



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
- Day 2
 - Model checking
 - 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

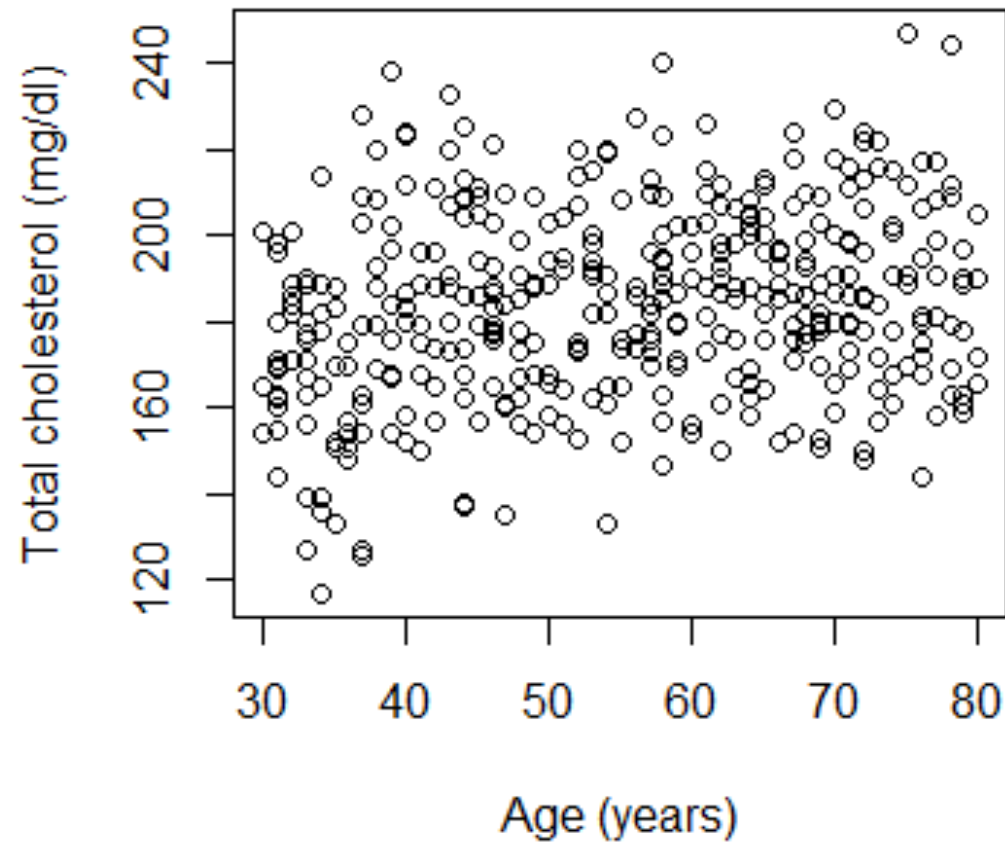
- Linear regression is concerned with a **continuous** outcome
- Data: Factors related to serum total cholesterol (continuous outcome), 400 individuals, 11 variables

```
> 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

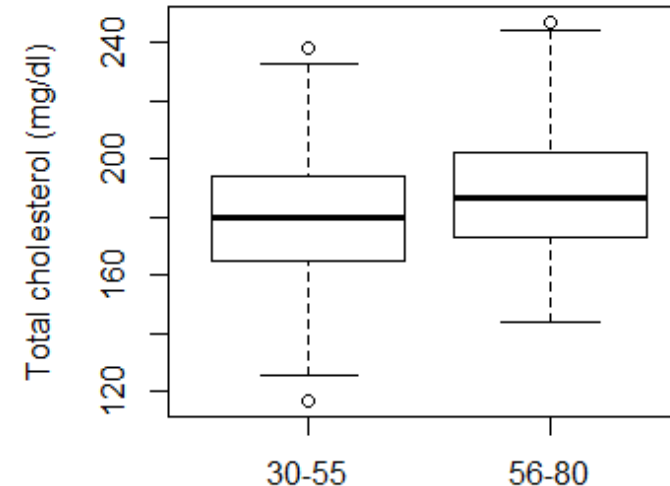
Motivation: Cholesterol Example



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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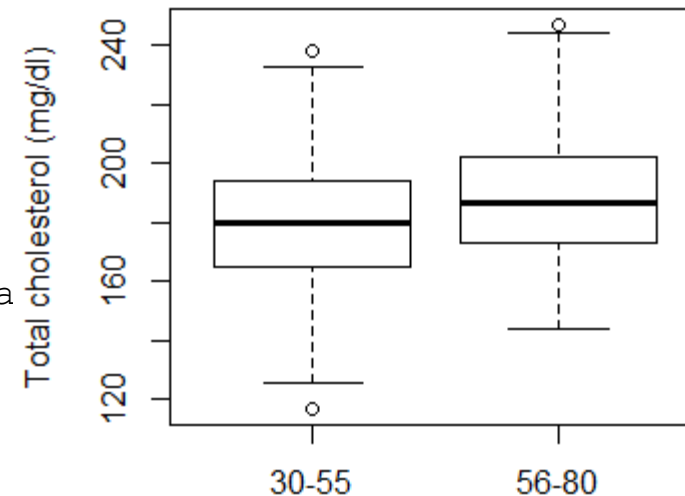
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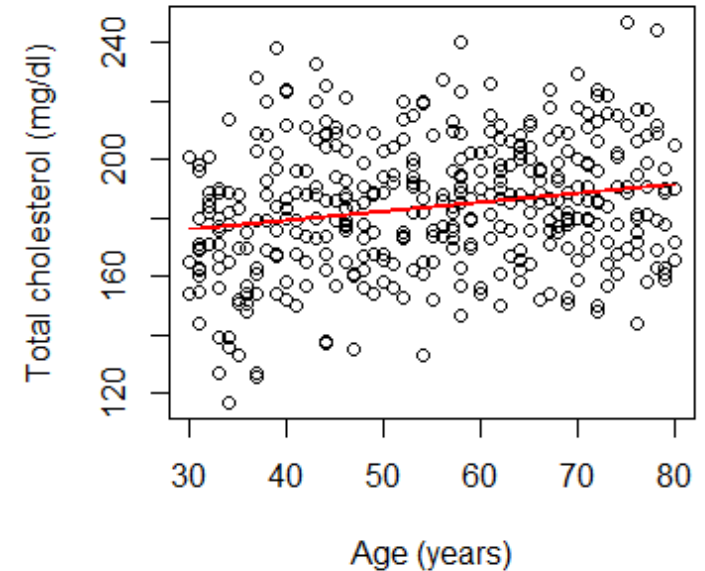


Motivation: Cholesterol Example

- 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?

