

# STATISTICS WITH

INTENSIVE WORKSHOP

2024

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# WORKSHOP SCHEDULE

- 4 days
  - 1. Intro to R and data analysis
  - 2. Statistical inference & hypothesis testing
  - 3. Modeling correlation and regression
  - 4. Machine Learning; MetaboAnalyst; Power Analysis
- Each day will include:
  - Frontal class (MORNING)
  - Practical training with R about the topics discussed in the morning. (AFTERNOON)

# DAY 3 – LECTURE OUTLINE

- Testing and summarizing relationship between 2 variables (**correlation**)
  - Pearson's analysis (parametric)
    - 2 numerical variables
  - Spearman test (not parametric)
    - 2 numerical variables (non linear relationships)
- Measures of **association**
  - Chi-Square test of independence
    - 2 categorical variables
  - Fisher's Exact Test
    - alternative to the Chi-Square Test of Independence
- Introduction of **regression analysis**
  - Simple linear regression models
  - Multiple Linear Regression models

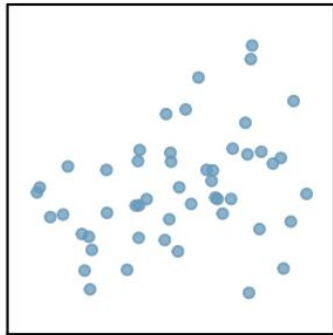
# Summarizing relationships between two variables

## Correlation

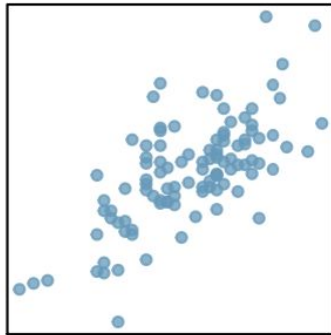
# Defining correlation

- **Correlation** is a numerical summary statistic that measures the *strength of a linear relationship* between two variables
  - denoted by **r** (correlation coefficient) which takes values **between -1 and 1**

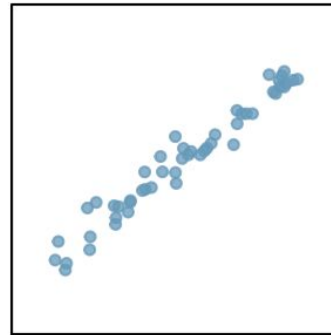
positive  
correlation



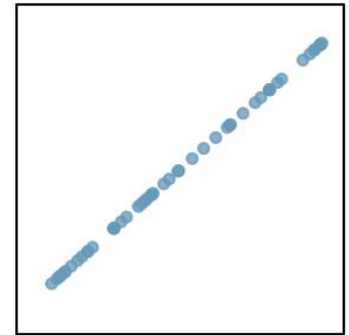
$R = 0.33$



$R = 0.69$

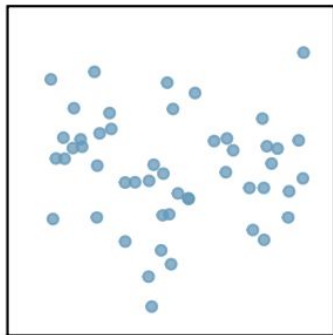


$R = 0.98$

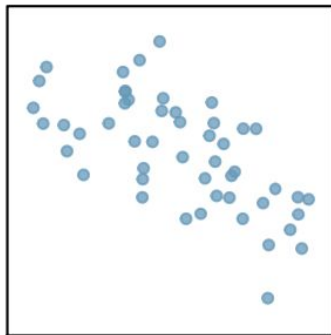


$R = 1.00$

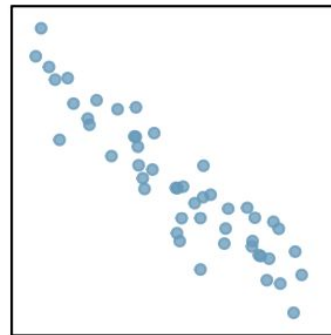
negative  
correlation



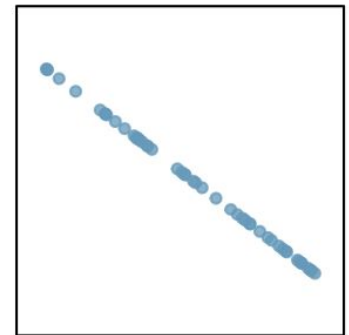
$R = -0.08$



$R = -0.64$



$R = -0.92$



$R = -1.00$

Source: Vu, J., & Harrington, D. (2021). *Introductory Statistics for the Life and Biomedical Sciences*. Retrieved from <https://www.openintro.org/book/biostat/>

# Most used measures of correlation

Correlation coefficient	Type of relationship	Levels of measurement	Data distribution
<b>Pearson's <math>r</math></b> ( for population)	Linear	Two <b>quantitative</b> (interval or <b>ratio</b> ) variables	Normal distribution
<b>Spearman's</b> ( for population)	Non-linear	Two <b>ordinal, interval or ratio</b> variables	Any distribution
<b>Cramér's <math>V</math></b> (Cramér's $\phi$ )	Non-linear	Two <b>nominal</b> variables	Any distribution
<b>Kendall's (<math>\tau</math>)</b>	Non-linear	Two <b>ordinal, interval or ratio</b> variables	Any distribution

# What is the link between correlation and covariance?

- **Covariance** is another helpful statistic that **tells whether both variables vary in the same direction** (positive covariance) **or in the opposite direction** (negative covariance)
  - Unlike in correlation, **there is no meaning of covariance numerical value only sign is useful**
  - **is**  $> 0$  --> vary in the same direction
  - **is**  $< 0$  --> vary in the opposite direction
  - **is**  $\sim 0$  --> vary independently from each other
- The general formula for **Covariance** is:
  - where  $\sigma_x$  is the standard deviation of x and  $\sigma_y$  is the standard deviation of y
  - dividing Covariance by  $\sigma_x \sigma_y$ , we obtain Correlation **r** with range  $[-1, +1]$
- Interesting to note that:

# Correlation between 2 numerical variables

Pearson's correlation (parametric test)



# Pearson's correlation

**Pearson correlation** ( $r$ ) measures a linear association between 2 CONTINUOUS variables ( $x$  and  $y$ ) or 2 dichotomous variables

- It's also known as a parametric correlation test because it depends to the distribution of the data.
- The Pearson correlation evaluates the linear relationship between two continuous variables.

## FORMULA

WHERE:

$x$  and  $y$  are two vectors of length  $n$

$\bar{x}$  and  $\bar{y}$  correspond to the means of  $x$  and  $y$ , respectively.

We can test the statistical significance of the correlation statistic as well.

The p-value (significance level) of the correlation can be determined by calculating

with

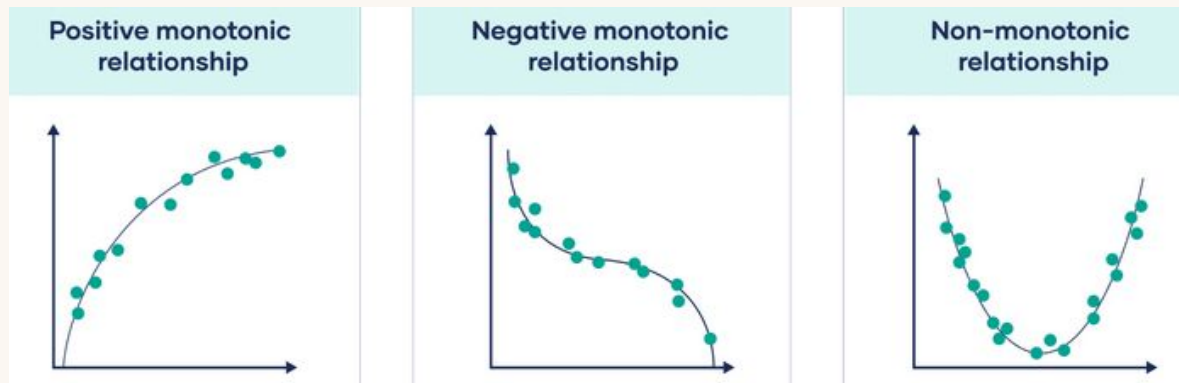
# Correlation between 2 numerical variables

Spearman's correlation (non parametric test)

# Spearman's rank order correlation coefficient

Spearman's correlation ( or ) is a **nonparametric alternative to Pearson's correlation**, used for

- continuous data with a **non linear, monotonic** relationships, or
- **ordinal** data (e.g. Likert scale survey questions: *strongly agree, agree, etc.*)



## FORMULA

- where:
  - is Spearman's coefficient of rank correlation.
  - is the difference between the ranks for each pair.
  - is the number of paired observations.

