On the Comparison of Umbrella Pattern Treatment Means with a Control Mean

Y. I. CHEN

Graduate Institute of Statistics, National Central University, ROC

Summary

This paper is concerned with comparing several increasing dose levels (treatments) with a zero dose control when the prior information about the umbrella pattern treatment means is available. The problem of testing whether there is at least one treatment which is better than the control is considered. Multiple test procedures are then proposed for deciding treatments (if any) which are better than the control. Some approximate criticial values of the proposed tests are reported. The results of a Monte Carlo power study are presented.

Key words: Monte Carlo study; Multiple test procedure; Umbrella pattern treatment means.

1. Introduction

The problem of comparing increasing dose levels (treatments) of a substance with a zero dose control together with the prior information that if there were a response to the substance the treatment means would be monotonically ordered was first considered in Williams (1971, 1972). However, monotonicity of dose-response relationship is far from universal. Many examples are available in medicine where increasing doses of therapies usually produce better (say, higher) treatment effects, but these therapies often become counter-productive at high doses. In such cases, an increasing dose-response relationship with a downturn in response at high doses is anticipated. These treatment effects are then expected to have an up-down ordering, hence, they are said to follow an umbrella pattern (see, for instance, MACK and WOLFE, 1981). The point which separates the treatment effects into the two different ordering groups is called the peak of the umbrella.

Suppose that X_{i1}, \ldots, X_{in_i} , $i = 0, 1, \ldots, k$ are k + 1 independent random samples from normal distributions $N(\mu_0, \sigma^2), N(\mu_1, \sigma^2), \ldots, N(\mu_k, \sigma^2)$, where μ_0 represents the control mean and μ_i the *i*th treatment mean, and σ^2 is the common variance. Specifically, we consider testing the null hypothesis $H_0: [\mu_0 = \mu_1 = \ldots = \mu_k]$ against the alternative hypothesis $H_A: [\mu_i > \mu_0]$ for at least one i]. In addition, we assume that, under $H_A, \mu_1 \leq \ldots \leq \mu_p \geq \ldots \geq \mu_k$, for some p, with at least one strict inequality.

In section 2 we propose an extension of Williams' test to the case of known umbrella peak. Estimation of the doses (if any) which are better than the control is also discussed. In section 3 we propose a test procedure for the case where the unknown peak group is expected to be relatively close to the kth population. A testing procedure for the more general unknown peak setting based on the method of estimating the umbrella peak suggested by Shi (1988) is also considered. In section 4 we report some approximate critical values of the tests proposed in sections 2 and 3, respectively. In section 5 we present the results of an extensive Monte Carlo simulation investigation of the relative powers of several competing tests for a variety of umbrella pattern treatment means configurations.

2. Case of Known Umbrella Peak

Suppose that, under H_A , the peak of the umbrella known to be at group p $(1 \le p \le k)$. Further, assume that $n_0 = c$ and $n_1 = \ldots = n_k = n$. Let $\bar{X}_0, \bar{X}_1, \ldots, \bar{X}_k$ be the sample means for the k+1 groups and let $\hat{\mu}_1^{(p)} \le \ldots \le \hat{\mu}_p^{(p)} \ge \ldots \ge \hat{\mu}_k^{(p)}$ be the isotonic regression of $\bar{X}_1, \ldots, \bar{X}_k$ under the restrictions $\mu_1 \le \ldots \le \mu_p \ge \ldots \ge \mu_k$. Note that if $\mu_p > \mu_0$, then H_A holds. Therefore, we propose to reject H_0 for large values of

$$T_p = (\hat{\mu}_p^{(p)} - \bar{X}_0) / (S \sqrt{n^{-1} + c^{-1}}), \tag{2.1}$$

where S^2 is an unbiased estimator of the common variance σ^2 independent of \bar{X}_0 , \bar{X}_1 , ..., \bar{X}_k and vS^2/σ^2 is distributed to chi-squared distribution with degrees of freedom v = k(n-1) + c - 1. Note that the test based on T_k is in fact Williams' test for comparing ordered treatment means with a control mean.

From the derivation of the isotonic regression $\hat{\mu}_1^{(p)} \leq ... \leq \hat{\mu}_p^{(p)} \geq ... \geq \hat{\mu}_k^{(p)}$ discussed in Chen and Wolfe (1990), we obtain

$$\hat{\mu}_{p}^{(p)} = \max_{1 \le s \le p \le i \le k} \sum_{i=s}^{l} \bar{X}_{i}/(t-s+1). \tag{2.2}$$

Therefore, the statistic T_p becomes

$$T_{p} = \max_{1 \le s \le p \le t \le k} \left\{ \sum_{i=s}^{t} \overline{X}_{i} / (t - s + 1) - \overline{X}_{0} \right\} / (S \sqrt{n^{-1} + c^{-1}}). \tag{2.3}$$

Hence, under H_0 , the distribution of T_p is the same as that of $(Y - Z_0)/W^{1/2}$, where $Y = \max_{1 \le s \le p \le t \le k} \sum_{i=s}^{t} Z_i/(t-s+1)$, W and the Z_i are independent random variables, Z_0 is distributed according to N(0, n/c), Z_1, \ldots, Z_k are standard normal random variables and cvW is distributed as $(c+n)\chi_v^2$.