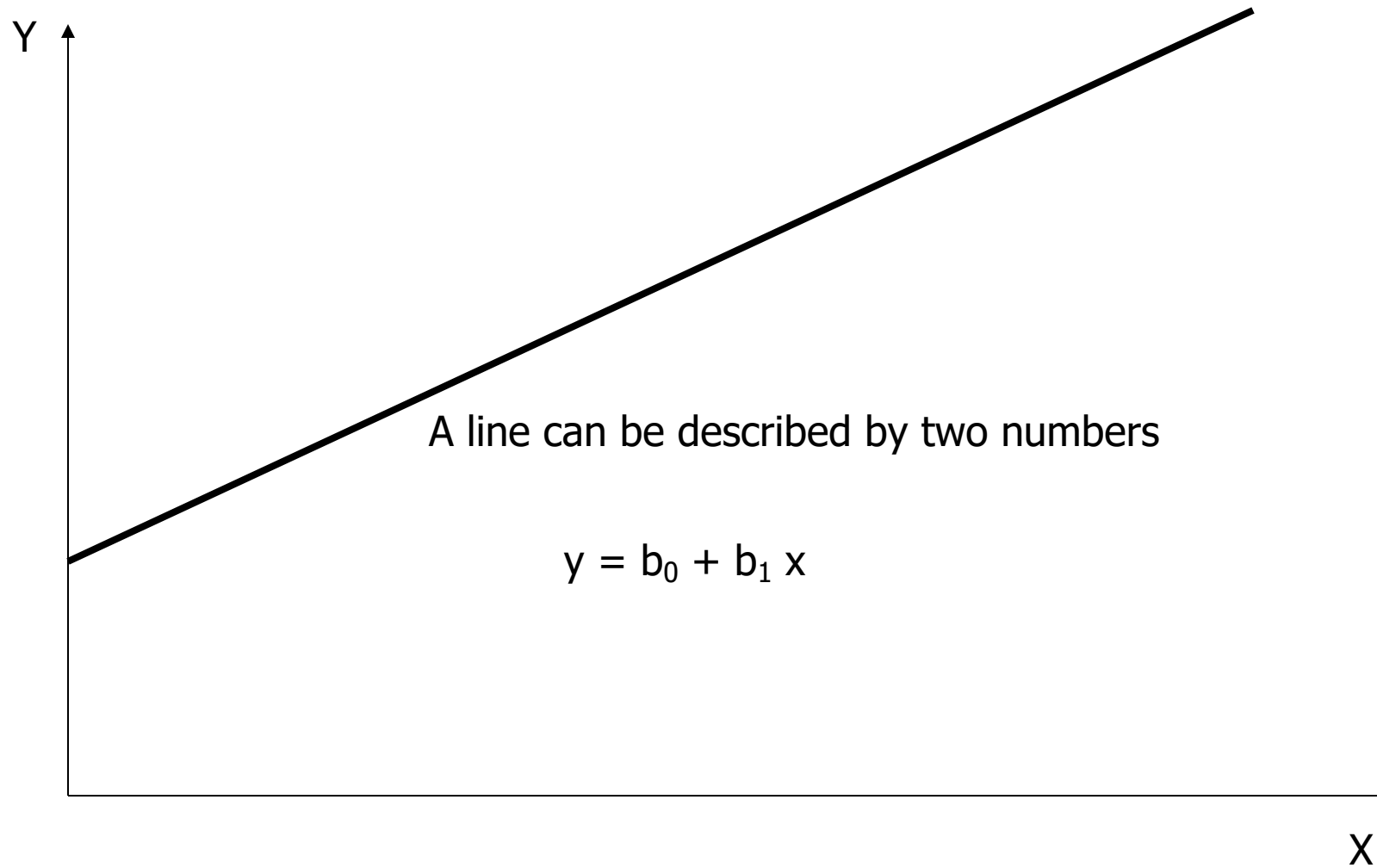


Linear Regression

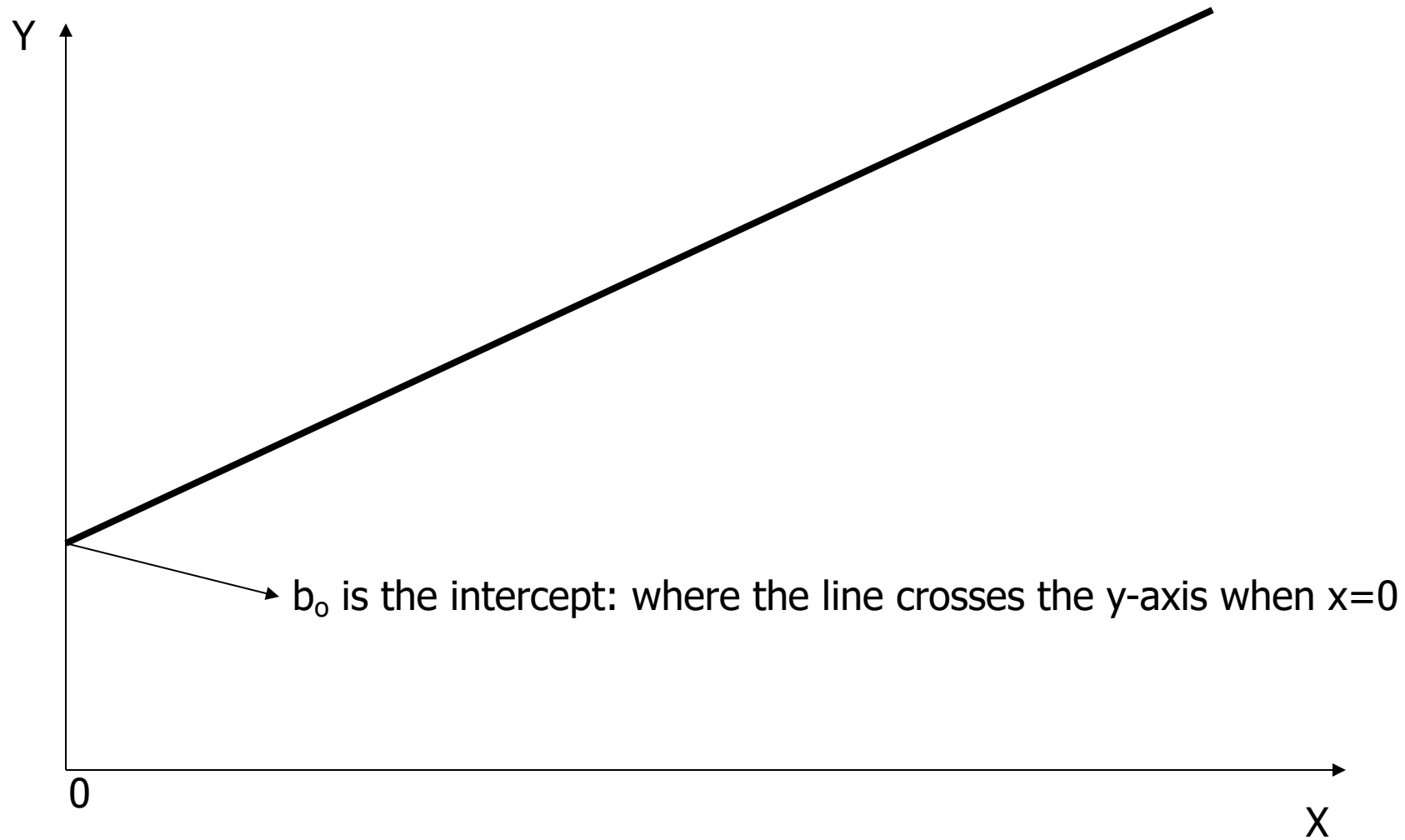
- A statistical method for modeling the relationship between a continuous variable [response/outcome/dependent] and other variables [predictors/exposure/independent]
 - Most commonly used statistical model
 - Flexible
 - Well-developed and understood properties
 - Easy interpretation
 - Building block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



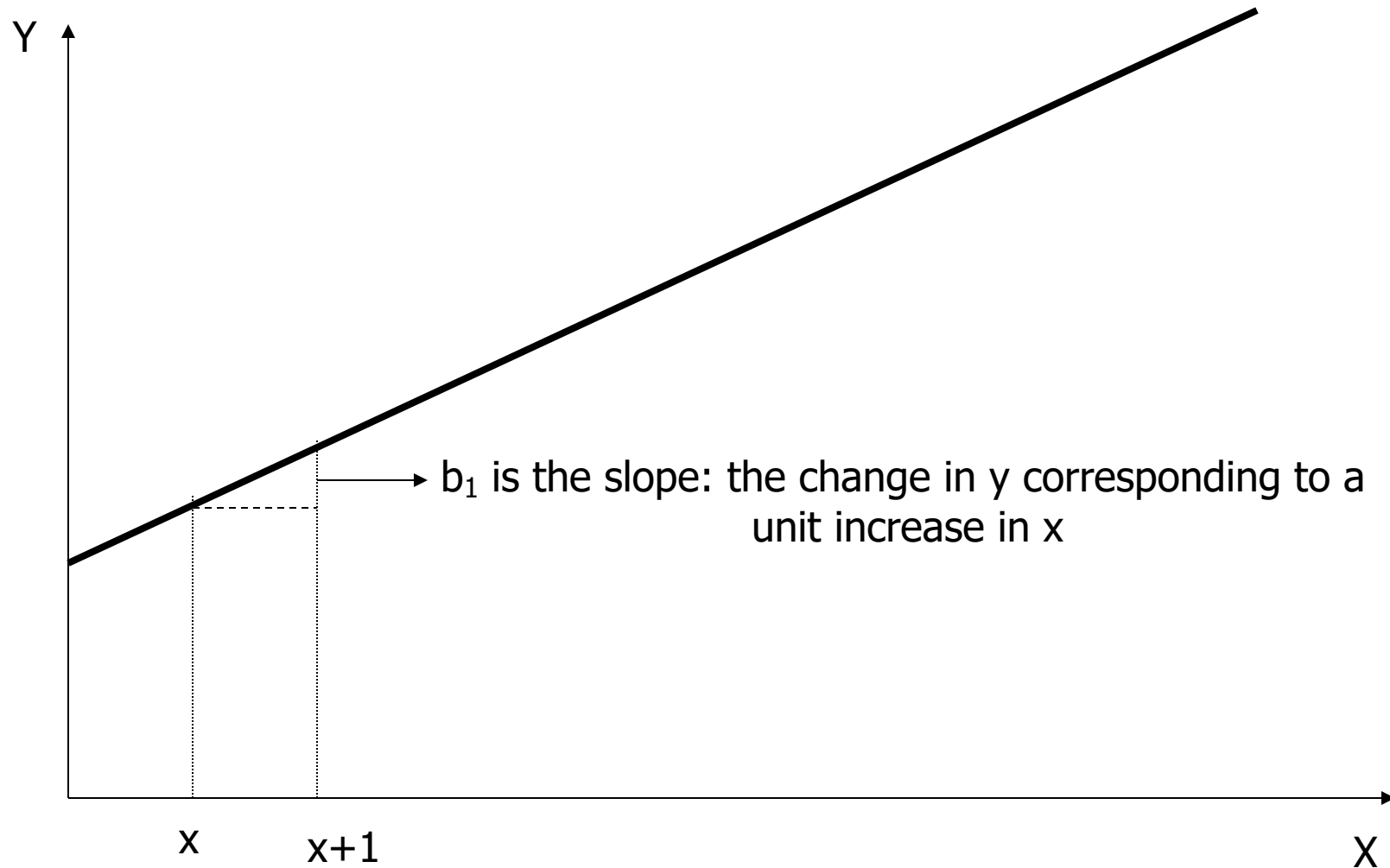
The straight line equation



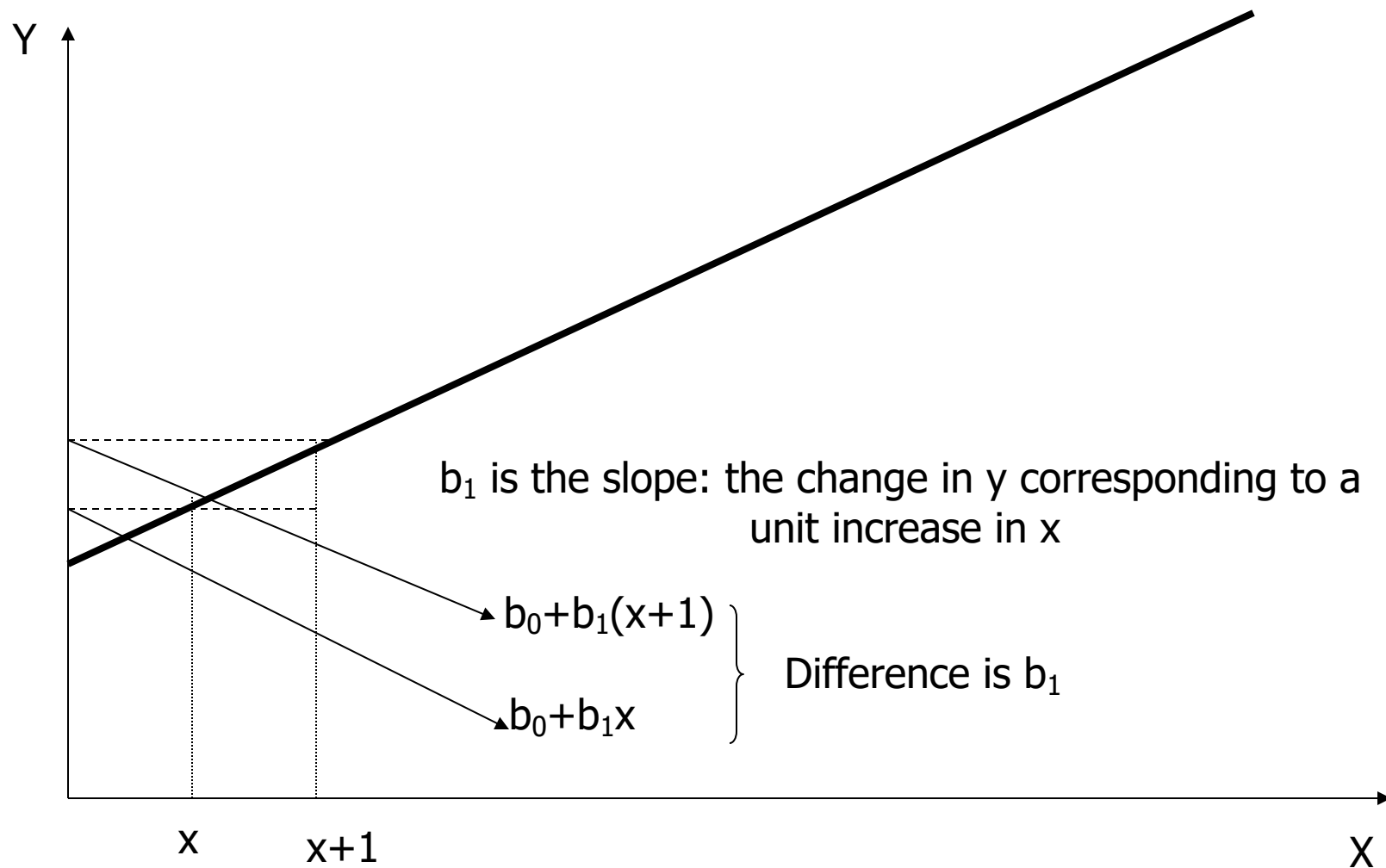
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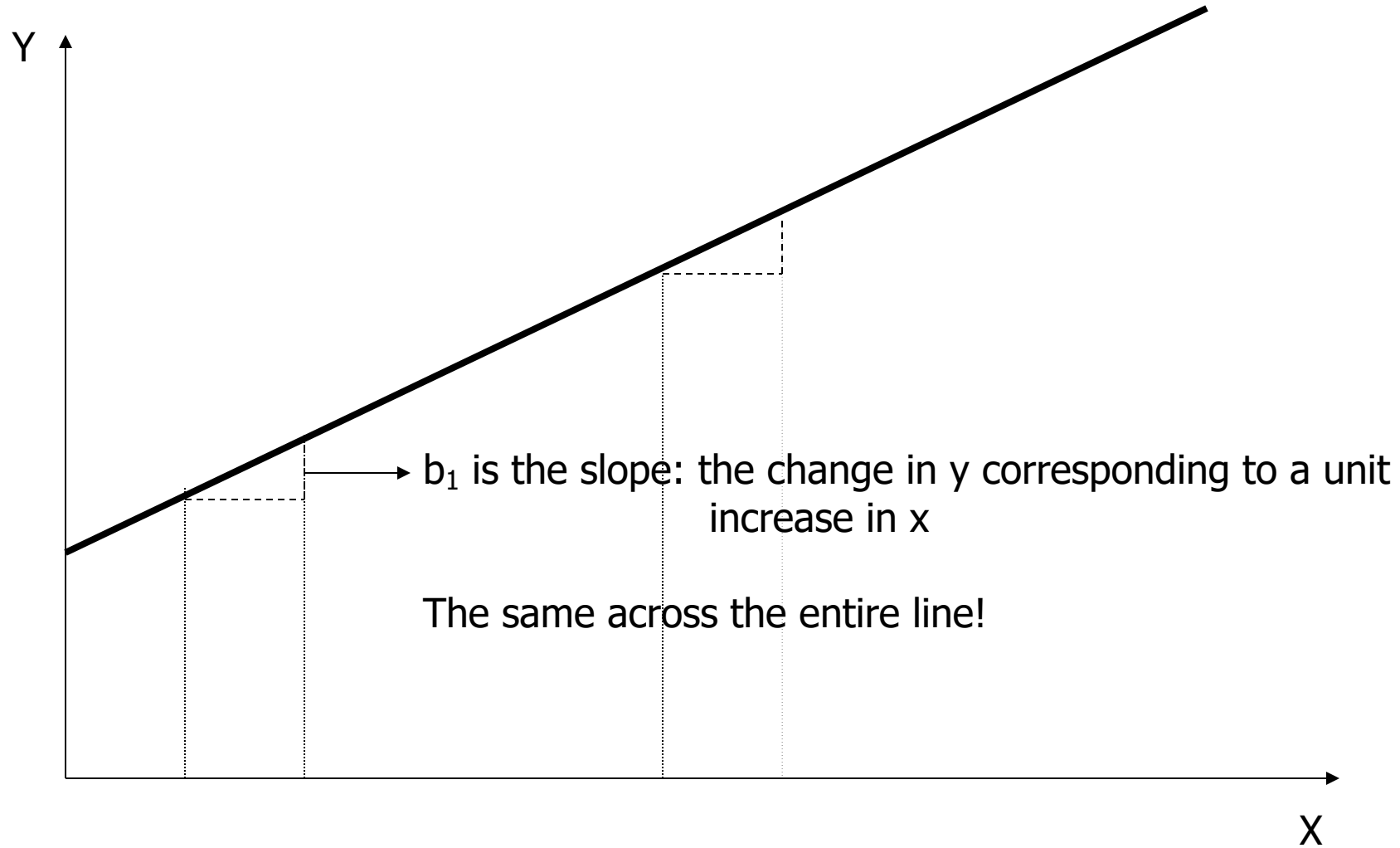
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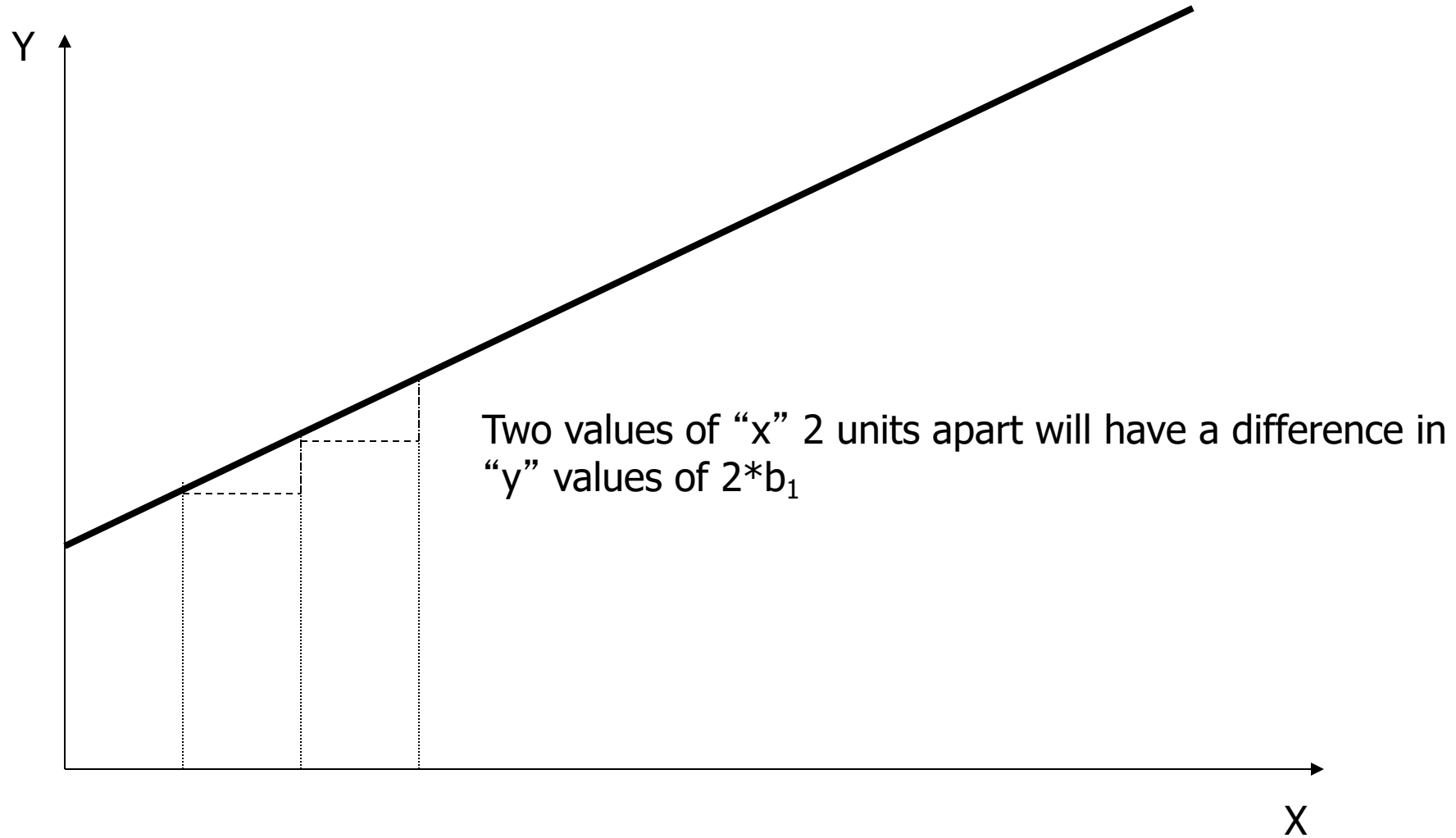
