2019-2

Introduction to Biostatistics - Lecture 1: Introduction and Descriptive Statistics

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Introduction to Biostatistics

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Outline

- Purpose
- Introduction to biostatistics
- Descriptive Statistics

Purpose of the course

- Basic principles and applications of statistics to problems in clinical and public health settings.
- Will cover tools for statistical inference: t-test, chi-square tests, ANOVA, Linear regression.
- Interpretation and presentation of the results
- Introductory foundation for the implementation of those techniques using R or R studio software.

References

- Multiple authors, Openstax College

  Introductory Statistics

  Publisher: OpenStx, Pubdate: 2013

https://open.umn.edu/opentextbooks/textbooks/introductory-statistics-2013

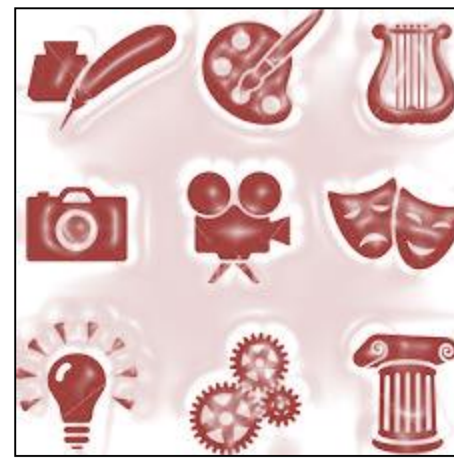
- Quick-R: https://www.statmethods.net/
- UCLA statistical computing: https://stats.idre.ucla.edu/

What is Statistics?

- **Statistics** is the **science** of learning from **data**, and of measuring, controlling, and communicating uncertainty; and it thereby provides the navigation essential for controlling the course of scientific and societal advances (*Davidian, M. and Louis, T. A., 10.1126/science.1218685*).

- **Statistics** is also an **ART** …

  of conducting a study, analyzing the data, and derive useful conclusions from numerical outcomes about real life problems…



What is Biostatistics?

- **Biostatistics** is the application of statistics in medical research, e.g.:
  - Clinical trials
  - Epidemiology
  - Pharmacology
  - Medical decision making
  - Comparative Effectiveness Research
  - etc.

Statistical Analysis

Key steps for a complete and accurate statistical analysis:

- State a valid research question
- Collect information (DATA) for answering this question
- Validate/clean/organize the collected information
- Exploratory Data Analysis (EDA)
- Analyze this information
- Translate numerical results into answers
- Interpret results and derive conclusions
- Present the results and communicate with people

Terms in Biostatistics

- **Data :**
  - all the information we collect to answer the research question
- **Variables :**
  - Outcome, treatment, study population characteristics
- **Subjects :**
  - units on which characteristics are measured
- **Observations :**
  - data elements
- **Population :**
  - all the subjects of interest
- **Sample :**
  - a subset of the population for which data are collected

Reference: Introductory Statistics, page 45-46

Sample from Population

	Population	**Sample**	
Descriptive Measure	Parameter	statistic	Summary of a characteristic
Size	N	n	Total # of subjects
Mean	μ	$\bar{x}$	Average
Variance	σ^2	s^2	Variance

Impossible/impractical to analyze the entire population →

→ thus we only analyze a sample

Statistical Inference

Collect and analyze data from samples →

→ Calculate summary statistics →

→ Make Inference about unknown population parameters (e.g., population average from sample mean)

The Framingham Heart Study

https://www.framinghamheartstudy.org/fhs-about/history/epidemiological-background/

- … *"a long term prospective study of the etiology of cardiovascular disease among a population of free living subjects in the community of Framingham, Massachusetts."* …
- Identifying risk factors for cardiovascular disease (CVD)
- N=4,434 participants (subset of the original sample)
- Follow-up period: 1956 – 1968
- Longitudinal data: measurements approximately every 6 years
- 1 to 3 observations for each participant (total 11,627 obs)

