Session 1a

Principles of statistics (1) – Summary measures and *P*-values

Outline

- Summarising data
- The role of chance
- Interpreting *P*-values
- Commonly used hypothesis tests
- Limitations of *P*-values

Summarising data

Why do we summarise data?

- To get a feel for the data
- To decide on the types of variables that we have and their distributions
- To check for possible errors, outliers or missing values
- To start to appreciate the relationships between pairs of variables
- To allow others to assess comparability with their own population

Types of data variables

Qualitative - (categorical)	*Binary:* 2 categories (eg. dead/alive)
	Nominal: >2 categories, no ordering to groups (eg. ethnicity)
	Ordinal: >2 categories, some inherent ordering (eg. severity of pain, age group)
Quantitative - (numerical)	*Discrete:* Can take only certain values in a range (eg. quality of life score, no. of sexual partners in a year)
	Continuous: Can take any value in a range (eg. height, weight, CD4 count)
Other types -	*Ranks, percentages, rates, ratios, scores*

Displaying the data graphically

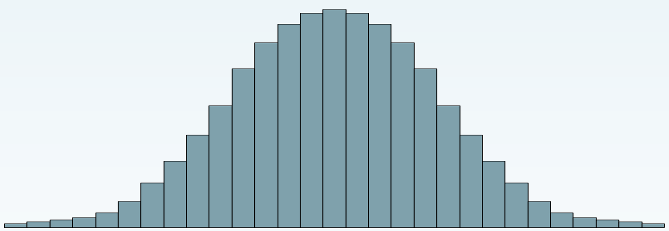
- One categorical variable
  - Pie chart, bar/column chart
- One numerical variable
  - Dot plot, histogram, box plot, stem-and-whisker plot
- Two categorical variables
  - Clustered/segmented bar/column charts
- Two numerical variables
  - Scatter plot

The distributions of quantitative data

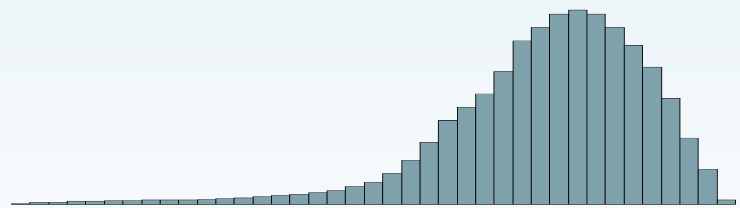
The choice of summary statistics and the most appropriate analytical method will depend on the shape of the distribution

Symmetrical, bell-shaped

‘Normal’ distribution

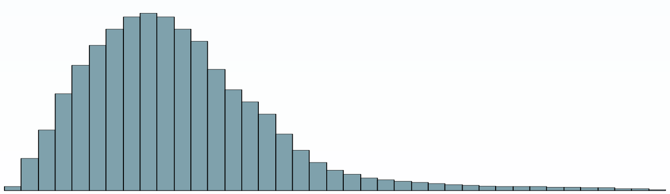


Negative skewness



Positive skewness

common in laboratory data
eg. CD4 counts in HIV+ves



Uniform distribution

Equal probability of taking any value in the range

Summarising quantitative data

- We usually quote two measures:
  - A measure of the *average* value
  - A measure of how *variable* the data are

Type of data	Average	Variability
Numerical, normally distributed	Mean	SD/variance
Numerical, skewed	Median	Range/IQR
Categorical, nominal	Mode	No suitable measure – give % in each category
Categorical, ordinal, only a few categories	Mode	
Categorical, ordinal, reasonable number of categories	Median	