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The straight line equation

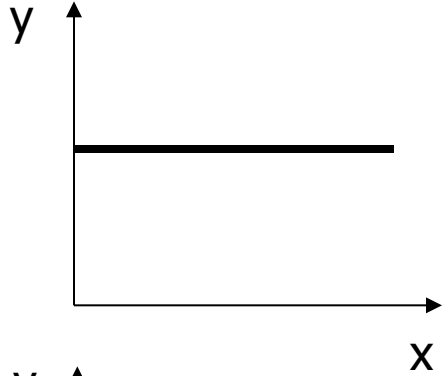




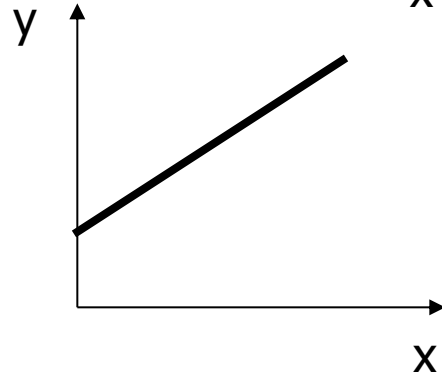
The straight line equation

- 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

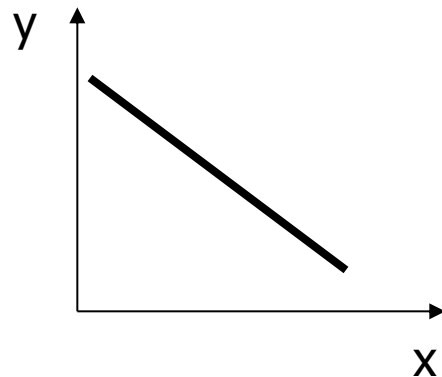
The straight line equation



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



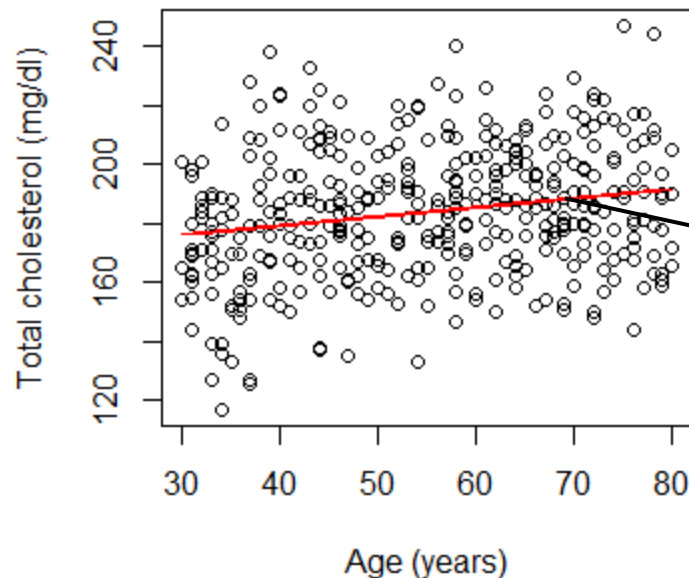
($b_1 > 0$) Positive association between x and y
(values of y increase as values of x increase)



($b_1 < 0$) 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:**

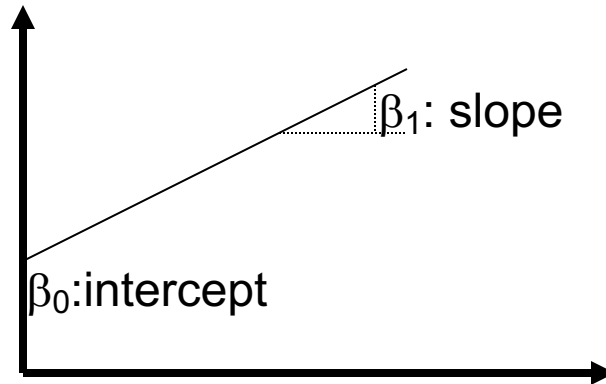
$$y = \beta_0 + \beta_1 x + \varepsilon, \quad \varepsilon \sim N(0, \sigma^2)$$

