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The principles of biostatistics

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Learning outcomes

At the end of this workshop, you should be able to

1. Describe about **population & sample, causality, level of measurement & distribution of data**
2. **Summarise categorical & numerical data**
3. **Use appropriate statistical test for bi-variable analyses**

Truth

We observe.

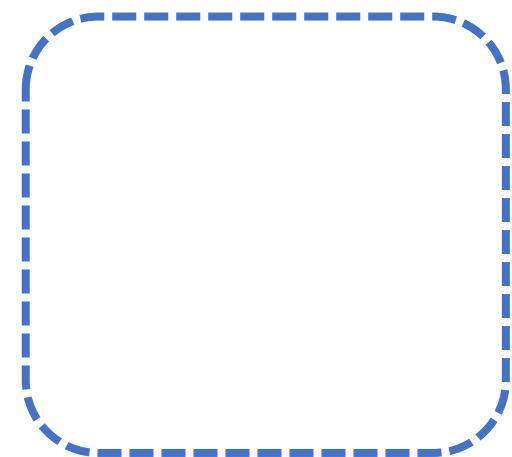
We believe what we observe.

What we observed might not be the truth.



One of the most important objective in research is to **represent** results from **sample** analysis to the **population**.

Population vs. Sample



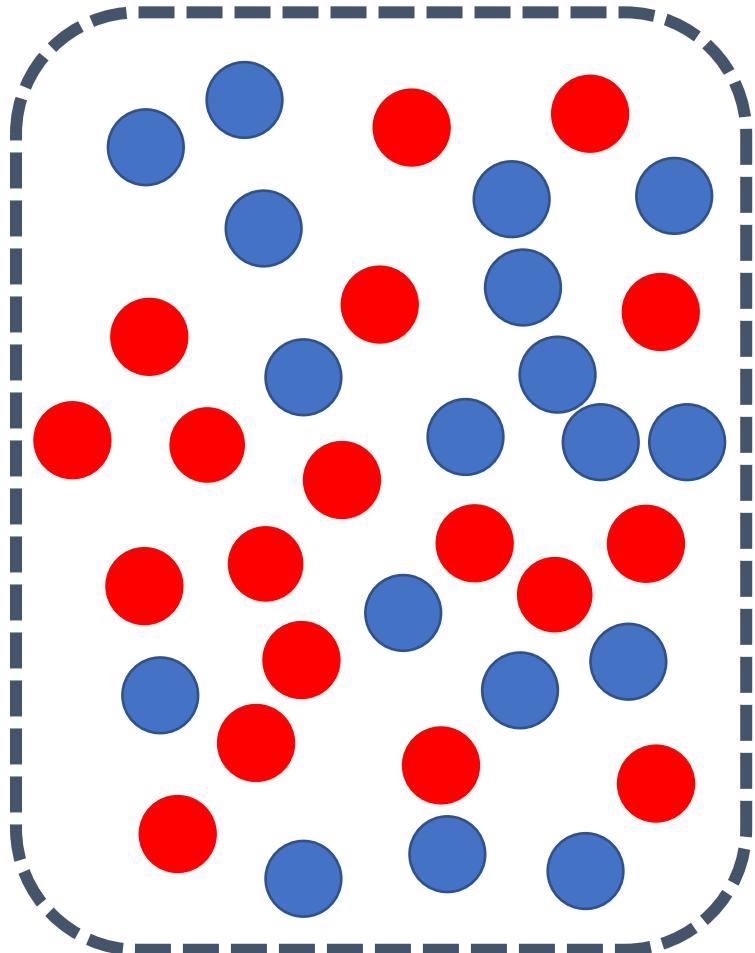
Parameter vs. Statistics

- **Parameter** - characteristic of the whole population
- **Statistics** - characteristic of a sample, presumably **measurable**.



Statistics estimate parameters

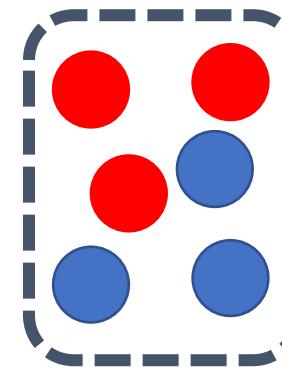
- Representative
- Sampling error
- Different samples yield different estimates
- Statistics = Parameter if sampling done properly
- How to prove?