691

If the test based on T_p rejects the null hypothesis H_0 , we conclude that there is a response to the substance and that at least the dose p is better than the control. However, it is possible that this response occurs not only at dose p. Let $t(\alpha; p, k)$ be the upper α th percentile for the null distribution of T_p . Set $T_{pi} = (\hat{\mu}_i^{(p)} - \bar{X}_0)/S \sqrt{n^{-1} + c^{-1}}$, i = 1, ..., k. If $T_{pa} < t(\alpha; k, p)$, $T_{pb} < t(\alpha; k, p)$ and $T_{pi} \ge t(\alpha; k, p)$ for $1 \le a and <math>a < i < b$, we then conclude that there is evidence for a response at doses a + 1, ..., b - 1. Since

$$\alpha = P\{T_p \ge t(\alpha; k, p) | H_0\} \ge P\{T_{pi} \ge t(\alpha; k, p), i = 1, ..., k | H_0\},$$

in the language of multiple comparison procedures, the experiment-wise error rate of the procedure stated above is controlled.

3. Case of Unknown Umbrella Peak

When treatment effects follow an umbrella pattern, it occurs frequently that this umbrella has a downturn at high dose levels (see, for example, SIMPSON and MARGOLIN (1986)). In this case, the peak group of the umbrella is expected to be relatively close to the kth population. Hence, we suggest to choose the peak group \tilde{p} such that

$$\tilde{p} = \max \left\{ i \colon \bar{X}_i > \frac{\bar{X}_1 + \dots + \bar{X}_{i-1}}{i-1} \right\}.$$

Finally, the null hypothese H_0 is rejected for large values of

$$T_{\tilde{p}} = \max_{1 \le s \le \tilde{p} \le t \le k} \left\{ \sum_{i=s}^{t} \bar{X}_i / (t - s + 1) - \bar{X}_0 \right\} / (S \sqrt{n^{-1} + c^{-1}}). \tag{3.1}$$

For the more general setting where the peak of the umbrella is unknown, we employ the method suggested by SHI (1988) to estimate the unknown peak. Let $\hat{\mu}_1^{(t)} \leq \ldots \leq \hat{\mu}_t^{(t)} \geq \ldots \geq \hat{\mu}_k^{(t)}$ be the isotonic regression of $\overline{X}_1, \ldots, \overline{X}_k$ under the restrictions $\mu_1 \leq \ldots \leq \mu_t \geq \ldots \geq \mu_k$ for $t = 1, \ldots, k$. We first select the group \hat{p} such that

$$\sum_{i=1}^{k} (\hat{\mu}_{i}^{(\hat{p})} - \bar{X}_{i})^{2} = \min_{1 \le i \le k} \sum_{i=1}^{k} (\hat{\mu}_{i}^{(i)} - \bar{X}_{i})^{2}.$$

The null hypothesis H_0 is then rejected for large values of

$$T_{\hat{p}} = \max_{1 \le s \le \hat{p} \le t \le k} \left\{ \sum_{i=s}^{t} \bar{X}_i / (t-s+1) - \bar{X}_0 \right\} / (S \sqrt{n^{-1} + c^{-1}}). \tag{3.2}$$

Let $t_{\tilde{p}}(\alpha; k)$ and $t_{\hat{p}}(\alpha; k)$ be the upper α th percentiles for the null distributions of $T_{\tilde{p}}$ and $T_{\hat{p}}$, respectively. If the test based on $T_{\tilde{p}}$ (or $T_{\hat{p}}$) rejects H_0 , a level

 $(1-\alpha)$ multiple comparison procedure similar to that described in section 2, but employing the critical value $t_{\tilde{p}}(\alpha; k)$ (or $t_{\hat{p}}(\alpha; k)$), can be used to estimate doses which are significantly better than the zero-dose control.

