# NONPARAMETRIC COMPARISONS OF UMBRELLA PATTERN TREATMENT EFFECTS WITH A CONTROL IN A ONE-WAY LAYOUT

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Key words and phrases : Isotonic regression; Monte Carlo study; multiple test procedure; one-way layout; umbrella pattern treatment effects.

#### ABSTRACT

Nonparametric tests for comparing umbrella pattern treatment effects with a control in a one-way layout were studied in Chen and Wolfe (1993). In this paper a recursive formula for deriving the isotonic regression which is useful for statistical inference under the umbrella pattern restriction is given. An alternative multiple test procedure is then considered for the setting where the peak of the umbrella is known. The results of a Monte Carlo power study are presented.

## 1. INTRODUCTION

A variety of nonparametric procedures have been developed for comparing several treatments with a control in a one-way layout setting. In particular, Dunn (1964) proposed a multiple rank test for the general setting in which no information about the pattern of treatment effects is available. For comparing increasing doses of a substance with a zero-dose control, Shirley (1977) suggested a nonparametric

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version of Williams' (1971, 1972, 1973) test procedure for the situation where the experimenter believes a priori that if there were a response to the substance the treatment effects would be monotonically ordered. Williams (1986) further proposed a modification of Shirley's procedure, although he did not show how well the modified procedure performs over the original Shirley's procedure. However, monotonicity of dose-response 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. Chen and Wolfe (1993) then considered nonparametric test procedures for comparing these treatments with the control when the experimenter has the prior information that if there were a response to the substance the treatment effects would follow an umbrella pattern (see, for example, Mack and Wolfe (1981)).

Suppose that  $X_{i1}, ..., X_{in_i}$ , i = 0, 1, ..., k, are k+1 independent random samples from populations with continuous distribution functions  $F_i(x) = F(x-\theta_i)$ , i = 0, 1, ..., k, respectively. The zero population (i=0) is the control and the other k populations are treatments. Under the prior belief of  $\theta_1 \le ... \le \theta_p \ge ... \ge \theta_k$  for some p, Chen and Wolfe (1993) considered multiple test procedures for deciding the i with  $\theta_i > \theta_0$  when the peak of the umbrella (p) is known or unknown. However, they did not investigate the power performances of these multiple test procedures.

In the following sections we discribe some previously proposed test procedures for either the peak known or unknown settings. A formula for the isotonic regression which is useful for statistical inference under the umbrella pattern restriction is derived. An alternative to the Chen-Wolfe procedure for comparing peak-known umbrella pattern treatment effects with a control is then suggested. Finally, we present the results of an extensive Monte Carlo simulation investigation of the relative powers of the competing multiple test procedures considered in this paper.

### 2. DESCRIPTION OF PREVIOUS TEST PROCEDURES

Let  $R_{ij}$  be the rank of  $X_{ij}$  among the  $N = \sum_{i=0}^{k} n_i$  observations and let  $\tilde{R}_i = \sum_{i=1}^{n_i} R_{ij}/n_i$  be the average rank of the ith sample, i= 0,1, ..., k. Dunn (1964)

suggested to claim that  $\theta_i > \theta_o$  if

$$D_{i} = (\bar{R}_{i} - \bar{R}_{0}) [\{N(N+1)/12\}(1/n_{i}+1/c)]^{-1/2} \ge d(\alpha; k)$$

where  $d(\alpha; k)$  is the upper  $\alpha$ th percentile of the null distribution of the statistic  $max(D_1, ..., D_k)$ .

For comparing ordered treatment effects with a control, Shirley (1977) proposed a nonparametric version of Williams (1971, 1972, 1975) procedure based on the statistics

$$S_{k:i} = (\hat{R}_i^{(k)} - \tilde{R}_o) [\{N(N+1)/12\}(1/n_i + 1/c)]^{-1/2}, i = 1, ..., k,$$

where  $\hat{R}_1^{(k)} \le ... \le \hat{R}_k^{(k)}$  be the isotonic regression of  $\tilde{R}_1, ..., \tilde{R}_k$  under the restriction

 $\theta_1 \le ... \le \theta_k$ . Let  $s(\alpha; i)$  be the upper  $\alpha$ th percentile of the null distribution of the statistic  $S_{i:i}$ . If  $S_{k:i} \ge s(\alpha; i)$  for i=k, k-1, ..., u, but  $S_{k:u-1} < s(\alpha; u-1)$ , Shirley's procedure then claims that there is evidence for a response at doses u, ..., k.

