Analysis of DUR

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This session was developed
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This session

- Measures of frequency
  - Prevalence
  - Incidence
- Measures of effect
  - Risk and rates
  - Risk and rate differences/ Risk and Rate ratios
  - Odds and odds ratios
- Inferential Statistics
  - 95% Confidence intervals
  - Continuous variables
    - T Test
    - ANOVA
  - Categorical variables
    - Chi-squared

Calculating statistics

- Free statistical packages:
  - r/ r studio
  - SAS Academic version (for students/academics)
  - Analysis toolpak for Excel (addin free if you have excel)
- Commercial packages
  - STATA
  - SPSS
  - XLSTAT. (excel based)
  - Minitab
  - Plus many more
- Simple statistics can be calculated by hand

Measures of frequency

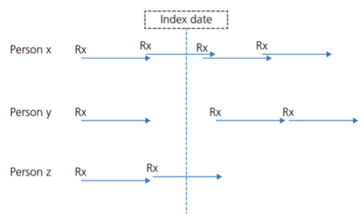
- Prevalence
- Incidence

Prevalence

- Proportion of people in a given population who have a particular disease at a point or interval of time

$$\text{Prevalence} = \frac{\text{Number of people with a disease}}{\text{Number of people in the population at risk}}$$

- Ranges from 0 to 1 (as a % from 0 to 100)



Person x and Person y are prevalent at the index date

From Drug Utilization Research Methods and applications, 2016

- Period prevalence
  - Measured over a period of time
    - Prevalence of antibiotic use over a 1 year period in a sample of women aged 30-39 was found to be 70.6%.
- Point prevalence
  - Measured at a single point in time
    - In a survey, 3% of parents reported their children under 10 years had used a short acting beta agonist in the past 24 hours.

Prevalence

- Factors affecting prevalence
  - Disease severity
    - ↑ deaths - ↓ prevalence
  - Duration of use
    - shorter duration - ↓ prevalence
  - Number of new cases
    - many cases - ↑ prevalence
- measures of prevalence useful for assessing the need for health care and the planning of health services.

Interpreting prevalence

Example:

In the Danish national prescription database, the 1-year prevalence of PPI use was 9.1% in 2012.

This implies that of 1000 people alive and resident in Denmark in January 2012, 91 would redeem a prescription during 2012

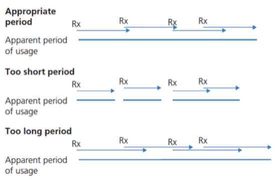
(Drug Utilization: Methods and Applications, 2016)

Interpreting prevalence

- Drug and usage dependent:
- a high period prevalence might represent a:
  - high rate of new users (e.g. for antibiotics),
  - high number of persistent users (e.g. for insulin)
  - high number of new and existing users (e.g. for nonsteroidal antiinflammatory drugs, NSAIDs).

Prevalence in DUR

- Need to be aware of what you are measuring
  - Medication dispensings or users
    - one user may have many dispensings
- Need to select an appropriate usage period



From Drug Utilization Research Methods and applications, 2016

Incidence in DUR

- Number of *NEW* users in a given time period
- Determines how often a medication is commenced

Incidence= Number of new users / Number of people in population at risk

e.g. 22 new opioid users in village A / 100 inhabitants in village A

=0.22

Incidence of opioid use in village A is 22%

This doesn't tell us how many total users there are

Incidence

- cumulative incidence
  - risk of individuals in the population commencing a medication during a specified period

$$CI = \frac{\text{Number of NEW users during a specified period}}{\text{All people in the population not using the medication at the beginning of the period}}$$

Incidence in DUR

- Need to consider a run-in period
  - New user if different to a previous user
- Run in period varies with the medication and the health care setting
  - Is the medication used intermittently or regularly?
  - How often are medications prescribed or supplied?

Prevalence and incidence in DUR

- prevalence measures the total drug use
- incidence measures new users

Prevalence = Incidence × Duration of use

- Study design to measure:
  - prevalence
    - prevalence or cross-sectional study
  - incidence
    - cohort study

Prevalence and incidence in DUR

- Choice of measure will relate to research question and the purpose of the study
  - Eg to determine how much medication should be kept on hand at a clinic
    - prevalent use
  - To determine if use is increasing over time
    - Incident use

Measures of association in DUR

- Often interested in association between two variables

Is use of a medication more common among women compared to me

Does dose of medication Y increase with age

Measures of association in DUR

- Measure used depends on type of data and study design
- Categorical data
  - Cohort or cross sectional study
    - Risk and rate ratios
  - Case control, cross sectional study
    - Odds ratios
- Continuous data
  - Correlation
  - Regression

Measures of association Categorical data

- Interested in the relationship between an exposure and an outcome

Example: Is use of medication X more common among women compared to men

Exposure:?
Outcome:?

