Statistics at Square One

XII—The t tests (continued)

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(2) Difference of sample mean from population mean

Estimations of plasma calcium concentration in Dr Pink's 18 patients with Everley's syndrome gave a mean of 3.2 mmol/l, with standard deviation 1.1. Previous experience from a number of investigations and published reports had shown that the mean was commonly close to 2.5 mmol/l in healthy people aged 20-44, the age range of Dr Pink's patients. Is the mean in his patients abnormally high?

We set the figures out as follows:

Mean of general population, μ 2.5 mmol/l
 Mean of sample, $\bar{x}$ 3.2 mmol/l
 Standard deviation of sample, SD 1.1 mmol/l
 Standard error of sample mean, $SD/\sqrt{n} = 1.1/\sqrt{18}$ 0.26 mmol/l
 Difference between means, $\mu - \bar{x} = 2.5 - 3.2$ -0.7 mmol/l
 t = difference between means divided by standard

$$\text{error of sample mean } \frac{\mu - \bar{x}}{SD/\sqrt{n}} = \frac{-0.7}{0.26} = -2.69$$

Degrees of freedom, $n - 1 = 18 - 1 = 17$.

Ignoring the sign of the t value, and entering table 11.1 at 17 degrees of freedom, we find that 2.69 comes between probability values of 0.02 and 0.01, in other words between 2% and 1%. It is therefore unlikely that the sample with mean 3.2 came from the population with mean 2.5, and we may conclude that the sample mean is, at least statistically, unusually high. Whether it should be regarded clinically as abnormally high is something that needs to be considered separately by the physician in charge of that case.

(3) Difference between means of two samples

Here we apply a modified procedure for finding the standard error of the difference between two means and testing the size of the difference by this standard error (see Part VIII for large samples). For large samples we used the standard deviation of each sample, computed separately, to calculate the standard error of the difference between the means. For small samples we calculate a combined standard deviation for the two samples. The following example illustrates the procedure.

The addition of bran to the diet has been reported to benefit patients with diverticulosis. Several different bran preparations are available, and Dr Silver wants to test the efficacy of two of them on his patients, since favourable claims have been made for each. Among the consequences of administering bran that he wants to test is the transit time through the alimentary canal. Does it differ in the two groups of patients taking these two preparations of bran?

Dr Silver assumes the null hypothesis that there is no difference. By a random method he selects two groups of patients aged 40 to 64 with diverticulosis of comparable severity. Sample 1 contains 15 patients who are given treatment A, and sample 2 contains 12 patients who are given treatment B. The transit times of food through the gut are measured by a standard technique with marked pellets and the results are recorded, in order of increasing time, in table 12.1.

TABLE 12.1—Transit times in hours of marker pellets through alimentary canal of patients with diverticulosis on two types of treatment: unpaired comparison

Transit times in hours		
	Sample 1 Treatment A	Sample 2 Treatment B
	44	52
	51	64
	52	68
	55	74
	60	79
	62	83
	66	84
	68	88
	69	95
	71	97
	71	101
	76	116
	82	
	91	
	108	
Total	1026	1001
Mean	68.40	83.42

With treatment A the mean transit time was 68.40 h and with treatment B 83.42 h. What is the significance of the difference, 15.02 h?

The procedure is as follows:

Find the sum of the squares of the observations in sample 1 . . . Σx_1^2
 Find the sum of the squares of the observations in sample 2 . . . Σx_2^2
 Find the square of the total of the observations in sample 1 . . . $(\Sigma x_1)^2$
 Find the square of the total of the observations in sample 2 . . . $(\Sigma x_2)^2$
 Divide the square of the total of the observations in sample 1
 by the number in sample 1 $\frac{(\Sigma x_1)^2}{n_1}$

Divide the square of the total of the observations in sample 2
 by the number in sample 2 $\frac{(\Sigma x_2)^2}{n_2}$

For each sample find the sum of the squares of the difference from their respective means:

$$\Sigma(x_1 - \bar{x}_1)^2 = \Sigma x_1^2 - \frac{(\Sigma x_1)^2}{n_1}; \Sigma(x_2 - \bar{x}_2)^2 = \Sigma x_2^2 - \frac{(\Sigma x_2)^2}{n_2}$$

The square of the standard deviation (variance) for the two samples combined is now as follows:

$$\frac{\Sigma(x_1 - \bar{x}_1)^2 + \Sigma(x_2 - \bar{x}_2)^2}{(n_1 - 1) + (n_2 - 1)} = SD^2$$

The divisors $n_1 - 1$ and $n_2 - 1$ represent degrees of freedom. They are referred to briefly above and in these circumstances are 1 less than the total in the sample.

