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

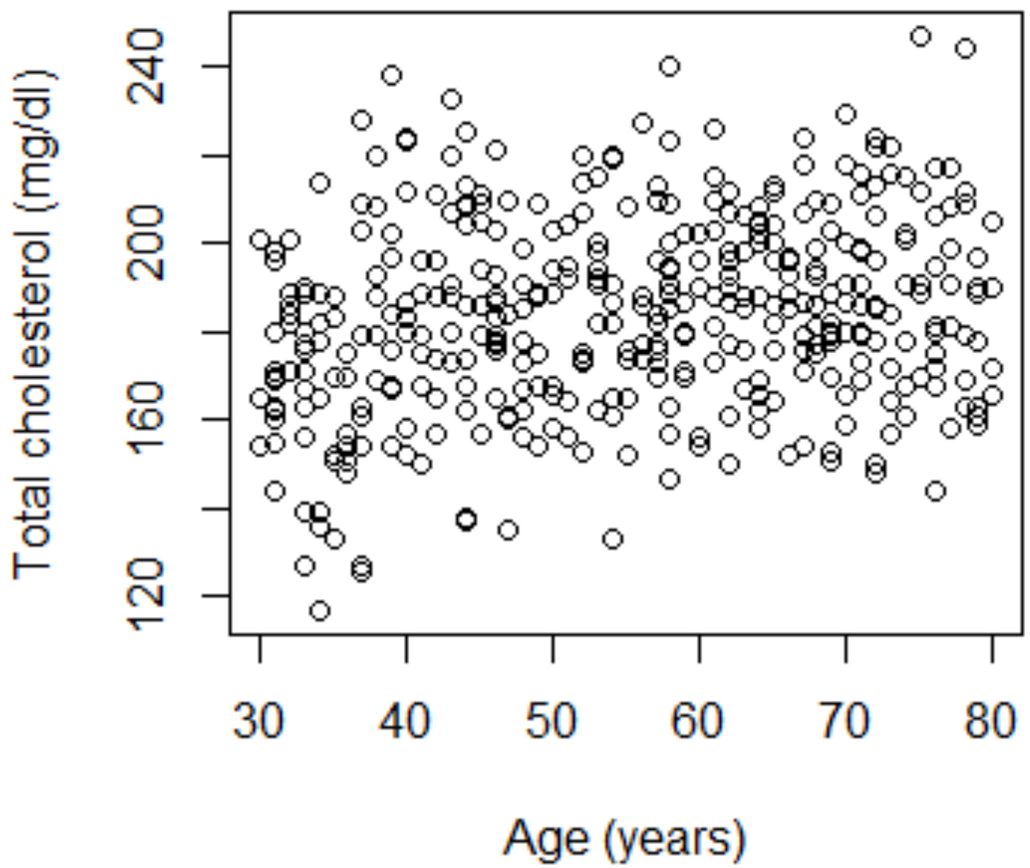
- Linear regression is concerned with a **continuous** outcome
- Data: Factors related to serum total cholesterol (continuous outcome), 400 individuals, 11 variables

```
> 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

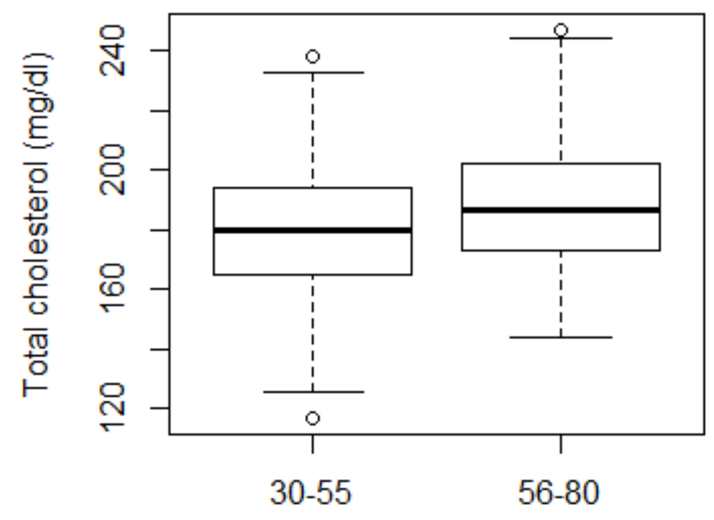
Motivation: Cholesterol Example



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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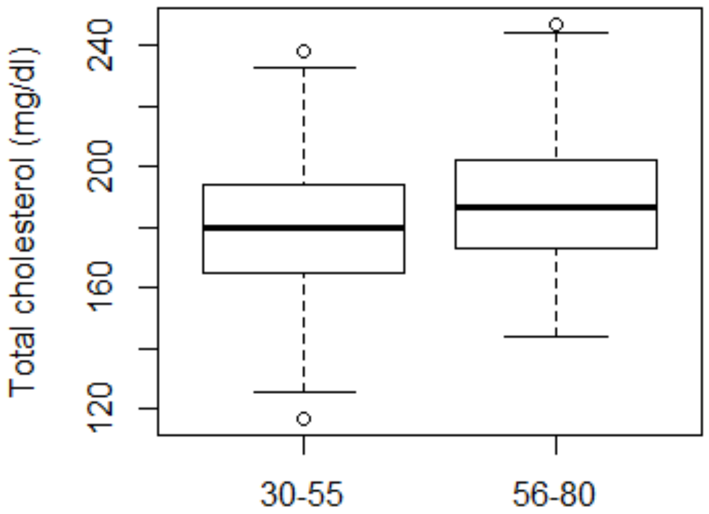


Motivation: Cholesterol Example

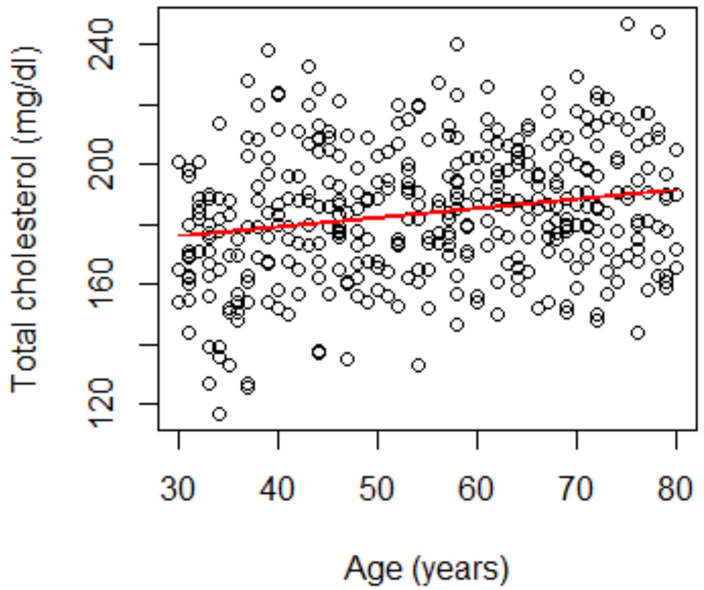