$$N = 35$$

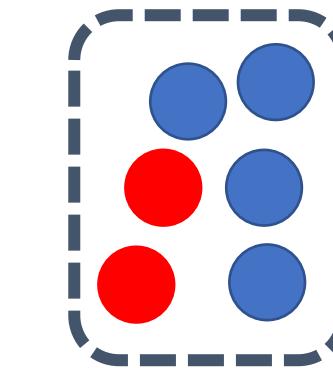
$$\text{Red} = 18/35 = 51.4\%$$

Parameter



$$N = 6$$

$$\text{Red} = 3/6 = 50\%$$



$$N = 6$$

$$\text{Red} = 2/6 = 33.3\%$$

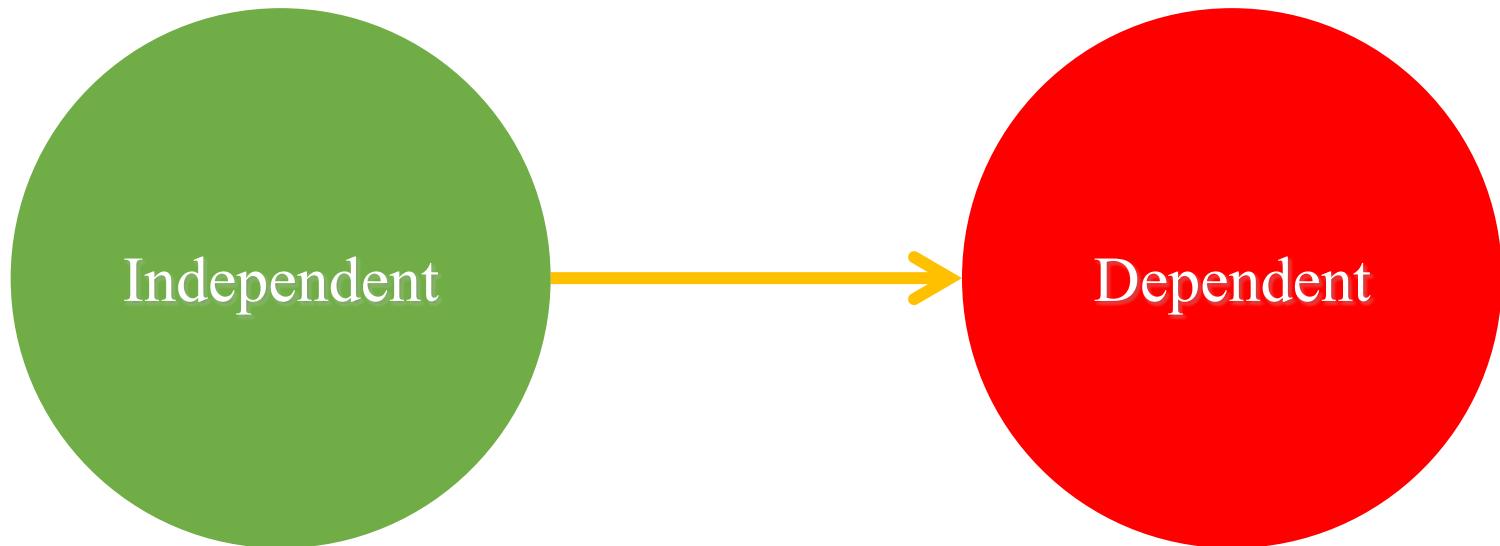
Statistics

$$\text{Average \% Red} = \frac{50\% + 33.3\% + 66.7\%}{3} = 50\%$$

Estimated
Parameter

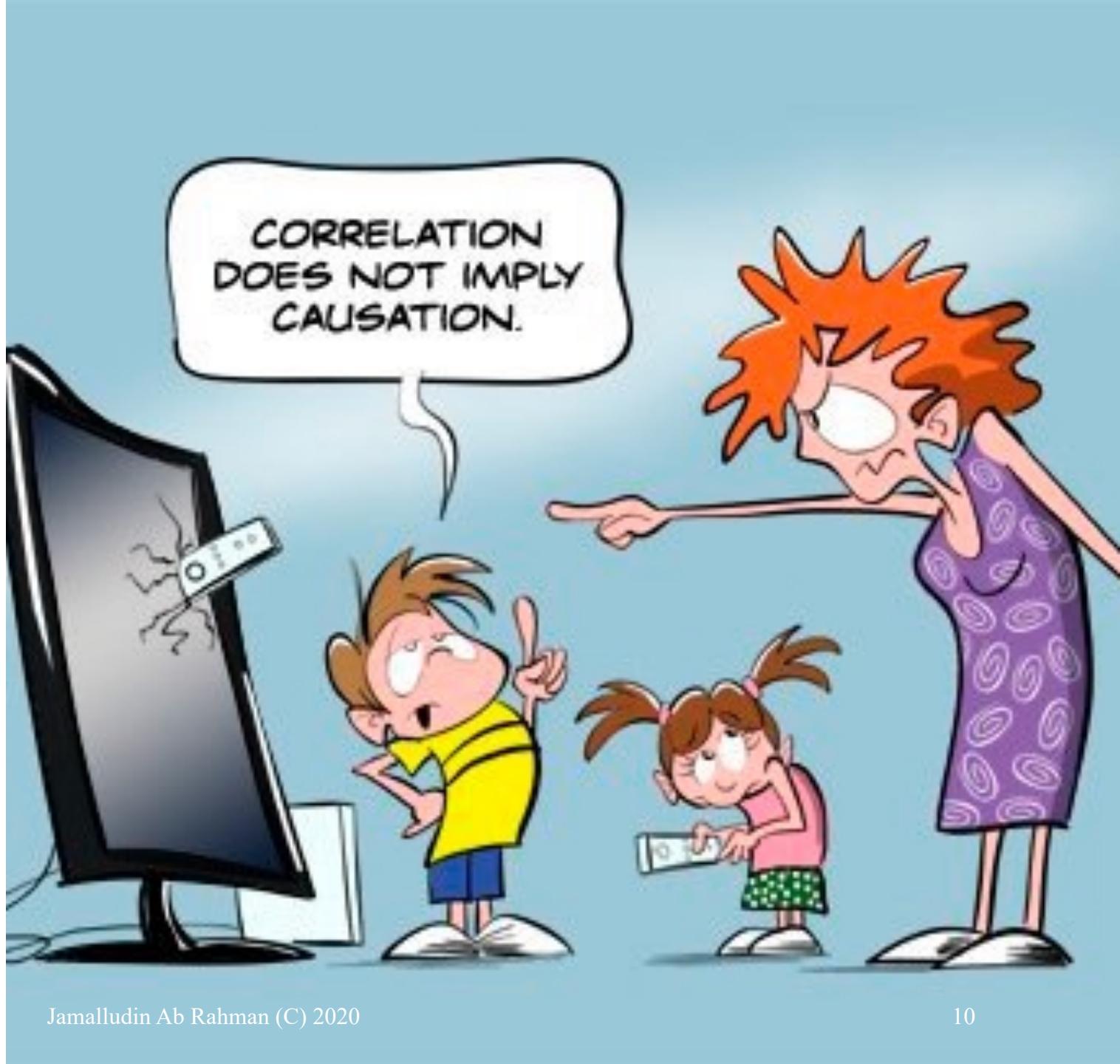
Variable & its role

- A value and whose associated value may be changed



Causation

- Relation of events (cause and effect)
- Correlation (between two events) does not (always) imply causation
- Rooster's crow does not cause the sun to rise
- Switch does not cause the bulb to light



Meeting January 14 1965

President's Address

The Env
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by Sir A
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Among
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ings with other Sectio
secondly, 'to make available information
the physical, chemical and psychological hazards
of occupation, and in particular about those that
are rare or not easily recognized'.

have to be
It will depend upon circum

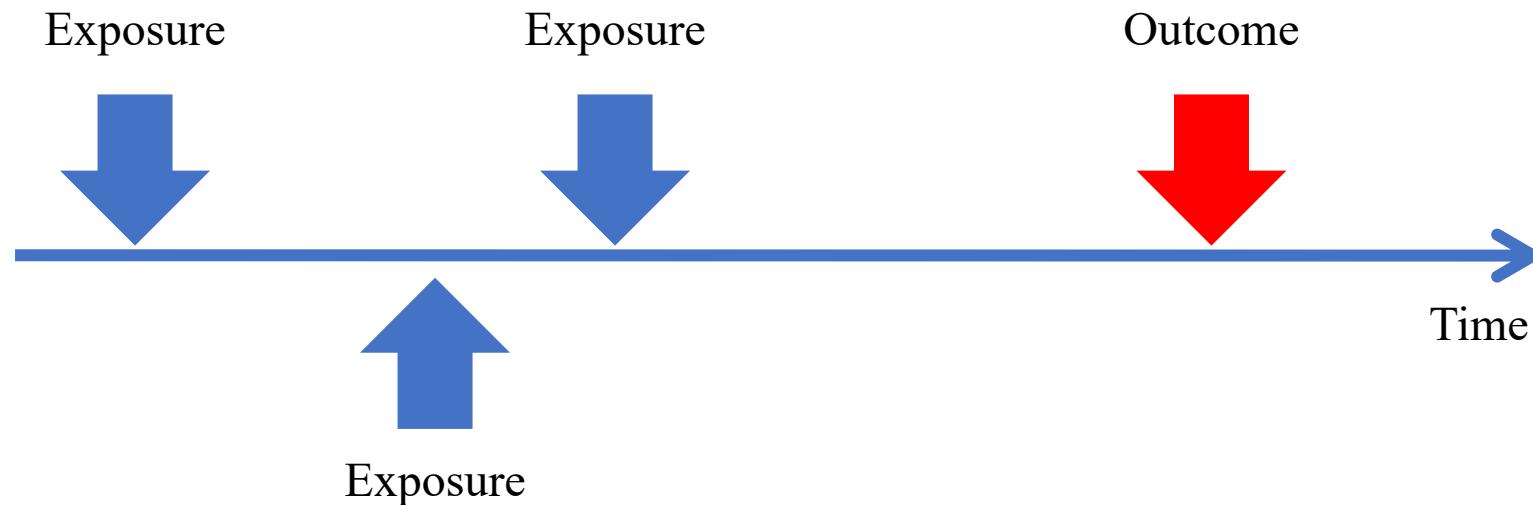
I have no wish, nor the skill, to embark upon a philosophical discussion of the meaning of 'causation'. The 'cause' of illness may be immediate and direct, it may be remote and indirect underlying the observed association. But with the aims of occupational, and almost synonymously preventive, medicine in mind the decisive question is whether the frequency of the undesirable event B will be influenced by a change in the environmental feature A. How such a

Hill's criteria

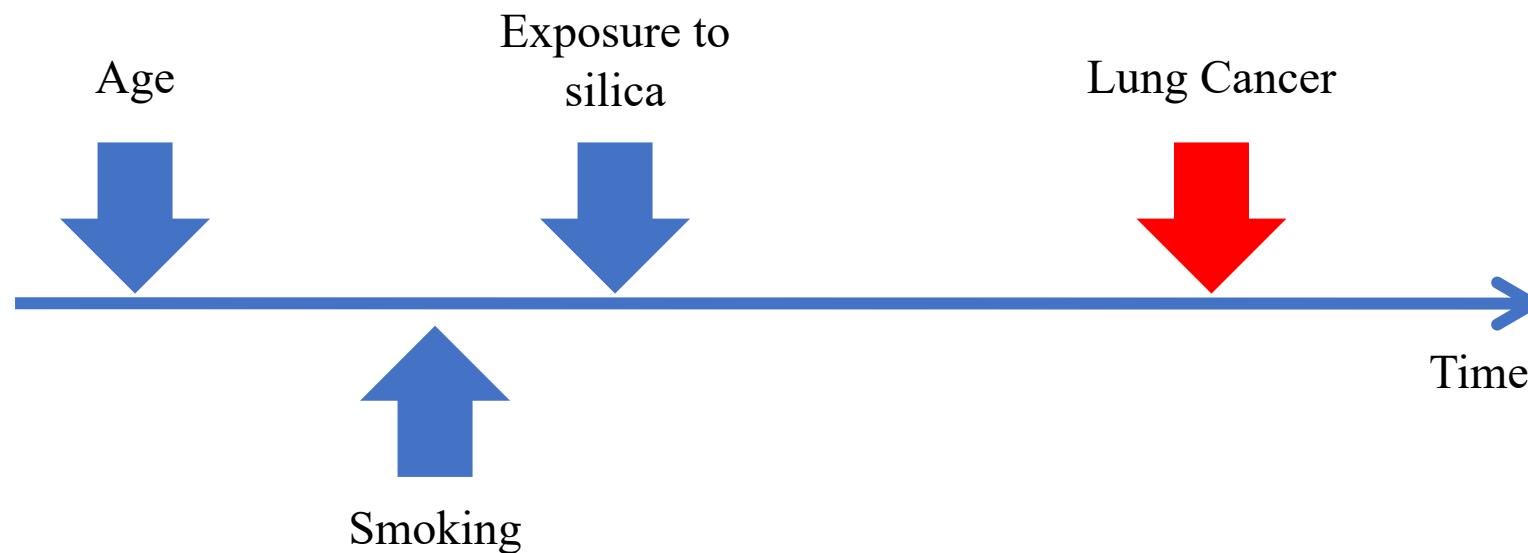
1. Strength of association
2. Consistency
3. Specificity
4. Temporality
5. Biological gradient
6. Plausibility
7. Coherence
8. Experiment
9. Analogy

Hill AB. The environment and disease:
Association or causation? Proceed Roy Soc
Medicine – London. 1965;58:295–300.

Time & causation



Time & causation (example)





Causal web

- Web of causation
- Conceptual framework
- Path analysis/web
- Relationship between variables
- Cause and effect