The role of chance

Hypothesis tests – background

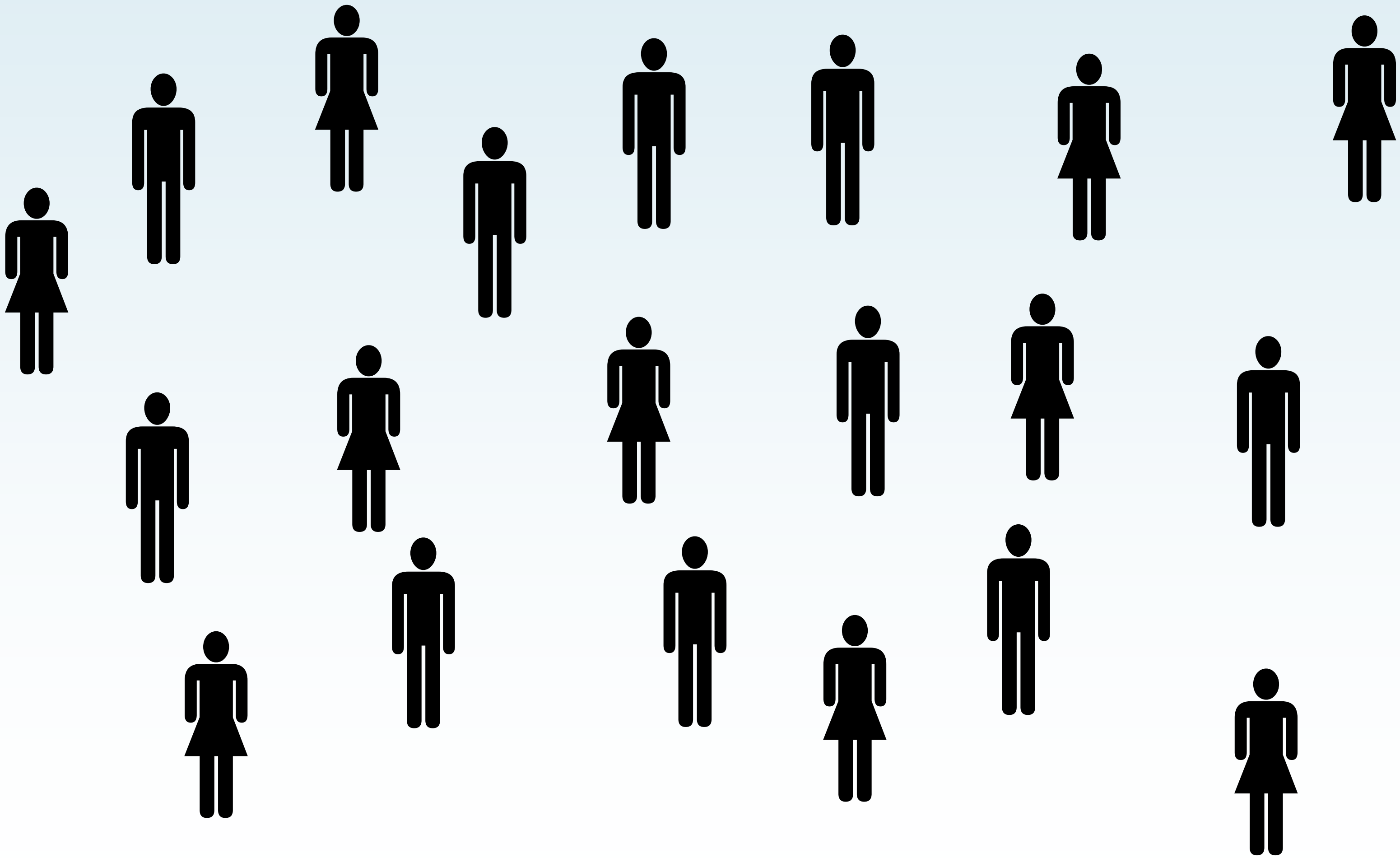
- Presentations of data in the medical world are littered with p-values - '$P<0.05$' is thought to be a magical phrase, guaranteed to ensure that your paper will be published
- But what do these *P*-values really tell us, and is a *P*-value <0.05 really that important?

P-values – what do they tell us?

Example – baseline imbalance in trials

- Imagine 20 participants in a trial, 50% of whom are female
- We randomise the group in a 1:1 manner to receive one of two regimens, A (red) or B (blue)
- We should end up with approximately 10 patients allocated to regimen A and 10 patients to regimen
- What happens in practice?

