Clinical Biostatistics

Inference about means

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Methods for inference about means

Large samples

➢ Single mean: Normal method (z method)

➢ Paired data: Normal method (z method)

➢ Two samples: Normal method (z method)

Small samples

➢ Single mean: One sample t method

➢ Paired data: Paired t method

➢ Two samples: Two sample t method (independent
samples t method, two group t method)

More than two samples, any size

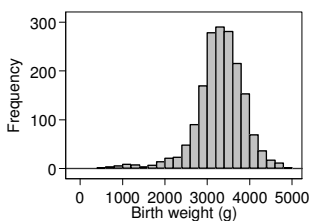➢ One-way analysis of variance (anova)

Single mean, large sample method

Confidence interval using the Normal distribution.

Method can be used for any large sample.

Data may be from any distribution.

Distribution of birthweight in 1749 singleton pregnancies to Caucasian mothers in South London.
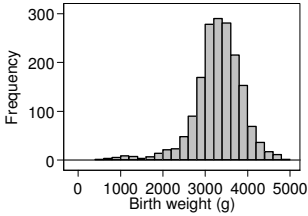

mean = 3296.0 g

standard deviation = 563.2 g.

standard error of
the mean = 13.5 g
$= 563.2 / \sqrt{1769}$

Single mean, large sample method

Confidence interval using the Normal distribution.

mean = 3296.0 g, standard deviation = 563.2 g ,
standard error of the mean = 13.5 g.

Large sample ➔ mean from Normal distribution with SD = 13.5 well estimated from data.

95% of observations from a Normal distribution are within 1.96 standard deviations from the mean.

95% confidence interval =
3296.0 – 1.96 × 13.5 g to
        3296.0 + 1.96 × 13.5 g

= 3270 to 3322 g.

Single mean, large sample method

Assumptions:

➢ The observations are independent. We should not have, for example, a group of 100 observations where there are 10 subjects with 10 observations on each.

➢ The sample is large enough for the standard errors to be well estimated. My rule of thumb is 100 for one group.

Paired data, large sample method

Confidence interval for mean difference using the Normal distribution.

Example: interventions for depression delivered using the internet.

Recruited 525 people with symptoms of depression identified in a survey.

Randomly allocated to websites:

▪ BluePages, information about depression (n = 166),

▪ MoodGYM, cognitive behaviour therapy (n = 182),

▪ attention placebo (n = 178).

Christensen H, Griffiths KM, Jorm AF. (2004) Delivering interventions for depression by using the internet: randomised controlled trial. *British Medical Journal* **328**, 265-268.

Paired data, large sample method

Baseline depression score (0-60) and fall after six weeks by treatment group for 525 patients with depression (Christensen *et al*., 2004)

		Baseline scores		Fall in scores	
	number	mean	SD	mean	SD
BluePages	165	21.1	10.4	3.9	9.1
MoodGYM	182	21.8	10.5	4.2	9.1
Controls	178	21.6	11.1	1.0	8.4

90 (17%) of subjects did not return post-intervention questionnaires and the authors assumed that their scores were unchanged.

Differences must have a large spike of at least 90 observations at zero.

They could not have a Normal distribution.

Paired data, large sample method

BluePages: 165 subjects, mean fall in depression score = 3.9, standard deviation = 9.1.

Standard error of the mean difference = 0.71.

95% confidence interval for the mean fall is
$$3.9 - 1.96 \times 0.71 \text{ to } 3.9 + 1.96 \times 0.71$$
$$= 2.5 \text{ to } 5.3 \text{ points on the depression scale.}$$

This is an interval estimate for the mean fall in depression score assuming non-responders do not change.

Paired data, large sample method

BluePages: 165 subjects, mean fall in depression score = 3.9, standard deviation = 9.1, standard error of the mean = 0.71.

Test of significance

▪ null hypothesis: mean change in population is zero,

▪ alternative hypothesis: there is a change, in either direction.

Large sample ➔ mean will be from a Normal distribution with standard deviation equal to the standard error of the mean.

Observed sample mean minus the unknown population mean divided by the standard error will be an observation from the Standard Normal distribution.

