CS4220: Knowledge Discovery Methods for Bioinformatics

Unit 1: Essence of Biostatistics

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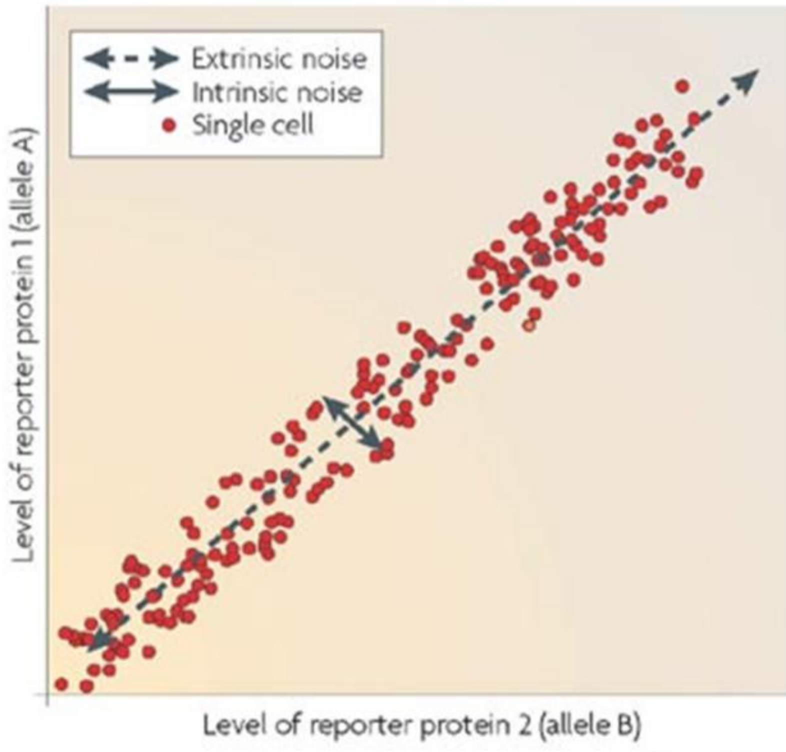
Outline

- **Basics of biostatistics**
- **Statistical estimation**
- **Hypothesis testing**
  - Measurement data: z-test, t-test
  - Categorical data: χ2-test, Fisher's exact test
  - Non-parametric methods
- **Ranking and rating**
- **Summary**

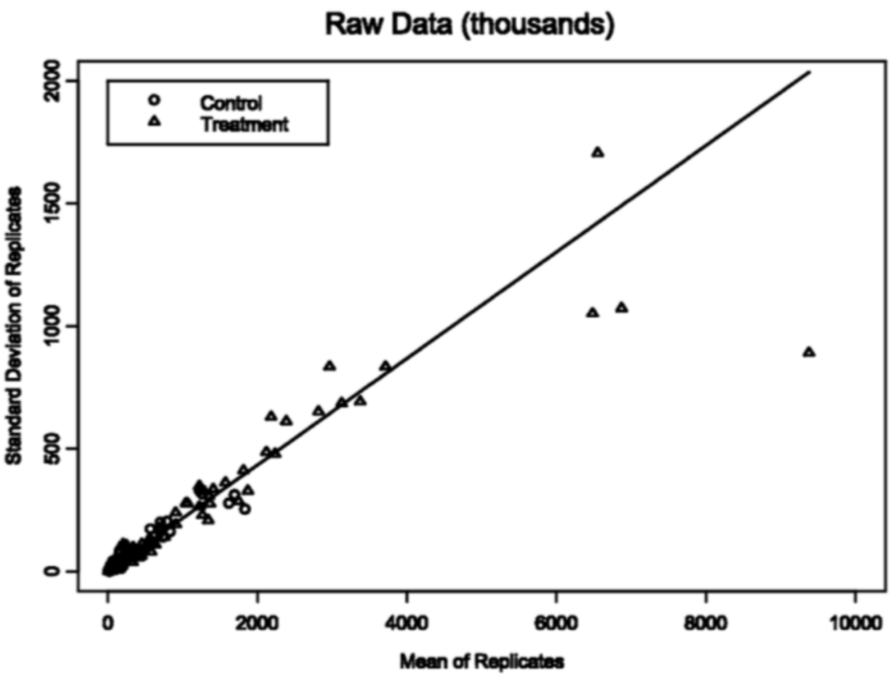
Why need biostatistics?

Intrinsic & extrinsic noise



Nat Rev Genet, 9:583-593, 2008

Measurement errors



J Comput Biol, 8(6):557-569, 2001

Why need to learn biostatistics?

- **Essential for scientific method of investigation**
  - Formulate hypothesis
  - Design study to objectively test hypothesis
  - Collect reliable and unbiased data
  - Process and evaluate data rigorously
  - Interpret and draw appropriate conclusions

- **Essential for understanding, appraisal and critique of scientific literature**

Type of statistical variables

- **Descriptive (categorical) variables**
  - Nominal variables (no order between values): gender, eye color, race group, …
  - Ordinal variables (inherent order among values): response to treatment: none, slow, moderate, fast

- **Measurement variables**
  - Continuous measurement variable: height, weight, blood pressure …
  - Discrete measurement variable (values are integers): number of siblings, the number of times a person has been admitted to a hospital …

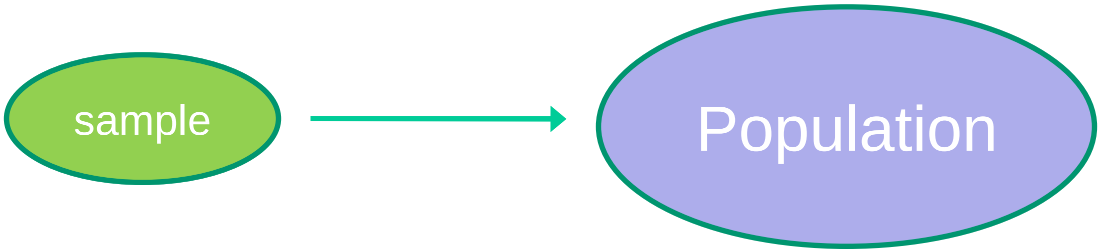
Statistical variables

- **It is important to be able to distinguish different types of statistical variables and the data they generate as the kind of statistical indices and charts and the type of statistical tests used depend on knowledge of these basics**

Types of statistical methods

- **Descriptive statistical methods**
  – Provide summary indices for a given data, e.g. arithmetic mean, median, standard deviation, coefficient of variation, etc.

- **Inductive (inferential) statistical methods**
  – Produce statistical inferences about a population based on information from a sample derived from the population, need to take variation into account



Estimating population values from sample values

Summarizing data

- **Statistic is “making sense of data”**
- **Raw data have to be processed and summarized before one can make sense of data**
- **Summary can take the form of**
  - Summary index: using a single value to summarize data from a study variable
  - Tables
  - Diagrams

Summarizing categorical data

patient	gende r	status
1	Male	alive
2	female	alive
3	male	dead
4	female	alive
etc	etc	etc

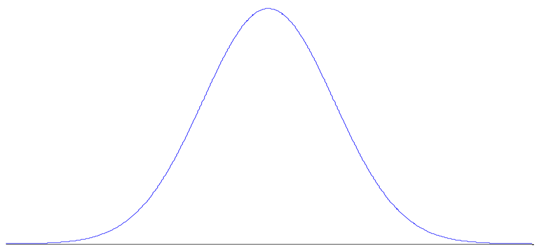
	Dead	Alive	Total
Female	12	25	37
male	23	26	49
Total	35	51	86

- **A Proportion is a type of fraction in which the numerator is a subset of the denominator**
  - proportion dead = 35/86 = 0.41
- **Odds are fractions where the numerator is not part of the denominator**
  - Odds in favor of death = 35/51 = 0.69
- **A Ratio is a comparison of two numbers**
  - ratio of dead: alive = 35: 51
- **Odds ratio: commonly used in case-control study**
  - Odds in favor of death for females = 12/25 = 0.48
  - Odds in favor of death for males = 23/26 = 0.88
  - Odds ratio = 0.88/0.48 = 1.84

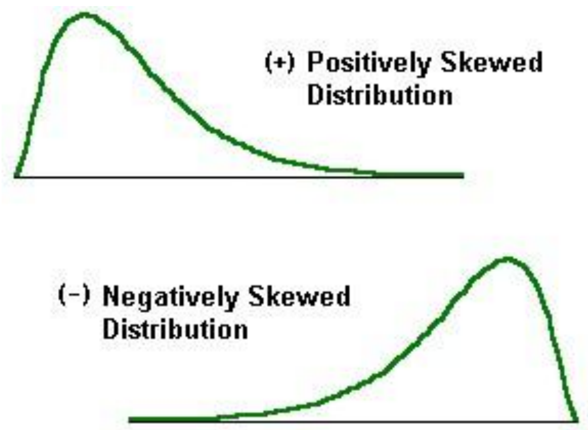
Summarizing measurement data

- **Distribution patterns**
  - Symmetrical (bell-shaped) distribution, e.g. normal distribution
  - Skewed distribution
  - Bimodal and multimodal distribution
- **Indices of central tendency**
  - Mean, median
- **Indices of dispersion**
  - Variance, standard deviation, coefficient of variance

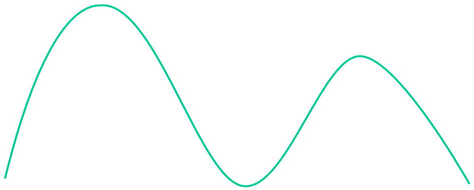
Distribution patterns



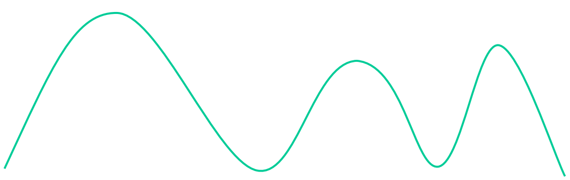
symmetrical distribution



Skewed distribution



Bimodal



Multimodal

Indices of central tendency

- **(Arithmetic) mean: Average of a set of values**

$$\bar{X} = \frac{\sum_{i=1}^{n} X_i}{n}$$

- **Mean is sensitive to extreme values**
- **Example: blood pressure reading**

x1	87	87
x2	95	95
x3	98	98
x4	101	101
x5	105.0	1050
mean	97.2	286.2

Robust measure of central tendency

- **Median: The number separating the higher half of a sample, a population, or a population from the lower half**
- **Median is less sensitive to extreme values**

