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Author(s): C. W. Dunnett

Source: Biometrics, Vol. 20, No. 3 (Sep., 1964), pp. 482-491

Published by: International Biometric Society Stable URL: http://www.jstor.org/stable/2528490

Accessed: 12/11/2008 10:21

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NEW TABLES FOR MULTIPLE COMPARISONS WITH A CONTROL

C. W. DUNNETT

Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y., U. S. A.

1. INTRODUCTION

Some time ago, a multiple comparison procedure for comparing several treatments simultaneously with a control or standard treatment was introduced by the present author (Dunnett [1955]). The procedure was designed to be used either to test the significance of the differences between each of the treatments and the control with a stated value 1-P for the *joint* significance level, or to set confidence limits on the true values of the treatment differences from the control with a stated value P for the *joint* confidence coefficient. Thus the procedure has the property of controlling the experimentwise, rather than the per-comparison, error rate associated with the comparisons, in common with the multiple comparison procedures of Tukey [unpublished] and Scheffé [1953].

In the earlier paper, tables were provided enabling up to nine treatments to be compared with a control with joint confidence coefficient either .95 or .99. Tables for both one-sided and two-sided comparisons were given but, as explained in the paper, the two-sided values were inexact for the case of more than two comparisons as a result of an approximation which had to be made in the computations.

The main purpose of the present paper is to give the exact tables for making two-sided comparisons. The necessary computations were done on a General Precision LGP-30 electronic computer, by a method described in section 3 below. The tables are given here as Tables II and III; these replace Tables 2a and 2b, respectively, of the previous paper. In addition to providing the exact values, a method is given for adjusting the tabulated values to cover the situation where the variance of the control mean is smaller than the variance of the treatment means, as occurs for example when a greater number of observations is allocated to the control than to any of the test treatments. Furthermore, the number of treatments which may be simultaneously compared with a control has been extended to twenty.

Comparisons between treatments and a control or standard are of frequent interest in biological experimentation. Whether in a particular situation of this type a multiple comparison procedure is required depends on the error rate of concern to the investigator; for a discussion, see Steel [1961]. In a screening-type experiment, in which each treatment is to be individually reported regarding the outcome of the experiment, a per-comparison error rate seems to be clearly in order and hence a multiple comparison procedure is in no way pertinent. On the other hand, if the experiment is to be reported as a unit and more attention is likely to be paid to the particular differences which turn out to be most striking, for example to those treatments which differ most from the control, then any significance or confidence statement concerning the treatment differences should take this into account. In the following section, an example is presented to show how the present procedure may be used to do this.

2. ILLUSTRATIVE EXAMPLE

In this section, we will illustrate the use of this multiple comparison procedure in making significance tests between a set of treatments and a control. As mentioned above, the procedure can also be used for making confidence statements; for an illustration of the latter, the reader is referred to the earlier paper.

The example to be considered is concerned with the effect of certain drugs on the fat content of the breast muscle in cockerels. In the experiment performed, 80 cockerels were divided at random into four treatment groups. The birds in group A were the untreated controls, while groups B, C and D received, respectively, stilbesterol and two levels of acetyl enheptin in their diets. Birds from each group were sacrificed at specified times for the purpose of making certain measurements. One of these was the fat content of the breast muscle and these data are shown in Table I below.

Also shown in Table I is the analysis of variance of the data. Strictly speaking, an analysis of variance is not a necessary part of the multiple comparisons procedure, but it is a convenient way to calculate the error variance which is required and, in the present example, it serves also to justify comparing the treatment groups on the basis of their over-all mean values, in view of the absence of an indication of an interaction between treatments and sacrifice times. (However, the contribution to this interaction from the difference between group C and the controls, though not significant, may be high enough to cause

I am indebted to Dr. G. Tonelli, Experimental Therapeutics Research, Lederle Laboratories, for allowing me to use the data from this experiment.