Paired data, large sample method

BluePages: 165 subjects, mean fall in depression score = 3.9, standard deviation = 9.1, standard error of the mean = 0.71.

Test of significance

▪ null hypothesis: mean change in population is zero.

If true then sample mean over standard error will be from a Standard Normal distribution.

$z = 3.9/0.71 = 5.49$.

$P = 0.00000004$.

Usually quote this as P<0.0001.

This is the large sample Normal test for a single mean, also called the z test for a single mean.

Paired data, large sample method

Assumptions:

➤ The observations are independent. We should not have, for example, a group of 100 observations where there are 10 subjects with 10 observations on each.

➤ The sample is large enough for the standard errors to be well estimated. My rule of thumb is 100 for one group.

➤ The mean and standard deviation of differences are constant, i.e. not related to the size of the variable.

Check by plotting difference against the average of the two measurements for the subject.

See later under paired t test.

Two means, large sample method

		Fall in scores		
	number	mean	SD	SE of mean
BluePages	165	3.9	9.1	0.71
MoodGYM	182	4.2	9.1	0.67
Controls	178	1.0	8.4	0.63

Confidence interval for difference between two means, BluePages minus MoodGYM.

Difference = −0.3

Standard error for the difference $= \sqrt{0.71^2 + 0.67^2} = 0.98$

N.B. This only works when the groups are independent.

95% CI = −0.3 − 1.96 × 0.98 to −0.3 + 1.96 × 0.98
        = −2.2 to +1.6

Two means, large sample method

```
                    Fall in scores
          number    mean    SD   SE of mean
BluePages  165      3.9     9.1     0.71
MoodGYM    182      4.2     9.1     0.67
Controls   178      1.0     8.4     0.63
```

Test of null hypothesis means are equal, BluePages versus MoodGYM.

Difference = −0.3, standard error for the difference = 0.98.

If null hypothesis true, difference/standard error will be from a Standard Normal distribution.

difference/standard error = −0.3/0.98 = −0.31.

From Normal distribution P = 0.8.

Large sample Normal or z test for two means.

Two means, large sample method

Assumptions:

➢ The observations and groups are independent. We should not have links between observations in the two groups, such as a matched study where each subject in one group is matched, e.g. by age and sex, with a subject in the other group.

➢ The samples are large enough for the standard errors to be well estimated. My rule of thumb is at least 50 in each group.

One sample t method for small samples

Example: nine patients with chronic non-healing wounds (Shukla *et al.*, 2004).

Biopsies were assessed using the microscopic angiogenesis grading system (MAGS) score, which provides an index of how well small blood vessels are developing and hence of epithelial regeneration.

High scores are good.

Observations: 20, 31, 34, 39, 43, 45, 49, 51, and 63.

mean = 41.7, standard deviation = 12.5,
standard error of the mean = 4.2.

Shukla VK, Rasheed MA, Kumar M, Gupta SK, Pandey SS. (2004) A trial to determine the role of placental extract in the treatment of chronic non-healing wounds. *Journal of Wound Care* **13**, 177-9,

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One sample t method for small samples

Observations: 20, 31, 34, 39, 43, 45, 49, 51, and 63.

mean = 41.7, standard deviation = 12.5,
standard error of the mean = 4.2.

95% confidence interval for the mean:

If the sample were large we could use

mean – 1.96 standard errors to mean + 1.96 standard errors.

We cannot use the large sample Normal method because the samples are too small.

The standard error will not be sufficiently well estimated.

One sample t method for small samples

Observations: 20, 31, 34, 39, 43, 45, 49, 51, and 63.

mean = 41.7, standard deviation = 12.5,
standard error of the mean = 4.2.

95% confidence interval for the mean:

mean – ? standard errors to mean + ? standard errors.

We use Student's t distribution.

For a small sample, we must assume that the differences themselves follow a Normal distribution.

95% confidence interval:

mean – $t_{0.05}$ standard errors to mean + $t_{0.05}$ standard errors.

One sample t method for small samples

Observations: 20, 31, 34, 39, 43, 45, 49, 51, and 63.

mean = 41.7, standard deviation = 12.5,
standard error of the mean = 4.2.