Measures of association Categorical data

- Interested in the relationship between an exposure and an outcome

Example: Is use of medication X more common among women compared to men

Exposure: Female gender
Outcome: Use of medication X

Measures of association

		Outcome		
		Yes	No	Row total
Exposure	Yes	a	b	?
	No	c	d	?
	Column total	?	?	?

Measures of association

		Outcome		
		Yes	No	
Exposure	Yes	a	b	
	No	c	d	

Measures of association

		Outcome		
		Yes	No	Row total
Exposure	Yes	a	b	a + b
	No	c	d	c + d
	Column total	a + c	b + d	a+b+c+d

Measures of association

Is use of medication X more common among women compared to men?

		Use of Medication X		
		Yes	No	Row total
Gender	Female	a	b	a + b
	Male	c	d	c + d
	Column total	a + c	b + d	a+b+c+d

Risk = Number of users
Total population who could be users

Measure of how likely an outcome is for the exposure group

		Use of Medication X		
		Yes	No	Row total
Gender	Female	40	50	90
	Male	60	50	110
	Column total	100	100	200

Risk = Number of users
Total population who could be users

Calculate the risk in this sample of using medication X for:

Females

Males

		Use of Medication X		
		Yes	No	Row total
Gender	Female	40	50	90
	Male	60	50	110
	Column total	100	100	200

Females:
Risk=40/(40+60)
=0.4 (or 40%)

Males:
Risk=60/(40+60)
=0.6 (or 60%)

		Use of Medication X		
		Yes	No	Row total
Gender	Female	40	50	90
	Male	60	50	110
	Column total	100	100	200

Comparing risk

- The chance of winning the lottery ticket is 1 in 20 million with a single ticket
- Which is correct?
  - "If I buy two lottery tickets I will double my chances of winning, increasing my chances by 100%."
  - "If I buy two lottery tickets, my chance of winning is 2 in 20 million, so an absolute increase in my chances of winning is 0.0001%"

Comparing risk

- The chance of winning the lottery ticket is 1 in 20 million with a single ticket
  - "If I buy two lottery tickets I will double my chances of winning, increasing my chances by 100%."
  - "If I buy two lottery tickets, my chance of winning is 2 in 20 million, so an absolute increase in my chances of winning is 0.0001%"
- Both are correct
- Different risk measures present the same information in different ways

Risk difference and Risk ratio

Risk difference: risk for females-risk for males

Risk ratio: risk for females/risk for males

		Use of Medication X		
		Yes	No	Row total
Gender	Female	40	50	90
	Male	60	50	110
	Column total	100	100	200

Females:

Risk=40/(40+60)

=0.4 (or 40%)

Males:

Risk=60/(40+60)

=0.6 (or 60%)

Risk difference: risk for females-risk for males

=0.4-0.6

=0.2

		Use of Medication X		
		Yes	No	Row total
Gender	Female	40	50	90
	Male	60	50	110
	Column total	100	100	200

Risk difference

Risk difference: risk for females-risk for males

=0.4-0.6

=0.2

- There were 20 less users per 100 population for females than males

Risk difference

- Sometimes called risk reduction
- Risk difference measure quantifies the difference in **incidence** between an exposed and an unexposed population.
- We use a difference measure to estimate the risk that is attributable to exposure in the exposed group.

Risk difference

- Compares between two different therapies or strategies
  - Comparison of pharmacist-led medication review versus no medication review

% medication related problems identified at dispensing	
Medication review	No medication review
8.2	1.5

- Absolute risk reduction= 8.2 - 1.5

  = 6.7%

Absolute risk reduction

- Absolute effect of exposure
- Does not generalise across populations
  - Varies by age, sex and other factors

Risk ratio

Females:

Risk=40/(40+60)

=0.4 (or 40%)

Males:

Risk=60/(40+60)

=0.6 (or 60%)

Risk ratio: risk for females/risk for males

=0.4/0.6

=2/3

=0.67 (ie 67%)

		Use of Medication X		
		Yes	No	Row total
Gender	Female	40	50	90
	Male	60	50	110
	Column total	100	100	200

Risk ratio

A ratio measure estimates the strength of association between a suspected risk factor and an outcome.

In our previous example
Risk ratio: risk for females/risk for males
=0.67 (ie 67%)

That is females have a 33% lower risk of using medication X compared to males

Interpreting Risk ratios

- association:
  - RR of 1 indicates no association
  - RR >1 indicates a positive association
  - RR <1 indicates a negative association
- Note: the prevalence ratio is the ratio of prevalence in A compared to prevalence in B but not used often

Relative risk reduction

- Relative risk reduction (RRR)
- Reduction in event rates expressed in a proportional manner in relation to the control event rate
- Relative risk reduction = 1-relative risk
  - Medication X RR =0.67 (females compared to males)

RRR=1-RR
=1-0.67
=0.33

Being female reduces the risk of using medication X by 33%"

- Lower the event rate in the control group the larger the difference between relative risk reduction and absolute risk reduction.