4. Null Distributions of the Proposed Tests

When, in particular, k = 3, p = 2, n = c, and the common variance σ^2 is known, we observe from section 2 that the statistic T_2 is distributed as

$$\max_{1 \le s \le 2 \le t \le 3} \left\{ \sum_{i=s}^{t} Z_i / (t-s+1) - Z_0 \right\} / \sqrt{2},$$

where the Z_i are independent standard normal random variables. According to the 6 different permutations of Z_1 , Z_2 and Z_3 , we obtain

$$\begin{split} \sqrt{2}\,T_2 &= \bar{Z}_{23} - Z_0, & \text{if } Z_2 < Z_3 \text{ and } \bar{Z}_{23} > Z_1 \\ &= \bar{Z}_{12} - Z_0, & \text{if } Z_1 > Z_2 \text{ and } \bar{Z}_{12} > Z_3 \\ &= Z_2 - Z_0, & \text{if } Z_1 < Z_2 \text{ and } Z_2 > Z_3 \\ &= \bar{Z}_{123} - Z_0, & \text{if } Z_1 < Z_3 \text{ and } \bar{Z}_{23} < Z_1 \text{ or } Z_1 > Z_3 \text{ and } \bar{Z}_{12} < Z_3, \end{split}$$

where $\bar{Z}_{si} = (Z_s + Z_t)/2$ for $1 \le s \le 2 \le t \le 3$ and $\bar{Z}_{123} = (Z_1 + Z_2 + Z_3)/3$. After some algebraic manipulations, we have

$$P\{T_{2} \ge t \mid H_{0}\} = \int_{0}^{\infty} \exp(-x^{2}/12) \, \Phi\{(x-6t)/4\sqrt{3}\} \, dx/2\sqrt{3\pi}$$

$$+ \int_{0}^{\infty} \int_{0}^{\infty} \exp\{-(2y-x)^{2}/12 - x^{2}/4\} \, \Phi\{(3t-x-y)/2\sqrt{3}\} \, dx \, dy/2\sqrt{3\pi}$$

$$+ \Phi(\sqrt{3}t/2) \int_{0}^{\infty} \exp(-x^{2}/4) \, \Phi(-3x/\sqrt{6}) \, dx/\sqrt{\pi} \, .$$

By using elementary numerical integration techniques to solve the equation $P\{T_2 \ge t(\alpha; 3, 2) | H_0\} = \alpha$, we obtain the critical values $t(\alpha; 3, 2)$ for $\alpha = .05$ and .10 in the following:

Table 1 Critical values $t(\alpha; 3, 2)$ of the test based on T_2 when n = c and σ^2 is known

α	.05	.10
ι(α; 2, 3)	1.7697	1.4402

Biom. J. 35 (1993) 6

Since the null distribution of the test statistic T_p becomes relatively complicated for $k \ge 4$ and that of the statistic $T_{\tilde{p}}$ is even more difficult to obtain, we employ simulation technique to estimate the critical values $t(\alpha; k, p)$ and $t_{\tilde{p}}(\alpha; k)$. For each value of k (and p for peak-known case), the number of treatments, the International Mathematical and Statistical Libraries (IMSL) routine RNNOR was used to generate appropriate normal random variates for which the statistics T_p and $T_{\tilde{p}}$ were respectively evaluated. Proceeding in this fashion, we obtained empirical cumulative distributions of T_p and $T_{\tilde{p}}$, respectively, based on a sample of size 10,000 from the corresponding true distributions. The estimated critical values for the T_p and $T_{\tilde{p}}$ tests then correspond to percentiles of their empirical distributions and are presented in Tables 2 and 3. When k=3 with infinite degrees of freedom, for example, the estimated 95th percentile for the null distribution of $T_{\tilde{p}}$ is 1.917.