95% confidence interval for the mean:

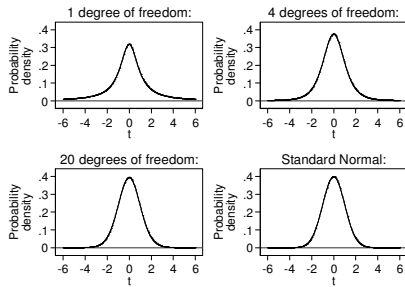mean – $t_{0.05}$ standard errors to mean + $t_{0.05}$ standard errors.

What is $t_{0.05}$?

This comes from Student's t distribution, defined as the distribution followed by a sample mean minus a population mean all divided by the standard error, when the observations follow a Normal distribution.

where $t_{0.05}$ is the two-sided 5% point of the t distribution with degrees of freedom = number of observations minus one.
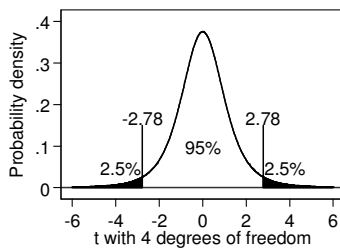
Student's t distribution

The t distribution family has one parameter, the degrees of freedom.

As the degrees of freedom increases, the t distribution becomes closer to the Standard Normal distribution.

Two tailed probability point of the t Distribution

Two tailed probability points of the t Distribution

D.f.	0.10 (10%)	0.05 (5%)	0.01 (1%)	0.001 (0.1%)	D.f.	0.10 (10%)	0.05 (5%)	0.01 (1%)	0.001 (0.1%)
	Probability					Probability			
1	6.31	12.70	63.66	636.62	16	1.75	2.12	2.92	4.02
2	2.92	4.30	9.93	31.60	17	1.74	2.11	2.90	3.97
3	2.35	3.18	5.84	12.92	18	1.73	2.10	2.88	3.92
4	2.13	2.78	4.60	8.61	19	1.73	2.09	2.86	3.88
5	2.02	2.57	4.03	6.87	20	1.73	2.09	2.85	3.85
6	1.94	2.45	3.71	5.96	21	1.72	2.08	2.83	3.82
7	1.90	2.36	3.50	5.41	22	1.72	2.07	2.82	3.79
8	1.86	2.31	3.36	5.04	23	1.71	2.07	2.81	3.77
9	1.83	2.26	3.25	4.78	24	1.71	2.06	2.80	3.75
10	1.81	2.23	3.17	4.59	25	1.71	2.06	2.79	3.73
11	1.80	2.20	3.11	4.44	30	1.70	2.04	2.75	3.65
12	1.78	2.18	3.06	4.32	40	1.68	2.02	2.70	3.55
13	1.77	2.16	3.01	4.22	60	1.67	2.00	2.66	3.46
14	1.76	2.15	2.98	4.14	120	1.66	1.98	2.62	3.37
15	1.75	2.13	2.95	4.07	∞	1.65	1.96	2.58	3.29

D.f. = Degrees of freedom
∞ = infinity, same as the Standard Normal Distribution

One sample t method for small samples

Observations: 20, 31, 34, 39, 43, 45, 49, 51, and 63.

mean = 41.7, standard deviation = 12.5,
standard error of the mean = 4.2.

95% confidence interval for the mean:

mean $- t_{0.05}$ standard errors to mean $+ t_{0.05}$ standard errors.

What is $t_{0.05}$?

$t_{0.05}$ is the two-sided 5% point of the t distribution with degrees of freedom = number of observations minus one.

This is the degrees of freedom for the sample variance.

We have 9 observations so $9 - 1 = 8$ degrees of freedom.

