

Training Course on Research & Biostatistics for Medical Professionals

For Hong Kong College of Family Physicians

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 30th August 2014*

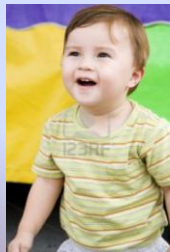
WHAT IS STATISTICS

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Mathematics and Statistics



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Fact and Truth

Great Philosopher said:

“If you want to learn more about **FACT**,
 please ask **STATISTICIAN**;

If you want to learn more about **TRUTH**,
 please ask **MATHEMATICIAN**.”

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Role of Medical Statistician

- Should be involved in the beginning of study
- Advise on study design
- Calculation of sample size (if appropriate)
- Choice of appropriate statistical test
- Data analysis
- Data management
- Interpretation of statistical result

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“To call in the statistician after the experiment is done may be no more than asking him to perform a post-mortem examination; he may be able to say what the experiment died of”

- Sir R.A. Fisher
Indian Statistical Congress (1938)



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CONTENT

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- Sample size calculation
- Sampling method
- Descriptive statistics
- Type of data and data management
- Statistical test and significant test
- Interpretation of statistical result
- Common statistical software

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SAMPLE SIZE CALCULATION

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Sample

- Subset of population
- Rarely use the entire population
- May be imperfect representation of population
- If sample is unbiased and large enough, it will give useful information

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If sample size too small

- 95% confidence interval will not be narrow enough to give precise estimate (mean, median or proportion)
- In a comparative test, a true difference may be missed
- Unethical to the subject involved and the society (if the intervention is beneficial with minimal side effect)

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If the sample size too large

- Wasting of resource, including time, money, manpower, etc.
- In naturalistic study, positive result (in comparative test) with low clinical significant will be detected.
- Unethical to society and subject (if intervention with no real effect but have serious side effect)

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Sample size for means estimation

- Information required
 - Standard deviation (SD) of the measure being estimated (can be from previous studies)
 - The desired width of the confidence interval (d)
 - The confidence interval (CI) (95%, 99% , 90%, etc)

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Sample size for means estimation

- $n = (CI)^2 \times 4 (SD)^2 / d^2$
 - For 95% confidence interval, CI = 1.96
 - For 90% confidence interval, CI = 1.64
 - For 99% confidence interval, CI = 2.58

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Sample size for proportion estimation

- Information required
 - The expected population proportion, p
 - The desired width of the confidence interval (d)
 - The confidence interval (CI)

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Sample size for proportion estimation

- $n = (CI)^2 \times 4 p(1-p) / d^2$
 - For 95% confidence interval, CI = 1.96
 - For 90% confidence interval, CI = 1.64
 - For 99% confidence interval, CI = 2.58

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Sample size for comparative studies

- Sample size calculation aim at minimize the type I and type II error
- Type I error – we conclude that there is a difference between groups in the target population when in fact there is not.
- Type II error – We conclude that there is no difference between the groups in the target population when in fact there is a real difference.

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Sample size for comparative studies

- Clinically important difference – the minimum clinically important difference is determined by physician who would not want the study miss it. It should be clinically meaningful but not statistically meaningful
- Significance level (α) – it is the probability of type I error
- The power of the test ($1 - \beta$) – where β is the probability of type II error

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Sample size for comparing means

- The information required:
 - The standard deviation (SD) of the measure being compared
 - The minimum difference (d) that is clinically important
 - The significance level (α)
 - The power of the test ($1 - \beta$)
 - n is the number of sample in each group
- $n = 2K(SD)^2 / d^2$

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Sample size for comparing proportions

- The information required:
 - The expected population proportions in group 1, P_1
 - The expected population proportions in group 2, P_2
 - The significance level (α)
 - The power of the test ($1 - \beta$)
 - n is the number of sample in each group
- $n = K[P_1(1 - P_1) + P_2(1 - P_2)] / (P_1 - P_2)^2$

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Value of K corresponding to α and β

Power ($1 - \beta$)	Significance level (α)		
	5%	1%	0.1%
80%	7.8	11.7	17.1
90%	10.5	14.9	20.9
95%	13.0	17.8	24.3
99%	18.4	24.1	31.6

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Assumption for sample size calculation

- There was no sample lost till the end of study once the samples was selected.
- There are equal sample size in each group of comparison
- Samples are simple random sample selected at individual level
- It is not applied to cluster sampling and regression
- The samples are large enough (> 50 in each group) to use large sample methods for analysis

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Other issues

- We can select more sample if we expected that there are sample lost during study
- Software can be used to calculate sample size
- Is calculation always needed:
 - Not if the study is a qualitative study
 - Not always for a small survey
 - Not always for a pilot study

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SAMPLING METHODS

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Different types of sampling

- Simple random sampling
- Systematic sampling
- Stratified sampling
- Cluster sampling
- Quota sampling
- Convenience sampling

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Simple Random Sampling

- You should have whole list of subjects in sample space
- Label each subject with a number
- If you want n sample from sample space, select n random number from computer or random number table
- Select the sample label with the random number selected.

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Simple Random Sampling

- Advantage
 - Gold standard of sampling
 - No detail of each sample is needed
 - Each individual has equal chance of being selected
- Disadvantage
 - You need to know the whole list in sampling frame

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Systematic sampling

- We got whole list in sampling frame and label the subject by natural number
- Calculate interval $I = \text{population size} / \text{sample size}$
- Randomly choose a number less than I from computer program or random number table and we select the first sample which label by the random number selected
- Then, select another sample by interval I till the end of the list.

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Systematic sampling

- Advantage
 - Easy to perform
 - If the list ranked in a group followed by another, it got the effect of stratified sampling
- Disadvantage
 - Cause sampling error if the list order in particular way (say, there must be a man followed by a woman)

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Stratified Sampling

- Put each subject into one of the strata in which each stratum must be mutually exclusive and all strata must include all subject.
- The characteristics of subjects in particular stratum should be homogenous.
- From each stratum, select a proportion of sample by simple random sampling or systematic sampling and form subsample (the proportion = sample size / population size)
- Combined all subsample.

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Stratified Sampling

- Advantage
 - We will not miss sample from minority group
 - Minimal sampling error
- Disadvantage
 - Time and manpower consuming
 - Some characteristic of each individual must be known
 - Resulting sample size may be larger than expected if there are too many strata, or there are some strata with few subjects only

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Cluster Sampling

- Divided the population into several clusters (the difference in characteristics of subjects in each cluster should be minimal)
- Randomly selected few clusters
- From each cluster, collect the list of sampling frame and selected certain number of sample from each cluster by simple random sampling, systematic sampling or stratified sampling.
- Combine all subsample

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Cluster Sampling

- Advantage
 - Whole list of the population is not necessary
 - Decreased traffic time
- Disadvantage
 - Increased sampling error
 - Different method of sample size calculation

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Quota Sampling

- Each interviewer assigned certain number of sample to be interviewed (location of selecting the sample may also be fixed)
- Certain proportion of characteristics are required (say, half should be female)
- If the number of sample achieved, the sampling process ended
- There was no randomization

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Convenience Sampling

- There was no limitation
- You can select any sample you like and agree to be interviewed or join the test
- Sampling error
- Convenience sampling should be avoided if possible

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Randomization

- Randomization reduces bias by equalising so-called factors (independent variables) that have not been accounted for in the experimental design
- It can be achieved by random number table, or generated by computer (like Excel)
- Pseudo-random number generated by computer

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DESCRIPTIVE STATISTICS

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Descriptive Statistics

- It described the main features of a collection of data quantitatively
- It aimed at summarize the dataset
- There are 4 degrees:
 - Location
 - Spread
 - Skewness
 - Kurtosis

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Location

- It is the first degree
- Mean: the arithmetic means or expected value of random variables
- Median: the value separating the higher half of a sample from the lower half
- Mode: The most common value among the group
- In normal distribution: mean = median = mode

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Spread

- It is a second degree
- Standard deviation: related to mean

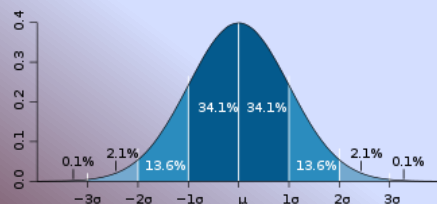
$$\sigma = \sqrt{E[(X - \mu)^2]}.$$
- Range and Percentile
- Interquartile range: related to median
 - It contain half of the sample inside the range
 - Upper quartile: separate the higher $\frac{1}{4}$ and lower $\frac{3}{4}$
 - Lower quartile: separate the lower $\frac{1}{4}$ and higher $\frac{3}{4}$

