Biostatistics
Week I

Ege Ülgen, M.D.

7 October 2021

ACIBADEM
MEHMET ALİ AYDINLAR
ÜNİVERSİTESİ

Statistics

- A discipline concerned with
  - **Collecting data** for a certain purpose
  - **Analysis** of the collected data
  - **Reaching conclusions** based on the analysis

Statistics

Collection

Organization

Analysis

Interpretation

Presentation

Biotatistics

- Does a novel drug affect survival in pancreatic cancer?
- Which mutation is most likely the cause of an inherited disease?
- Can health status of advanced AIDS patients be improved by a novel treatment?

Descriptive/Inferential Statistics

- Descriptive Statistics
  - Organization of collected data, calculation of mean and dispersion, presentation as tables, graphics, etc.
- Inferential Statistics
  - Building hypothesis concerning the population based on sample findings, hypothesis testing, interpretation.

Population vs. Sample

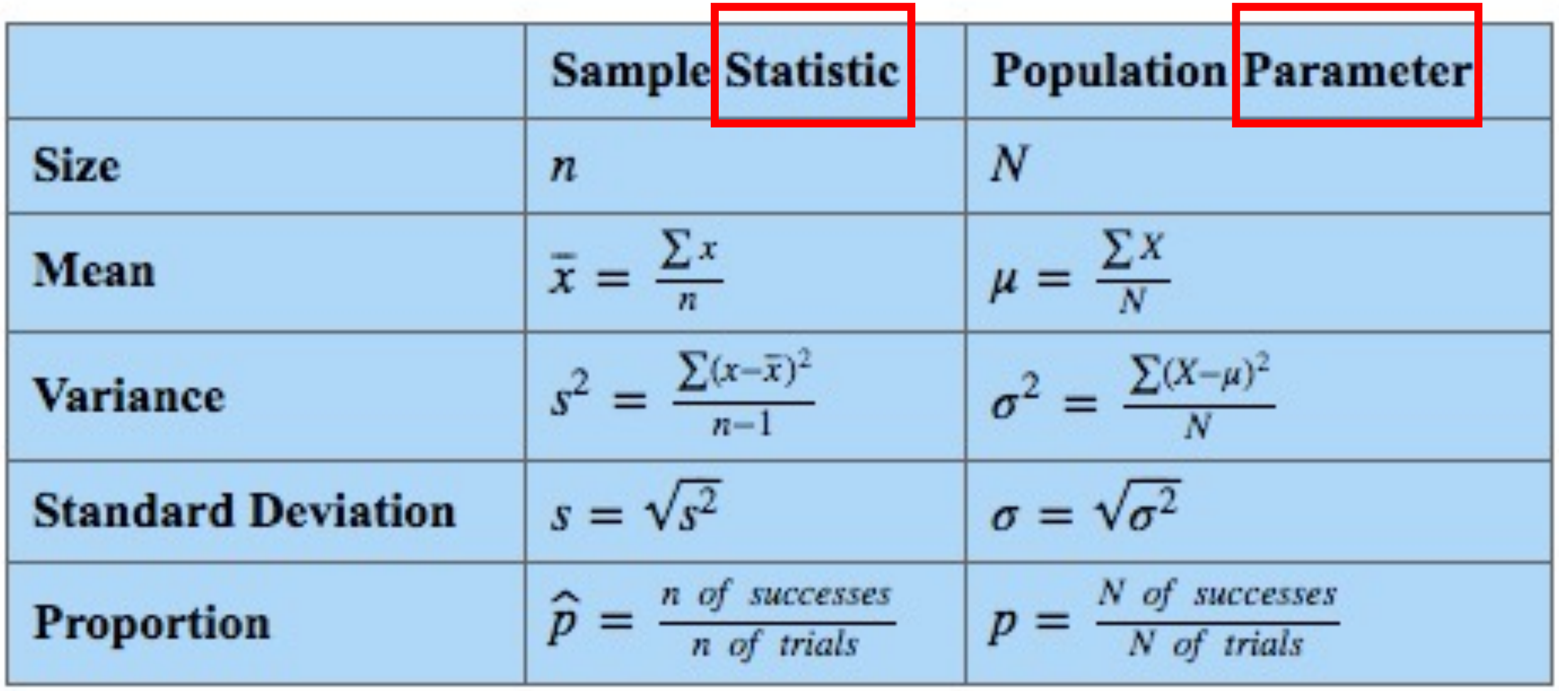
- Population
  - All subjects under consideration that have the same properties
  - E.g., everyone living in Istanbul

  N = 15.52 million (as of 31 Dec 2019)

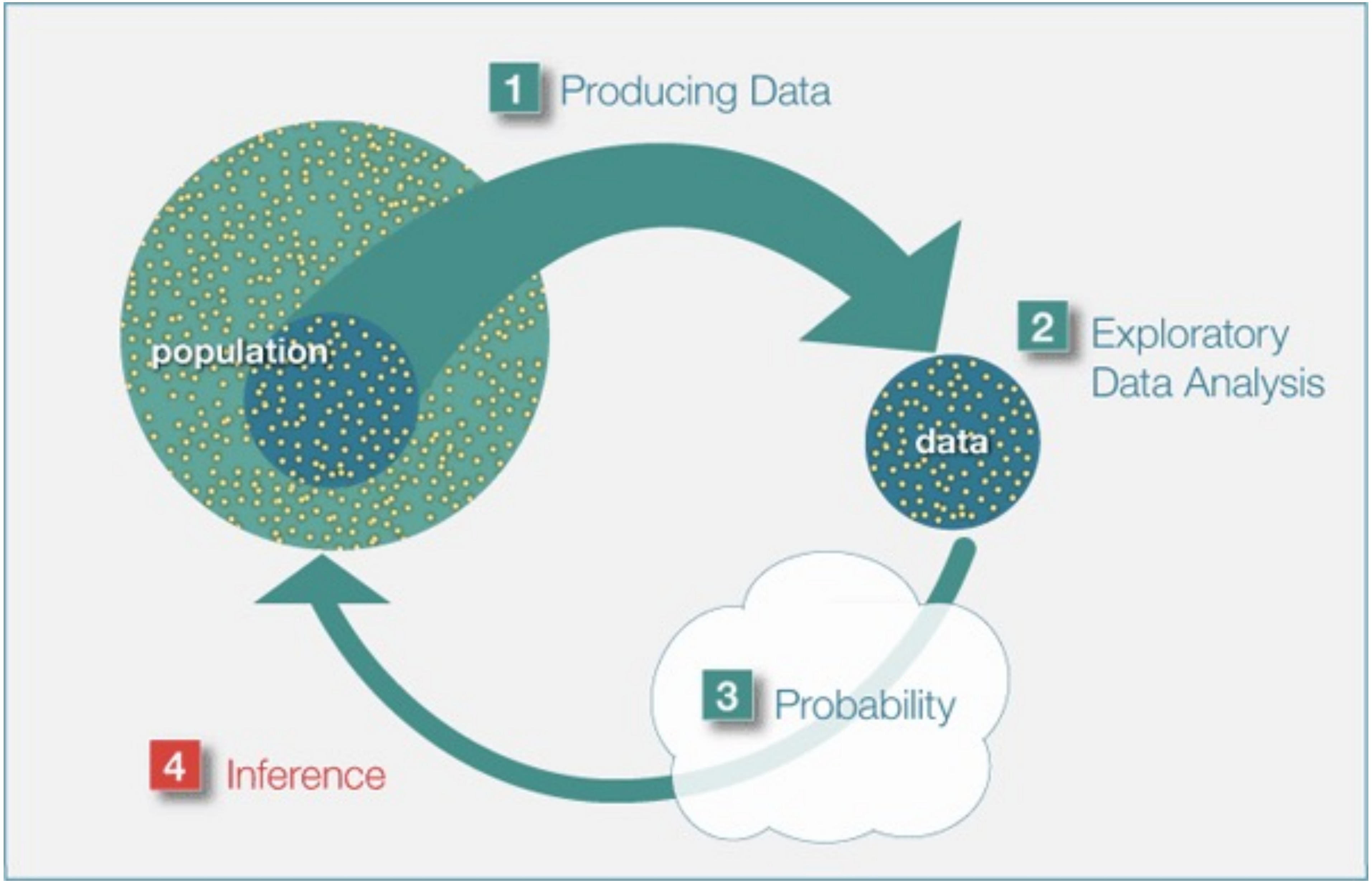
- Sample
  - A proportion of the population (ideally randomly selected)
  - E.g., **n** = 500, 1000, 5000, …

  (n might be decided based on sample size calculations – Week 11)

Terminology/Notation



	Sample Statistic	Population Parameter
Size	n	N
Mean	$\bar{x} = \frac{\sum x}{n}$	$\mu = \frac{\sum X}{N}$
Variance	$s^2 = \frac{\sum(x-\bar{x})^2}{n-1}$	$\sigma^2 = \frac{\sum(X-\mu)^2}{N}$
Standard Deviation	$s = \sqrt{s^2}$	$\sigma = \sqrt{\sigma^2}$
Proportion	$\hat{p} = \frac{n\ of\ successes}{n\ of\ trials}$	$p = \frac{N\ of\ successes}{N\ of\ trials}$



Unit 4a: introduction to statistical inference [Internet]. [cited 2021 Sep 27]. Available from: https://bolt.mph.ufl.edu/6050-6052/unit-4/

Data/Variable

- Items of information, often numeric, that are collected through observation
    - Age
    - Gender
    - Ethnicity
    - Systolic blood pressure
    - Treatment type

  …

Example Study

- Main question
    - Can the health status of advanced AIDS patients be improved by a novel drug treatment?