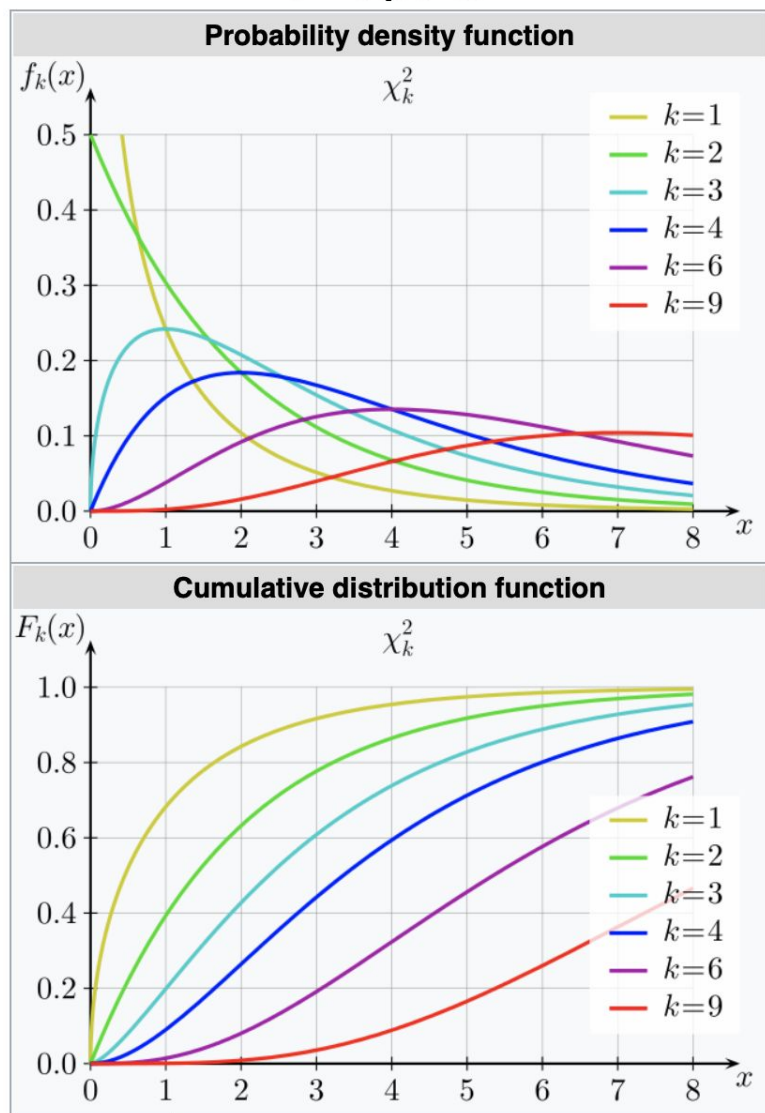
Hypothesis Test: Rank Correlation

# Chi Squared Distributions

A widely used analytical tool

# The chi-squared distribution

## chi-squared



- The **chi-squared distribution** () is a family of continuous probability distributions
- It results from the sum of squares of  $k$  normally distributed random variables, where  $k$  is the number of degrees of freedom ( $df$ )
- The **mean** is equal to the  $df$  and the **variance** is equal to  $2 \times df$

<b>Notation</b>	$\chi^2(k)$ or $\chi_k^2$
<b>Parameters</b>	$k \in \mathbb{N}^*$ (known as "degrees of freedom")
<b>Support</b>	$x \in (0, +\infty)$ if $k = 1$ , otherwise $x \in [0, +\infty)$
<b>PDF</b>	$\frac{1}{2^{k/2} \Gamma(k/2)} x^{k/2-1} e^{-x/2}$
<b>CDF</b>	$\frac{1}{\Gamma(k/2)} \gamma\left(\frac{k}{2}, \frac{x}{2}\right)$
<b>Mean</b>	$k$
<b>Median</b>	$\approx k \left(1 - \frac{2}{9k}\right)^3$
<b>Mode</b>	$\max(k - 2, 0)$
<b>Variance</b>	$2k$

# Applications of the Chi-Square Test

- Unlike the **Normal distribution**, very few real-world observations follow a **chi-square distribution**, but it is used extensively in hypothesis testing (also due to its close relationship with the normal).
  - As **k** increases, the distribution looks more and more similar to a normal distribution
- The **Chi-square test** helps to answer the following questions:
  - 1. Independence test**
    - Are two categorical variables independent of each other?
      - for example, does gender have an impact on whether a person has a Netflix subscription or not?
  - 2. Distribution (or Goodness of fit) test**
    - Are the observed values of two categorical variables equal to the expected values?
      - One question could be, is one of the three video streaming services Netflix, Amazon, and Disney subscribed to above average?
  - 3. Homogeneity test**
    - Are two or more samples from the same population?
      - One question could be whether the subscription frequencies of the three video streaming services Netflix, Amazon and Disney differ in different age groups.

# Correlation between 2 categorical variables

Chi Squared test of independence

# A useful tool for categorical variables: contingency tables

- A **contingency table** summarizes data for 2 categorical variables (each value in the table representing the times a particular combination of outcomes occurs)
- Below we see 2 categorical variables “**gender**” (male, female) and “**has Netflix subscription**” (yes, no)

Frequency			SUM
	Male	Female	
Netflix yes	10	13	<b>23</b>
Netflix no	15	14	<b>29</b>
<b>SUM</b>	<b>25</b>	<b>27</b>	

- The **row totals** (counts across each row) and the **column totals** (counts across each column) are the **marginal totals**
- Frequencies can also be shown as proportions



# Computing the Chi-Square Test of Independence

- E.g. suppose we are testing the independence of the two categorical variables “**gender**” (male, female) and “**has Netflix subscription**” (yes, no)
- The test performs a **comparison** of these two contingency tables:

<u>Observed</u> Frequency		
	Male	Female
Netflix yes	10	13
Netflix no	15	14

<u>Expected</u> Frequency		
	Male	Female
Netflix yes	$(23 \times 25) / 52 = 11.06$	$(23 \times 27) / 52 = 11.94$
Netflix no	$(29 \times 25) / 52 = 13.94$	$(29 \times 27) / 52 = 15.06$

## IMPORTANT ASSUMPTIONS TO NOTICE:

- The assumption for the **chi-squared ()** test statistic is that the expected frequencies per cell are  $> 5$
- The **chi-squared ()** test uses only the categories but NOT rankings

# Computing the Chi-Square Test of Independence (computation)

- Let's compute the example for the two variables “gender” and “has Netflix subscription”

Observed Frequency		
	Male	Female
Netflix yes	10	13
Netflix no	15	14

Expected Frequency		
	Male	Female
Netflix yes	$(23 \times 25) / 52 = 11.06$	$(23 \times 27) / 52 = 11.94$
Netflix no	$(29 \times 25) / 52 = 13.94$	$(29 \times 27) / 52 = 15.06$

- The **chi-squared ()** test statistic is calculated via:
- where:
  - observed frequency and
  - Expected frequency**
    - calculated for each cell in the contingency table
- The test assumptions are:
  - $H_0$ : (null hypothesis) The two variables are independent.
  - $H_1$ : (alternative hypothesis) The two variables are not independent. (i.e. they are associated)
  -

# Interpreting the Chi-Square Test of Independence

- The **chi-squared ()** test statistic calculated value:
- BY THE CRITICAL REGION: Looking at the distribution, for a significance level of 5% and a *df* of 1, the **critical chi-squared value = 3.841**
  - → Since the **calculated chi-squared value=0.35** is smaller, we **FAIL TO REJECT the null** ( $H_0$ : *The two categorical variables are independent*)
- BY THE p VALUE: Also, the **p-value** associated to the and is **0.5541**.
  - → Since this p-value is not less than 0.05, we fail to reject the null hypothesis.
- This means we do not have sufficient evidence to say that there is an association between gender and political having a Netflix account!

# Chi Squared test (another application)

Goodness of Fit Test for one categorical variable

# Chi-Square Goodness of Fit Test

- GOAL: a Chi-Square goodness of fit test is used to **determine whether or not a categorical variable follows a hypothesized distribution.**
  - With **high** goodness of fit, the values expected based on the model are **close to** the observed values
  - With **low** goodness of fit, the values expected based on the model are **far from** the observed values
- EXAMPLES OF APPLICATION:
  - *Is this sample drawn from a population with 90% right-handed and 10% left-handed people?*
  - *Do offspring have with an equal probability of inheriting all possible genotypic combinations (i.e., unlinked genes)?*
- HYPOTHESIS FORMULATION
  - Null Hypothesis ( $H_0$ ): The population follows the specified distribution.
  - Alternative Hypothesis ( $H_a$ ): The population does not follow the specified distribution.

# Chi-Square Goodness of Fit Test (computation)

- FORMULA: The formula is essentially the same as in the independence test
- where  $O_i$  = Observed Frequencies and  $E_i$  = Expected Frequencies
- ... with  $k$  (number of groups minus 1)
- WHEN SHOULD WE USE IT? (assumptions)
  1. We are testing the distribution of **one categorical variable**
    - if you have a continuous variable, it should be converted to categorical (this is called *data binning*) or a different test can be used (like the Kolmogorov–Smirnov goodness of fit test for continuous variables)
  2. The sample was randomly selected from the population.
  3. There are a minimum of 5 observations expected in each group.

# Chi-Square Goodness of Fit Test (example)

- GOAL: examine the appropriateness of hypothesized distribution for a dataset
- CASE: In the FAMuSS study (we'll see later in the lab) volunteers were observed at a university, so we test if their distribution by categorical variable **race** is the same as (i.e. *representative of*) the general US population?

Race	African.American	Asian	Caucasian	Other	Total
FAMuSS (Observed)	27	55	467	46	595
US Census (Expected)	76.16	5.95	478.38	34.51	595

- where  $O_i$  = Observed Frequencies and  $E_i$  = Expected Frequencies
- ... with  $k$  (number of groups minus 1)
- The  $\chi^2$  statistic is extremely large, and the associated p-value  $< 0.001 \rightarrow$
- We **reject the null hypothesis** (= the sample proportions should equal the population proportions)... in fact, we can see for example the higher Asian representation in sample

# Correlation between 2 categorical variables - Fisher's Exact Test

(alternative to the Chi-Square Test of  
Independence)



# Fisher's Exact Test

- Fisher's Exact Test is used to determine whether or not there is a significant association between two categorical variables.
- It is typically used as an alternative to the Chi-Square Test of Independence when one or more of the cell counts in a 2×2 table is less than 5.
- Fisher's Exact Test uses the following null and alternative hypotheses:
  - $H_0$ : (null hypothesis) The two variables are independent.
  - $H_1$ : (alternative hypothesis) The two variables are not independent.