The standard error of the difference between the means is

$$SE \text{ diff} = \sqrt{\frac{SD^2}{n_1} + \frac{SD^2}{n_2}}$$

When the difference between the means is divided by this standard error the result is t .

$$\text{Thus } t = \frac{\bar{x}_1 - \bar{x}_2}{\sqrt{\frac{SD^2}{n_1} + \frac{SD^2}{n_2}}}$$

The table of the t distribution (table 11.1) is entered at $(n_1 - 1) + (n_2 - 1)$ degrees of freedom.

Dr Silver's figures work out like this:

	Treatment A	Treatment B
n	= 15	12
Σx	= 1026	1001
$\bar{x}$	= 68.4	83.42
Σx^2	= 73978	86921
$(\Sigma x)^2$	= 1052676	1002001
$\frac{(\Sigma x)^2}{n}$	= 70178.4	83500.083
$\Sigma(x - \bar{x})^2$	= 3799.6	3420.917
SD^2	$= \frac{3799.6 + 3420.917}{(15 - 1) + (12 - 1)} = 288.82$	

$$\begin{aligned} SE \text{ diff} &= \sqrt{\frac{288.82}{15} + \frac{288.82}{12}} \\ &= \sqrt{288.82 \left(\frac{1}{15} + \frac{1}{12} \right)} \\ &= 6.582 \\ t &= \frac{83.42 - 68.4}{6.582} = 2.282 \end{aligned}$$

The table of t distribution shows that at 25 degrees of freedom, that is $(15 - 1) + (12 - 1)$, when $t = 2.282$, it lies between 2.060 and 2.485. Consequently, $0.05 > P > 0.02$.

This degree of probability is just smaller than the conventional level of 5%. The null hypothesis that there is no significant difference between the means is therefore somewhat unlikely. There probably is a real difference on average between the alimentary transit times in patients on these two preparations of bran.

Exercise 12. In Dr Pink's 18 patients the mean level of plasma phosphate was 1.7 mmol/l, standard deviation 0.8. If the mean level in the general population is taken as 1.2 mmol/l, what is the significance of the difference between that mean and the mean in Dr Pink's patients? *Answer:* $t = 2.652$, $0.02 > P > 0.01$.

In two wards for elderly women in a geriatric hospital the following levels of haemoglobin were found: Ward A: 12.2, 11.1, 14.0, 11.3, 10.8, 12.5, 12.2, 11.9, 13.6, 12.7, 13.4, 13.7 g/dl; Ward B: 11.9, 10.7, 12.3, 13.9, 11.1, 11.2, 13.3, 11.4, 12.0, 11.1 g/dl. What is the difference between the mean levels in the two wards, and what is its significance? *Answer:* 0.56 g/dl; $t = 1.243$, $DF = 20$, $0.5 > P > 0.1$.

Today's Treatment

Diseases of the cardiovascular system

Hypertension—II

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Methyldopa

The use of low doses of methyldopa (500-750 mg/day) either alone or in combination with other drugs reduces the troublesome adverse effects, such as drowsiness, that occasionally limit its usefulness as a single drug used in high doses (2 g/day or more). The explanation of the mode of action has undergone considerable change. The main hypotensive action of methyldopa is now believed to be mediated through the action of a metabolite, perhaps α -methylnoradrenaline, on the central nervous system to stimulate central alpha-receptors rather than through peripheral effects. Methyldopa also lowers renin activity.

An appreciable reduction in blood pressure may be obtained within three to six hours in the bedfast patient if a high initial oral dose (750-1000 mg) is used. Such doses are rarely employed because rapid and dramatic reduction of blood pressure is indicated only in the severest grades of hypertension. Furthermore, the starting of methyldopa treatment is often delayed because it interferes with the estimation of catecholamines to show a false-positive reaction in the screening test for pheochromocytoma. Used in conventional doses (500-3000 mg/day) methyldopa reduces supine, erect, and post-exercise blood pressures. Few carefully controlled comparative studies have been carried out but it appears that the hypotensive efficacy is at least equivalent to that of beta-blockers, adrenergic neurone blockers, and clonidine. When added to other hypotensive agents a lower starting dose (375-500 mg/day) should be used and the dose of the other agent also reduced until the effectiveness of the combination can be assessed. If a further hypotensive effect is required or tolerance develops increases in doses are usually by 250 mg increments at intervals of two to three days, preferably at night because of possible sedation. Methyldopa is largely excreted by the kidney and smaller doses are recommended in renal insufficiency. A rise in blood urea may occur

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