
  - For $x = 46$

$$\hat{y} = 181.2 \quad \text{95\% CI: (178.7, 183.7)}$$

$$\hat{y}^* = 181.2 \quad \text{95\% CI: (138.5, 223.9)}$$

  - Question: Why are the confidence intervals for $\hat{y}$ and $\hat{y}^*$ of differing widths?
  - Answer: The interval is broader when we make a prediction for a cholesterol level for a single individual because it must incorporate random variability around the mean.
  - Note: Unlike confidence intervals, the formula for the prediction interval depends on the normality assumption regardless of sample size.

Exercise

- Let's put some of the concepts we have been discussing into practice
- Open up the Labs file and R Studio and follow the directions to load the class data set and install the R packages you will need for this module
- Work on Exercises 1-3
  - Try each exercise on your own
  - Make note of any questions or difficulties you have
  - At **10:15PT** we will meet as a group to go over the solutions and discuss your questions