

Exact Confidence Bounds for All Contrasts of Three or More Regression Lines



John D. Spurrier

Journal of the American Statistical Association, Vol. 94, No. 446. (Jun., 1999), pp. 483-488.

Stable URL:

<http://links.jstor.org/sici?sici=0162-1459%28199906%2994%3A446%3C483%3AECBFAC%3E2.0.CO%3B2-Z>

Journal of the American Statistical Association is currently published by American Statistical Association.

Your use of the JSTOR archive indicates your acceptance of JSTOR's Terms and Conditions of Use, available at <http://www.jstor.org/about/terms.html>. JSTOR's Terms and Conditions of Use provides, in part, that unless you have obtained prior permission, you may not download an entire issue of a journal or multiple copies of articles, and you may use content in the JSTOR archive only for your personal, non-commercial use.

Please contact the publisher regarding any further use of this work. Publisher contact information may be obtained at <http://www.jstor.org/journals/astata.html>.

Each copy of any part of a JSTOR transmission must contain the same copyright notice that appears on the screen or printed page of such transmission.

JSTOR is an independent not-for-profit organization dedicated to creating and preserving a digital archive of scholarly journals. For more information regarding JSTOR, please contact support@jstor.org.

Exact Confidence Bounds for All Contrasts of Three or More Regression Lines

John D. SPURRIER

It is desired to compare $k \geq 3$ treatments. Under the assumption of iid normal errors, it is well known that the Scheffé method produces exact simultaneous confidence bounds for all contrasts of the treatment means. Furthermore, it is known that the Scheffé method is conservative when one desires confidence bounds for a specific subset of contrasts of means. Exact methods, such as those due to Tukey and Dunnett, yield tighter bounds than the Scheffé method for specific subsets of contrasts of means. In this article, multiple comparisons of the k treatments are done not in terms of their means, but rather in terms of a parametric function. The parametric function of interest is the simple linear regression model, $E(Y|x)$. It is desired to find simultaneous confidence bounds for all contrasts of the k simple linear regression models. Although the Scheffé method can be used to find such bounds, this is extremely conservative. The union-intersection method is used to develop simultaneous confidence bounds for these contrasts under the assumption of equal design matrices for each treatment. The method is based on a pivotal quantity whose distribution function is a linear combination of F distribution functions. Thus probability points can be computed using standard computing packages. The Scheffé bounds are about 5% wider than the exact bounds for $k = 3$ and about 13% wider for $k = 6$.

KEY WORDS: Multiple comparison; Scheffé method; Simple linear regression; Simultaneous confidence; Union intersection.

1. INTRODUCTION

There is a wealth of literature on comparing the means of $k \geq 3$ groups under the assumption of iid normal errors. Major contributions to the area are due to Dunnett (1955, 1964), Scheffé (1959), and Tukey (1953), who developed simultaneous confidence intervals for all pairwise differences of means, all contrasts of means, and all pairwise differences with a control or standard treatment. Other authors have also made numerous contributions. Hochberg and Tamhane (1987) and Hsu (1996) provided excellent summaries of this literature. The Scheffé method, which is derived by inverting an F test for a hypothesis involving the general linear model parameter vector, is applicable to a wider range of problems than multiple comparisons of univariate means.

At times, one wishes to compare $k \geq 3$ groups based on some parametric function other than the mean. For example, Masuda, Saito, and Inui (1997) studied the effects of three treatments on the accumulation of the chemotherapy agent [^3H]methotrexate in rat renal tissue as a function of time. The agent is eliminated from the body through urine. Failure to accumulate enough of the agent in the kidneys can lead to possible toxicity. Figure 1 suggests a linear relationship between accumulation and time for each treatment in the time interval used in the study. Comparison of the three treatments involves performing multiple comparisons of the regression models.

In this article I restrict attention to multiple comparisons for all contrasts of simple linear regression lines under the assumptions that the errors are iid $N(0, \sigma^2)$ and that the same design matrices are used for the k groups. Although these assumptions are too restrictive for many applications, this article demonstrates the need to develop new multi-

ple comparison procedures as one moves from comparing means to comparing more complicated parametric functions.