- Sub-questions
    - Are there differences between treatments in terms of health benefits?
    - Do health benefits differ with respect to gender?
    - Do health benefits differ with respect to age?

Example Study (cont.)

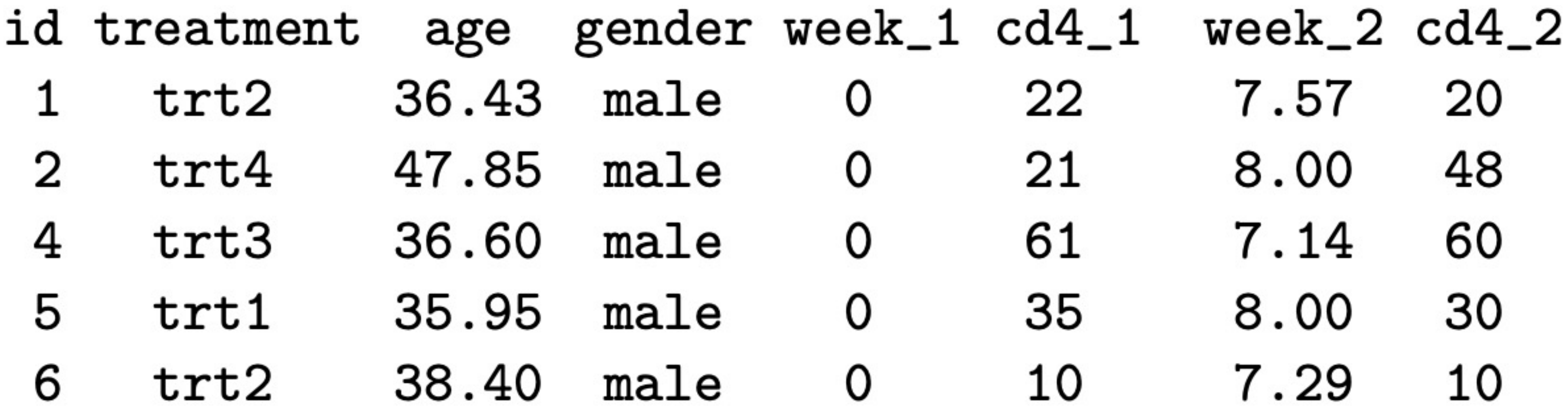
- Randomized clinical trial
- 1178 patients
  - 289, 288, 293, and 308 patients per treatment arm
- Data collection at baseline (week = 0) Do health benefits differ with respect to age?
- 5 more follow-ups with 8-week intervals

Example Study (cont.)

- Variables
    - Identification number
    - Treatment arm
    - Age
    - Gender
    - CD4 cell count at each follow-up
    - Time of follow-up (in weeks since baseline)

Example Study (cont.)

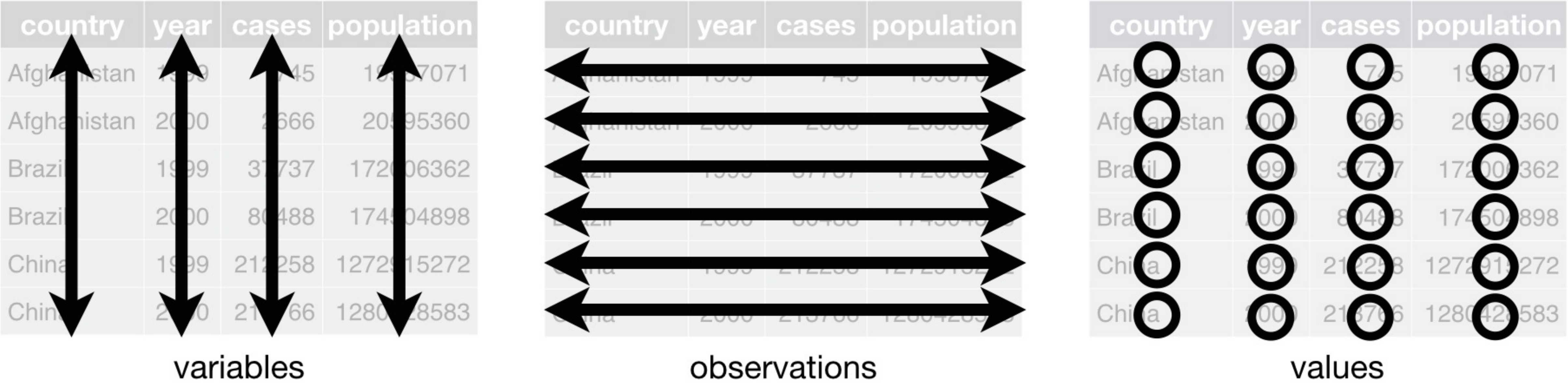
First 5 patients’ data, out of 1,178 (only for the first two weeks)



id	treatment	age	gender	week_1	cd4_1	week_2	cd4_2
1	trt2	36.43	male	0	22	7.57	20
2	trt4	47.85	male	0	21	8.00	48
4	trt3	36.60	male	0	61	7.14	60
5	trt1	35.95	male	0	35	8.00	30
6	trt2	38.40	male	0	10	7.29	10

Applied longitudinal analysis [Internet]. [cited 2021 Sep 27].
Available from: https://content.sph.harvard.edu/fitzmaur/ala2e/

«Clean» Data



12 tidy data | r for data science [Internet]. [cited 2021 Sep 27]. Available from: https://r4ds.had.co.nz/tidy-data.html

Variable Types

- **Discrete/Categorical/Qualitative**
    - Measured in a discrete manner

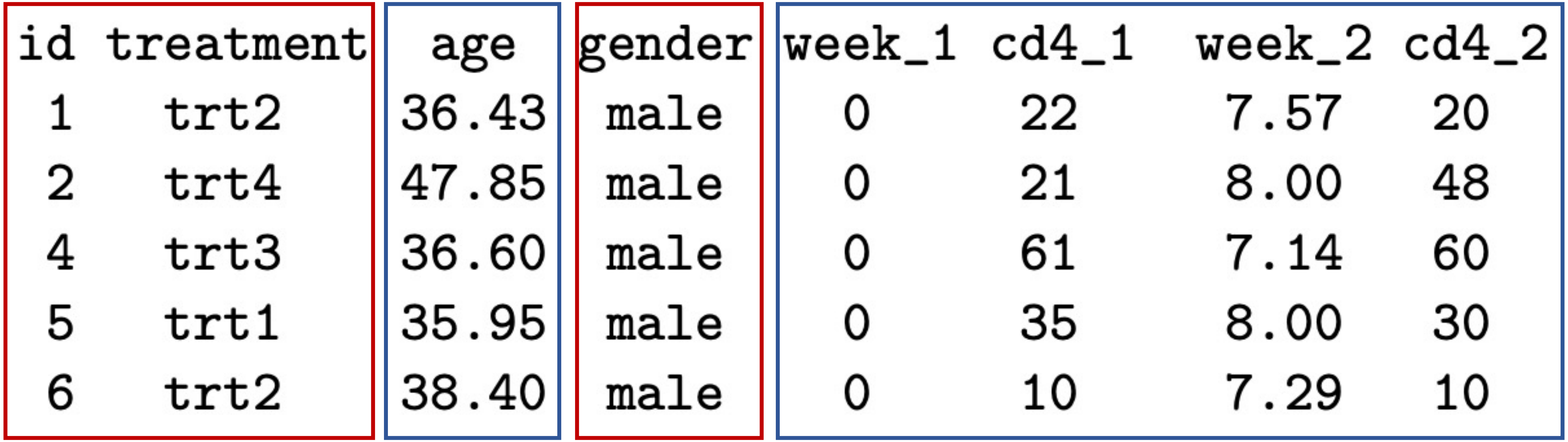
    - **Nominal**: no natural ordering. E.g., eye color, zip-code
    - **Dichotomous/binary**: only takes two values. E.g., dead/alive, female/male
    - **Ordinal**: natural ordering. E.g., agree/neutral/disagree, bad/fair/good
    - **Count**: counted values. E.g., number of tumor occurrences in one month

Variable Types

- **Continuous/Quantitative**
  - Measured in a continuous manner

  - **Interval:** real number (+/- including 0). E.g., temperature, location
  - **Ratio:** positive values (**0 indicates none**). E.g., height, age, daily calcium consumption (mg).

Example Study (cont.)



id	treatment	age	gender	week_1	cd4_1	week_2	cd4_2
1	trt2	36.43	male	0	22	7.57	20
2	trt4	47.85	male	0	21	8.00	48
4	trt3	36.60	male	0	61	7.14	60
5	trt1	35.95	male	0	35	8.00	30
6	trt2	38.40	male	0	10	7.29	10