The Framingham Heart Study

- Information:
  - ID
  - Age
  - Sex
  - Period (1^{st}, 2^{nd}, or 3^{rd} exam)
  - Systolic Blood Pressure (mmHg)
  - Diastolic Blood Pressure (mmHg)
  - Use of Anti-hypertensive medication at exam (yes/no)
  - Current smoking status (yes/no)
  - Average number of cigarettes smoked/day
  - Prevalent coronary Heart disease (yes/no)
  - … etc

The Framingham Heart Study

RStudio

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Lec1.R × | dat1 ×

Filter

	sex	randid	totchol	age	sysbp	diabp	cursmoke	cigpday	bmi	diabetes	bpmeds	heartrte
1	1	2448	195	39	106.0	70.0	0	0	26.97	0	0	
2	1	2448	209	52	121.0	66.0	0	0	NA	0	0	
3	2	6238	250	46	121.0	81.0	0	0	28.73	0	0	
4	2	6238	260	52	105.0	69.5	0	0	29.43	0	0	
5	2	6238	237	58	108.0	66.0	0	0	28.50	0	0	
6	1	9428	245	48	127.5	80.0	1	20	25.34	0	0	
7	1	9428	283	54	141.0	89.0	1	30	25.34	0	0	
8	2	10552	225	61	150.0	95.0	1	30	28.58	0	0	
9	2	10552	232	67	183.0	109.0	1	20	30.18	0	0	
10	2	11252	285	46	130.0	84.0	1	23	23.10	0	0	
11	2	11252	343	51	109.0	77.0	1	30	23.48	0	0	
12	2	11252	NA	58	155.0	90.0	1	30	24.61	0	0	
13	2	11263	228	43	180.0	110.0	0	0	30.30	0	0	
14	2	11263	230	49	177.0	102.0	0	0	31.36	0	1	
15	2	11263	220	55	180.0	106.0	0	0	31.17	1	1	
16	2	12629	205	63	138.0	71.0	0	0	33.11	0	0	
17	2	12629	220	70	149.0	81.0	0	0	36.76	0	0	
18	2	12806	313	45	100.0	71.0	1	20	21.68	0	0	
19	2	12806	NA	51	109.5	72.5	1	30	22.19	0	0	
20	2	12806	320	57	110.0	46.0	1	30	22.02	0	0	
21	1	14367	260	52	141.5	89.0	0	0	26.36	0	0	
22	1	14367	292	58	132.0	90.0	0	0	25.39	0	0	
23	1	14367	280	64	168.0	100.0	0	0	25.72	0	0	
24	1	16365	225	43	162.0	107.0	1	30	23.61	0	0	

Showing 1 to 26 of 11,627 entries

Statistical Concepts: Example 1
The Framingham Heart Study

- **Data :**
  –
- **Variables :**
  –
- **Subjects :**
  –
- **Observations :**
  –
- **Population :**
  –
- **Sample :**
  –

Statistical Concepts: Example 1
The Framingham Heart Study

- **Data :**
  - all the collected information for the purposes of this study
- **Variables :**
  -
- **Subjects :**
  -
- **Observations :**
- **Population :**
- **Sample :**

Statistical Concepts: Example 1
The Framingham Heart Study

- **Data :**
  - all the collected information for the purposes of this study
- **Variables :**
  - “randid”, “period”, “sex”, “age”, “totchol”, “cursmoke”, .., etc
- **Subjects :**
  -
- **Observations :**
- **Population :**
- **Sample :**

Statistical Concepts: Example 1
The Framingham Heart Study

- **Data :**
  - all the collected information for the purposes of this study
- **Variables :**
  - "randid", "period", "sex", "age", "totchol", "cursmoke", .., etc
- **Subjects :**
  - participants (each one with unique ID number "randid")
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- **Population :**
- **Sample :**

Statistical Concepts: Example 1
The Framingham Heart Study

- **Data :**
  - all the collected information for the purposes of this study
- **Variables :**
  - “randid”, “period”, “sex”, “age”, “totchol”, “cursmoke”, .., etc
- **Subjects :**
  - participants (each one with unique ID number “randid”)
- **Observations :**
  - Each element of the dataset, e.g. for participant with “randin”=9428 :
    - “period”=2, “totchol”=283, “age”=54, … etc.
- **Population :**