TABLE I

NUMERICAL DATA ON FAT CONTENT OF BREAST MUSCLE IN

COCKERELS ON DIFFERENT TREATMENTS

		Percenta	ige Fat of	Fresh Tis	sue	
~		T	reatment	Group		
Sacrifice Time	A (contro	ols)	В	\mathbf{C}	D	Sums
1 week	2.84		2.43	1.95		
	2.49		1.85	2.67	2.20	
	2.50		2.42	2.23	2.32	
	2.42		2.73	2.31	2.79	
	2.61		2.07	2.53	2.94	
	12.86	1	11.50	11.69	$\overline{13.46}$	49.51
3 weeks	2.23		2.83	2.32	2.45	
	2.48		2.59	2.36	2.49	
	2.48		2.53	2.46	2.95	
	2.23		2.73	2.04	2.05	
	2.65		2.26	2.30	2.31	
	12.07]	12.94	11.48	$\phantom{00000000000000000000000000000000000$	48.74
5 weeks	2.30		2.50	2.25	2.53	
	2.30		1.84	2.45	2.03	
	2.38		2.20	2.52	2.45	
	2.05		2.31	1.90	2.34	
	2.13		2.20	2.19	1.92	
	11.16	-	11.05	11.31	11.27	44.79
7 weeks	2.41		2.48	2.96	2,15	
	2.46		1.46	2.05	2.63	
	3.17		2.96	1.60	2.38	
	2.87		2.73	1.47	2.93	
	2.86		2.84	2.23	2.80	
	13.77		12.47	10.31	12.89	49.44
Sums	49.86		47.96	44.79	49.87	192.48
\mathbf{Means}	2.493		2.398	2.24	0 2.494	
Source of	and a tion	Ano	alysis of V		Mean square	F-ratio
Treatmen		a.j. 3	0.86	-	.2867	2.64
Sacrifice t		э 3	0.30		.2525	2.33
	$ts \times Times$	9	1.19		.1323	$\frac{2.33}{1.22}$
		-				
Residual		64	6.94		.1086	1.22

some concern; also, Tukey's [1949] test for non-additivity approaches significance. The low mean value for group C at seven weeks appears to be the cause, rather than anything that might be remedied by a transformation of the data.)

The main comparisons of interest to the experimenter are between each of the three treatments and the control. The one differing most from the control is treatment C. To test the significance of this treatment difference, we calculate a Student t-statistic in the usual way. On the assumption that the four treatment groups have homogeneous variances, and following the 'fixed effects' model of the analysis of variance which dictates the use of the residual mean square to estimate the error variance, we obtain for the t-statistic

$$t = \frac{\bar{X}_t - \bar{X}_c}{s\sqrt{(1/n_t) + (1/n_c)}} = \frac{2.240 - 2.493}{\sqrt{.1086}\sqrt{2/20}} = -2.43.$$
 (1)

However, to allow for the fact that we have selected the most extreme of three treatment differences, we refer to the p=3 column of Table II or Table III instead of the usual Student t-tables (the values of the latter appear in the p=1 column of the tables). For 64 degrees of freedom, the critical values are seen to be 2.41 for the .05 significance level and 3.02 for the .01 level. Thus we can state that this treatment differs significantly from the control at the .05 probability level. The other two treatment differences can be tested in the same way, using the same critical values, but it is obvious in this example that neither of them is significant.

Hence we have found one statistically significant difference from the control (group C), and it is a bit surprising that it should be this group, since group D which received the same drug at twice the dose does not show any apparent difference from the control. Whether one should conclude in this instance that a real treatment effect has been demonstrated, which for some reason is not manifested at the higher dose level, would depend on the experimenter's prior knowledge regarding the properties of this particular drug together with his assessment of the likelihood of the observed effect's being due to a chance occurrence or a flaw in the conduct of the experiment. Had the significance test been performed using the usual tables of Student's t, the treatment effect would have appeared to be more significant than it really is, since the value of t calculated in (1) above actually exceeds the 2% critical value of Student's t.

If the sacrifice times had corresponded to 'blocks' of some sort which would have to be considered as a random rather than a fixed effect, the analysis of variance model would be of the 'mixed' type. This would call for the interaction mean square as the proper error variance for the treatment comparisons. The multiple comparisons test between treatments and control could be applied using the formula in (1), but with the interaction mean square to estimate the variance,

$$t = \frac{\bar{X}_t - \bar{X}_c}{s\sqrt{(1/n_t) + (1/n_c)}} = \frac{2.240 - 2.493}{\sqrt{.1323}\sqrt{2/20}} = -2.20,$$

and of course the tables should be entered with the degrees of freedom associated with interaction.