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Standard Deviation



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Skewness

- It is the third degree
- It measure the asymmetry of the distribution
- It is calculated by

$$\gamma_1 = E\left[\left(\frac{X-\mu}{\sigma}\right)^3\right] = \frac{\mu_3}{\sigma^3} = \frac{E[(X-\mu)^3]}{(E[(X-\mu)^2])^{3/2}} = \frac{\kappa_3}{\kappa_2^{3/2}},$$

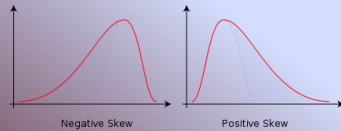
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Skewness

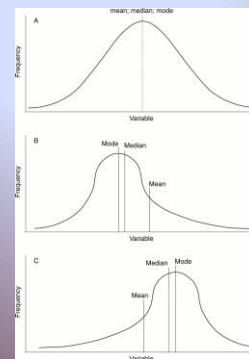
- Looked at the tail of the distribution
- Positive (right) skewed (mean > median > mode)
- Negative (left) skewed (mean < median < mode)



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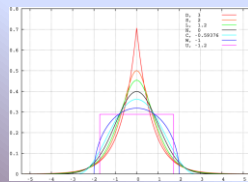
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Kurtosis

- It is the fourth degree
- It is a measure of “peakedness” of the distribution

$$g_2 = \frac{m_4}{m_2^2} - 3 = \frac{\frac{1}{n} \sum_{i=1}^n (x_i - \bar{x})^4}{\left(\frac{1}{n} \sum_{i=1}^n (x_i - \bar{x})^2 \right)^2} - 3$$



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Visualize the data

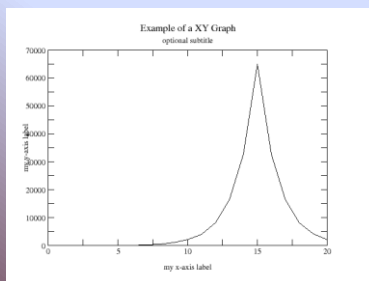
- Graph
- Histogram
- Boxplot
- Stemplot
- Scattergram

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Graph

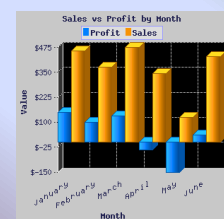
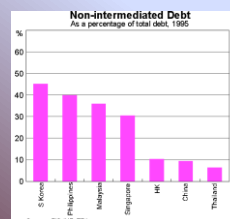


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Histogram

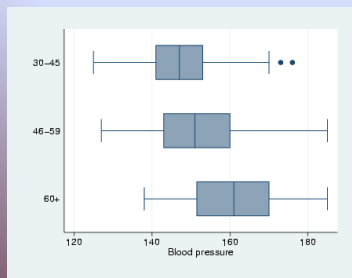


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Boxplot

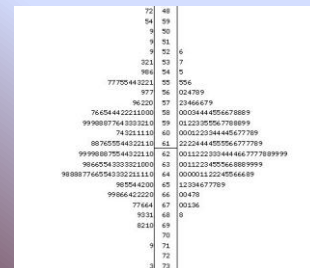


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Stemplot

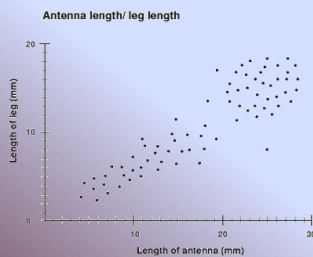


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Scattergram



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Normal Distribution

- How to realize the data is normally distributed or not from descriptive statistics
 - Mean = median = mode
 - ~~Mean = median~~ (It can occur in bimodal symmetrical distribution)
 - Mean and standard deviation (if 2 standard deviation from the mean is out of the normal range of the variable, it is unlikely to be normally distributed)
 - histogram

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DATA TYPES AND DATA MANAGEMENT

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Types of Data

- Either quantitative or categorical
- A variable is a quantity that is measured or observed in an individual and which varies from person to person
- A statistics (test statistics) is any quantity that is calculated from a set of data

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Quantitative data

- Can be measured numerically
- Continuous data – lie on a continuum and can take any value between two limits
- Discrete data – can take certain value (count)
- Interval scale – differences between values at different points of the scale have the same meaning
- Ratio scale – ratio of two measures has same meaning (temperature scale)
- Ordinal data – data values can be arranged in a numerical order from the smallest to the largest.

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Categorical data

- Individuals fall into a number of separate categories or classes
- Number was assigned for coding purpose, it can be ordinal but not interval data because the “distance” has no real measure
- Distinguish between ordered and non-ordered data
- Dichotomous data – only 2 classes
- Categorizing continuous data
 - Dichotomizing – potentially very problematic
 - Into several groups – less effect on statistical power when compared with dichotomizing

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Data Entry

- Give a unique identifier to each subject
- Code the data before entry (remember the meaning of the code)
- Excel or statistical program
- Can be directly transfer form electronic data form
- Double entry can reduce the rate of error during data transfer

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Data storing and transporting

- Paper forms
 - File systematically to allow easy access
 - Stored securely
 - Store identifying detail separately from data form
 - Keeping a copy in one location if they are being transported
 - If data are valuable, a copy should always be kept in a different place.

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Data storing and transporting

- Electronic files
 - Identifying details should always be removed when transporting the file
 - Password protected and encrypted
 - Keep more than one copy of the data in two separate locations
 - Useful to use file names that show the version or date where files are updated

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Data Checking

- Check early
- Range checks
- Consistency
- Original forms
- Missing data
- Snowballing errors
- Digit preference (round up problem)
- Scatter plot
- Statistical analysis

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Correcting errors

- Check the original data form wherever possible to identify the source of potential data error
- Not to make assumptions or guesses where data values look unusual or are missing
- An outlying value should not be deleted simply because it is unusual.
- Keep a record of any changes that are made to the dataset and keep dated copies of datasets as changes are made.

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STATISTICAL TEST AND ITS INTERPRETATION

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Hypothesis test

Hypothesis testing

- Set up hypothesis
- Find value of test statistics
- Look up critical value
- Is test statistics smaller (or greater) than critical value
- Decide reject the hypothesis or not

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Hypothesis test

- We decide that we should “reject” the hypothesis or not.
- If we want to know whether A is true
- We set a null hypothesis – A
- Then, by means of rejecting null hypothesis to prove A is true
- Why?

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Hypothesis test

- We cannot check all the case in the world to prove the hypothesis is true
- But once there is a contra-example, we can disprove a statement or hypothesis
- So, it is easier to reject a null hypothesis rather than test all the case in the world to check a hypothesis
- It is the concept of Falsifiability or Refutability.

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Falsifiability

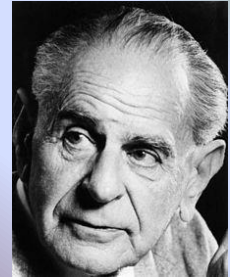
A theory can be contradicted by an observation or the outcome of a physical experiment. That something is "falsifiable" does not mean it is false; rather, that if it is false, then some observation or experiment will produce a reproducible result that is in conflict with it.

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- **Sir Karl Raimund Popper** (1902 – 1994)
- From 1930 to 1936, he taught secondary school. Popper published his first book, *Logik der Forschung* (*The Logic of Scientific Discovery*) in 1934, in which he introduced the concept of Falsifiability.



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Null / Alternative Hypothesis

- The **null hypothesis** typically corresponds to a general or default position, that are capable of being proven false using a test of observed data.
- It is typically paired with a second hypothesis, the alternative hypothesis, which asserts a particular relationship between the phenomena.
- It is important to understand that the **null hypothesis can never be proven**. Your data can only **reject** a null hypothesis or **fail to reject it**.

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Hypothesis of one sided test

$$H_0 : M_A \leq M_B$$

$$H_1 : M_A > M_B$$

Where H_0 is null hypothesis
and H_1 is alternative hypothesis

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Hypothesis of one sided paired test

$$H_0 : M_{A-B} \leq 0$$

$$H_1 : M_{A-B} > 0$$

Where H_0 is null hypothesis
and H_1 is alternative hypothesis

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Hypothesis of two sided test

$$H_0 : M_A = M_B$$

$$H_1 : M_A \neq M_B$$

Where H_0 is null hypothesis
and H_1 is alternative hypothesis

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Hypothesis of two sided paired test

$$H_0 : M_{A-B} = 0$$

$$H_1 : M_{A-B} \neq 0$$

Where H_0 is null hypothesis
and H_1 is alternative hypothesis

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Reject the hypothesis

- The hypothesis is rejected if a sample is selected whose values are one of the 5% most extreme outcomes that might occur if the hypothesis were true.
- In case of one way testing, 5% in one side
- In case of two way testing, 2.5% in each side.

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P value

- P value is the probability of obtaining a test statistic at least as extreme as the one that was actually observed, assuming that the null hypothesis is true
- $P < 0.05$ is usually regarded as statistically significant
- Not significant does not mean “there is no difference” or “there is no effect”. It means there is insufficient evidence for a difference or effect
- Exact p values should be given with estimates and confidence intervals wherever possible.