Median is unchanged → x3

x1	87	87
x2	95	95
x3	**98**	**98**
x4	101	101
x5	105.0	1050

Indices of central tendency: Quantiles

- **Quantiles: Dividing the distribution of ordered values into equal-sized parts**
  - Quartiles: 4 equal parts
  - Deciles: 10 equal parts
  - Percentiles: 100 equal parts

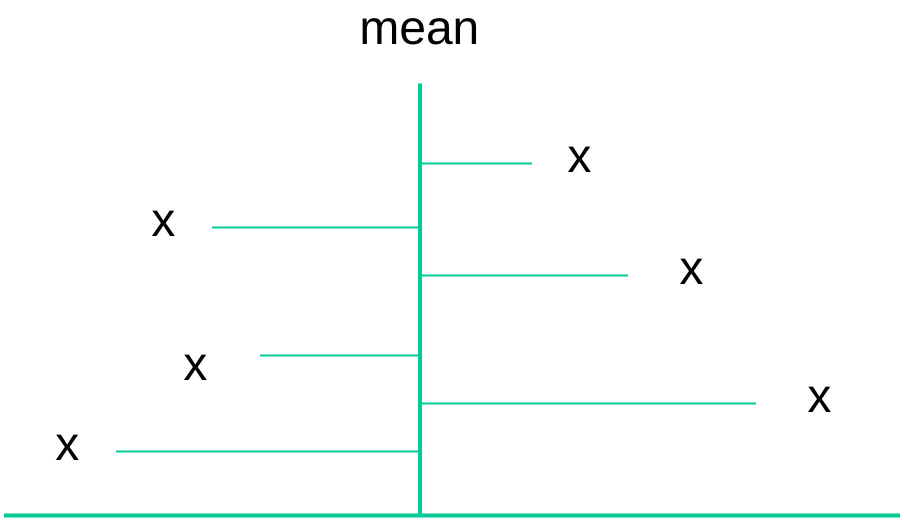
First 25% **Second 25%** **Third 25%** **Fourth 25%**

Q_1 Q_2 Q_3

Q_1: first quartile
Q_2 : second quartile = median
Q_3: third quartile

Indices of dispersion

- **Summarize the dispersion of individual values from some central value like the mean**
- **Give a measure of variation**



Indices of dispersion: Variance

- **Variance : Average of squares of deviation from the mean**

$$\frac{\sum_{i=1}^{n}(X_i - \overline{X})^2}{n}$$

- **Variance of a sample: Usually subtract 1 from n in the denominator**

$$\frac{\sum_{i=1}^{n}(X_i - \overline{X})^2}{n-1}$$

effective sample size, also called degree of freedom

Indices of dispersion: Standard deviation

- **Problem with variance: Awkward unit of measurement as value are squared**

- **Solution: Take square root of variance => standard deviation**

- **Sample standard deviation (s or sd)**

$$\sqrt{\frac{\sum_{i=1}^{n}(X_i - \overline{X})^2}{n-1}}$$

Standard deviation

- **Caution must be exercised when using standard deviation as a comparative index of dispersion**

Weights of newborn elephants (kg)	
929	853
878	939
895	972
937	841
801	826

n=10, $\bar{X}$ = 887.1, sd = 56.50

Weights of newborn mice (kg)	
0.72	0.42
0.63	0.31
0.59	0.38
0.79	0.96
1.06	0.89

n=10, $\bar{X}$ = 0.68, sd = 0.255

Incorrect to say that elephants show greater variation for birth-weights than mice because of higher standard deviation

Coefficient of variance

- **Coefficient of variance expresses standard deviation relative to its mean**

$$cv = \frac{s}{\overline{X}}$$

Weights of newborn elephants (kg)	
929	853
878	939
895	972
937	841
801	826

n=10, $\overline{X}$ = 887.1
s = 56.50, cv = 0.0637

Weights of newborn mice (kg)	
0.72	0.42
0.63	0.31
0.59	0.38
0.79	0.96
1.06	0.89

n=10, $\overline{X}$ = 0.68
s = 0.255, cv = 0.375

Mice show greater birth-weight variation

When to use coefficient of variance

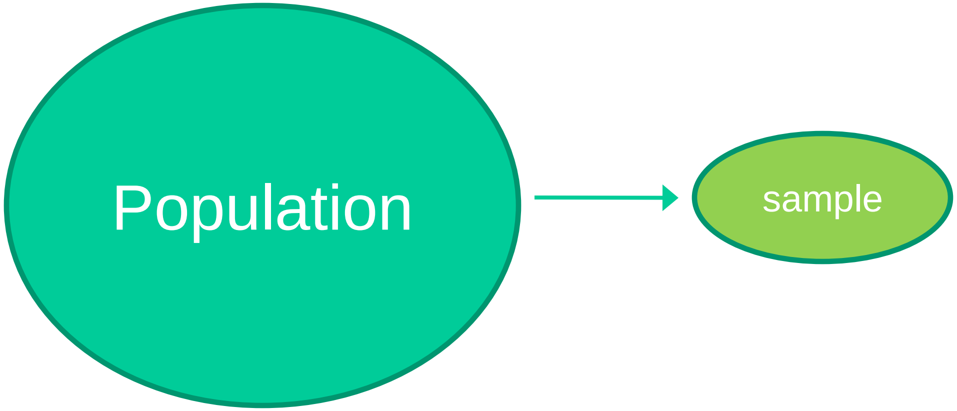
- **When comparison groups have very different means (CV is suitable as it expresses the standard deviation relative to its corresponding mean)**

- **When different units of measurements are involved, e.g. group 1 unit is mm, and group 2 unit is mg (CV is suitable for comparison as it is unit-free)**

- **In such cases, standard deviation should not be used for comparison**

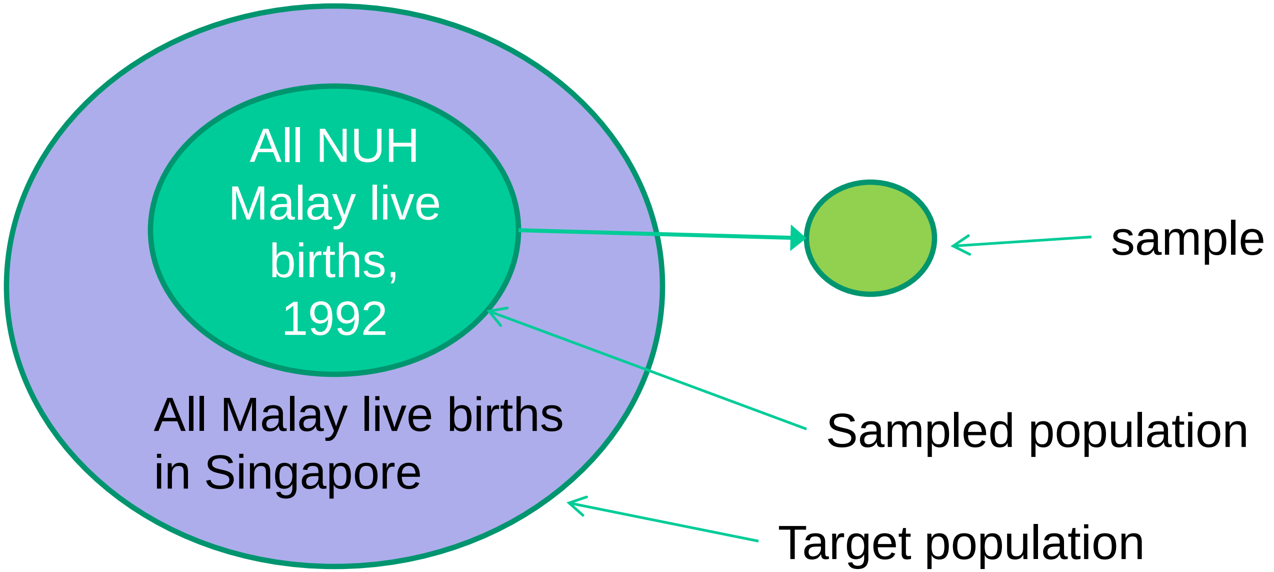
Sample and population

- **Populations are rarely studied because of logistical, financial and other considerations**
- **Researchers have to rely on study samples**
- **Many types of sampling design**
- **Most common is simple random sampling**

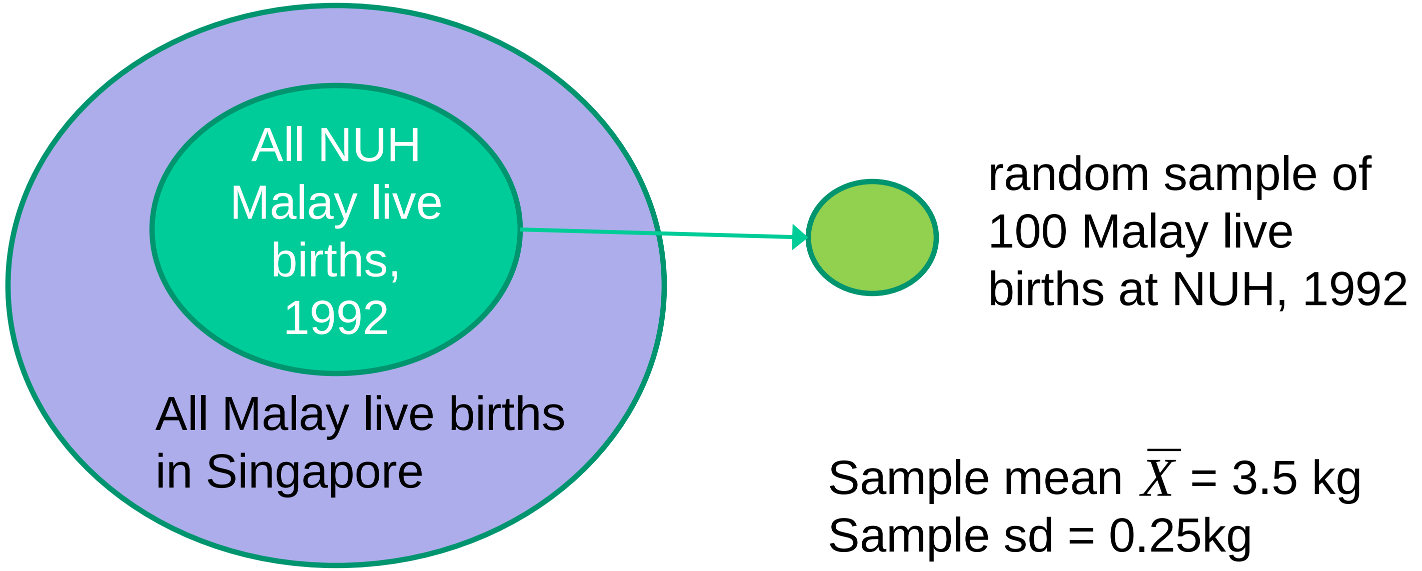


Random sampling

- **Suppose that we want to estimate the mean birth-weights of Malay male live births in Singapore**
- **Due to logistical constraints, we decide to take a random sample of 100 Malay live births at the National University Hospital in a given year**