Discrete - nominal

Contin.-
ratio

Discrete –
nominal
/binary

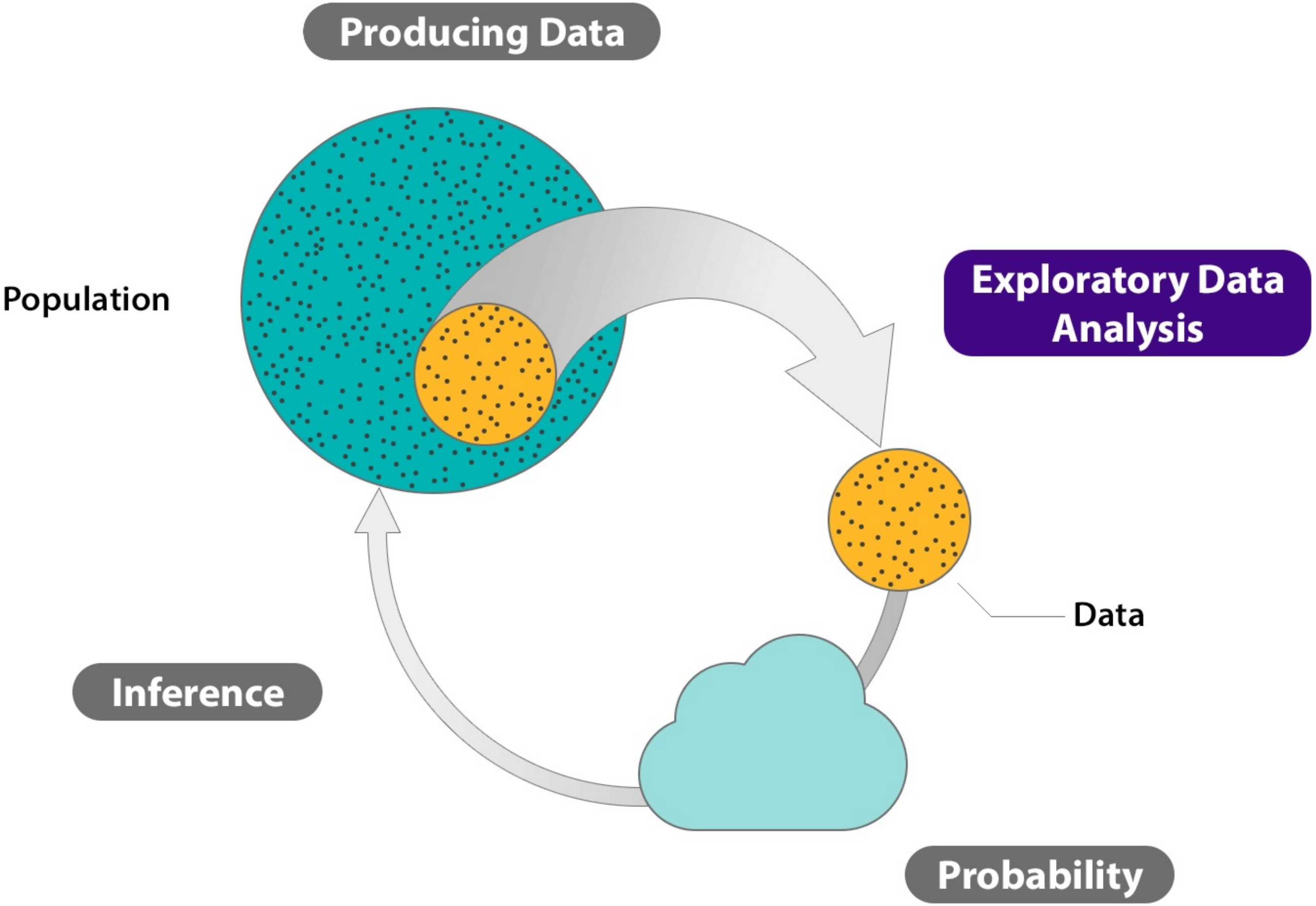
Discrete - count
Contin. - ratio

Applied longitudinal analysis [Internet]. [cited 2021 Sep 27].
Available from: https://content.sph.harvard.edu/fitzmaur/ala2e/

Same variable – different classifications

1. Time after study entry
   0, 1.2, 2.5, 3.1, 4.6, 5.2, 6.6, 7.1, 8 weeks
   Continuous - ratio
2. Time after study entry
   < 4 weeks, ≥ 4 weeks
   Categorical - binary
3. Time after study entry
   < 2 weeks, ≥ 2 and < 4 weeks, ≥ 4 weeks
   Categorical - ordinal
4. Time after study entry
   -4.6, -3.4, -2.1, -1.5, 0, 0.6, 2, 2.5, 3.4 weeks
   Continuous - interval

The Big Picture



Unit 1: exploratory data analysis [Internet]. [cited 2021 Sep 27]. Available from: https://bolt.mph.ufl.edu/6050-6052/unit-1/

Exploratory Data Analysis (EDA)

- Examining Distributions — exploring data **one variable at a time**.
- Examining Relationships — exploring data **two variables at a time**.

Frequency Tables – Categorical Variable

- Eye colors of 10 individuals:

  blue, green, brown, blue, brown, blue, blue, green, brown, brown

Frequency Tables – Categorical Variable

- Eye colors of 10 individuals:

  blue, green, brown, blue, brown, blue, blue, green, brown, brown

Eye Color	Frequency
Blue	4
Brown	4
Green	2

Frequency Tables – Categorical Variable

- Eye colors of 10 individuals:

  blue, green, brown, blue, brown, blue, blue, green, brown, brown

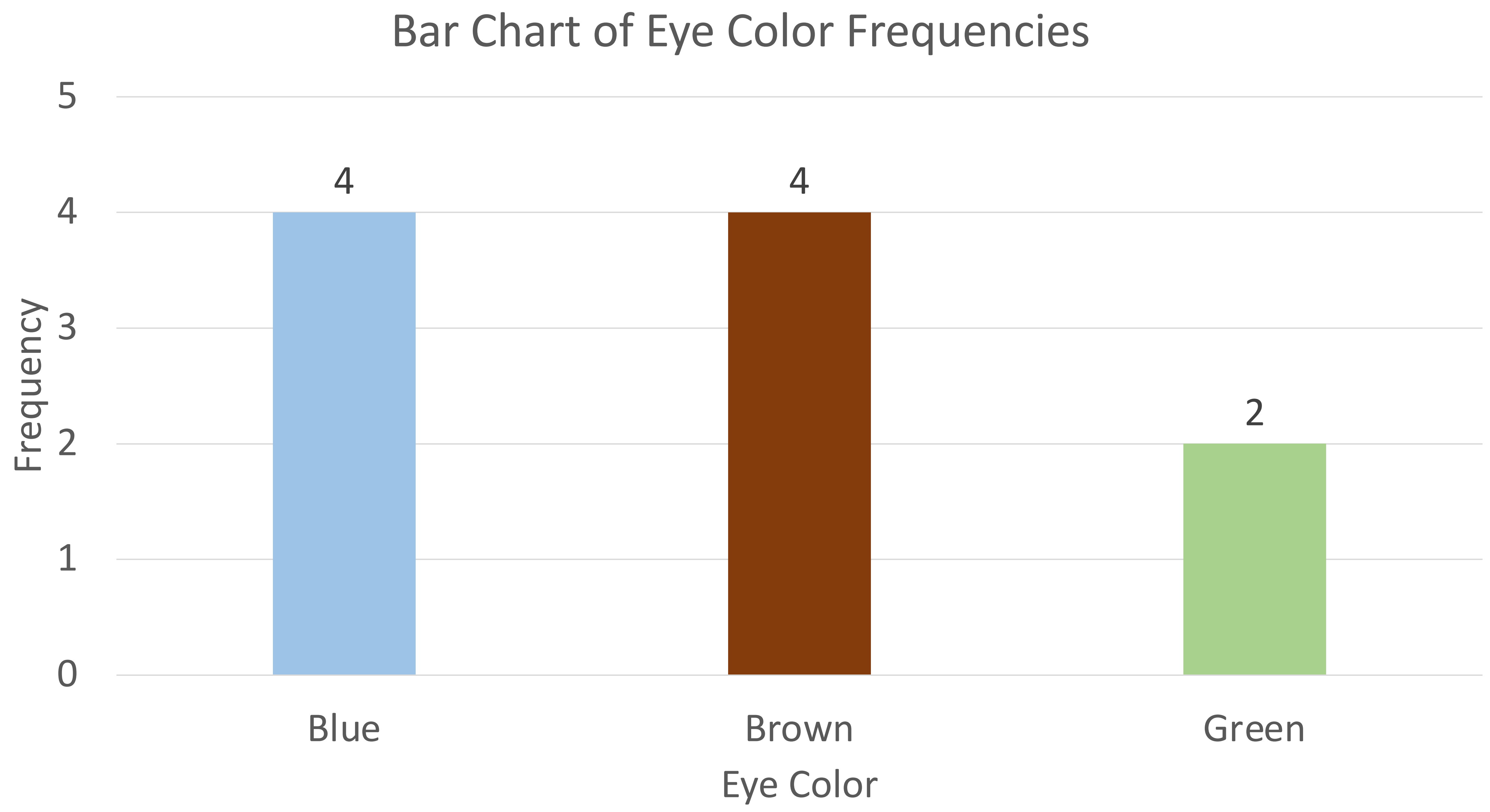
Eye Color	Frequency	Relative Freq.
Blue	4	4/10 = 0.4
Brown	4	4/10 = 0.4
Green	2	2/10 = 0.2