Another point to be noted concerning the analysis of this example is the assumption that the four groups have the same variance. In many situations, this assumption is quite reasonable; however, in the present example, the within groups variance for the control turns out to be significantly smaller than for the three treatments. If one is unwilling to accept the assumption of equal variances in these circumstances, separate control and treatment variances could be estimated from the data and a t-statistic calculated using the formula appropriate for comparing two groups with unequal variances instead of (1). In this example, we would obtain $s_c^2 = .0448$ (16 d.f.) and $s_t^2 = .1298$ (48 d.f.) for the two variances, and the appropriate t-statistic would be

$$t = \frac{\bar{X}_t - \bar{X}_c}{\sqrt{(s_t^2/n_t) + (s_c^2/n_c)}} = \frac{2.240 - 2.493}{\sqrt{(.1298 + .0448)/20}} = -2.71.$$

Following the method of Cochran and Cox (see Anderson and Bancroft [1952], p. 52), the number of degrees of freedom to be associated with this statistic is the weighted average of the degrees of freedom associated with the two variances, using s_t^2/n_t and s_c^2/n_c as weights. The result in this instance is 40 d.f., and entering Table II with p=3 and d.f. = 40, we find that 2.44 is the .05 critical value. This value should, however, be adjusted for the unequal variances as described in the next part of this section, by calculating $1 - n_t s_c^2/n_c s_t^2 = .655$, which when multiplied by the superscript number on the value taken from Table II gives the percentage increase required in the critical value (.655 \times 2.2 = 1.4% is the percentage increase, so the correct critical value is $1.014 \times 2.44 = 2.47$).

Allocating more observations to the control.

In the example described, the experiment was designed to provide equal numbers of observations on the control and on each treatment. In this case, assuming homogeneous variances, the critical values of t are read directly from the table. If, however, relatively more observations are provided on the control than on any of the test treatments,

the critical values of t require some adjustment. This may be done through the use of the numbers shown as superscripts in the tables.

The method of adjusting the critical values of t when more observations have been allocated to the control is as follows. Calculate $1 - n_t/n_c$, where n_t and n_c are the numbers of observations on the treatment and on the control, respectively, and multiply the resulting fraction by the superscript on the appropriate value of t in the table. The result represents the percentage by which the tabular value of t should be increased to allow for the greater number of observations on the control. (More generally, calculate $1 - \sigma_c^2/\sigma_t^2$ where σ_c^2 is the variance of the control mean and σ_t^2 the variance of each treatment mean; this reduces to $1 - n_t/n_c$ when the variance per observation is the same in each group.)

For example, suppose the 80 cockerels had been allocated 32 to the control and 16 to each treatment group, in which case $1 - n_t/n_c = 0.5$. Then the percentage increase required in the tabular value of t is (0.5)(2.1) = 1.1%, making the correct critical value (1.011)(2.41) = 2.44, for the .05 significance level.

Although a slight increase in the critical value of t is entailed, there is a gain achieved by the allocation of relatively more observations to the control as a result of the decrease in the standard error of the treatment difference which appears in the denominator of (1). To achieve the optimum gain, the ratio n_c/n_t should be taken to be approximately equal to the square root of the number of treatments.

3. CONSTRUCTION OF THE TABLES

The method of determining the tabular values of t in Tables II and III was essentially the same as that used previously to compute the one-sided tables, except that no previously computed tables were available for the two-sided case so that the entire calculations had to be done by machine. This involved the numerical evaluation of a double integral expression of the type shown as formula (7.2) in Gupta and Sobel [1957]. For each value of p shown in the tables and for d.f. = 5, 10, 20 and ∞ , this double integral expression was evaluated numerically for three successive values of t differing by 0.05 such that the desired value of P was bracketed. Then the value of t was determined by fitting a 3-point curve and the result checked by direct computation of the value of P. For the intermediate degrees of freedom, the tabular values were obtained by interpolation using the reciprocal of the degrees of freedom as argument. The results obtained were rounded to the two decimal places shown in the tables and should be correct to this number of places.

Table of t for Two-Sided Comparisons Between p Treatments and a Control for a Joint Confidence Coefficient of P=95%TABLE II