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:



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

Mean population value of Y at X=x

- Random component:

$$\text{Var}[Y | X = x] = \sigma^2$$

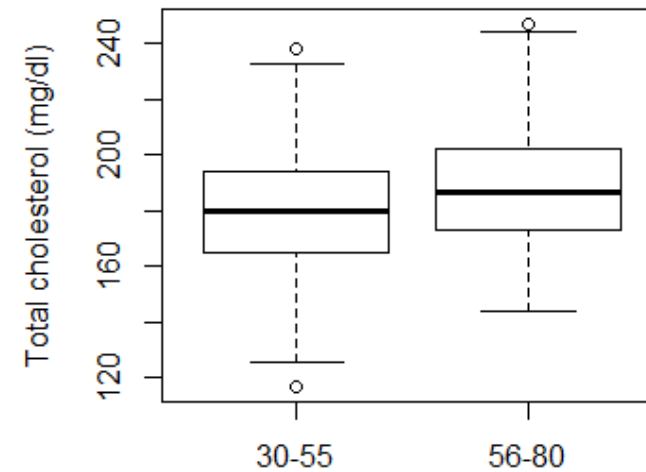
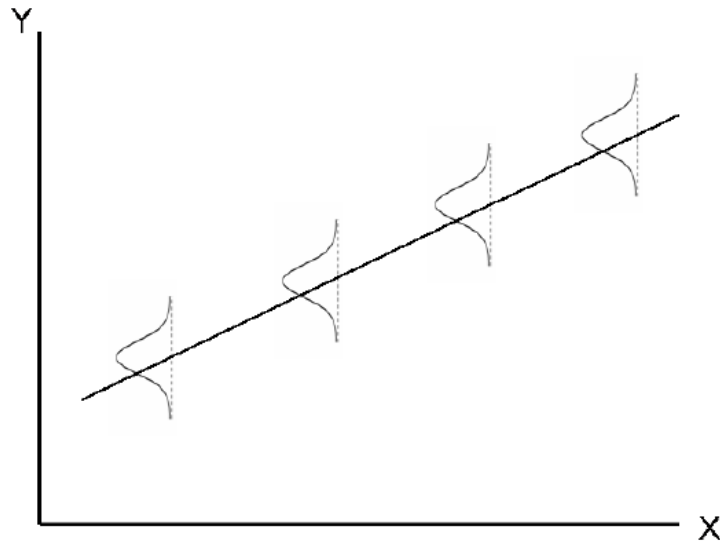
Variance does not depend on x

Simple Linear Regression: Assumptions

MODEL: $E[Y | X = x] = \beta_0 + \beta_1 x$

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

Distribution of Y at different x values:



Compare with the boxplots for two age groups



Simple Linear Regression: Interpreting model coefficients

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

- **Question:** How do you interpret β_1 ?