Sample, sampled population, and target population



Sample mean $\bar{X}$ = 3.5 kg
Sample sd = 0.25kg

- **Suppose that we know the mean birth weight of sampled population μ to be 3.27kg with σ = 0.38kg**
- **$\bar{X} - \mu$ = 0.23kg**

Sampling error

- **Could the difference of 0.23 kg =(3.5kg-3.27kg) be real or could it be due purely to chance in sampling?**
- **'Apparent' different betw population mean and the random sample mean that is due purely to chance in sampling is called sampling error**
- **Sampling error does not mean that a mistake has been made in the process of sampling but variation experienced due to the process of sampling**
  - Sampling error reflects the difference betw the value derived from the sample and the true population value
- **The only way to eliminate sampling error is to enumerate the entire population**

Estimating sampling error

All NUH live births, 1992

Sample size = constant = 100

$\bar{X}$=3.5 kg

$\bar{X}$=2.9 kg

$\bar{X}$=3.8 kg

$\bar{X}$=3.1 kg

$\bar{X}$=2.8 kg

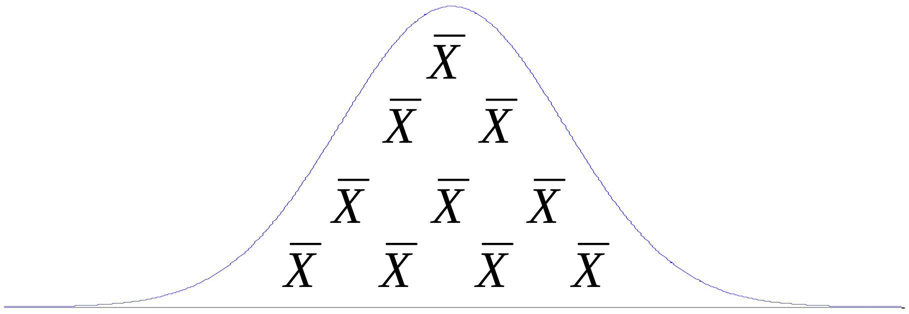
$\bar{X}$=3.5 kg

etc

Repeated sampling with replacement using the same sample size

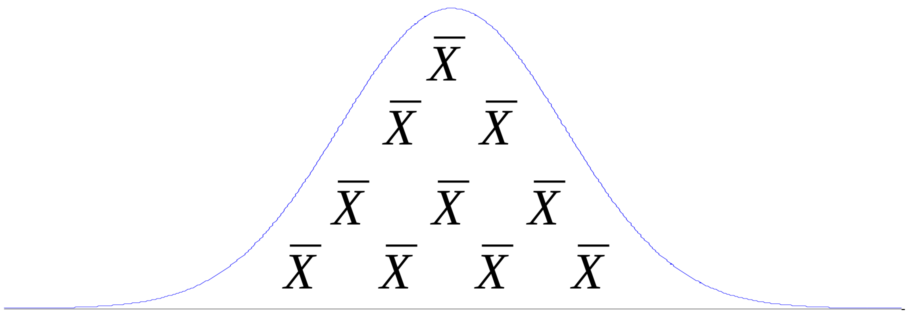
Distribution of sample means

- **Also known as sampling distribution of the mean**
- **Each unit of observation in the sampling distribution is a sample mean**
- **Spread of the sampling distribution gives a measure of the magnitude of sampling error**



Sampling distribution of the mean

- **Central limit theorem: When sample sizes are large, sampling distribution generated by repeated random sampling with replacement is invariably a normal distribution regardless of the shape of the population distribution**



- **Mean of sampling distribution = population mean = μ**

- **Standard error of the sample mean =**

$$\text{S.E.}_{\bar{X}} = \frac{\sigma}{\sqrt{n}}$$

Standard deviation vs. standard error

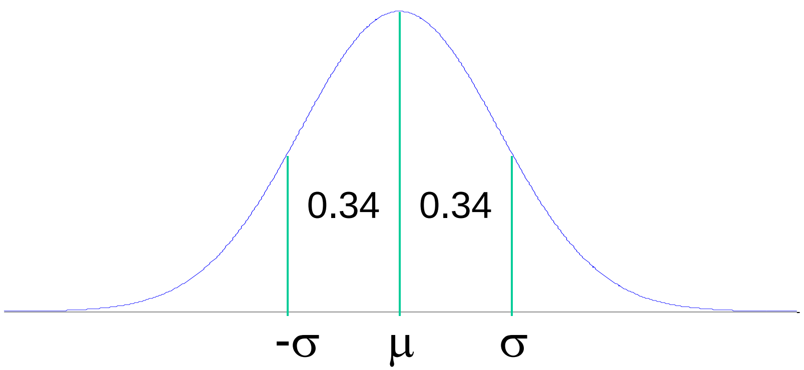
- **Standard deviation (s.d.) tells us variability among individuals**

- **Standard error (S.E.$_{\bar{X}}$) tells us variability of sample means**

- **Standard error of the mean = S.E.$_{\bar{X}}$ = $\dfrac{\sigma}{\sqrt{n}}$**

  – σ : standard deviation of the population

Properties of normal distribution



- **Unimodal and symmetrical**

- **Probability distribution**
  - Area under normal curve is 1

- **For a normal distribution w/ mean μ and standard deviation σ**
  - $\mu \pm 1\sigma$ is ~68% of area under the normal curve
  - $\mu \pm 1.96\sigma$ is ~95% of area under the normal curve
  - $\mu \pm 2.58\sigma$ is ~99% of area under the normal curve

Roadmap

- **Basics of biostatistics**
- **Statistical estimation**
- **Hypothesis testing**
  - Measurement data
  - Categorical data
  - Non-parametric methods
- **Ranking and rating**
- **Summary**

Central dogma of biostatistics: Estimation and hypothesis testing

- **Statistical estimation**
  - Estimating population parameters based on sample statistics
  - Application of the "Confidence interval"

- **Hypothesis testing**
  - Testing certain assumptions about the population by using probabilities to estimate the likelihood of the results obtained in the sample(s) given the assumptions about the population
  - Application of "Test for statistical significance"

Statistical estimation

- **Two ways to estimate population values from sample values**
  - Point estimation
    - **Using a sample statistic to estimate a population parameter based on a single value**
      - *e.g. if a random sample of Malay births gave $\bar{X}$ =3.5kg, and we use it to estimate μ, the mean birthweight of all Malay births in the sampled population, we are making a point estimation*
    - **Point estimation ignores sampling error**
  - Interval estimation
    - **using a sample statistic to estimate a population parameter by making allowance for sample variation (error)**

Interval estimation

- Provide an estimation of the population parameter by defining an interval or range within which the population parameter could be found with a given probability or likelihood
- This interval is called Confidence interval
- In order to understand confidence interval, we need to return to the discussion of sampling distribution

Central limit theorem

- **Repeated sampling with replacement gives a distribution of sample means which is normally distributed and with a mean which is the true population mean, μ**

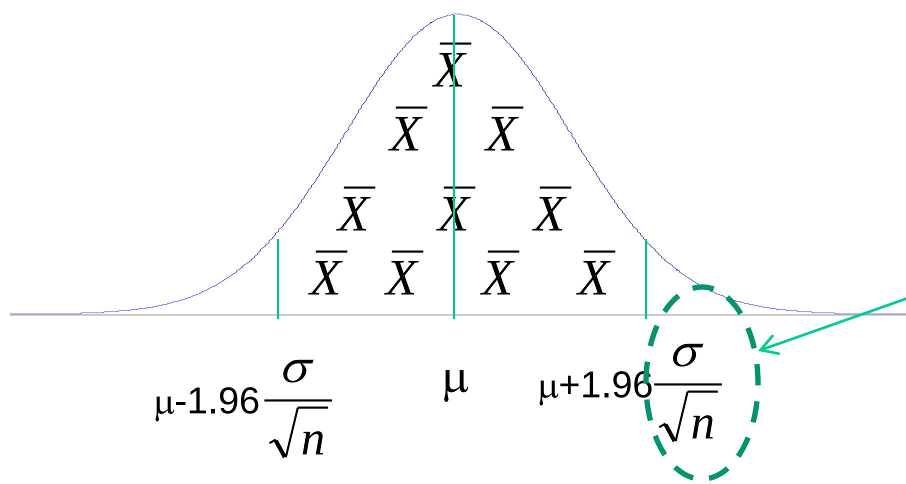
- **Assumptions:**
  - Large and constant sample size
  - Repeated sampling with replacement
  - Samples are randomly taken

Sampling distribution of the mean

- **95% sample means of the sampling distribution can be found within the limit of $\mu \pm 1.96 \dfrac{\sigma}{\sqrt{n}}$**

- **Can be rewritten as**

$$\Pr\Big(\underbrace{\bar{X} - 1.96\frac{\sigma}{\sqrt{n}} <= \mu <= \bar{X} + 1.96\frac{\sigma}{\sqrt{n}}}_{\text{95\% confidence interval}}\Big) = 0.95$$



Standard error of the sample mean S.E.$_{\bar{X}}$

95% confidence interval

95% chance of finding μ within this interval

$$\bar{X} - 1.96\frac{\sigma}{\sqrt{n}} \qquad \bar{X} \qquad \bar{X} + 1.96\frac{\sigma}{\sqrt{n}}$$

Standard error of the sample mean S.E.$_{\bar{X}}$

- **The 95% confidence interval gives an interval of values within which there is a 95% chance of locating the true population mean μ**