Rate measures

- Used when there is movement into or out of a cohort
  - ie cohort members contribute different lengths of time to the study
- Used in the same way as risk measures

Rate measures

Example of a Rate Ratio
To identify the population most likely to benefit from an intervention to reduce antibiotic use, a study was conducted to see if antibiotic use in children was associated with gender.

The incidence rate of children using antibiotics who were female who did was measured over one year and compared with the incidence rate in male children in the same community who were using antibiotics.

Since the children could have antibiotics more than one time in the study period, the researchers used the incidence rate of antibiotics, as this takes into account the number of times a child used an antibiotic.
The measured incidence rates of antibiotic use (per 100 person-years) were:
For male children= 3
For female children= 0.6
Therefore:
Rate Ratio = 5

So in this study, the incidence rate of antibiotic use was five times higher in male children compared to female children.

Odds

- ratio of the number of people with the outcome to the number of people without it in a particular population.

Odds

- Cross sectional study looking at association between salbutamol use and hayfever in 11 year old children

		Hayfever		
		Yes	No	Total
Salbutamol user	Yes	141	420	561
	No	928	13 525	14 453
	Total	1069	13 945	15 522

Odds of using salbutamol for those with hayfever

=a/c

=141/928

=0.15

Odds of using salbutamol for those without hayfever

=b/d

=420/13945

=0.03

Odds in DUR

- Difficult to interpret
- What does an odds of 0.15 mean?

Odds Ratio

a measure of association used for case-control studies

way of comparing whether the probability of a certain event is the same for two groups

estimates the relative risk

Odds Ratio (OR) $= \dfrac{a / c}{b / d}$

$= \dfrac{a \times d}{b \times c}$

Odds ratios in DUR

Interpretation

- *For rare events the odds ratio approximates the relative risk*
- *OR=1 no association*
- *OR<> 1 event is more likely in one of the two groups*

Odds Ratio

- Cross sectional study looking at association between salbutamol use and hayfever in 11 year old children

		Hayfever		
		Yes	No	Total
Salbutamol user	Yes	141	420	561
	No	928	13 525	14 453
	Total	1069	13 945	15 522

- Odds ratio= (a x d)/(b x c)

  = (141 x 13 525)/(928 x 420)

  = 4.89

Odds ratio interpretation

- In our study into salbutamol use and hayfever OR=5
- In this study, the children who used salbutamol had nearly five times the odds of having hayfever as the children who do not use salbutamol

Odds ratios interpretation

- In case control studies the OR is the odds of having the exposure among those with the outcome
- If our salbutamol/ hayfever example was a case control study
  - We would interpret this as the odds of using salbutamol is 5 times higher among children with hayfever than those without.

Interpreting risk

- How do you interpret this?

•If the chance of a disease occurring is 1% (ie 1 on 100) and treatment reduces this to 0.5%
  •Absolute risk reduction is 0.5%
  •Relative risk reduction is 50%
•Need baseline information to interpret risk

Descriptive statistics

- **Descriptive Statistics**
- Describe a set of data.
- Common descriptive statistics:
  - Categorical data: proportions
  - Continuous data: mean, standard deviation, median, interquartile range, range

Inferential statistics

- Uses methods of probability theory to draw conclusions about a population using data from a sample.
- Methods of estimation and hypothesis testing are the basis of inferential statistics.
- Choice of test depends on study design.

Choosing a statistical test

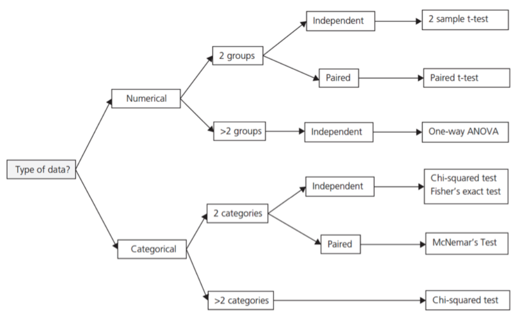


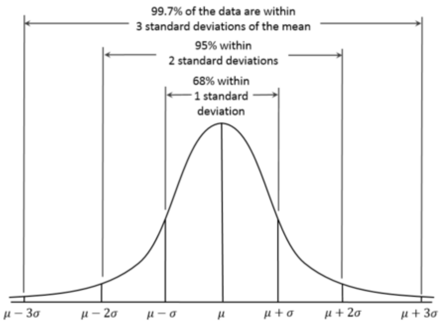
Figure 9.2 Flowchart for determining which standard statistical test is appropriate.