The model for the n observations from the i th group is

$$Y_{ij} = \alpha_i + \beta_i x_j + \varepsilon_{ij} \quad (1)$$

for $i = 1, \dots, k$ and $j = 1, \dots, n$. Define the n -dimensional vectors $\mathbf{1} = (1, \dots, 1)'$ and $\mathbf{x} = (x_1, \dots, x_n)'$. Without loss of generality, assume that the predictor variable values have been centered and scaled such that $\mathbf{x}'\mathbf{1} = 0$ and $\mathbf{x}'\mathbf{x} = 1$. Let $\hat{\alpha}_i$ and $\hat{\beta}_i$ denote the least squares estimators of α_i and β_i , $i = 1, \dots, k$. Let $\hat{\sigma}^2$ denote the pooled error mean square with $\nu = k(n-2)$ df, let $\bar{\alpha}$ and $\bar{\beta}$ denote the sample means of the $\hat{\alpha}_i$'s and $\hat{\beta}_i$'s, and let C denote the set of vectors $\mathbf{c} = (c_1, \dots, c_k)$ such that

$$\sum_{i=1}^k c_i = 0.$$

Using the traditional form of the point estimate plus or minus a probability point times the estimated standard error, the $100(1 - \alpha)\%$ simultaneous confidence bounds are

$$\sum_{i=1}^k c_i(\alpha_i + \beta_i x) \in \sum_{i=1}^k c_i(\hat{\alpha}_i + \hat{\beta}_i x) \pm b\hat{\sigma} \left[(1/n + x^2) \sum_{i=1}^k (c_i^2) \right]^{1/2} \quad (2)$$

for all \mathbf{c} in C and all real x , where b is a probability point that depends on k , ν , and α . The primary results of this article are an algorithm for computing b for exact simultaneous confidence bounds and a comparison of the exact simultaneous confidence bounds to the existing Scheffé bounds. Although Scheffé's method yields exact simultaneous confidence bounds for all contrasts of means, I show that the

John D. Spurrier is Professor, Department of Statistics, University of South Carolina, Columbia, SC 29208 (E-mail: spurrier@stat.sc.edu). The author thanks Ken-ichi Inui of Kyoto University for providing the example data and the editor, associate editor, and two referees for helpful comments.

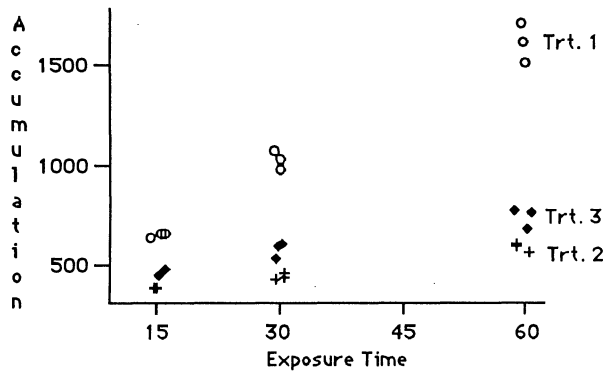


Figure 1. Accumulation of $[^3\text{H}]$ Methotrexate (fmol/mg protein) Versus Exposure Time (m) With Three Treatments.

Scheffé confidence bounds for all contrasts of regression lines are extremely conservative.

In Section 2 the union-intersection method is used to determine the appropriate pivotal quantity, an algorithm is developed for computing b , and a table of probability points is presented. The exact and Scheffé bounds are compared in Section 3. The Masuda et al. (1997) $[^3\text{H}]$ methotrexate data are used to illustrate the exact bounds in Section 4. Concluding remarks are given in Section 5. Most derivations are given in the Appendix.

2. DETERMINATION OF THE PROBABILITY POINT

For each \mathbf{c} in C and each real x , define the random variable

$$T_{\mathbf{c},x} = \frac{\sum_{i=1}^k c_i[(\hat{\alpha}_i - \alpha_i) + (\hat{\beta}_i - \beta_i)x]}{\hat{\sigma}[(1/n + x^2) \sum_{i=1}^k (c_i^2)]^{1/2}}. \quad (3)$$

By the union-intersection principle, the constant b is the solution to the equation

$$P(|T_{\mathbf{c},x}| \leq b \quad \forall \text{ real } x \text{ and } \forall \mathbf{c} \text{ in } C) = 1 - \alpha \quad (4)$$

or, equivalently, the positive solution to

$$P[\sup(T_{\mathbf{c},x}^2) \leq b^2] = 1 - \alpha, \quad (5)$$

where the supremum is taken over \mathbf{c} in C and all x . Inverting (5) yields the exact $100(1 - \alpha)\%$ simultaneous confidence bounds in (2).