Causal webs in epidemiology

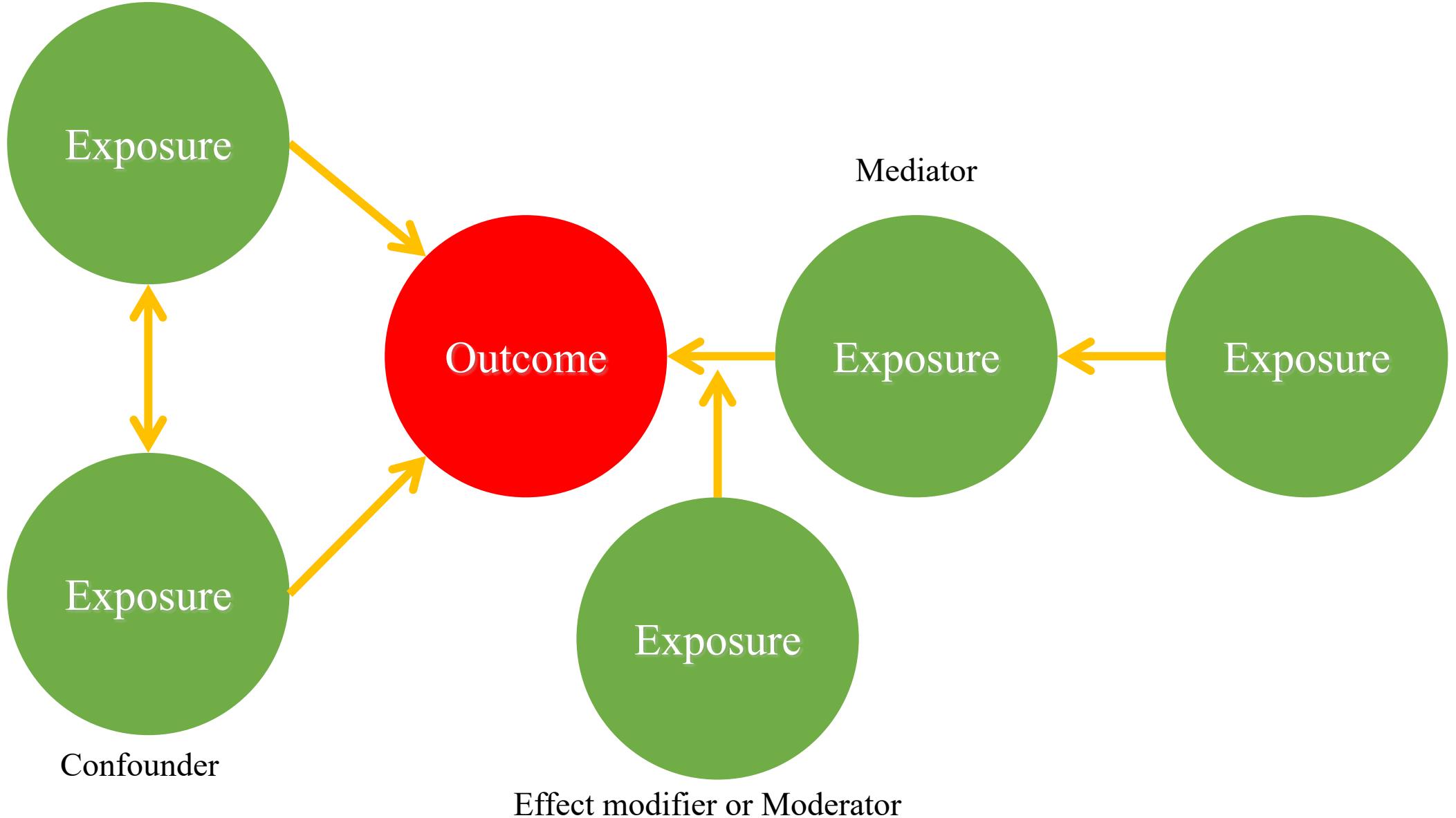
Federica Russo

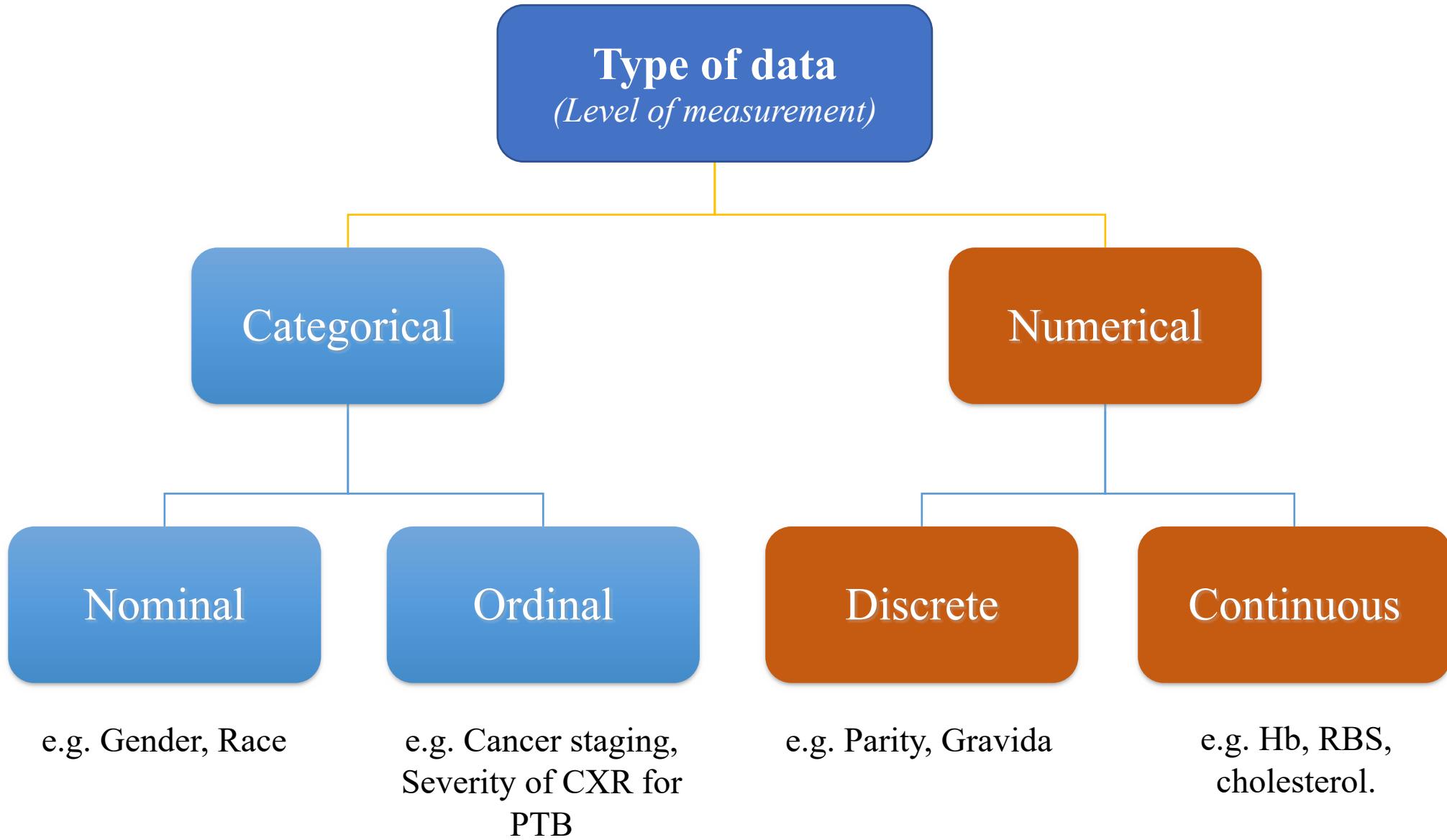
Philosophy, Kent

Draft of 30 October 2009

To appear in *Paradigmi* – Special issue on the Philosophy of Medicine.

Abstract. The notion of ‘causal web’ emerged in the epidemiological literature in the early Sixties and had to wait until the Nineties for a thorough critical appraisal. Famously, Nancy Krieger argued that such a notion isn’t helpful unless we specify what kind of spiders create the webs. This means, according to Krieger, (i) that the role of the spiders is to provide an explanation of the yarns of the web and (ii) that the sought spiders have to be biological and social. This paper contributes to the development of the notion of causal web, elaborating on the two following points: (i) to catch the spiders we need multi-fold evidence—specifically, mechanistic and difference-making—and (ii) for the eco-social to be explanatory, the web has to be mechanistic in a sense to be specified.





Distribution (shape) of data

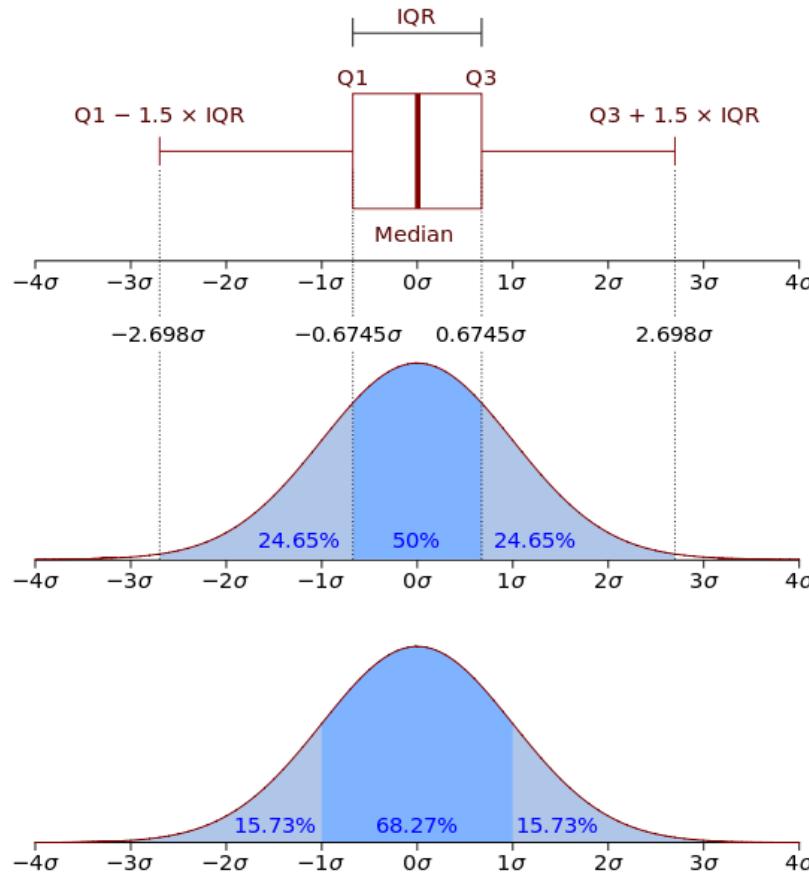
- Applicable to **numerical** value
- Discrete or Continuous
- Discrete \sim *Binomial, Poisson, Negative Binomial, Hypergeometry, Multinomial etc.*
- Continuous \sim *Normal, t, chi-square, F etc.*



Knowing about the distribution means knowing the probability.

Knowing the probability will assists in reasoning.