Source Drug Utilization Research: Methods and Applications

Confidence intervals

- With a good study design the sample subjects will be representative of a wider population.
- Based on this we can apply our conclusions from the study sample to the population.
- Any single measure has a degree of uncertainty around it in terms of representing the TRUE population value.
- The confidence interval estimates the imprecision around the sample estimate

Confidence intervals



Confidence intervals

- 95% confidence interval
  - Normal distribution 95% of data lies within 2 standard deviations of the mean
- **For a given 95% confidence interval around an estimate (mean, mean difference, proportion, difference in proportions, risk ratio, odds ratio) we are 95% confident that the TRUE population value lies within the interval.**

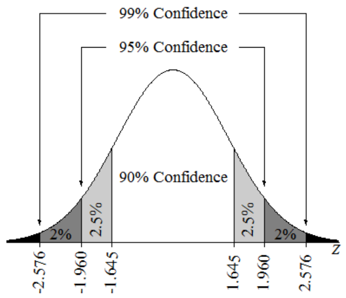
Confidence Interval

- Confidence intervals can be calculated with most statistical software
  - But you usually have to ask for them.
- For non-ratio estimates

95% CI=estimate ± 1.95 x Standard error (estimate)

- For risk, rate and ratio measures
  - A little more complex but still do-able by hand
  - See http://sphweb.bumc.bu.edu/otlt/MPH-Modules/QuantCore/PH717_ComparingFrequencies/PH717_ComparingFrequencies-TOC.html

- If we calculate a 99% Confidence interval will it be wider or narrower than the 95% CI?



Continuous outcomes

- T-test or Z-test
  - Z test easier without statistical software
- Paired t-test
- ANOVA
- Assumptions:
  - Outcome variable is normally distributed.
- How can we assess the distribution of the outcome variable?

t-test

- To determine if a difference in a continuous outcome could be due to chance.
- Example
  - Mean number of drugs in 100 women=8.5 drugs
  - Mean number of drugs in 130 men=7.2 drugs
- Does the number of drugs differ between men and women?

t-test

- What are your:
- Null Hypothesis:
- Alternate Hypothesis:

t-test

- Null Hypothesis: there is no difference in the mean number of drugs between men and women.
  - $\text{mean}^{\text{women}}=\text{mean}^{\text{men}}$
- Alternate Hypothesis: there is a difference in the mean number of drugs between men and women.
  - $\text{mean}^{\text{women}}\neq\text{mean}^{\text{men}}$

t-Test

$$t = \frac{M_x - M_y}{\sqrt{\frac{S_x^2}{n_x} + \frac{S_y^2}{n_y}}}$$

M = mean
n = number of scores per group

$$S^2 = \frac{\sum (x - M)^2}{n - 1}$$

x = individual scores
M = mean
n= number of scores in group

t-test

- Example: You want to know if women from clinic A are using more medicines than women from clinic B. You ask the next 8 women who visit each clinic how many medicines they are taking.

Clinic A	Clinic B
5	8
7	1
5	4
3	6
5	6
3	4
3	1
1	2

t-test

- Example: You want to know if women from clinic A are using more medicines than women from clinic B. You ask the next 8 women who visit each clinic how many medicines they are taking.

What is the null hypothesis:

What is the alternate hypothesis:

t-test

- Example: You want to know if women from clinic A are using more medicines than women from clinic B. You ask the next 8 women who visit each clinic how many medicines they are taking.

Null hypothesis: mean clinic A=mean clinic B

Alternate hypothesis: mean clinic A<>mean clinic B

t-test

- What is the mean number of medications used in each clinic?

Clinic A	Clinic B
5	8
7	1
5	4
3	6
5	6
3	4
3	1
9	2
M_1=	M_1=

t-test

- What is the mean number of medications used in each clinic?

Clinic A	Clinic B
5	8
7	1
5	4
3	6
5	6
3	4
3	1
9	2
M_1=5	M_2=4

t-test

$$t = \frac{M_x - M_y}{\sqrt{\frac{S_x^2}{n_x} + \frac{S_y^2}{n_y}}}$$ M = mean, n = number of scores per group

$$S^2 = \frac{\sum (x-M)^2}{n-1}$$ x = individual scores, M = mean, n= number of scores in group

Clinic A (n=8)	X_1-M_1	$(X_1-M_1)^2$	S^2	Clinic B (n=8)	X_2-M_2	$(X_2-M_2)^2$	S^2
5				8			
7				1			
5				4			
3				6			
5				6			
3				4			
3				1			
9				2			
M_1=5				M_2=4			

t-test

$$t = \frac{M_x - M_y}{\sqrt{\frac{S_x^2}{n_x} + \frac{S_y^2}{n_y}}}$$ M = mean, n = number of scores per group

$$S^2 = \frac{\sum (x-M)^2}{n-1}$$ x = individual scores, M = mean, n= number of scores in group