# Calculate **effect size** after a Chi-Square Test

3 alternatives to assess “strength” of the association (if any)

# Three Ways to Calculate Effect Size for a Chi-Square Test

- So, we have seen 2 commonly used **Chi-Square tests**:
  - **Chi-Square Test for Independence**: Used to determine whether or not there is a significant association between two categorical variables from a single population.
  - **Chi-Square Test for Goodness of Fit**: Used to determine whether or not a categorical variable follows a hypothesized distribution
- For both of these tests, we obtain a **p-value** that tells us “if” an association is found (i.e. we should reject the null hypothesis of the test or not).
- Then, we may wonder about the **effect size** of the test (i.e. “how strong” an association is)
- There are 3 ways to measure **effect size**:
  1. **Phi** ( $\phi$ )
    - for 2 x 2 contingency table
  2. **odds ratio** (OR)
    - for 2 x 2 contingency table
  3. **Cramer's V** (V)
    - for larger tables
      - example in lab

# Correlation between... 1 numerical variable and 1 categorical variables

... we have actually met before 🤔

# Correlation between 1 numerical variable and 1 categorical variables

- Recall that we have already encountered methods for comparing **numerical** data across groups in the previous lessons
  1. Using **side-by-side boxplots** for visual comparison of how the distribution of a numerical variable differs by category
  2. Using **One-Way ANOVA** for testing relationships between Numerical and Categorical variables
    - i.e. the extension of the t-test for more than 2 groups

# When and why do Regression Analysis?

- Regression the most widely used method of comparison in data analysis. It can be specified as:
  1. **Simple Regression Analysis** uncovers mean-dependence between 2 variables
  2. **Multiple Regression Analysis** involves more variables
- Regression is a method used for different purposes:
  1. In **CAUSAL ANALYSIS**: to uncover the effect of one variable on another variable
  2. In **PREDICTIVE ANALYSIS** : to assess what to expect of a variable for various values of another variable

*...more on this distinction coming up in Lecture #?*

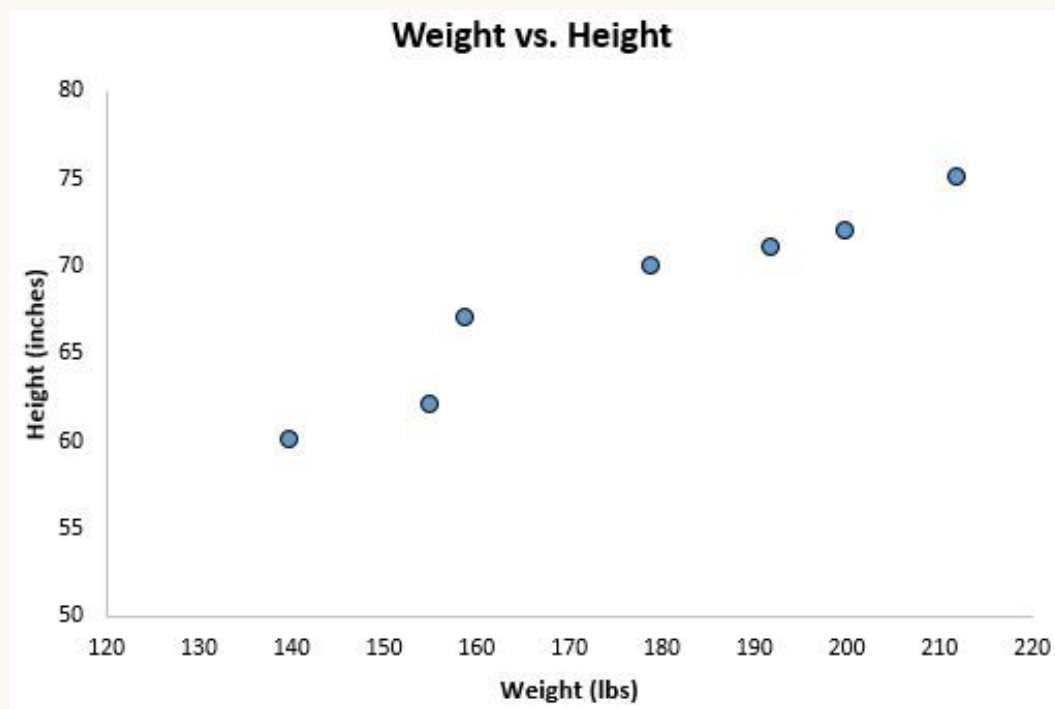
# Simple Linear Regression

Regression analysis is a widely used method for **prediction** and – *given the proper experimental conditions* – for **causal explanation**

# Simple linear regression: example

- Regression models are highly valuable, as they are one of the most common ways to make inferences and predictions
- Linear regression is OK with data that exhibit linear or approximately linear relationships
- **Simple linear regression** is a statistical method you can use to understand the relationship between two variables, (the **predictor variable**) and (the **response variable**)

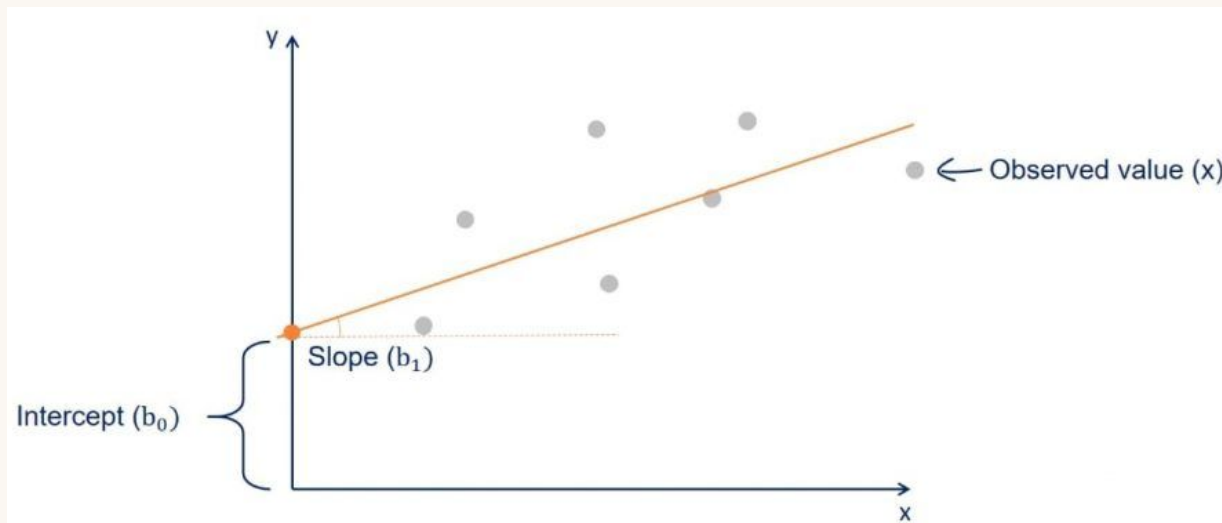
Weight (lbs)	Height (inches)
140	60
155	62
159	67
179	70
192	71
200	72
212	75





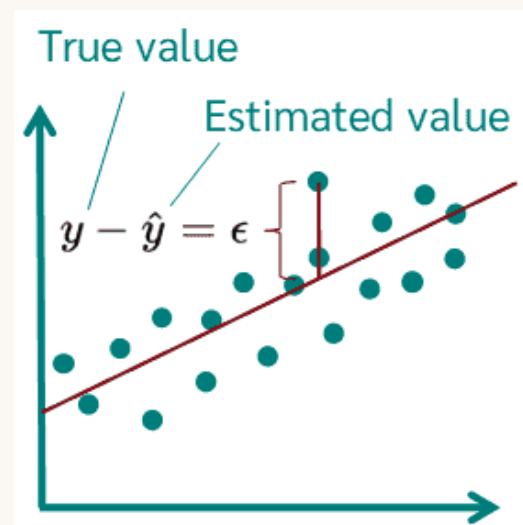
# Functional (linear) relationship and regression

- The **correlation coefficient** gave us information about the degree to which points (corresponding to  $x$  and  $y$  pairs) were clustered around a straight line ... but nothing about the **slope** of that line
- **regression analysis**, instead, provides this kind of information:
  - we want to know exactly how those 2 variables are related
  - (given we hypothesized a linear relationship) the model has a **functional form** that provides an **intercept** and a **slope**:



# Linear regression (Ordinary Least Square)

- The **OLS regression line** is chosen as to minimize the difference between estimated values and actual ones
  - in fact, OLS seeks the minimum sum of squared distances between each point and the regression line
  - it is the “best fitting” line given any data of points
- **NOTE:** like with previous **inferential statistics methods**, we are making statements on the **population** of interest based on some **sample** data available



Population data of interest	<u>Sample data we have</u>
= <b>true</b> Y values (dependent/response variable)	= <b>estimated</b> (or predicted) Y values based on X values
= <b>true</b> X values (independent/explanatory variable)	= <b>sample</b> X values
= <b>true</b> intercept	= <b>estimated</b> intercept
= <b>true</b> slope/coefficient on x	= <b>estimated</b> slope/coefficient on x
= <b>true</b> residual or unobserved part of y	= <b>estimated</b> residual (error), or unobserved part of Y