Table 2 Estimated critical values of T_n for $n_0 = n_1 = ... = n_t$

						(a)	$\alpha = 0.05$				
J C	k		3		4		5			6	
d . f.	p	2	3	3	4	3	4	5	4	5	6
5		2.285	2.247	2.252	2.228	2.346	2.346	2.242	2.292	2.262	2.192
6		2.163	2.083	2.172	2.101	2.200	2.187	2.192	2.210	2.185	2.145
7		2.165	2.111	2.153	2.104	2.129	2.112	2.029	2.139	2.101	2.074
8		2.033	1.991	2.067	2.050	2.092	2.076	2.026	2.069	2.089	2.024
9		2.066	2.012	2.043	1.990	2.048	2.061	1.990	2.064	2.054	1.992
10		1.989	1.981	1.976	1.938	1.985	2.024	1.945	2.050	2.041	1.967
11		2.051	1.946	1.977	1.942	2.008	2.053	1.976	2.035	2.041	1.930
12		1.932	1.894	1.980	1.884	2.005	1.982	1.922	1.983	1.966	1.913
13		1.943	1.888	1.956	1.902	1.998	2.008	1.942	1.972	1.994	1.912
14		1.945	1.861	1.950	1.892	1.948	1.923	1.893	1.958	1.933	1.912
15		1.931	1.893	1.938	1.890	1.981	1.993	1.947	1.967	1.965	1.919
16		1.913	1.847	1.879	1.877	1.905	1.909	1.851	1.978	1.957	1.914
17		1.910	1.877	1.913	1.864	1.936	1.957	1.905	1.937	1.949	1.895
18		1.890	1.866	1.897	1.864	1.929	1.948	1.891	1.944	1.945	1.889
19		1.879	1.845	1.887	1.857	1.913	1.938	1.874	1.940	1.932	1.884
20		1.860	1.832	1.878	1.849	1.911	1.931	1.873	1.941	1.928	1.894
22		1.852	1.813	1.867	1.837	1.907	1.909	1.849	1.931	1.919	1.876
24		1.848	1.813	1.860	1.824	1.904	1.916	1.844	1.912	1.913	1.875
26		1.852	1.815	1.855	1.823	1.903	1.910	1.845	1.896	1.892	1.853
28		1.848	1.798	1.861	1.827	1.895	1.898	1.828	1.897	1.882	1.842
30		1.839	1.787	1.858	1.815	1.881	1.878	1.813	1.898	1.891	1.857
35		1.836	1.796	1.846	1.804	1.883	1.873	1.805	1.874	1.870	1.828
40		1.828	1.770	1.834	1.792	1.894	1.876	1.815	1.876	1.867	1.826
60		1.816	1.756	1.821	1.775	1.850	1.832	1.787	1.859	1.847	1.800
120		1,795	1.744	1.825	1.751	1.833	1.817	1.775	1.823	1.841	1.797
∞		1.770	1.730	1.779	1.740	1.771	1.778	1.740	1.795	1.802	1.760

Table 2 (continued)

						(b)	$\alpha = 0.10$				
	k		3		4		5			6	
d.f.	<i>p</i>	2	3	3	4	3	4	5	4	5	6
5		1.729	1.684	1.767	1.696	1.775	1.786	1.699	1.779	1.756	1.679
6		1.638	1.635	1.679	1.614	1.727	1.715	1.663	1.731	1.694	1.635
7		1.657	1.609	1.672	1.626	1.672	1.658	1.595	1.686	1.657	1.629
8		1.596	1.548	1.624	1.583	1.646	1.641	1.560	1.655	1.656	1.613
9		1.620	1.557	1.601	1.567	1.639	1.619	1.565	1.632	1.621	1.564
10		1.560	1.521	1.576	1.516	1.604	1.615	1.574	1.626	1.616	1.553
11		1.576	1.535	1.560	1.529	1.616	1.614	1.569	1.617	1.601	1.531
12		1.532	1.472	1.578	1.534	1.590	1.595	1.533	1.566	1.557	1.514
13		1.543	1.506	1.547	1.507	1.594	1.585	1.550	1.603	1.586	1.529
14		1.547	1.495	1.559	1.507	1.542	1.529	1.485	1.563	1.560	1.508
15		1.544	1.509	1.537	1.505	1.587	1.594	1,552	1.584	1.578	1.507
16		1.508	1.476	1.520	1.472	1.544	1.539	1.492	1.592	1.567	1.523
17		1.519	1.495	1.524	1.500	1.574	1.573	1.529	1.569	1.566	1.516
18		1.510	1.487	1.511	1.486	1.572	1.559	1.516	1.573	1.564	1.515
19		1.496	1.476	1.504	1.486	1.569	1.556	1.506	1.572	1.561	1.507
20		1.493	1.471	1.497	1.484	1.561	1.544	1.504	1.565	1.563	1.503
22		1.488	1.461	1.490	1.469	1.550	1.531	1.491	1.565	1.557	1.493
24		1.483	1.453	1.478	1.462	1.546	1.541	1.487	1.553	1.542	1.492
26		1.482	1.451	1.477	1,451	1.538	1.541	1.484	1.542	1.527	1.475
28		1.471	1.442	1.482	1.459	1.529	1.535	1.478	1.541	1.531	1.477
30		1.478	1.445	1.476	1.450	1.521	1.527	1.475	1.534	1.537	1.484
35		1.480	1.448	1.466	1.444	1.524	1.518	1.466	1.527	1.522	1.476
40		1.469	1.436	1.459	1.441	1.532	1.532	1.470	1.525	1.521	1.482
60		1.460	1.430	1.446	1.436	1.495	1.453	1.553	1.502	1.503	1.470
120		1.449	1.420	1.460	1.427	1.479	1.493	1.447	1.489	1.505	1.465
∞		1.440	t.390	1.444	1.419	1.460	1.461	1.419	1.481	1.475	1.434