Frequency Tables – Categorical Variable

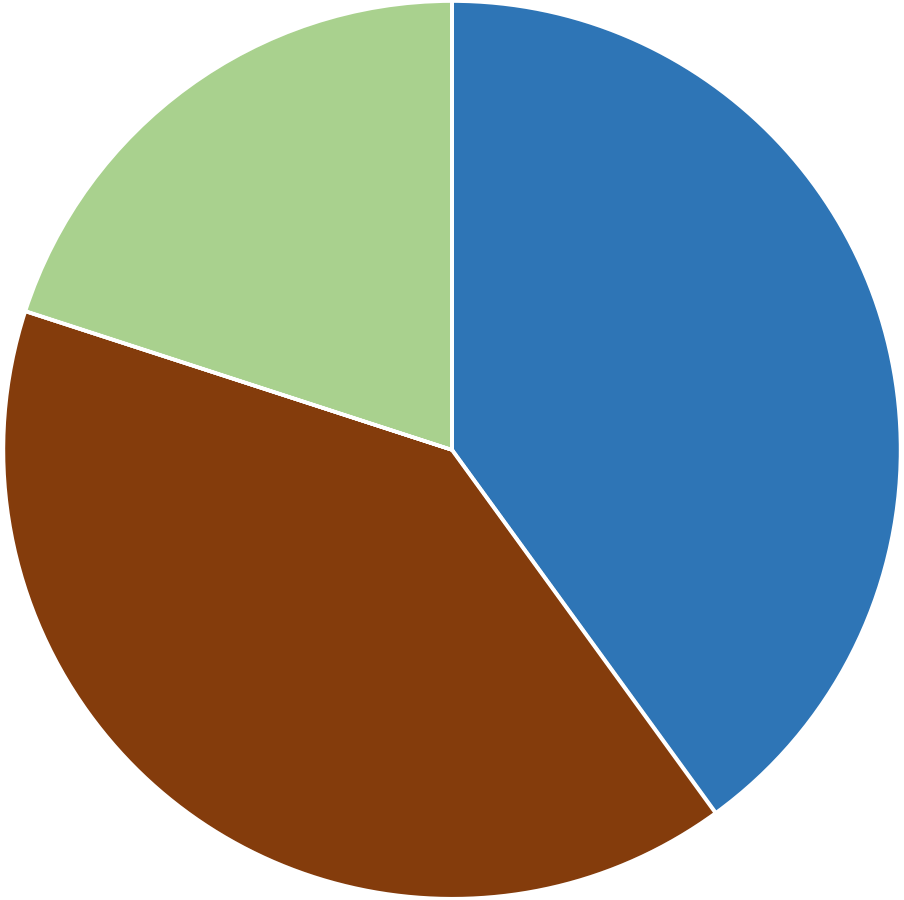
- Eye colors of 10 individuals:

  blue, green, brown, blue, brown, blue, blue, green, brown, brown

Eye Color	Frequency	Relative Freq.	%
Blue	4	4/10 = 0.4	40
Brown	4	4/10 = 0.4	40
Green	2	2/10 = 0.2	20


Bar Chart of Eye Color Frequencies
5
4
3
2
1
0
Frequency
4
4
2
Blue
Brown
Green
Eye Color

Do not use pie charts!



Contingency table/Cross tabulation/Crosstab

- Tables in which two categorical variables are investigated together

	Male	**Female**
No education	4	10
Primary school	3	5
High school	2	8
Bachelor’s degree	7	9

Frequency Tables – Continuous Variable

Cholesterol levels of 40 patients:

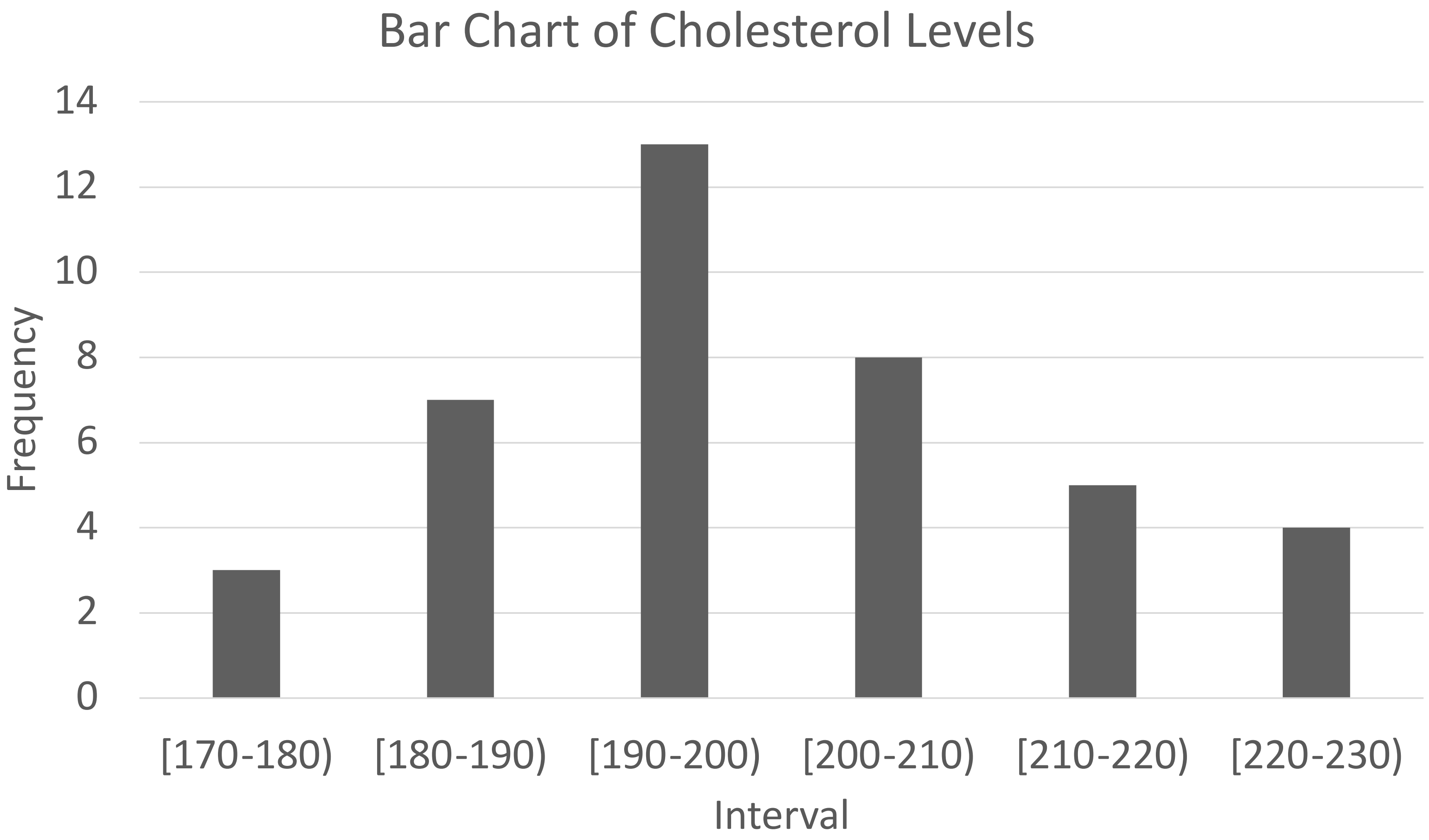
Original data

213, 174, 193, 196, 220, 183, 194, 200, 192, 200, 200, 199, 178, 183, 188, 193, 187, 181, 193, 205, 196, 211, 202, 213, 216, 206, 195, 191, 171, 194, 184, 191, 221, 212, 221, 204, 204, 191, 183, 227