I now derive a closed-form expression for $\sup(T_{\mathbf{c},x}^2)$. Let

$$Z_{1i} = n^{1/2}(\hat{\alpha}_i - \alpha_i)/\sigma$$

and

$$Z_{2i} = (\hat{\beta}_i - \beta_i)/\sigma \quad \text{for } i = 1, \dots, k. \quad (6)$$

Under the design constraints, these random variables are iid standard normal. Let \bar{Z}_1 and \bar{Z}_2 denote the sample means of the Z_{1i} 's and the Z_{2i} 's. Theorem 1 gives a closed-form expression for $\sup(T_{\mathbf{c},x}^2)$. The proof is given in the Appendix.

Theorem 1. The pivotal quantity $\sup(T_{\mathbf{c},x}^2) = Q/(\hat{\sigma}^2/\sigma^2)$, where

$$Q = \{Q_{11} + Q_{22} + [4R^2Q_{11}Q_{22} + (Q_{22} - Q_{11})^2]^{1/2}\}/2,$$

with $Q_{jj'} = \sum_{i=1}^k (Z_{ji} - \bar{Z}_j)(Z_{j'i} - \bar{Z}_{j'})$, j and $j' = 1, 2$, and $R = Q_{12}/[Q_{11}Q_{22}]^{1/2}$.

I now derive the distribution of $\sup(T_{\mathbf{c},x}^2)$. Under the design constraints, (Z_{11}, \dots, Z_{1k}) and (Z_{21}, \dots, Z_{2k}) are independent sets of k iid standard normal random variables. The variable $Q_{jj'}$ is the numerator of the sample variance of the j th set, $j = 1, 2$. The variable R is the sample correlation coefficient computed on (Z_{1i}, Z_{2i}) , $i = 1, \dots, k$. Moreover, the Z_{ji} 's depend on the original regression data only through the $\hat{\alpha}_i$'s and $\hat{\beta}_i$'s.

It follows from Anderson (1958, p. 154) and Graybill (1976) that Q_{11} , Q_{22} , $\nu(\hat{\sigma}^2/\sigma^2)$, and R are mutually independent. The first three variables have chi-squared distributions with $k - 1$, $k - 1$, and ν df. The density of R is

$$\frac{\Gamma[(k - 1)/2](1 - r^2)^{(k-4)/2}}{\Gamma[(k - 2)/2](\pi)^{1/2}} \quad \text{for } -1 \leq r \leq 1. \quad (7)$$

Theorem 2 shows that the distribution function of $\sup(T_{\mathbf{c},x}^2)$ is a linear combination of F distribution functions. There are different expressions for odd and even k . Let F_{ν_1, ν_2} denote the distribution function of the F distribution with ν_1 and ν_2 df and let $p_i = \prod_{j=1}^i (2j - 1)$ for positive integer i .

Theorem 2. For odd $k \geq 3$,

$$\begin{aligned} P[\sup(T_{\mathbf{c},x}^2) \leq b^2] &= \frac{k - 1}{2^{(k-1)/2}} F_{k-1, \nu}[2b^2/(k - 1)] \\ &\quad - \frac{\pi^{1/2} b^{k-2} \Gamma[(\nu + k - 2)/2]}{\Gamma[(k - 1)/2] \Gamma(\nu/2) \nu^{(k-2)/2} [1 + (b^2/\nu)]^{[(\nu+k-2)/2]}} \\ &\quad \times F_{1, \nu+k-2}[b^2(\nu + k - 2)/(b^2 + \nu)] \\ &\quad + \frac{1}{\Gamma[(k - 1)/2] 2^{(k-1)/2}} \\ &\quad \times \sum_{i=1}^{(k-5)/2} \frac{(k - 3 - 2i) \Gamma[(k - 1 + 2i)/2]}{p_i} \\ &\quad \times F_{k-1+2i, \nu}[2b^2/(k - 1 + 2i)], \end{aligned}$$

where the summation is defined to be 0 for $k = 3$ or 5. For even $k \geq 4$,

$$\begin{aligned} P[\sup(T_{\mathbf{c},x}^2) \leq b^2] &= \{\Gamma(k/2) 2^{(k-2)/2} [F_{k, \nu}(b^2/k) - F_{k-2, \nu}(b^2/(k - 2))]\} \\ &\quad + \sum_{i=1}^{(k-2)/2} \frac{\Gamma(k - 2 - i) i}{2^{(k-2)/2 - i} \Gamma(k/2 - i)} \\ &\quad \times F_{2(k-i-2), \nu}[b^2/(k - i - 2)]\} / p_{(k-2)/2}. \end{aligned}$$

The proof is given in the Appendix. As most statistical packages compute F distribution functions, it is easy to calculate $P[\sup(T_{\mathbf{c},x}^2) \leq b^2]$.