Table 3 Estimated critical values of $T_{\tilde{p}}$ for $n_0 = n_1 = \dots = n_k$

d.f.			(a) α	= 0.05		(b) $\alpha = 0.10$				
υ	k	3	4	5	6	3	4	5	6	
5		2.515	2.633	2.719	2.711	1.953	2.075	2.122	2.118	
6		2.342	2.509	2.613	2.606	1.825	1.976	2.045	2.057	
7		2.387	2.450	2.481	2.490	1.863	1.975	1.965	2.014	
8		2.237	2.373	2.401	2.442	1.786	1.913	1.960	1.991	
9		2.230	2.330	2.377	2.414	1.786	1.884	1.916	1.945	
10		2.200	2.294	2.330	2.351	1.765	1.841	1.910	1.911	
11		2.175	2.249	2.353	2.349	1.744	1.837	1.905	1.926	
12		2.116	2.242	2.291	2.283	1.710	1.817	1.852	1.852	
13		2.115	2.206	2.284	2.301	1.716	1.824	1.876	1.908	
14		2.120	2.201	2.227	2.257	1.720	1.805	1.809	1.865	

695

Table 3 (continued)

d.f.		(a) α	= 0.05			(b) α	= 0.10	
v k	3	4	5	6	3	4	5	6
15	2.107	2.192	2.260	2.271	1.712	1.800	1.871	1.888
16	2.070	2.146	2.214	2.248	1.682	1.748	1.813	1.869
17	2.079	2.174	2.218	2.254	1.698	1.789	1.838	1.870
18	2.065	2.159	2.202	2.245	1.681	1.780	1.828	1.870
19	2.039	2.149	2.188	2.244	1.666	1.771	1.816	1.857
20	2.028	2.134	2.190	2.245	1.655	1.762	1.811	1.863
22	2.015	2.113	2.173	2.229	1.646	1.752	1.792	1.850
24	2.012	2.098	2.167	2.220	1.642	1.745	1.796	1.840
26	2.018	2.101	2.168	2.197	1.640	1.742	1.794	1.826
28	1.999	2.110	2.156	2.183	1.632	1.745	1.785	1.818
30	1.999	2.103	2.131	2.197	1.629	1.736	1.780	1.824
35	1.985	2.080	2.123	2.164	1.633	1.724	1.775	1.808
40	1.961	2.071	2.127	2.167	1.624	1.711	1.780	1.803
60	1.946	2.054	2.079	2.135	1.616	1.692	1.761	1.786
120	1.913	2.036	2.065	2.112	1.595	1.683	1.748	1.775
∞	1.917	2.045	2.038	2.073	1.605	1.700	1.708	1.745

5. Monte Carlo Power Study

To examine the relative powers of the proposed tests based on T_p , $T_{\tilde{p}}$ and $T_{\hat{p}}$, Shi's tests based on $\tilde{\chi}_p^2$ and $\tilde{\chi}_{\hat{p}}^2$, Williams' test based on W and Dunnett's test based on D for comparing umbrella pattern treatment means with a control mean, we conducted a Monte Carlo Study. In this study, we consider k=4 treatments, with known σ^2 and c/n=1 and 3, where $n_0=c$ and $n_1=\ldots=n_k=n$, and a variety of different umbrella pattern treatment means.

The power performances of the test procedures considered in this paper are evaluated via the experiment-wise power (probability of detecting at least one treatment which is better than the control) and the comparison-wise power (probability of correctly detecting the treatments which are better than the control, available only for multiple test procedures). For each of these settings, appropriate normal variates were generated by using the IMSL routines RNNOR. In each case, we used 10,000 replications in obtaining the various power estimates. Approximate level $\alpha = 0.05$ and 0.10 critical values were used. The simulated power estimates for the seven tests are presented in Tables 4 and 5. The designated umbrella pattern treatment means correspond to values of $\mu_{10} = \mu_1 - \mu_0, \dots, \mu_{k0} = \mu_k - \mu_0$.

We observe from the simulation results that Williams' test has excellent experiment-wise power when the treatment means have a monotonic ordering. Likewise, the test based on T_p provides excellent experiment-wise power against umbrella pattern treatment means when the peak is correctly chosen. This is not