- **Sample :**

Statistical Concepts: Example 1
The Framingham Heart Study

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  - all the collected information for the purposes of this study
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- **Sample :**
  -

Statistical Concepts: Example 1
The Framingham Heart Study

- **Data :**
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- **Population :**
  - … "*a population of free living subjects in the community of Framingham, Massachusetts.*" …
- **Sample :**
  - Subset of the population of size n=4,434

Classification of Variables

Discrete

Nominal

- Name only.

Ex., *Gender*:
- Male
- Female

Ordinal

- Order implied.

Ex., *Self-reported health status*:
- Excellent
- Very good
- Good
- Fair
- Poor

Continuous (interval, ratio)

Measurements in scale

Ex., age,
height,
weight,
cholesterol level,
SBP,
DBP, etc.

Reference: Introductory Statistics, Chapter 1.3

Classification of Variables: Example

The Framingham Heart Study

- Discrete Variables:
  - Nominal:
  - Ordinal:

- Continuous Variables:

The Framingham Heart Study

RStudio

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Lec1.R dat1

Filter

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10	2	11252	285	46	130.0	84.0	1	23	23.10	0	0	
11	2	11252	343	51	109.0	77.0	1	30	23.48	0	0	

Classification of Variables: Example
The Framingham Heart Study

- Discrete Variables:
  - Nominal: “sex”, “cursmoke”, etc.
  - Ordinal: “period”

- Continuous Variables:
  - “sysbp”, “bmi”, etc

Descriptive statistics for Discrete variables

- **Frequency (f):** Number (#) of subjects in each category.
- **Relative frequency ($\frac{f}{n} \cdot 100$):** Proportion (%) of subjects in each category.

Example: calculate number/proportion of subjects in each period

Period	Frequency (f)	Relative Frequency (%)	Cumulative Relative Frequency (%)
1	4434	$\frac{4434}{11627} \cdot 100 = 38.1$	38.1
2	3930	33.8	71.9
3	3260	28.1	100
Total	**11627**	**100**	

Descriptive statistics for Discrete variables

- **Frequency (f):** Number (#) of subjects in each category.
- **Relative frequency ($\frac{f}{n} \cdot 100$):** Proportion (%) of subjects in each category.

Example: calculate number/proportion of subjects in each period in R

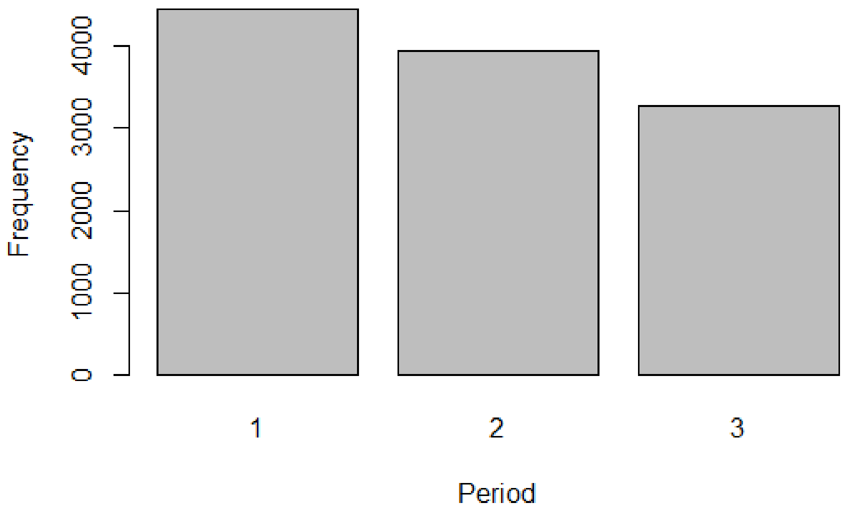
```
## frequency and relative frequency of period ##
tab1 = table(dat1$period)
n = sum(tab1)
rel_tab1 = tab1/n*100 ## alternative way: prop.table(tab1)*100
cum_tab1 = cumsum(rel_tab1)
cbind(tab1, rel_tab1, cum_tab1)
```

