

obstructive lung disease, severe cardiomegaly, mild cardiac failure, pregnancy, allergic rhinitis, diabetes mellitus, and sinus bradycardia. In these instances the potential benefits of beta-blockade must be weighed against the disadvantages.

Many adverse reactions have been associated with beta-blockers. Nausea, anorexia, and vomiting may be reduced by taking them before food. A rise in blood urea levels and deterioration in renal function have been reported as with other hypotensive agents. On the other hand, successful use of beta-blockers and a reduction in the plasma half life of propranolol have also been described in renal failure. The avoidance of high doses (say, over 400 mg propranolol or oxprenolol daily) may reduce the occurrence of symptoms of mild fatigue, lassitude, light-headedness, ataxia, anxiety, mental confusion, hallucinations, insomnia, vivid dreams, and a hypertensive response, which have been reported in some patients. In cold climates cold extremities, aggravation of Raynaud's phenomenon, and symptoms of peripheral vascular disease may be troublesome. Rashes have been reported with most agents. Several minor adverse reactions have also been described. In severe ischaemic heart disease withdrawal of beta-blockers should not be abrupt, as deaths from cardiac arrhythmia and myocardial infarction have been reported. The principal adverse drug interaction

concerns antidiabetic treatment. Signs of hypoglycaemia may be masked and the hypoglycaemic effects of concurrent treatment increased.

A validated case of the oculomucocutaneous syndrome associated with practolol treatment has not yet been reported with any other beta-blocker. Careful monitoring of patients on beta-blockers, particularly the newer agents, is required. The cause of the reaction has not been determined.

References

- ¹ Kannel, W B, and Dawber, T R, *British Journal of Hospital Medicine*, 1974, **11**, 508.
- ² Veterans Administration Co-operative Study Group, *Journal of the American Medical Association*, 1967, **202**, 1028.
- ³ Veterans Administration Co-operative Study Group, *Journal of the American Medical Association*, 1970, **203**, 1143.
- ⁴ Veterans Administration Co-operative Study Group, *Circulation*, 1972, **45**, 991.
- ⁵ Taguchi, J, and Freis, E D, *New England Journal of Medicine*, 1974, **291**, 329.
- ⁶ American Heart Association Report, *Circulation*, 1967, **36**, 980.

Statistics at Square One

XI—The t tests

T D V SWINSCOW

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Previously we have considered how to test the null hypotheses that there is no difference between the mean of a sample and the population mean, and no difference between the means of two samples. We obtained the difference between the means by subtraction, and then divided this difference by the standard error of the difference. If the difference is 1.96 times its standard error, or more, it is likely to occur with a frequency of only 1 in 20, or less. The probability attached to other ratios of the difference divided by the standard error appeared in table 7.1.

But with small samples, where more chance variation must be allowed for, these ratios are not entirely accurate. Some modification of the procedure of dividing the difference by its standard error is needed, and the technique to use is the *t* test. Its foundations were laid by W S Gossett under the pseudonym "Student,"¹ so that it is sometimes known as Student's *t* test. The procedure does not differ greatly from the one used for large samples, but it is preferable when the number of observations is fewer than about 60, and certainly when they amount to only 30 or less.

The application of the *t* distribution to four types of problem will now be considered:

(1) The mean and standard deviation of a sample are known (or can be calculated). What is the probability that the population

mean, which is unknown, lies within a certain range of the sample mean?

(2) The mean and standard deviation of a sample are known (or can be calculated) and a value is postulated for the mean of the population. How significantly does the sample mean differ from the postulated population mean?

(3) The means and standard deviations of two samples are known (or can be calculated). How significant is the difference between the means?

(4) Paired observations are made on two samples (or in succession on one sample). What is the significance of the difference between the means of the two sets of observations?

In each case the problem is essentially the same—namely, to establish multiples of standard errors to which probabilities can be attached. These multiples are the number of times a difference can be divided by its standard error. We have seen that with large samples 1.96 times the standard error has a probability of 5% or less, and 2.576 times the standard error a probability of 1% or less (table 7.1). With small samples these multiples of standard error are larger, and the smaller the sample the larger they become.