Two tailed probability points of the t Distribution

D.f.	Probability				D.f.	Probability			
	0.10	0.05	0.01	0.001		0.10	0.05	0.01	0.001
	(10%)	(5%)	(1%)	(0.1%)		(10%)	(5%)	(1%)	(0.1%)
1	6.31	12.70	63.66	636.62	16	1.75	2.12	2.92	4.02
2	2.92	4.30	9.93	31.60	17	1.74	2.11	2.90	3.97
3	2.35	3.18	5.84	12.92	18	1.73	2.10	2.88	3.92
4	2.13	2.78	4.60	8.61	19	1.73	2.09	2.86	3.88
5	2.02	2.57	4.03	6.87	20	1.73	2.09	2.85	3.85
6	1.94	2.45	3.71	5.96	21	1.72	2.08	2.83	3.82
7	1.90	2.36	3.50	5.41	22	1.72	2.07	2.82	3.79
8	1.86	2.31	3.36	5.04	23	1.71	2.07	2.81	3.77
9	1.83	2.26	3.25	4.78	24	1.71	2.06	2.80	3.75
10	1.81	2.23	3.17	4.59	25	1.71	2.06	2.79	3.73
11	1.80	2.20	3.11	4.44	30	1.70	2.04	2.75	3.65
12	1.78	2.18	3.06	4.32	40	1.68	2.02	2.70	3.55
13	1.77	2.16	3.01	4.22	60	1.67	2.00	2.66	3.46
14	1.76	2.15	2.98	4.14	120	1.66	1.98	2.62	3.37
15	1.75	2.13	2.95	4.07	∞	1.65	1.96	2.58	3.29

D.f. = Degrees of freedom
∞ = infinity, same as the Standard Normal Distribution

One sample t method for small samples

Observations: 20, 31, 34, 39, 43, 45, 49, 51, and 63.

mean = 41.7, standard deviation = 12.5,
standard error of the mean = 4.2.

95% confidence interval for the mean:

mean $- t_{0.05}$ standard errors to mean $+ t_{0.05}$ standard errors.

$t_{0.05} = 2.31$

95% confidence interval for the mean:

$41.7 - 2.31 \times 4.2$ to $41.7 + 2.31 \times 4.2$

= 32.0 to 51.4 MAGS units.

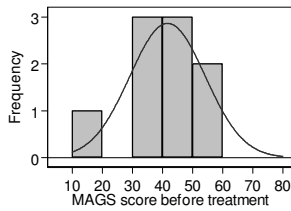**One sample t method for small samples**

Assumptions:

➢ The observations are independent.

➢ The observations are from a Normal distribution.

One sample t method for small samples

Assumption: the observations are from a Normal distribution.

Hard to check with a histogram for a small sample:

We can check the assumption of a Normal distribution with a Normal plot.

Normal plot

Order the observations.

| 20 | 31 | 34 | 39 | 43 | 45 | 49 | 51 | 63 |

What would we expect the first observation of a Normal sample with 9 observations to be?

The average value for the smallest observation in a sample of 9 observations from a Standard Normal distribution is −1.28.

We can do this for what we expect the 2nd, 3rd, 4th, etc., to be:

−1.28 −0.84 −0.52 −0.25 0.00 0.25 0.52 0.84 1.28

Normal plot

Order the observations.

  20   31   34   39   43   45   49   51   63

The average values for the 1st, 2nd, 3rd, etc.
observations of a Standard Normal sample with 9
observations are:

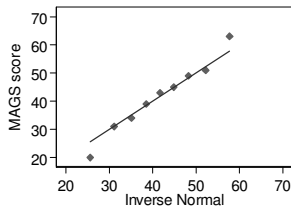 −1.28 −0.84 −0.52 −0.25 0.00 0.25 0.52 0.84 1.28

For a Normal sample with the same mean and standard
deviation as MAGS, we multiply by standard
deviation = 12.5 and add mean = 41.7:

 25.6 31.1 35.1 38.5 41.7 44.8 48.2 52.2 57.7

Normal plot
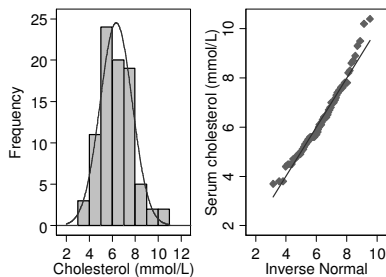
MAGS: 20   31   34   39   43   45   49   51   63
Normal: 25.6 31.1 35.1 38.5 41.7 44.8 48.2 52.2 57.7

If we plot MAGS score against the expected Normal value,
we should get a straight line if the MAGS score follows a
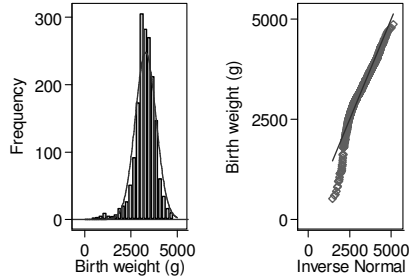Normal distribution.