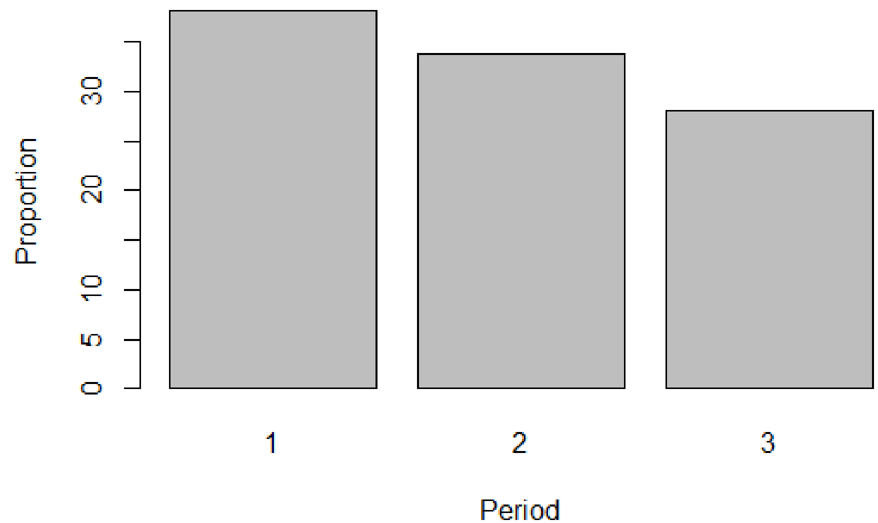
```
> cbind(tab1, rel_tab1, cum_tab1)
  tab1 rel_tab1  cum_tab1
1 4434 38.13537  38.13537
2 3930 33.80064  71.93601
3 3263 28.06399 100.00000
```

Graphical Methods for Discrete variables

- **Bar plots :** indicate frequency or relative frequency distribution

```
barplot(tab1, xlab="Period", ylab = "Frequency")
barplot(rel_tab1, xlab="Period", ylab="Proportion")
```





Descriptive statistics for Discrete variables

- **Frequency and relative frequency ($\frac{f}{n} \cdot 100$) by groups**

  Example: calculate number/proportion of subjects in each period in R by sex (female if sex=2)

```
## period by sex ##
tab2 = table(dat1$period, dat1$sex)
tab2
rel_tab2 = prop.table(tab2, margin=2)*100 ## the option margin = 2 for column sum to be 100%
rel_tab2

cbind(tab2, rel_tab2)
```

```
> ## period by sex ##
> tab2 = table(dat1$period, dat1$sex)
> tab2

       1    2
  1 1944 2490
  2 1691 2239
  3 1387 1876
> rel_tab2 = prop.table(tab2, margin=2)*100 ## the option margin = 2 for column sum to be 100%
> rel_tab2

           1        2
  1 38.70968 37.69871
  2 33.67184 33.89856
  3 27.61848 28.40273
>
> cbind(tab2, rel_tab2)
     1    2        1        2
1 1944 2490 38.70968 37.69871
2 1691 2239 33.67184 33.89856
3 1387 1876 27.61848 28.40273
```

Descriptive statistics for Continuous variables

Measures of location	Measures of dispersion
Indicate where the collected values of a variable are “located” compared to the range of possible values it can take.	Indicate how dispersed the collected values of a variable are.