Williams (1986) further considered a modification of Shirley's procedure by finding all relevant statistics from the observations in the first i treatment groups and the control group. Set  $N_i = \sum_{t=0}^{i} n_t$ , i = 1, ..., k. The  $N_i$  observations are ranked from smallest to largest and the average ranks,  $\bar{R}_{ri}$ , for r = 0, 1, ..., i, are obtained. Let  $\hat{R}_{1i}^{(i)} \le ... \le \hat{R}_{ii}^{(i)}$  be the isotonic regression of  $\bar{R}_{1i}$ , ...,  $\bar{R}_{ii}$  under the restriction  $\theta_1 \le ... \le \theta_i$ . Williams then suggested a multiple test procedure similar to the one proposed by Shirley (1976), but utilizing different statistics

$$W_i = (\hat{R}_{ii}^{(1)} - \bar{R}_{oi}) [\{N_i(N_i+1)/12\}(1/n_i+1/c)]^{-1/2}, i= 1, ..., k.$$

Owing to the fact that monotonicity of dose-response is far from universal, Chen and Wolfe (1993) considered comparing umbrella pattern treatment effects with a control. Suppose that the peak of the umbrella is known to be at group p  $(1 \le p \le k)$ . Let  $\hat{R}_1^{(p)} \le ... \le \hat{R}_p^{(p)} \ge ... \ge \hat{R}_k^{(p)}$  be the isotonic regression of  $\bar{R}_1$ , ...,  $\bar{R}_k$ under the restriction  $\theta_1 \le ... \le \theta_p \ge ... \ge \theta_k$ . For the case of  $n_0 = c$  and  $n_1 = ... = n_k = n$ , Chen and Wolfe suggested a multiple test procedure based on the statistics

$$T_{p:i} = (\hat{R}_{i}^{(p)} \cdot \tilde{R}_{0}) [\{N(N+1)/12\}(1/n+1/c)\}^{-1/2}, i=1, ..., k.$$

Note that the statistics  $T_{k:i}$  are actually Shirley's statistics  $S_{k:i}$ , i=1, ..., k. Let  $t(\alpha; k, p)$  be the upper  $\alpha$ th percentile of the null distribution of  $T_{p:p}$ . If  $T_{p:p} \ge t(\alpha; k, p)$ , the Chen-Wolfe procedure then claims that at least the dose p is better than the control. However, it is possible that this response occurs not only at dose p. They then suggested starting from both the doses p-land p+1 to search for those doses which were more effective than the control. If  $T_{p:p-1} < t(\alpha; k, p)$  and  $T_{p:p+1} < t(\alpha; k, p)$ , they concluded that there was evidence for a response only at dose p. If, however,  $T_{p:p-1} \ge t(\alpha; k, p)$  (and/or  $T_{p:p+1} \ge t(\alpha; k, p)$ ), they claimed that there was evidence for a response at doses p and p-1 (and/or p+1) and then suggested testing for a response at dose p-2 (and/or p+2). This procedure is continued until dose levels u and v are obtained for which  $T_{p:u-1} < t(\alpha; k, p)$  and  $T_{p:v+1} < t(\alpha; k, p)$ , where  $1 \le u . Finally, they concluded that there was evidence for a response at doses u, ..., v.$ 

For the more general setting where the peak of the umbrella is unknown but is believed to be relatively close to the kth population, Chen and Wolfe (1993) employed the method suggested by Simpson and Margolin (1986) to obtain an estimate of the unknown peak. Let  $U_{ij}$  be the usual Mann-Whitney statistic corresponding to the number of observations in sample j that exceed observations in sample i and let  $Q_j = \sum_{i=1}^{j-1} U_{ij}$ , j=2, ..., k. Set  $\hat{p}_s = \max_{2 \le j \le k} \{j: Q_j \ge (j-1)n^2/2\}$ . In this case, they proposed a multiple test procedure similar to that described above, but employing the test statistics

$$\Gamma_{\hat{\mathbf{p}}_{s}:i} = (\hat{\mathbf{R}}_{i}^{\hat{\mathbf{p}}_{s}} \cdot \tilde{\mathbf{R}}_{0}) [\{\mathbf{N}(\mathbf{N}+1)/12\}(1/n+1/c)]^{-1/2}, i=1, ..., k,$$
(2.4)

and critical values of the test based on  $T_{\hat{p}_s, \hat{p}_s}$ , to determine which treatments are better than the control.