# OLS Linear regression interpretation

- The formula for the line of best fit is written as:
$$\hat{y} = \beta_0 + \beta_1 x$$
  - where  $\hat{y}$  is the predicted value of the response variable (**height**),  $\beta_0$  is the **y-intercept**,  $\beta_1$  is the **regression coefficient**, and  $x$  is the value of the predictor variable (**weight**).
- For example, in the case of :
$$\hat{y} = 32.7830 + 0.2001x$$
  - $\beta_0 = 32.7830$ . This means **when the predictor variable **weight** is 0 pounds, the predicted **height** is 32.7830 inches.**
    - Sometimes the value for  $\beta_0$  can be useful to know, but not in this specific example
  - $\beta_1 = 0.2001$ . This means that for a **one unit increase in the variable, the variable is predicted to increase(decrease) by 0.2001 units.** Here, a one pound increase in **weight** is associated with a 0.2001 inch increase in (**expected height**), on average.
    - NOTE: just like with previous hypothesis testing on sample means etc., we are testing the coefficients ( $\beta_0$  and  $\beta_1$ ) for statistical significance under  $H_0$ : the coefficient = 0

# Assumptions of linear regression

- For the results of a linear regression model to be valid and reliable, we need to check that the following four assumptions are met:
  1. **Linear relationship:** There exists a linear relationship between the independent variable,  $x$ , and the dependent variable,  $y$
  2. **Normality:** The residuals of the model are normally distributed.
    - Check normality (OF RESIDUALS) with the known methods (QQplot, Shapiro-Wilk, Kolmogorov Smirnov)
  3. **Homoscedasticity:** The residuals have constant variance at every level of  $x$ .
  4. **Independence:** The residuals are independent. In particular, there is no correlation between consecutive residuals in time series data.
    - This is mostly relevant when working with time series data. Ideally, we don't want there to be a pattern among consecutive residuals.

# Diagnostic plotting: residuals

A **residual** is the vertical distance between a data point and the regression line.  $y_i - \hat{y}_i$

- $y_i$ : The **actual response** value for the  $i$ th observation
- $\hat{y}_i$ : The **predicted response** value based on the multiple linear regression model

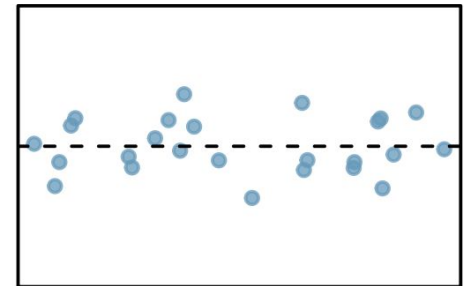
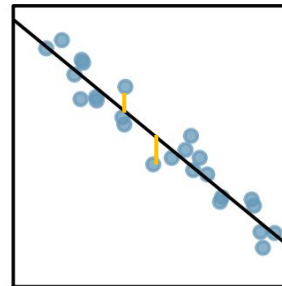
*We want to see a residual plot where data shows random scatter above and below the horizontal line*

In the example on the right:

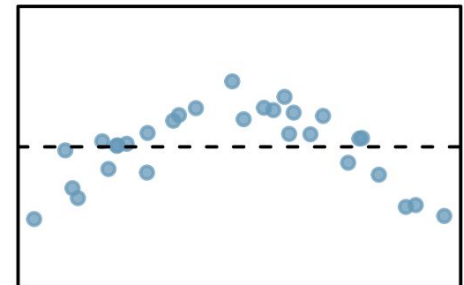
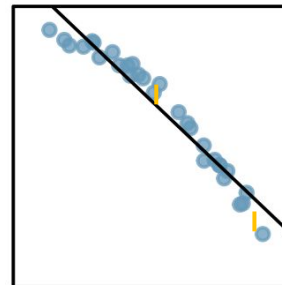
- **Case 1)** linear model is a **particularly good fit!**
- **Case 2)** the original data cycles below and above the regression line
- **Case 3)** the variability of the residuals is not constant; the residuals are slightly more variable for larger predicted values.

Best fitting  
line

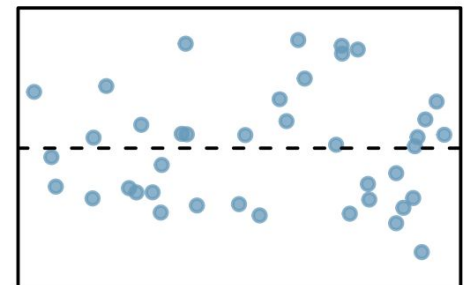
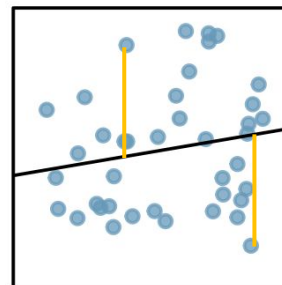
(corresponding)  
Residual plots



1



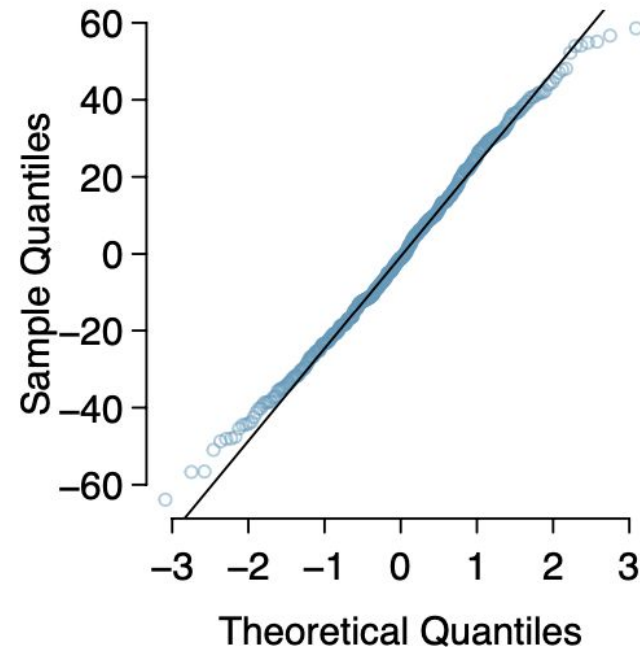
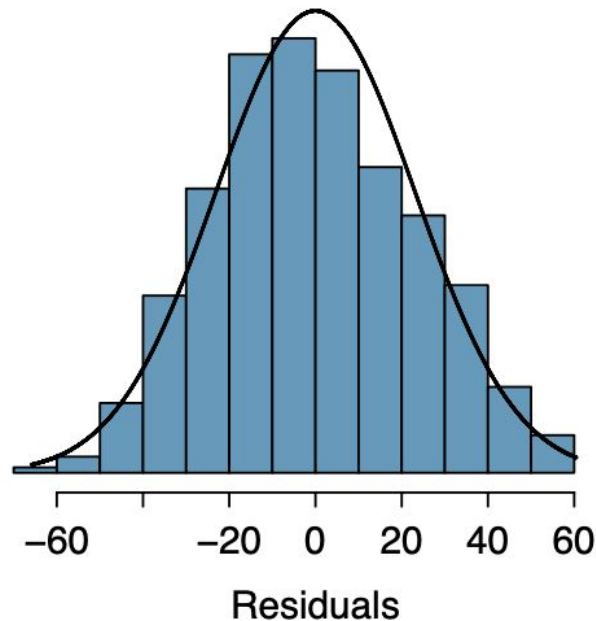
2



3

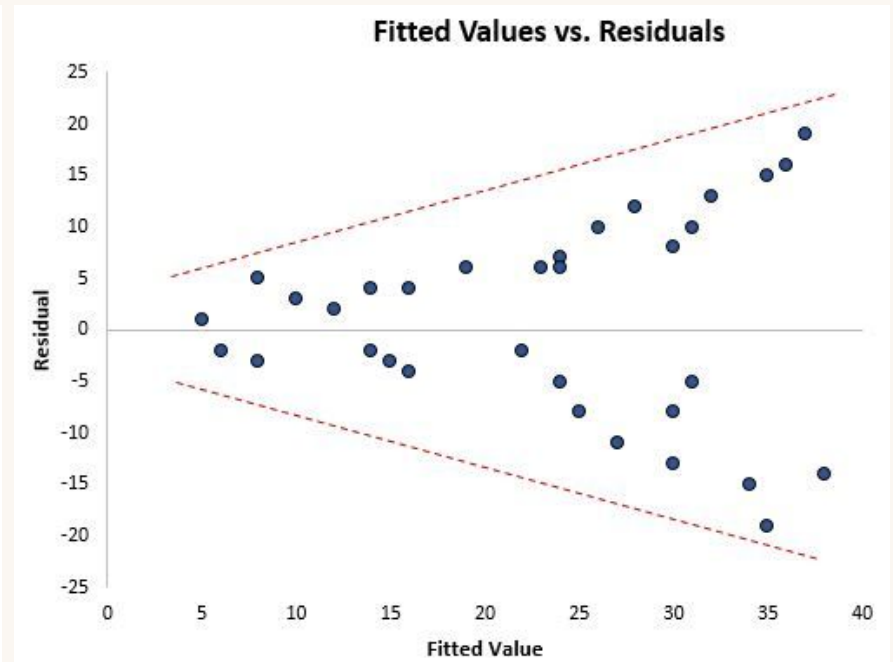
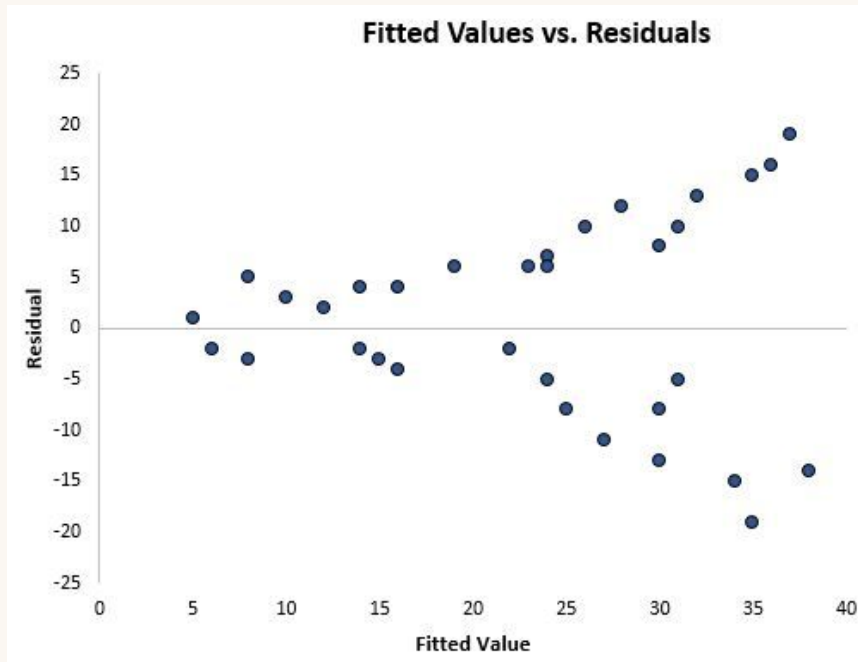
# Diagnostic plotting: normality of residuals