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History of Statistics

- 1532 – First weekly data on deaths in London (Sir W. Petty)
- 1539 – start of data collection on birth, marriages and deaths in France
- 1662 – First published demographic study based on bills of mortality (J. Braunt)
- Publication of *Ars Conjectandi* (J Bernoulli)
- 1834 – establishment of Royal Statistical Society

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- 1839 – Establishment of American Statistical Association (Boston)
- 1889 - Publication of *Natural Inheritance* (F. Galton)
- 1900 – development of chi-squared test (K Pearson)
- 1901 – publication of first issue of *Biometrika* (F. Galton)
- 1903 – development of Principal Component Analysis (K Pearson)

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- 1908 – publication of *The Probable error of a mean* (“Student”)
- 1920 – Pearson create the role of medical statistician
- 1925 – Publication of *Statistical Methods for Research Worker* (R A Fisher)
- 1935 – Publication of *The Design of Experiments* (R A Fisher)

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- 1946 – first clinical trial conducted by British Medical Research Council
- 1972 – Publication of *Regression models and life tables* (D R Cox)
- 1979 – Publication of *Bootstrap methods: another look at the jackknife* (B Efron)

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SEX DIFFERENCES IN TUBERCULOSIS MORTALITY

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TABLE I
RESPIRATORY TUBERCULOSIS MORTALITY AND SOCIAL CLASS, 1930-2
(Rates calculated for 100,000 living for the 3-yr period 1930-2)

Age	16-	20-	25-	35-	45-	55-	65-	70-	75
	199	319	323	383	454	377	269	177	87
	196	165	188	261	242	264	211	142	142
	148	112	131	203	172	258	211	165	80
	182	111	130	275	386	271	272	179	80
	166	112	123	416	497	377	240	176	101
	228	359	363	488	605	518	398	270	138
	317	562	486	690	359	179	102	—	31
	306	315	262	199	145	125	103	82	64
	—	—	124	91	84	85	—	—	—
	—	199	171	131	99	94	84	132	68
	—	295	300	289	145	127	110	132	67
	—	290	271	297	165	126	97	81	54
	—	396	379	342	271	197	160	138	95
	—	—	105	70	26	17	—	—	—
	308	379	371	250	170	132	125	94	68
	—	—	199	454	—	—	—	—	—
	—	188	202	204	124	91	71	113	—
	—	223	131	147	145	176	168	—	129
	—	129	451	445	286	193	130	—	—
	—	119	444	346	399	273	210	—	—
	—	349	596	493	362	188	114	109	84
	—	—	—	—	—	—	—	—	43

Rates not calculated for any age group in which there were less than ten deaths.

Source: Registrar-General's Decennial Supplement for 1931, Part IIA Occupational Mortality, Tables 4A, 4B, 4C, pp. 215-325.

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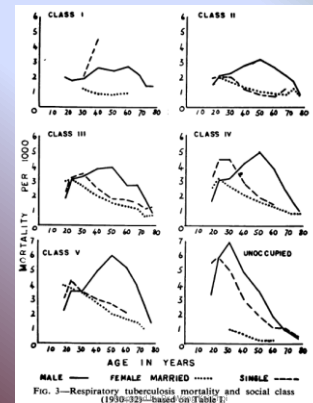


FIG. 3—Respiratory tuberculosis mortality and social class (1930-32)—based on Table I.

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Drawbacks of using significant test in medical research

Can Statistical Results apply to clinical setting?

Can collective phenomena explain individual behavior?



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- Macroscopically, the survival rate of a particular disease is $n\%$
- Microscopically, if a patient survives, survival rate is 100%; if patient dies, survival rate is 0% - all or none
- Use of multiple regression analysis can partially solve the problem and try to individualize the treatment.

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Deduction vs Induction

Deductive Reasoning

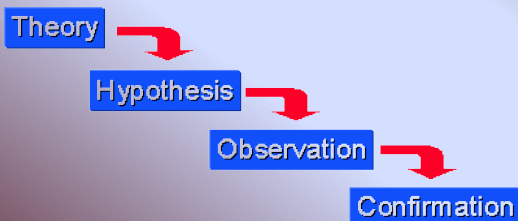
Deductive logic, is reasoning which constructs or evaluates deductive arguments. Deductive arguments are attempts to show that a conclusion necessarily follows from a set of premises. A deductive argument is valid if the conclusion must be true provided that the premises are true. A deductive argument is sound if it is valid and its premises are true.

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Deductive Reasoning



Inductive Reasoning

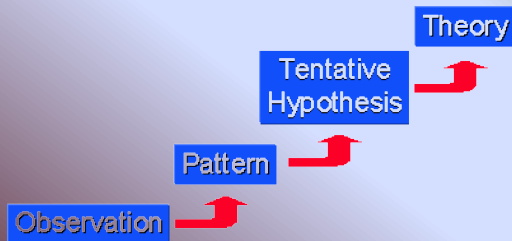
Inductive logic, is a kind of reasoning that constructs or evaluates propositions that are abstractions of observations. It is commonly construed as a form of reasoning that makes generalizations based on individual instances. In this sense it is often contrasted with deductive reasoning

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Inductive Reasoning



Clinical Inductive / Deductive Reasoning

- Inductive Reasoning – symptoms of a patient is ..., and we draw a list of differential diagnoses
- Deductive Reasoning – we have a particular diagnosis in mind and compare the symptoms of the patient to see whether he fit the diagnosis or not.

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Deductive Reasoning

- We can only acquire part of the truth with deductive reasoning, depends on the hypothesis we set.
- Example: investigator can only prove there is tail or a head in coin

5%?

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Why 5% is chosen?

- Fisher played a major role in the canonization of the 5% level as a criterion for statistical significance.
- In 1925, in his book “Statistical Methods for Research Workers” he fixed 5% as the only significance level in Table VI (F-distribution).
- 5% is arbitrary, as Fisher knew, but fulfils a general social purpose.

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Table T Critical Values of the t Distribution

One-Tail = α	Two-Tail = α	.25	.20	.15	.10	.05	.025	.01	.005	.001	.0005
df		1	2	3	4	5	6	7	8	9	10
1	0.825	1.000	1.078	1.151	1.225	1.301	1.377	1.457	1.539	1.626	1.696
2	0.789	0.816	0.886	0.958	1.033	1.101	1.171	1.250	1.327	1.412	1.479
3	0.771	0.797	0.865	0.937	1.012	1.080	1.150	1.229	1.306	1.393	1.458
4	0.761	0.787	0.855	0.927	1.001	1.069	1.139	1.218	1.295	1.382	1.447
5	0.753	0.778	0.846	0.918	0.992	1.060	1.130	1.209	1.286	1.373	1.438
6	0.748	0.772	0.840	0.912	0.985	1.054	1.124	1.203	1.280	1.367	1.432
7	0.744	0.768	0.836	0.908	0.981	1.050	1.120	1.199	1.276	1.363	1.428
8	0.741	0.765	0.833	0.905	0.978	1.047	1.117	1.196	1.273	1.360	1.425
9	0.738	0.762	0.830	0.902	0.975	1.044	1.114	1.193	1.270	1.357	1.422
10	0.736	0.760	0.828	0.900	0.973	1.042	1.112	1.191	1.268	1.355	1.420
11	0.734	0.758	0.826	0.898	0.971	1.040	1.110	1.189	1.266	1.353	1.418
12	0.732	0.756	0.824	0.896	0.969	1.038	1.108	1.187	1.264	1.351	1.416
13	0.731	0.755	0.823	0.895	0.968	1.037	1.107	1.186	1.263	1.350	1.415
14	0.729	0.753	0.821	0.893	0.966	1.035	1.105	1.184	1.261	1.348	1.413
15	0.728	0.752	0.820	0.892	0.965	1.034	1.104	1.183	1.260	1.347	1.412
16	0.727	0.751	0.819	0.891	0.964	1.033	1.103	1.182	1.259	1.346	1.411
17	0.726	0.750	0.818	0.890	0.963	1.032	1.102	1.181	1.258	1.345	1.410
18	0.725	0.749	0.817	0.889	0.962	1.031	1.101	1.180	1.257	1.344	1.409
19	0.724	0.748	0.816	0.888	0.961	1.030	1.100	1.179	1.256	1.343	1.408
20	0.723	0.747	0.815	0.887	0.960	1.029	1.099	1.178	1.255	1.342	1.407
21	0.722	0.746	0.814	0.886	0.959	1.028	1.098	1.177	1.254	1.341	1.406
22	0.721	0.745	0.813	0.885	0.958	1.027	1.097	1.176	1.253	1.340	1.405
23	0.720	0.744	0.812	0.884	0.957	1.026	1.096	1.175	1.252	1.339	1.404
24	0.719	0.743	0.811	0.883	0.956	1.025	1.095	1.174	1.251	1.338	1.403
25	0.718	0.742	0.810	0.882	0.955	1.024	1.094	1.173	1.250	1.337	1.402
26	0.717	0.741	0.809	0.881	0.954	1.023	1.093	1.172	1.249	1.336	1.401
27	0.716	0.740	0.808	0.880	0.953	1.022	1.092	1.171	1.248	1.335	1.400
28	0.715	0.739	0.807	0.879	0.952	1.021	1.091	1.170	1.247	1.334	1.399
29	0.714	0.738	0.806	0.878	0.951	1.020	1.090	1.169	1.246	1.333	1.398
30	0.713	0.737	0.805	0.877	0.950	1.019	1.089	1.168	1.245	1.332	1.397
40	0.710	0.734	0.803	0.875	0.947	1.016	1.087	1.166	1.243	1.330	1.395
60	0.707	0.731	0.801	0.873	0.945	1.014	1.085	1.164	1.241	1.328	1.393
80	0.705	0.729	0.800	0.871	0.943	1.013	1.084	1.163	1.240	1.327	1.391
100	0.704	0.728	0.799	0.870	0.942	1.012	1.083	1.162	1.239	1.326	1.390
∞	0.703	0.727	0.798	0.869	0.941	1.011	1.082	1.161	1.238	1.325	1.389