Descriptive statistics for Continuous variables

Measures of location	Measures of dispersion
Indicate where the collected values of a variable are "located" compared to the range of possible values it can take.	Indicate how dispersed the collected values of a variable are.
• Mean • Median • Quartiles • Mode • Min • Max	• Range • Variance • Standard Deviation • Interquartile range (IQR) • Mean Absolute Deviation (MAD) • Coefficient of variation

Measures of Location : Mean ($\bar{x}$)

Definition	Formula
• Average value. • A typical value for the variable of interest.	$\bar{x} = \frac{\sum_{i=1}^{n} X_i}{n}$

- Sample of n=7
- X= Systolic Blood Pressure in mmHg:

X_1	X_2	X_3	X_4	X_5	X_6	X_7
121	110	114	100	160	130	130

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- X= Systolic Blood Pressure in mmHg:

X_1	X_2	X_3	X_4	X_5	X_6	X_7
121	110	114	100	160	130	130

$$\bar{x} = \frac{\sum_{i=1}^{n} X_i}{n} = \frac{X_1 + X_2 + X_3 + \cdots + X_7}{n} = \frac{121+110+114+\cdots+130}{7} = \frac{865}{7} = 123.57 \approx 123.6$$

Measures of Location : Median

Definition	Formula
• The middle value of the variable of interest. • 50% of the collected values are less and 50% are greater than the median.	• If n odd: the $\frac{(n+1)}{2}^{th}$ observation • If n even: mean of the $\frac{n}{2}^{th}$ and the $(\frac{n}{2}+1)^{th}$ observations in the **ordered** sample

Unordered	X_1	X_2	X_3	X_4	X_5	X_6	X_7
	121	110	114	100	160	130	130
Ordered	$X_{(1)}$	$X_{(2)}$	$X_{(3)}$	$X_{(4)}$	$X_{(5)}$	$X_{(6)}$	$X_{(7)}$
	100	110	114	121	130	130	160

Measures of Location : Median

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Unordered	X_1	X_2	X_3	X_4	X_5	X_6	X_7
	121	110	114	100	160	130	130
Ordered	$X_{(1)}$	$X_{(2)}$	$X_{(3)}$	$X_{(4)}$	$X_{(5)}$	$X_{(6)}$	$X_{(7)}$
	100	110	114	121	130	130	160

Median

n=7 → odd # → median: $\frac{(7+1)}{2}$ = 4th observation in the ordered sample

→ median = $X_{(4)}$ = 121

Measures of Location : **Median**

Unordered	X_1	X_2	X_3	X_4	X_5	X_6
	121	110	114	100	160	130
Ordered	$X_{(1)}$	$X_{(2)}$	$X_{(3)}$	$X_{(4)}$	$X_{(5)}$	$X_{(6)}$
	100	110	114	121	130	130

Measures of Location : **Median**

Unordered	X_1	X_2	X_3	X_4	X_5	X_6
	121	110	114	100	160	130
Ordered	$X_{(1)}$	$X_{(2)}$	$X_{(3)}$	$X_{(4)}$	$X_{(5)}$	$X_{(6)}$
	100	110	114	121	130	130

3th **4th**

n=6 → even # → **median**: **mean** of the $(\frac{6}{2})$=**3th** and the $(\frac{6}{2}+1)$=**4th** observations in the ordered sample

$$\rightarrow \text{median} = \frac{X_{(3)}+X_{(4)}}{2} = \frac{114+121}{2} = 117.5$$

Measures of Location : **Quartiles**

Definition
• First (**Q_1**): 25% of the collected values are less than Q_1.   • Second (**Q_2**): 50% of the collected values are less than Q_2 (**median**).   • Third (**Q_3**): 75% of the collected values are less than Q_3.

Measures of Location : **Percentiles**

Definition

- $\mathbf{q_p}$: p% of the collected values are less than q_p.
- E.g., q_1 is that value of the population (or sample) with 1% of the observed values being less and 99% being grater than it.

Measures of Location : **Mode / Min / Max**

Definition
• **Min**: the minimum of the collected values ($\mathbf{X_{(1)}}$). • **Max**: the maximum of the collected values ($\mathbf{X_{(n)}}$). • **Mode**: the most frequent of the collected values.