- The residuals of the model are normally distributed.
- Check normality (OF RESIDUALS) with the known methods (QQplot, Shapiro-Wilk, Kolmogorov Smirnov)



# Diagnostic plotting: Homoscedasticity

- ASSUMPTION: The residuals (i.e. the error term) have constant variance at every level of  $x$  (“homoscedasticity”)
- When this is not true, the results of the regression model might be unreliable
- This assumption can be verified by:
  - the “Residual vs. Fitted” plot
  - the Breusch-Pagan Test or the White Test



# The Coefficient of Determination or “R Squared” ( $R^2$ )

- One way to measure how well the least squares regression line “fits” the data is using the **coefficient of determination**, denoted as  $R^2$ .
- $R^2$  is the proportion of the variance in the response variable that can be explained by the predictor variable.
- $R^2$  can range **from 0 to 1**.
  - A **value close to 0** indicates that data is very **spread around the regression line** (this doesn't necessarily mean that the model is a bad fit, rather that the data is naturally noisy)
  - A **value close to 1** indicates that the response variable can be perfectly explained without error by the predictor variable.
- For example, an  $R^2$  of 0.2 indicates that 20% of the variance in the response variable can be explained by the predictor variable; an  $R^2$  of 0.77 indicates that 77% of the variance in the response variable can be explained by the predictor variable
- **BEWARE OF MISINTERPRETATION:** measures variability around a regression line... it **doesn't tell if the model is a good fit or even reasonable !!**
  - To assess the performance of linear models,  $R^2$  must be considered along with other measures (e.g. the Residual Standard Error or the significance level of the regression)



# Multiple Linear Regression

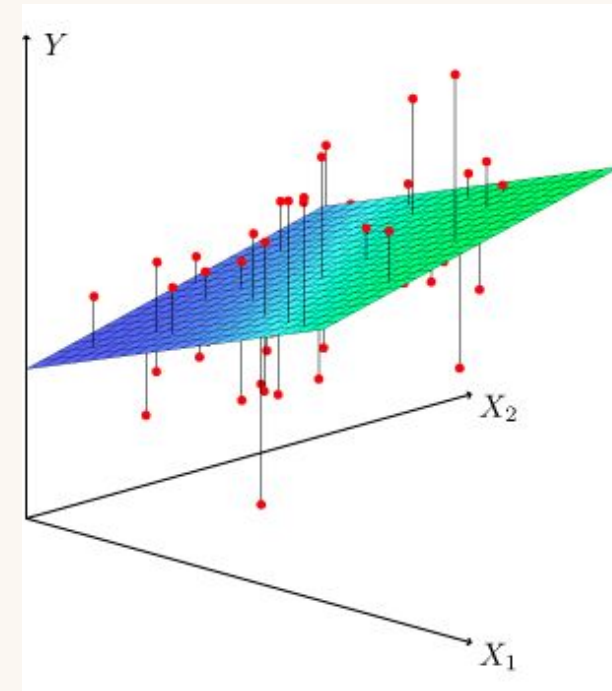
Regression analysis can be used to estimate the linear relationship between a response variable and several predictors

# Multiple linear regression: formally

- A multiple linear regression model takes the form:
- where:
  - $Y$ : The response variable
  - $X_j$ : The  $j$ th predictor variable
  - $\beta_j$ : The average effect on  $Y$  of a one unit increase in  $X_j$ , holding all other predictors fixed
  - $\epsilon_i$ : The error term
- The values for  $\beta_0, \beta_1, \dots, \beta_k$  are chosen using the least square method, which minimizes the sum of squared residuals (RSS):

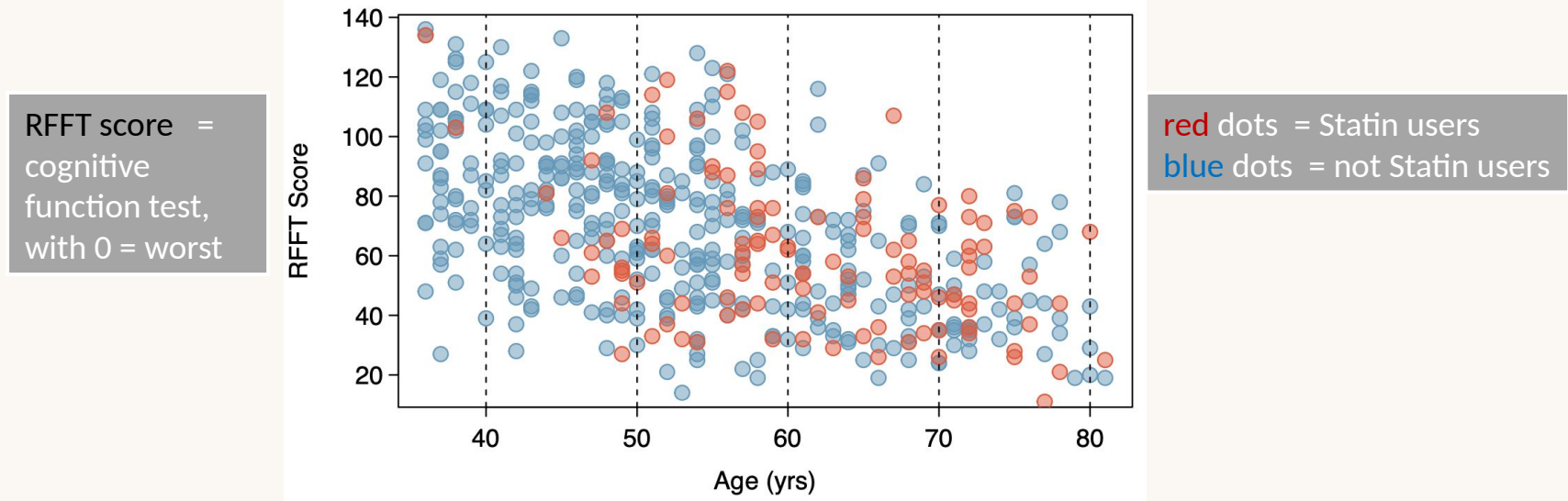
$$RSS =$$

- where:
  - $\sum$ : A greek symbol that means sum
  - $y_i$ : The actual response value for the  $i$ th observation
  - $\hat{y}_i$ : The predicted response value based on the multiple linear regression model



# Multiple linear regression: example

- [We'll revisit this in the lab, using the PREVEND dataset]
- STUDY: **Statins** are a class of drugs widely used to lower cholesterol (which can increase risk for adverse cardiovascular events). However, treatment with a statin might be associated with an increased risk of **cognitive decline**. Adults of **older age** are at increased risk for cardiovascular disease, but also for cognitive decline
- GOAL: Examine the association of **statin use** with **cognitive ability** in an observational cohort, but also accounted for **age** in the analysis as it could be a potential **confounder** in this setting
- HYPOTHETICAL MODEL:



Source: Vu, J., & Harrington, D. (2021). *Introductory Statistics for the Life and Biomedical Sciences*. Retrieved from <https://www.openintro.org/book/biostat/>

# Multiple linear regression: interpreting predictors coefficients

Given our model, we have obtained this prediction equation:

- ESTIMATE for a coefficient is the predicted mean change in corresponding to a 1 unit change in , when the values of all other predictors remain constant. E.g.:
  - an increase of 1 year of age is associated with a decrease of -1.2710 in RFFT score, when statin use is the same
  - for 2 individuals of the same age, the RFFT score will be 0.8509 higher for the one taking statins
- [STD. ERROR, T-STATISTIC, P-VALUE]: For each coefficient the model tests the  $H_0 : = 0$ 
  - the association between RFFT score and statin use is not statistically significant, but the association between RFFT score and age is significant

```
Call:
lm(formula = rfft ~ statin + age, data = prevend)
```

```
Residuals:
```

```
      Min       1Q   Median       3Q      Max
-63.855 -16.860  -1.178   15.730   58.751
```

```
Coefficients:
```