Normal plot

Skew distributions produce a clear bend or curve.

Normal plot

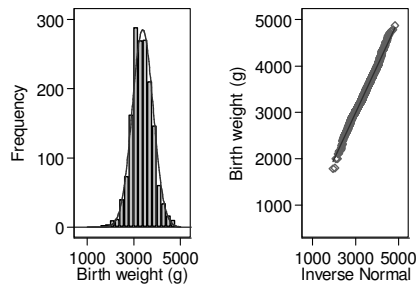Skew distributions produce a clear bend or curve.

All births:

Normal plot

Distributions close to the Normal produce a straight line.

Term births:

Normal plot

There are several ways of drawing Normal plots.

Some programs, such as SPSS, put the expected Normal values on the vertical axis and the observed data on the horizontal axis. A downward curve then indicates positive skewness, an upward curve negative skewness.

Some programs use the Standard Normal expected values rather than those for a Normal distribution with the same mean and standard deviation as the data.

Some offer a Normal probability plot rather than a Normal quantile plot, but these look very similar and are interpreted in the same way.

Paired t method

```
MAGS score before and after treatment with topical
placental extract in 9 patients with non-healing
wounds (Shukla et al., 2004)
Subject    Before    After    Difference
   1         20        32         12
   2         31        47         16
   3         34        43          9
   4         39        43          4
   5         43        55         12
   6         45        52          7
   7         49        61         12
   8         51        55          4
   9         63        71          8
Mean                             9.33
Standard deviation               4.03
Standard error of mean           1.34
```

Paired t method

For a small sample, we must assume that the differences themselves follow a Normal distribution.

95% confidence interval:

mean difference – $t_{0.05}$ standard errors to
mean difference + $t_{0.05}$ standard errors.

where $t_{0.05}$ is the two-sided 5% point of the t distribution with degrees of freedom = number of observations minus one.

Test of significance: refer mean difference / standard error to the t distribution with degrees of freedom = number of observations minus one.

Paired t method

Example: Increase in MAGS score

Mean difference = 9.33, SE = 1.34 litres/min.

9 differences, hence 9 – 1 = 8 degrees of freedom.

```
            Two tailed probability points of the t Distribution

D.f.          Probability          D.f.          Probability
      0.10  0.05  0.01  0.001            0.10  0.05  0.01  0.001
      (10%) (5%)  (1%)  (0.1%)           (10%) (5%)  (1%)  (0.1%)
 1    6.31 12.70 63.66 636.62      16    1.75  2.12  2.92  4.02
 2    2.92  4.30  9.93  31.60      17    1.74  2.11  2.90  3.97
 3    2.35  3.18  5.84  12.92      18    1.73  2.10  2.88  3.92
 4    2.13  2.78  4.60   8.61      19    1.73  2.09  2.86  3.88
 5    2.02  2.57  4.03   6.87      20    1.73  2.09  2.85  3.85
 6    1.94  2.45  3.71   5.96      21    1.72  2.08  2.83  3.82
 7    1.90  2.36  3.50   5.41      22    1.72  2.07  2.82  3.79
 8    1.86  2.31  3.36   5.04      23    1.71  2.07  2.81  3.77
 9    1.83  2.26  3.25   4.78      24    1.71  2.06  2.80  3.75
10    1.81  2.23  3.17   4.59      25    1.71  2.06  2.79  3.73
11    1.80  2.20  3.11   4.44      30    1.70  2.04  2.75  3.65
12    1.78  2.18  3.06   4.32      40    1.68  2.02  2.70  3.55
13    1.77  2.16  3.01   4.22      60    1.67  2.00  2.66  3.46
14    1.76  2.15  2.98   4.14     120    1.66  1.98  2.62  3.37
15    1.75  2.13  2.95   4.07      ∞     1.65  1.96  2.58  3.29
D.f. = Degrees of freedom
∞ = infinity, same as the Standard Normal Distribution
```

Paired t method

Example: Increase in MAGS score

Mean difference = 9.33, SE = 1.34 litres/min.