(1) Where does population mean lie?

A rare congenital disease, Everley's syndrome, generally causes a reduction in concentration of blood sodium. This is thought to provide a useful diagnostic sign as well as a clue to the efficacy of treatment. Little is known about the subject, but Dr Pink, who is director of a dermatological department in a London teaching hospital, is known to be interested in the

disease and has seen more cases than anyone else. Even so, he has seen only 18. The patients were all aged between 20 and 44.

From study of his 18 cases Dr Pink has found that their mean blood sodium concentration was 155 mmol/l, with standard deviation of 12 mmol/l. For future guidance where may one expect the mean to lie in cases of this disease? What are the 95% confidence limits within which the mean of the total population of such cases may be expected to lie?

Dr Pink's data are set out as follows:

Number of observations	18
Mean blood sodium concentration	115 mmol/l
Standard deviation	12 mmol/l
Standard error of mean	.. SD/ \sqrt{n} = 12/ $\sqrt{18}$ =	2.83 mmol/l

To find the 95% confidence limits above and below the mean we now have to find a multiple of the standard error. In large samples we have seen that the multiple is 1.96 (Part VII). For small samples we use the table of t . As the sample becomes smaller t becomes larger for any particular level of probability. Conversely, as the sample becomes larger t becomes smaller and approaches the values given in table 7.1, reaching them for infinitely large samples.

Since the size of the sample influences t it is taken into account in relating it to probabilities in the table. Some useful parts of the full t table appear in table 11.1. The left-hand column is headed DF for "degrees of freedom." The use of these was noted in the calculation of the standard deviation (Part III). In practice they amount in these circumstances to 1 less than the number of observations in the sample. With Dr Pink's data we have $18 - 1 = 17$. This is because only 17 observations plus the total number of observations are needed to specify the sample, the 18th being determined by subtraction.

To find the number by which we must multiply the standard error to give the 95% confidence limits we enter the table at 17 in the left-hand column and read across to the column headed 0.05. There the number 2.110 appears. The 95% confidence limits of the mean are now set as follows:

$$\begin{aligned} \text{Mean} + 2.110 \text{ SE} \\ \text{Mean} - 2.110 \text{ SE} \end{aligned}$$

Dr Pink's figures come out as follows:

$$\begin{aligned} 115 + (2.110 \times 2.83) &= 120.97 \text{ mmol/l} \\ 115 - (2.110 \times 2.83) &= 109.03 \text{ mmol/l} \end{aligned}$$

We therefore conclude that the chance of the population mean lying below 109.03 or above 120.97 mmol/l is only 5% or less.

Likewise from table 11.1 the 1% confidence limits of the mean are as follows:

$$\begin{aligned} \text{Mean} + 2.898 \text{ SE} \\ \text{Mean} - 2.898 \text{ SE} \end{aligned}$$