The probability point for the exact simultaneous intervals in (2) is found by solving (5) for $b > 0$. From Theorem 2, (5)

can be written as a nonlinear equation in b . This equation can be solved using root finding techniques. Table 1 gives values of b for $\alpha = .05$ and various n .

If $\alpha_1 = \alpha_2 = \dots = \alpha_k$ and $\beta_1 = \beta_2 = \dots = \beta_k$, then the random variable $\sup(T_{c,x}^2)$ equals the statistic

$$T^2 = \{S_{11} + S_{22} + [4(S_{12})^2 + (S_{22} - S_{11})^2]^{1/2}\}/(2\hat{\sigma}^2), \quad (8)$$

where

$$S_{11} = n \sum_{i=1}^k (\hat{\alpha}_i - \bar{\alpha})^2, \quad S_{22} = \sum_{i=1}^k (\hat{\beta}_i - \bar{\beta})^2,$$

and

$$S_{12} = n^{1/2} \sum_{i=1}^k (\hat{\alpha}_i - \bar{\alpha})(\hat{\beta}_i - \bar{\beta}).$$

It follows that all bounds in (2) contain 0 if and only if $T^2 \leq b^2$.

3. COMPARISON OF METHODS

Inverting the F test for testing the simultaneous null hypothesis $\alpha_1 = \alpha_2 = \dots = \alpha_k$ and $\beta_1 = \beta_2 = \dots = \beta_k$ versus the alternative of any possible difference yields the Scheffé simultaneous confidence intervals

$$\sum_{i=1}^k (c_i \alpha_i + d_i \beta_i) \in \sum_{i=1}^k (c_i \hat{\alpha}_i + d_i \hat{\beta}_i) \pm [(2k-2)F_{\alpha, 2k-2, \nu}]^{1/2} \hat{\sigma} \left[\sum_{i=1}^k (c_i^2/n + d_i^2) \right]^{1/2} \quad (9)$$

for all vectors \mathbf{c} and \mathbf{d} in C , where $F_{\alpha, 2k-2, \nu}$ is the upper α probability point of the F distribution with $2k-2$ and ν df. Scheffé simultaneous confidence bounds for all contrasts of the regression lines are obtained by restricting attention to the case where $\mathbf{d} = \mathbf{x}\mathbf{c}$. The resulting bounds are identical to those in (2), except b is replaced by $[(2k-2)F_{\alpha, 2k-2, \nu}]^{1/2}$.

The Scheffé bounds for all contrasts of regression lines are conservative for $k \geq 3$, because the restriction $\mathbf{d} = \mathbf{x}\mathbf{c}$

severely limits the choices of \mathbf{d} in C . The Scheffé bounds become more conservative as k increases. The Scheffé bounds are exact for comparing two lines.

More insight into the conservative nature of the Scheffé bounds is gained by looking at the closed-form expression for $\sup(T_{c,x}^2)$. Note that Q is bounded below by the maximum of two independent chi-squared random variables with $k-1$ df ($R^2 = 0$) and bounded above by the sum of the same two random variables ($R^2 = 1$). If R^2 in Q were replaced by 1, then the resulting simultaneous confidence bounds would match the Scheffé bounds. As k increases, the probability that R^2 is close to 1 decreases, and the Scheffé bounds become more conservative.

Replacing b^2 by $(2k-2)F_{\alpha, 2k-2, \nu}$ in Theorem 2 yields the coverage probability for the Scheffé bounds. Table 2 presents the coverage probability for nominal 95% Scheffé bounds and the ratio of the Scheffé bound width to the exact bound width for selected values of k and ν with $\alpha = .05$. Scheffé's procedure is quite conservative when $k = 3$ and becomes more conservative as k increases. The degree of conservatism increases slightly as ν increases from 24 to 48.

The bound width ratios in Table 2 show that the Scheffé bounds are about 5% wider than the exact bounds for $k = 3$ and about 13% wider for $k = 6$. To put these percentages in perspective, Scheffé intervals are about 4.5% wider than Tukey bounds for all pairwise differences of normal means for $k = 3, \nu = 24$, and $\alpha = .05$ and 23% wider for $k = 6, \nu = 24$, and $\alpha = .05$.