Unordered	X_1	X_2	X_3	X_4	X_5	X_6	X_7
	121	110	114	100	160	130	130
Ordered	$X_{(1)}$	$X_{(2)}$	$X_{(3)}$	$X_{(4)}$	$X_{(5)}$	$X_{(6)}$	$X_{(7)}$
	100	110	114	121	130	130	160

Measures of Location : **Mode / Min / Max**

Definition

- **Min**: the minimum of the collected values ($\mathbf{X_{(1)}}$).
- **Max**: the maximum of the collected values ($\mathbf{X_{(n)}}$).
- **Mode**: the most frequent of the collected values.

Unordered	X_1	X_2	X_3	X_4	X_5	X_6	X_7
	121	110	114	100	160	130	130
Ordered	$X_{(1)}$	$X_{(2)}$	$X_{(3)}$	$X_{(4)}$	$X_{(5)}$	$X_{(6)}$	$X_{(7)}$
	100	110	114	121	130	130	160

Min

Max

Mode = 130

Measures of Dispersion: **Variance (s^2)**

Definition	Formula
• Average squared deviation from the mean.	$S^2 = \frac{\sum_{i=1}^{n}(X_i - \bar{X})^2}{n-1}$

- $\bar{X}$ = 123.6

X_1	X_2	X_3	X_4	X_5	X_6	X_7
121	110	114	100	160	130	130

Measures of Dispersion: **Variance (s^2)**

Definition	**Formula**
• Average squared deviation from the mean.	$S^2 = \frac{\sum_{i=1}^{n}(X_i - \bar{X})^2}{n-1}$

- $\bar{X}$ = 123.6

X_1	X_2	X_3	X_4	X_5	X_6	X_7
121	110	114	100	160	130	130

$$S^2 = \frac{\sum_{i=1}^{n}(X_i - \bar{X})^2}{n-1} = \frac{(X_1-\bar{X})^2 + \cdots + (X_7-\bar{X})^2}{n-1} = \frac{(121-123.6)^2 + \cdots + (130-123.6)^2}{7-1} =$$

$$= \frac{2247.72}{6} = 374.62 \approx 374.6$$

Other Measures of Dispersion:

Definition	Formula
• Standard deviation	$s = \sqrt{\frac{\sum_{i=1}^{n}(X_i - \bar{X})^2}{n-1}}$
• Mean Absolute Deviation (MAD)	MAD = $\frac{\sum_{i=1}^{n} \lvert X_i - \bar{X} \rvert}{n}$
• Range	Max – Min
• Interquartile Range (IQR)	$Q_3 - Q_1$
• Coefficient of variation	$\frac{s}{\bar{X}}$

Descriptive Statistics for Continuous Variables Example: The Framingham Heart Study

```
> ## the overall summary stat for sysbp ##
> describe(dat1$sysbp)
   vars     n   mean   sd median trimmed   mad  min max range skew kurtosis   se
X1    1 11627 136.32 22.8    132  134.34 20.76 83.5 295 211.5 0.94     1.37 0.21
>
> ## the summary stat for sysbp by sex ##
> describeBy(dat1$sysbp, dat1$sex)

 Descriptive statistics by group
group: 1
   vars    n   mean   sd median trimmed   mad  min max range skew kurtosis   se
X1    1 5022 135.07 20.3    132  133.37 19.27 83.5 235 151.5 0.86     0.93 0.29
---------------------------------------------------------------------
group: 2
   vars    n   mean    sd median trimmed   mad  min max range skew kurtosis  se
X1    1 6605 137.28 24.49    133  135.15 22.24 83.5 295 211.5 0.93     1.28 0.3
```