- Using the t-test:
  - There is a statistically significant association between cholesterol and age

  - 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

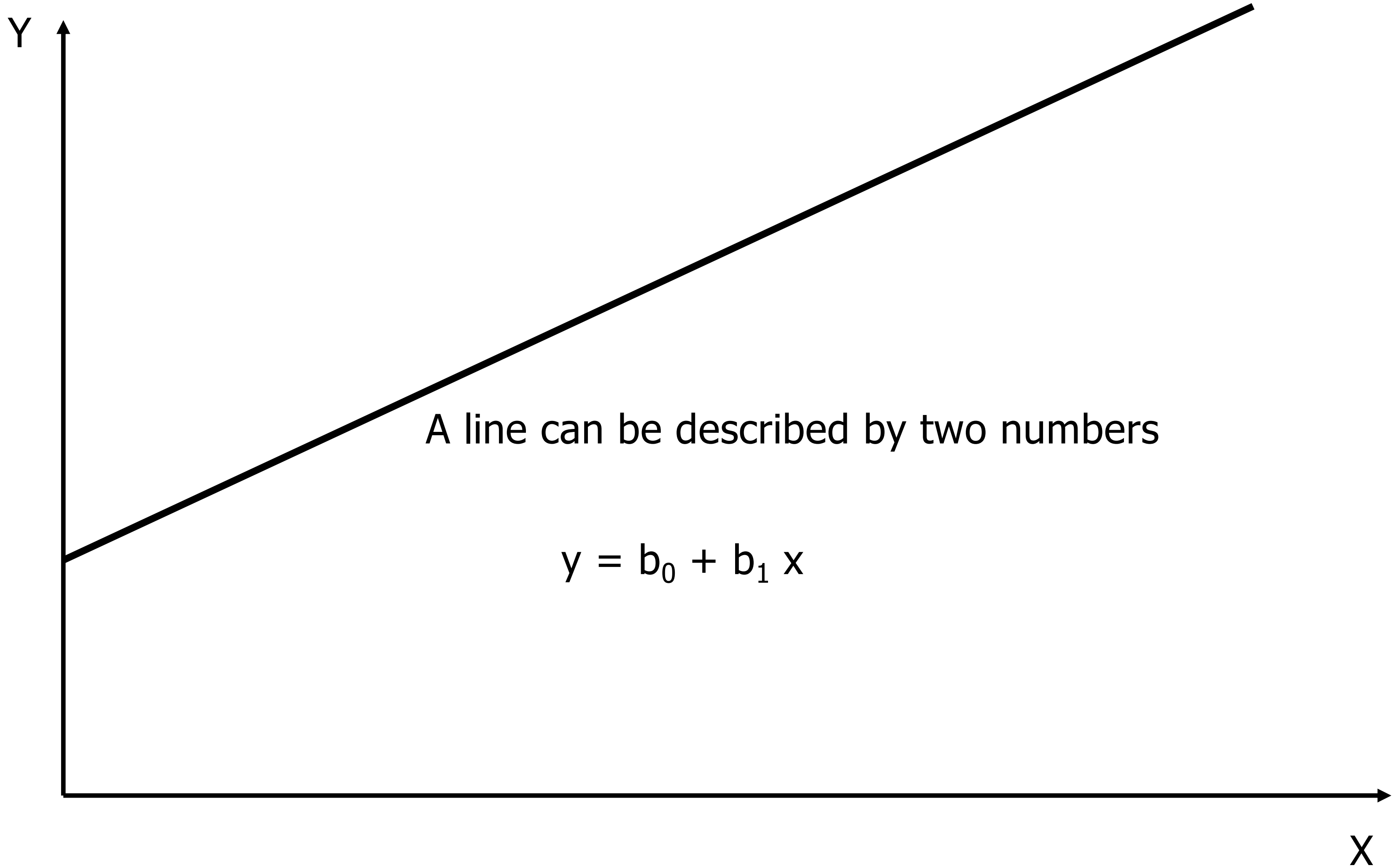
- A statistical method for modeling the relationship between a continuous variable [response/outcome/dependent] and other variables [predictors/exposure/independent]
  - Most commonly used statistical model
  - Flexible
  - Well-developed and understood properties
  - Easy interpretation
  - Building 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

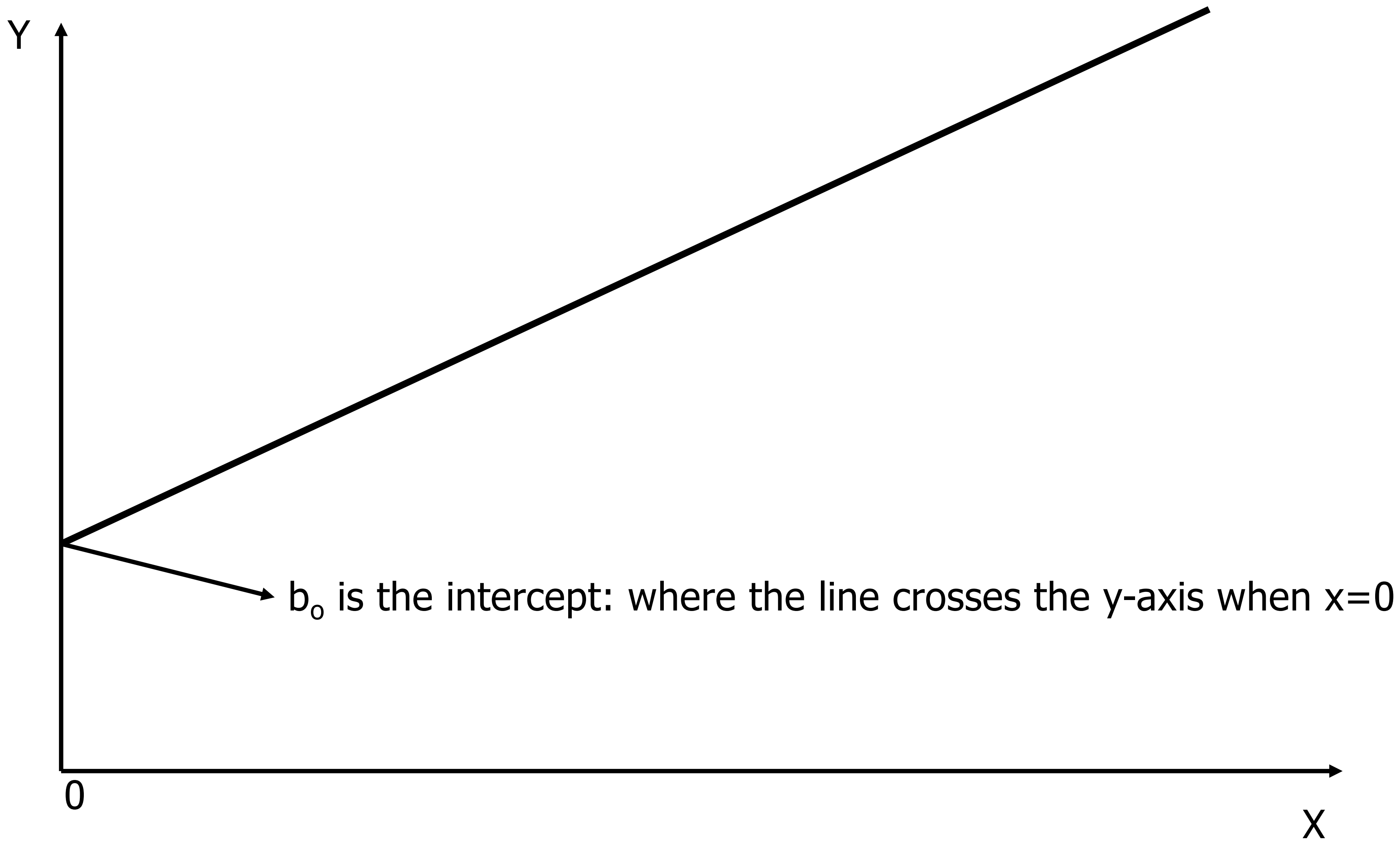
The straight line equation