20 trial participants



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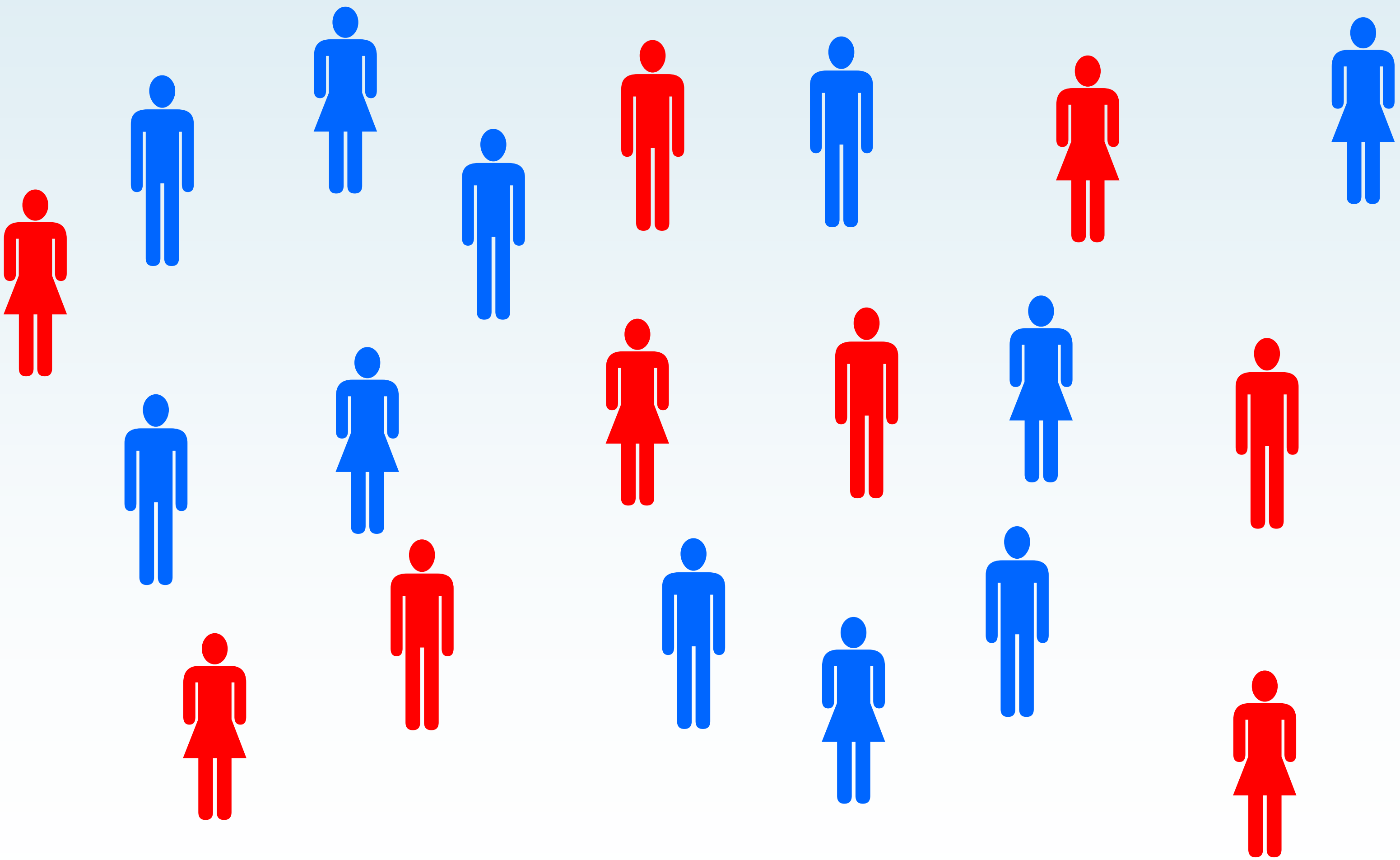