1	ı																						
	20	4.429.4	$4.11^{9.0}$	3.918.6	3.768.2	3.657.9	3.571.1	3.507.5	3.457.8	$3.40^{7.1}$	3.367.0	3.336.8	3.306.7	3.276.6	3.256.6	3.236.4	3.226.3	3.166.0	3.115.8	$3.06^{5.5}$	3.005.1	2.954.8	2.914.5
	15	4.268.7	3.978.2	3.787.8	3.647.5	3.537.2	3.457.0	3.396.8	$3.34^{6.6}$	3.296.5	3.266.3	3.236.2	$3.20^{6.1}$	$3.18^{6.0}$	$3.16^{5.9}$	$3.14^{5.8}$	3.125.7	3.075.5	$3.02^{5.2}$	2.975.0	2.924.7	2.874.4	2.834.1
	12	4.148.0	3.867.8	3.677.2	$3.54^{6.9}$	3,446.7	3.366.5	$3.30^{6.3}$	$3.25^{6.1}$	3.216.0	3.185.8	3.155.7	3.125.6	$3.10^{5.5}$	3.085.4	3.065.4	3.055.3	3.005.1	2.954.8	2.904.6	2.864.4	2.814.1	2.773.8
	11	4.097.8	3.817.4	$3.63^{7.0}$	$3.50^{6.7}$	$3.40^{6.5}$	3.334.2	$3.27^{6.1}$	3.225.9	3.185.8	$3.14^{5.6}$	3.125.5	3.095.4	3.075.3	$3.05^{5.3}$	3.035.2	3.025.1	2.974.9	2.924.7	2.874.5	2.834.2	2.794.0	2.743.7
ve control)	10	4.037.5	3.767.1	3.586.7	3.466.5	3.366.2	3.296.0	3.235.8	3.185.7	3.145.5	3.115.4	3.085.3	3.065.2	3.035.1	3.015.1	$3.00^{5.0}$	2.984.9	2.944.7	2.894.5	2.854.3	2.804.1	2.763.8	2.723.6
cluding th	6	3.977.2	3.716.8	3.536.5	3.416.2	3.325.9	3.245.7	3.195.6	3.145.4	$3.10^{5.3}$	3.075.2	3.045.1	3.025.0	3.004.9	2.984.8	2.964.8	2.954.7	2.904.5	2.864.3	2.814.1	2.773.9	2.733.7	2.693.5
= number of treatment means (excluding the control)	∞	3.906.8	$3.64^{6.4}$	3.476.1	3.355.9	3.265.6	3.195.4	3.145.3	3.095.1	3.065.0	3.024.9	3.004.8	2.974.7	2.954.7	2.944.6	2.924.5	2.904.5	2.864.3	2.824.1	2.773.9	2.733.7	2.693.5	2.653.3
reatment	7	3.826.4	$3.57^{6.0}$	3.415.7	3.295.5	$3.20^{5.3}$	3.145.1	3.084.9	$3.04^{4.8}$	3.004.7	2.974.6	2.954.6	2.924.4	2.904.4	2.894.3	2.874.2	2.864.2	2.814.0	2.773.9	2.733.7	2.693.5	2.653.3	$2.61^{3.1}$
umber of t	9	3.735.9	$3.49^{5.6}$	3.335.3	3.225.1	$3.14^{4.9}$	3.074.7	3.024.6	2.984.4	2.944.3	2.914.2	2.894.2	2.874.1	2.854.0	2.834.0	2.813.9	2.803.9	2.763.7	2.723.6	2.683.4	$2.64^{3.3}$	2,603.1	2.572.9
u = d	ಬ	3.625.4	$3.39^{5.0}$	$3.24^{4.8}$	3.134.5	3.054.4	2.994.2	$2.94^{4.1}$	2.904.0	2.873.9	2.843.8	2.823.8	2.803.7	2.783.6	2.763.6	2.753.5	2.733.5	2.703.4	2.663.2	2.623.1	2.583.0	2,552.8	$2.51^{2.7}$
	4	3.484.6	3.264.3	3.124.1	3.023.9	2.953.8	2.893.6	2.843.5	2.813.4	2.783.4	2.753.3	2.733.2	2.713.2	2.693.1	2.683.1	$2.66^{3.1}$	2,653.0	$2.61^{2.9}$	2,582.8	$2.54^{2.7}$	$2.51^{2.6}$	2,472.5	2.442.3
	က	3.293.6	$3.10^{3.4}$	2.973.2	2.883.1	2.813.0	2.762.9	$2.72^{2.8}$	2.682.7	2.652.7	$2.63^{2.6}$	2.612.6	2.592.5	2.582.5	2.562.5	$2.55^{2.5}$	2.542.4	2.512.3	2.472.3	2,442.2	$2.41^{2.1}$	2.382.0	2.351.9
	83	3.032.3	$2.86^{2.1}$	$2.75^{2.0}$	2.672.0	2.611.9	2.571.8	2.531.8	2.501.7	2,481.7	2.461.7	2.441.7	2.421.6	2.411.6	2,401.6	2.391.6	2,381.6	2,351.5	2.321.5	2,291.4	2.271.4	2.241.3	2.211.3
	H	2.57	2.45	2.36	2.31	2.26	2.23	2.20	2.18	2.16	2.14	2.13	2.12	2.11	2.10	2.09	2.09	2.06	2.04	2.03	2.00	1.98	1.96
	d.f.	70	9	_	∞	- О	10	11	12	13	14	15	16	17	18	19	20	24	30	40	09	120	8