A line can be described by two numbers

$$y = b_0 + b_1 x$$

The straight line equation



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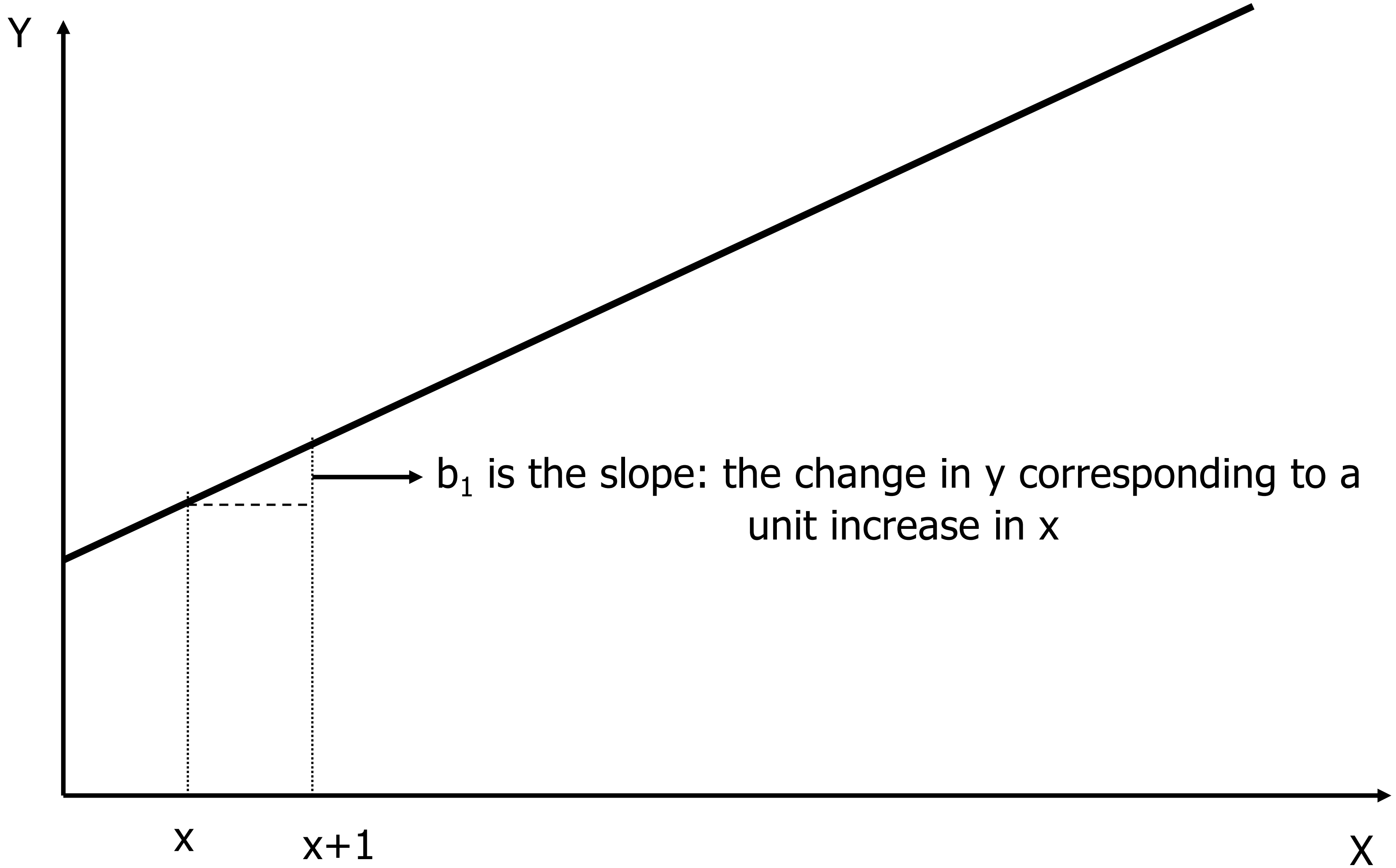

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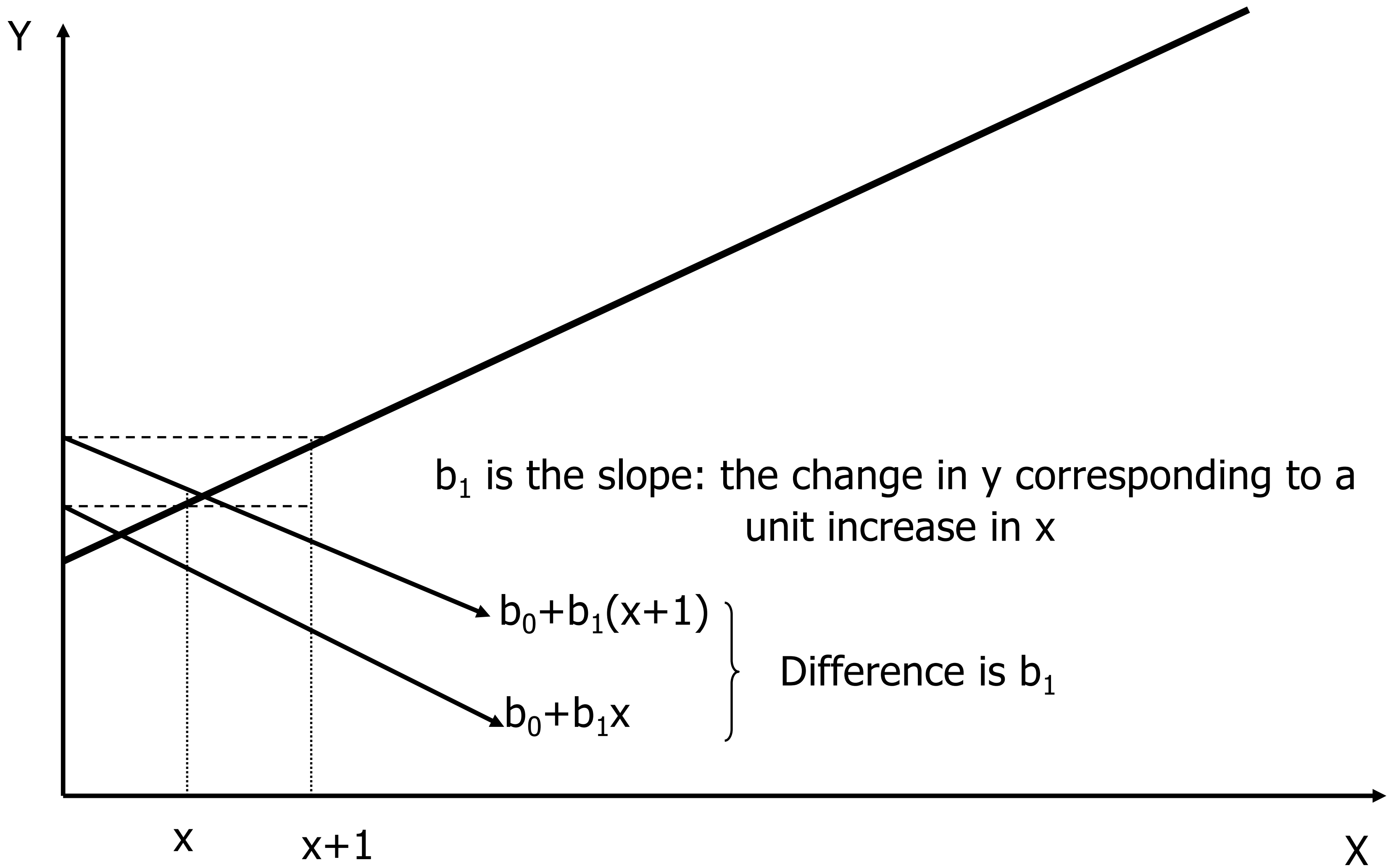
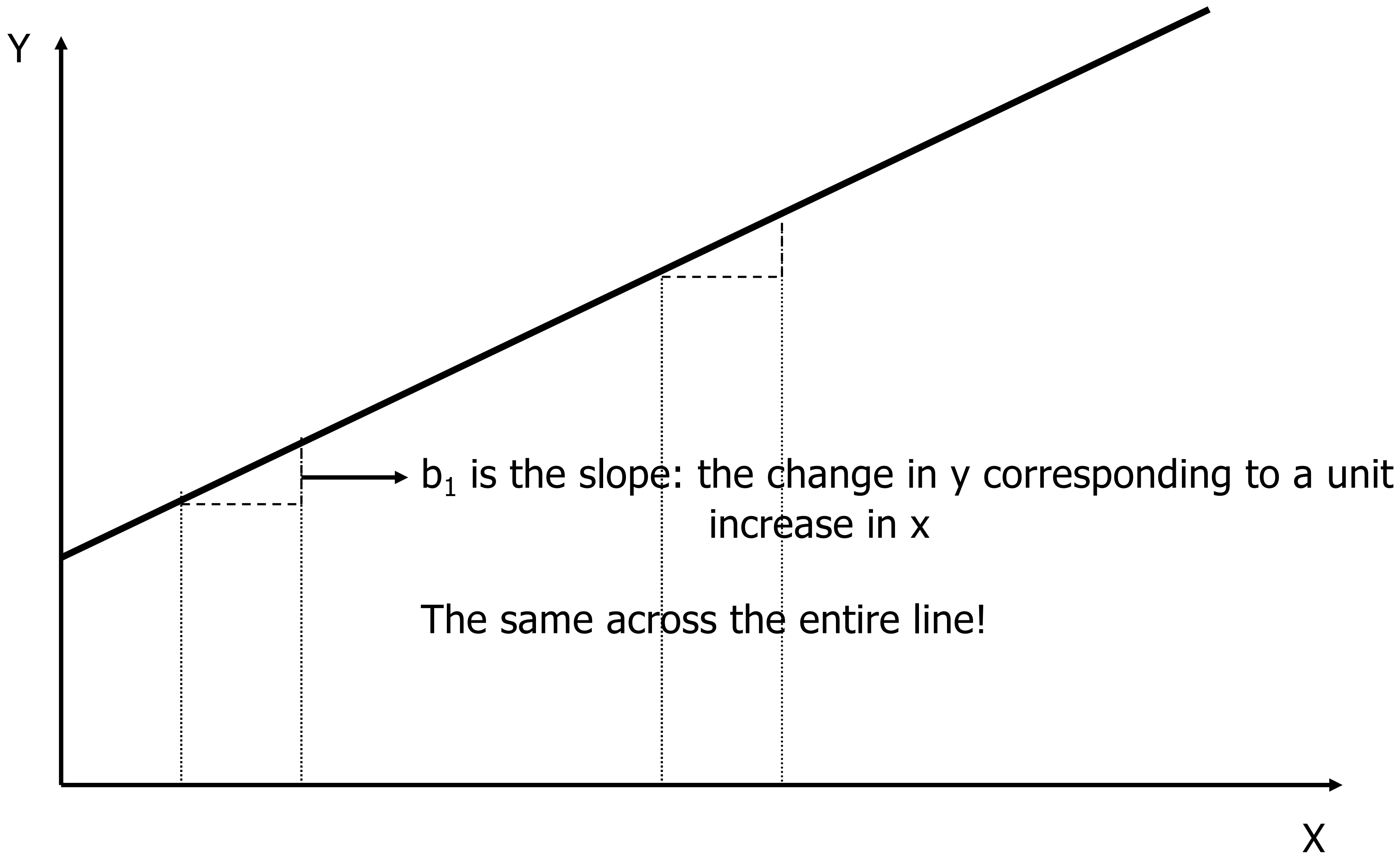
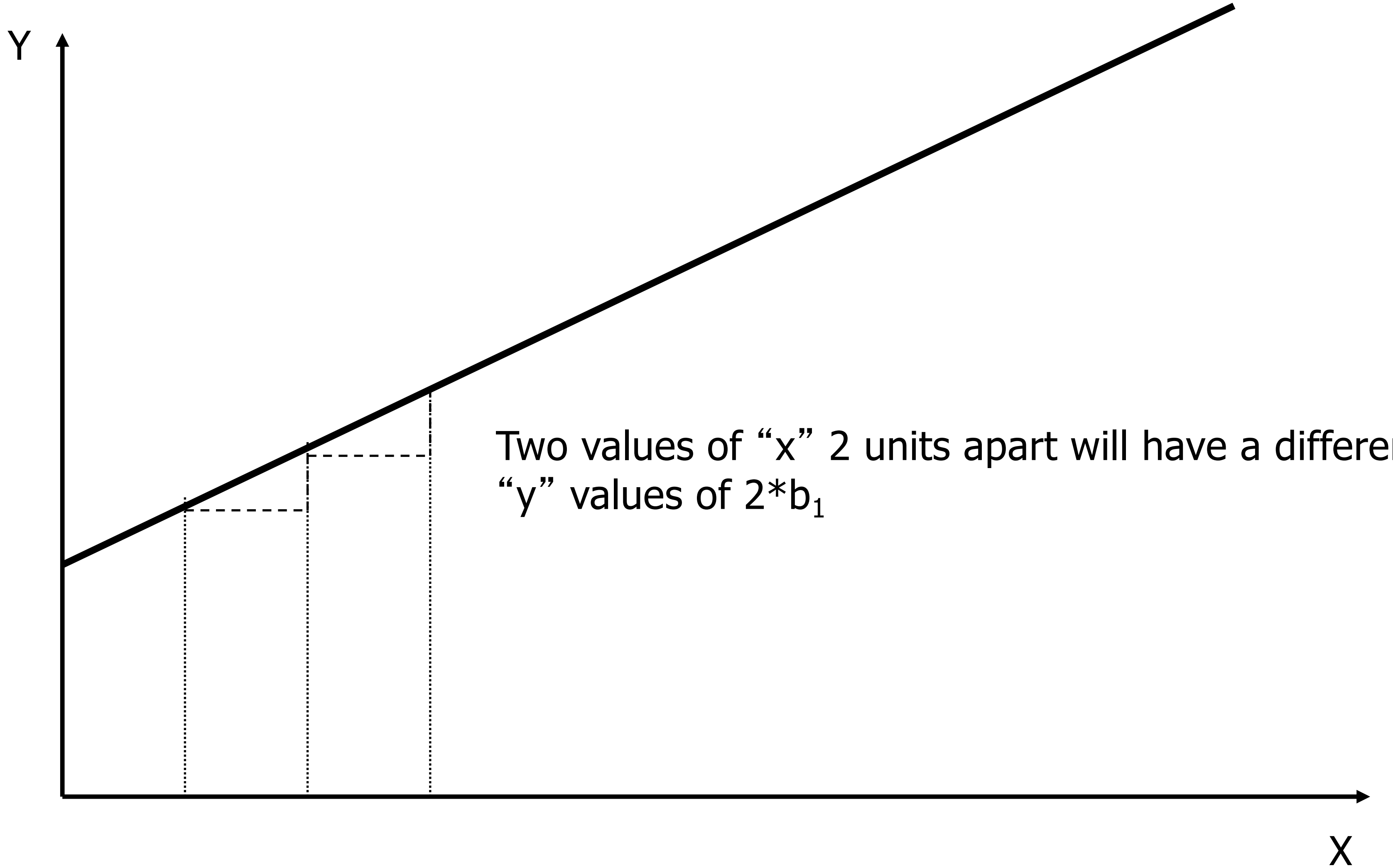


b_1 is the slope: the change in y corresponding to a unit increase in x

The straight line equation



The straight line equation

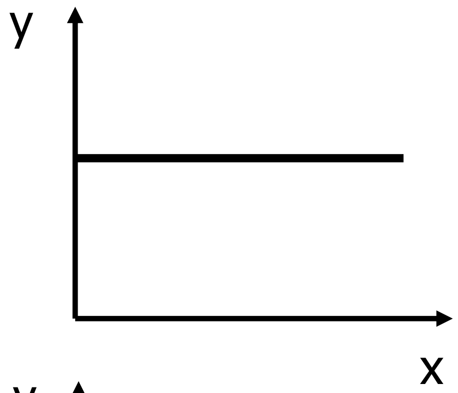


Two values of “x” 2 units apart will have a difference in “y” values of $2*b_1$