SEX = 1 for male, 2 for female

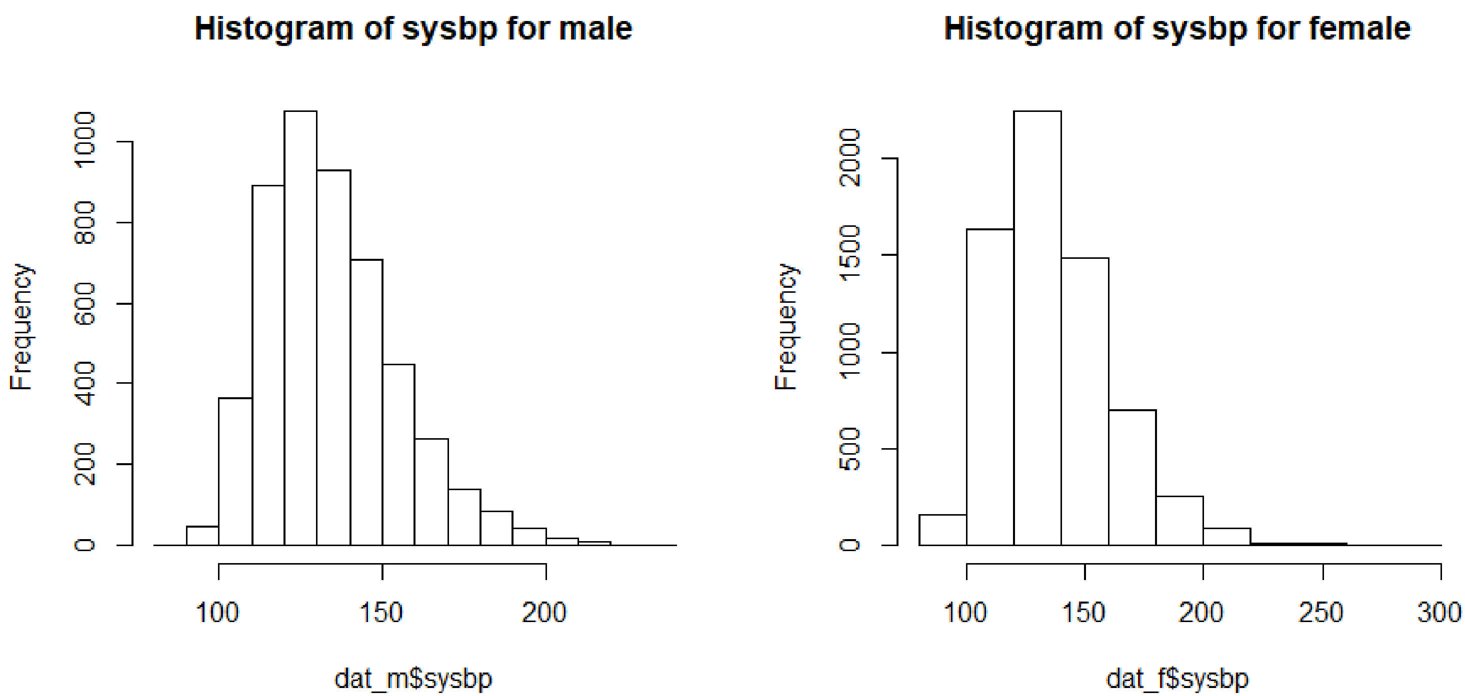
Std.dev = $Var(X_i)$ to explain variation of sysbp