	Estimate	Std. Error	t value	Pr(> t )
(Intercept)	137.8822	5.1221	26.919	<2e-16 ***
statin	0.8509	2.5957	0.328	0.743
age	-1.2710	0.0943	-13.478	<2e-16 ***

```
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

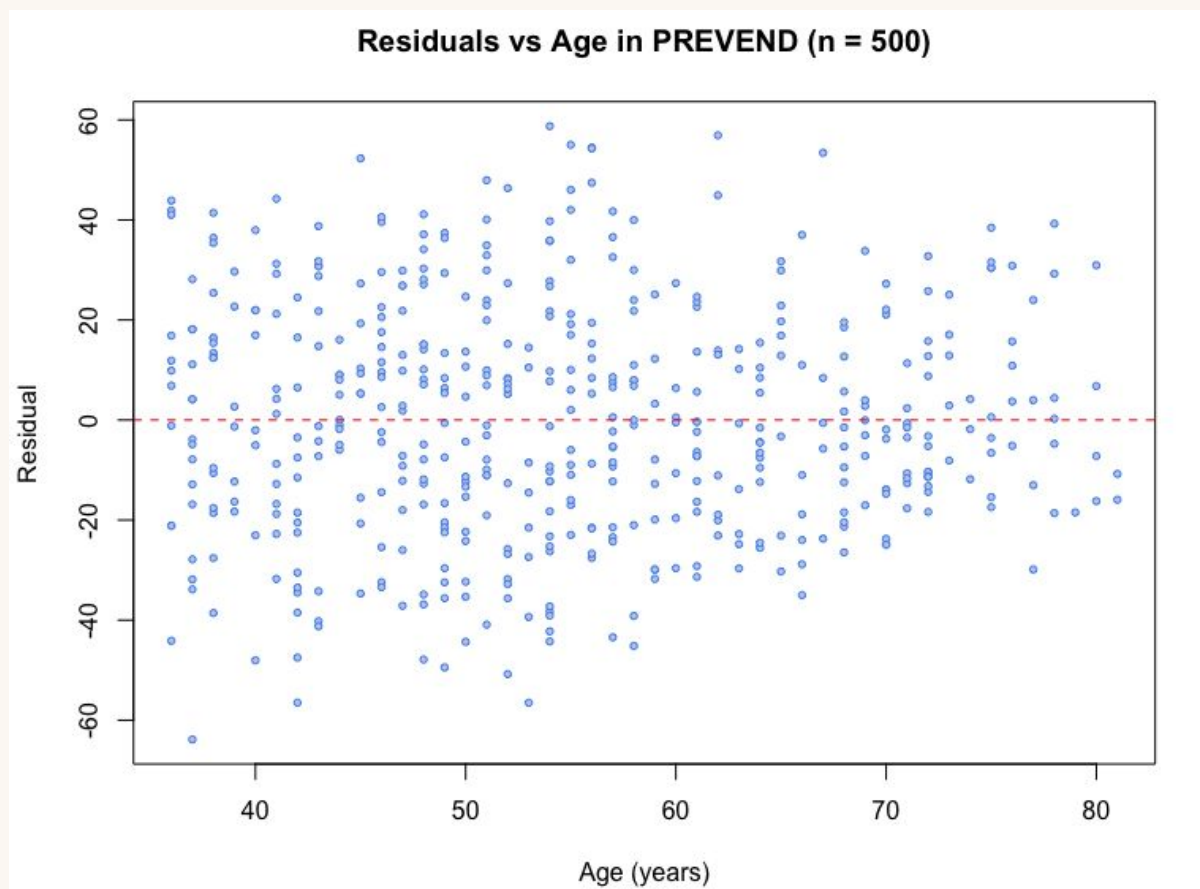
# Assumptions for (multiple) linear regression

Similar to those of simple linear regression...

1. **Linearity** : For each predictor variable , change in the predictor is linearly related to change in the response variable when the value of all other predictors is held constant.
  - It is not possible to make a scatterplot of a response against several simultaneous predictors. Instead, we use a **modified residual plot** to assess linearity
2. **Normality of residuals**: The residuals are approximately normally distributed.
  - Verified with normal probability plots (Q-Q plots etc.)
3. **Homoscedasticity** (constant variability): The residuals have approximately constant variance at every level of x.
  - Verified by plotting the residual values on the **y-axis** and the predicted values on the **x-axis**
4. **Independent observations**: Each set of observations ( ) is independent
5. **(NEW!) No multicollinearity**: i.e. no situations when there is a strong linear correlation between the independent variables, conditional on the other variables in the model
  - multicollinearity may lead to imprecision or instability of the estimated parameters when a variable changes

## Using residuals to check model assumption 1 (on individual predictors)

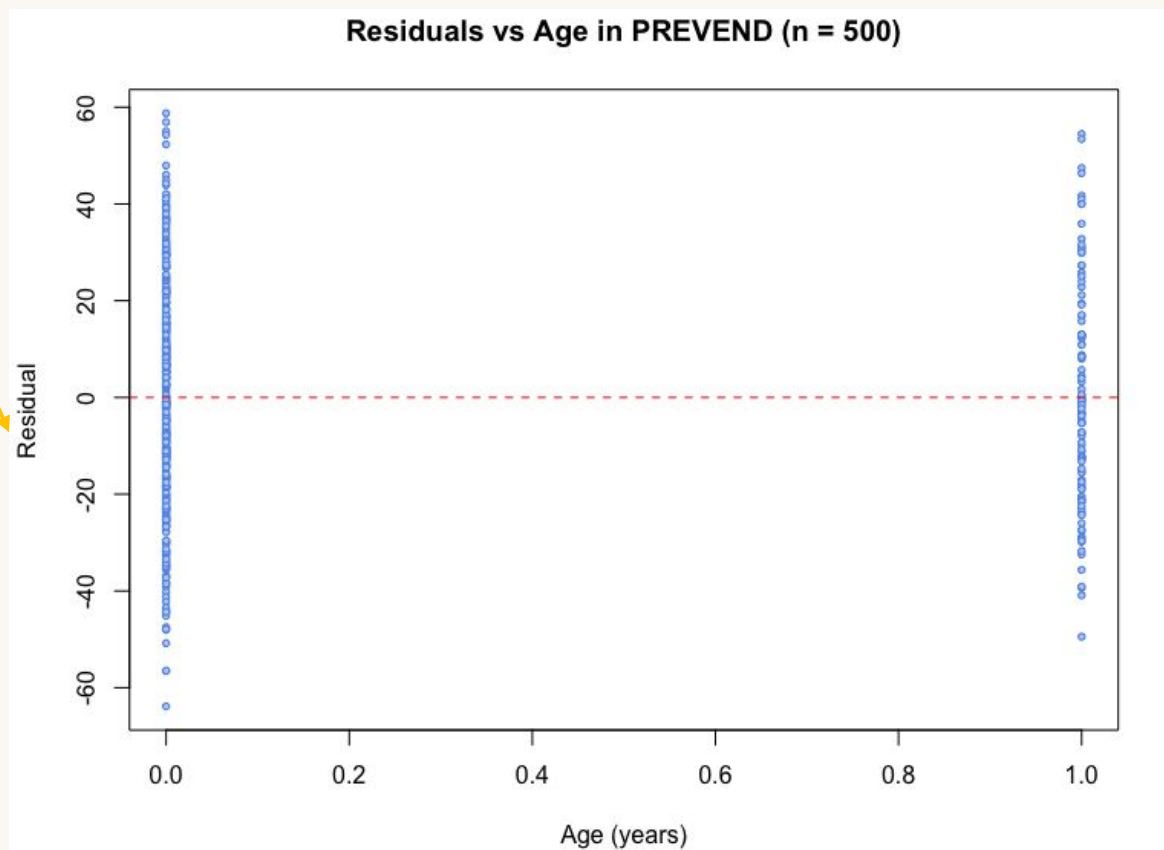
- Assess **linearity** with respect to **age** using a scatterplot with **residual values** on the **y-axis** and values of **age** on the **x-axis**
  - There does not seem to be remaining nonlinearity with respect to **age** after the model is fit.



## Using residuals to check model assumption 1 (on individual predictors)

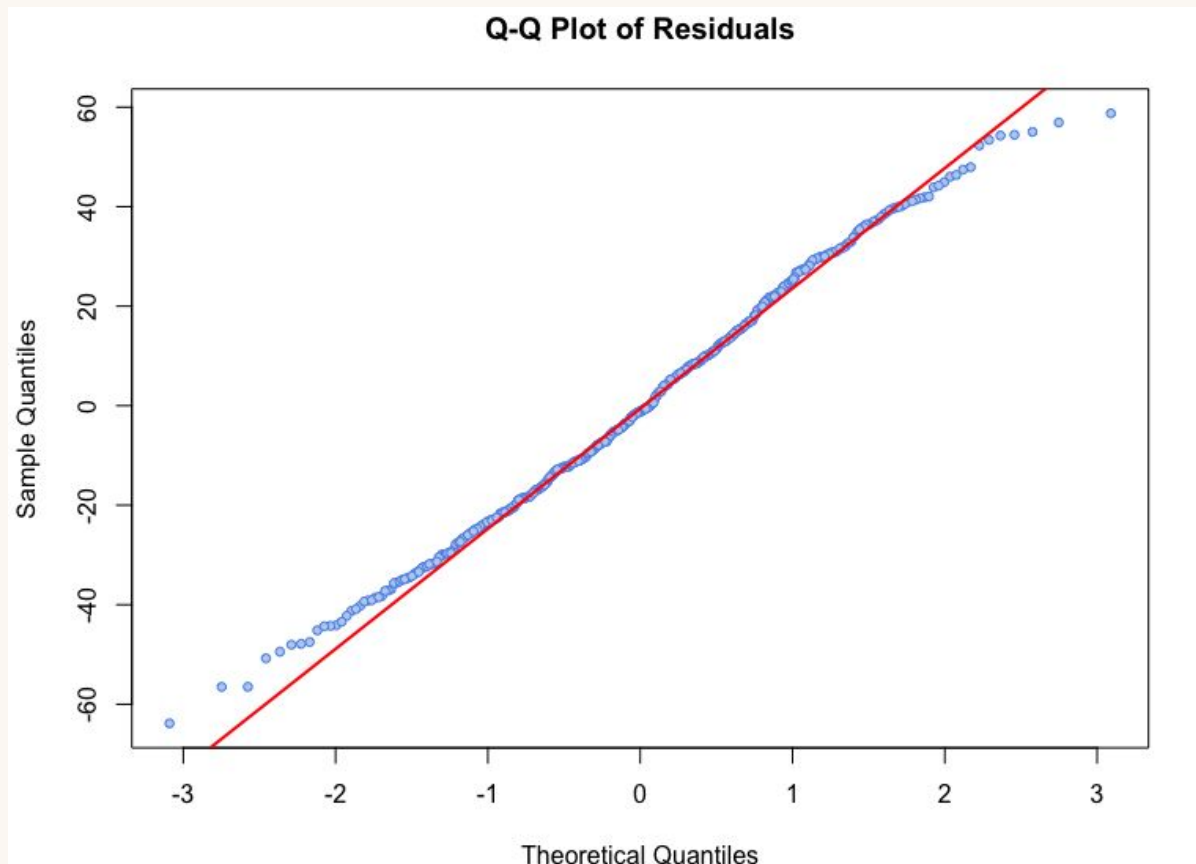
- Assess **linearity** with respect to **statin use** using a scatterplot with **residual values** on the **y-axis** and values of **age** on the **x-axis**