Clinic A (n=8)	X_1-M_1	$(X_1-M_1)^2$	S^2	Clinic B (n=8)	X_2-M_2	$(X_2-M_2)^2$	S^2
5	0	0	0	8	4	16	2.714
7	2	4	0.5714	1	-3	9	1.286
5	0	0	0	4	0	0	0
3	-2	4	0.5714	6	2	4	0.5714
5	0	0	0	6	2	4	0.5714
3	-2	4	0.5714	4	0	0	0
3	-2	4	0.5714	1	-3	9	1.286
9	4	16	2.2857	2	-2	4	0.5714
M_1=5			Sum S^2= 4.5714	M_2=4			Sum S^2= 6.571

t-test

$$t = \frac{M_x - M_y}{\sqrt{\frac{S_x^2}{n_x} + \frac{S_y^2}{n_y}}}$$ M = mean, n = number of scores per group

In our example:

M_1= 5
M_2= 4
$S^2_{(1)}$= 4.571
$S^2_{(2)}$= 6.571
N_1=8
n_2=8

$$= \frac{5-4}{\sqrt{\frac{4.571}{8} + \frac{6.571}{8}}}$$

$$= \frac{1}{\sqrt{.571 + .821}}$$

$$= \frac{1}{1.18}$$

t = .847

Interpreting the t-statistic

- Use statistical tables to determine the probability of achieving an estimate as large as that obtained by chance

- In our example

t=0.847

df = $n_1 + n_2 - 2$

=

Interpreting the t-statistic

- Use statistical tables to determine the probability of achieving an estimate as large as that obtained by chance

- In our example

t=0.847

df = $n_1 + n_2 - 2$

=14

Degrees of freedom=n1 +n2-2

Table A2 Percentage points of the *t* distribution

	One-sided *P* value								
	0.25	0.1	0.05	0.025	0.01	0.005	0.0025	0.001	0.0005
	Two-sided *P* value								
d.f.	0.5	0.2	0.1	0.05	0.02	0.01	0.005	0.002	0.001
1	1.00	3.08	6.31	12.71	31.82	63.66	127.32	318.31	636.62
2	0.82	1.89	2.92	4.30	6.96	9.92	14.09	22.33	31.60
3	0.76	1.64	2.35	3.18	4.54	5.84	7.45	10.21	12.92
4	0.74	1.53	2.13	2.78	3.75	4.60	5.60	7.17	8.61
5	0.73	1.48	2.02	2.57	3.36	4.03	4.77	5.89	6.87
6	0.72	1.44	1.94	2.45	3.14	3.71	4.32	5.21	5.96
7	0.71	1.42	1.90	2.36	3.00	3.50	4.03	4.78	5.41
8	0.71	1.40	1.86	2.31	2.90	3.36	3.83	4.50	5.04
9	0.70	1.38	1.83	2.26	2.82	3.25	3.69	4.30	4.78
10	0.70	1.37	1.81	2.23	2.76	3.17	3.58	4.14	4.59
11	0.70	1.36	1.80	2.20	2.72	3.11	3.50	4.02	4.44
12	0.70	1.36	1.78	2.18	2.68	3.06	3.43	3.93	4.32
13	0.69	1.35	1.77	2.16	2.65	3.01	3.37	3.85	4.22
14	0.69	1.34	1.76	2.14	2.62	2.98	3.33	3.79	4.14
15	0.69	1.34	1.75	2.13	2.60	2.95	3.29	3.73	4.07
16	0.69	1.34	1.75	2.12	2.58	2.92	3.25	3.69	4.02

Interpreting p values

- The p value gives the probability of obtaining an estimate as large as the one obtained in your sample by chance.

- *If p is low then the probability that you rejected the null hypothesis and found a difference is unlikely to be due to chance*
  - *We conclude that there is very strong evidence to suggest that the difference in mean number of medications between men and women*

In our example p is between 0.2 and 0.5

What in your interpretation of this?

In our example p is between 0.2 and 0.5

A p value of 0.5>p>0.2 indicates that we should not reject the null hypothesis that there is no difference between the number of medicines used by women in clinic A compared to women in clinic B.

P values and significance

- p is an estimate of the chance of finding the observed outcome and rejecting the null hypothesis when TRUE difference exists
  - This called type 1 error or alpha
  - Traditionally set at 0.05

Paired t-test

- Which of the following questions uses paired data?
  - Is anticholinergic burden measured by the anticholingeric burden scale higher than that measure by the drug burden index among nursing home residents?
  - Is the number of medications in men higher than in women?
  - Are people living in Windhoek more likely to use opioids than people living in Sydney?

Paired t-test

- Which of the following questions uses paired data?
  - Is anticholinergic burden measured by the anticholingeric burden scale higher than that measure by the drug burden index among nursing home residents?
    - As for this question we are using two measurements from the one person. One for the anticholinergic burden scale and one for the drug burden index

ANOVA

- Comparison of means among more than 2 groups (can use it for 2 groups but t or z test easier)
- ANOVA compares between-group variation and within-group variation. i.e the amount of variation in the data due to differences between the group means with the amount of variation in the data due to random differences between observations within groups.