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Degrees of Freedom	Probability of a larger value of χ^2							
	0.99	0.95	0.90	0.75	0.50	0.25	0.10	0.05
1	0.000	0.004	0.016	0.102	0.455	1.32	2.71	3.84
2	0.010	0.103	0.211	0.575	1.386	2.77	4.61	5.99
3	0.115	0.352	0.584	1.212	2.366	4.11	6.25	7.81
4	0.297	0.711	1.064	1.923	3.357	5.39	7.78	9.49
5	0.554	1.145	1.610	2.675	4.351	6.63	9.24	11.07
6	0.872	1.635	2.204	3.455	5.348	7.84	10.64	12.59
7	1.239	2.167	2.833	4.255	6.346	9.04	12.02	14.07
8	1.647	2.733	3.490	5.071	7.344	10.22	13.36	15.51
9	2.088	3.325	4.168	5.899	8.343	11.39	14.68	16.92
10	2.558	3.940	4.865	6.757	9.342	12.55	15.99	18.31
11	3.053	4.575	5.578	7.584	10.341	13.70	17.28	19.68
12	3.571	5.226	6.304	8.438	11.340	14.85	18.55	21.03
13	4.107	5.892	7.042	9.299	12.340	15.98	19.81	22.36
14	4.660	6.571	7.790	10.165	13.339	17.12	21.06	23.68
15	5.229	7.261	8.547	11.037	14.339	18.25	22.31	25.00
16	5.812	7.962	9.312	11.912	15.338	19.37	23.54	26.30
17	6.408	8.672	10.085	12.792	16.338	20.49	24.77	27.59
18	7.015	9.390	10.865	13.675	17.338	21.60	25.99	28.87
19	7.633	10.117	11.651	14.562	18.338	22.72	27.20	30.14
20	8.260	10.851	12.443	15.452	19.337	23.83	28.41	31.41
22	9.542	12.338	14.041	17.240	21.337	26.04	30.81	33.92
24	10.856	13.848	15.659	19.037	23.337	28.24	33.20	36.42
26	12.198	15.379	17.292	20.843	25.336	30.43	35.56	38.89
28	13.565	16.928	18.939	22.657	27.336	32.62	37.92	41.34
30	14.953	18.493	20.599	24.478	29.336	34.80	40.26	43.77
40	22.164	26.509	29.051	33.660	39.335	45.62	51.80	55.76
50	27.707	34.764	37.689	42.942	49.335	56.33	63.17	67.50
60	37.485	43.188	46.459	52.794	59.335	66.98	74.40	79.08

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i	95% quantiles of $F(i, j)$									
	1	2	3	4	5	6	7	8	9	10
1	4052	4999.5	5403	5625	5764	5878	5978	6062	6132	6190
2	98.50	99.00	99.17	99.25	99.30	99.33	99.36	99.37	99.39	99.40
3	34.12	30.82	29.46	28.73	28.24	27.91	27.67	27.49	27.35	27.23
4	21.20	18.00	16.69	15.98	15.52	15.21	14.98	14.80	14.66	14.55
5	16.26	13.27	12.00	11.29	10.97	10.67	10.46	10.29	10.16	10.05
6	13.75	10.92	9.78	9.15	8.75	8.47	8.26	8.10	7.98	7.87
7	12.25	9.55	8.45	7.85	7.46	7.19	6.99	6.84	6.72	6.62
8	11.26	8.65	7.59	7.01	6.63	6.37	6.18	6.03	5.91	5.81
9	10.56	8.02	6.99	6.42	6.06	5.80	5.61	5.47	5.35	5.26
10	10.04	7.56	6.55	5.99	5.64	5.39	5.20	5.06	4.94	4.85
11	9.65	7.21	6.22	5.67	5.32	5.07	4.89	4.74	4.63	4.54
12	9.33	6.93	5.95	5.41	5.06	4.82	4.64	4.50	4.39	4.30
13	9.07	6.70	5.74	5.21	4.86	4.62	4.44	4.30	4.19	4.10
14	8.86	6.51	5.56	5.03	4.69	4.45	4.27	4.13	4.02	3.93
15	8.68	6.36	5.42	4.89	4.56	4.32	4.14	4.00	3.89	3.80
16	8.53	6.23	5.29	4.77	4.44	4.20	4.03	3.89	3.78	3.69
17	8.40	6.11	5.18	4.67	4.34	4.10	3.93	3.79	3.68	3.59
18	8.29	6.01	5.09	4.58	4.25	4.01	3.84	3.71	3.60	3.51
19	8.18	5.93	5.01	4.50	4.17	3.94	3.77	3.65	3.52	3.43
20	8.10	5.85	4.94	4.43	4.10	3.87	3.70	3.58	3.46	3.37
21	8.02	5.78	4.87	4.37	4.04	3.81	3.64	3.51	3.40	3.31
22	7.95	5.72	4.82	4.31	3.99	3.76	3.59	3.47	3.35	3.26
23	7.88	5.66	4.76	4.26	3.94	3.71	3.54	3.41	3.30	3.21
24	7.82	5.61	4.72	4.22	3.90	3.67	3.50	3.38	3.26	3.17
25	7.77	5.57	4.68	4.18	3.86	3.63	3.46	3.32	3.22	3.13
26	7.72	5.53	4.64	4.14	3.82	3.59	3.42	3.29	3.18	3.09
27	7.68	5.49	4.60	4.11	3.78	3.56	3.39	3.26	3.15	3.06
28	7.64	5.45	4.57	4.07	3.75	3.53	3.36	3.23	3.12	3.03
29	7.60	5.42	4.54	4.04	3.73	3.50	3.33	3.20	3.09	3.00
30	7.56	5.39	4.51	4.02	3.70	3.47	3.30	3.17	3.07	2.98
40	7.31	5.18	4.31	3.83	3.51	3.29	3.12	2.99	2.89	2.80
50	7.08	4.98	4.13	3.65	3.34	3.12	2.95	2.82	2.72	2.63
100	6.65	4.79	3.95	3.48	3.17	2.96	2.79	2.66	2.56	2.47
∞	6.63	4.68	3.85	3.38	3.07	2.86	2.69	2.56	2.46	2.37

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5% - evidence based?

- The value is fixed in 1925 when the medical statistics and clinical trial is not well established.
- 5% is reasonable for social research, as Fisher knew, but it may not reasonable in medical research
- Before we have evidence to show we should choose 5% as significant level, we cannot say that we are practicing "evidence based medicine"

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T TEST

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History

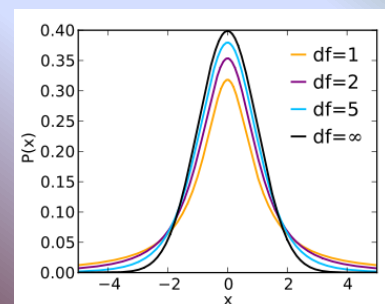
- The t-statistic was introduced in 1908 by William Sealy Gosset, a chemist working in Dublin, Ireland ("Student" was his pen name).
- He published the test in *Biometrika* in 1908



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T-test for 2 independent means

- Details of the test
 - Compares means from 2 independent sample
 - Based on sampling distribution of difference of two samples
 - Allow calculate a difference and confidence interval of the difference
 - Can be calculated by formula or statistical program

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T-test for 2 independent means

- Null hypothesis
 - Two samples come from population with same means
- Assumptions of test
 - Continuous data with normal distribution
 - Variances are the same

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T-test for 2 independent means

- If assumptions do not hold
 - The statistical test is dubious and the p value may be wrong
 - Try transformation of the data
 - It is robust to slight skewness (2 samples with same size) but is less robust if variances are clearly different
 - Skewness and different variance can be corrected by transformation.