  - It is not necessary to assess linearity with respect to **statin use** since it is measured as a **categorical variable**. A line drawn through two points (that is, the mean of the two groups defined by a binary variable) is necessarily linear

NOT  
MEANINGFUL  
with respect  
to categorical  
explanatory  
variable!



## Using residuals to check model assumption 2 (Normality of residuals)

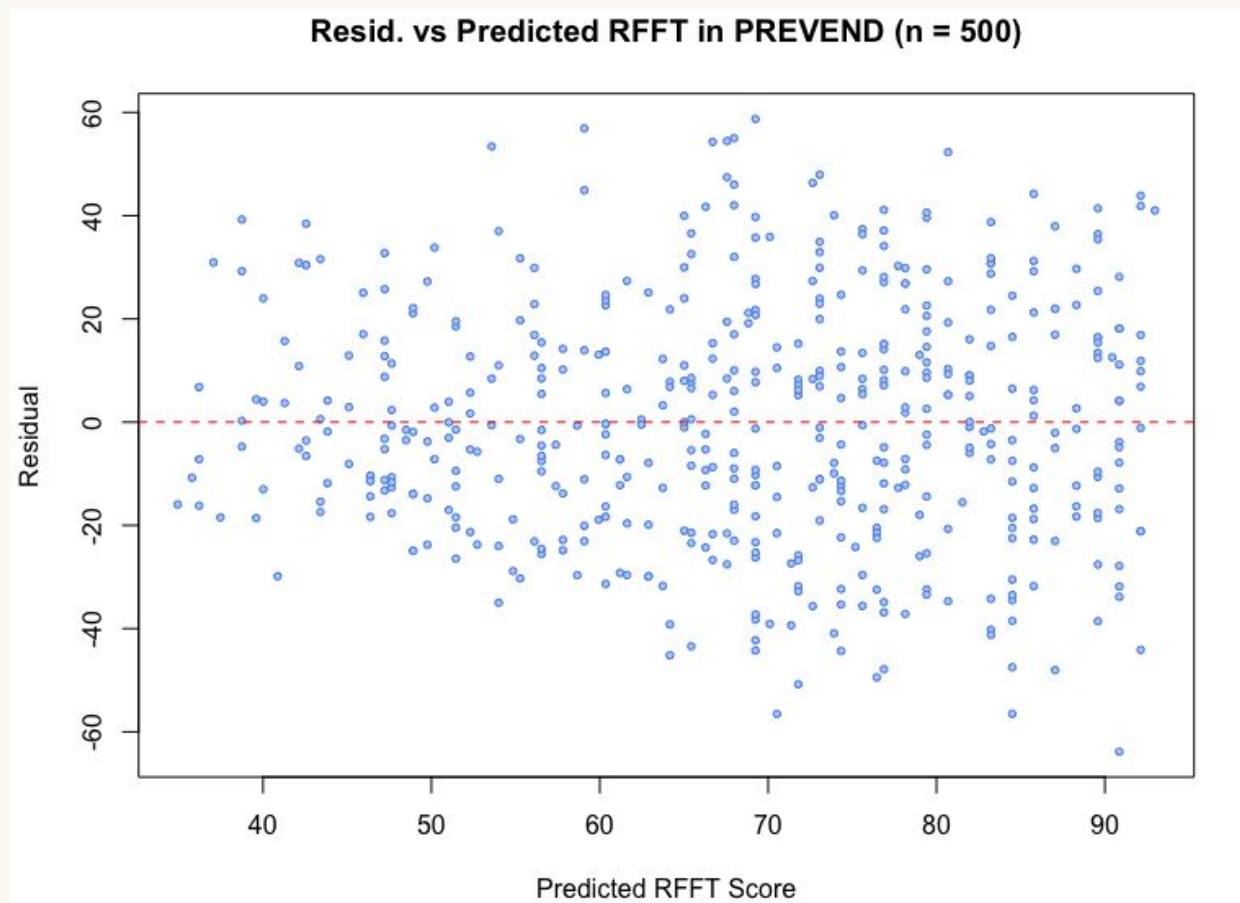
- As in Simple Regression we use Q-Q plots
  - The residuals are reasonably normally distributed, with only slight departures from normality in the tails.





# Using residuals to check model assumption 3 (Homoscedasticity)

- As in Simple Regression we plot the residual values on the **y-axis** and the predicted values on the **x-axis**
  - It seems reasonable to assume approximately constant variance.



# Checking assumption n 6 (no multicollinearity)

- It can be assessed by studying the correlation between each pair of independent variables, or even better, by computing the **variance inflation factor (VIF)**
  - The **VIF** measures how much the variance of an estimated regression coefficient increases, relative to a situation in which the explanatory variables are strictly independent.
  - A **high value of VIF is a sign of multicollinearity** (the threshold is generally at 5 or 10)
  - The easiest way to reduce the VIF is to remove some correlated independent variables, or eventually to standardize the data.

Not an  
issue in our  
dataset/  
model



# Variability in the response explained by the model: $R^2$ and Adj. $R^2$ in multiple regression

- As in simple regression, represents the proportion of variability in the response variable explained by the model
  - As variables are added, always increases
- incorporates a *penalty* for including predictors that do not contribute much towards explaining observed variation in the response variable
  - does not have an inherent interpretation, but it is useful while comparing models with different explanatory variables
- **Resid. Std. Err.** (square root of the residual mean squared errors ) is the estimated standard deviation of the error of the regression equation and is a good measure of the accuracy of the regression line.