## 3. ISOTONIC REGRESSION UNDER UMBRELLA PATTERN RESTRICTION AND A NEW MULTIPLE TEST PROCEDURE

An algorithm related to a quadratic programming problem for solving the isotonic regression under umbrella pattern restictions was proposed by Chen and Wolfe (1990). In their paper, however, the explicit form of the isotonic regression of  $\bar{R}_1$ , ...,  $\bar{R}_k$  under the restriction  $\theta_1 \leq ... \leq \theta_p \geq ... \geq \theta_k$ , namely,  $\bar{R}_1^{(p)} \leq ... \leq \bar{R}_p^{(p)} \geq ... \leq \theta_k$ 

 $... \ge \hat{R}_k^{(p)}$ , is not given, yet we only observe

$$\hat{R}_{p}^{(p)} = \max_{1 \le u \le p \le v \le k} \sum_{i=u}^{v} \bar{R}_{i} / (v - u + 1).$$

If we let a and b be the smallest and the largest integers such that  $\sum_{i=a}^{b} \overline{R}_{i}/(b-a+1) = \hat{R}_{p}^{(p)}$ , where  $1 \le a \le p \le b \le k$ , then it can seen that  $\hat{R}_{i}^{(p)} = \hat{R}_{p}^{(p)}$ , i=a, ..., b. Since Chen and Wolfe (1990) pointed out that  $\hat{R}_{1}^{(p)} \le ... \le \hat{R}_{p}^{(p)} \ge ... \ge \hat{R}_{k}^{(p)}$  is the solution to the quadratic programming problem :

$$\min \sum_{i=1}^{k} (r_i - \overline{R}_i)^2$$

subject to the constraints  $r_1 \le ... \le r_p \ge ... \ge r_k$ . We observe, for  $a \ge 2$  and/or  $b \le k-1$ ,

$$\min \sum_{i=1}^{k} (r_i - \overline{R}_i)^2 = \sum_{i=a}^{b} (\overline{R}_p^{(p)} - \overline{R}_i)^2 + \min \sum_{i=1}^{a-1} (r_i - \overline{R}_i)^2 + \min \sum_{i=b+1}^{k} (r_i - \overline{R}_i)^2.$$

Therefore,  $\hat{R}_{1}^{(p)} \leq ... \leq \hat{R}_{a-1}^{(p)}$  and  $\hat{R}_{b+1}^{(p)} \geq ... \geq \hat{R}_{k}^{(p)}$  can be respectively solved by applying the recursive formulas proposed by Puri and Singh (1990). That is, let

$$A_{a-1}^{(p)} = \max_{1 \le s \le a-1} \sum_{r=s}^{a-1} \overline{R_r}/(a-s)$$

and

$$\hat{R}_{b+1}^{(p)} = \max_{b+1 \le s \le k} \sum_{r=b+1}^{s} \overline{R}_{r}/(s-b).$$

If a≥3, set

$$\hat{R}_{i}^{(p)} = \max_{1 \le s \le i} \left\{ \sum_{r=s}^{a-1} \bar{R}_{r} - \sum_{w=i+1}^{a-1} \hat{R}_{w} \right\} / (i-s+1) \text{ for } i=a-2, ..., 1$$

and, if  $b \le k-2$ , set

$$\hat{R}_{j}^{(p)} = \max_{j \le s \le k} \left\{ \sum_{r=b+1}^{s} \bar{R_{r}} - \sum_{w=b+1}^{j-1} \hat{R_{w}} \right\} / (s-j+1) \text{ for } j=b+2, ..., k.$$

Based on the results in Williams (1986) and the above recursive formula for deriving the isotonic regression of  $\bar{R}_1$ , ...,  $\bar{R}_k$  under umbrella pattern restrictions, we consider a modification of the Chen-Wolfe (1993) procedure for comparing peak-known umbrella pattern treatment effects with a control. If  $T_{p:p} \ge t(\alpha; k, p)$ ,