4. EXAMPLE

Masuda et al. (1997) studied the effects of $k = 3$ treatments on the accumulation of the chemotherapy agent [^3H]methotrexate in rat renal tissue. They measured the accumulation (fmol/mg protein) in three independent replicates for each treatment after exposure time, $t = 15, 30$, and 60 minutes. Thus $n = 9$. Different tissue samples were used for the different times. Centering and rescaling the predictor variable yields

$$x = (t - 35)/(4,200)^{1/2}. \quad (10)$$

The fitted regression lines are

$$Y = 1,099.26 + 1,370.90x = 358.89 + 21.15t,$$

$$Y = 471.96 + 298.19x = 310.92 + 4.60t,$$

and

$$Y = 596.63 + 381.55x = 390.57 + 5.89t \quad (11)$$

Table 1. Values of b for Exact 95% Bounds for All Contrasts of k Simple Regression Lines Using the Same n Design Points

n	$k = 3$	$k = 4$	$k = 5$	$k = 6$	$k = 7$	$k = 8$
3	5.712	5.566	5.556	5.607	5.688	5.784
4	4.036	4.255	4.451	4.634	4.806	4.970
5	3.617	3.898	4.134	4.345	4.537	4.717
6	3.428	3.732	3.984	4.205	4.407	4.592
7	3.321	3.636	3.896	4.123	4.329	4.519
8	3.251	3.574	3.838	4.069	4.278	4.470
9	3.203	3.530	3.797	4.031	4.242	4.435
10	3.167	3.497	3.767	4.003	4.215	4.409
11	3.140	3.472	3.744	3.981	4.194	4.389
12	3.118	3.452	3.725	3.963	4.177	4.373
15	3.074	3.411	3.687	3.926	4.142	4.339
20	3.034	3.373	3.651	3.893	4.110	4.308
25	3.011	3.352	3.631	3.874	4.092	4.291
30	2.997	3.339	3.619	3.862	4.080	4.280
40	2.979	3.322	3.603	3.847	4.066	4.266
50	2.969	3.313	3.594	3.839	4.058	4.258
60	2.963	3.307	3.588	3.833	4.052	4.253

Table 2. Coverage Probability of Nominal 95% Scheffé Bounds and Ratio of 95% Scheffé Bound Width to 95% Exact Bound Width

k	n	ν	Coverage	Ratio	n	ν	Coverage	Ratio
3	10	24	.964	1.05	18	48	.965	1.05
4	8	24	.973	1.09	14	48	.975	1.08
6	6	24	.983	1.13	10	48	.985	1.13
8	5	24	.988	1.16	8	48	.991	1.15

for treatments 1, 2, and 3. The pooled estimate is $\hat{\sigma} = 45.58$.

Using $b = 3.203$, the exact bounds in (2) yield simultaneous 95% confidence for all contrasts. I illustrate the simultaneous confidence bounds through two of the contrasts. Letting $c_1 = 1, c_2 = -1$, and $c_3 = 0$ gives the confidence bounds

$$627.30 + 1,072.71x \pm 3.203(45.58)\{2[(1/9) + x^2]\}^{1/2} \quad (12)$$

for the expected accumulation with treatment 1 minus the expected accumulation with treatment 2 as a function of x . The bounds are illustrated in Figure 2 using the original exposure time scale. For exposure times greater than 4.3 minutes, the expected accumulation with treatment 1 is greater than the expected accumulation with treatment 2.

Letting $c_1 = 1, c_2 = -1/2$, and $c_3 = -1/2$ gives the confidence bounds

$$564.965 + 1,031.03x \pm 3.203(45.58)\{1.5[(1/9) + x^2]\}^{1/2} \quad (13)$$

for the expected accumulation with treatment 1 minus the average of the expected accumulations with treatments 2 and 3 as a function of x . For exposure times greater than 5.8 minutes, the expected accumulation with treatment 1 is greater than the average expected accumulations for treatments 2 and 3.

5. CONCLUDING REMARKS

Although the Scheffé method is quite versatile, it is quite conservative for comparing $k \geq 3$ regression lines. An exact method has been established for comparing simple regression lines under the assumption of identical design matrices for each group. The exact method produces narrower confidence bounds than the Scheffé method.

Though conservative, the Scheffé method can be used for the case of unequal design matrices. The union-intersection method could be used to produce exact bounds for this more general case, but the maximization process and the distribution theory become much more complex.

In many situations, there are upper and lower bounds for the possible values of the predictor variable. In such situa-

tions, the maximization in (A.5) would be over a subinterval of $[0, 1]$, and the resulting bounds would be narrower than those in (2). The distribution theory would be more complicated.

Exact simultaneous confidence intervals could also be developed for all contrasts of multiple or polynomial regression lines using similar arguments. Again, the distribution theory would be more complicated.