TABLE 11.1—Distribution of t

DF	Probability					
	0.5	0.1	0.05	0.02	0.01	0.001
1	1.000	6.314	12.706	31.821	63.657	636.619
2	0.816	2.920	4.303	6.965	9.925	31.598
3	0.765	2.353	3.182	4.541	5.841	12.941
4	0.741	2.132	2.776	3.747	4.604	8.610
5	0.727	2.015	2.571	3.365	4.032	6.859
6	0.718	1.943	2.447	3.143	3.707	5.959
7	0.711	1.895	2.365	2.998	3.499	5.405
8	0.706	1.860	2.306	2.896	3.355	5.041
9	0.703	1.833	2.262	2.821	3.250	4.781
10	0.700	1.812	2.228	2.764	3.169	4.587
11	0.697	1.796	2.201	2.718	3.106	4.437
12	0.695	1.782	2.179	2.681	3.055	4.318
13	0.694	1.771	2.160	2.650	3.012	4.221
14	0.692	1.761	2.145	2.624	2.977	4.140
15	0.691	1.753	2.131	2.602	2.947	4.073
16	0.690	1.746	2.120	2.583	2.921	4.015
17	0.689	1.740	2.110	2.567	2.898	3.965
18	0.688	1.734	2.101	2.552	2.878	3.922
19	0.688	1.729	2.093	2.539	2.861	3.883
20	0.687	1.725	2.086	2.528	2.845	3.850
21	0.686	1.721	2.080	2.518	2.831	3.819
22	0.686	1.717	2.074	2.508	2.819	3.792
23	0.685	1.714	2.069	2.500	2.807	3.767
24	0.685	1.711	2.064	2.492	2.797	3.745
25	0.684	1.708	2.060	2.485	2.787	3.725
26	0.684	1.706	2.056	2.479	2.779	3.707
27	0.684	1.703	2.052	2.473	2.771	3.690
28	0.683	1.701	2.048	2.467	2.763	3.674
29	0.683	1.699	2.045	2.462	2.756	3.659
30	0.683	1.697	2.042	2.457	2.750	3.646
40	0.681	1.684	2.021	2.423	2.704	3.551
60	0.679	1.671	2.000	2.390	2.660	3.460
120	0.677	1.658	1.980	2.358	2.617	3.373
∞	0.674	1.645	1.960	2.326	2.576	3.291

Table 11.1 is taken by permission of the authors and publishers from table III of Fisher and Yates: *Statistical Tables for Biological, Agricultural and Medical Research*, published by Longman Group Ltd, London (previously published by Oliver & Boyd, Edinburgh).

Dr Pink's figures have the following limits at the 1% probability level:

$$\begin{aligned} 115 + (2.898 \times 2.83) &= 123.20 \\ 115 - (2.898 \times 2.83) &= 106.80 \end{aligned}$$

Reference

- "Student," *Biometrika*, 1908, 6, 1.

Exercise 11. In 22 patients with an unusual liver disease the plasma alkaline phosphatase was found in a certain laboratory to have a mean value of 39 King-Armstrong units, standard deviation 3.4 units. What are the 95% confidence limits within which the mean of the population of such cases whose specimens come to the same laboratory may be expected to lie? *Answer:* 37.5 and 40.5.

In the last four years I have seen three cases of chickenpox in children in which they have developed a strikingly severe bilateral parotitis when they were in the convalescent stage of the chickenpox. Clinically the picture was of mumps in each case and this was diagnosed. Is this a recognised combination?

I have never heard of an association between chickenpox and parotitis and could find no reference to it in 10 textbooks on infectious diseases. Perhaps these cases were just coincidences, and the children also had mumps. Chickenpox may cause lymph node enlargement. Are you sure that the swelling really was parotitis?

What is the legal responsibility of the parents and the maternity hospital when the parents refuse to take their mongol baby home?

The hospital has a legal duty to care for the abandoned child until the local authority assumes this responsibility. A parent legally liable to maintain a child is deemed to have neglected him if he has failed to

provide adequate food, clothing, medical aid, or lodging.¹ Conviction of breach of this duty may lead to a fine or imprisonment. By leaving the child in hospital, however, the parents can hardly be said to have neglected him within the meaning of the Act, making prosecution unlikely. The hospital staff will have tried to persuade the parents to take the child home if this is considered to be in his best interests, but if the parents refuse the staff should report the case to the local social service department. Every local authority must make available advice, guidance, and help to promote the welfare of children.² If a child is abandoned by his parents the local authority is obliged to receive him into its care if this is thought to be necessary in the interests of his welfare.³ In the eyes of the law, a child is in need of care if he is likely to suffer unnecessarily through not receiving such care, protection, and guidance as a good parent may reasonably be expected to give.⁴ After the child has been taken into care by the usual procedures, the parents may be ordered to pay towards the cost of his care.⁴

¹ *The Children and Young Persons Act 1933*. London, HMSO, 1933.

² *The Children and Young Persons Act 1963*. London, HMSO, 1963.

³ *The Children Act 1948*. London, HMSO, 1948.

⁴ *The Children and Young Persons Act 1969*. London, HMSO, 1969.