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we claim that at least the doses a, ..., p, ..., b are better than the control. Recall that  $\hat{R}_{1i}^{(j)} \leq ... \leq \hat{R}_{ii}^{(j)}$  is the isotonic regression of  $\tilde{R}_{1i}$ , ...,  $\tilde{R}_{ii}$  under the restriction  $\theta_1 \leq ... \leq \theta_i$ , where the  $\tilde{R}_{ti}$  is the average rank of the rth sample calculated from the  $N_i = \sum_{t=0}^{i} n_t$  observations. For  $a \geq 2$ , to compare the first a-1 treatments with the control, we claim that treatments u, ..., a-1 are better than the control when  $W_i \geq s(\alpha; i)$  for  $u \leq i \leq a-1$ , but  $W_{u-1} < s(\alpha; u)$ . If  $b \leq k-1$ , to compare the last k-b+1 treatments with the control, we set  $N_j^* = n_0 + \sum_{t=j}^{k} n_t$ , j = b+1, ..., k. The  $N_j^*$ 

observations are then ranked from smallest to largest to obtain the average ranks,  $\tilde{R}_{sj}^*$ , for s=0, j, ..., k. Let  $\hat{R}_{jj}^{(j)*} \ge ... \ge \hat{R}_{kj}^{(j)*}$  be the isotonic regression of  $\tilde{R}_{jj}^*$ , ...,

 $\bar{R}_{ki}^*$  under the restriction  $\theta_i \ge ... \ge \theta_k$ . Set

$$W_{j}^{*} = (\hat{R}_{jj}^{(j)*} - \hat{R}_{oj}^{*})[\{N_{j}^{*}(N_{j}^{*}+1)/12\}(1/n_{j}+1/c)]^{-1/2}, j=b+1, ..., k.$$

If  $W_j^* \ge s(\alpha; k-j+1)$  for  $b+1 \le j \le v$ , but  $W_{v+1}^* < s(\alpha; k-v)$ , we then claim that

treatments b+1, ..., v are also better than the control. Finally, we conclude that there is evidence for a response at doses u, ..., v. Note that, for comparing ordered treatment effects with a control, this new procedure is in fact the modified Shirley's procedure proposed by Williams (1986).

#### 4. MONTE CARLO POWER STUDY

To investigate the relative power performances of Dunn's (1964) procedure, D, Shirley's (1977) procedure, S, Williams' (1986) procedure, W, the Chen-Wolfe (1993) procedures, CW(p) and CW( $p_s$ ), and the proposed modified Chen-Wolfe procedure, MCW(p), for comparing umbrella pattern treatment effects with a control, we conducted a Monte Carlo power study. The pairwise power, denoted by  $\pi_{io}$  (probability of declaring the ith treatment better than the control), and the comparison-wise power (probability of correctly detecting the treatments which are better than the control) were utilized to evaluate the power performances of these multiple test procedures.

In this study, we considered k= 3, 4 and 5 treatments, with  $n_0$ = 5 and 10 observations for the control sample, and  $n_1$ =...= $n_k$ = 5 observations per treatment

TABLEI

Pairwise power estimates for  $\alpha = .05$ ,  $n_1 = ... = n_3 = 5$  and  $n_0 = 5/10$ (a) Normal

θ <sub>lo</sub>	θ20	θ30		CW(p)	MCW(p)	S	W	CW(p <sub>s</sub> )	D
0	.5	1	π <sub>10</sub>	.015/.013	.020/.023	.017/.014	.020/.023	.009/.011	.011/.013
			π <sub>20</sub>	.107/.133	.122/.145	.112/.137	.122/.145	.079/.109	.070/.095
			π <sub>30</sub>	.401/.496	.401/.496	.401/.496	.401/.496	.298/.412	.243/.338
.5	ł	1	πlo	.085/.109	.092/.144	.086/.113	.092/.144	.065/.096	.061/.088
			π <sub>20</sub>	.284/.375	.292/.384	.286/.383	.292/.384	.271/.375	.236/.333
			π <sub>30</sub>	.450/.569	.450/.569	.450/.569	.450/.569	.313/.423	.242/.338
.5	1	0	π <sub>10</sub>	.098/.138	.107/.163	.050/.057	.049/.064	.091/.124	.071/.097
			π <sub>20</sub>	.384/.501	.384/.501	.096/.124	.101/.124	.277/.386	.237/.335
			<sup>π</sup> 30	.012/.013	.024/.045	.105/.129	.105/.129	.021/.028	.012/.016
.5	1	.5	π <sub>10</sub>	.100/.141	.107./.169	.078/.094	.076/.112	.084/.117	.069/.098
			π <sub>20</sub>	.407/.527	.407/.527	.203/.257	.202/.258	.286/.387	.249/.344
			<sup>π</sup> 30	.101/.136	.106/.168	.251/.308	.251/.308	.106/.150	.072/.102
1	.5	0	π <sub>10</sub>	.395/.507	.395/.507	.070/.079	.063/.080	.274/.379	.237/.335
			<sup>π</sup> 20	.114/.142	.121/.146	.076/.087	.073/.087	.095/.127	.073/.096
			<sup>π</sup> 30	.020/.018	.018/.025	.063/.100	.082/.100	.015/.022	.011/.017
1	.5	.5	π <sub>10</sub>	.422/.523	.422/.523	.114/.144	.101/.146	.246/.335	.250/.347
			<sup>л</sup> 20	.138/.171	.143/.176	.133/.166	.126/.165	.107/.146	.072/.100
			π <sub>30</sub>	.063/.079	.064/.091	.203/.254	.196/.254	.091/.130	.071/.103