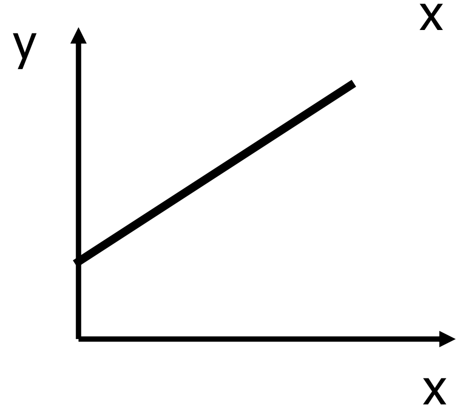
The straight line equation

- 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

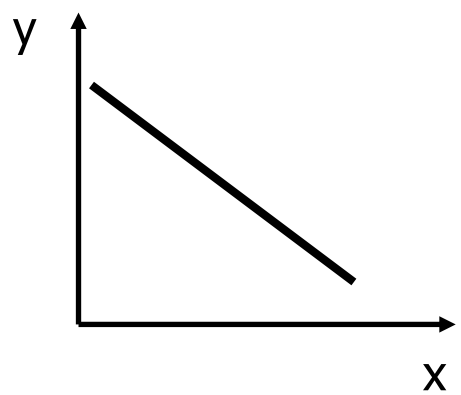
The straight line equation



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



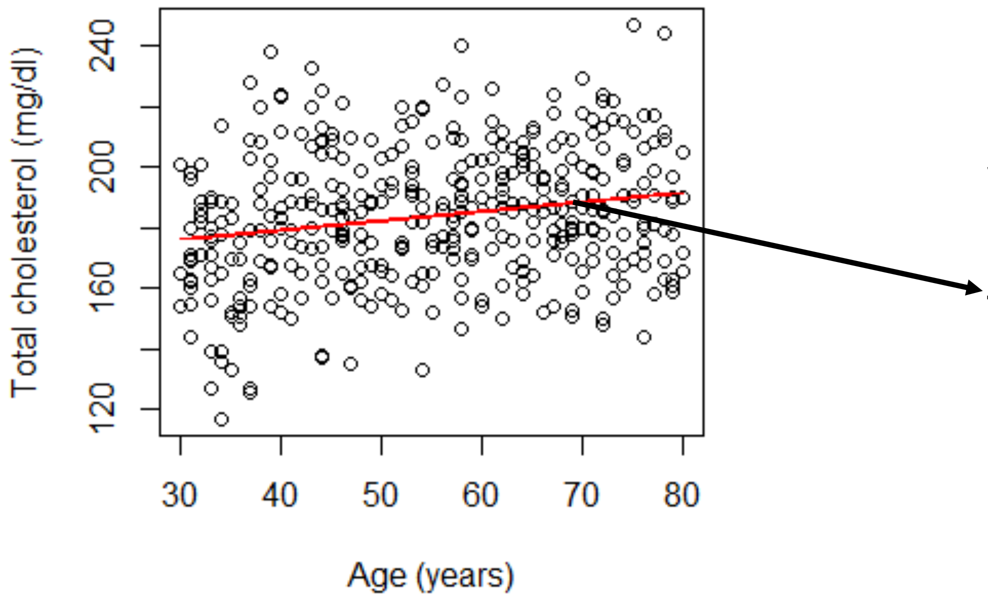
($b_1 > 0$) Positive association between x and y
(values of y increase as values of x increase)



($b_1 < 0$) 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**:

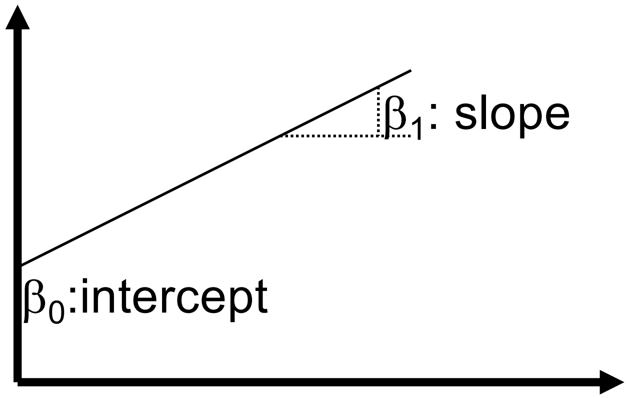
$$y = \beta_0 + \beta_1 x + \varepsilon, \quad \varepsilon \sim N(0, \sigma^2)$$