```
Coefficients:
              Estimate Std. Error t value Pr(>|t|)
(Intercept) 137.8822    5.1221   26.919  <2e-16 ***
statin        0.8509    2.5957    0.328    0.743
age         -1.2710    0.0943  -13.478  <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 23.21 on 497 degrees of freedom
Multiple R-squared:  0.2852,    Adjusted R-squared:  0.2823
F-statistic: 99.13 on 2 and 497 DF,  p-value: < 2.2e-16
```

# F statistic in multiple regression

- Again, the **F-test of overall significance** indicates whether this linear regression model provides a **better fit to the data** than a hypothetical model that contains no independent variables (known as the “**intercept model**”)
  - $H_0$ : (null hypothesis) The **intercept model** fits the data as well as your model.
  - $H_1$ : (alternative hypothesis) Your model fits the data better than the intercept-only model
- In this case **p-value** is extremely small, we have sufficient evidence to conclude that this model fits the data better than intercept-only model
- NOTE: in general, if none of the independent variables are statistically significant, the overall F-test is also not statistically significant

```
Coefficients:
              Estimate Std. Error t value Pr(>|t|)
(Intercept) 137.8822    5.1221   26.919  <2e-16 ***
statin       0.8509     2.5957    0.328    0.743
age        -1.2710     0.0943  -13.478  <2e-16 ***
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Residual standard error: 23.21 on 497 degrees of freedom
Multiple R-squared:  0.2852,    Adjusted R-squared:  0.2823
F-statistic: 99.13 on 2 and 497 DF,  p-value: < 2.2e-16
```

# Model performance: ideas for further investigation

- The **PREVEND** data came from a **cross-sectional study**, i.e. not from a study in which participants were followed as they aged (i.e., a **longitudinal study**)
- So, while the model indicates that older patients tend to have lower RFFT scores, **we cannot conclude that RFFT scores decline with age in individuals**
  - only **repeated measurements** of RFFT taken as (the same) individual participants aged could rule out some explanatory effect of unobserved differences across different age cohorts
- We found that **age** was a *confounder*: **was it the only one?**
  - Other **potential confounders** could be **education level** (also associated to access to health care) and the **presence of cardiovascular disease** (can lead to vascular dementia and cognitive decline)
  - **Residual confounders** —frequent in observational studies— can be other variables in a dataset that have not been examined, or variables that were not measured in the study
- A **randomized experiment** is the best way to eliminate **residual confounders**, since it ensures that, at least on average, all predictors are not associated with the exposure (i.e. one source of confounding: **selection bias**).

*The details of how a study was designed and how data were collected should always be taken into account when interpreting study results.*

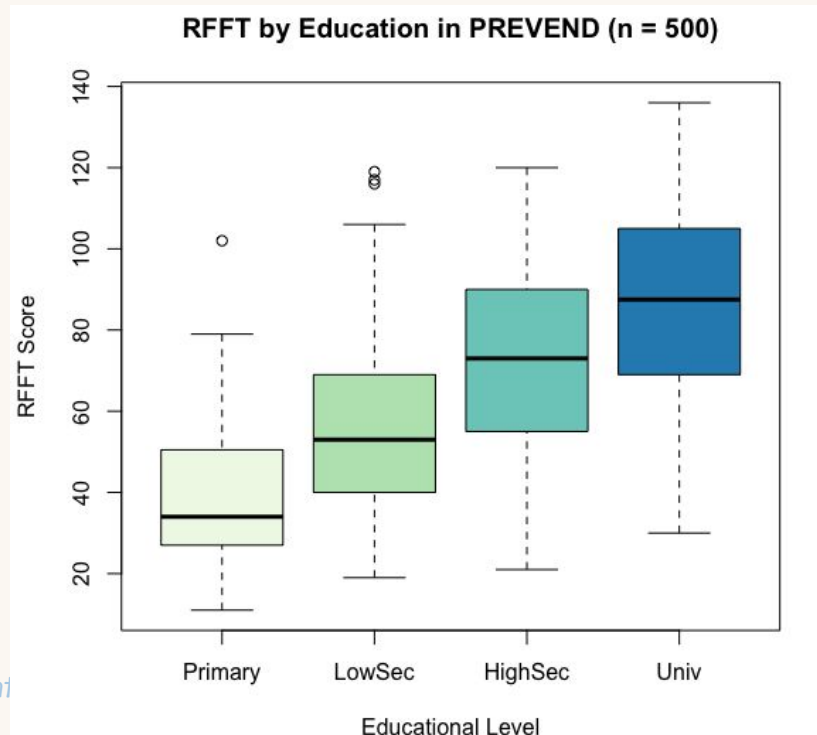
# Adding a categorical predictor with several levels to the model

- In a regression model with a **categorical variable with more than two levels** (e.g. education level), **one of the categories is set as the reference category**. The remaining categories each have an estimated coefficient
  - Each predictor levels can be thought of as binary variables that can take on either 0 or 1

- **EXAMPLE:** predicted RFFT for individuals in **Lower Secondary Education** level

= 55.72

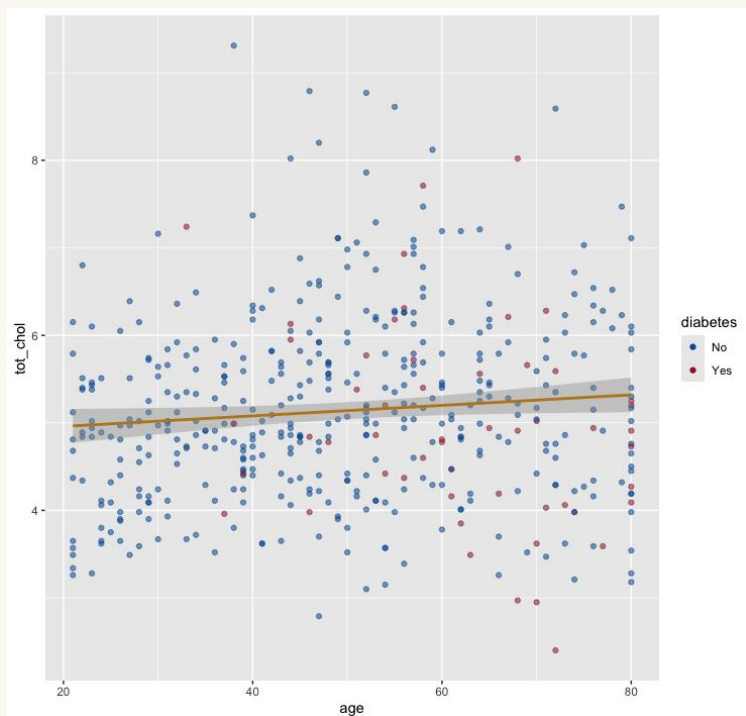
is not in the model because it is the **implicit reference level** (i.e. the intercept value 40.94)



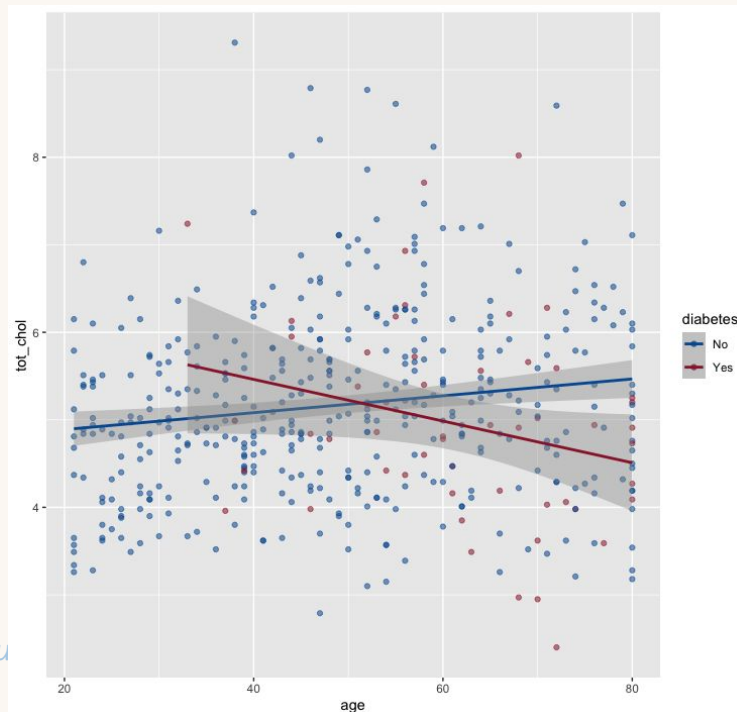
# Adding a **interaction term** to the model specification

- A statistical interaction occurs when the effect of one explanatory variable  $X_1$  on the response  $Y$  **depends on the level of another explanatory variable  $X_2$**
- Let's go back to the NHANES dataset and consider a linear model that predicts total **cholesterol level (mmol/L)** from **age (yrs.)** and diabetes status.
- Comparing 2 alternative models:
  - MLR without interaction:
  - MLR with interaction:  $+\beta_2(\text{Diabetes} \times \text{Age})$
- Model 2 *acknowledges the relationship between cholesterol and age depends on diabetes status* (i.e. it “allows” the relationship of with the to vary based on the values of)

Linear model on entire sample



Linear model by category (Diabetics or not)





# Multiple linear regression: recap

- **Multiple linear regression** is a generalization of simple linear regression to address the relationship between a **response variable** and **several predictors**, where  $k$  is the number of predictors
  - including logical, interval/ratio, or categorical predictors, as well as interaction terms
  - to interpret categorical predictors (>2 levels) one of the category's levels is set as the reference, each remaining level has an estimated coefficient = estimated change relative to the reference
- **Typical applications** of multiple linear regression are:
  1. **PRIMARY PREDICTOR:** Estimating an association between a response variable and **primary predictor** of interest, while adjusting for **possible confounding variables**
    - this is the case of the previous example! (Examining the association between **statin use** and **cognitive ability**, adjusting by **age**)
  2. **EXPLANATORY MODELS:** Constructing a model that effectively explains the observed variation in the response variable; in other words, to **build a predictive model for a response variable**
    - different techniques may be adopted in model selection (i.e. different **specifications** where we add/subtract explanatory variables)
    - A **parsimonious model (few variables)** is usually preferred over a complex model
    - **$R^2$**  and **Adjusted  $R^2$**  can be useful to compare models
    - In particular **Adjusted  $R^2$**  helps to balance predictive ability with complexity in a multiple regression model



# More advanced topics on REGRESSION...

- This lecture is just an introduction but there is a wide array of topics pertaining to regression analysis...
- Here are some of the many variants and advancements over the linear regression model:
  - **LOGISTIC REGRESSION**: if the dependent variable is dichotomous (0,1) or nominally scaled
  - **POISSON REGRESSION**: if the dependent variable is count over a period of time
  - **COX PROPORTIONAL HAZARDS REGRESSION**: for modeling censored data
  - **FUNCTIONAL TRANSFORMATIONS**: quadratic, exponential ....
  - **GENERALIZED LINEAR MODELS (GLMs)**: an extension of the linear model where the modelling of error is not Gaussian
  - **PANEL REGRESSION MODELS**: special regression models that can make use of both the temporal and the inter-individual variation if you have longitudinal data (or time-series cross-sectional or panel data)