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θ10	θ20	θ <sub>30</sub>		CW(p)	MCW(p)	S	W	CW(∮ <sub>s</sub> )	D
0	.5	1	π10	.025/.024	.028/.035	.029/.026	.028/.035	.018/.018	.020/.020
			π <sub>20</sub>	187/.227	.218/.260	.189/.234	.218/.260	.133/.175	.103/.141
			π <sub>30</sub>	.568/.698	.568/.698	.568/.698	.568/.698	.462/.614	.397/.529
.5	1	1	π <sub>lo</sub>	.157/.194	.188/.292	.158/.202	.188/.292	.118/.154	.102/.133
			<sup>π</sup> 20	.491/.627	.526/.656	.494/.637	.526/.656	.446/.583	.409/.528
			π <sub>30</sub>	.632/.763	.632/.763	.632/.763	.632/.763	.492/.629	.402/.530
.5	1	0	πlo	.181/.224	.188/.296	.098/.112	.113/.140	.141/.181	.111/.138
			<sup>π</sup> 20	.563/.707	.563/.707	.169/.194	.173/.195	.449/.592	.396/.529
			π <sub>30</sub>	.019/.021	.030/.045	.174/.195	.172/.195	.030/.035	.019/.020
.5	1	.5	π <sub>lo</sub>	.192/.243	.197/.303	.168/.204	.177/.260	.157/.195	.128/.158
			<sup>π</sup> 20	.615/.753	.615/.753	.374/.473	.386/.478	.489/.624	.453/.580
			<sup>π</sup> 30	.193/.240	.196/.303	.400/.492	.400/.492	.176/.221	.130/.158
1	.5	0	π <sub>lo</sub>	.575/.715	.575/.715	.132/.148	.130/.151	.443/.586	.402/.535
			π <sub>20</sub>	.193/.240	.214/.263	.135/.150	.132/.152	.140/.188	.103/.138
			π <sub>30</sub>	.028/.028	.026/.034	.144/.159	.140/.159	.024/.027	.019/.020
1	.5	.5	$\pi_{lo}$	.629/.749	.629/.749	.256/.328	.259/.337	.439/.553	.460/.586
			π <sub>20</sub>	.242/.305	.284/.330	.265/.337	.274/.342	.194/.242	.126/.155
			π <sub>30</sub>	.130/.159	.165/.214	.321/.410	.330/.410	.149/.185	.128/.155
			•						

TABLE II Pairwise power estimates for  $\alpha$ =.05,  $n_1$ = ...= $n_4$ = 5 and  $n_o$ = 5 /10 (a) Normal