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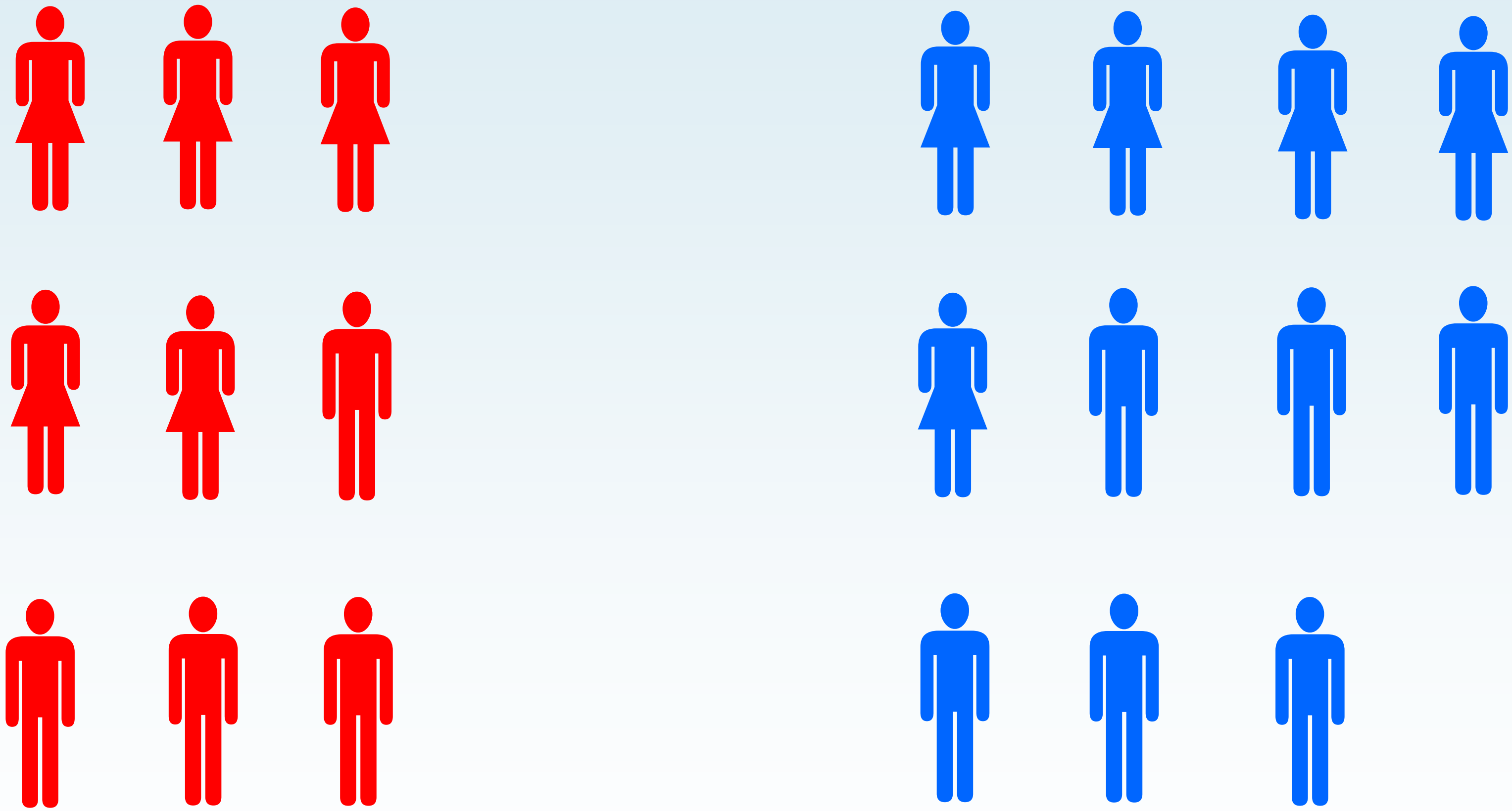

Regimen A **Regimen B**

20 trial participants - % female

	Regimen			
	A		B	
Trial number	N	N (%) female	N	N (%) female
1	9	5 (55.6)	11	5 (45.5)

20 trial participants - % female

	Regimen			
	A		B	
Trial number	N	N (%) female	N	N (%) female
1	9	5 (55.6)	11	5 (45.5)
2	10	5 (50.0)	10	5 (50.0)
3	7	3 (42.9)	13	7 (53.8)
4	15	7 (46.7)	5	3 (60.0)
5	8	5 (62.5)	12	5 (41.7)
6	8	4 (50.0)	12	6 (50.0)
7	10	5 (50.0)	10	5 (50.0)
8	10	6 (60.0)	10	4 (40.0)
9	11	7 (63.6)	9	3 (33.3)
10	10	3 (30.0)	10	7 (70.0)

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100 trial participants - % female

	Regimen			
	A		B	
Trial number	N	N (%) female	N	N (%) female
1	54	28 (51.9)	46	22 (47.8)
2	53	24 (45.3)	47	26 (55.3)
3	61	30 (49.2)	39	20 (51.3)
4	51	25 (49.0)	49	25 (51.0)
5	57	29 (50.9)	43	21 (48.8)
6	50	24 (48.0)	50	26 (52.0)
7	51	22 (43.1)	49	28 (57.1)
8	54	30 (55.6)	46	20 (43.5)
9	57	28 (49.1)	43	22 (51.2)
10	47	20 (42.6)	53	30 (56.6)