Estimating standard error

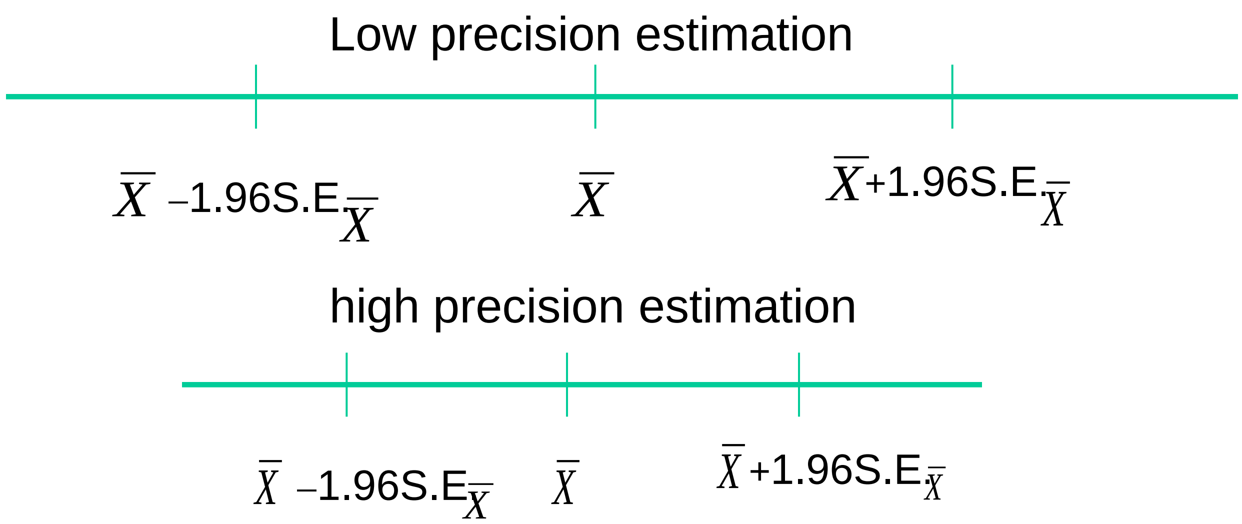
- **The sampling distribution is only a theoretical distribution as in practice we take only one sample and not repeated sample**

- **Hence S.E.$_{\overline{X}}$ is often not known but can be estimated from a single sample**

$$S.E._{\overline{X}} = \frac{s}{\sqrt{n}}$$

Where s is sample standard deviation and n is the sample size

Precision of statistical estimation



- **Width of a confidence interval gives a measure of the precision of the statistical estimation**

$\Rightarrow$ **Estimation of population value can achieve higher precision by minimizing S.E.** $\overline{X}$, **which depends on the population s.d. and sample size, that is S.E.** $\overline{X}$ **can be minimized by maximizing sample size (up to a certain point)**

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Hypothesis testing

- **Another way of statistical inference in which we want to ask a question like**
  - How likely is the mean systolic blood pressure from a sampled population (e.g. biomedical researchers) the same as those in the general population?
    - **i.e. $\mu_{researchers} = \mu_{general}$?**
  - Is the difference between $\bar{X}_1$ and $\bar{X}_2$ statistically significant for us to reject the hypothesis that their corresponding u_1 and u_2 are the same?
    - **i.e. $\mu_{male} = \mu_{female}$?**

Steps for test of significance

- **A test of significance can only be done on a difference, e.g. difference betw $\bar{X}$ and μ, $\bar{X}_1$ and $\bar{X}_2$**

1. **Decide the difference to be tested, e.g. difference in pulse rate betw those who were subjected to a stress test and the controls, on the assumption that the stress test significantly increases pulse rate (the hypothesis)**
2. **Formulate a Null Hypothesis, e.g. no difference in pulse rate betw the two groups,**
   - i.e. H0: $\mu_{test}=\mu_{control}$
   - Alternative hypothesis H1 : $\mu_{test} \neq \mu_{control}$

Steps for test of significance

3. Carry out the appropriate test of significance. Based on the test statistic (result), estimate the likelihood that the difference is due purely to sample error
4. On the basis of likelihood of sample error, as measured by the Pr value, decide whether to reject or not reject the Null Hypothesis
5. Draw the appropriate conclusion in the context of the biomedical problem, e.g. some evidence, from the dataset, that subjects who underwent the stress test have higher pulse rate than the controls on average

Test of significance: An example

- **Suppose a random sample of 100 Malay male live births delivered at NUH gave a sample mean weight of 3.5kg with an sd of 0.9kg**

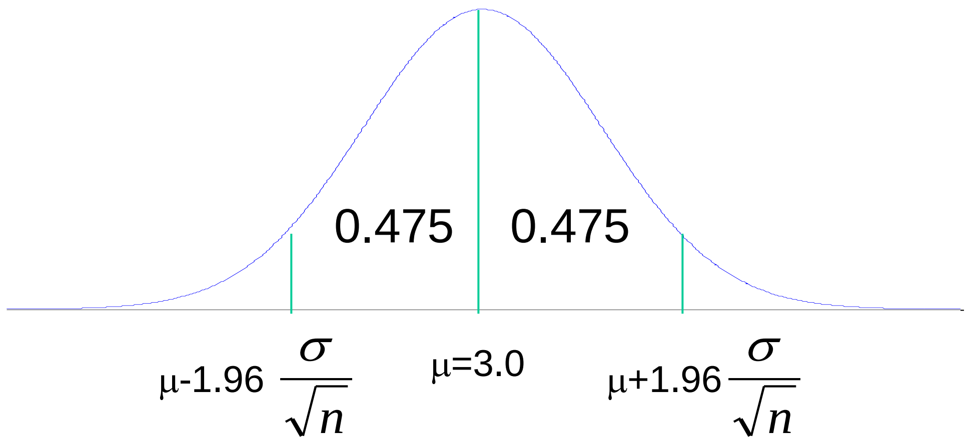
- **Question of interest: What is the likelihood that the mean birth weight from the sample population (all Malay male live birth delivered at NUH) is the same as the mean birth weight of all Malay male live births in the general population, after taking sample error into consideration?**

Test of significance: An example

- **Suppose: $\bar{X}$ = 3.5kg, sd = 0.9kg,**
  μ_{pop} = 3.0 kg σ_{pop} = 1.8kg
- **Difference betw means = 3.5–3.0 = 0.5kg**
- **Null Hypothesis, H0: $\mu_{NUH} = \mu_{pop}$**
- **Test of significance makes use of the normal distribution properties of the sampling distribution of the mean**

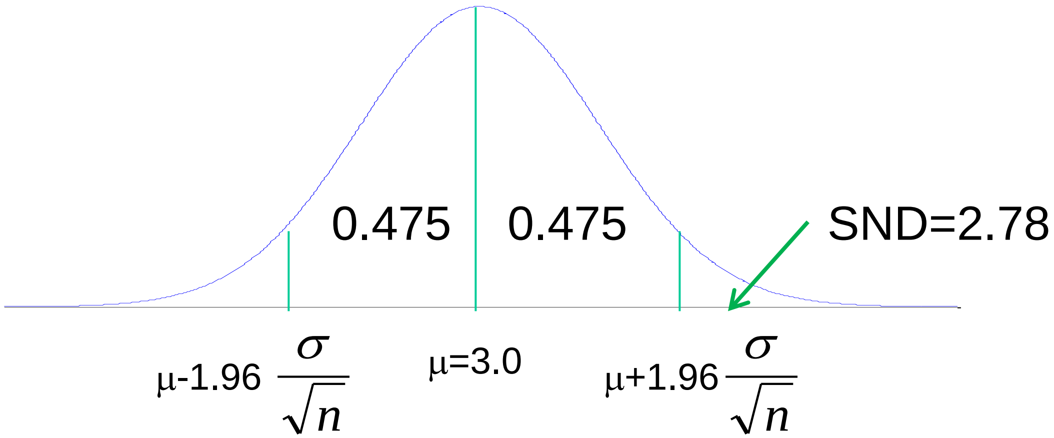
Test of significance

- **Where does our sample mean of 3.5kg lie on the sampling distribution?**
- **If it lies outside the limit of $\mu \pm 1.96\frac{\sigma}{\sqrt{n}}$, the likelihood that the sample belongs to the same population is equal or less than 0.05 (5%)**



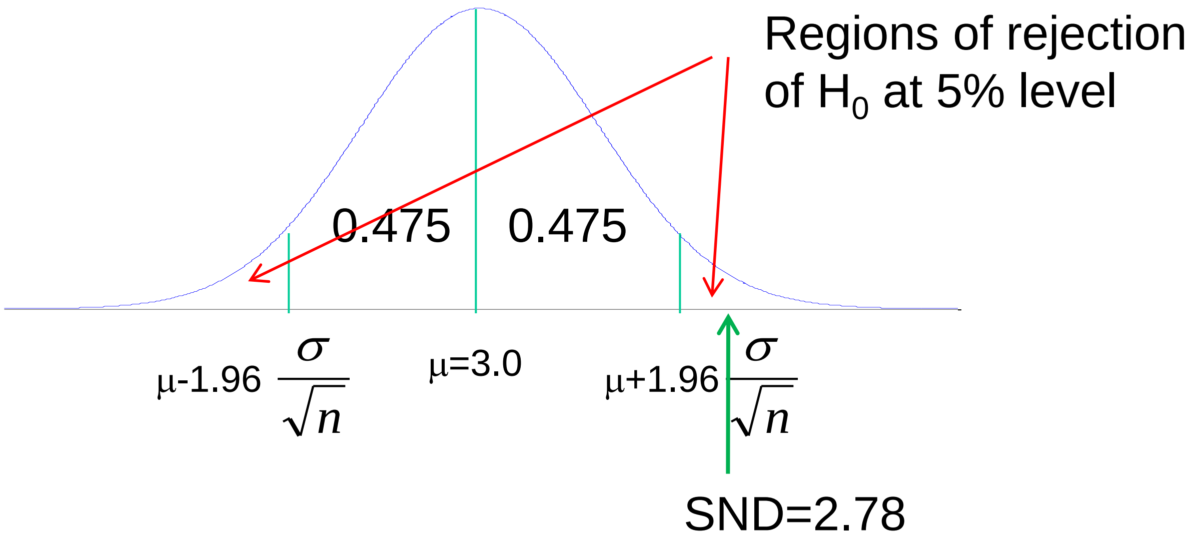
Test of significance: z-test

- **Test is given by $\frac{\bar{X}-\mu}{SE_{\bar{X}}}$ = standard normal deviate (SND or z)**
- **SND expresses the difference in standard error units on a standard normal curve with μ= 0 and σ=1**
- **For our example, SND = $\frac{3.5-3.0}{1.8/\sqrt{100}}$ = 2.78**