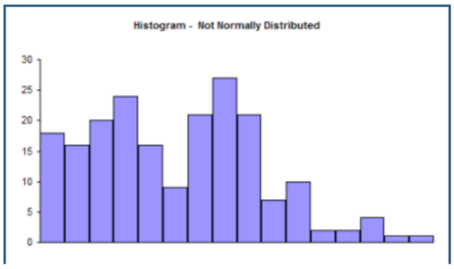
ANOVA

- ANOVA assumptions
- The outcome variable is normally distributed.
- The true (population) standard deviations are assumed to be approximately equal between the groups being compared.

ANOVA

- The statistic calculated is the F statistic and the tables used to determine the p value are for the F distribution

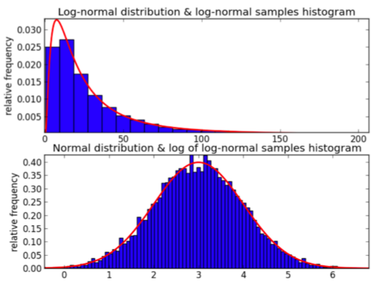
What is your data is not normally distributed?



- Cannot meet the assumption of normality
- Cannot used t-test or ANOVA

- Two options
  - Transform your data
  - Use a non-parametric test

Log transformation



Log transformation changes the distribution to a normal distribution

All testing then happens on the transformed data and presented for the transformed data.

Other transformations can also be used.

Non parametric testing of continuous outcomes

- Wilcoxon rank sum test
  - Also known as Mann-Whitney U-test
- Rank all observations in ascending order

Mean number of medicines in nursing home residents versus older community dwelling individuals (by health clinic)

Health clinics (n=7)	Nursing homes (n=9)
8.50	8.27
9.48	8.20
8.65	8.25
8.16	8.14
8.83	9.00
7.76	8.10
8.63	7.20
	8.32
	7.70

Health clinics	Nursing homes	Rank
7.20		1
7.70		2
	7.76	3
8.10		4
8.14		5
	8.16	6
8.20		7
8.25		8
8.27		9
8.32		10
	8.50	11
	8.63	12
	8.65	13
	9.83	14
9.00		15
	9.48	16

N=number of nonzero matches under null hypothesis
N=16

Ho:mean health clinics =mean nursing home

HA: mean health clinics<> mean nursing homes

- Chose the one group and sum the ranks

T=1+2+4+5+7+8+9+10 +15

T=61

N=16

Using the relevant tables

Health clinics	Rank
7.20	1
7.70	2
8.10	4
8.14	5
8.20	7
8.25	8
8.27	9
8.32	10
9.00	15

Table A4 Critical values for the Wilcoxon matched pairs signed rank test

N = number of non-zero differences; *T* = smaller of T_+ and T_-; Significant if *T* < critical value.

	One-sided *P*-value					One-sided *P*-value			
	0.05	0.025	0.01	0.005		0.05	0.025	0.01	0.005
	Two-sided *P*-value					Two-sided *P*-value			
N	0.1	0.05	0.02	0.01	*N*	0.1	0.05	0.02	0.01
5	1				30	152	137	120	109
6	2	1			31	163	148	130	118
7	4	2	0		32	175	159	141	128
8	6	4	2	0	33	188	171	151	138
9	8	6	3	2	34	201	183	162	149
10	11	8	5	3	35	214	195	174	160
11	14	11	7	5	36	228	208	186	171
12	17	14	10	7	37	242	222	198	183
13	21	17	13	10	38	256	235	211	195
14	26	21	16	13	39	271	250	224	208
15	30	25	20	16	40	287	264	238	221
16	36	30	24	19	41	303	279	252	234

N=16

T=61

Table A4 Critical values for the Wilcoxon matched pairs signed rank test

N = number of non-zero differences; *T* = smaller of T_+ and T_-; Significant if *T* < critical value.

	One-sided *P*-value					One-sided *P*-value			
	0.05	0.025	0.01	0.005		0.05	0.025	0.01	0.005
	Two-sided *P*-value					Two-sided *P*-value			
N	0.1	0.05	0.02	0.01	*N*	0.1	0.05	0.02	0.01
5	1				30	152	137	120	109
6	2	1			31	163	148	130	118
7	4	2	0		32	175	159	141	128
8	6	4	2	0	33	188	171	151	138
9	8	6	3	2	34	201	183	162	149
10	11	8	5	3	35	214	195	174	160
11	14	11	7	5	36	228	208	186	171
12	17	14	10	7	37	242	222	198	183
13	21	17	13	10	38	256	235	211	195
14	26	21	16	13	39	271	250	224	208
15	30	25	20	16	40	287	264	238	221
16	36	30	24	19	41	303	279	252	234

N=16

T=61

P>0.1

- If N=16, T=61 then p>0.1
- There is no evidence that we should reject the null hypothesis that the mean number of medicines are equal. Therefor there is no evidence that the mean number of medicines per health clinic is different to the mean number of medicines per nursing home.