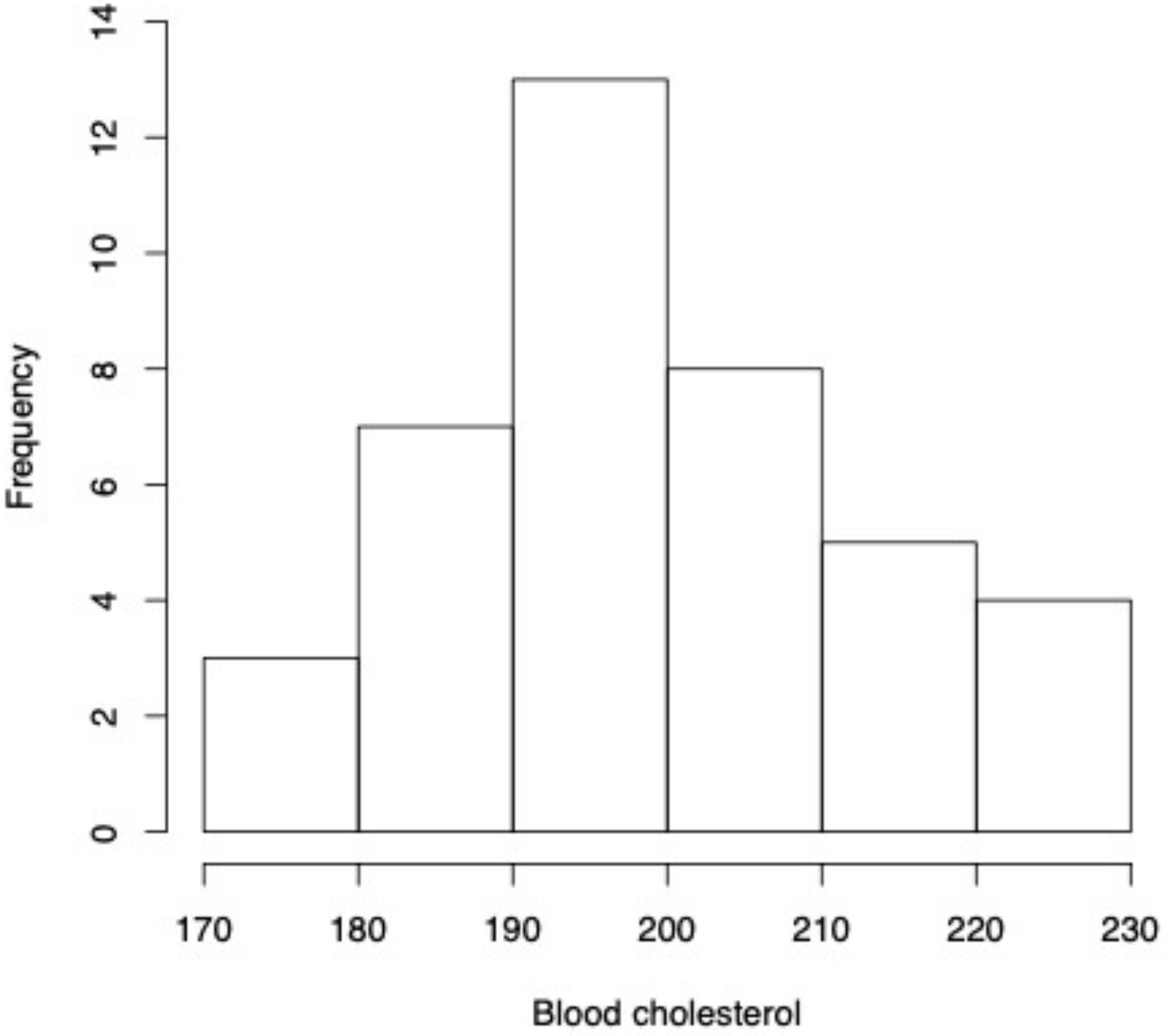
Sorted data

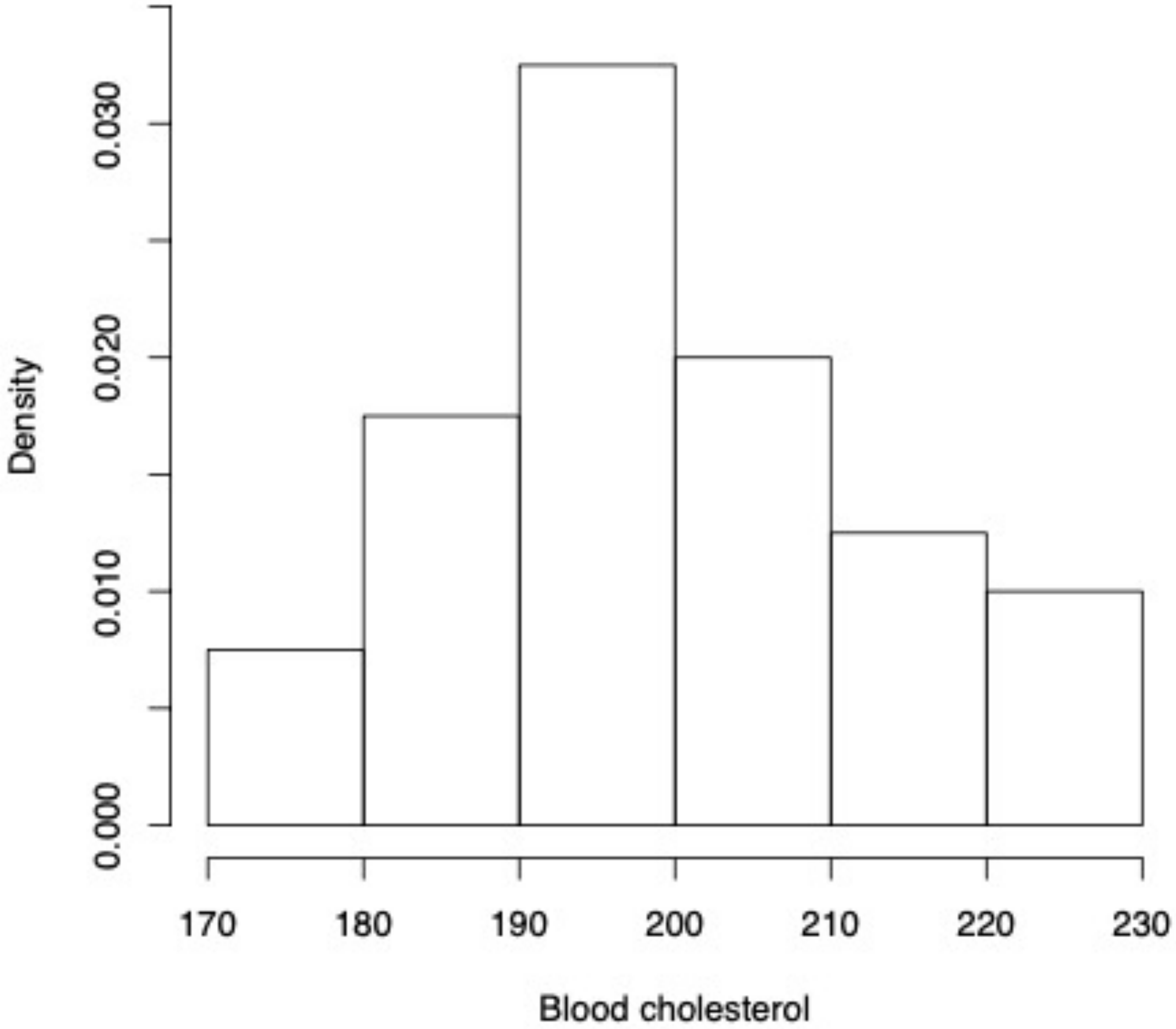
171, 174, 178, 181, 183, 183, 183, 184, 187, 188, 191, 191, 191, 192, 193, 193, 193, 194, 194, 195, 196, 196, 199, 200, 200, 200, 202, 204, 204, 205, 206, 211, 212, 213, 213, 216, 220, 221, 221, 227

Interval	Frequency	Relative Freq.	%
[170-180)	3	3/40 = 0.075	7.5
[180-190)	7	7/40 = 0.175	17.5
[190-200)	13	13/40 = 0.325	32.5
[200-210)	8	8/40 = 0.200	20.0
[210-220)	5	5/40 = 0.125	12.5
[220-230)	4	4/40 = 0.100	10.0

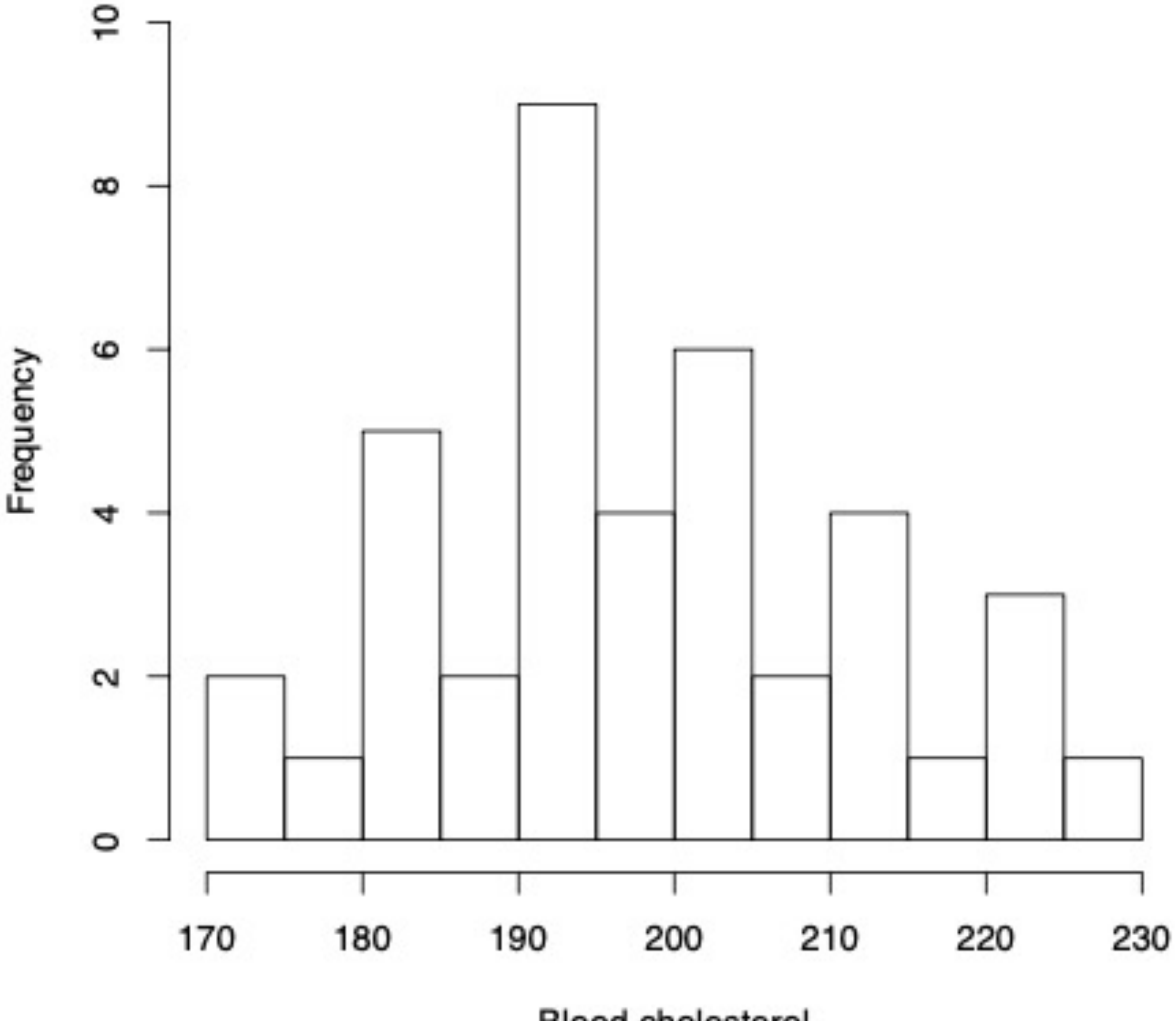

Bar Chart of Cholesterol Levels
14
12
10
8
6
4
2
0
Frequency
[170-180)
[180-190)
[190-200)
[200-210)
[210-220)
[220-230)
Interval

Histogram


Frequency
0
2
4
6
8
10
12
14
170
180
190
200
210
220
230
Blood cholesterol


Density
0.000
0.010
0.020
0.030
170
180
190
200
210
220
230
Blood cholesterol

Histogram



Frequency
0
2
4
6
8
10
170
180
190
200
210
220
230
Blood cholesterol

Ross, S. M. (2017). Introductory statistics. Amsterdam: Elsevier/AP.