Normal Distribution



$$f(x; \mu, \sigma^2) = \frac{1}{\sigma\sqrt{2\pi}} e^{-\frac{1}{2}(\frac{x-\mu}{\sigma})^2}$$

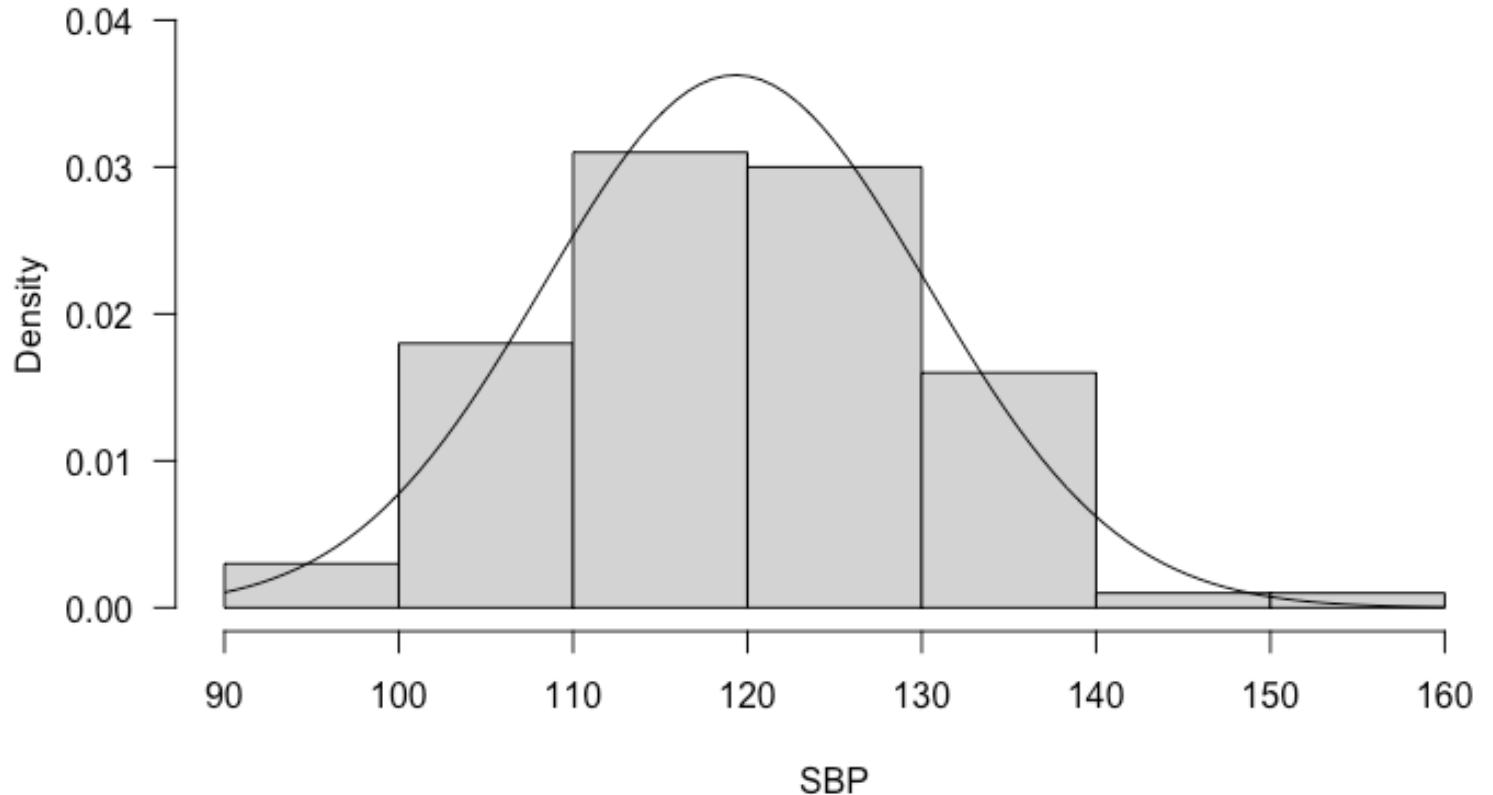
Why Normal?

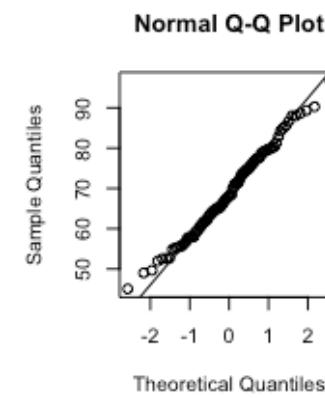
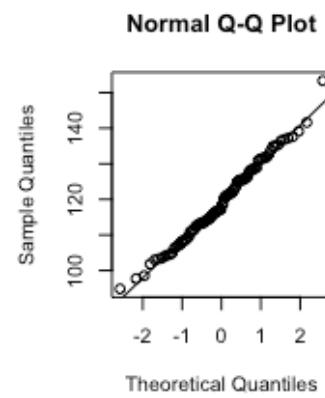
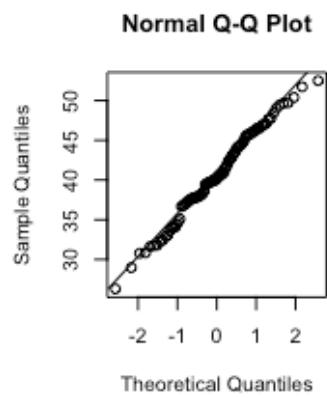
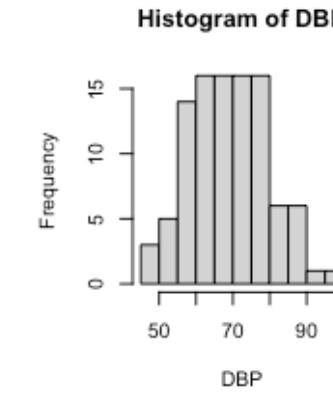
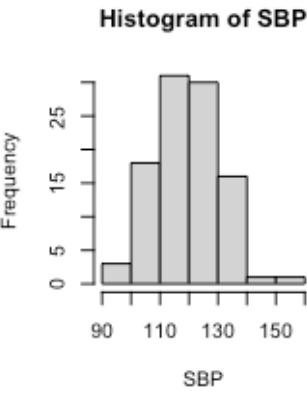
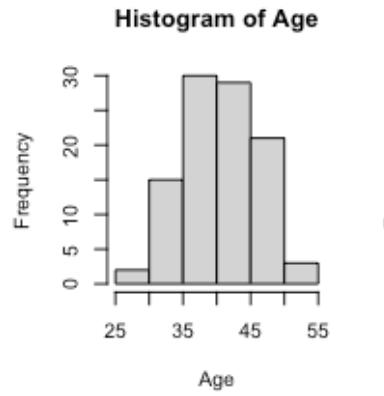
- Because many biological & psychological variables are distributed normally
- Many predictive models assume Normal distribution

Characteristics

- Bell shaped curve
- Symmetrical
- Unimodal

Distribution of SBP





Checking distribution

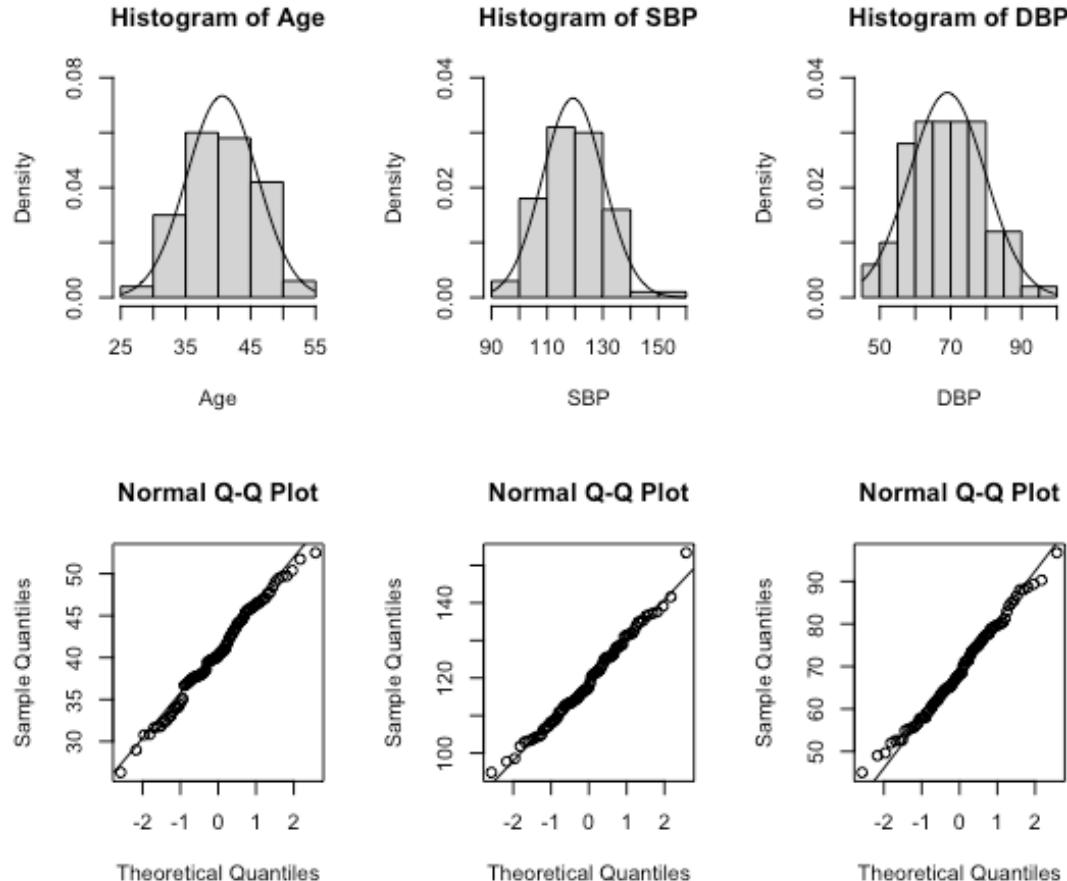
Visually

```
par(mfrow= c(2,3))
hist(Age)
hist(SBP)
hist(DBP)
```

```
qqnorm(Age)
qqline(Age)
```

```
qqnorm(SBP)
qqline(SBP)
```

```
qqnorm(DBP)
qqline(DBP)
```