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$$t = \frac{\bar{X}_1 - \bar{X}_2}{s_{\bar{X}_1 - \bar{X}_2}}$$

Where

$$s_{\bar{X}_1 - \bar{X}_2} = \sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}$$

Degree of freedom

$$\text{d.f.} = \frac{(s_1^2/n_1 + s_2^2/n_2)^2}{(s_1^2/n_1)^2/(n_1 - 1) + (s_2^2/n_2)^2/(n_2 - 1)}$$

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T test for paired (matched) data

- Also called one sample t-test
- It analyses mean difference in paired sample
- Null hypothesis: means difference is zero
- Assumption
 - differences follow a normal distribution
 - variance are constant
- If assumption do not hold – transform the raw data (not the difference)

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$$t = \frac{\bar{X}_D - \mu_0}{s_D / \sqrt{n}}$$

Where \bar{X}_D and s_D is the average and standard deviation of the differences

The degree of freedom is $n-1$

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Z TEST

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Z test

- Compares proportions from two independent samples
- Based on sampling distribution of the difference of proportions
- Allow calculation of differences and a confidence interval for the difference
- Is equivalent to chi-squared test
- Can be calculated by formula and statistical program

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Z test

- Null hypothesis
 - Two samples come from populations with the same proportions
- Assumption of the test
 - Binary data
 - Sample is large. Both subjects with or without characteristics should be greater than 5 in both groups.

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$$z = \frac{\hat{p}_1 - \hat{p}_2}{\sqrt{\hat{p}(1-\hat{p})\left(\frac{1}{n_1} + \frac{1}{n_2}\right)}}$$

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CHI SQUARED TEST

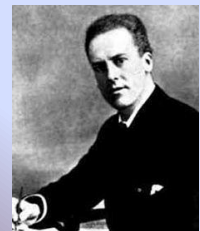
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History

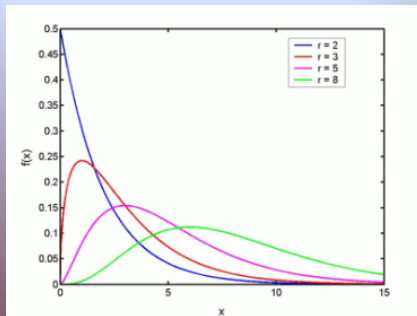
- **Pearson's chi-square test** is the best-known of several chi-square tests – statistical procedures whose results are evaluated by reference to the chi-square distribution.
- Its properties were first investigated by Karl Pearson in 1900.



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Chi-squared test

- Tests for association between two categorical variables
- When each variables has only 2 categories, it is equivalent to z test
- Based on the chi-squared distribution with n degree of freedom
- $n = (\text{no. of row} - 1) \times (\text{no. of column} - 1)$
- It gives p value but not direct estimate or confidence interval as z test

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Chi-squared test

- Rationale of test
 - Calculates the frequencies that would be expected if there was no association
 - It compares the observed frequencies and expected values
 - If they are very different, this provides evidence that there is an association
 - The test uses a formula based on chi-squared distribution to give p value

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Chi-squared test

- Null hypothesis
 - There is no association between the two variables in the population from which the samples come
- Assumptions of test
 - Large sample size
 - At least 80% of expected frequencies must be greater than 5

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Chi-squared test

- If assumption do not hold
 - Collapsing the table
 - Continuity correction (Yates' correction)
 - Fisher's exact test
- Doing chi-squared test
 - Always use with frequencies, never use percentage
 - The formula works with all size tables
 - Can be done by computer program

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$$\chi^2 = \sum_{i=1}^n \frac{(O_i - E_i)^2}{E_i}$$

where

χ^2 = Pearson's cumulative test statistic, which asymptotically approaches a χ^2 distribution.

O_i = an observed frequency;

E_i = an expected (theoretical) frequency, asserted by the null hypothesis;

n = the number of cells in the table.

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Yates' Correction

- Chi-squared test based on frequencies (discrete) whilst the chi-squared distribution is continuous.
- The fit is not good in small sample size
- Yates' correction modified the chi-squared formula to make better fit
- Corrected p value (slightly bigger) should be reported

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$$\chi^2_{\text{Yates}} = \sum_{i=1}^N \frac{(|O_i - E_i| - 0.5)^2}{E_i}$$

where:

O_i = an observed frequency

E_i = an expected (theoretical) frequency, asserted by the null hypothesis

N = number of distinct events

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FISHER'S EXACT TEST

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History

- Fisher is said to have devised the test following a comment from Muriel Bristol, who claimed to be able to detect whether the tea or the milk was added first to her cup in 1922



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Fisher's Exact test

- Useful for small samples where chi-squared test is invalid
- Tests for an association between 2 categorical variables
- Normally used for 2 x 2 tables, but computer program allow for bigger tables
- Evaluating the probabilities associated with all possible tables which have the same row and column totals as the observed data, assuming the null hypothesis is true

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Fisher's Exact test

- Based on exact probabilities, it is computationally intensive and may be slow or fail for large sample size.
- Give p values but not direct estimate or confidence interval

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Fisher's Exact test

- Null hypothesis
 - No association between the two variables in the population from which the samples come
 - Same null hypothesis as the chi-squared test
- Assumptions of test
 - none

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Fisher's exact test

- Always use with frequencies, never use percentages for calculation
- No simple formula, statistical program needed
- Unless with good reason, use the two-sided p value
- It gives p values at least as big as the chi-squared test. For large sample size, p values are similar
- If in doubt about the sample size, use Fisher's exact test instead of chi-squared test.

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a	b	a + b
c	d	c + d
a + c	b + d	a + b + c + d

$$p = \frac{\binom{a+b}{a} \binom{c+d}{c}}{\binom{n}{a+c}} = \frac{(a+b)!(c+d)!(a+c)!(b+d)!}{a!b!c!d!n!}$$

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CORRELATION

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Pearson's correlation

- It investigate the strength of a linear relationship between two continuous variables
- It is used when neither variable can be assumed to predict the other
- It gives an estimate, the correlation coefficient and a p value
- A confidence interval can be calculated

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Pearson's correlation

- Assumption
 - The relationship is linear
 - Normal distribution
 - For significant test – at least one variable to be normally disturbed
 - For confidence intervals – both variables should be normally distributed
 - A random sample within the range of interest

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$$r = \frac{\sum_{i=1}^n (X_i - \bar{X})(Y_i - \bar{Y})}{\sqrt{\sum_{i=1}^n (X_i - \bar{X})^2} \sqrt{\sum_{i=1}^n (Y_i - \bar{Y})^2}}$$

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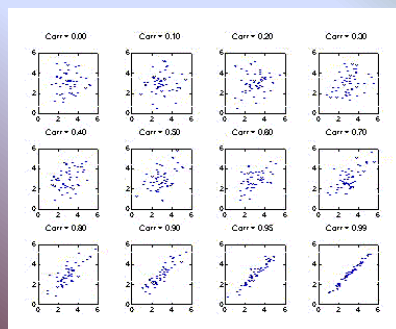
Interpretation of r

- r tells us how close is the linear relationship between two variables
- It lies between +1 and -1
- Negative (positive) values indicate negative (positive) linear relationship
- $r = 0$ indicate that is no linear relationship
- The closer the value +1 or -1, the stronger relationship between two variables

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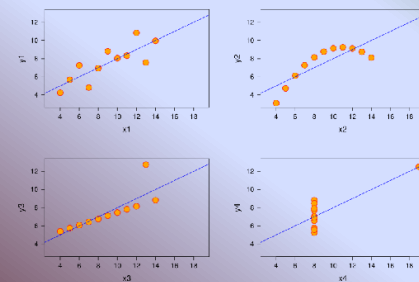
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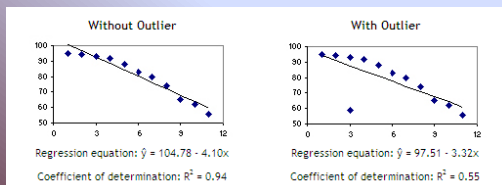
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Outlier

- If outlier is removed, r is closer to +1 or -1



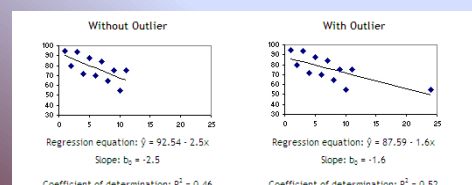
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Influential point

- If influential point is removed, r is closer to 0



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Test and estimate of r

- A significant test can be done with null hypothesis that $r = 0$
- A confidence interval of r can be calculated
- Statistical significance of r directly related to sample size
 - If sample size is large, it may be statistically significant even the relationship is weak

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Interpretation of correlation coefficients

A recently published article by Ko et al¹ illustrates a commonly encountered problem with the interpretation of correlation coefficients in medical research. The authors stated the correlation coefficient ranged from -0.002 to 0.15. If the P value was greater than 0.05, they interpreted the findings as indicating no correlation. Otherwise, there was weak correlation. The t value of the correlation coefficient was given by:

$$t = r \sqrt{\frac{n-2}{1-r^2}}$$

where r is the correlation coefficient and n the sample size.²

From this we can infer that if the sample size or correlation coefficient increases, so will the t value, and hence P value will decrease and thus tend to increase statistical significance. Thus, if there is a huge sample size, the result will be significant even when there is very weak association. However, if the sample size is small, the result will remain non-significant even though the correlation coefficient

is large. Theoretically, if the sample size approaches infinity, the test will always be highly significant ($P < 0.001$) though the correlation coefficient tends to zero.