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:

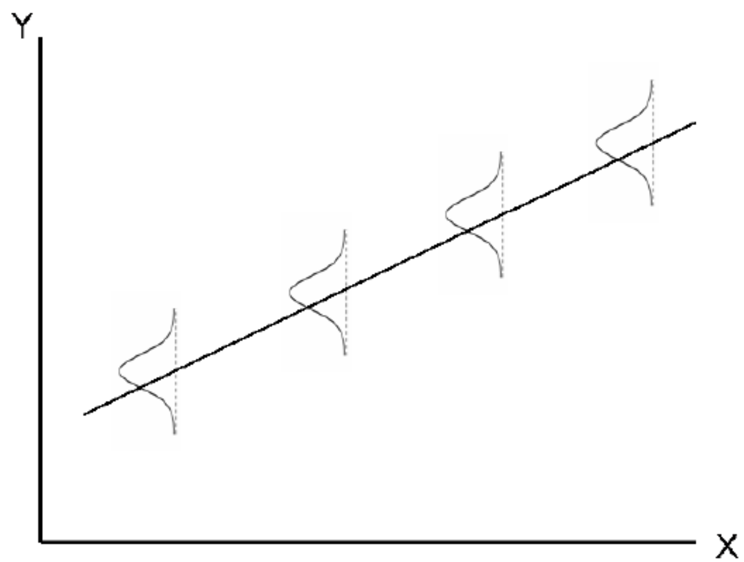
$$Var[Y \mid X = x] = \sigma^2$$

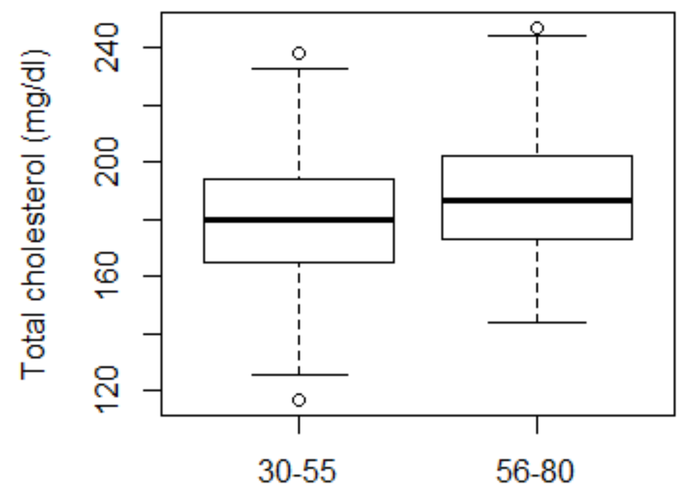
Variance does not depend on x

Simple Linear Regression: Assumptions

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

Distribution of Y at different x values:





Compare with the boxplots for two age groups

Simple Linear Regression: Interpreting model coefficients

- Model: $E[Y|x] = \beta_0+\beta_1 x$ $Var[Y|x] = \sigma^2$

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

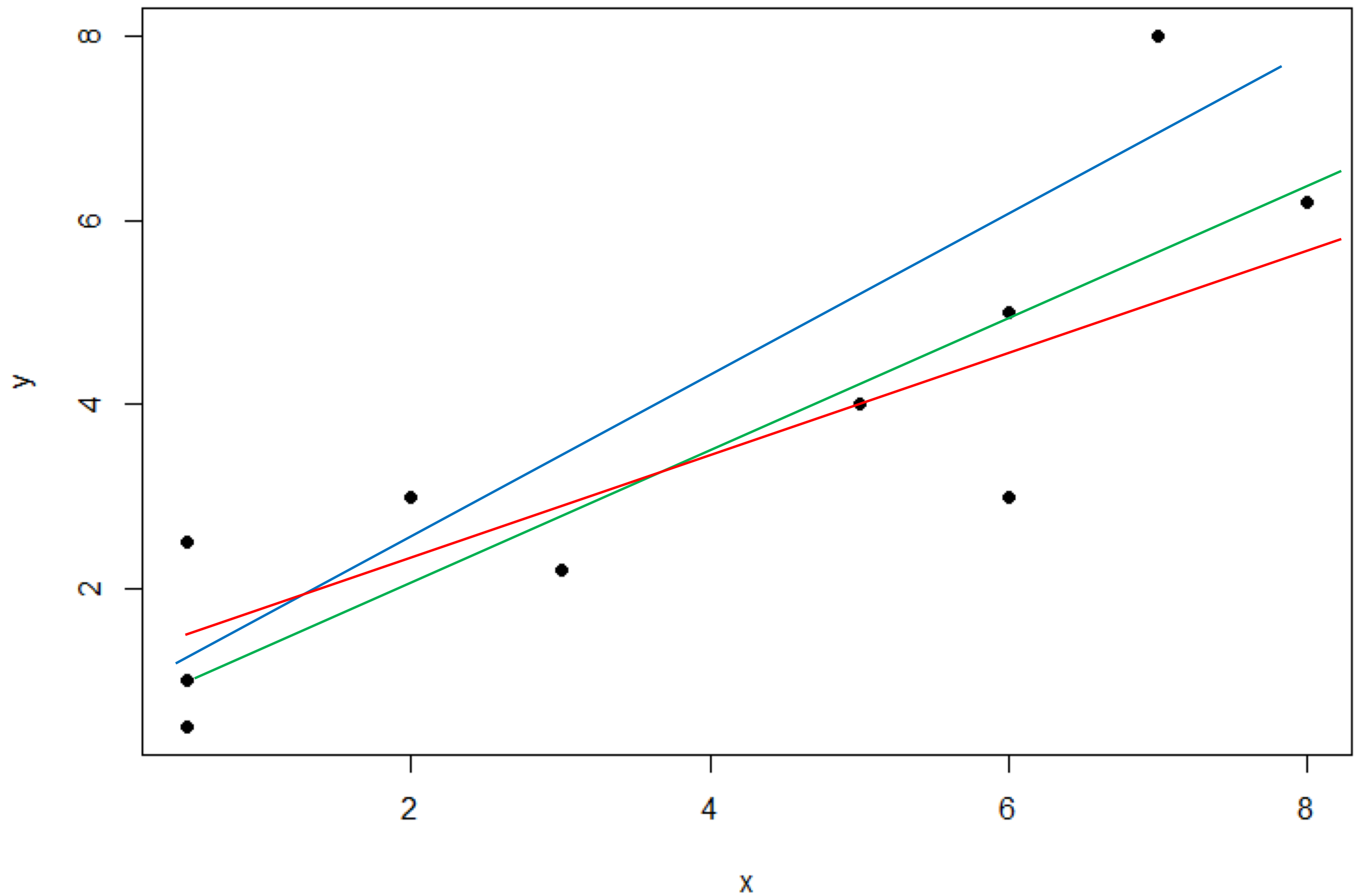
- Question: How do you interpret β_1?