Histogram

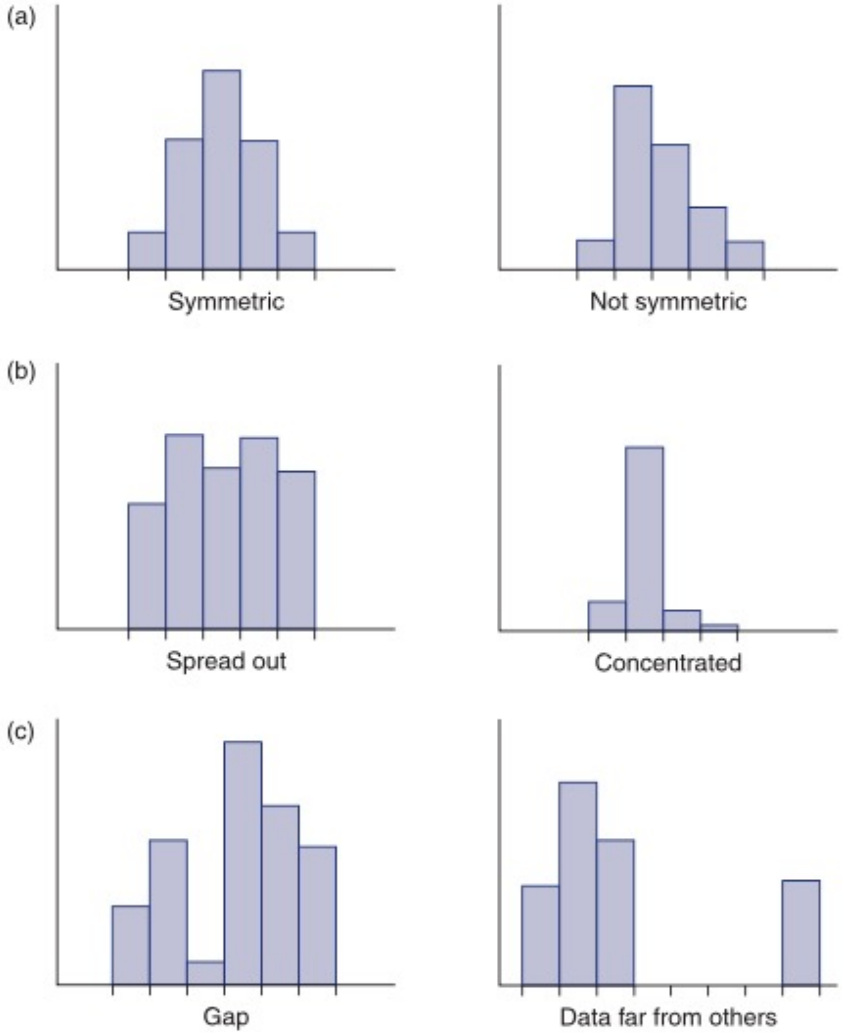


FIGURE 2.8

Characteristics of data detected by histograms. (a) symmetry, (b) degree of spread and where values are concentrated, and (c) gaps in data and data far from others.

Ross, S. M. (2017). Introductory statistics. Amsterdam: Elsevier/AP.

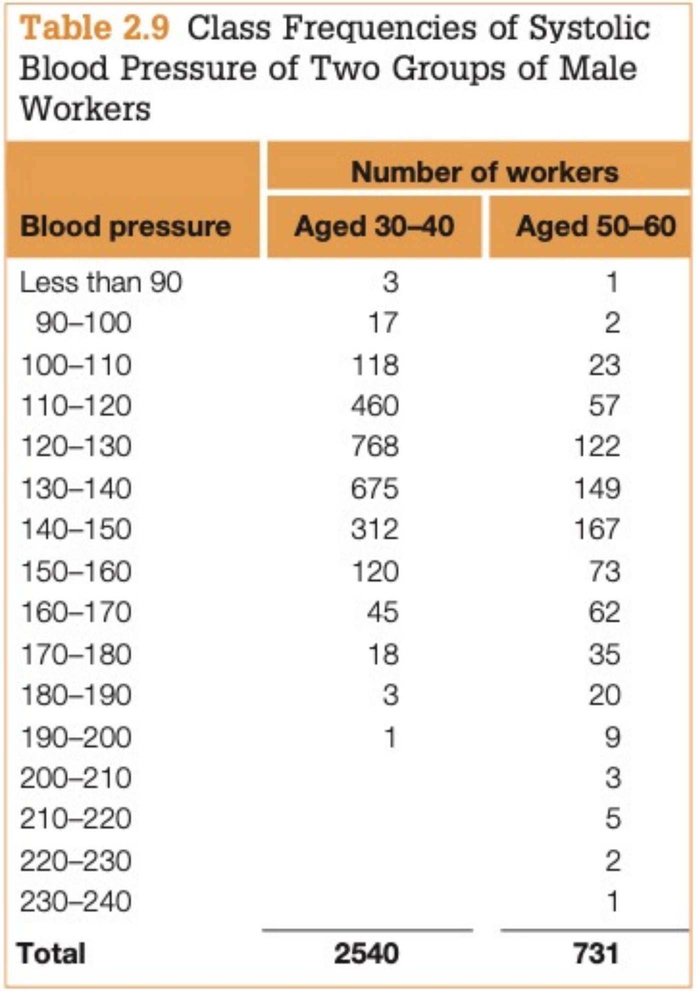


Table 2.9 Class Frequencies of Systolic Blood Pressure of Two Groups of Male Workers

	Number of workers	
Blood pressure	**Aged 30–40**	**Aged 50–60**
Less than 90	3	1
90–100	17	2
100–110	118	23
110–120	460	57
120–130	768	122
130–140	675	149
140–150	312	167
150–160	120	73
160–170	45	62
170–180	18	35
180–190	3	20
190–200	1	9
200–210		3
210–220		5
220–230		2
230–240		1
Total	**2540**	**731**

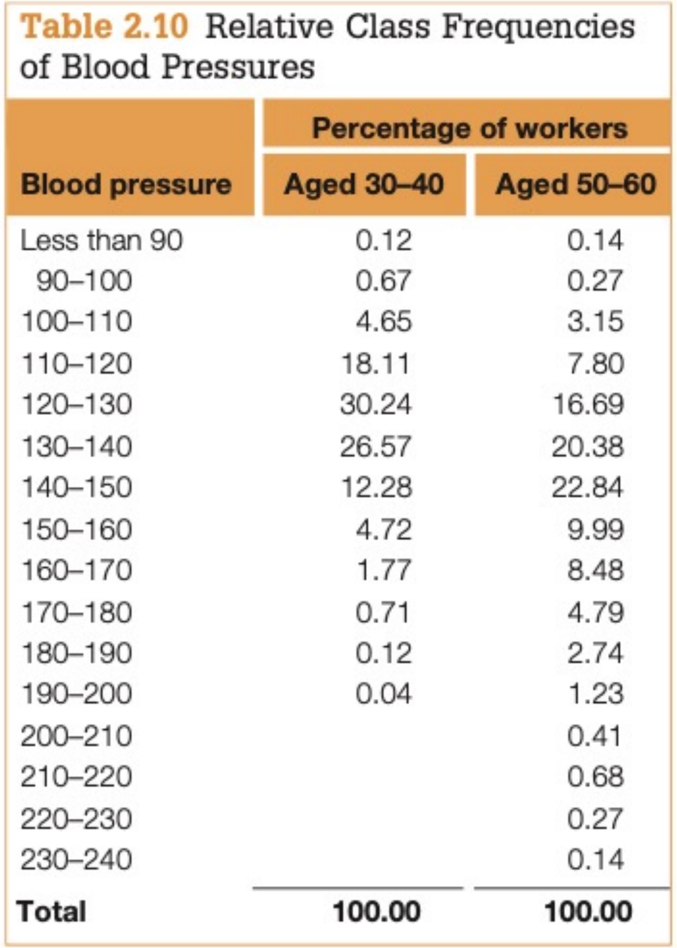


Table 2.10 Relative Class Frequencies of Blood Pressures

	Percentage of workers	
Blood pressure	**Aged 30–40**	**Aged 50–60**
Less than 90	0.12	0.14
90–100	0.67	0.27
100–110	4.65	3.15
110–120	18.11	7.80
120–130	30.24	16.69
130–140	26.57	20.38
140–150	12.28	22.84
150–160	4.72	9.99
160–170	1.77	8.48
170–180	0.71	4.79
180–190	0.12	2.74
190–200	0.04	1.23
200–210		0.41
210–220		0.68
220–230		0.27
230–240		0.14
Total	**100.00**	**100.00**

Ross, S. M. (2017). Introductory statistics. Amsterdam: Elsevier/AP.