Table 4
Experiment-wise power estimates for k = 4 when σ^2 is known

				(a)	$\alpha = 0$.	05					
μ_{10}	μ ₂₀	μ_{30}	μ_{40}	c/n	T_p	W	$\bar{\chi}_p^2$	$T_{\tilde{p}}$	$T_{\hat{ ho}}$	$\bar{\chi}^2_{\hat{p}}$	D
0	0	0	2.4	1	.493	.493	.518	.371	.326	.336	.325
				3	.637	.637	.568	.515	.463	.372	.463
0	0	1.2	2.4	1	.509	.509	.567	.390	.350	.384	.350
				3	.661	.661	.641	.544	.502	.454	.502
C	1.2	1.2	2.4	1	.513	.513	.522	.401	.371	.356	.371
				3	.669	.669	.654	.562	.536	.476	.536
1.2	2.4	2.4	3.6	1	.826	.826	.786	.743	.726	.643	.725
				3	.951	.951	.949	.918	.912	.884	.912
0	0	2.4	0	í	.472	.153	.512	.337	.322	.393	.322
				3	.633	.198	.548	.466	.457	.428	.457
0	1.2	2.4	0	1	.491	.170	.551	.373	.347	.432	.346
				3	.660	.228	.618	.525	.498	.508	.498
)	1.2	2.4	1.2	1	.505	.326	.502	.370	.369	.387	.368
				3	.682	.464	.613	.525	.533	.507	.533
1.2	2.4	3.6	1.2	1	.812	.525	.769	.721	.695	.666	.694
				3	.948	.747	.915	.893	.884	.863	.884
0	2.4	0	0	1	.480	.090	.511	.311	.320	.401	.319
				3	.649	.098	.547	.422	.456	.442	.456
0	2.4	1.2	0	1	.496	.140	.542	.344	.346	.430	.345
				3	.674	.186	.609	.475	.496	.508	.496
1.2	2.4	1.2	0	1	.510	.153	.516	.389	.367	.413	.366
				3	.694	.207	.633	.545	.531	.535	.531
1.2	3.6	2.4	1.2	1	.808	.491	.760	.688	.699	.670	.698
				3	.948	.716	.904	.870	.884	.859	.884
2.4	0	0	0	1	.482	.072	.512	.101	.323	.387	.322
				3	.647	.074	.530	.123	.456	.432	.456
2.4	1.2	0	0	1	.500	.098	.550	.213	.348	.426	.347
				3	.671	.106	.593	.299	.496	.503	.496
2.4	1.2	1.2	0	1	.505	.144	.500	.262	.369	.390	.367
				3	.679	.184	.590	.377	.528	.517	.528
3.6	2.4	2.4	1.2	1	.821	.501	.739	.635	.722	.646	.721
				3	.956	.733	.914	.851	.909	.883	.909

				(b)	$\alpha = 0.$	10					
μ_{10}	μ_{20}	μ ₃₀	μ_{40}	c/n	T_{p}	W	$\bar{\chi}_{P}^{2}$	$T_{\tilde{\rho}}$	$T_{\hat{p}}$	$\bar{\chi}_{\hat{p}}^2$	D
0	0	0	2.4	1	.614	.614	.652	.510	.458	.464	.456
				3	.755	.755	.695	.637	.584	.499	.584
0	0	1.2	2.4	1	.631	.631	.694	.533	.490	.516	.488
				3	.785	.785	.760	.670	.631	.583	.630
0	1.2	1.2	2.4	1	.639	.639	.660	.549	.516	.488	.515
				3	.795	.795	.774	.693	.669	.609	.668

Table 4 (continued)

				(b)	$\alpha = 0.$	10					
μ10	μ_{20}	μ_{30}	μ_{40}	c/n	T_{ρ}	W	$\bar{\chi}_p^2$	$T_{\tilde{p}}$	$T_{\hat{ ho}}$	$\bar{\chi}^2_{\hat{p}}$	D
1.2	2.4	2.4	3.6	1	.899	.899	.872	.850	.834	.760	.833
				3	.982	.982	.978	.962	.959	.936	.959
0	0	2.4	0	1	.610	.262	.645	.468	.451	.524	.450
				3	.754	.332	.687	.591	.582	.561	.582
0	1.2	2.4	0	1	.631	.294	.681	.517	.486	.569	.485
				3	.781	.379	.749	.660	.632	.636	.631
)	1.2	2.4	1.2	1	.647	.470	.627	.516	.512	.522	.511
				3	.803	.629	.743	.670	.671	.634	.670
1.2	2.4	3.6	1.2	1	.894	.680	.859	.833	.814	.784	.813
				3	.978	.872	.960	.948	.941	.922	.941
)	2.4	0	0	1	.602	.161	.644	.436	.456	.535	.455
				3	.754	.186	.681	.539	.582	.573	.581
)	2.4	1.2	0	1	.622	.246	.675	.486	.491	.572	.489
				3	.782	.317	.733	.615	.631	.639	.630
1.2	2.4	1.2	0	1	.638	.268	.657	.538	.516	.549	.515
				3	.802	.351	.757	.685	.669	.666	.668
1.2	3.6	2.4	1.2	1	.888	.635	.851	.806	.812	.783	.811
				3	.975	.840	.950	.934	.941	.917	.941
2.4	0	0	0	1	.620	.143	.641	.195	.455	.521	.454
				3	.759	.151	.659	.228	.582	.563	.582
2.4	1.2	0	0	1	.640	.188	.675	.342	.486	.564	.485
				3	.789	.221	.718	.441	.626	.630	.626
2.4	1.2	1.2	0	1	.647	.265	.631	.407	.512	.528	.511
				3	.798	.334	.720	.536	.664	.642	.664
3.6	2.4	2.4	1.2	1	.901	.665	.832	.777	.833	.763	.832
				3	.982	.868	.956	.928	.956	.932	.956