Showing Normal curve

```
hist(Age, ylim=c(0,.08), probability = TRUE)
curve(dnorm(x, mean=mean(Age), sd=sd(Age)), add=TRUE)
```

```
hist(SBP, ylim=c(0,0.04), probability = TRUE)
curve(dnorm(x, mean=mean(SBP), sd=sd(SBP)), add=TRUE)
```

```
hist(DBP, ylim=c(0,0.04), probability = TRUE)
curve(dnorm(x, mean=mean(DBP), sd=sd(DBP)), add=TRUE)
```

Q-Q Plot

```
qqnorm(Age)
qqline(Age)
```

```
qqnorm(SBP)
qqline(SBP)
```

```
qqnorm(DBP)
qqline(DBP)
```

Characteristics of a normal distribution

1. Shape of the curve – smooth symmetrical bell-shaped
2. Mean=Median
3. Skewness ~ 0 (usually ± 2)
4. Kurtosis ~ 0 (usually ± 2)

```
> library(psych)
> describe(Age)
  vars   n   mean    sd median trimmed   mad    min    max range skew kurtosis    se
x1     1 100 40.62 5.44  40.18     40.7 5.18 26.31 52.5  26.2 -0.12    -0.47 0.54
> describe(SBP)
  vars   n   mean    sd median trimmed   mad    min    max range skew kurtosis    se
x1     1 100 119.32 11 117.81   119.12 11.49 94.85 153.37 58.52 0.24    -0.23 1.1
> describe(DBP)
  vars   n   mean    sd median trimmed   mad    min    max range skew kurtosis    se
x1     1 100 69.09 10.7  68.12    68.84 11.7 45.07 96.75 51.68 0.15    -0.58 1.07
```

Test of Normality

- Anderson–Darling Test
- Corrected Kolmogorov–Smirnov Test
(Lilliefors Test)
- Cramér–von-Mises Criterion
- D'agostino's K-squared Test
- Jarque–Bera Test
- Pearson's Chi-square Test
- Shapiro–Francia
- Shapiro–Wilk Test

```
> # Normality test
>
> shapiro.test(Age)

Shapiro-Wilk normality test

data: Age
W = 0.98956, p-value = 0.6295

> shapiro.test(SBP)

Shapiro-Wilk normality test

data: SBP
W = 0.98957, p-value = 0.6297

> shapiro.test(DBP)

Shapiro-Wilk normality test

data: DBP
W = 0.99029, p-value = 0.688
```

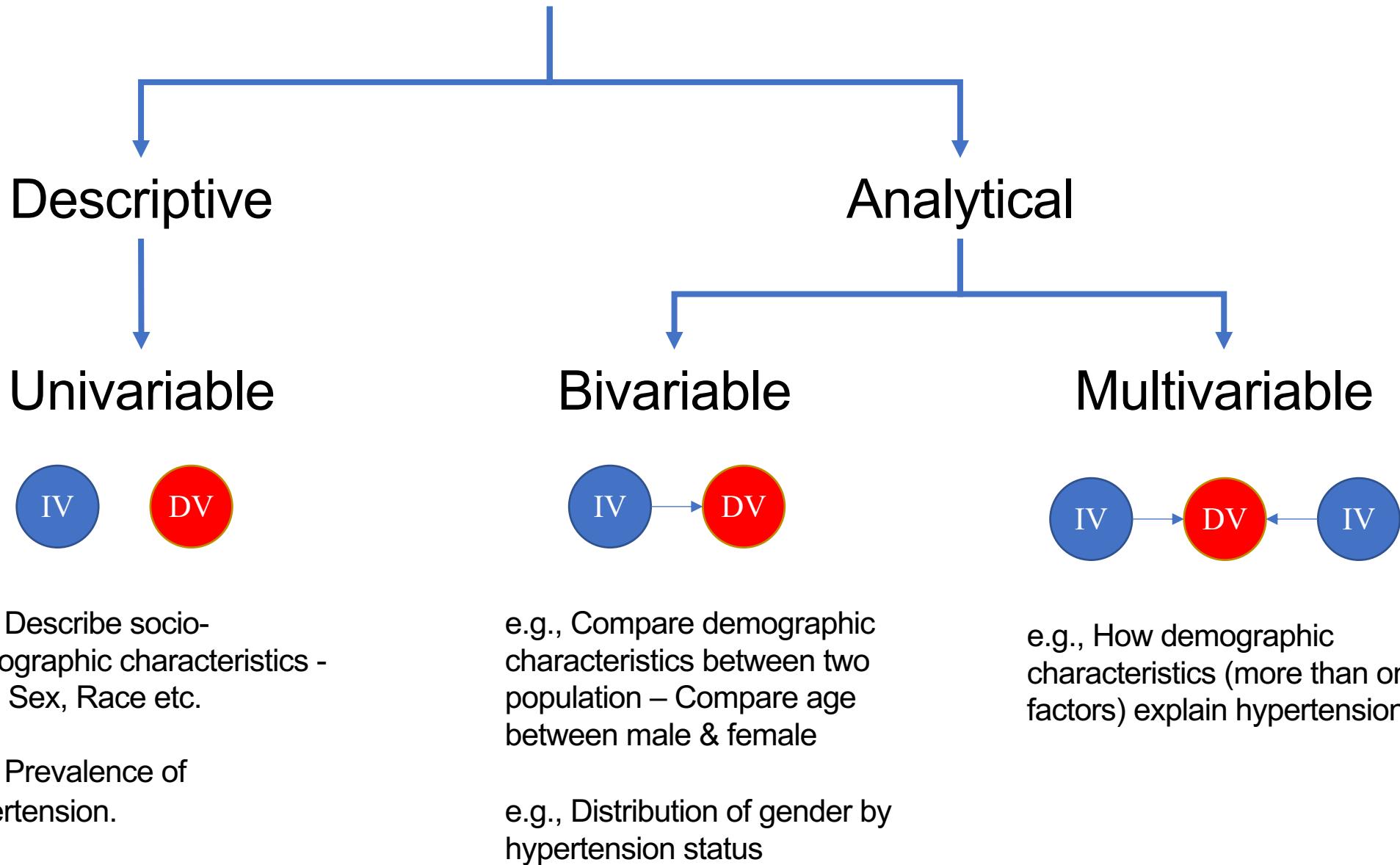
Use Normality test with caution

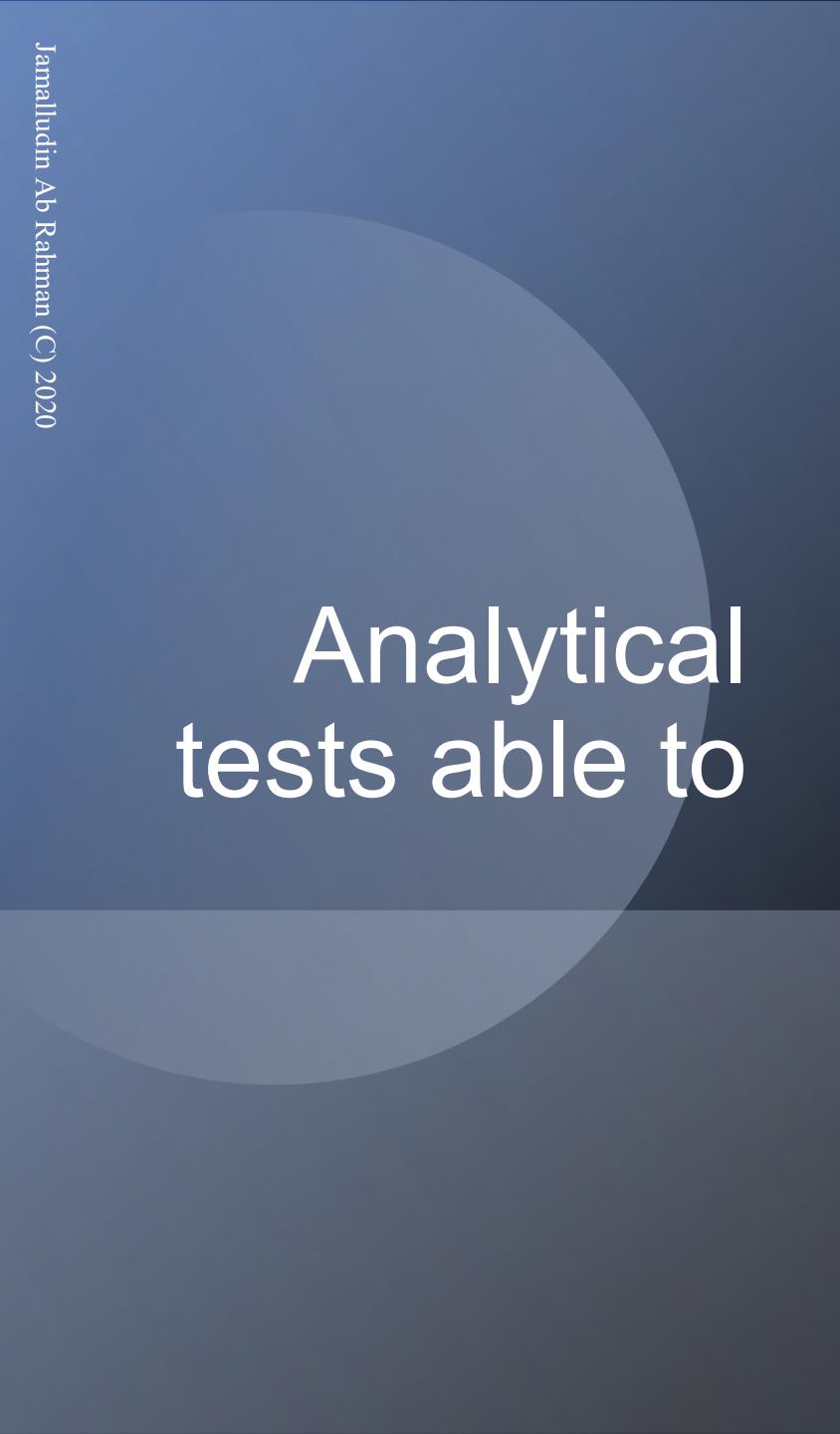
- Small samples almost always pass a normality test. *Normality tests have little power to tell whether or not a small sample of data comes from a Gaussian distribution.*
- With large samples, minor deviations from normality may be flagged as statistically significant, *even though small deviations from a normal distribution won't affect the results of a t test or ANOVA.*

What would you do if the distribution is not normal?