- **Answer:**

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

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

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

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:**

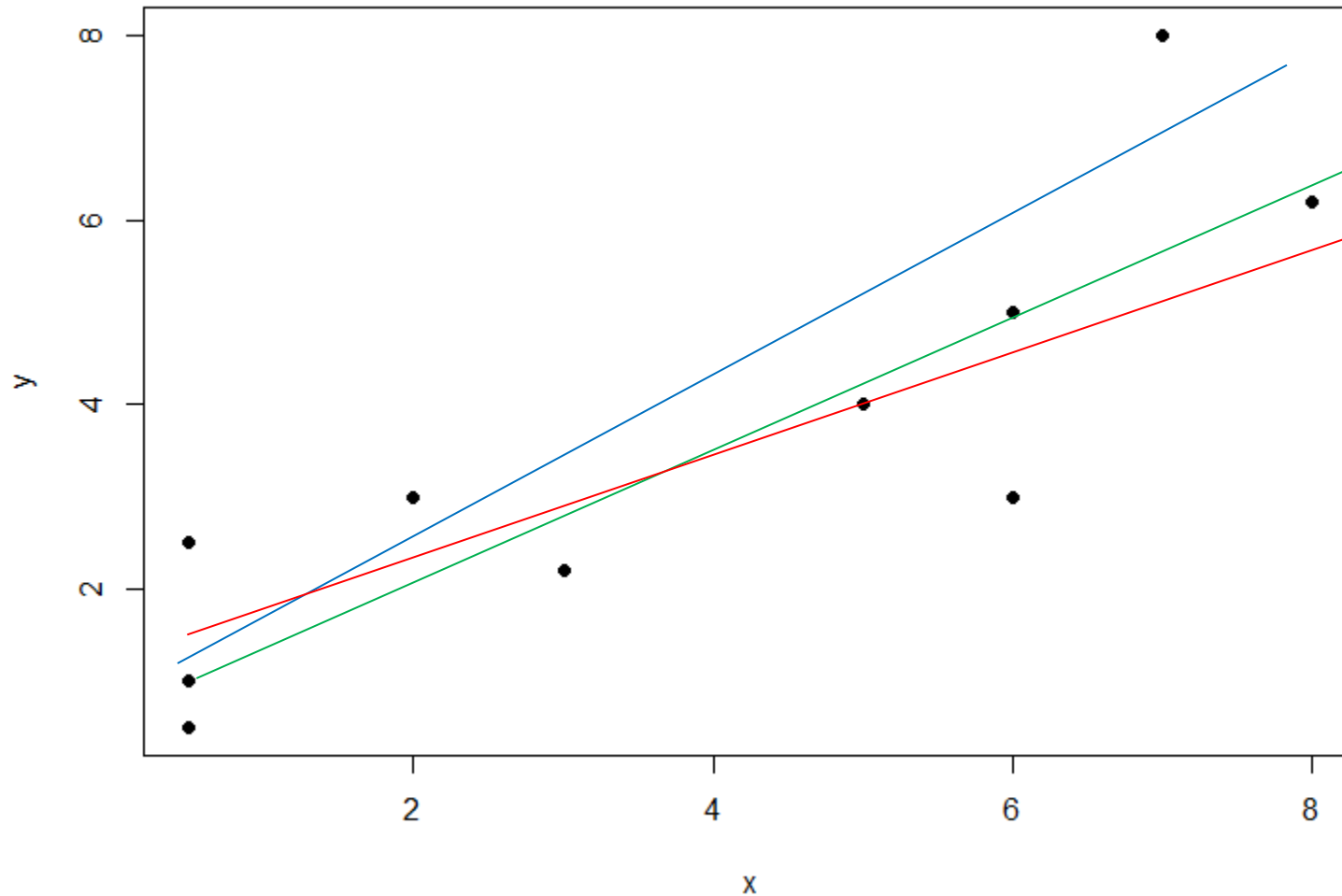


Example: Cholesterol and age

- **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

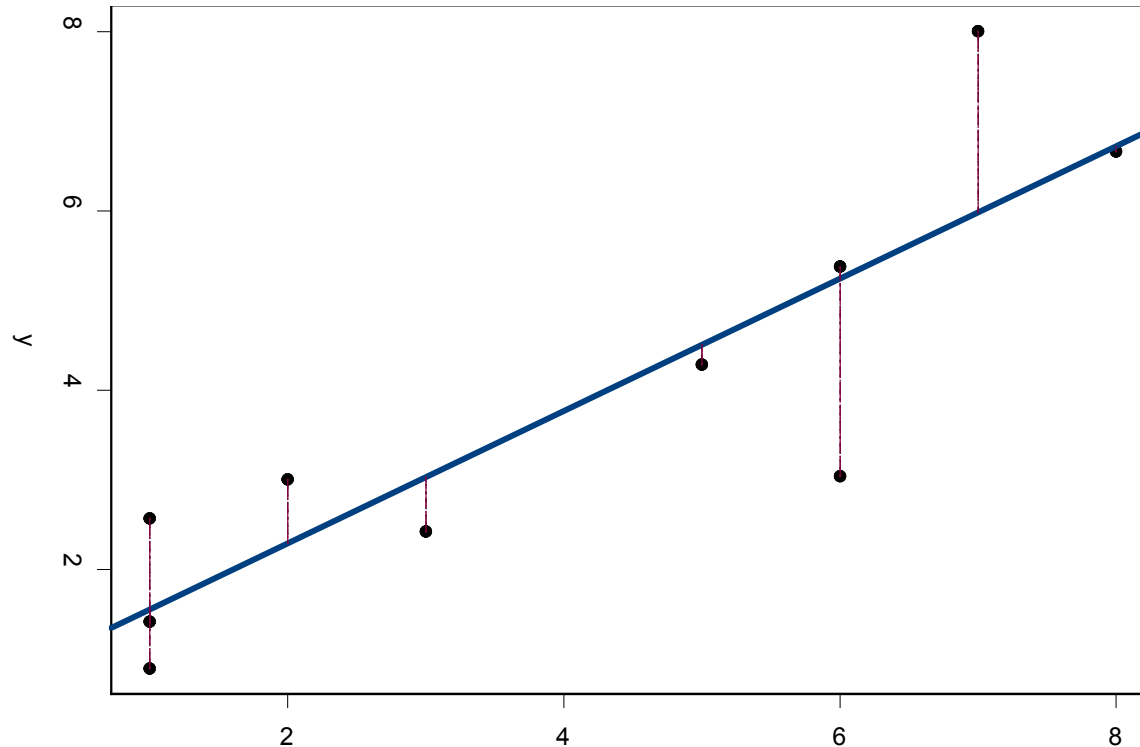
Least Squares Estimation

- 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:

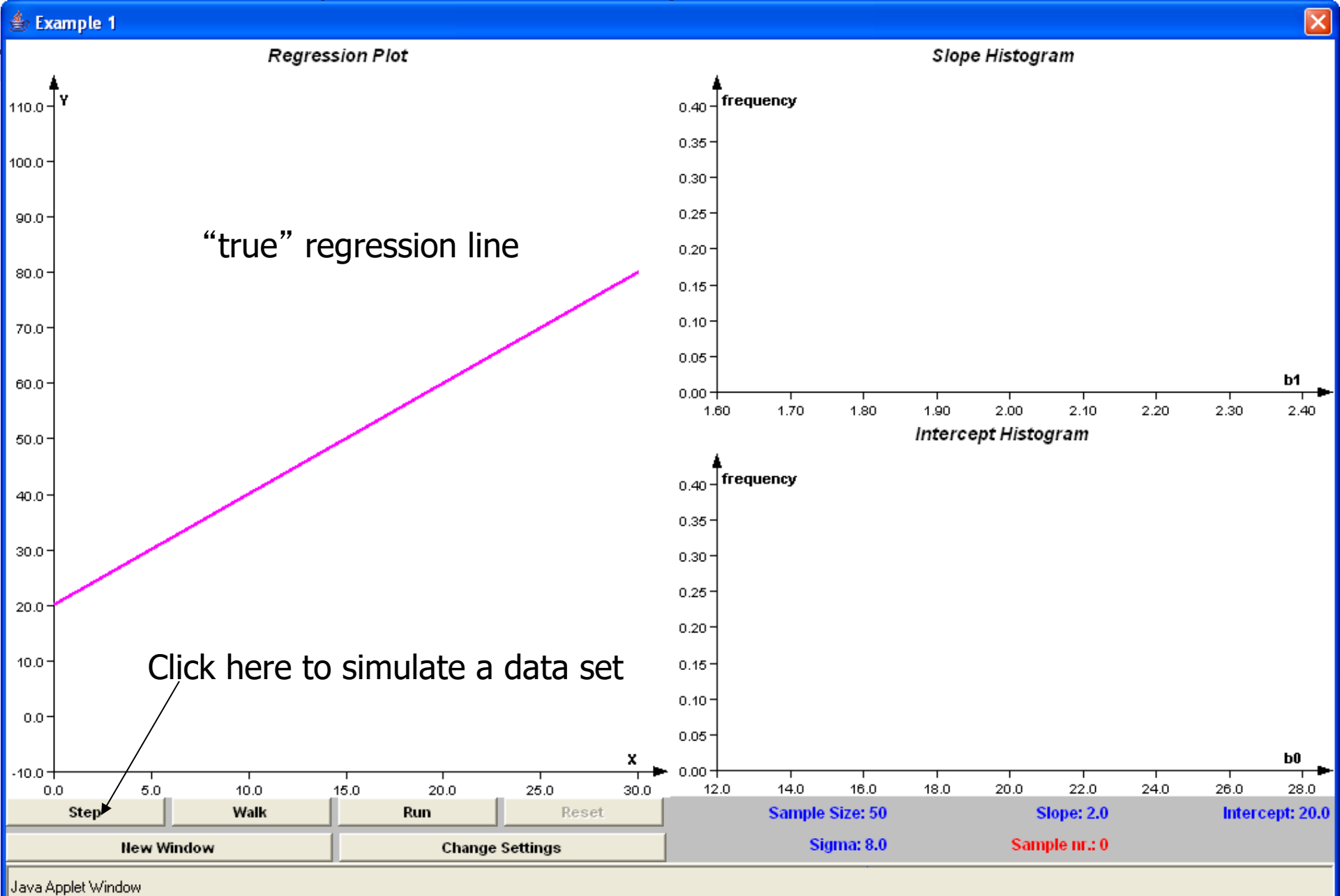
$$\hat{\sigma}^2 = \frac{\sum_{i=1}^n r_i^2}{n-2} = \frac{\sum_{i=1}^n (y_i - \hat{y}_i)^2}{n-2} = \frac{\sum_{i=1}^n (y_i - \hat{\beta}_0 - \hat{\beta}_1 x_i)^2}{n-2}$$

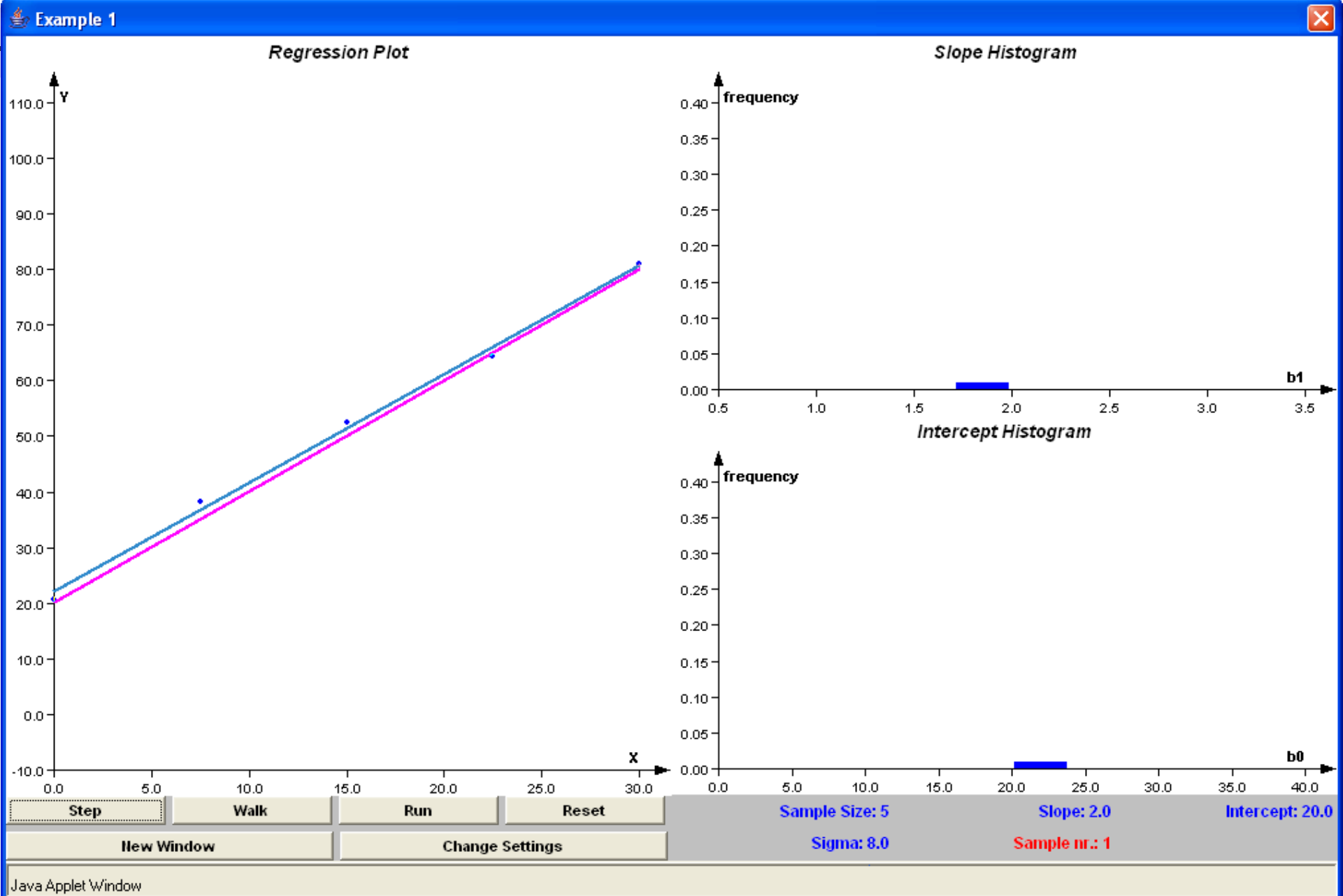


Estimated Standard Errors

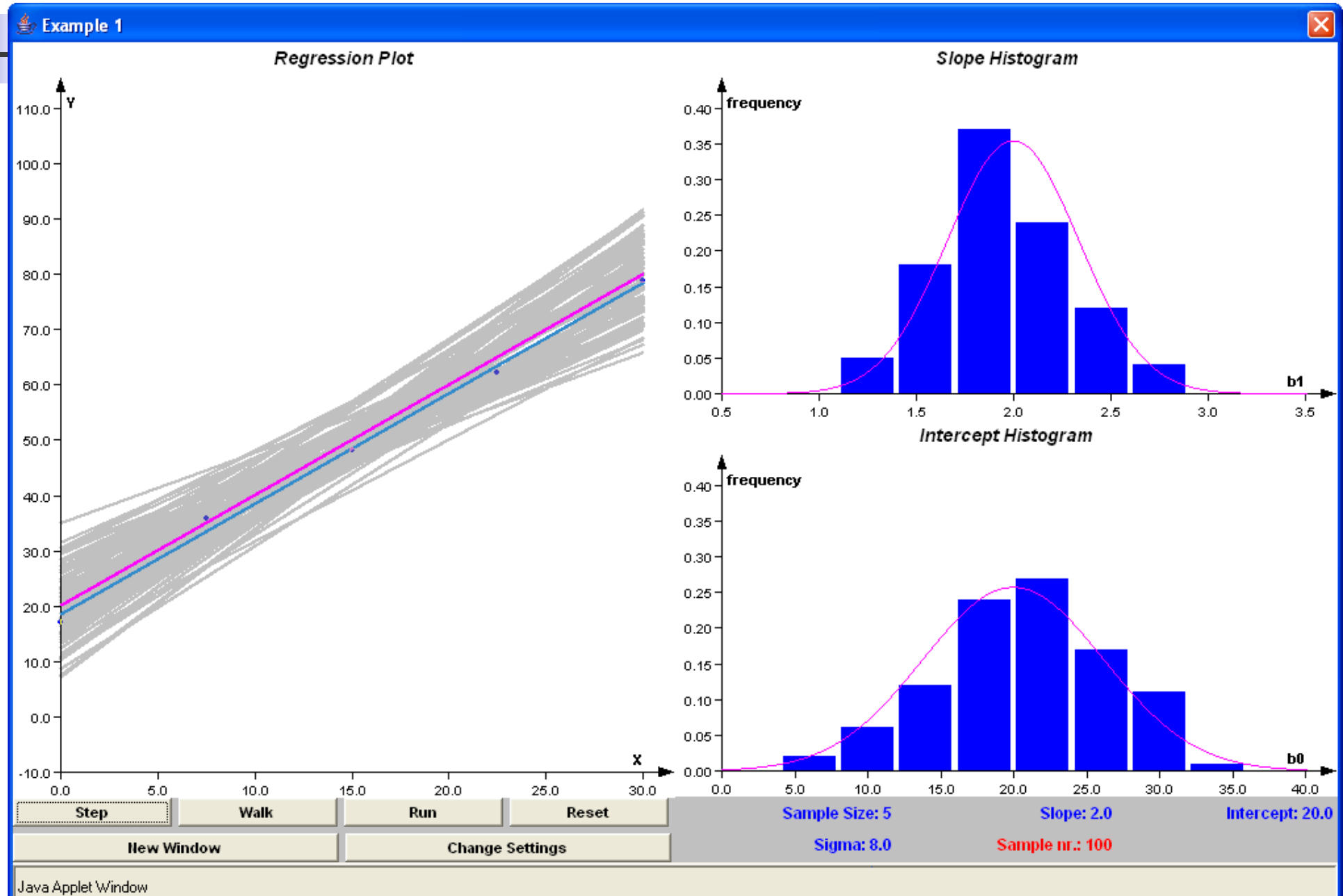
- Recall that, when estimating parameters from a sample, there will be **sampling variability** in the estimates
- This is true for regression parameter estimates