$\overline{\theta_{10}}$	θ20	θ <sub>30</sub>	θ40		CW(p)	MCW(p)	S	w	CW(p <sub>s</sub> )	D
0	0	.5	1	<sup>π</sup> 10	.006/.005	.010/.007	.007/.006	.010/.007	.003/.002	.010/.012
				π20	.020/.017	.030/.022	.022/.019	.030/.022	.008/.008	.010/.012
				π30	.112/.146	.130/.154	.117/.151	.130/.154	.071/.085	.058/.083
				π <sub>40</sub>	.390/.512	.390/.512	.390/.512	.390/.512	.284/.358	.213/.291
.5	1	1	1.5	π10	.060/.093	.090/.139	.063/.094	.090/.139	.027.042	.040/.062
				<sup>π</sup> 20	.239/.339	.288/.377	.249/.356	.228/.377	.154/.220	.192/.270
				<sup>π</sup> 30	.382/.527	.422/.552	.387/.532	.422/.552	.274/.374	.180/.273
				π <sub>40</sub>	.710/.850	.710/.850	.710/.850	.710/.850	.566/.708	.475/.630
0	.5	I	0	<sup>π</sup> 10	.015/.016	.017/.023	.011/.011	.015/.016	.009/.008	.010/.012
				π <sub>20</sub>	.109/.147	.113/.148	.059/.065	.062/.073	.071/.089	.061/.082
				<sup>π</sup> 30	.383/.509	.383/.509	.102/.131	.106/.140	.256/.337	.208/.294
				<sup>π</sup> 40	.027/.035	.036/.042	.112/.144	.112/.144	.025!.027	.011/.010
.5	1	1.5	.5	π <sub>10</sub>	.074/.113	.095/.152	.068/.101	.082/.137	.043/.059	.061/.066
				π <sub>20</sub>	.321/.459	.352/.467	.242/.330	.254/.357	.243/.322	.236/.281
				<sup>π</sup> 30	.687/.843	.687/.843	.360/.491	.357/.507	.545/.688	.538/.634
				<sup>π</sup> 40	.103/.137	.143/.200	.365/.512	.365/.512	.087/.116	.064/.069
0	1	.5	0	π <sub>lo</sub>	.023/.032	.025/.041	.014/.014	.015/.019	.015/.014	.015/.012
				<sup>π</sup> 20	.363/.497	.363/.497	.074/.084	.078/.091	.212/.268	.261/.294
				<sup>π</sup> 30	.103/.113	.125/.147	.078/.092	.085/.100	.101/.134	.084/.082
				<sup>π</sup> 40	.011/.012	.027/.022	.094/.113	.094/.113	.019/.017	.016/.010
1	1.5	.5	.5	π <sub>lo</sub>	.303/.427	.291/.477	.153/.230	.151/.244	.229/.303	.243/.281
				<sup>π</sup> 20	.689/.831	.689/.831	.216/.306	.211/.311	.488/.612	.538/.630
				<sup>π</sup> 30	.119/.127	.173/.208	.217/.312	.213/.314	.085/.121	.061/.068
				<sup>π</sup> 40	.042/.041	.087/.094	.250/.362	.250/.362	.058/.077	.065/.066
1	.5	0	0	πlo	.385/.516	.385/.516	.036/.037	.037/.035	.226/.292	.256/.304
				<sup>π</sup> 20	.113/.151	.128/.157	.041/.036	.041/.037	.082/.096	.083/.081
				<sup>π</sup> 30	.022/.019	.030/.022	.042/.039	.043/.040	.014/.018	.016/.013
				π <sub>40</sub>	.007/.005	.011/.007	.060/.064	.060/.064	.014/.014	.016/.010
1.5	1	1	.5	π <sub>10</sub>	.716/.851	.716/.851	.249/.383	.246/.382	.451/.557	.538/.636
				<sup>π</sup> 20	.384/.541	.422/.551	.271/.390	.270/.399	.281/.381	.236/.269
				<sup>π</sup> 30	.237/.361	.294/.379	.291/.424	.293/.430	.237/.319	.234/.274
				π <sub>40</sub>	.060/.100	.113/.143	.312/.456	.312/.456	.051/.078	.058/.062