Table 5
Comparison-wise power estimates for k = 4 when σ^2 is known

(a) $\alpha = 0.05$												
μ_{10}	μ_{20}	μ_{30}	μ_{40}	c/n	T_p	W	$T_{\widetilde{p}}$	$T_{\hat{p}}$	D			
0	0	0	2.4	1	.444	.441	.347	.301	.286			
				3	.593	.588	.494	.437	.424			
0	0	1.2	2.4	1	.140	.135	.083	.053	.049			
				3	.194	.194	.114	.068	.066			
)	1.2	1.2	2.4	1	.087	.086	.045	.028	.018			
				3	.111	.116	.052	.030	.019			
1.2	2.4	2.4	3.6	1	.160	.177	.085	.062	.044			
				3	.199	.221	.107	.069	.046			
)	0	2.4	0	1	.404	.000	.276	.289	.282			
				3	.560	.000	.397	.424	.419			
)	1.2	2.4	0	1	.116	.000	.069	.050	.050			
				3	.173	.000	.100	.066	.066			

Table 5 (continued)

(a) $\alpha = 0.05$												
μ_{10}	μ_{20}	μ_{30}	μ_{40}	c/n	T_{ρ}	W	$T_{\widetilde{p}}$	$T_{\hat{p}}$	D			
0	1.2	2.4	1.2	1	.058	.110	.037	.022	.020			
				3	.072	.152	.041	.024	.022			
1.2	2.4	3.6	1.2	1	.072	.176	.035	.021	.018			
				3	.078	.222	.040	.027	.024			
0	2.4	0	0	1	.412	.000	.251	.288	.281			
				3	.573	.000	.358	.425	.419			
0	2.4	1.2	0	1	.120	.000	.090	.049	.049			
				3	.185	.000	.131	.066	.066			
1.2	2.4	1.2	0	1	.059	.000	.032	.019	.017			
				3	.075	.000	.032	.022	.020			
1.2	3.6	2.4	1.2	1	.073	.186	.036	.021	.018			
				3	.083	.238	.040	.027	.024			
2.4	0	0	0	1	.434	.000	.000	.295	.281			
				3	.600	.000	.000	.429	.417			
2.4	1.2	0	0	1	.136	.000	.147	.051	.048			
				3	.198	.000	.217	.068	.066			
2.4	1.2	1.2	0	1	.089	.000	.050	.026	.017			
				3	.120	.000	.059	.027	.018			
3.6	2.4	2.4	1.2	1	.159	.468	.096	.066	.048			
				3	.212	.670	.116	.074	.049			

(b) $\alpha = 0.10$												
μ_{10}	μ_{20}	μ_{30}	μ_{40}	c/n	T_{ρ}	W	$T_{\tilde{P}}$	$T_{\hat{p}}$	D			
0	0	0	2.4	1	.519	.513	.453	.404	.376			
				3	.663	.656	.591	.534	.506			
0	0	1.2	2.4	1	.202	.192	.143	.099	.091			
				3	.285	.278	.187	.124	.117			
0	1.2	1.2	2.4	1	.149	.138	.088	.060	.042			
				3	.197	.192	.101	.061	.039			
1.2	2.4	2.4	3.6	1	.258	.289	.166	.123	.094			
				3	.322	.359	.190	.139	.096			
0	0	2.4	0	1	.477	.000	.354	.383	.370			
				3	.613	.000	.467	.518	.504			
0	1.2	2.4	0	1	.171	.000	.119	.087	.087			
				3	.246	.000	.161	.113	.113			
0	1.2	2.4	1.2	1	.105	.171	.071	.046	.042			
				3	.129	.242	.079	.048	.045			
1.2	2.4	3.6	1.2	1	.142	.290	.085	.052	.046			
				3	.154	.359	.079	.061	.055			
\mathbf{c}	2.4	0	0	1	.473	.000	.316	.389	.373			
				3	.612	.000	.412	.520	.505			

Biom. J. **35** (1993) 6

Table 5 (continued)