APPENDIX: PROOFS OF THEOREMS

Proof of Theorem 1

By substitution of (6) and by the fact that $c'1 = 0$,

$$T_{c,x}^2 = \frac{\{\sum_{i=1}^k c_i[(1/n^{1/2})(Z_{1i} - \bar{Z}_1) + x(Z_{2i} - \bar{Z}_2)]\}^2}{(\hat{\sigma}^2/\sigma^2)(1/n + x^2)\sum_{i=1}^k (c_i^2)}. \quad (A.1)$$

Holding x fixed, the Cauchy-Schwarz inequality gives that $T_{c,x}^2$ is maximized over c in C when

$$c_i = (1/n^{1/2})(Z_{1i} - \bar{Z}_1) + x(Z_{2i} - \bar{Z}_2) \quad \text{for } i = 1, \dots, k. \quad (A.2)$$

Denote this maximum value of $T_{c,x}^2$ for fixed x by

$$\begin{aligned} T_x^2 &= \frac{\sum_{i=1}^k [(1/n^{1/2})(Z_{1i} - \bar{Z}_1) + x(Z_{2i} - \bar{Z}_2)]^2}{(\hat{\sigma}^2/\sigma^2)(1/n + x^2)} \\ &= \frac{aQ_{11} + 2[a(1-a)]^{1/2}Q_{12} + (1-a)Q_{22}}{\hat{\sigma}^2/\sigma^2}, \end{aligned} \quad (A.3)$$

where

$$a = 1/(1 + nx^2)$$

and

$$Q_{jj'} = \sum_{i=1}^k (Z_{ji} - \bar{Z}_j)(Z_{j'i} - \bar{Z}_{j'}), \quad j \text{ and } j' = 1, 2. \quad (A.4)$$

Now,

$$\begin{aligned} \sup(T_{c,x}^2) &= \max \frac{aQ_{11} + 2[a(1-a)]^{1/2}Q_{12} + (1-a)Q_{22}}{\hat{\sigma}^2/\sigma^2}, \end{aligned} \quad (A.5)$$

where the maximization is taken with respect to a in $[0, 1]$. Standard maximization arguments yield that the maximum occurs at

$$a = [1 - V/(1 + V^2)^{1/2}]/2, \quad (A.6)$$

where $V = (Q_{22} - Q_{11})/(2|Q_{12}|)$ provided that $|Q_{12}| \neq 0$. This follows after a straightforward argument that

$$\sup(T_{c,x}^2) = \frac{Q}{\hat{\sigma}^2/\sigma^2}, \quad (A.7)$$

where $Q = \{Q_{11} + Q_{22} + [4R^2Q_{11}Q_{22} + (Q_{22} - Q_{11})^2]^{1/2}\}/2$ and $R = Q_{12}/[Q_{11}Q_{22}]^{1/2}$. If $Q_{12} = 0$, then (A.7) still holds, as the numerators of the right sides of (A.5) and Q both equal $\max(Q_{11}, Q_{22})$. The proof is complete.

Let G_{ν_1} denote the distribution function of the chi-squared distribution with ν_1 df. Note that $G_1(q) = \text{erf}[(q/2)^{1/2}]$, where erf is the error function.

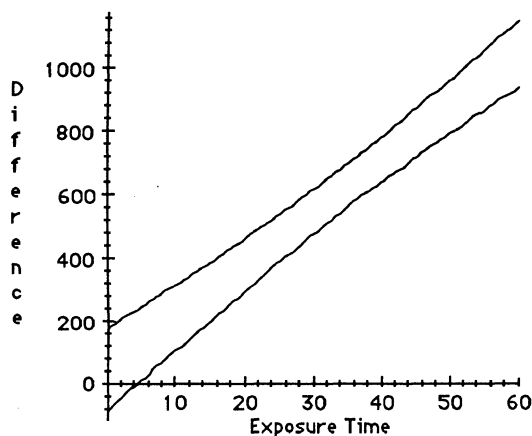


Figure 2. Confidence Bounds for Expected Accumulation (fmol/mg protein) for Treatment 1 Minus Expected Accumulation for Treatment 2 as a Function of Exposure Time (m).

Lemma 1. Let $a \geq -1$ be an odd integer. Then

$$\begin{aligned} & \frac{1}{\Gamma[(a+2)/2]2^{(a+2)/2}} \int_0^z q^{a/2} \exp(-q/2) \operatorname{erf} [(q/2)^{1/2}] dq \\ &= [G_1(z)]^2/2 + (1/\pi) \sum_{i=1}^{(a+1)/2} [\Gamma(i)G_{2i}(2z)/p_i] \\ & \quad - (2/\pi)^{1/2} G_1(z) \sum_{i=1}^{(a+1)/2} [z^{i-(1/2)} \exp(-z/2)/p_i], \end{aligned}$$

where the summations are defined to be 0 if $a = -1$.