- Looking at the formulas for $\hat{\beta}_0$ and $\hat{\beta}_1$, we can see that they are just complicated means
- In repeated sampling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

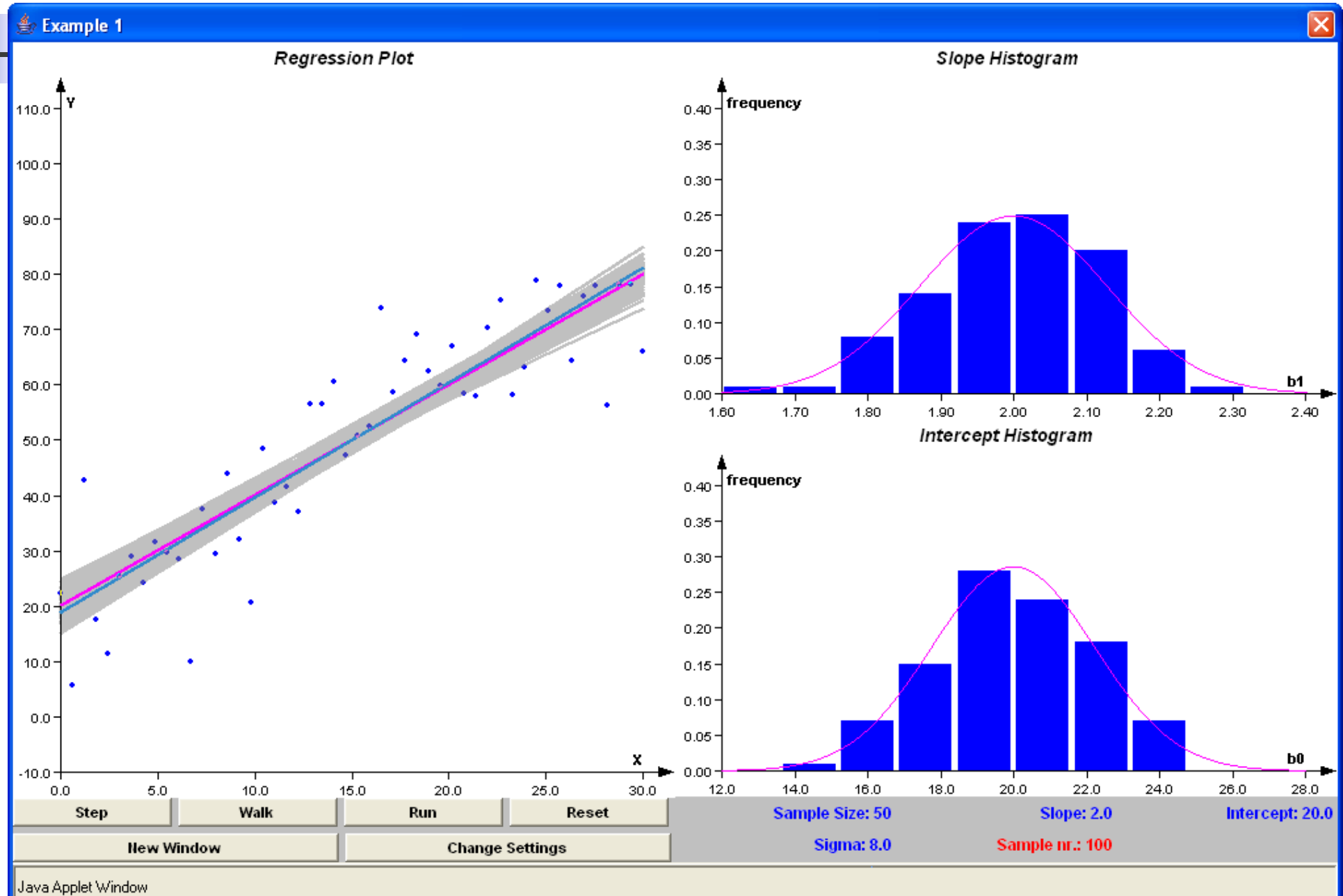




Sampling Distribution



Sampling Distribution





Inference

- About regression model parameters

- Hypothesis testing: $H_0: \beta_j = 0$ ($j=0,1$)

- Test Statistic:

- Large Samples:

$$\frac{\hat{\beta}_j - (\text{null hyp})}{se(\hat{\beta}_j)} \sim N(0,1)$$

- Small Samples:

$$\frac{\hat{\beta}_j - (\text{null hyp})}{se(\hat{\beta}_j)} \sim t_{n-2}$$

- Confidence Intervals:

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

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

Inference: Hypothesis Testing

Null Hypothesis: $\beta_j = 0$

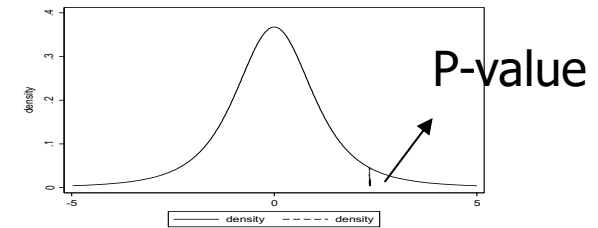
T=test statistic

Alternative

P-Value

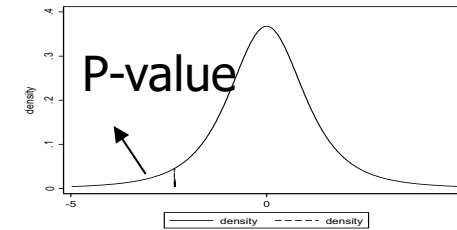
$$\beta_j > 0$$

$$P(t_{n-2} > T)$$



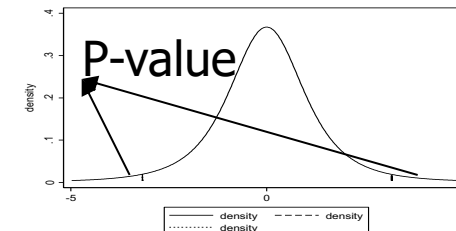