1. Validate data entry
2. Transform the data
3. Use a non-parametric test

Statistical analysis





Analytical
tests able to

1. Determine **presence of difference** (or similarity)
2. Determine **degree of difference**
3. Determine the **direction of changes (trend)**
4. **Predict changes** (outcomes)

Is there any difference between A & B?

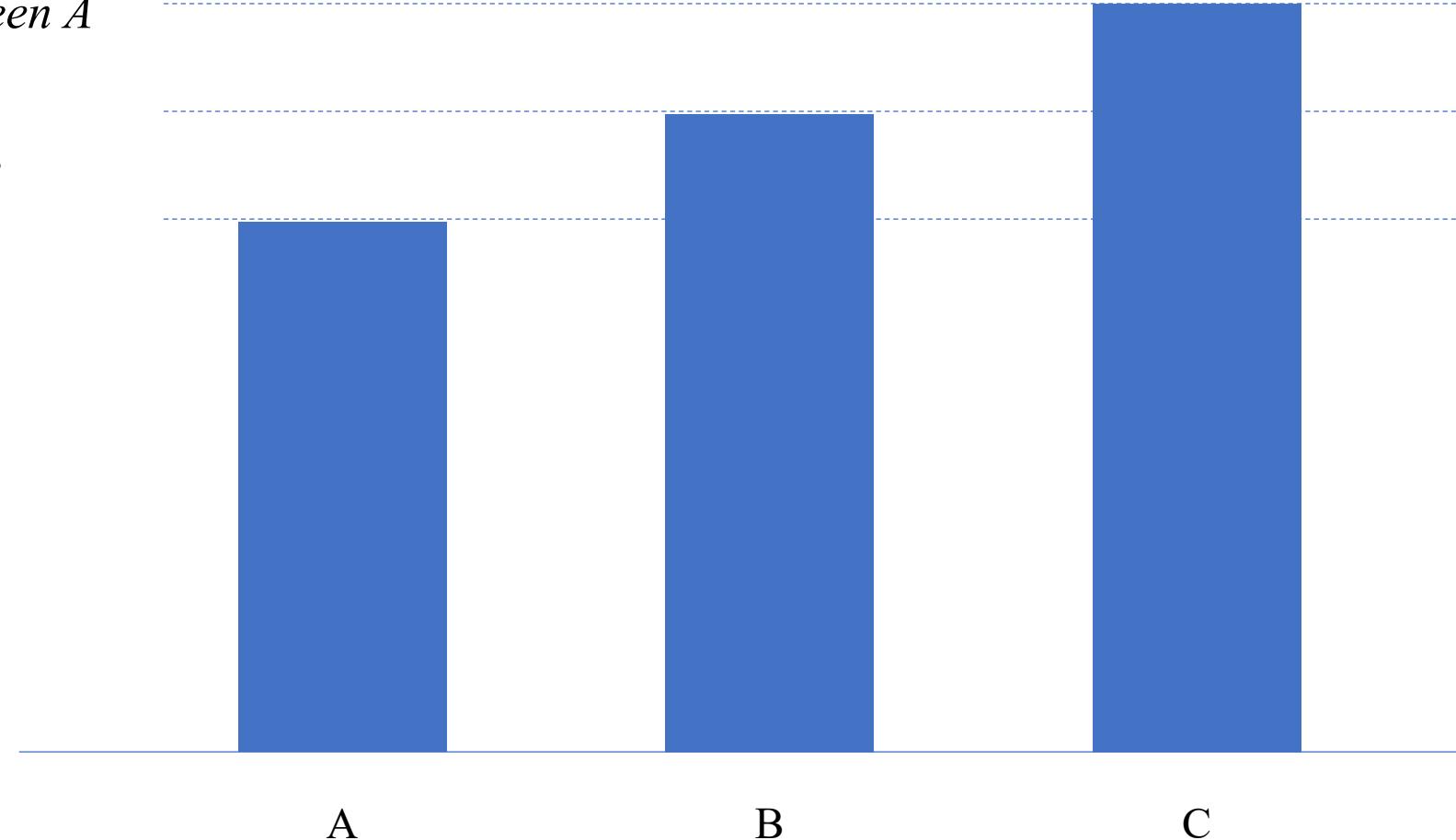
Which one is taller? A or B?

How big is the difference between A & B?

Is C different from A & B?

Is there any pattern now?

If there will be D, can you predict how tall is D?



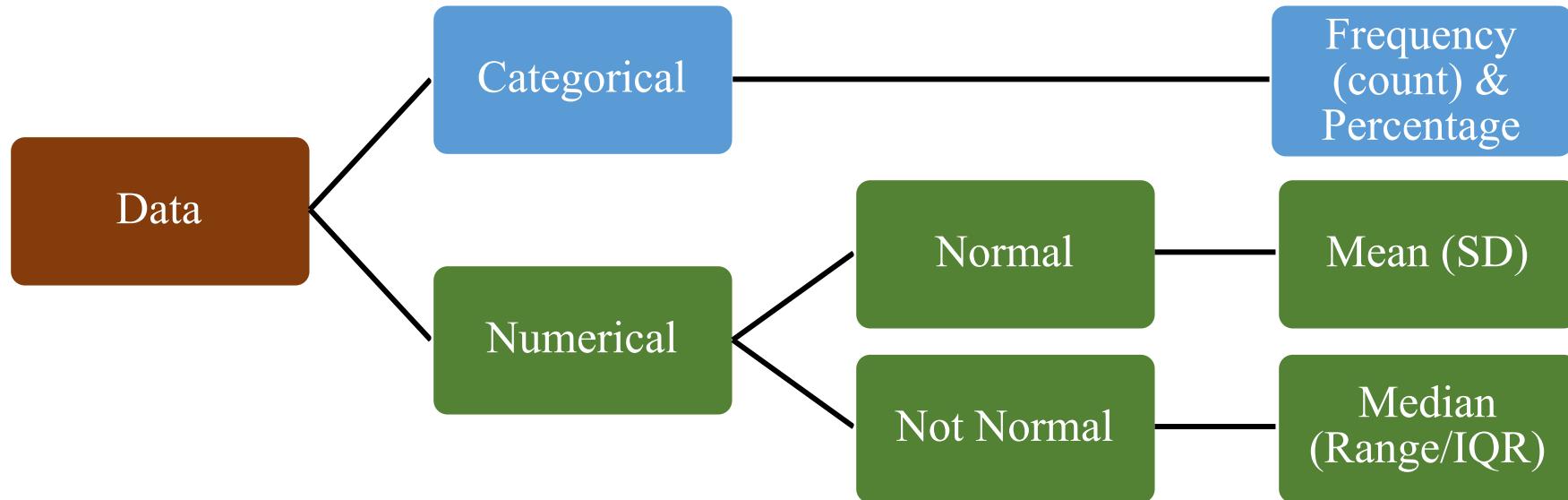
Descriptive statistics

Basic Biostatistics
Jamalludin Ab Rahman

Descriptive Statistics

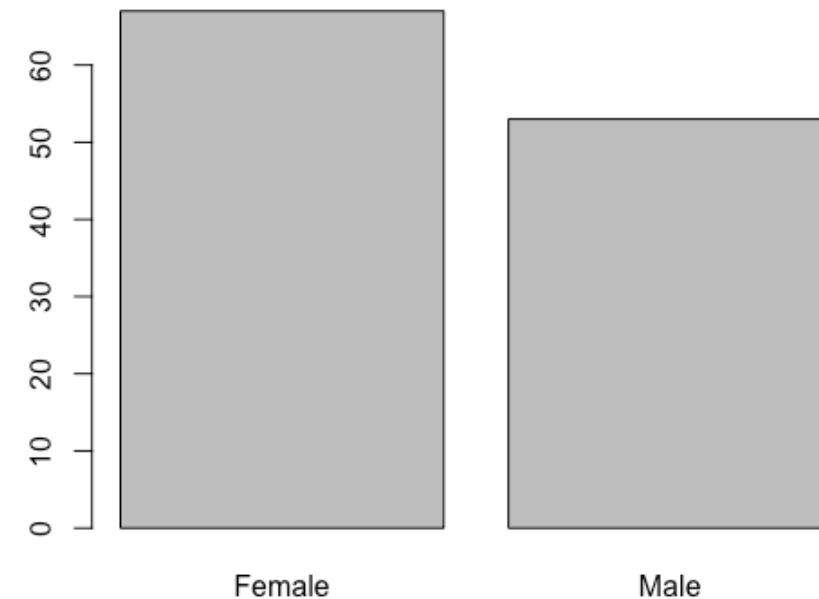
- Explain **one variable** at one time
- Method based on level of measurement
 - Categorical
Frequency (Percentage)
 - Numerical
*Central measures (e.g. mean, median)
& Dispersion (e.g. variance, standard deviation, range, min-max, interquartile range)*