- Answer:

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

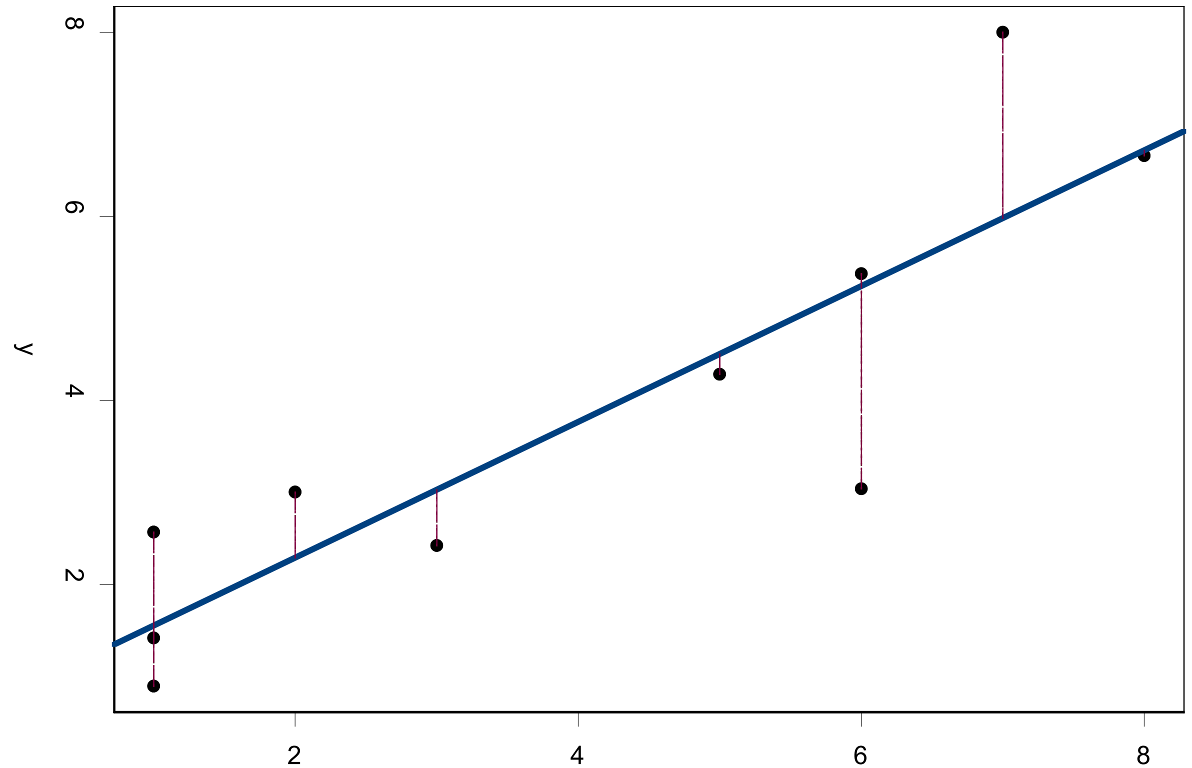
Least Squares Estimation

- 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:

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

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

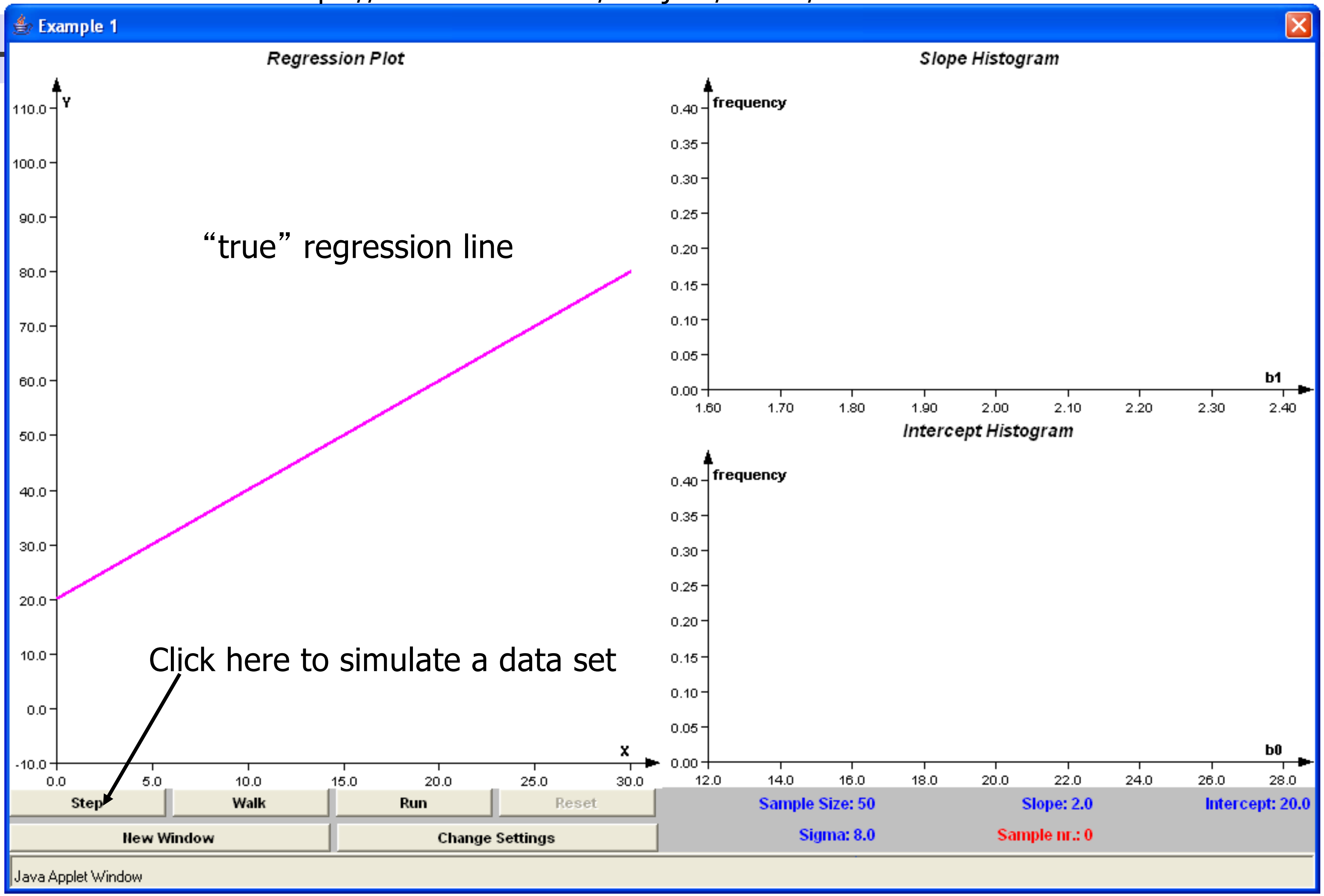
- We estimate the variance as:

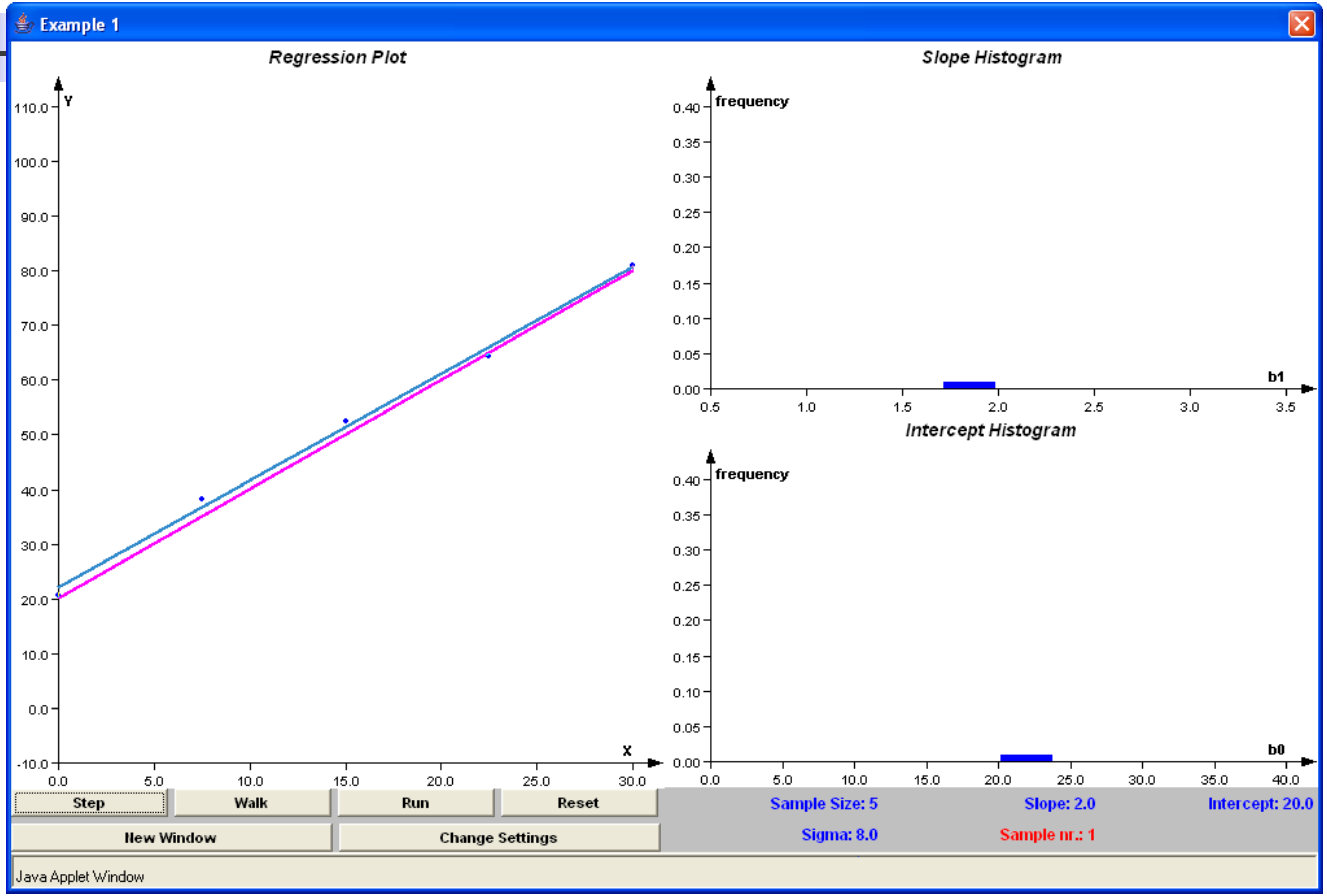
$$\hat{\sigma}^2 = \frac{\sum_{i=1}^{n} r_i^2}{n-2} = \frac{\sum_{i=1}^{n} (y_i - \hat{y}_i)^2}{n-2} = \frac{\sum_{i=1}^{n} (y_i - \hat{\beta}_0 - \hat{\beta}_1 x_i)^2}{n-2}$$

Estimated Standard Errors

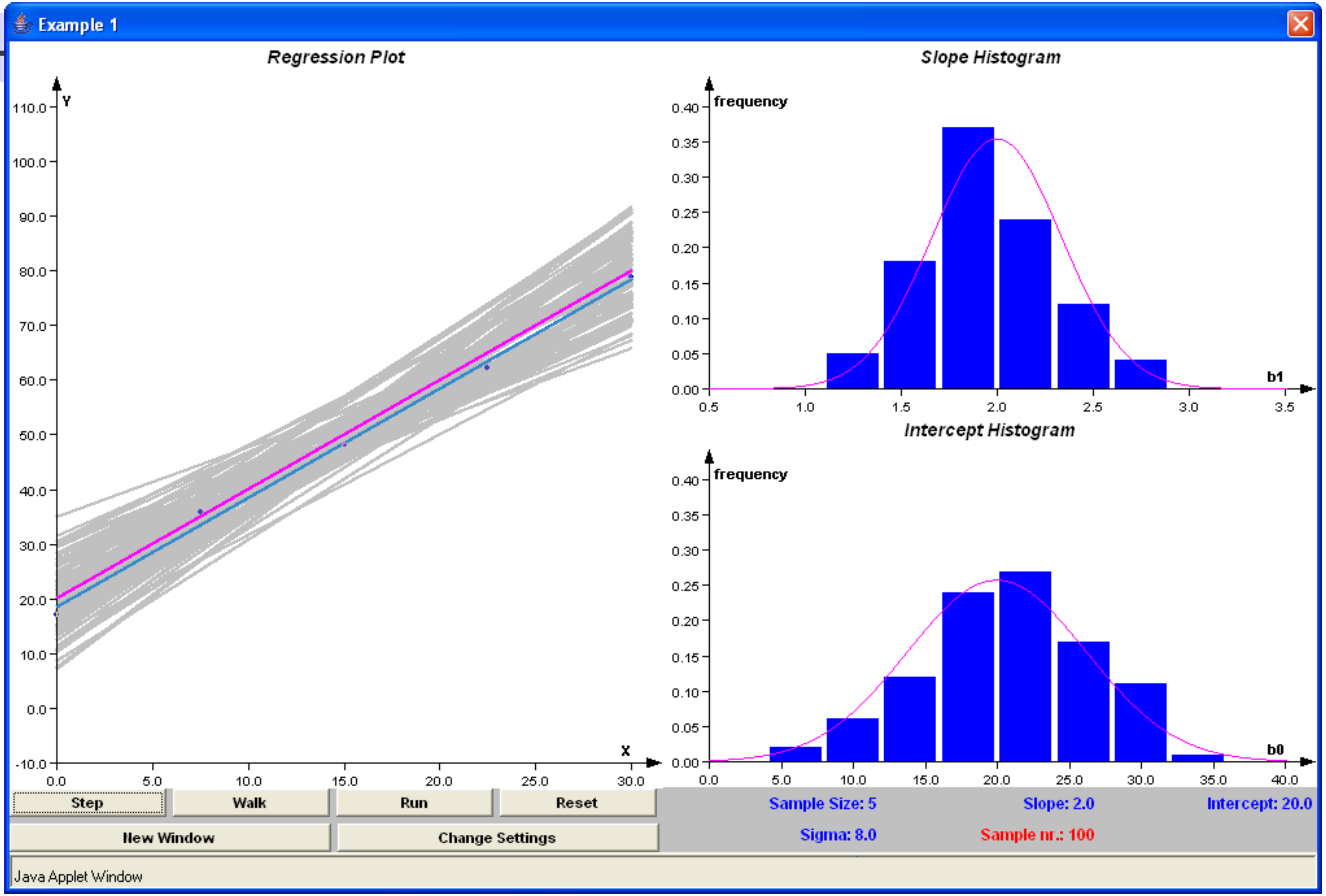
- Recall that, when estimating parameters from a sample, there will be sampling variability in the estimates
- This is true for regression parameter estimates
- Looking at the formulas for $\hat{\beta}_0$ and $\hat{\beta}_1$, we can see that they are just complicated means