The role of 'chance'

- So even if we randomly subdivide patients into two groups, their characteristics may be imbalanced
- The size of the imbalance generally gets smaller as the trial increases in size
- Random baseline covariate imbalance is not usually a problem in a trial (unless it is big) as statistical methods can deal with this
- However, if we are describing outcomes rather than baseline covariates, then there is more cause for concern

Trial participants - % viral load <50 cps/ml

	Regimen			
	A		B	
Trial number	N	N (%) VL<50 copies/ml	N	N (%) VL<50 copies/ml
1	54	28 (51.9)	46	22 (47.8)
2	53	24 (45.3)	47	26 (55.3)
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14% difference in outcome

What is the *P*-value?

- *P*-value: probability of obtaining an effect at least as big as that observed if the null hypothesis is true (i.e. there is no real effect)
- Large *P*-value – results are consistent with chance variation
  - *Insufficient evidence that effect is real*
- Small *P*-value – results are inconsistent with chance variation
  - *Sufficient evidence that effect is real*

What is large and what is small?

By convention:

$P<0.05$ – SMALL

$P>0.05$ – LARGE

Hypothesis testing - how do we obtain a *P*-value?

The general approach to hypothesis testing

- Start by defining two hypotheses:
  - Null hypothesis: There is no real difference in viral load response rates between the two regimens
  - Alternative hypothesis: There is a real difference in viral load response rates between the two regimens
- Conduct trial and collect data
- Use data from that trial to perform a hypothesis test (e.g. Chi-squared test, t-test, ANOVA)
- Obtain a *P*-value

Choosing the right hypothesis test

All statistical tests will generate a *P*-value - the choice of statistical test will be based on a number of factors, including:

- The hypotheses being studied
- The variables of particular interest
- The distribution of their values
- The number of individuals who will be included in the analysis
- The number of 'groups' being studied
- The relationship (if any) between these groups

Choosing the right hypothesis test

Tests that may be used (a small selection):

Comparing proportions

- Chi-squared test
- Chi-squared test for trend
- Fisher's exact test
- Relative risk
- Odds ratio

Comparing numbers

- Unpaired *t*-test
- Paired *t*-test
- Mann-Whitney U test
- ANOVA
- Kruskal-Wallis test

Example – the Chi-squared test

- Two groups
- Interested in whether the proportion of individuals with an outcome differs between these groups
- Measurement of interest is categorical
- Can draw up a table of responses in the groups
- Expected numbers in each cell of the table are >5

Example – Define hypotheses

We wish to know whether patients receiving a new treatment regimen (A) are more likely to achieve viral load suppression than those receiving standard-of-care (B)

Hypotheses:

H_0: There is no real difference in the proportion of patients with a VL$\leq$50 copies/ml between those receiving regimen A and those receiving regimen B

H_1: There is a real difference in the proportion of patients with a VL$\leq$50 copies/ml between those receiving regimen A and those receiving regimen B

Example – Collect data

	VL≤50 copies/ml	VL >50 copies/ml	Total
Regimen	N (%)	N (%)	N (%)
A	28 (52)	26 (48)	54 (100)
B	22 (48)	24 (52)	46 (100)
Total	50 (50)	50 (50)	100 (100)

Example – Interpret *P*-value

- Computer output gives Chi-squared value of 0.04
- *P*-value associated with this test value =0.84
- If there really was no difference in viral load response between the two groups, and we repeated the study 100 times, we would have observed a difference of this size (or greater) on 84 of the 100 occasions
- As *P*>0.05, there is insufficient evidence of a real difference in viral load response rates between the two regimens

Points to note

- We have not proven that the difference was due to chance, just that there was a reasonable probability that it might have been
- We can never prove the null hypothesis
- We take an ‘innocent until proven guilty’ approach

Limitation of *P*-values

- Although *P*-values are helpful in telling us which effects are likely to be real, they also suffer from limitations (see session 1b)
- An estimate of the size of the effect and its corresponding confidence interval provides complementary information
- The limitations of *P*-values, as well as the use of confidence intervals, will be studied in Session 1b