$$\beta_j < 0$$

$$P(t_{n-2} < T)$$



$$\beta_j \neq 0$$

$$2P(t_{n-2} > |T|)$$





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 %
(Intercept)	158.5171656	175.2861949
age	0.1624211	0.4582481

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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:

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

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

$\hat{\beta}_0$: 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:

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

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

- 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:

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

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- 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 value**, for any value of x_i as

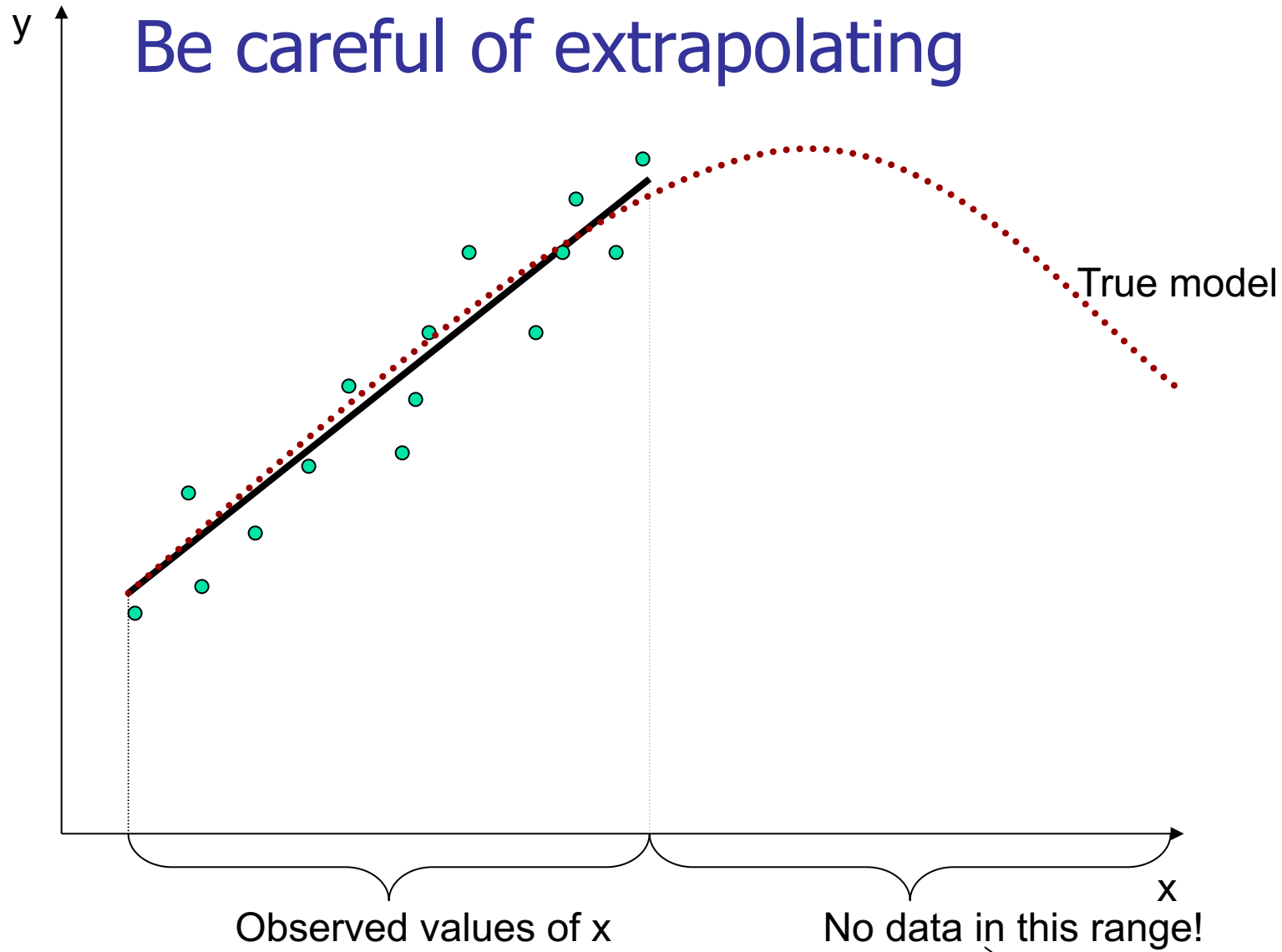
$$\hat{y}_i = \hat{\beta}_0 + \hat{\beta}_1 x_i$$

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