# TABLE II Continued

(b) Exponential

$\overline{\theta_{10}}$	θ20	θ30	θ40		CW(p)	MCW(p)	S	W	CW(∲ <sub>s</sub> )	D
0	0	.5	1	<sup>π</sup> 10	.008/.008	.012/.009	.010/.008	.012/.009	.004/.003	.019/.016
				π <sub>20</sub>	.029/.032	.037/.036	.032/.033	.037/.036	.013/.013	.019/.015
				π <sub>30</sub>	.188/.247	.222/.267	.189/.249	.222/.267	.117/.143	.115/.121
				π <sub>40</sub>	.548/.713	.548/.713	.548/.713	.548/.713	.426/.555	.399/.470
.5	1	1	1.5	<sup>π</sup> 10	.108/.159	.191/.297	.116/.160	.191/.297	.056/.800	.084/.085
				<sup>π</sup> 20	.407/.556	.525/.659	.411/.564	.525/.659	.294/.397	.364/.411
				<sup>π</sup> 30	.542/.715	.628/.763	.543/.720	.628/.763	.431/.565	.355/.407
				π <sub>40</sub>	.844/.953	.844/.953	.844/.953	.844/.953	.758/.889	.742/.850
0	.5	1	0	πlo	.025/.027	.028/.033	.020/.020	.023/.025	.014/.014	.020/.017
				π <sub>20</sub>	.178/.244	.213/.265	.110/.116	.130/.139	.117/.137	.117/.111
				π30	.530/.710	.530/.710	.167/.194	.178/.206	.400/.525	.397!.472
				π40	.035/.044	.032/.049	.180/.203	.180/.203	.035/.039	.018/.016
.5	I	1.5	.5	πιο	.140/.193	.188/.299	.143/.187	.183/.293	.088/.109	.105/.100
				π <sub>20</sub>	.507/.675	.565/.704	.430/.573	.472/.624	.411/.529	.403/.455
				π30	.836/.953	.836/.953	.528/.690	.536/.706	.748/.879	.743/.851
				π <sub>40</sub>	.161/.212	.191/.315	.537/.701	.537/.701	.124/.155	.100/.103
0	1	.5	0	<sup>π</sup> 10	.033/.038	.032/.044	.023/.023	.020/.027	.024/.024	.019/.017
				<sup>π</sup> 20	.530/.699	.530/.699	.141/.153	.136/.168	.327/.427	.390/.472
				<sup>π</sup> 30	.176/.220	.206/.262	.143/.159	.137/.169	.168/.210	.119/.117
				π <sub>40</sub>	.026/.023	.027/.038	.146/.172	.146/.172	.026/.030	.021/.017
1	1.5	.5	.5	π <sub>io</sub>	.481/.643	.443/.691	.328/.465	.329/.504	.383/.498	.386/.447
				π <sub>20</sub>	.844/.950	.844/.950	.384/.513	.379/.533	.695/.824	.738/.856
				π <sub>30</sub>	.188/.209	.288/.340	.385/.521	.379/.534	.146/.190	.100/.108
				<sup>π</sup> 40	.082/.097	.159/.216	.399/.556	.399/.556	.081/.106	.099/.102
1	.5	0	0	π <sub>10</sub>	.550/.716	.550/.716	.069/.070	.073/.072	.358/.465	.400/.472
				<sup>π</sup> 20	.188/.258	.219/.269	.072/.068	.073/.072	.124/.148	.118/.113
				<sup>π</sup> 30	.031/.037	.039/.037	.073/.071	.074/.073	.024/.027	.021/.018
				π <sub>40</sub>	.009/.010	.011/.013	.091/.097	.091/.097	.020/.021	.021/.017
1.5	1	1	.5	π <sub>10</sub>	.849/.953	.849/.953	.445/.629	.446/.636	.662/.792	.740/.849
				π <sub>20</sub>	.550/.723	.624/.763	.455/.623	.456/.637	.444/.585	.363/.412
				π30	.409/.570	.525/.656	.463/.637	.464/.645	.363/.467	.371/.407
				π <sub>40</sub>	.112/.167	.190/.293	.475/.654	.475/.654	.073/.104	.087/.088

TABLE III Pairwise power estimates for  $\alpha$ =.05,  $n_1$ = ...= $n_5$ = 5 and  $n_0$ =5/10 (a) Normal