Test of significance

- **There is a less than 5% chance that a difference of this magnitude (0.5kg) could have occurred on either side of the distribution, if the random sample of the 100 Malay males had come from a population whose mean birth weight is the same as that of the general population**



NORMAL CURVE AREAS

Entries in the body of the Table give the area under the Standard Normal Curve from 0 to z

z	.00	.01	.02	.03	.04	.05	.06	.07	.08	.09
0.0	.0000	.0040	.0080	.0120	.0160	.0596	.0636	.0675	.0714	.0753
0.1	.0398	.0438	.0478	.0517	.0557	.0596	.0636	.0675	.0714	.0753
0.2	.0793	.0832	.0871	.0910	.0948	.0987	.1026	.1064	.1103	.1141
0.3	.1179	.1217	.1255	.1293	.1331	.1368	.1406	.1443	.1480	.1517
0.4	.1554	.1591	.1628	.1664	.1700	.1736	.1772	.1808	.1844	.1879
0.5	.1915	.1950	.1985	.2019	.2054	.2088	.2123	.2157	.2190	.2224
0.6	.2257	.2291	.2324	.2357	.2389	.2422	.2454	.2486	.2517	.2549
0.7	.2580	.2611	.2642	.2673	.2704	.2734	.2764	.2794	.2823	.2852
0.8	.2881	.2910	.2939	.2967	.2995	.3023	.3051	.3078	.3106	.3133
0.9	.3159	.3186	.3212	.3238	.3264	.3289	.3315	.3340	.3365	.3389
1.0	.3413	.3438	.3461	.3485	.3508	.3531	.3554	.3577	.3599	.3621
1.1	.3643	.3665	.3686	.3708	.3729	.3749	.3770	.3790	.3810	.3830
1.2	.3849	.3869	.3888	.3907	.3925	.3944	.3962	.3980	.3997	.4015
1.3	.4032	.4049	.4066	.4082	.4099	.4115	.4131	.4147	.4162	.4177
1.4	.4192	.4207	.4222	.4236	.4251	.4265	.4279	.4292	.4306	.4319
1.5	.4332	.4345	.4357	.4370	.4382	.4394	.4406	.4418	.4429	.4441
1.6	.4452	.4463	.4474	.4484	.4495	.4505	.4515	.4525	.4535	.4545
1.7	.4554	.4564	.4573	.4582	.4591	.4599	.4608	.4616	.4625	.4633
1.8	.4641	.4649	.4656	.4664	.4671	.4678	.4686	.4693	.4699	.4706
1.9	.4713	.4719	.4726	.4732	.4738	.4744	.4750	.4756	.4761	.4767
2.0	.4772	.4778	.4783	.4788	.4793	.4798	.4803	.4808	.4812	.4817
2.1	.4821	.4826	.4830	.4834	.4838	.4842	.4846	.4850	.4854	.4857
2.2	.4861	.4864	.4868	.4871	.4875	.4878	.4881	.4884	.4887	.4890
2.3	.4893	.4896	.4898	.4901	.4904	.4906	.4909	.4911	.4913	.4916
2.4	.4918	.4920	.4922	.4925	.4927	.4929	.4931	.4932	.4934	.4936
2.5	.4938	.4940	.4941	.4943	.4945	.4946	.4948	.4949	.4951	.4952
2.6	.4953	.4955	.4956	.4957	.4959	.4960	.4961	.4962	.4963	.4964
2.7	.4965	.4966	.4967	.4968	.4969	.4970	.4971	.4972	.4973	.4974
2.8	.4974	.4975	.4976	.4977	.4977	.4978	.4979	.4979	.4980	.4981
2.9	.4981	.4982	.4982	.4983	.4984	.4984	.4985	.4985	.4986	.4986
3.0	.4987	.4987	.4987	.4988	.4988	.4989	.4989	.4989	.4990	.4990

SND(z) = 2.78

Pr (two-tailed)
= 2 x (0.5 -0.4973)
= 2 x 0.0027
= 0.0054

One-tailed vs. two-tailed test

- **So far, we have been testing for a difference that can occur on both sides of the standard normal distribution**

- **In our example, the z-value of 2.78 gave a P-value of 0.0054**

- **For a one-tailed test, a z-score of 2.78 will give a P-value of 0.0027 (=0.0054/2). That is occurred when we are absolutely sure that the mean birth weight of our sample always exceeds that of the general population**

One-tailed vs. two-tailed tests

- **Two-side tests are conventionally used because most of the time, we are not sure of the direction of the difference**
- **One-tailed test are used only when we can anticipate a priori the direction of a difference**
- **One-tailed tests are tempting because they are more likely to give a significant result**
- **Given the same z-score, the P-value is halved for one tailed test**
- **It also mean that they run a greater risk of rejecting the Null Hypothesis when it is in fact correct --- type I error**

Type I and type II errors

- **If the difference is statistically significant, i.e. H0 is incorrect, failure to reject H0 would lead to type II error**

True situation

Conclusion from hypothesis testing

	Difference exists (H_0 is incorrect)	No difference (H_0 is correct)
Difference exists (reject H_0)	Correct action (power or 1-β)	Type I or α error
No difference (Accept H_0)	Type II or β error	Correct action

Statistical significance vs. clinical significance

- **We should not be obsessed with carrying out test of significance. Sometimes a statistically significant result can have little or no clinical significance**

- **Example: Given large sample sizes, a difference in 5 beats per minutes in pulse rate in a clinical trial involving two drugs can give a statistically significant difference when the average difference may hardly bring about a drastic metabolic change between the two groups**

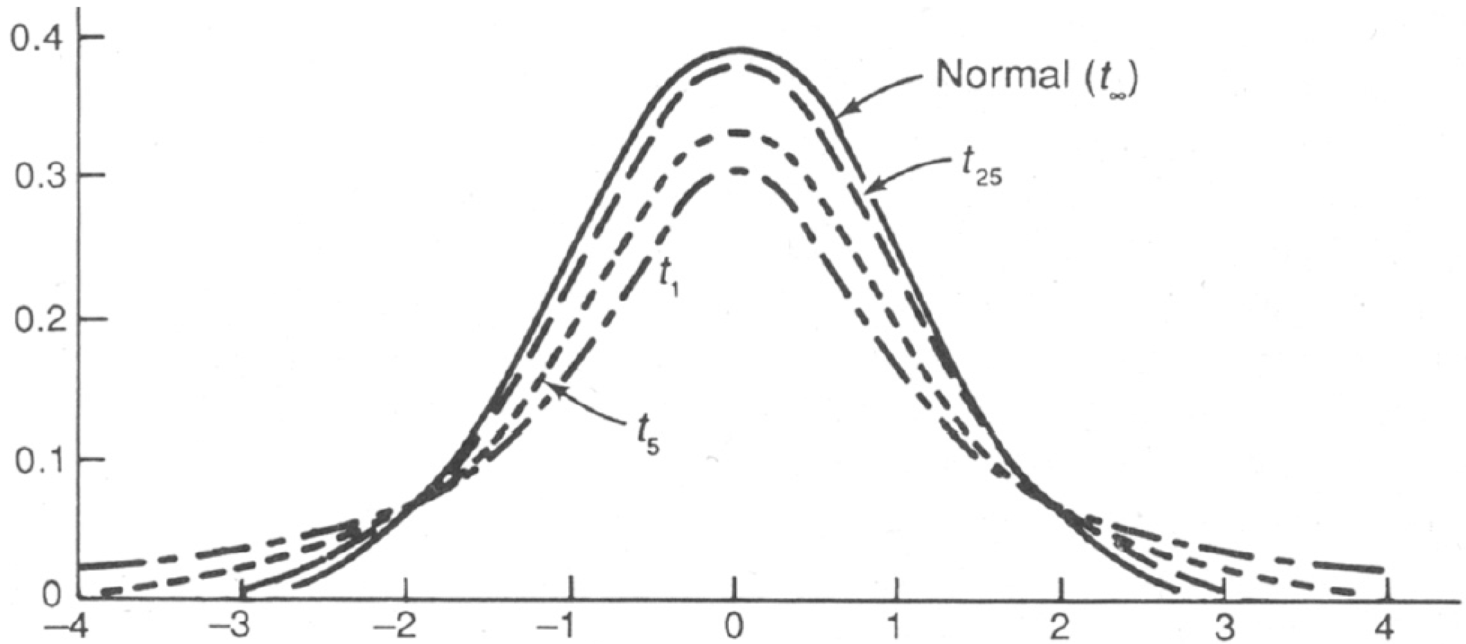
t-test

- **The assumption that the sampling distribution will be normally distributed holds for large samples but not for small samples**
- **Sample size is large, use z-test**
- **t-test is used when sample size is small**
  - Statistical concept of t-distribution
  - Comparing means for 2 independent groups
    - **unpaired t-test**
  - Comparing means for 2 matched groups
    - **paired t-test**

t-distribution

- **Sampling distribution based on small samples will be symmetrical (bell shaped) but not necessarily normal**
- **Spread of these symmetrical distributions is determined by the specific sample size. The smaller the sample size, the wider the spread, and hence the bigger the standard error**
- **These symmetrical distributions are known as student's t-distribution or simply, t-distribution**
- **The t-distribution approaches the normal distribution when sample size tends to infinity**

Family of t-distributions



t-test for 2 independent samples or unpaired t-test

- $\bar{X}_1 - \bar{X}_2$ **= 0.08157-0.03943 = 0.04**
- **Question: What is the probability that the difference of 0.04 units between the two sample means has occurred purely by chance, i.e. due to sampling error alone?**

Blood Pb concentrations

	Battery workers (occupationally exposed)	Control (not occupationally exposed)
	0.082	0.040
	0.080	0.035
	0.079	0.036
	0.069	0.039
	0.085	0.040
	0.09	0.046
	0.086	0.040
mean	**0.08157**	**0.03943**
std dev	**0.0067047**	**0.0035523**

Unpaired t-test

- **We are testing the hypothesis that battery workers could have higher blood Pb levels than the control group of workers as they are occupationally exposed**

Blood Pb concentrations

	Battery workers (occupationally exposed)	Control (not occupationally exposed)
	0.082	0.040
	0.080	0.035
	0.079	0.036
	0.069	0.039
	0.085	0.040
	0.09	0.046
	0.086	0.040
mean	**0.08157**	**0.03943**
std dev	**0.0067047**	**0.0035523**

- **Note: conventionally, a P-value of 0.05 is generally recognized as low enough to reject the Null Hypothesis of "no difference"**

Unpaired t-test

- **Null Hypothesis: No difference in mean blood Pb level between battery workers and control group, i.e.**

  H0: $\mu_{battery} = \mu_{control}$

- **t-score is given by**

$$t = \frac{\overline{X}_1 - \overline{X}_2}{SE_{(\overline{X}_1 - \overline{X}_2)}} = \frac{\overline{X}_1 - \overline{X}_2}{\sqrt{(\frac{1}{n_1} + \frac{1}{n_2})\frac{(n_1 - 1)s_1^{\ 2} + (n_2 - 1)s_2^{\ 2}}{n_1 + n_2 - 2}}}$$

  with (n1+n2–2) degrees of freedom

Unpaired t-test

- For the given exampl

$$t = \frac{0.08157 - 0.03943}{0.002868}$$

= 14.7 with 12 d.f.