9 differences, hence 9 − 1 = 8 degrees of freedom.

Using the 8 d.f. row, we get $t_{0.05}$ = 2.31.

The 95% confidence interval:

$9.33 − 2.31 \times 1.34$ to $9.33 + 2.31 \times 1.34$
= 6.2 to 12.4.

Test of significance:

Mean/SE = 9.33/1.34 = 6.96

Paired t method

Example: Increase in MAGS score

Mean difference = 9.33, SE = 1.34 litres/min.

9 differences, hence 9 − 1 = 8 degrees of freedom.

Using the 8 d.f. row, we get $t_{0.05}$ = 2.31.

The 95% confidence interval:

$9.33 − 2.31 \times 1.34$ to $9.33 + 2.31 \times 1.34$
= 6.2 to 12.4.

Test of significance:

Mean/SE = 9.33/1.34 = 6.96

From t table, P<0.001. From computer program,
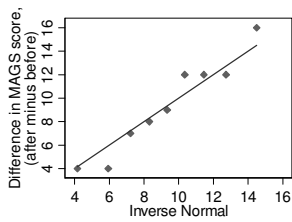P=0.0001.

Paired t method

Assumptions:

➤ The observations are independent.

➤ The differences follow a Normal distribution.

➤ The mean and standard deviation of differences are constant, i.e. not related to the size of the variable.

Paired t method

Assumptions of the paired t method

The differences follow a Normal distribution.

Check with histogram, Normal plot.
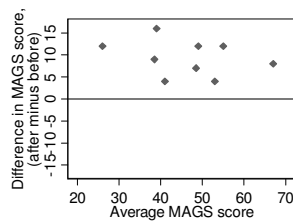

Paired t method

Assumptions of the paired t method

The differences follow a Normal distribution.

Check with histogram, Normal plot.

The mean and SD of the differences are constant, i.e. unrelated to magnitude.

Check with plot of difference against average.

Paired t method

Deviations from assumptions

1. The differences follow a Normal distribution.

   Need at least 100 observations to ignore non-Normal. However, differences tend to have a symmetrical distribution, so this assumption is usually met.

2. The mean and SD of the differences are constant, i.e. unrelated to magnitude.

   Essential, can be dealt with by transformation.

Two sample t method

This is also called the unpaired t method or test and the two group t method, Student's two sample t test.

Example: Capillary density (per mm^2) in the feet of ulcerated patients and a healthy control group (data supplied by Marc Lamah)

```
------------------------------------------
         Controls          Ulcerated patients
------------------------------------------
   17.5 34.5 36.5  52.0     9.0 18.5 23.0 27.5
   27.5 31.0 38.0          11.0 20.0 23.0 28.0
   27.0 35.5 40.0          12.5 20.0 24.0 28.5
   29.5 33.5 39.5          18.0 22.0 26.5 29.0
   27.0 35.5 40.0          18.0 22.5 26.5 44.5
   29.0 34.0 40.0          18.0 22.5 27.0
------------------------------------------
Number      19                    23
Mean        34.08                 22.59
SD           7.29                  7.31
------------------------------------------
```

Two sample t method

We cannot use the large sample Normal method because the samples are too small.

The standard error will not be sufficiently well estimated.

The distribution of the standard error estimate depends on the distribution of the observations themselves.

We must make two assumptions about the data:

1. the observations come from Normal distributions,

2. the distributions in the two populations have the same variance. (N.B. The populations, not the samples from them, have the same variance.)

Two sample t method

If the distributions in the two populations have the same variance, we need only one estimate of variance. We call this the common or pooled variance estimate.

The degrees of freedom are number of observations minus 2.