- In repeated sampling we would 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/

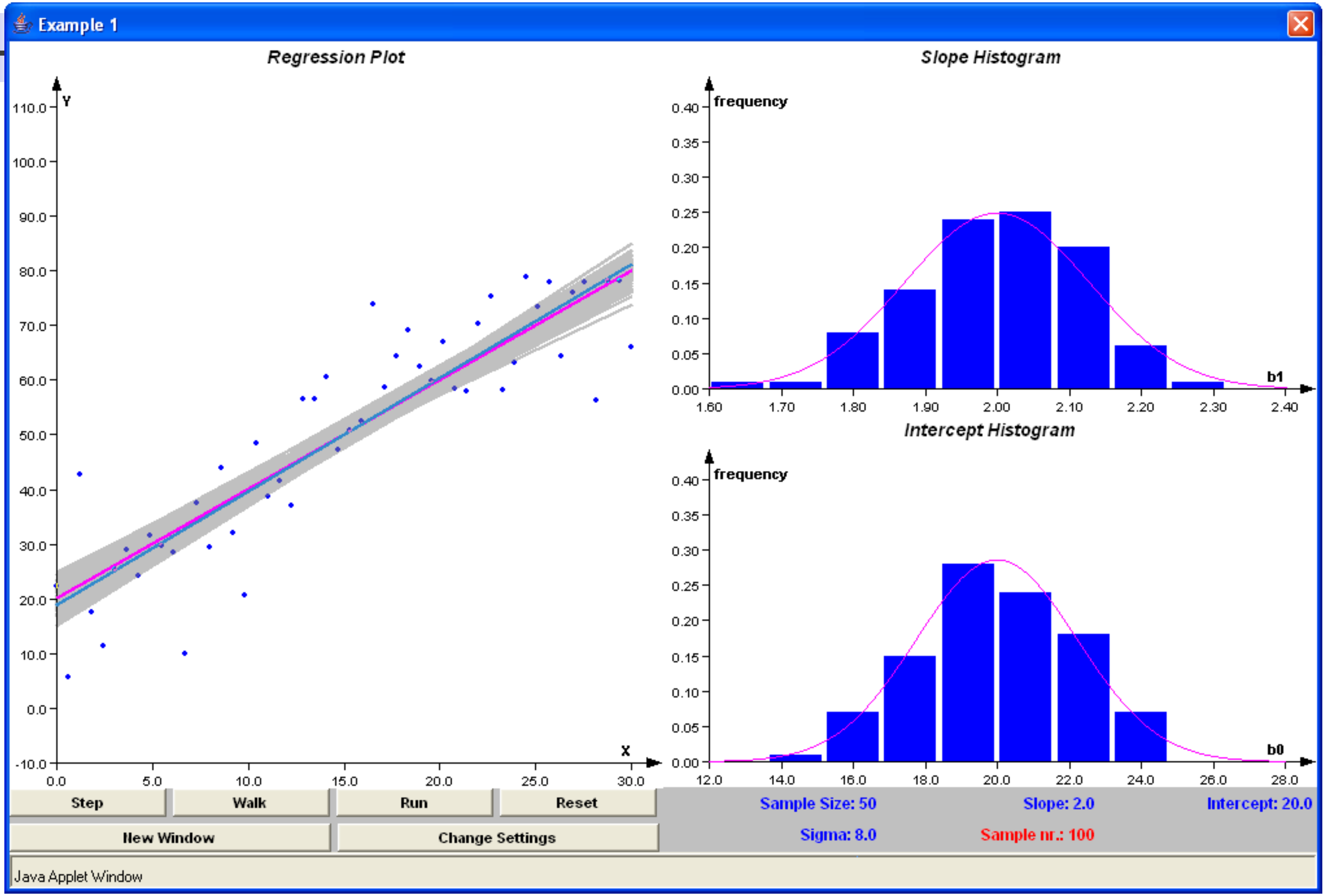



Example 1
Regression Plot
Y
X
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
0.0
5.0
10.0
15.0
20.0
25.0
30.0
Slope Histogram
frequency
b1
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
0.5
1.0
1.5
2.0
2.5
3.0
3.5
Intercept Histogram
frequency
b0
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
0.0
5.0
10.0
15.0
20.0
25.0
30.0
35.0
40.0
Step
Walk
Run
Reset
New Window
Change Settings
Sample Size: 5
Slope: 2.0
Intercept: 20.0
Sigma: 8.0
Sample nr.: 1
Java Applet Window

Sampling Distribution



Sampling Distribution



Inference

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

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

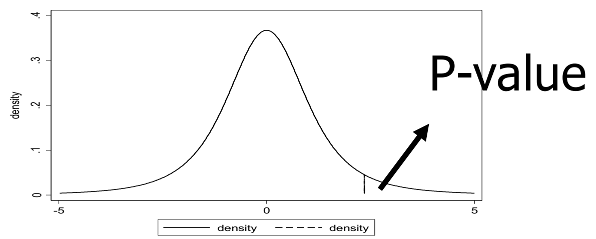
[Don't worry about these formulae: we will use R to fit the models!]