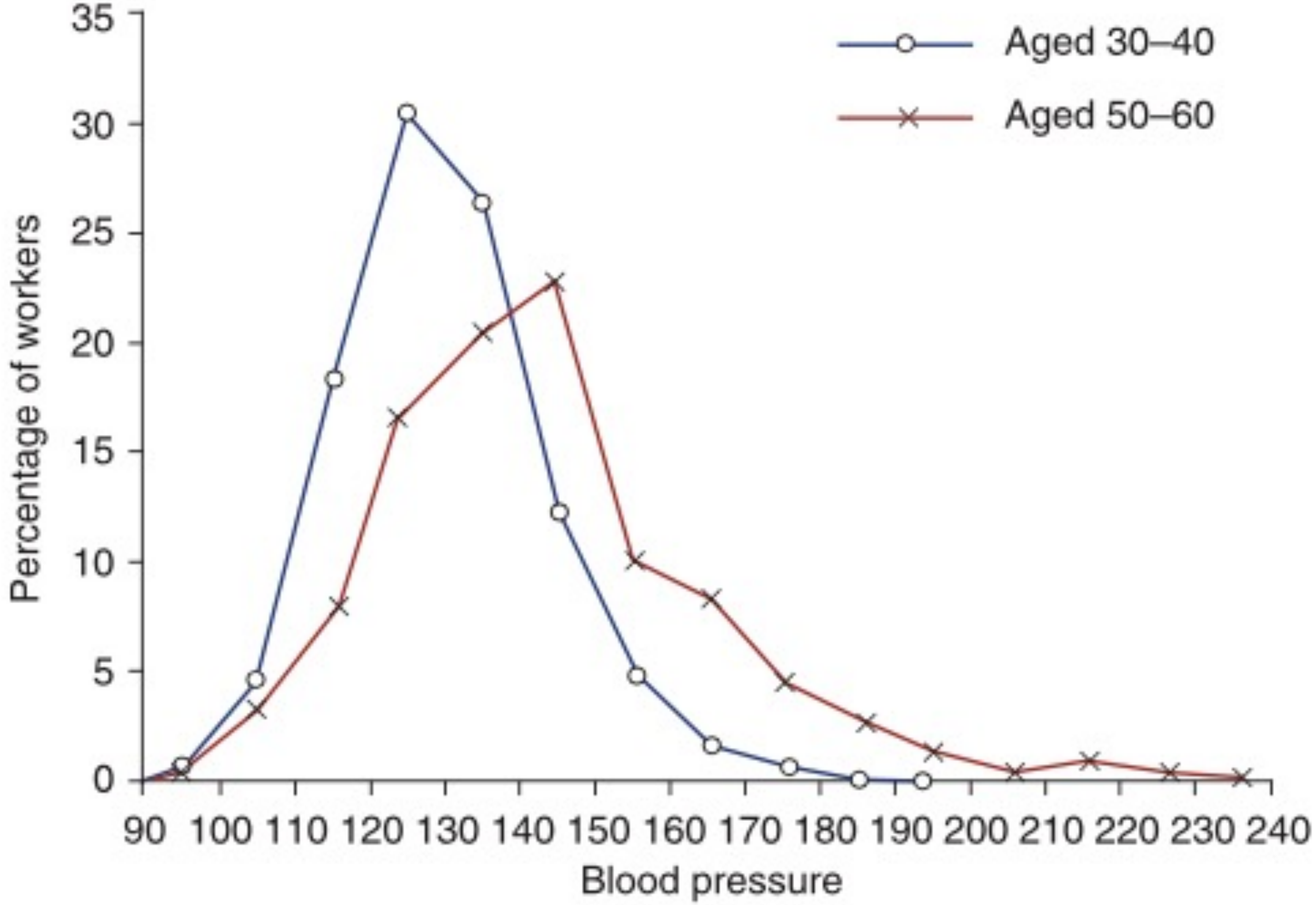


FIGURE 2.10

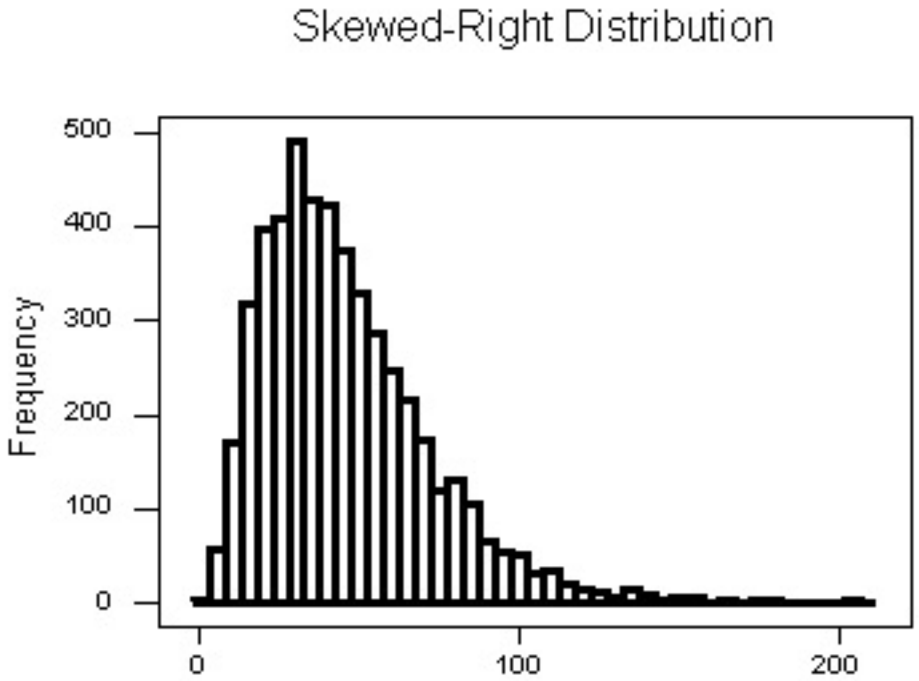
Relative frequency polygons for the data of Table 2.10.

Describing Distributions

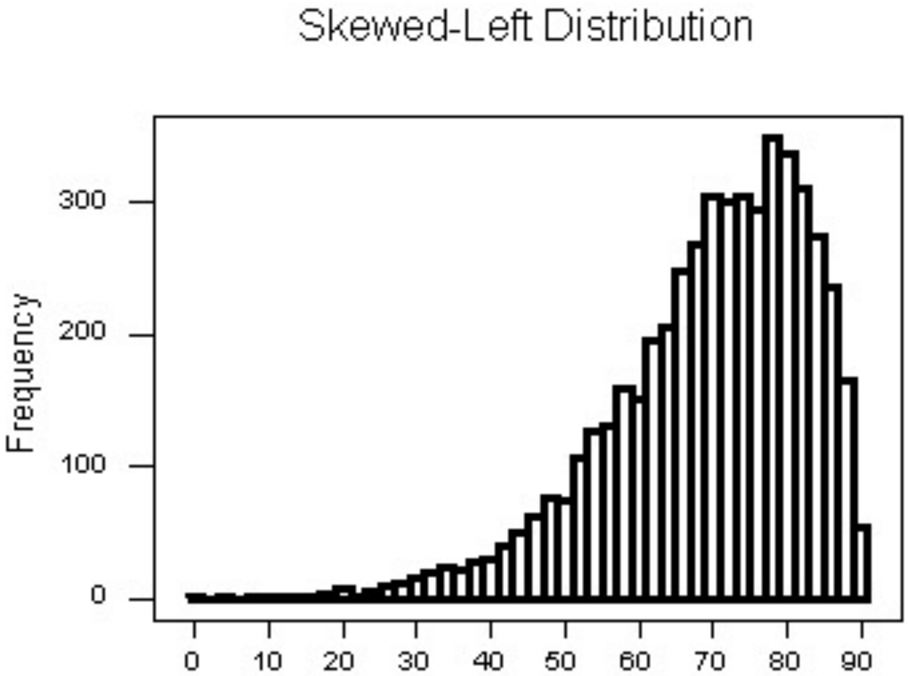
- **Shape**
- **Center**
- Spread
- Outliers

Shape

- **Symmetry/Skewness** of the distribution
- **Peakedness (modality)**
  - The number of peaks (modes) the distribution has



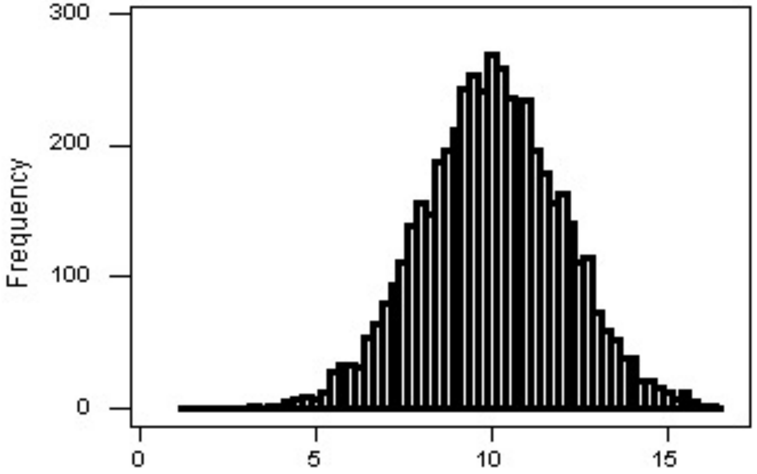
Skewed-Right Distribution



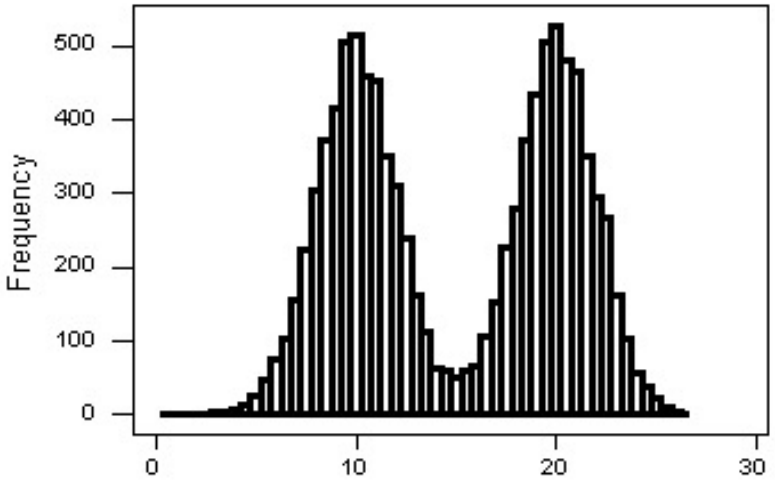
Skewed-Left Distribution

Describing distributions [Internet]. [cited 2021 Oct 1]. Available from: https://bolt.mph.ufl.edu/6050-6052/unit-1/one-quantitative-variable-introduction/describing-distributions/