plied by $(1-2\rho)/(1-\rho)$ or $1-n_t/n_c$, gives the percentage increase required in the critical value of t valid for .125 $< \rho <$.5 or $n_c/n_t > 1$.

Table of t for Two-Sided Comparisons Between p Treatments and a Control for a Joint Confidence Coefficient of P=99%TABLE III

d.f.	1	7	က	4	ಒ	9	7	∞	6	10	11	12	15	20
2	4.03	4.631.8	4.983.0	5.223.9	5.414.6	5.565.2	5.695.7	5.806.1	5.896.5	5.986.9	6.057.2	6.127.4	6.308.1	6.529.0
9	3.71	$4.21^{1.6}$	$4.51^{2.7}$	4.713.5	4.874.1	5.004.6	$5.10^{5.1}$	$5.20^{6.5}$	5.285.8	5.356.1	5.416.4	5.476.7	5.627.3	5.818.1
^	3.50	3.951.5	4.212.4	4.393.1	4.533.7	4.644.2	4.744.6	4.825.0	4.895.3	4.955.6	5.016.8	5.066.1	5.196.7	5.367.4
∞	3.36	3.771.3	$4.00^{2.2}$	4.172.9	4.293.4	4.403.9	4.484.2	4.564.6	4.624.9	4.685.1	4.735.4	4.785.6	4.906.1	5.056.9
6	3.25	$3.63^{1.2}$	3.852.1	$4.01^{2.7}$	4.123.2	4.223.6	4.303.9	4.374.2	4.434.5	4.484.8	$4.53^{6.0}$	4.575.2	4.685.7	4.826.4
10	3.17	$3.53^{1.2}$	3.741.9	3.882.5	3.993.0	4.083.4	4.163.7	4.224.0	4.284.2	4.334.5	4.374.7	4.424.9	4.525.4	4.656.0
11	3.11	$3.45^{1.1}$	$3.65^{1.8}$	3.792.4	$3.89^{2.8}$	3.983.2	4.053.5	4.113.8	4.164.0	4.214.2	4.254.4	4.294.6	4.395.1	4.526.7
12	3.05	3.391.1	3.581.7	3.712.3	3.812.7	3.893.0	3.963.3	4.023.6	4.073.8	4.124.0	4.164.2	4.194.4	4.294.8	4.415.4
13	3.01	3.331.0	3.521.7	$3.65^{2.2}$	3.742.6	3.822.9	3.893.2	3.943.4	3.993.6	4.043.8	4.084.0	4.114.2	4.204.6	4.326.2
14	2.98	3.291.0	3.471.6	$3.59^{2.1}$	3.692.5	3.762.8	3.833.0	3.883.3	3.933.5	3.973.7	4.013.9	4.054.0	4.134.4	4.245.0
15	2.95	3,250.9	3.431.5	$3.55^{2.0}$	3.642.4	3.712.7	3.782.9	3.833.2	3.883.4	3.923.6	3.953.7	3.993.9	4.074.3	4.184.8
16	2.92	$3.22^{0.9}$	3,391.6	$3.51^{1.9}$	$3.60^{2.3}$	3.672.6	$3.73^{2.8}$	3.783.1	3.833.3	3.873.4	3.913.6	3.943.8	4.024.1	4.134.6
17	2.90	$3.19^{0.9}$	3.361.5	$3.47^{1.9}$	$3.56^{2.2}$	3.632.5	3.692.7	3.743.0	3.793.2	3.833.3	3.863.5	3.903.6	3.984.0	4.084.5
18	2.88	3.170.9	3.331.4	$3.44^{1.8}$	$3.53^{2.2}$	$3.60^{2.4}$	$3.66^{2.7}$	3.712.9	$3.75^{3.1}$	3.793.2	3.833.4	3.863.5	3.943.9	4.044.4
19	2.86	$3.15^{0.9}$	3.311.4	$3.42^{1.8}$	$3.50^{2.1}$	3.572.4	3.632.4	3.682.8	3.723.0	3.763.2	3.793.3	3.833.4	$3.90^{3.8}$	4.004.3
20	2.85	3,130.8	3.291.4	3.401.7	3.482.1	3.552.3	3.602.5	3.652.7	3.692.9	3.733.1	3.773.2	3.803.4	3.873.7	3.974.2
24	2.80	3.070.8	3.221.3	3.321.6	3.401.9	$3.47^{2.1}$	3.522.4	3.572.8	$3.61^{2.7}$	$3.64^{2.8}$	3.683.0	3.703.1	3.783.4	3.873.8
30	2.75	$3.01^{0.7}$	$3.15^{1.2}$	$3.25^{1.5}$	3.331.8	3.392.0	$3.44^{2.2}$	3.492.3	$3.52^{2.5}$	3.562.6	$3.59^{2.7}$	$3.62^{2.8}$	3.693.1	3.783.5
40	2.70	$2.95^{0.7}$	3.091.1	$3.19^{1.4}$	3.261.6	$3.32^{1.8}$	3.372.0	$3.41^{2.1}$	3,442.3	3.482.4	3.512.5	3.532.6	$3.60^{2.8}$	3.683.2
09	2.66	2.900.6	3.031.0	$3.12^{1.3}$	$3.19^{1.5}$	3.251.6	3.291.8	3.331.9	3,372.0	$3.40^{2.1}$	3.422.2	$3.45^{2.3}$	3.512.5	3.592.8
120	2.62	2.850.6	2.970.9	3.061.1	$3.12^{1.3}$	3.181.5	3.221.6	3.261.7	3.291.8	3,321.9	$3.35^{2.0}$	3.372.1	3,432.2	3.512.5
8	2, 58	9.007.6	9.000.6	3 001.0	2 081.2	0 111 2		2			1			