We use this common estimate of variance to estimate the standard error of the difference between the means.

Capillary density example:

Common variance = 53.31, SD = 7.30 capillaries/mm², df = 19 + 23 − 2 = 40.

SE of difference = 2.26 capillaries/mm².

Difference (control − ulcer) = 34.08 − 22.59 = 11.49 capillaries/mm².

Two sample t method

Capillary density example:

Common variance = 53.31, SD = 7.30 capillaries/mm², df = 19 + 23 − 2 = 40.

SE of difference = 2.26 capillaries/mm².

Difference (control − ulcer) = 34.08 − 22.59 = 11.49 capillaries/mm².

95% confidence interval for difference:

11.49 − ? × 2.26 to 11.49 + ? × 2.26.

? comes not from the Normal distribution but the t distribution with 40 degrees of freedom.

Two tailed probability points of the t Distribution

D.f.	Probability				D.f.	Probability			
	0.10	0.05	0.01	0.001		0.10	0.05	0.01	0.001
	(10%)	(5%)	(1%)	(0.1%)		(10%)	(5%)	(1%)	(0.1%)
1	6.31	12.70	63.66	636.62	16	1.75	2.12	2.92	4.02
2	2.92	4.30	9.93	31.60	17	1.74	2.11	2.90	3.97
3	2.35	3.18	5.84	12.92	18	1.73	2.10	2.88	3.92
4	2.13	2.78	4.60	8.61	19	1.73	2.09	2.86	3.88
5	2.02	2.57	4.03	6.87	20	1.73	2.09	2.85	3.85
6	1.94	2.45	3.71	5.96	21	1.72	2.08	2.83	3.82
7	1.90	2.36	3.50	5.41	22	1.72	2.07	2.82	3.79
8	1.86	2.31	3.36	5.04	23	1.71	2.07	2.81	3.77
9	1.83	2.26	3.25	4.78	24	1.71	2.06	2.80	3.75
10	1.81	2.23	3.17	4.59	25	1.71	2.06	2.79	3.73
11	1.80	2.20	3.11	4.44	30	1.70	2.04	2.75	3.65
12	1.78	2.18	3.06	4.32	40	1.68	2.02	2.70	3.55
13	1.77	2.16	3.01	4.22	60	1.67	2.00	2.66	3.46
14	1.76	2.15	2.98	4.14	120	1.66	1.98	2.62	3.37
15	1.75	2.13	2.95	4.07	∞	1.65	1.96	2.58	3.29

D.f. = Degrees of freedom
∞ = infinity, same as the Standard Normal Distribution

Two sample t method

Capillary density example:

Common variance = 53.31, SD = 7.30 capillaries/mm^2, df = 19 + 23 − 2 = 40.

SE of difference = 2.26 capillaries/mm^2.

Difference (control − ulcer) = 34.08 − 22.59 = 11.49 capillaries/mm^2.

95% confidence interval for difference:

11.49 − ? × 2.26 to 11.49 + ? × 2.26.

? comes not from the Normal distribution but the t distribution with 40 degrees of freedom.

11.49 − 2.02 × 2.26 to 11.49 + 2.02 × 2.26
= 6.92 to 16.07 capillaries/mm^2.

Two sample t method

Capillary density example:

Common variance = 53.31, SD = 7.30 capillaries/mm^2, df = 19 + 23 − 2 = 40.

SE of difference = 2.26 capillaries/mm^2.

Difference (control − ulcer) = 34.08 − 22.59 = 11.49 capillaries/mm^2.

Test of significance, null hypothesis that in the population the difference between means = 0:

(difference − 0)/SE = 11.49/2.26 = 5.08.

If the null hypothesis were true, this would be an observation from the t distribution with 40 degrees of freedom.

Two sample t method

Capillary density example:

Test of significance, null hypothesis that in the population the difference between means = 0:

(difference − 0)/SE = 11.49/2.26 = 5.08.

If the null hypothesis were true, this would be an observation from the t distribution with 40 degrees of freedom.

From the table, the probability of such an extreme value is less than 0.001.