- P-value <0.001, reject Null hypothesis

⇒Some evidence, from the data, that battery workers in our study have higher blood Pb level than the control group on average

Blood Pb concentrations

	Battery workers (occupationally exposed)	Control (not occupationally exposed)
	0.082	0.040
	0.080	0.035
	0.079	0.036
	0.069	0.039
	0.085	0.040
	0.09	0.046
	0.086	0.040
mean	**0.08157**	**0.03943**
std dev	**0.0067047**	**0.0035523**

t-table

From our example:
t=14.7 with 12 d.f.

Value far exceeds 4.318, the critical value for statistical significance at the Pr=0.001 (0.1%) level when df=12 i.e. Pr < 0.001

	Probability			
df	.05	.02	.01	.001
1	12.706	31.821	63.657	636.619
2	4.303	6.965	9.925	31.598
3	3.182	4.541	5.841	12.924
4	2.776	3.747	4.604	8.610
5	2.571	3.365	4.032	6.869
6	2.447	3.143	3.707	5.959
7	2.365	2.998	3.499	5.408
8	2.306	2.896	3.355	5.041
9	2.262	2.821	3.250	4.781
10	2.228	2.764	3.169	4.587
11	2.201	2.718	3.106	4.437
12	2.179	2.681	3.055	4.318
13	2.160	2.650	3.012	4.221
14	2.145	2.624	2.977	4.140
15	2.131	2.602	2.947	4.073
16	2.120	2.583	2.921	4.015
17	2.110	2.567	2.898	3.965
18	2.101	2.552	2.878	3.922
19	2.093	2.539	2.861	3.883
. . .	. . .	. . .	. . .	. . .
25	2.060	2.485	2.787	3.725
26	2.056	2.479	2.779	3.707
27	2.052	2.473	2.771	3.690
28	2.048	2.467	2.763	3.674
29	2.045	2.462	2.756	3.659
30	2.042	2.457	2.750	3.646
40	2.021	2.423	2.704	3.551
60	2.000	2.390	2.660	3.460
120	1.980	2.358	2.617	3.373
α	1.960	2.326	2.576	3.291

Unpaired t-test assumptions

- **Data are normally distributed in the population from which the two independent samples have been drawn**
- **The two samples are random and independent, i.e. observations in one group are not related to observations in the other group**
- **The 2 independent samples have been drawn from populations with the same (homogeneous) variance, i.e. $\sigma_1=\sigma_2$**

Paired t-test

- **Previous problem uses un-paired t-test as the two samples were matched**
  - i.e. the two samples were independently derived
- **Sometimes, we may need to deal with matched study designs**

Patient	Fasting cholesterol	Postprandial cholesterol
1	198	202
2	192	188
3	241	238
4	229	226
5	185	174
6	303	315

Study involves 6 subjects acting as their own control (best match)

Paired t-test

- **Null hypothesis: No difference in mean cholesterol levels between fasting and postprandial states**

  H0: $\mu_{fasting} = \mu_{postprandial}$

Patient	Fasting cholesterol	Postprandial cholesterol	Difference (d)
1	198	202	-4
2	192	188	+4
3	241	238	+3
4	229	226	+3
5	185	174	+11
6	303	315	-12

$\bar{d}$ = 0.833
s_d = 7.885
n= 6

Paired t-test

- **t-score given by**

$$t = \frac{\bar{d}}{SE_{\bar{d}}} = \frac{\bar{d}}{s_d / \sqrt{n}}$$

$$= \frac{0.833}{3.219} = 0.259$$

with (n-1) degrees of freedom, where n is the # of pairs

Patient	Difference (d)
1	-4
2	+4
3	+3
4	+3
5	+11
6	-12

$\bar{d}$ = 0.833
s_d = 7.885
n= 6

t-table

From our example:
t=0.259 with 5 d.f.

Value is very much lower than 2.571, the critical value for statistical significance at the Pr=0.05 (5%) level when df=5
i.e. Pr > 0.05

df	Probability .05	.02	.01	.001
1	12.706	31.821	63.657	636.619
2	4.303	6.965	9.925	31.598
3	3.182	4.541	5.841	12.924
4	2.776	3.747	4.604	8.610
5	2.571	3.365	4.032	6.869
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17	2.110	2.567	2.898	3.965
18	2.101	2.552	2.878	3.922
19	2.093	2.539	2.861	3.883
...	...	...	...	...
25	2.060	2.485	2.787	3.725
26	2.056	2.479	2.779	3.707
27	2.052	2.473	2.771	3.690
28	2.048	2.467	2.763	3.674
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120	1.980	2.358	2.617	3.373
α	1.960	2.326	2.576	3.291

Paired t-test

Patient	Fasting cholesterol	Postprandial cholesterol
1	198	202
2	192	188
3	241	238
4	229	226
5	185	174
6	303	315

- **Action: Should not reject the Null Hypothesis**

- **Conclusion: Insufficient evidence, from the data, to suggest that postprandial cholesterol levels are, on average, higher than fasting cholesterol levels**

Common errors relating to t-test

- **Failure to recognize assumptions**
  - If assumption does not hold, explore data transformation or use of non-parametric methods
- **Failure to distinguish between paired and unpaired designs**

Roadmap

- **Basics of biostatistics**
- **Statistical estimation**
- **Hypothesis testing**
  - Measurement data
  - Categorical data
  - Non-parametric methods
- **Ranking and rating**
- **Summary**

Hypothesis testing involving categorical data

- **Chi-square test for statistical association involving 2x2 tables and RxC tables**
  - Testing for associations involving small, unmatched samples
  - Testing for associations involving small, matched samples

Association

- **Examining relationship betw 2 categorical variables**
- **Some examples of association:**
  - Smoking and lung cancer
  - Ethic group and coronary heart disease
- **Questions of interest when testing for association betw two categorical variables**
  - Does the presence/absence of one factor (variable) influence the presence/absence of the other factor (variable)?
- **Caution**
  - presence of an association does not necessarily imply causation

Relating to comparison betw proportions

Treatment	Improvement	No improvement	Total
Arthritic drug	18	6	24
placebo	9	11	20
Total	27	17	44

- **Proportion improved in drug group = 18/24 = 75%**
- **Proportion improved in placebo group = 9/20 = 45.0%**

- **Question: What is the probability that the observed difference of 30% is purely due to sampling error, i.e. chance in sampling?**
- **Use $\chi 2$ –test**

Chi-square test for statistical association

treatment	Improvement	No improvement	Total
Arthritic drug	18 (a)	6 (b)	24
placebo	9 (c)	11 (d)	20
Total	27	17	44

- **Prob of selecting a person in drug group = 24/44**
- **Prob of selecting a person with improvement = 27/44**
- **Prob of selecting a person from drug group who had shown improvement= (24/44)*(27/44) = 0.3347 (assuming two independent events)**
- **Expected value for cell (a) =0.3347*44 = 14.73**

Chi-square test for statistical association

treatment	Improvement	No improvement	Total
Arthritic drug	18 (14.73)	6 (9.27)	24
placebo	9 (12.27)	11 (7.73)	20
Total	27	17	44

- **General formula for $\chi 2$**

$$\chi^2 = \sum \frac{(obs - \exp)^2}{\exp}$$

- **$\chi 2$ –test is always performed on categorical variables using absolute frequencies, never percentage or proportion**

Chi-square test for statistical association

- **For the given problem:**

$$\sum \frac{(obs-\exp)^2}{\exp} = \frac{(18-14.73)^2}{14.73} + \frac{(6-9.27)^2}{9.27} + \frac{(9-12.27)^2}{12.27} + \frac{(11-7.73)^2}{7.73}$$

$$= 4.14 \text{ with 1 degree of freedom}$$

- **χ2 degree of freedom is given by:**
  (no. of rows-1)*(no. of cols-1)
  = (2-1)*(2-1) = 1

18	6	24
9	11	20
27	17	44

How many of these 4 cells are free to vary if we keep the row and column totals constant?