So the P value for the correlation coefficient just tells us whether the coefficient is or is not reliable, it cannot determine whether there is correlation between two factors. For example, in the article referred to, for $r=0.15$ and $P=0.003$, we should interpret as "the correlation coefficient is reliable and there is weak correlation between two factors". In another example with $r=-0.002$ and $P=0.97$, we should interpret as "there is no adequate evidence to show whether two factors are correlated or not" rather than "they are not correlated" as stated in the article.

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References

1. Ko FHL, Choi AM, Chan HSE, et al. Are Hong Kong doctors following the Global Initiative for Asthma guidelines: a questionnaire "Survey on Asthma Management". *Hong Kong Med J* 2010;16:88-93.
2. Armitage P, Berry G, Matthews JN. *Statistical methods in medical research*. 4th ed. Massachusetts: Blackwell Publishing; 2002:198.

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Spearman's correlation

- It is used when none of the 2 variables follows a normal distribution – it is assumption for Pearson's correlation.
- Null hypothesis
 - There is no tendency for one variable either to increase or to decrease as the other increases
- Assumption
 - The variables can be ranked
 - Monotonic relationship between 2 variables

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Spearman's correlation

- This is calculated using same formula as for Pearson's correlation but uses the ranks of the data rather than the data values themselves
- It gives a values between -1 and +1
- p value can be obtained from statistical program

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MANN WHITNEY U TEST (WILCOXON TWO SAMPLE SIGNED RANK TEST)

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History

- It is also called as Wilcoxon two sample signed ranked test.
- It was proposed initially by Frank Wilcoxon in 1945, for equal sample sizes, and extended to arbitrary sample sizes and in other ways by Henry Mann and his student Donald Ransom Whitney in 1947

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Mann-Whitney U test

- It is based on the rank of the data
- It gives p value but no estimate
- Given a table of cut-offs, the test is easy to do by hand
- If the sample is very small (both smaller than four observations), then statistical significance is impossible.

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Mann-Whitney U test

- The samples should be unrelated (independent)
- The test can be applied to ordinal data
- The population distributions should have the same shape (it tests the whole distribution)
- Tied values in the data
 - If number of ties is small, it is still satisfactory
 - If data are ordinal and fall into only 3 or 4 categories, it is better to use chi-squared test

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WILCOXON MATCHED PAIRS TEST

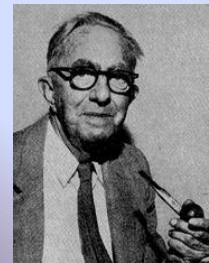
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History

- It is also called Wilcoxon signed rank test
- The test is named for Frank Wilcoxon (1892–1965) who, in a single paper, proposed both it and the rank-sum test for two independent samples (Wilcoxon, 1945)



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Wilcoxon matched pairs test

- Based on the signs of the differences in the pairs and the relative sizes of differences rather than the actual values
- It gives p values but no estimate
- Given a table of cut-offs, the test is easy to do by hand
- If the sample is smaller than 6, then statistical significance is impossible

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Wilcoxon matched pairs test

- The data should be paired
- The data should consist of numerical measurements (interval data)
- The distribution of the differences should be symmetrical. It is difficult to know in practice whether the distribution is symmetrical or not, but we can apply it with small sample size
- The zero difference (tie) should be omitted

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SIMPLE LINEAR REGRESSION

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Simple Linear Regression

- Estimate the nature of linear relationship between two continuous variables
 - Dependent (response) variable
 - Independent (explanatory) variables
- The calculation based on least squared method – It minimize the sum of the squares of these residual (= observed value – fitted values)

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Simple Linear Regression

- Slope or regression coefficient is given by

$$\begin{aligned}\hat{\beta} &= \frac{\sum_{i=1}^n (x_i - \bar{x})(y_i - \bar{y})}{\sum_{i=1}^n (x_i - \bar{x})^2} = \frac{\sum_{i=1}^n x_i y_i - \frac{1}{n} \sum_{i=1}^n x_i \sum_{j=1}^n y_j}{\sum_{i=1}^n x_i^2 - \frac{1}{n} (\sum_{i=1}^n x_i)^2} \\ &= \frac{\bar{xy} - \bar{x}\bar{y}}{\bar{x}^2 - \bar{x}^2} = \frac{\text{Cov}[x, y]}{\text{Var}[x]} = r_{xy} \frac{s_y}{s_x}, \\ \hat{\alpha} &= \bar{y} - \hat{\beta} \bar{x},\end{aligned}$$

- The line goes through the mean point: (\bar{x}, \bar{y})
- Therefore the intercept is given by: $a = \bar{y} - b\bar{x}$

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Interpretation of the equation

- Regression coefficient gives the change in the outcome (y) for a unit change in the predictor variable (x)
- The intercept gives the value of y when x is 0
- The line gives the mean or expected value of y for each value of x

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Simple Linear Regression

- If there is no relationship between x and y, the true regression coefficient b will be 0
- Can be tested using a form of t test
- The regression coefficient b is a useful summary to show how the two variables related
- 95% confidence interval can be calculated for b
- The equation of the line can be used for prediction

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Simple Linear Regression

- Assumption
 - The relationship is linear
 - The distribution of the residuals is normal
 - The variance of the outcome y is constant over x
- Predication
 - Within sample prediction
 - Prediction outside the sample

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Multivariate Analysis

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Multivariate?

- When there is more than one predictor variable on predicting the outcome variable
 - E.g., head size (predictor) and recall (criterion)
 - Recall Performance (in words) = 0.32 (head size in cm) + 1.67
 - ...but how about other variables, such as IQ?
- Linear combination of variables

$$Y' = a + b_1(x_1) + b_2(x_2) + \dots + b_k(x_k)$$
 - k is number of predictor variables

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Multivariate Statistics: the basics

- To examine the relationship between variables, e.g., multiple regression
 - The relationship between predictor variables (can be discrete—e.g., gender, or continuous—e.g., income) and a continuous outcome variable
 - Predicting the performance in a certain task (e.g., memory) based on subjects' performance in other tasks (e.g., attention) and group status (e.g., showing hypertension)

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Multivariate Statistics: the basics

- Costs
 - Requires larger sample sizes
- Benefits
 - Increases precision using multiple measures of a construct
 - Including more variables to capture genuine relationships in the multidimensional and multicausal real world

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Multivariate Statistics: Data screening

- Relationships with other variables
 - **Multicollinearity** — strong inter-correlations among predictor variables ($|r| > 0.8$)
 - Observed in inter-correlation matrices
 - Redundancy among the predictor variables
 - Tolerance $1 - R^2$ ("Collinearity Statistics")
 - Larger = Better
 - If < 0.2 — multicollinear

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Multivariate Statistics: Data screening

- How to tackle multicollinearity problems?
 - To combine closely related variables into a composite variable (e.g., averaging)—this requires some theoretical justifications
 - To use **centering**: transforming the closely related variables by subtracting the mean (averaged across all samples) from each sample

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Multiple Regression

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Multiple Regression

- To assess the relationship between one **continuous** outcome variable (Y) and several discrete/or continuous predictor variables (X)
 - The best *prediction* of a outcome variable (Y') from the combination of predictor variables

$$Y' = a + b_1(x_1) + b_2(x_2) + \dots + b_k(x_k)$$
 - b = unstandardized regression coefficient of each predictor variable
 - Show how much Y' would change with a one unit increase in x
 - Regression analyses—to come up with b values that make Y (data) and Y' (prediction) as close as possible

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Multiple Regression: Type

- Standard
 - All variables are simultaneously entered into the regression equation
 - The regression coefficient of **each** predictor is estimated while {holding constant/ partialling out/ controlling for} the other predictor variables