How to describe a data



Describe categorical variable

```
> # Describe categorical variable  
> table(Sex)  
Sex  
Female   Male  
  67      53  
> round(prop.table(table(Sex))*100,  
digit=1)  
Sex  
Female   Male  
  55.8    44.2  
>  
> par(mfrow= c(1,1))  
> plot(Sex)
```



Describe numerical variable

```
> # Describe numerical variables (Age, SBP & DBP)
> library(psych)
> describe(Age)
  vars   n   mean     sd median trimmed   mad   min     max range skew kurtosis     se
X1     1 120 40.01  4.48   40.02   39.94  4.35  29.9  52.43  22.53  0.19    -0.15  0.41
> describe(SBP)
  vars   n   mean     sd median trimmed   mad   min     max range skew kurtosis     se
X1     1 120 119.93  9.21  120.19  119.95  9.34  98.47 142.03  43.56 -0.02    -0.44  0.84
> describe(DBP)
  vars   n   mean     sd median trimmed   mad   min     max range skew kurtosis     se
X1     1 120 70.54 10.72   70.97   70.91 10.55  44.83 100.84  56.01 -0.16     0.05  0.98
```

“Table 1”

```
# Using gtsummary to describe all variables
library(gtsummary)
library(tidyverse)

detach(data2)
data2 %>%
 tbl_summary(
    statistic = all_continuous() ~ c("{mean} ({sd}),",
                                       "{median} ({p25}), {p75}),",
                                       "{min} - {max}"),
    digits = all_continuous() ~ 1
)
```

Characteristic	N = 120 [†]
ID	60.5 (34.8), 60.5 (30.8, 90.2), 1.0 - 120.0
Age	40.0 (4.5), 40.0 (37.1, 43.0), 29.9 - 52.4
Sex	
Female	67 (56%)
Male	53 (44%)
SBP	119.9 (9.2), 120.2 (113.3, 125.7), 98.5 - 142.0
DBP	70.5 (10.7), 71.0 (63.9, 77.9), 44.8 - 100.8

[†] Statistics presented: Mean (SD), Median (IQR), Range; n (%)

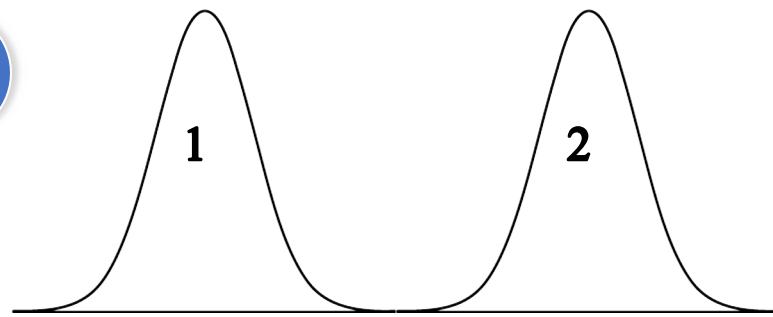


Analytical statistics

Basic Biostatistics
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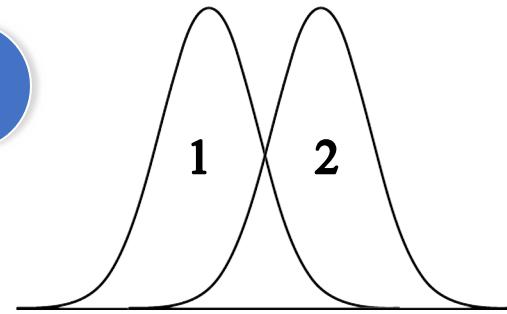
Comparing difference

A

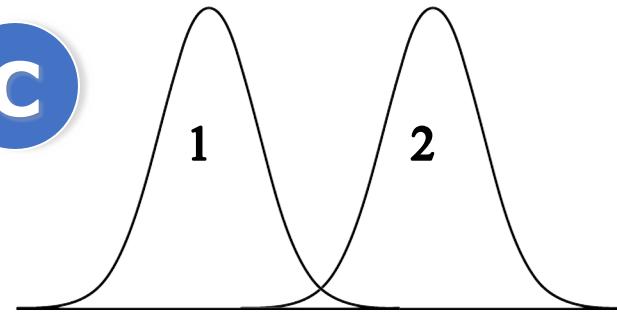


Which of the following shows true difference between the two populations?