Setting	Parametric Methods	Non-Parametric Methods
Single sample	t-test (or z-test)	Wilcoxon signed rank test
Two independent samples	Two-sample t-test (or two-sample z-test)	Wilcoxon rank sum test (also called Mann-Whitney U test)
Two paired samples	Paired t-test (or paired z-test)	Wilcoxon signed rank test

Inference testing categorical data

- Normal distribution is no longer expected
- An **association** exists between two categorical variables if the distribution of one variable varies according to the value of the other.
- Can see this using a 2x2 table.

Chi-squared test

$$\chi^2 = \Sigma \frac{(O-E)^2}{E}$$

Where O= the observed outcome
E= expected outcome if null hypothesis true

		Outcome		
		Yes	No	Row total
Exposure	Yes	a	b	a + b
	No	c	d	c + d
	Column total	a + c	b + d	a+b+c+d

To calculate E for each cell= (row total x column total)/total number

Chi-squared test

- Very easy to calculate by hand
  - And even easier with software!
- To interpret the chi-squared use the chi-squared distribution
- Degrees of freedom   df = (r-1) ×(c-1)

Table A3 Percentage points of the χ^2 distribution

In the comparison of two proportions (2 × 2 χ^2 or Mantel–Haenszel χ^2 test) or in the assessment of a trend, the percentage points give a two-sided test. A one-sided test may be obtained by halving the *P* values. (Concepts of one- and two-sidedness do not apply to larger degrees of freedom, as these relate to tests of multiple comparisons.)

	P value							
d.f.	0.5	0.25	0.1	0.05	0.025	0.01	0.005	0.001
1	0.45	1.32	2.71	3.84	5.02	6.63	7.88	10.83
2	1.39	2.77	4.61	5.99	7.38	9.21	10.60	13.82
3	2.37	4.11	6.25	7.81	9.35	11.34	12.84	16.27
4	3.36	5.39	7.78	9.49	11.14	13.28	14.86	18.47
5	4.35	6.63	9.24	11.07	12.83	15.09	16.75	20.52
6	5.35	7.84	10.64	12.59	14.45	16.81	18.55	22.46
7	6.35	9.04	12.02	14.07	16.01	18.48	20.28	24.32
8	7.34	10.22	13.36	15.51	17.53	20.09	21.96	26.13
9	8.34	11.39	14.68	16.92	19.02	21.67	23.59	27.88
10	9.34	12.55	15.99	18.31	20.48	23.21	25.19	29.59
11	10.34	13.70	17.28	19.68	21.92	24.73	26.76	31.26
12	11.34	14.85	18.55	21.03	23.34	26.22	28.30	32.91
13	12.34	15.98	19.81	22.36	24.74	27.69	29.82	34.53

You conduct a study of 100 health clinic patients with depression to determine if women more likely to be prescribed an antidepressant than men.

		Antidepressant user		
		Yes	No	Row total
Gender	Male	18	7	25
	Female	42	33	75
	Column total	60	40	100

You conduct a study of 100 health clinic patients with depression to determine if women more likely to use antidepressants than men

- What is the null hypothesis?
- What is the alternate hypothesis?

You conduct a study of 100 health clinic patients with depression to determine if women more likely to use antidepressants than men

- Null hypothesis: no difference in the number of users by gender
- Alternate hypothesis: number of antidepressant users differs by gender

What is the frequency of antidepressant use for each gender?
Male?
Female?
What is the odds ratio?

		Antidepressant user		
		Yes	No	Row total
Gender	Female	18	7	25
	Male	42	33	75
	Column total	60	40	100

Look at frequency of use by gender
18/25=72% of women use an antidepressant
42/75=56% of men use an antidepressant

OR=18 x 33/42 x 7
=2.02 (women compared to men)

		Antidepressant user		
		Yes	No	Row total
Gender	Female	18	7	25
	Male	42	33	75
	Column total	60	40	100

- Calculate the expected values for each cell if there is no association
- Remember expected value
  = row total x column total / total number

		Antidepressant user		
		Yes	No	Row total
Gender	Female			25
	Male			75
	Column total	60	40	100

- Calculate the expected values for each cell if there is no association
- Remember expected value
  = row total x column total / total number

		Antidepressant user		
		Yes	No	Row total
Gender	Female	15	10	25
	Male	45	30	75
	Column total	60	40	100