Using a computer program: P = 0.0000, which we write P<0.0001.
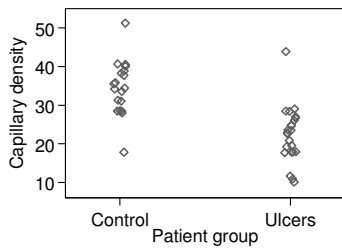
17

Two sample t method

Assumptions of two sample t method
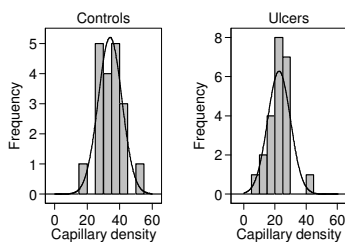
➢ Observations are independent.

➢ Distribution of capillary density follows a Normal distribution in each population.

➢ Variances are the same in each population.

Two sample t method

Assumptions of two sample t method

➢ Distribution of capillary density follows a Normal distribution in each population.

➢ Variances are the same in each population.

Two sample t method

Assumptions of two sample t method

➢ Distribution of capillary density follows a Normal distribution in each population.

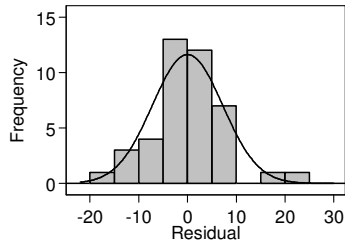➢ Variances are the same in each population.

Not enough observations to judge.

Two sample t method

Assumptions of two sample t method

Could combine the two graphs by subtracting the group mean from each observation to give **residuals**.
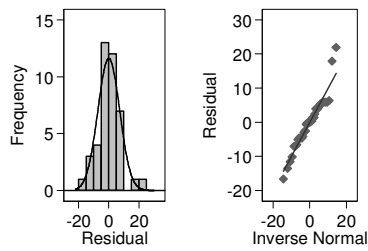
Residuals have mean = 0.

Looks fairly symmetrical, but few observations.

A better way: Normal plot.

Two sample t method

Example: capillary density

Distribution close to Normal.

Two sample t method

Example: capillary density

```
-----------------------------------------
                Controls    Ulcerated patients
-----------------------------------------
Number            19              23
Mean            34.08           22.59
SD               7.29            7.31
-----------------------------------------
```

Standard deviations very similar.

Two sample t method

Effect of deviations from assumptions

Methods using the t distribution depend on some strong assumptions about the distributions from which the data come.

In general for two equal sized samples the t method is very resistant to deviations from Normality, though as the samples become less equal in size the approximation becomes less good.

The most likely effect of skewness is that we lose power.

P values are too large and confidence intervals too wide.

We can usually correct skewness by a transformation.

Two sample t method

Effect of deviations from assumptions

If we cannot assume uniform variance, the effect is usually small if the two populations are from a Normal Distribution.

Unequal variance is often associated with skewness in the data, in which case a transformation designed to correct one fault often tends to correct the other as well.

If distributions are Normal, can use the Satterthwaite correction to the degrees of freedom.

Two sample t method

Unequal variances: Satterthwaite correction to the degrees of freedom.

If variances are unequal, we cannot estimate a common variance.

Instead we use the large sample form of the standard error of the difference between means. We replace the t value for confidence intervals by t with fewer degrees of freedom.

Degrees of freedom depend on the relative sizes of the variances. The larger variance dominates and if one is much larger than the other the degrees of freedom for that group are the only degrees of freedom.

Two sample t method

Unequal variances: Satterthwaite correction to the degrees of freedom.

For the capillary density example:

Degrees of freedom: 40 (= 19 + 23 − 2)

Satterthwaite's degrees of freedom: 38.56

We round this down to 38 to use the t table.

Equal variances: 95% CI = 6.92 to 16.07, P<0.0001.
Unequal variances: 95% CI = 6.91 to 16.07, P<0.0001.

N.B. Satterthwaite's method is an approximation for use in unusual circumstances. The equal variance method is the standard t test.

More than two groups

One way analysis of variance (anova)

We shall omit this.

Assumptions as for two sample t test, whatever the sample size.