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Multiple Regression: Type

- Sequential (block entry or hierarchical)
 - Predictor variables are entered in two or more steps
 - To evaluate the relationships between a **subset** of predictor variables and an outcome variable, after controlling for the effects of other subsets of predictor variables on the outcome variable
 - Based on theories
 - Determine the significance of the change in R^2 at each step to see if each newly added predictor makes a significant **improvement** in the predictive power of the regression equation

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Multiple Regression: Example 1

$$JobSatisfaction = 2.411 + (0.512)(SocialSupport) + (-0.109)(Stress) + (0.106)(Income)$$

- If all other variables are held constant:
 - Predicted job satisfaction increases by 0.512 for the increase of an unit of social support
 - Predicted job satisfaction decreases by 0.109 for the increase of an unit of stress
 - Predicted job satisfaction increases by 0.106 for the increase of an unit of income

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Multiple Regression: Example 1

- How important are our predictor variables?
 - Regression coefficients and tests of significance (t-test)—If the coefficient is not significantly different from zero, that predictor will serve *no use*
 - Common mistake:** relative sizes of b_i reflect the relative importance of the predictors
 - E.g., Income is more important than Social Support because b is larger?
- $$JobSatisfaction = 2.411 + (0.512)(SocialSupport) + (-0.109)(Stress) + (0.106)(Income)$$

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Multiple Regression: Example 1

- When considering **relative** magnitudes of the coefficients, we should take into account the *SD* of the predictor variables
 - Solving the regression using *standardized variables (beta)*

Coefficients ^a					
Model	Unstandardized Coefficients		Standardized Coefficients		Sig.
	B	Std. Error	Beta	t	
1					
(Constant)	2.411	.328		7.359	.000
social support at work	.512	.057	.592	9.019	.000
degree of stress at work	-.109	.053	-.115	-2.053	.041
monthly income at work	.198	.050	.192	2.112	.036

$$\text{JobSatisfaction}_z = (0.502)(\text{SocialSupport}_z) + (-0.115)(\text{Stress}_z) + (0.102)(\text{Income}_z)$$

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Multiple Regression: Example 1

- $Y' = a + b_1(x_1) + b_2(x_2) + \dots + b_k(x_k)$
- Common mistake:** X_1 and Y are strongly correlated \rightarrow b_1 has to be a significant regression coefficient in multiple regression models
 - A test of a predictor variable is done in the context of all other variables in the regression equation
 - After X_2, X_3, X_4, \dots and X_k are partialled out (or held constant), X_1 may no longer be useful for predicting the Y
 - b_1 is coefficient for regression of Y on X_1 when we *partial out* the effect of X_2, \dots , and X_k
 - E.g., math exam score and students' quantitative IQ

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Multiple Regression: Points to note

- Sample size** considerations (rules of thumb)
 - $50 + 8 * (\text{number of predictors})$, or
 - Number of predictor variables should be smaller than (the number of subjects divided by 10)
- Limitations
 - Predictability does not tell us anything about the direction of **causality** in regression analyses
 - Similar to "Correlation does not mean causation"
 - Regression assumes no measurement error
 - Must ensure **reliability** and validity of the variables

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Multiple Regression: Points to note

- Should all *available* variables be entered in the regression models?
 - Adding more predictor variables can change the betas of all other predictors
 - Excludes relevant variables (e.g., intelligence) \rightarrow estimation of coefficients for the remaining variables may not reflect the whole pictures
 - Includes irrelevant variables (e.g., preference to ice-cream flavor in salary and success in universities) \rightarrow increase the error variance and weaken the statistical power of the model

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Multiple Regression: Points to note

- Assumptions
 - Absence of multicollinearity among predictor variables
 - Normality, linearity, and homoscedasticity
 - If the underlying function between one or more of the predictors and the criterion is *not* linear, then the betas will be biased and unreliable, so it is important to look at all bivariate plots prior to the analyses

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Logistic Regression

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Logistic Regression

- Can be used when the outcome (*i.e.*, **Y**) is **dichotomous**
- Examples:
 - Does a sample have early-stage Alzheimer's disease?
 - Does a cancer patient respond to therapy?
 - Does a secondary school student smoke?
- Compare to continuous outcomes
 - Global cognitive function
 - Tumor size
 - Packs/week

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Logistic Regression

- To predict the membership in discrete groups (outcome variable, e.g., binary) from several predictor variables (which can be discrete or continuous)
 - E.g., predicting the occurrence of dementia (healthy old adults vs. earliest-stage Alzheimer's diseases) based on subjects' performance in cognitive tests
 - Binary outcome variable is most common, code reference group as 0 and occurrence group as 1 (useful for odd ratio interpretation)

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Logistic Regression

- Goal = to find the best **linear** combination of predictors to maximize the likelihood of obtaining the observed outcome frequencies

$$\ln\left(\frac{p}{1-p}\right) = b_0 + b_1x$$

- p is the probability that the event Y occurs, $p(Y=1)$
- $p/(1-p)$ is the *odds ratio*
- $\ln[p/(1-p)]$ is the log odds ratio, or *logit*
- Can be standard or sequential

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Logistic Regression: Points to note

- Assumptions about variable distributions are not required, but may have more power if there are multivariate normality, and linearity among predictors
- Problems may occur if too few cases relative to predictor variables
- Absence of **multicollinearity** across predictor variables

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OTHERS

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Bonferroni Correction

- It is a simple method to correct the cut-off for statistical significant for multiple testing
- For $\alpha = 0.05$, if the test repeated for 20 times, there should be 1 false positive
- If there is n repeated testing, we need $(1 - \alpha)^n = 0.95$, which approximately equal to $1 - n\alpha$. So, α is approximately equal to $0.05 / n$
- Disadvantage – too conservative

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Estimate for test of proportion

- Risk difference ($p_1 - p_2$)
 - Use if actual size of difference is of interest
 - Most straight forward and useful for survey
- Relative risk (p_1 / p_2)
 - Use if relative risk is of interest
 - Useful when comparing the size of effect for several factor
 - Easier to interpret
 - Do not use for case control test

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Estimate for test of proportion

- Odds ratio (ad / bc where a, b, c and d are 2×2 tables frequencies)
 - Use for case-control studies
 - Approximately equal to relative risk when the outcome is rare
 - Can be misinterpreted when the outcome is common
 - Can adjust for others factors using logistics regression

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Confidence Interval

- In statistics, a **confidence interval (CI)** is a particular kind of interval estimate of a population parameter and is used to indicate the **reliability** of an estimate. It is an observed interval, in principle **different from sample to sample**, that frequently includes the parameter of interest, if the experiment is repeated. How frequently the observed interval contains the parameter is determined by the **confidence level** or **confidence coefficient**.

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Others

- Analysis of variance
- Poisson Regression
- Kappa (inter-rater reliability)
- McNamer test
- Epidemiology
- Principle component analysis
-

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COMMON STATISTICAL SOFTWARE

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Choosing a package

- | | |
|----------------------|---------------------------------|
| • Cost | • Size of datasets |
| • Support | • Transferring between packages |
| • Your institution | • Testing |
| • Usability | • Operating system |
| • Data management | • License versus perpetual copy |
| • Type of analysis | • Upgrades |
| • Specialized method | • Discounted versions |
| • Graphics | |

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Commonly used package

Free

- Epi-info (CDC)
- OpenEpi (CDC)
- R (Programming language)
- WinBUGS (for Bayesian analysis)

Commercial

- Microsoft Excel
- SPSS
- STATA
- Minitab
- SAS
- STATISTICA

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POST TEST

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Variable	OCD (n = 50)	Schizophrenia (n = 47)	χ^2 (degrees of freedom), p value
Mean (standard deviation) age (years)	29 (9)	36 (11)	514 (506), 0.38
Sex			
Male	37 (74)	38 (81)	1.29 (2), 0.52
Female	13 (26)	9 (19)	
Marital status			
Single	14 (28)	10 (21)	1.66 (4), 0.79
Married	34 (68)	36 (77)	
Widowed	2 (4)	-	
Separated	-	1 (2)	
Occupation			
Professional	13 (26)	6 (13)	38.8 (48), 0.82
Clerical / shop owner	3 (6)	6 (13)	
Farmer	2 (4)	1 (2)	
Skilled worker	10 (20)	9 (19)	
Semi-skilled / unskilled worker	1 (2)	14 (30)	
Unemployed	10 (20)	6 (13)	
Housewife	-	1 (2)	
Retired	11 (22)	4 (9)	

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	OCD (n = 50)	Schizophrenia (n = 47)	t Value, p value
IDEAS			
Self-care	0.1 (0.3)	0.3 (0.4)	-2.3, 0.03
Interpersonal activities	0.5 (0.5)	1.2 (0.9)	-4.3, <0.01
Communication and understanding	0.4 (0.5)	0.7 (0.6)	-2.0, 0.04
Work	0.9 (0.7)	1.8 (1.5)	-3.9, <0.01
Global disability	5.9 (1.3)	7.7 (2.8)	-4.5, <0.01
GAF	66.6 (10.5)	55.0 (20.1)	3.7, <0.01