SE.mean = $\sqrt{Var(\bar{X})}$ to explain variation of MEAN sysbp

Graphical Methods for Continuous variables

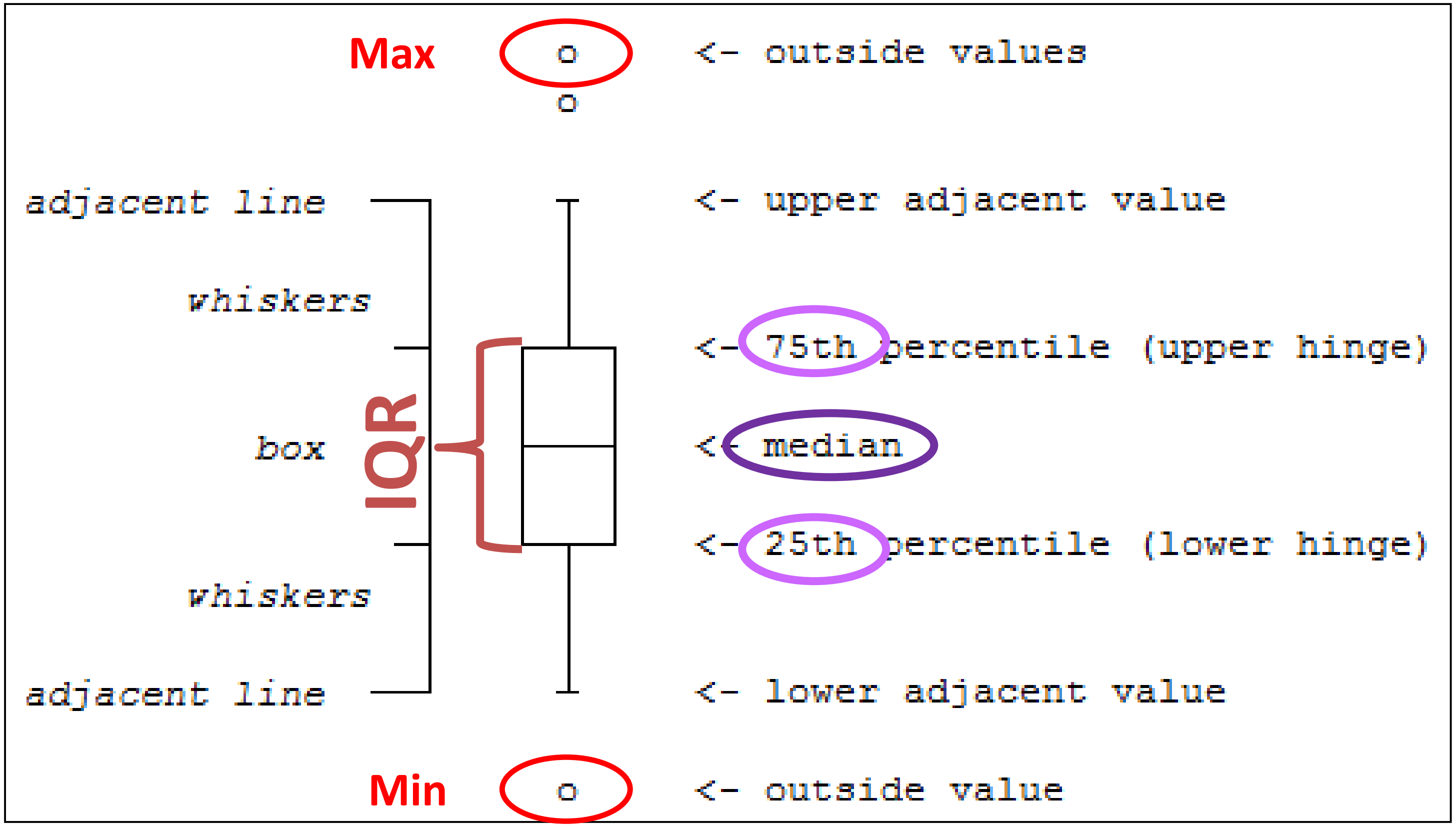
- **Histogram :** indicate the distribution of the values of a continuous variable.

```
## Histogram of sysbp by sex ##
dat_m = subset(dat1, sex==1) ## get a subset for male
dat_f = subset(dat1, sex==2) ## get a subset for female
par(mfrow = c(1,2)) ## to draw two plots side by side
hist(dat_m$sysbp, main="Histogram of sysbp for male")
hist(dat_f$sysbp, main="Histogram of sysbp for female")
```



Graphical Methods for Continuous variables

Box - Plot : indicate the distribution of the values of a continuous variable, pointing out the following quantities:



Outliers

- Observations above Q3 + 1.5IQR or
  below Q1 – 1.5IQR

  are called, “outliers”, in the box plot.
- Outliers are not caused by typo or errors.
- Outliers are simply part of data, which can not be ignored.
- Outliers explain how many extreme values are located at tails of a distribution.

Graphical Methods for Continuous variables

- **Box-Plot** : the distribution of the values of a continuous variable.

```
## A box plot of sysbp by sex ##
par(mfrow = c(1,1))
boxplot(sysbp ~ sex, data=dat1, main="Box plot of sysbp by sex")
```