(b) $\alpha = 0.10$											
μ_{10}	μ_{20}	μ_{30}	μ_{40}	c/n	T_p	W	$T_{\widetilde{p}}$	$\mathcal{T}_{\hat{p}}$	D		
0	2.4	1.2	0	1	.170	.000	.145	.090	.089		
				3	.248	.000	.200	.117	.116		
1.2	2.4	1.2	0	1	.101	.000	.065	.044	.040		
				3	.133	.000	.070	.047	.043		
1.2	3.6	2.4	1.2	1	.135	.302	.086	.052	.046		
				3	.153	.378	.080	.060	.054		
2.4	0	0	0	1	.525	.000	.000	.400	.371		
				3	.665	.000	.000	.531	.503		
2.4	1.2	0	0	1	.204	.000	.234	.099	.089		
				3	.287	.000	.320	.124	.117		
2.4	1.2	1.2	0	1	.147	.000	.100	.060	.039		
				3	.205	.000	.118	.060	.041		
3.6	2.4	2.4	1.2	1	.263	.626	.172	.128	.098		
				3	.334	.826	.202	.141	.099		

surprising since both tests are designed to detect for their respective special classes of alternatives. However, the power of Williams' test drops sharply when there is a downturn in the umbrella. Similarly, we would expect the power of the test based on T_p to decline when the peak of the umbrella in incorrectly selected. In addition, the comparison-wise power performance of Williams' procedure is similar to that of the multiple test procedure proposed in section 2 for comparing ordered treatment means with a control mean. For comparing umbrella pattern treatment means with a control mean, however, Williams' procedure may not be as powerful as the proposed procedure, especially for the case where the kth treatment mean of this umbrella is the same as the control mean.

Simulation results indicate that with equal treatment replication Shi's tests based on $\bar{\chi}_p^2$ and $\bar{\chi}_{\hat{p}}^2$, respectively, are better than the corresponding T_p and $T_{\hat{p}}$ tests when some of the μ_{i0} are zero. When treatments are all better than the control, however, the tests based on T_p and $T_{\hat{p}}$ compare more favorably with the corresponding $\bar{\chi}_p^2$ and $\bar{\chi}_{\hat{p}}^2$ tests. In particular, when the control replication is increased, the tests based on T_p and $T_{\hat{p}}$ are superior to $\bar{\chi}_p^2$ and $\bar{\chi}_{\hat{p}}^2$ tests, respectively. Moreover, Shi's tests for umbrella alternatives only provide single tests. In comparing several umbrella pattern treatment means with a control mean, however, experimenters usually prefer procedures which can be used to determine which treatments (if any) are more effective than the control.

In general, the statistic $T_{\tilde{p}}$ provides a better test procedure than does either $T_{\hat{p}}$ or D for the unknown peak setting when the peak group is relatively close to the kth population. When, however, the location of the peak group is relatively far away from the kth population, the procedure based on $T_{\tilde{p}}$ performs poorly.

In these cases, the test procedures based on $T_{\hat{p}}$ and D, respectively, are both superior to the one based on $T_{\tilde{p}}$. Finally, we observe that the power performance of the procedure based on $T_{\hat{p}}$ is similar to that of Dunnett's procedure based on D for comparing general umbrella pattern treatment means with a control mean.

According to the simulation results, we, therefore, have several recommendations. When the prior information that the treatment means have an umbrella pattern under the alternative is available, the procedure based on T_{ρ} should be used if one is relatively confident of the location of the peak group. The procedure based on $T_{\tilde{\rho}}$ is recommended if the peak group of the umbrella is unknown, but is believed to be relatively close to the kth population. For the case where no information about the location of the peak group is available, Dunnett's procedure is suggested since it is computationally less complicated than the power-equivalent procedure based on $T_{\hat{\rho}}$.

Acknowledgement

This work was supported in part by NSC80-0208-M008-09 from National Science Council of Taiwan. The author wishes to thank Ms. Chang, Shu-Ching for providing partial computing assistance.

References

- CHEN, Y. I. and WOLFE, D. A., 1990: A study of distribution-free tests for umbrella alternatives. Biom. J. 32, 47-57.
- DUNNETT, C. W., 1955: A multiple comparisons procedure for comparing several treatment with a control. J. Amer. Statist. Assoc. 50, 1096-1121.
- MACK, G. A. and WOLFE, D. A., 1981: K-sample rank tests for umbrella alternatives. J. Amer. Statist. Assoc. 76, 175-181.
- SHI, N. Z., 1988: A test of homogeneity for umbrella alternatives and tables of the level probabilities. Comm. Statist.-Theor. Meth. 17, 657-670.
- SIMPSON, D. G. and MARGOLIN, B. H., 1986: Recursive nonparametric testing for dose-response relationships subject to downturns at high doses. Biometrika 73, 589-596.
- WILLIAMS, D. A., 1971: A test for differences between treatment means when several dose levels are compared with a zero dose control. Biometrics 27, 103-117.
- WILLIAMS, D. A., 1972: The comparison of several dose levels with a zero dose control. Biometrics 28, 519-531.

Received June 1992

YUH-ING CHEN Graduate Institute of Statistics National Central University Chung-Li, Taiwan 32054 R.O.C.