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	Adults (< 65 years) [n = 7]	Elderly (≥ 65 years) [n = 12]	Chi-square	p Value
Psychiatric diagnoses				
Organic brain syndrome	2 (29%)	0	3.83	0.05
Dementia	0	8 (67%)	8.06	0.01
Mental retardation	4 (57%)	0	8.69	0.003
Schizophrenia	3 (43%)	4 (33%)	0.17	0.68
Delusional disorder	0	2 (17%)	1.30	0.25
Depression	1 (14%)	1 (8%)	0.17	0.68
Bipolar affective disorder	2 (29%)	0	3.83	0.05
Physical diagnoses				
Neurological	4 (57%)	4 (33%)	1.03	0.31
Gastro-intestinal / hepatic	2 (29%)	1 (8%)	1.36	0.24
Orthopaedic	1 (14%)	2 (17%)	0.02	0.89
Respiratory	0	2 (17%)	1.30	0.25
Endocrine	1 (14%)	2 (17%)	0.02	0.89
Urological	0	1 (8%)	0.62	0.43
Sensory	0	1 (8%)	0.62	0.43
Cardiovascular	1 (14%)	2 (17%)	0.02	0.89
Treatment factors				
Extrapyramidal symptom	3 (43%)	1 (8%)	3.17	0.08
Typical antipsychotics	5 (71%)	10 (83%)	0.38	0.54
Atypical antipsychotics	4 (57%)	1 (8%)	5.43	0.02
Anticonvulsants	4 (57%)	4 (33%)	1.03	0.31
Benzodiazepines	6 (86%)	1 (8%)	11.38	0.001
Anticholinergics	5 (71%)	6 (50%)	0.83	0.36
Antidepressants	1 (14%)	2 (17%)	0.02	0.89

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Variable	Pearson's correlation (r)	Significance
Age	0.12	p < 0.05
Depression	0.25	p < 0.01
Hopelessness	0.21	p < 0.01
Risk rescue score	0.13	p < 0.05

intent than those without morbidity (Table 1). There was a clinically significant correlation between suicidal intent and age, hopelessness, depression, and lethality of the attempt (Table 2).

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TABLE 3 Univariate analysis of potential factors affecting preferences for developing a Health Call Centre

Characteristic	Chi squared test		X ²	P value
	Agree to develop a Call Centre % (No.)	Disagree to develop a Call Centre % (No.)		
Gender				
Male	49.3 (168)	51.7 (31)	0.118	0.780
Female	50.7 (173)	49.3 (29)		
Age (years)				
18-30	6.8 (23)	3.3 (2)	36.269	<0.001
31-64	78.5 (266)	45.3 (29)		
>65	14.7 (46)	45.3 (29)		
Education				
Primary school or below	26.1 (96)	61.0 (36)	25.764	<0.001
Secondary school	58.2 (199)	27.1 (16)		
University or above	13.7 (47)	11.8 (7)		
Marital status				
Married	82.5 (282)	81.7 (49)	0.022	0.856
Others	17.5 (60)	18.3 (11)		
Working status ^a				
Working	48.2 (164)	31.7 (19)	5.641	0.024
Not working	51.8 (176)	68.3 (41)		
Individual monthly income				
No income (\$0)	38.9 (128)	63.2 (36)	11.694	0.001
Received income	61.1 (201)	36.6 (21)		

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Health status				
No difference – much better	68.0 (230)	56.9 (33)	2.760	0.100
Worse – much worse	32.0 (109)	43.1 (25)		
Being cared for by other people				
Yes	9.6 (33)	20.0 (12)	5.501	0.026
No	90.4 (309)	80.0 (48)		
Caregiver				
Yes	19.7 (67)	8.5 (5)	4.288	0.043
No	80.3 (273)	91.5 (54)		
Health insurance coverage				
Yes	32.9 (112)	18.3 (11)	5.111	0.023
None	67.1 (228)	81.7 (49)		
Fee waiver				
Yes	27.5 (94)	28.3 (17)	0.018	0.877
None	72.5 (248)	71.7 (43)		

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Types of fee waiver ^a				
CSSA/disability allowance	26.7 (94)	56.3 (8)	5.545	0.037
Civil servant/HA benefits	73.3 (66)	43.8 (7)		
Presence of chronic disease				
Yes	41.3 (141)	31.7 (19)	1.995	0.198
None	58.7 (200)	68.3 (41)		
Treatment on health problem last time				
Yes	2.9 (10)	6.7 (4)	2.127	0.141
No treatment	97.1 (332)	93.3 (56)		
Methods of solving health problem last time				
Ask health professional/others	80.1 (274)	83.3 (50)	0.781	0.677
Self (internet/books/others)	7.6 (26)	8.3 (5)		
Both	12.3 (42)	8.3 (5)		
Used health hotline before				
Yes	2.7 (9)	1.7 (1)	0.204	1.000
No	97.3 (330)	98.3 (58)		

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Table 4. Association of symptoms, insight, and social support with medication adherence among patients with schizophrenia.^a

Variable	Simple linear regression		Multiple linear regression	
	Crude regression coefficient (95% CI)	p Value	Adjusted regression coefficient (95% CI)	p Value
MSPSS	2.21 (0.89 to 3.52)	0.85		
BPRS	-0.13 (-0.24 to -0.02)	< 0.05	-0.12 (-0.24 to -0.01)	< 0.05
ITAQ	0.04 (-0.02 to 0.09)	0.19		

Abbreviations: BPRS = Brief Psychiatric Rating Scale; CI = confidence interval; ITAQ = Insight and Treatment Attitude Questionnaire; MSPSS = Multidimensional Scale of Perceived Social Support.

^a Forward, backward and stepwise multiple linear regression methods were applied. Model assumption was fulfilled. No multicollinearity was detected. Coefficient of determination (r^2) = 0.08.

The relationships of social support, insight, and psychopathology with medication adherence were explored by regression analysis. The relationships were examined using SLR, followed by MLR. All the variables that met the initial screening criteria ($p < 0.25$) were entered into MLR. After controlling for insight, the MLR analysis showed a significant negative linear relationship between psychopathology and total MARS score. Increase in the total BPRS by 1 reduced the MARS total score by 0.13

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Table 3. Association between demographic factors with medication adherence among patients with schizophrenia.^a

	Simple linear regression crude regression coefficient (95% CI)	p Value	Multiple linear regression adjusted regression coefficient (95% CI)	p Value
Age	-0.03 (-0.07 to 0.003)	0.08		
Gender	-0.80 (-1.43 to -0.18)	0.01		
Education level	-0.19 (-0.76 to 0.38)	0.51		
Marital status	-0.13 (-0.56 to 0.30)	0.54		
Occupation	-0.32 (-0.97 to 0.33)	0.32		
Income	-0.007 (-0.28 to 0.27)	0.95		
Duration of illness	-0.23 (-0.59 to 0.12)	0.19		
Frequency of admission	0.59 (-1.05 to -0.13)	0.01	-0.55 (-0.99 to -0.10)	< 0.05
Type of antipsychotic	0.08 (-0.49 to 0.66)	0.76		

Abbreviation: CI = confidence interval.

^a Forward, backward, and stepwise regression methods were applied. Model assumption was fulfilled. There were no interactions among dependent variables. No multicollinearity was detected. Coefficient of determination (r^2) = 0.08.

We concluded that if adherence could be addressed appropriately, the number of admissions and severity of psychopathology could be improved, leading to better patient outcomes. In a recent systematic review, Hayness et

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TO SUM UP

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You should learn...

- Basic concept of hypothesis test
- Interpretation of the test result
- Sampling method
- Identify and avoid common mistake in medical statistics
- At least, you should know when, how and where to seek advice

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- *Oxford Handbook of Medical Statistics* JL Peacock, PJ Peacock. Oxford University Press. 2011
- *Statistical Methods in Medical Research* 4th edition. P Armitage, G Berry, LNS Matthews. Blackwell Publishing. 2002
- *Elementary Statistics Tables*. HR Neave. Routledge. 1989
- <http://www.cct.cuhk.edu.hk/stat/>
– Sample size estimation (CUHK)
- <http://udel.edu/~mcdonald/statintro.html>
– Handbook of Biological Statistics
- <http://www.york.ac.uk/depts/maths/histstat/>
– History of Statistics (The University of York)

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To sum up

- Now, you may forget half of the content
- You will forget 90% of the talk within 1 week
- Learn it and revise it if you use it
- Consult statistician if necessary (better at the beginning of the study)
- Compared with mathematics, medical statistics is a “kid”.
- My e-mail: kc@drkcwong.com

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Thank You