χ^2 table

Critical values in the distributions of chi-squared
for different degrees of freedom

	Probability			
df	.05	.02	.01	.001
1	3.841	5.412	6.635	10.827
2	5.991	7.824	9.210	13.815
3	7.815	9.837	11.345	16.266
4	9.488	11.668	13.277	18.467
5	11.070	13.388	15.086	20.515
6	12.592	15.033	16.812	22.457
7	14.067	16.622	18.475	24.322
8	15.507	18.168	20.090	26.125
9	16.919	19.679	21.666	27.877
10	18.307	21.161	23.209	29.588
11	19.675	22.618	24.725	31.264
12	21.026	24.054	26.217	32.909
13	22.362	25.372	27.688	34.528
14	23.585	26.873	29.141	36.123
15	24.996	28.259	30.578	37.697
16	26.296	29.633	32.000	39.252
17	27.587	30.995	33.409	40.790
18	28.869	32.346	34.805	42.312
19	30.144	33.687	36.191	43.820
20	31.410	35.020	37.566	35.315
21	32.671	36.343	38.932	46.797
22	33.924	37.659	40.289	48.268
23	35.172	38.968	41.638	49.728
24	36.415	40.270	42.980	51.179
25	37.652	41.566	44.314	52.620
26	38.885	42.856	45.642	54.052
27	40.113	44.140	46.963	55.476
28	41.337	45.419	48.278	56.893
29	42.557	46.693	49.588	58.302
30	43.773	47.962	50.892	59.703

observed χ^2 value of 4.14 exceeds critical value of 3.841 for P=0.05 but not critical value of 5.412 for P=0.02 at 1 d.f.

i.e. 0.05 > P > 0.02

Chi-square test for statistical association

- **Probability of getting an observed difference of 30% in improvement rates if the Null hypothesis of no association is correct is betw 2% and 5%**

- **Hence, there is some statistical evidence from this study to suggest that treatment of arthritic patient with the drug can significantly improve grip strength**

Yate's correction for continuity

- In the $\chi 2$ test, we are using a discrete statistic which is approx by a continuous $\chi 2$ distribution. To correct for the use of the discrete statistic, a correction is applied to the original $\chi 2$ value to improve the fit

$$\chi_c^{\ 2} = \sum \frac{(|obs - \exp| - 0.5)^2}{\exp}$$

- Yate's correction for continuity is particularly useful when dealing with small sample size studies
- Yate's correction does not apply to contingency tables larger than 2x2. For non-2x2 tables, low cell frequencies are resolved by pooling (collapsing) adjacent cells

Extending to RxC tables

Type of vaccines	Had flu	Avoided flu	total
I	43	237	280
II	52	198	250
III	25	245	270
IV	48	212	260
V	57	233	290
Total	225	1125	1350

- **Null hypothesis assumes all vaccines tested had equal efficacy**

Computation of the $\chi 2$

Type of vaccines	Had flu	$(O-E)^2/E$	Avoided flu	$(O-E)^2/E$
I	43 (46.7)	0.293	237 (233.3)	0.059
II	52 (41.7)	2.544	198 (208.3)	0.509
III	25 (45.0)	8.889	245 (225.0)	1.778
IV	48 (43.3)	0.510	212 (216.7)	0.102
V	57 (48.3)	1.567	233 (241.7)	0.313
Total	225	13.803	1125	2.761

- **$\chi 2$ =13.803+2.761 = 16.564 with 4 d.f.**

χ^2 table

Critical values in the distributions of chi-squared
for different degrees of freedom

df	Probability .05	.02	.01	.001
1	3.841	5.412	6.635	10.827
2	5.991	7.824	9.210	13.815
3	7.815	9.837	11.345	16.266
4	9.488	11.668	13.277	18.467
5	11.070	13.388	15.086	20.515
6	12.592	15.033	16.812	22.457
7	14.067	16.622	18.475	24.322
8	15.507	18.168	20.090	26.125
9	16.919	19.679	21.666	27.877
10	18.307	21.161	23.209	29.588
11	19.675	22.618	24.725	31.264
12	21.026	24.054	26.217	32.909
13	22.362	25.372	27.688	34.528
14	23.585	26.873	29.141	36.123
15	24.996	28.259	30.578	37.697
16	26.296	29.633	32.000	39.252
17	27.587	30.995	33.409	40.790
18	28.869	32.346	34.805	42.312
19	30.144	33.687	36.191	43.820
20	31.410	35.020	37.566	35.315
21	32.671	36.343	38.932	46.797
22	33.924	37.659	40.289	48.268
23	35.172	38.968	41.638	49.728
24	36.415	40.270	42.980	51.179
25	37.652	41.566	44.314	52.620
26	38.885	42.856	45.642	54.052
27	40.113	44.140	46.963	55.476
28	41.337	45.419	48.278	56.893
29	42.557	46.693	49.588	58.302
30	43.773	47.962	50.892	59.703

observed χ^2 value of 16.564 with 4 d.f. exceeds critical value of 13.277 for P=0.01 but not critical value of 18.467 for P=0.001.

i.e. 0.01 > P > 0.001

Computation of the $\chi 2$

Type of vaccines	Had flu	$(O-E)^2/E$	Avoided flu	$(O-E)^2/E$
I	43 (46.7)	0.293	237 (233.3)	0.059
II	52 (41.7)	2.544	198 (208.3)	0.509
III	**25 (45.0)**	**8.889**	**245 (225.0)**	**1.778**
IV	48 (43.3)	0.510	212 (216.7)	0.102
V	57 (48.3)	1.567	233 (241.7)	0.313
Total	225	13.803	1125	2.761

- **Vaccine III contributes to the overall $\chi 2$= (8.889+1.778)/16.564 = 64.4%**

$\chi 2$ with Vaccine III removed

Type of vaccines	Had flu	Avoided flu	total
I	43	237	280
II	52	198	250
IV	48	212	260
V	57	233	290

- **$\chi 2$ =2.983 with 3 d.f.**
- **$0.1<p<0.5$, not statistically significant**

Vaccine III vs. rest

Type of vaccines	Had flu	Avoided flu	total
III	25	245	270
I, II, IV, V	200	880	1080
Total	225	1125	1350

- **$\chi 2$ =12.7 with 1 d.f.**
- **P<0.001**
- **There appear to be strong statistical evidence that the protective effect of vaccine III is significantly better than the other vaccines**

Handling extremely small samples

- **For extremely small samples, $\chi 2$ -test even with Yate's correction is NOT recommended**
- **Fisher's exact test should be used when there are small expected frequencies**
  - Involves calculating the exact probability of a table as extreme or more extreme than the one observed, given that the null hypothesis is correct
- **When to use fisher's exact test (rule of thumb)**
  - When the overall sample size < 20
  - Overall sample size is between 20 and 40 and the smallest of the four expected value < 5

Calculating Fisher's exact probability

- **Exact probability of observing a particular set of frequencies in a 2x2 table when the row and column totals are fixed is given by the hypergeometric distribution**

$$P(x=k)=\frac{\binom{m}{k}\binom{N-m}{n-k}}{\binom{N}{n}}$$

	Yes	No	Tota l
Yes	k	m-k	**m**
No	n-k	N+k-m-n	**N-m**
total	**n**	**N-n**	**N**

Comparing proportion for matched data

- **100 women in a fertility drug trial were matched in pairs for age, race group and duration of marriage. By random allocation, one woman in each pair was given a fertility drug while the other was given a placebo.**
- **Success is recorded if, within 12 months, a study subject became pregnant and failure otherwise**
- **Point to note about the study**
  - Matched design
  - Compare proportion of successes between fertility drug and placebo

McNemar's test

		placebo	
		success	failure
drug	success	20 (a)	12(b)
	failure	2 (c)	16 (d)

- **McNemar's test (based on discordant pairs)**

$$\chi^2 = \frac{(|b-c|-1)^2}{b+c} = \frac{81}{14} = 5.79$$

- **0.01<p<0.02**
- **Strong statistical evidence that the fertility drug produces a higher success rate than the placebo**

Roadmap

- **Basics of biostatistics**
- **Statistical estimation**
- **Hypothesis testing**
  - Measurement data
  - Categorical data
  - Non-parametric methods
- **Ranking and rating**
- **Summary**

Why non-parametric methods

- **Certain statistical tests like the t-test require assumptions of the distribution of the study variables in the population**
  - t-test requires the underlying assumption of a normal distribution
  - Such tests are known as parametric tests

- **There are situations when it is obvious that the study variable cannot be normally distributed, e.g.,**
  - # of hospital admissions per person per year
  - # of surgical operations per person

Why non-parametric methods

- **The study variable generates data which are scores and so should be treated as a categorical variable with data measured on ordinal scale**
  - E.g., scoring system for degree of skin reaction to a chemical agent:
    - **1: intense skin reaction**
    - **2: less intense reaction**
    - **3: No reaction**
- **For such type of data, the assumption required for parametric tests seem invalid => non-parametric methods should be used**
- **Aka distribution-free tests, because they make no assumption about the underlying distribution of the study variables**

Wilcoxon rank sum test (aka Mann-Whitney U test)

- **Non-parametric equivalent of parametric t-test for 2 independent samples (unpaired t-test)**
- **Suppose the waiting time (in days) for cataract surgery at two eye clinics are as follows:**

Patients at clinic A (n_A=18)	1, 5, 15, 7, 42, 13, 8, 35, 21, 12, 12, 22, 3, 14, 4, 2, 7, 2
Patients at clinic B (n_B=15)	4, 9, 6, 2, 10, 11, 16, 18, 6, 0, 9, 11, 7, 11, 10

Wilcoxon rank sum test

1. Rank all observations (n_A+n_B) in ascending order (least time to longest) along with the group identity each observation belongs
2. Resolve tied ranks by dividing sum of the ranks by the number of entries for a particular set of ties, i.e. average the ranks

time	rank	clinic	time	rank	clinic
0	1	B	8	15	A
1	2	A	9	16.5	B
2	4	A	9	16.5	B
2	4	B	10	18.5	B
2	4	A	10	18.5	B
3	6	A	11	21	B
4	7.5	A	11	21	B
4	7.5	B	11	21	B
5	9	A	12	23.5	A
6	10.5	B	12	23.5	A
6	10.5	B	13	25	A
7	13	A	etc	etc	etc
7	13	A			
7	13	B			

Wilcoxon rank sum test

3. **Sum up ranks separately for the two groups. If the two populations from which the samples have been drawn have similar distributions, we would expect the sum of ranks to be close. If not, we would expect the group with the smaller median to have the smaller sum of ranks**
4. **If the group sizes in both groups are the same, take the group with the smaller sum of ranks**

   If both groups have unique sample sizes, then use the sum of ranks of the smaller group
5. **Test for statistical significance**

Wilcoxon rank sum test

- **In this example**
  - sum of group A ranks = 324.5
  - sum of group B ranks = 236.5
- **T= 236.5 (sum of ranks of the smaller group)**
- **If $n=n_A+n_B$ <=25, then looking up table giving critical values of T for various size of n_A and n_B**
- **If n>25, we assume that T is practically normally distributed with**

$$\mu_T = \frac{n_A(n_A + n_B + 1)}{2}, \text{where } n_A < n_B$$

$$SE_T = \sqrt{\frac{n_B \mu}{6}}$$

Wilcoxon rank sum test

- **For our problem, T=236.5, n_A=18, n_B=15**

$$z = \frac{T - \mu_T}{SE_T} = \frac{236.5 - 255}{27.66} = 0.67$$

- **Result is not statistically significant at 5% (P=0.05) level**

$\Rightarrow$ **No strong evidence to show that the difference in waiting time for the two clinics are statistically significant**