B

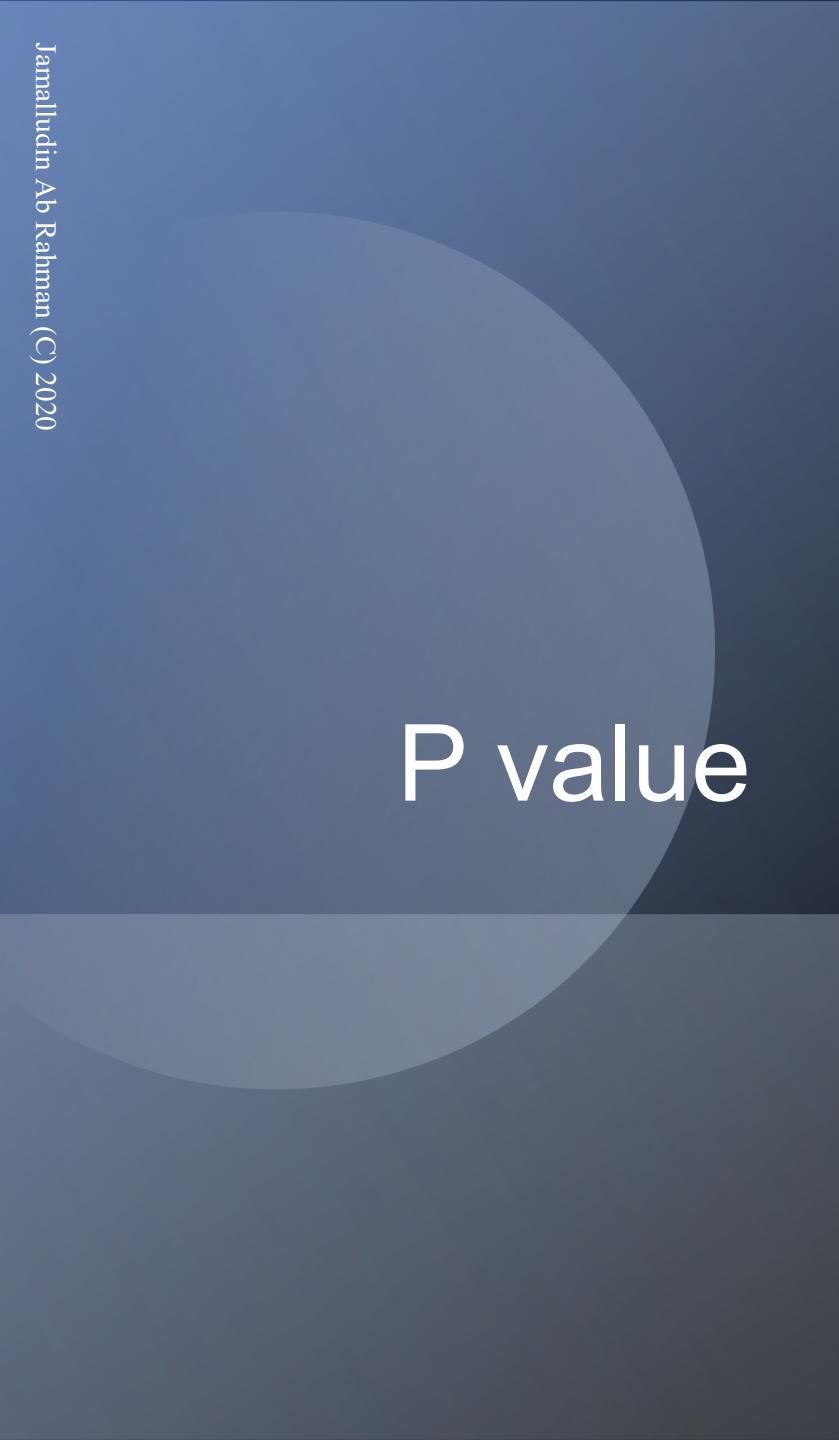


C



3 statistics to compare values

1. P-value
2. Confidence interval
3. Effect size



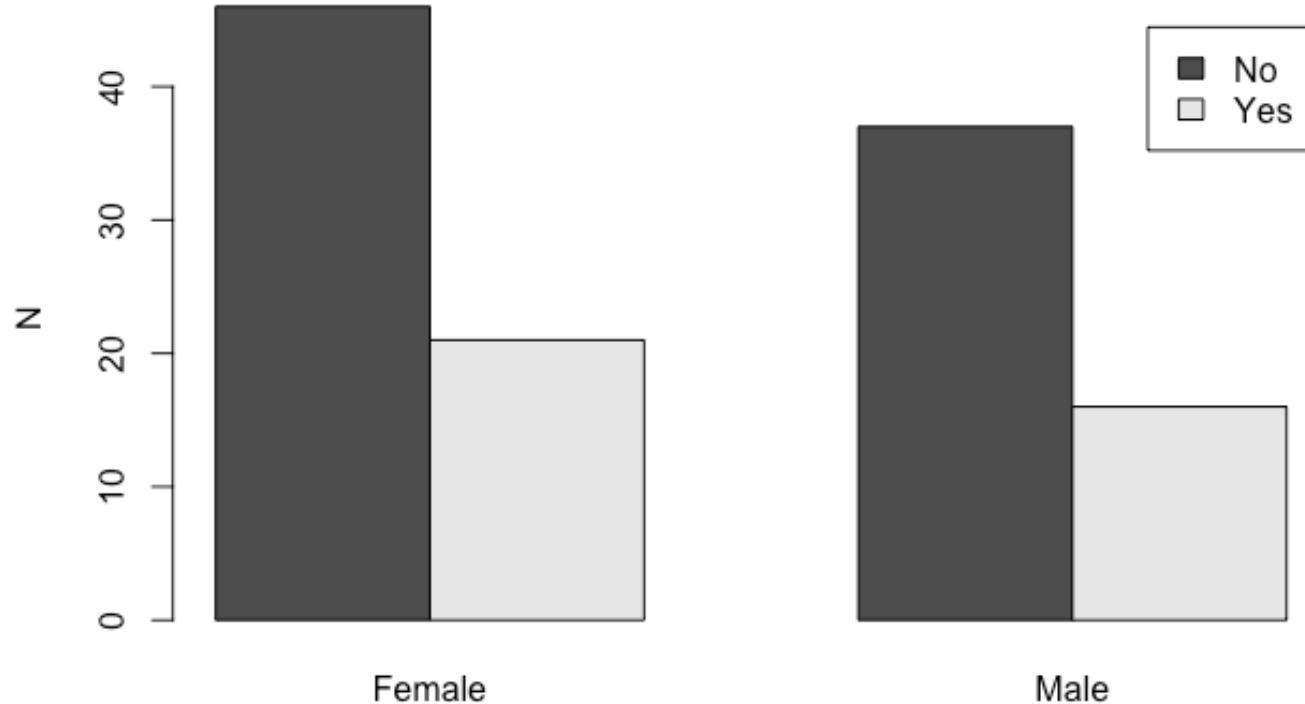
P value

- P-value is ‘likely’ or ‘unlikely’ that H_0 is true
- Taking 0.05 as the cut-off point (α), if $P \leq 0.05$, it is then ‘unlikely’ H_0 is true, therefore reject H_0

Hypothesis Testing using bivariable analysis

- Try to prove that there is relationship between Smoking and Sex
- H_0 : No difference in proportion of smoking between male and female

Distribution of Smoking by Sex



```
> # Cross-tabulate Sex with Smoking  
> x <- table(Smoking, Sex)  
> barplot(x, ylab="N",  
+           beside = TRUE,  
+           legend.text = TRUE,  
+           main = "Distribution of Smoking by Sex")
```

```
> ftable(x)  
      Sex Female Male
```

Smoking

	Female	Male
No	46	37
Yes	21	16

```
> round(prop.table(x)*100, digit=1)  
      Sex
```

	Female	Male
No	38.3	30.8
Yes	17.5	13.3

```
> chisq.test(x)
```

Pearson's Chi-squared test with Yates' continuity correction

Confidence Interval

- Range of plausible values
- Narrow interval → high precision
Wide interval → poor precision
- How narrow is narrow? And how wide is wide? Use your clinical judgment, or in some cases can use RSE (Relative Standard Error)

```

> # Error bars
> library(tidyverse)
> library(ggpubr)
>
> ggerrorplot(data=data3, x="Smoking",
y="SBP", main = "Distribution of SBP by
smoking status",
+             desc_stat = "mean_ci",
+             add = "jitter",
+             add.params = list(color =
"darkgray"))
>
> t.test(SBP~Smoking)

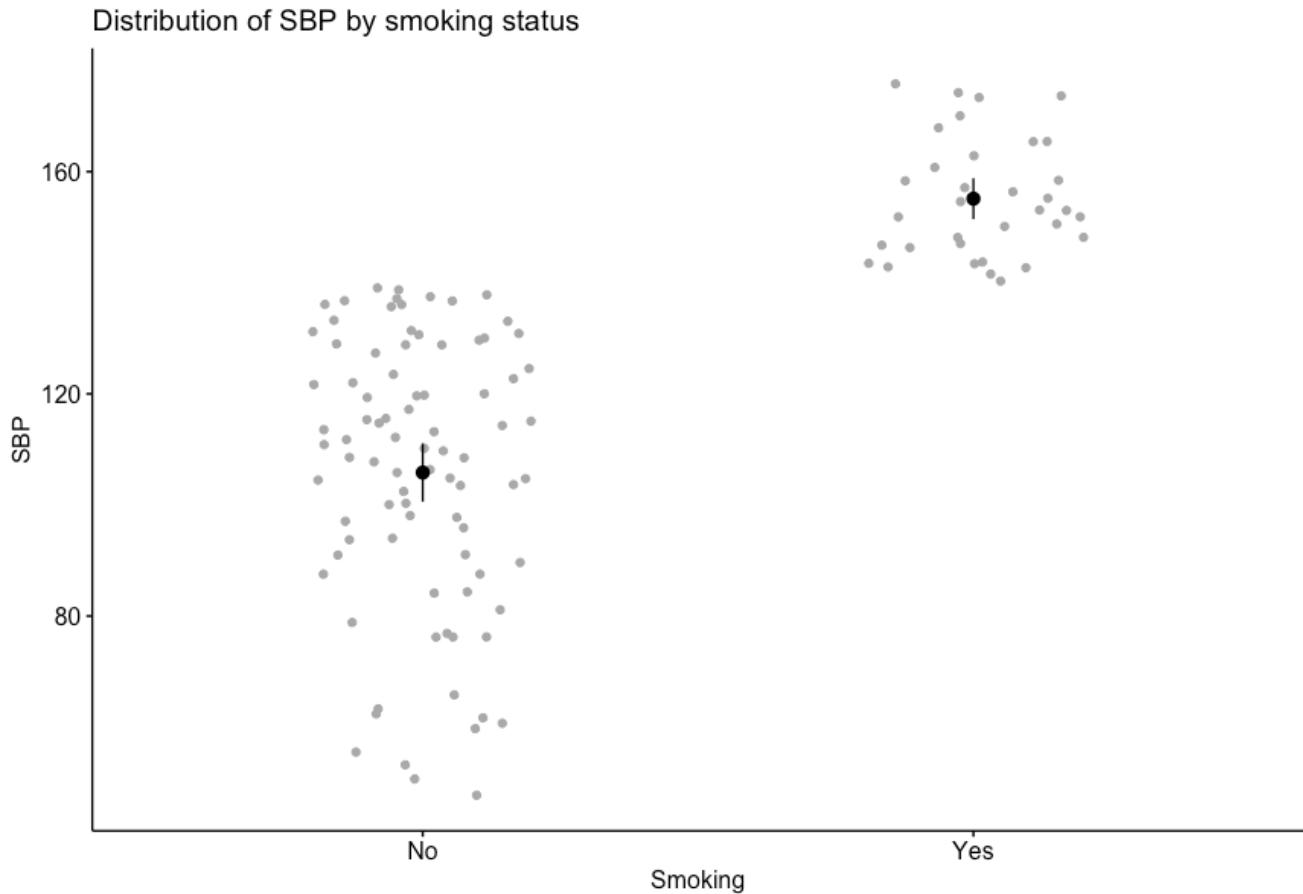
```

Welch Two Sample t-test

```

data: SBP by Smoking
t = -15.392, df = 117.07, p-value < 2.2e-16
alternative hypothesis: true difference in
means is not equal to 0
95 percent confidence interval:
-55.64642 -42.95939
sample estimates:
mean in group No mean in group Yes
105.8336      155.1365

```



Effect size

- The measure of effect irrespective of sample size
- Cohen (1988) classify effect size into
 - Low (<0.3)
 - Medium (0.3-0.7)
 - Large (> 0.7)
- Manual calculation or web based calculation

EDITORIAL

Using Effect Size—or Why the P Value Is Not Enough

GAIL M. SULLIVAN, MD, MPH
RICHARD FEINN, PhD

Statistical significance is the least interesting thing about the results. You should describe the results in terms of measures of magnitude—not just, does a treatment affect people, but how much does it affect them.

-Gene V. Glass¹

The primary product of a research inquiry is one or more measures of effect size, not P values.

-Jacob Cohen²

Statistical significance is the probability that the observed difference between two groups is due to chance. If the *P* value is larger than the alpha level chosen (eg, .05), any observed difference is assumed to be explained by sampling variability. With a sufficiently large sample, a statistical test

```
> # Effect size
> library(effectsize)
>
> model <- aov(SBP ~ Smoking, data=data3)
> omega_squared(model)
For one-way between subjects designs, partial omega squared is
equivalent to omega squared.
Returning omega squared.
Parameter | Omega2 | 90% CI
-----
Smoking | 0.51 | [0.41, 0.60]
> interpret_omega_squared(0.51, rules = "field2013")
[1] "large"
(Rules: field2013)
```

What test to use?

Variable 1	Variable 2	Test
Categorical	Categorical	Chi-square
Categorical (2 pop)	Numerical (Normal)	Independent sample t-test
Categorical (2 pop)	Numerical (Not Normal)	Mann-Whitney U test
Categorical (> 2 pop)	Numerical (Normal)	One-way ANOVA
Categorical (> 2 pop)	Numerical (Not Normal)	Kruskal-Wallis test
Numerical (Normal)	Numerical (Normal)	Pearson Correlation Coefficient Test
Numerical (Normal/ Not Normal)	Numerical (Not Normal)	Spearman Correlation Coefficient Test
Numerical (Normal)	Numerical (Normal) – Paired	Paired t-test
Numerical (Not Normal)	Numerical (Not Normal) – Paired	Wilcoxon Signed Rank Test

Summary

1. Identify & define variables
2. Type – independent vs. dependent
3. Level of measurements – nominal, ordinal or continuous
4. Check distribution – Normal vs. Not Normal
5. Decide what to do - descriptive vs. analytical