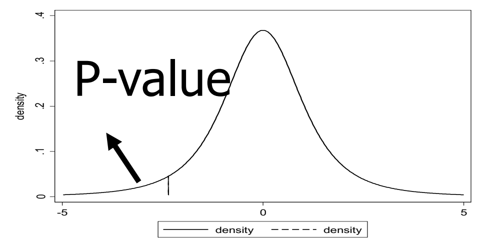
Inference: Hypothesis Testing

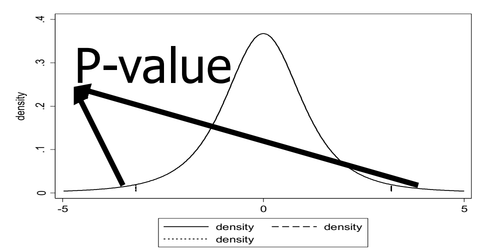
Null Hypothesis: $\beta_j = 0$

T=test statistic

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







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:

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

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

$\hat{\beta}_0$: 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:

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

    $\hat{\beta}_1 = 0.31$ 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 $\hat{\beta}_0, \quad \hat{\beta}_1$ we can find the **predicted** $\hat{y}_i$ **value**, for any value of x_i as

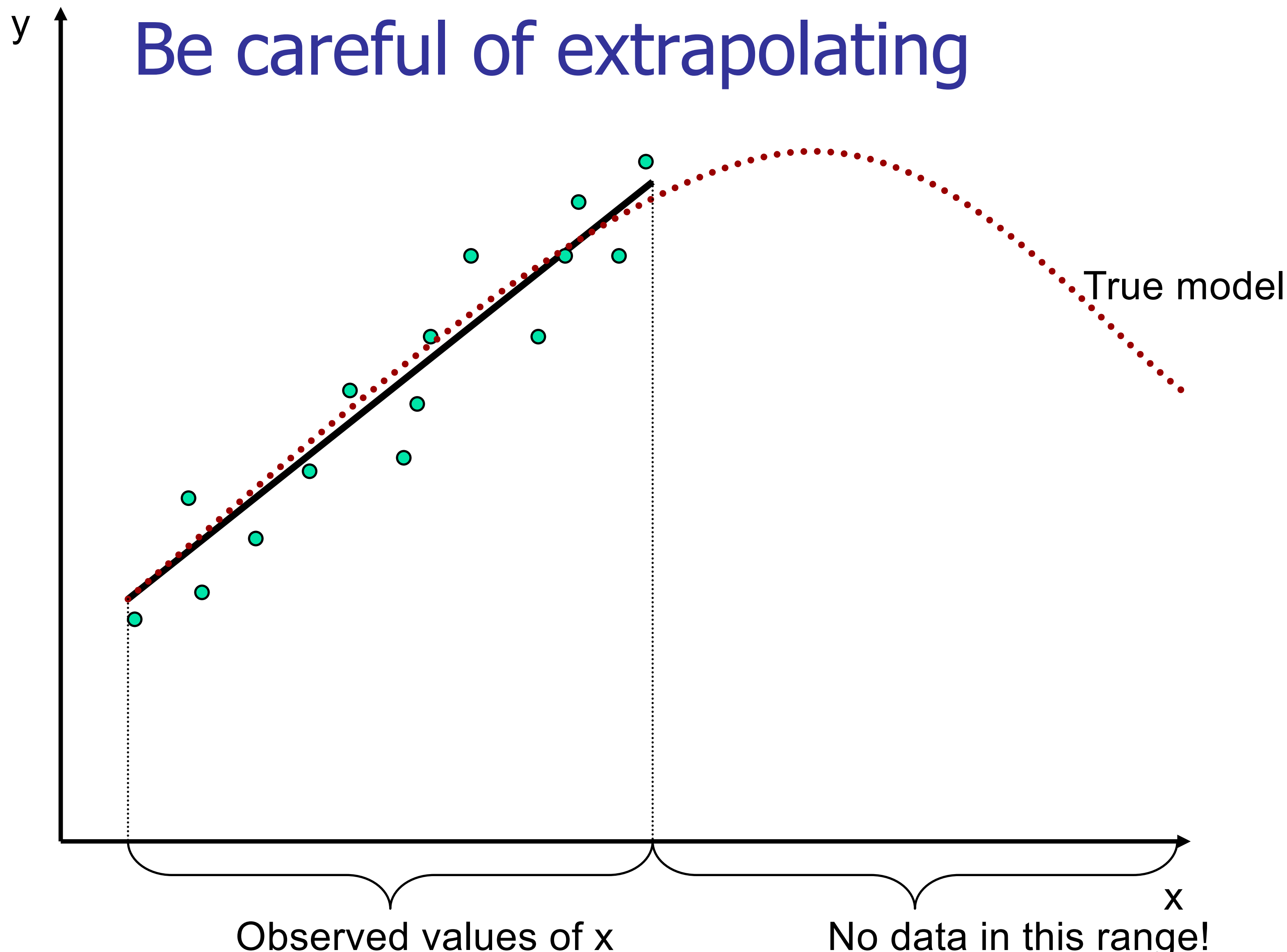
$$\hat{y}_i = \hat{\beta}_0 + \hat{\beta}_1 x_i$$

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

Be Cautious: This assumes the model is true.

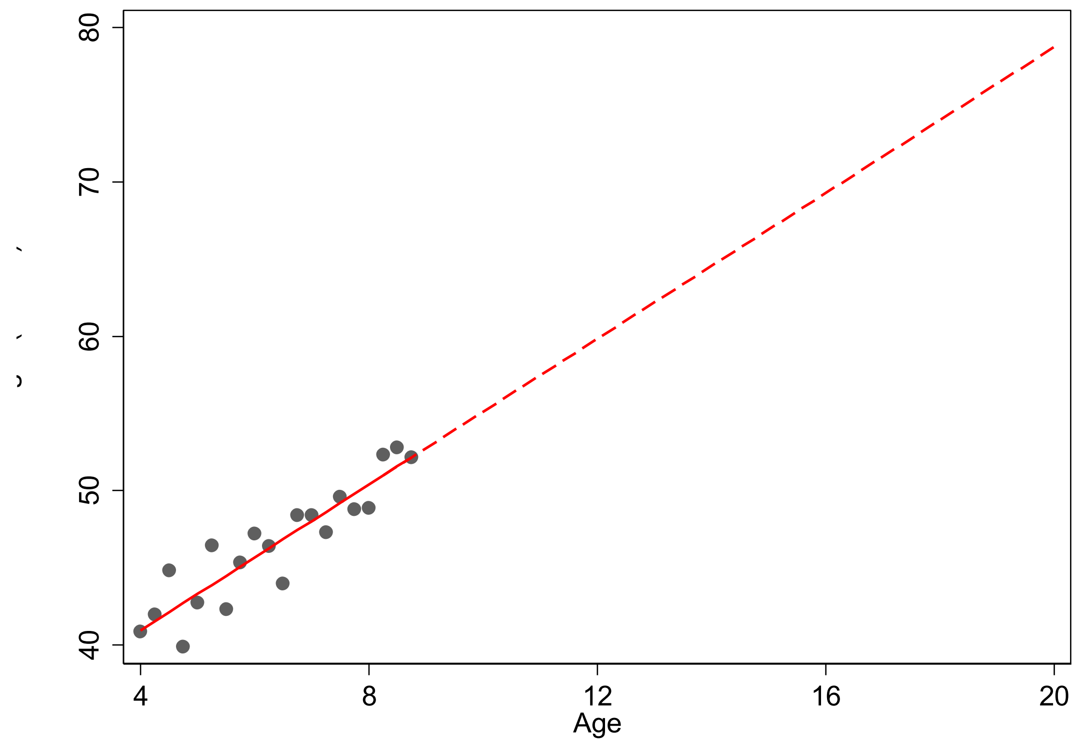
  - May be a reasonable assumption within the range of your data.
  - It may not be true outside the range of your data!

Be careful of extrapolating



Would you use the regression line to "extrapolate"??

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: $se(\hat{y}^*) = \hat{\sigma}\sqrt{1 + \frac{1}{n} + \frac{(x-\overline{x})^2}{\sum_{i=1}^{n}(x_i - \overline{x})^2}}$
  - 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 $x = 46$

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

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

  - 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 $x = 46$

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

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

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Example:

Scientific Question: Is cholesterol associated with age?

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

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

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

  - 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 **1:15PT** we will meet as a group to go over the solutions and discuss your questions