Wilcoxon matched pairs signed ranks test

- **Non-parametric equiv of parametric paired t-test**
- **Suppose the anxiety scores recorded for 10 patients receiving a new drug and a placebo in random order in a cross-over clinical trial are:**

Patients	1	2	3	4	5	6	7	8	9	10
Drug score	19	11	14	17	23	11	15	19	11	8
Placebo score	22	18	17	19	22	12	14	11	19	7

- **Question: Is there any statistical evidence to show that the new drug can significantly lower anxiety scores when compared with the placebo?**

Wilcoxon matched pairs signed ranks test

1. **Take the difference for each pair of readings**

Patients	1	2	3	4	5	6	7	8	9	10
Drug score	19	11	14	17	23	11	15	19	11	8
Placebo score	22	18	17	19	22	12	14	11	19	7
difference	-3	-7	-3	-2	1	-1	1	8	-8	1

Wilcoxon matched pairs signed ranks test

2. **Rank the differences from the smallest to the largest, ignoring signs and omitting 0 differences**

Patients	1	2	3	4	5	6	7	8	9	10
Drug score	19	11	14	17	23	11	15	19	11	8
Placebo score	22	18	17	19	22	12	14	11	19	7
difference	-3	-7	-3	-2	1	-1	1	8	-8	1
rank	6.5	8	6.5	5	2.5	2.5	2.5	9.5	9.5	2.5

Wilcoxon matched pairs signed ranks test

3. Put back the signs to the ranks

Patients	1	2	3	4	5	6	7	8	9	10
Drug score	19	11	14	17	23	11	15	19	11	8
Placebo score	22	18	17	19	22	12	14	11	19	7
difference	-3	-7	-3	-2	1	-1	1	8	-8	1
Rank -	6.5	8	6.5	5		2.5			9.5	
Rank +					2.5		2.5	9.5		2.5

Wilcoxon matched pairs signed ranks test

4. Add up ranks of positive differences and ranks of negative differences. Call the sum of the smaller group T

Patients	1	2	3	4	5	6	7	8	9	10
Drug score	19	11	14	17	23	11	15	19	11	8
Placebo score	22	18	17	19	22	12	14	11	19	7
difference	-3	-7	-3	-2	1	-1	1	8	-8	1
Rank -	6.5	8	6.5	5		2.5			9.5	
Rank +					2.5		2.5	9.5		2.5

- **Sum of + ranks: 17 (n+ =4)**
- **Sum of – ranks: 38 (n– = 6)**
- **T (sum of ranks of smaller group) = 17**

Wilcoxon matched pairs signed ranks test

5. Test for statistical significance

- If n≤25, then look up table giving critical values of T for various size of n
- If n>25, we can assume that T is practically normally distributed with

$$\mu_T = \frac{n(n+1)}{4}$$

$$SE_T = \sqrt{\frac{n(n+1)(2n+1)}{24}} = \sqrt{\frac{\mu_T(2n+1)}{6}}$$

- **For our problem, T=17 and n=10, hence we look up table** critical value for P=0.05 at N=10 is 8 (for 2-tailed test)

Note that critical values go progressively smaller as P gets smaller

Table B **Table of Critical Values of T in the Wilcoxon's Matched-Pairs Signed-Ranks Test**

	Level of significance for one-tailed test		
	0.025	0.01	0.005
N	Level of significance for two-tailed test		
	0.05	0.02	0.01
6	0	-	-
7	2	0	-
8	4	2	0
9	6	3	2
10	8	5	3
11	11	7	5
12	14	10	7
13	17	13	10
14	21	16	13
15	25	20	16
16	30	24	20
17	35	28	23
18	40	33	28
19	46	38	32
20	52	43	38
21	59	49	43
22	66	56	49
23	73	62	55
24	81	69	61
25	89	77	68

Wilcoxon matched pairs signed ranks test

- **For our problem, we found that T value of 17 is higher than the critical value for statistical significance at the 5% level**

$\Rightarrow$ **There is insufficient evidence to show that the new drug can significantly lower anxiety scores than the placebo. Therefore, we cannot rule out the possibility that the observed differences among scores are due to sampling error.**

Non-parametric vs. parametric methods

- **Advantages:**
  - Do not requires the assumption needed for parametric tests. Therefore useful for data which are markedly skewed
  - Good for data generated from small samples. For such small samples, parametric tests are not recommended unless the nature of population distribution is known
  - Good for observations which are scores, i.e. measured on ordinal scale
  - Quick and easy to apply and yet compare quite well with parametric methods

Non-parametric vs. parametric methods

- **Disadvantages**
  - Not suitable for estimation purposes as confidence intervals are difficult to construct
  - No equivalent methods for more complicated parametric methods like testing for interactions in ANOVA models
  - Not quite as statistically efficient as parametric methods if the assumptions needed for the parametric methods have been met

Roadmap

- **Basics of biostatistics**
- **Statistical estimation**
- **Hypothesis testing**
  - Measurement data
  - Categorical data
  - Non-parametric methods
- **Ranking and rating**
- **Summary**

Ranking and rating

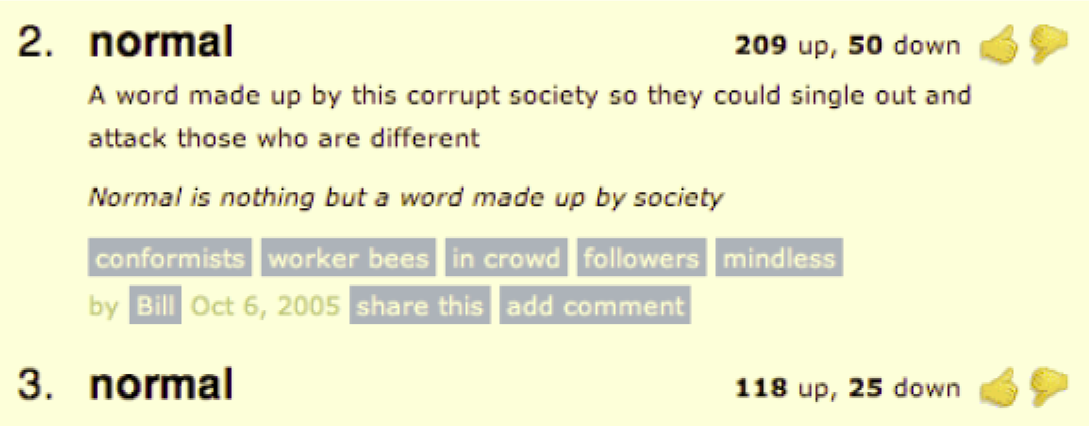
- **PROBLEM: You are a web programmer. You have users. Your users rate stuff on your site. You want to put the highest-rated stuff at the top and lowest-rated at the bottom. You need some sort of "score" to sort by**

PROBLEM: You are a web programmer. You have users. Your users rate stuff on your site. You want to put the highest-rated stuff at the top and lowest-rated at the bottom. You need some sort of "score" to sort by.

WRONG SOLUTION #1: Score = (Positive ratings) - (Negative ratings)

Why it is wrong: Suppose one item has 600 positive ratings and 400 negative ratings: 60% positive. Suppose item two has 5,500 positive ratings and 4,500 negative ratings: 55% positive. This algorithm puts item two (score = 1000, but only 55% positive) above item one (score = 200, and 60% positive). WRONG.

Sites that make this mistake: Urban Dictionary



PROBLEM: You are a web programmer. You have users. Your users rate stuff on your site. You want to put the highest-rated stuff at the top and lowest-rated at the bottom. You need some sort of "score" to sort by.

WRONG SOLUTION #2: Score = Average rating = (Positive ratings) / (Total ratings)

Why it is wrong: Average rating works fine if you always have a ton of ratings, but suppose item 1 has 2 positive ratings and 0 negative ratings. Suppose item 2 has 100 positive ratings and 1 negative rating. This algorithm puts item two (tons of positive ratings) below item one (very few positive ratings). WRONG.

Sites that make this mistake: Amazon.com

PROBLEM: You are a web programmer. You have users. Your users rate stuff on your site. You want to put the highest-rated stuff at the top and lowest-rated at the bottom. You need some sort of "score" to sort by.

- **A possible solution is the lower bound of the normal approximation interval**

$$\hat{p} \pm z_{1-\alpha/2}\sqrt{\frac{\hat{p}\left(1-\hat{p}\right)}{n}}$$

where $\hat{p}$ is the proportion of successes in a Bernoulli trial process estimated from the statistical sample, $z_{1-\alpha/2}$ is the $1-\alpha/2$ percentile of a standard normal distribution, α is the error percentile and n is the sample size. For example, for a 95% confidence level the error (α) is 5%, so $1-\alpha/2 = 0.975$ and $z_{1-\alpha/2} = 1.96$.

- **An improvement is the lower bound of the Wilson interval**

$$\frac{\hat{p} + \frac{1}{2n}z^2_{1-\alpha/2} \pm z_{1-\alpha/2}\sqrt{\frac{\hat{p}(1-\hat{p})}{n} + \frac{z^2_{1-\alpha/2}}{4n^2}}}{1 + \frac{1}{n}z^2_{1-\alpha/2}}$$

Summary

- **Statistical estimation**
  - Confidence interval
- **Ranking & rating**
  - Binomial proportion confidence intervals
    - **Normal approx interval**
    - **Wilson interval**
- **Hypothesis testing**
  - Large sample size: z-test
  - Measurement data
    - **Small sample size & normal distribution: unpaired t-test & paired t-test**
  - Categorical data
    - **Small sample size: χ2-test**
    - **Extremely small sample size: Fisher's exact test**
  - Non-parametric methods
    - **Wilcoxon rank sum test**
    - **Wilcoxon matched pairs signed ranks test**

Summary

- **Many software available to do hypothesis testing**
  - MATLAB, R, SPSS …
- **More important for us to know**
  - When to use which test
  - Interpret the results and draw proper conclusions

Topics not covered

- **Summarizing data with graphs**
  - Bar charts, pie charts, histograms, boxplots, scatter plots, …
- **Hypothesis testing involving >2 samples**
  - ANOVA
- **Association on 3-way contingency tables**
  - Cochran-Mantel-Haenszel (CMH) test
- **Liner correlation and regression**
- **Survival analysis**
- **Sample size estimation**
- **……**

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