Sketch of Proof of Lemma 1

Let X and Y denote independent chi-squared random variables with 1 and $a+2$ df. Now,

$$\begin{aligned} P(X \leq Y \leq z) &= \frac{1}{\Gamma[(a+2)/2]2^{(a+2)/2}} \\ & \quad \times \int_0^z q^{a/2} \exp(-q/2) \operatorname{erf} [(q/2)^{1/2}] dq \quad (\text{A.8}) \end{aligned}$$

and

$$P(Y \leq X \leq z) = \int_0^z (2\pi x)^{-1/2} \exp(-x/2) G_{a+2}(x) dx.$$

Using the independence of X and Y ,

$$P(X \leq Y \leq z) = P(X \leq z)P(Y \leq z) - P(Y \leq X \leq z). \quad (\text{A.9})$$

The result follows after using equation 26.4.8 of Zelen and Severo (1964) to rewrite the right side of (A.9) and simplifying.

Proof of Theorem 2

First, derive the density of $Q, f(q)$. Define $W_1 = \min(Q_{11}, Q_{22})$, $W_2 = \max(Q_{11}, Q_{22})$, and $W_3 = R^2$. By a standard change of variables, the joint density of (W_1, W_2, W_3) is

$$\frac{(w_1 w_2)^{(k-3)/2} \exp[-(w_1 + w_2)/2] (1 - w_3)^{(k-4)/2}}{2^{(k-2)} (\pi w_3)^{1/2} \Gamma[(k-1)/2] \Gamma[(k-2)/2]} \quad (\text{A.10})$$

for $0 \leq w_1 \leq w_2 < \infty, 0 < w_3 \leq 1$.

I now wish to find the joint density of (W_1, W_2, Q) . Note that $W_3 = (Q - W_1)(Q - W_2)/(W_1 W_2)$. By a standard change of variables, the joint density of (W_1, W_2, Q) is

$$\frac{\exp[-(w_1 + w_2)/2] [q(w_1 + w_2 - q)]^{(k-4)/2} (2q - w_1 - w_2)}{2^{(k-2)} [\pi(q - w_1)(q - w_2)]^{1/2} \Gamma[(k-1)/2] \Gamma[(k-2)/2]} \quad (\text{A.11})$$

for $0 \leq w_1 \leq w_2 < q \leq w_1 + w_2 < \infty$.

Making a third change of variables, let

$$X_1 = \frac{2Q - W_1 - W_2}{Q}$$

and

$$X_2 = \frac{Q - W_1}{2Q - W_1 - W_2}. \quad (\text{A.12})$$

This leads to the inverse functions

$$W_1 = Q(1 - X_1 X_2)$$

and

$$W_2 = Q[1 - X_1(1 - X_2)]. \quad (\text{A.13})$$

The joint density of (X_1, X_2, Q) is

$$\frac{q^{(k-2)} \exp(-q + qx_1/2) x_1 (1 - x_1)^{(k-4)/2}}{2^{(k-2)} [\pi x_2 (1 - x_2)]^{1/2} \Gamma[(k-1)/2] \Gamma[(k-2)/2]} \quad (\text{A.14})$$

for $0 < x_1 < 1, 1/2 < x_2 < 1, 0 < q < \infty$. Integrating with respect to x_2 and x_1 yields

$$\begin{aligned} f(q) &= \frac{(\pi)^{1/2} q^{(k-2)} \exp(-q)}{2^{(k-1)} \Gamma[(k-1)/2] \Gamma[(k-2)/2]} \\ & \quad \times \int_0^1 x_1 (1 - x_1)^{(k-4)/2} \exp(x_1 q/2) dx_1. \quad (\text{A.15}) \end{aligned}$$

First consider the case of even $k \geq 4$. After repeatedly integrating by parts and collecting terms, one has

$$\begin{aligned} f(q) &= \left\{ \exp(-q/2) q^{(k-4)/2} (q - k + 2)/2 \right. \\ & \quad \left. + \sum_{i=1}^{(k-2)/2} \frac{i q^{k-3-i} \exp(-q)}{2^{(k-2)/2-i} \Gamma(k/2 - i)} \right\} / p_{(k-2)/2}, \\ & \quad 0 < q < \infty. \quad (\text{A.16}) \end{aligned}$$