Be Cautious: This assumes the model is true.

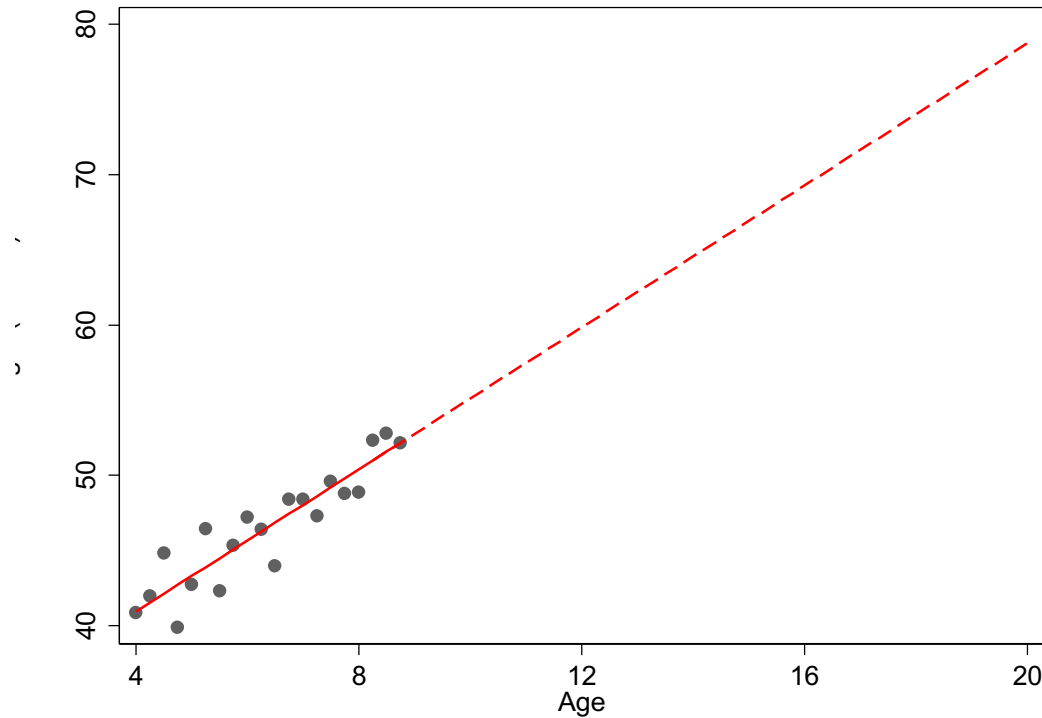
- May be a reasonable assumption within the range of your data.
- It may not be true outside the range of your data!

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

- 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 $x = 46$

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

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

- **Question:** How do our interpretations for \hat{y} and \hat{y}^* differ?



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- **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 $x = 46$

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

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

- **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 $x = 46$

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

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

- **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