- For each cell calculate observed –expected
- Then calculate $(\text{observed-expected})^2$
- Then calculated the sum of $(\text{observed-expected})^2$
- N=100, df = (rows-1)(columns-1)
  df= (2-1)(2-1)
  =1

Observed	Expected	Observed - expected	$(\text{Observed-expected})^2$	Cumulative frequency (Observed-expected
18	15	3	9	9
7	10	-3	9	18
42	45	-3	9	27
33	30	3	9	36

- For each cell calculate observed –expected

Observed	Expected	Observed - expected	$(\text{Observed-expected})^2$	Cumulative frequency (Observed-expected
18	15			
7	10			
42	45			
33	30			

- For each cell calculate observed –expected
- Then calculate (observed-expected)^2

Observed	Expected	Observed - expected	(Observed-expected)^2	Cumulative frequency (Observed-expected
18	15	3		
7	10	-3		
42	45	-3		
33	30	3		

- For each cell calculate observed –expected
- Then calculate (observed-expected)^2
- Then calculate (observed-expected)^2/ observed

Observed	Expected	Observed - expected	(Observed-expected)^2	(Observed-expected)2/ observed
18	15	3	9	0.50
7	10	-3	9	1.29
42	45	-3	9	0.21
33	30	3	9	0.27

- For each cell calculate observed –expected
- Then calculate (observed-expected)^2
- Then calculate (observed-expected)^2/ observed
- Then calculate the sum of (observed-expected)^2/ observed
  - This is the chi-squared value ie **chi-squared=2.27**
- How many degrees of freedom are there?

Observed	Expected	Observed - expected	(Observed-expected)^2	(Observed-expected)2/ observed
18	15	3	9	0.50
7	10	-3	9	1.29
42	45	-3	9	0.21
33	30	3	9	0.27
			Sum=	2.27

- For each cell calculate observed –expected
- Then calculate (observed-expected)^2
- Then calculated the sum of (observed-expected)^2
  - This is the chi-squared value ie **chi-squared=2.27**
- N=100, df = (rows-1)(columns-1)

  df = (2-1)(2-1)

  df =1

Observed	Expected	Observed - expected	(Observed-expected)^2	Cumulative frequency (Observed-expected
18	15	3	9	9
7	10	-3	9	18
42	45	-3	9	27
33	30	3	9	36

- What is the p-value for chi-squared=36 with 1 degree of freedom?

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- What is the p-value for chi-squared=36 with 1 degree of freedom?

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In the comparison of two proportions (2 × 2 χ^2 or Mantel–Haenszel χ^2 test) or in the assessment of a trend, the percentage points give a two-sided test. A one-sided test may be obtained by halving the *P* values. (Concepts of one- and two-sidedness do not apply to larger degrees of freedom, as these relate to tests of multiple comparisons.)

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7	6.35	9.04	12.02	14.07	16.01	18.48	20.28	24.32
8	7.34	10.22	13.36	15.51	17.53	20.09	21.96	26.13
9	8.34	11.39	14.68	16.92	19.02	21.67	23.59	27.88
10	9.34	12.55	15.99	18.31	20.48	23.21	25.19	29.59

- For chi-squared=36 and df=1 0.25>p>0.1

That is there is no evidence against the null hypothesis that there is no difference in prescribing of antidepressants between men and women. Women are not more likely to use antidepressants than men (p>0.1).

- For chi-squared=36 and df=1 0.25>p>0.1

That is there is no evidence against the null hypothesis that there is no difference in prescribing of antidepressants between men and women. Women are not more likely to use antidepressants than men (p>0.1).

The 95% confidence interval around the odds ratio is from 0.75 to 5.41

How would you interpret this?

- OR=2 (95%CI: 0.75 to 5.41)

We are 95% confident that the true odds ratio lies between 0.75 and 5.41, that is it could be as low as 0.75 or as high as 5.41. Since this interval includes OR=1 there is no evidence to conclude that the odds of women receiving an antidepressant than men.

Paired categorical data

- Not common in DUR
- Example: looking at medication use before and after hospitalization.
- Both observations are on the one person
  - Observations are no longer independent
  - Cannot use a chi-squared test
- McNemars test

Choosing a statistical test

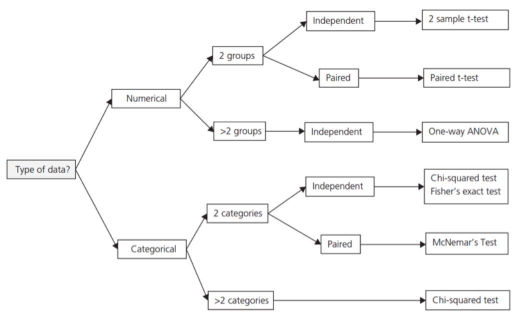

Figure 9.2 Flowchart for determining which standard statistical test is appropriate.

Source Drug Utilization Research: Methods and Applications