It follows by standard integration techniques that

$$\begin{aligned} P(Q \leq q) &= \left\{ \Gamma(k/2) 2^{(k-2)/2} [G_k(q) - G_{k-2}(q)] \right. \\ & \quad \left. + \sum_{i=1}^{(k-2)/2} \frac{i \Gamma(k-2-i)}{2^{(k-2)/2-i} \Gamma(k/2 - i)} G_{2(k-2-i)}(2q) \right\} \\ & \quad \div p_{(k-2)/2}. \quad (\text{A.17}) \end{aligned}$$

Let $h(u)$ denote the density of $U = \hat{\sigma}^2/\sigma^2$. By conditioning on u , one has

$$\begin{aligned} P[\sup(T_{c,x}^2) \leq b^2] \\ &= P(Q \leq b^2 U) = \int_0^\infty P(Q \leq b^2 u) h(u) du. \quad (\text{A.18}) \end{aligned}$$

The result follows after substituting (A.17) into (A.18), distributing the summation, and using the fact that the ratio of independent chi-squared random variables divided by their degrees of freedom has an F distribution.

Now consider the case of odd $k \geq 3$. After repeatedly integrating by parts and collecting terms, one has

$$\begin{aligned} f(q) &= \frac{1}{\Gamma[(k-1)/2] 2^{(k-1)/2}} \\ & \quad \times \left\{ \sum_{i=1}^{(k-3)/2} \frac{2i q^{k-3-i} \exp(-q)}{p_{(k-1)/2-i}} \right. \\ & \quad \left. + q^{(k-3)/2} \exp(-q) + (2\pi)^{1/2} \operatorname{erf} [(q/2)^{1/2}] \right. \\ & \quad \left. \times \exp(-q/2) q^{(k-4)/2} (q - k + 2)/2 \right\}, \\ & \quad 0 < q < \infty, \quad (\text{A.19}) \end{aligned}$$

where the summation is defined to be 0 for $k = 3$.

Using standard integration techniques and Lemma 1 and combining terms, one has

$$\begin{aligned}
 P(Q \leq q) &= \frac{k-1}{2^{(k-1)/2}} G_{k-1}(2q) \\
 &\quad - \frac{\pi^{1/2} (q/2)^{[(k-2)/2]} \exp(-q/2)}{\Gamma[(k-1)/2]} G_1(q) \\
 &\quad + \frac{1}{\Gamma[(k-1)/2] 2^{(k-1)/2}} \\
 &\quad \times \sum_{i=1}^{(k-5)/2} \frac{(k-3-2i)\Gamma[(k-1)/2+i]}{p_{i+1}} \\
 &\quad \times G_{k-1+2i}(2q), \tag{A.20}
 \end{aligned}$$

where the summation is defined to be 0 if $k = 3$ or 5 . The result follows by conditioning on U and using arguments analogous to those in the other case.

[Received October 1997. Revised July 1998.]

REFERENCES

- Anderson, T. W. (1958), *An Introduction to Multivariate Statistical Analysis*, New York: Wiley.
- Dunnett, C. W. (1955), "A Multiple Comparison Procedure for Comparing Several Treatments With a Control," *Journal of the American Statistical Association*, 50, 482-491.
- (1964), "New Tables for Multiple Comparisons With a Control," *Biometrics*, 20, 482-491.
- Graybill, F. A. (1976), *Theory and Application of the Linear Model*, Belmont, CA: Wadsworth.
- Hochberg, Y., and Tamhane, A. C. (1987), *Multiple Comparison Procedures*, New York: Wiley.
- Hsu, J. C. (1996), *Multiple Comparisons: Theory and Methods*, London: Chapman and Hall.
- Masuda, S., Saito, H., and Inui, K-I. (1997), "Interactions of Nonsteroidal Anti-inflammatory Drugs With Rat Renal Organic Anion Transporter, OAT-K1," *The Journal of Pharmacology and Experimental Therapeutics*, 283, 1039-1042.
- Scheffé, H. (1959), *The Analysis of Variance*, New York: Wiley.
- Tukey, J. W. (1953), "The Problem of Multiple Comparisons," mimeographed monograph.
- Zelen, M., and Severo, N. (1964), "Probability Functions," in *Handbook of Mathematical Functions With Formulas, Graphs, and Mathematical Tables*, eds. M. Abramowitz and I. A. Stegun, Washington, DC: U.S. Government Printing Office, pp. 925-995.