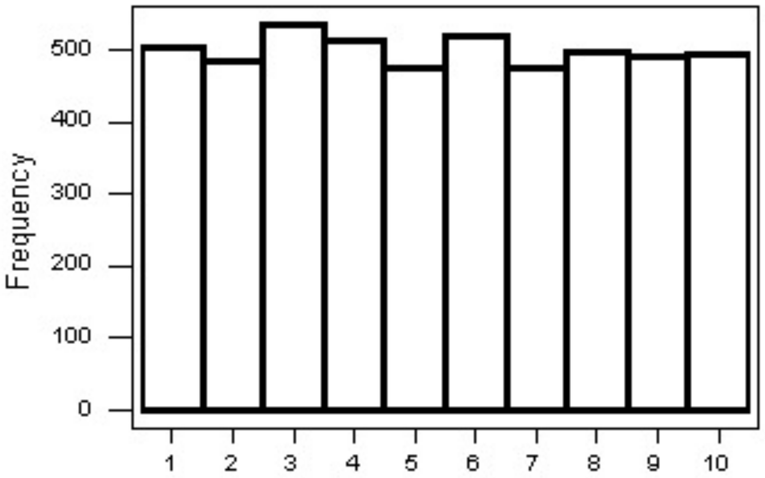
Symmetric, Single-peaked (Unimodal) Distribution



Symmetric, Double-peaked (Bimodal) Distribution



Symmetric, Uniform, Distribution



Describing distributions [Internet]. [cited 2021 Oct 1]. Available from: https://bolt.mph.ufl.edu/6050-6052/unit-1/one-quantitative-variable-introduction/describing-distributions/

Center

- Mean
- Median
- Mode

Center - Mean

$$\bar{x} = \frac{\sum_{i=1}^{n} x_i}{n}$$

Cholesterol levels of 40 patients:

213, 174, 193, 196, 220, 183, 194, 200, 192, 200, 200, 199, 178, 183, 188, 193, 187, 181, 193, 205, 196, 211, 202, 213, 216, 206, 195, 191, 171, 194, 184, 191, 221, 212, 221, 204, 204, 191, 183, 227

$$\bar{x} = \frac{213+174+...+227}{40} = 197.625$$

Mean

If $y_i = x_i + c$ (c is a constant) $\bar{y} = \bar{x} + c$

$$\bar{x} = \frac{213+174+...+227}{40} = 197.625$$

$$\bar{y} = \frac{(213+5)+(174+5)+...+(227+5)}{40} = 202.625$$

Mean

If $y_i = x_i$ x c (c is a constant) $\bar{y} = \bar{x}$ x c

x: 1, 2, 3, 4, 5

y: 3 (1 * 3), 6 (2 * 3), 9 (3 * 3), 12 (4 * 3), 15 (5 * 3)
$\Rightarrow c = 3$

$\bar{x} = 3,\ \bar{y} = 9 \Rightarrow \bar{y} = 3 * \bar{x}$

Mean

- Even a small change in a single value affects the mean

213, 174, 193, 196, 220, 183, 194, 200, 192, 200, 200, 199, 178, 183, 188, 193, 187, 181, 193, 205, 196, 211, 202, 213, 216, 206, 195, 191, 171, 194, 184, 191, 221, 212, 221, 204, 204, 191, 183, 227

- If the maximal value was 700 (instead of 227), the mean would be 209.45 (instead of 197.625)

Median

- It is calculated as the:
  - middle value of the sorted values (if n is odd)
  - average of two middle values of the sorted values (if n is even)

2, 5, 3, 10, 4
2, 3, $\underline{4}$, 5, 10 => median = 4

5, 3, 10, 4
3, $\underline{4}$, $\underline{5}$, 10 => median = 4.5

Median

Cholesterol levels of 40 patients:

Original data

213, 174, 193, 196, 220, 183, 194, 200, 192, 200, 200, 199, 178, 183, 188, 193, 187,
181, 193, 205, 196, 211, 202, 213, 216, 206, 195, 191, 171, 194, 184, 191, 221, 212,
221, 204, 204, 191, 183, 227

Sorted dataa

171, 174, 178, 181, 183, 183, 183, 184, 187, 188, 191, 191, 191, 192, 193, 193, 193,
194, 194, 195, 196, 196, 199, 200, 200, 200, 202, 204, 204, 205, 206, 211, 212, 213,
213, 216, 220, 221, 221, 227

Mean = 197.625

Median = 195.5

Median

171, 174, 178, 181, 183, 183, 183, 184, 187, 188, 191, 191, 191, 192, 193, 193, 193, 194, 194, 195, 196, 196, 199, 200, 200, 200, 202, 204, 204, 205, 206, 211, 212, 213, 213, 216, 220, 221, 221, **227**

Mean = 197.625

Median = 195.5

171, 174, 178, 181, 183, 183, 183, 184, 187, 188, 191, 191, 191, 192, 193, 193, 193, 194, 194, 195, 196, 196, 199, 200, 200, 200, 202, 204, 204, 205, 206, 211, 212, 213, 213, 216, 220, 221, 221, **700**

Mean = 209.45

Median = 195.5

Mode

- The mode is the value that appears most often in a set of data values

- Systolic blood pressures of 12 patients:

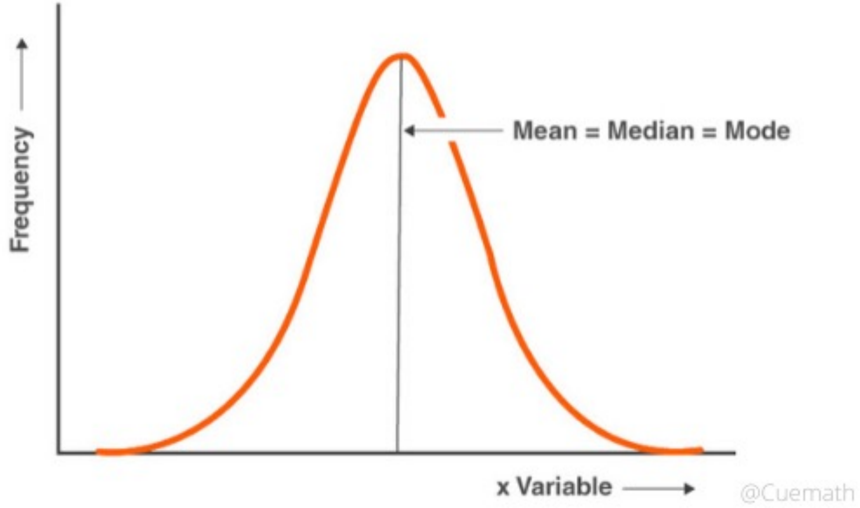
90, 80, **100**, 110, **100**, 120, **100**, 90, **100**, 110, 120, 110

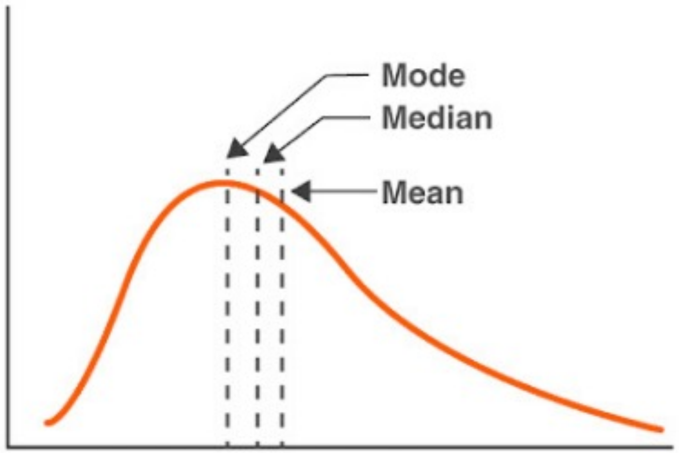
Mode = 100

Mean = 102.5

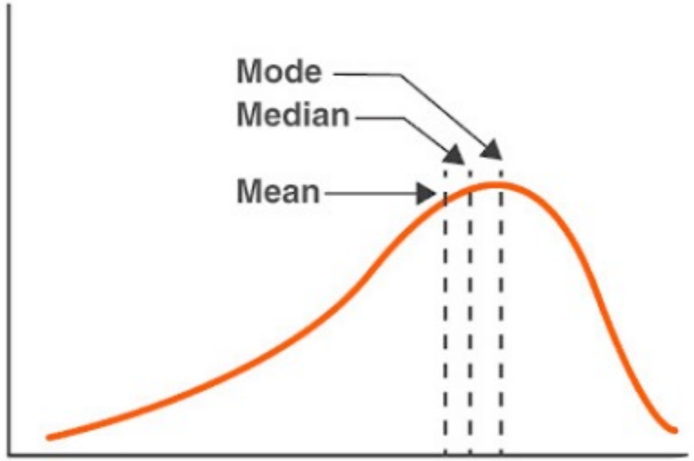
Median = 100

Mean – Median – Mode Relationship





Positively skewed frequency distribution



Negatively skewed frequency distribution

Brief Summary

- Statistics is a discipline concerned with collection, organization, analysis and interpretation of data
- The aim is to infer information regarding the population using sample data
- There are two kinds of variables:
  - Categorical – nominal, binary, ordinal, count
  - Continuous – interval, ratio
- We may summarize a categorical variable using frequency, relative frequency and/or percentage tables
- We may visually display a categorical variable using bar charts, etc.
- We may visually inspect the distribution of a continuous variable using histograms
- To determine the center of a continuous variable, one can use mean, median, mode
- The mean is very sensitive to outliers, while the median is robust to outliers