plied by $(1-2\rho)/(1-\rho)$ or $1-n_t/n_o$, gives the percentage increase required in the critical value of t valid for .125 $< \rho <$.5 or $n_o/n_t > 1$.

If there are more observations on the control than on any test treatment, or if for any other reason the variance of the control mean is smaller than the variance of the treatment means, the effect is to alter the correlation coefficient between the treatment minus the control differences. This correlation coefficient is $\rho = \sigma_c^2/(\sigma_c^2 + \sigma_t^2)$ where σ_c^2 and σ_t^2 are the respective variances of the control and treatment means; when the variances are homogeneous this becomes $n_t/(n_c + n_t)$ which takes the value $\frac{1}{2}$ when $n_c = n_t$ but is less than $\frac{1}{2}$ when $n_c > n_t$. In order to determine the effect of ρ on the value of t, the computations described in the preceding paragraph were done for $\rho = 0$, .125, .25, .375 and .50. It was found that over the range .125 $< \rho <$.50 the resulting values of t were very nearly linearly related to the reciprocal of $1-\rho$. This served as the basis for the method adopted for adjusting the tabular values of t. The numbers given as superscripts in the table actually represent 1.5 times the percentage increase of the critical value of t for $\rho = .25$ over the value for $\rho = .50$. By multiplying the value given in the superscript by $(1 - 2\rho)/(1 - \rho) = 1 - \sigma_c^2/\sigma_t^2$, or by $1 - n_t/n_c$ when the variances are homogeneous but the numbers of observations on control and treatment are different, an approximation is obtained for the percentage increase required in the tabular value of t which is accurate before rounding to one unit in the second decimal place over the range $.125 < \rho < .5$ (corresponding to a ratio n_c/n_t ranging as high as seven-fold). For $\rho = 0$ (corresponding to n_c/n_t approaching infinity), this method gives a value which is too high, but even then by only approximately three units at most in the second place before rounding. Thus for all practical purposes the method of adjusting the tabular value should be quite adequate.

ACKNOWLEDGEMENTS

The LGP-30 programs used in the computations were written by the author utilizing subroutines for the normal distribution written by R. A. Lamm. I wish to acknowledge my gratitude to R. A. Lamm and F. Ogden for their advice on the programming, and to F. Odgen and D. Dwyer for their help in performing the computations. Thanks are also due to R. M. DeBaun and to J. D. Haynes for helpful suggestions in connection with the analysis of the example.

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