$\overline{\theta_{1o}\theta_{2o}\theta_{3o}\theta_{4o}\theta_{5o}}$	CW(p)	MCW(p)	S	W	CW(p <sub>s</sub> )	D
00.511.5 π	o .004/.004	.010/.008	.004/.004	.010/.008	:001/.001	.006/.006
π	013/.013	.027/.023	.014/.014	.027/.023	.005/.004	.006/.007
π3	o .084/.124	.121/.155	.093/.126	.121/.155	.042/.058	.004/.006
π_	o .317/.449	.354!.477	.339/:451	.354/.477	.215/.296	.182/.235
π	o .675/.821	.675/.821	.675/.821	.675/.821	.524/.690	.424/.568
$.5.5$ 1 1 1.5 $\pi_1$	o .038/.052	.065/.100	.042/053	.065/.100	.013/.019	.042/.056
π2	o .097/.122	.137/.161	.100/124	.137/.161	.037/.055	.042/.054
π3	o .267/.370	.301/.412	.275/.375	.301/.412	.157/.230	.184/.253
π⊿	.393/.544	.423/.574	.412/.547	.423/.574	.276/.377	.195/.244
π	.717/.851	.717/.851	.717/.851	.717/.851	.564/.717	.472/.601
0.5 1.5 1 0 π	.011/.015	.020/.026	.010/.012	.018/.021	.004/.004	.006/.006
π <sub>2</sub>	o .114/.154	.142/.177	.073/.089	.095/.108	.059/.079	.042/.054
- π <sub>3</sub>	.668/.821	.668/.821	.188/.262	.208/.268	.403/.544	.429/.568
π4	.292/.310	.319/.430	.189/.273	.211/.273	.311/.424	.181/.236
π.	.012/.015	.026/.039	.210/.272	.210/.271	.015/.021	.005/.007
.5 1 1.5 1 .5 π <sub>1</sub>	.081/.114	.101/.155	.071/.099	.090/.134	.038/.054	.041/.055
<sup>π</sup> 2	.348/.467	.360/.476	.232/.324	.259/.345	.218/.303	.190/.250
π3	.725/.864	.725/.864	.326/.473	.353/.481	.474/.602	.491/.628
π4	.350/.458	.364/.471	.337/.491	.364/.491	.301/.397	.190/.242
πς	.091/.129	.101/.158	.377/.505	.377/.505	.071/.100	.035/.054
1.5 1 .5 0 0 π <sub>1</sub>	.679/.828	.679/.828	.071/.086	.077/.085	.429/.562	.445/.578
π <sub>2</sub>	.350/.463	.360/.486	.072/.082	.080/.086	.225/.318	.180/.237
<sup>π</sup> 3	.095/.132	.124/.153	.069/.085	.080/.087	.057/.082	.040/.057
π4	.015/.017	.027/.024	.092/.089	.079/.088	.009/.012	.005/.007
<sup>π</sup> 5	.005/.005	.010/.008	.092/.102	.092/.102	.006/.011	.005/.008
1.5 1 1 .5 .5 π <sub>1</sub>	o .726/.857	.726/.857	.199/.297	.200/.294	.397/.497	.474/.600
π2	.423/.558	.433/.579	.206/.300	.217/.304	.263/.364	.191/.250
<sup>л</sup> з	.281/.387	.304/.412	.209/.315	.227/.318	.222/.313	.181/.252
<sup>π</sup> 4	.100/.132	.135/.161	.217/.326	.229/.324	.073/.097	.045/.054
π5	.043/.056	.065/.084	.275/.371	.275/.371	.055/.075	.043/.055

# TABLE III Continued

(b) Exponential

$\overline{\theta_{10}\theta_{20}\theta_{30}\theta_{40}\theta_{50}}$	CW(p)	MCW(p)	S	W	CW(ps)	D
0.0 5 1 15 -	005/000	012/010	005/005			
$00.511.5\pi_{10}$	.005/.000	.013/.010	.005/.005	.013/.010	.001/.001	.009/.011
<sup>π</sup> 20	.021/.023	.038/.032	.024/.023	.038/.032	.005/.007	.011/.011
<sup>π</sup> 30	.162/.197	.225/.263	.147/.195	.225/.263	.061/.100	.064/.073
<sup>π</sup> 40	.489/.641	.549/.714	.502/.644	.549/.714	.301/.472	.279/.353
π <sub>50</sub>	.810/.934	.810/.934	.810/.934	.810/.934	.656/.853	.616/.804
$.5.5111.5\pi_{10}$	.087/.110	.169/.219	.092/.111	.169/.219	.020/.043	.073/.081
<sup>π</sup> 20	.180/.221	.284/.326	.189/.225	.284/.326	.071/.116	.074/.084
<sup>л</sup> зо	.459/.600	.565/.704	.478/.608	.568/.704	.281/.432	.333/.403
π <sub>40</sub>	.597/.747	.650/.803	.609/.750	.650/.803	.420/.596	.332/.406
π50	.863/.955	.863/.955	.863/.955	.863/.955	.746/.900	.710/.849
0.5 1.5 1 0 π <sub>10</sub>	.020/.022	.030/.038	.019/.021	.028/.035	.005/.009	.010/.011
π <sub>20</sub>	.173/.208	.224/.268	.129/.150	.181/.207	.074/.111	.063/.071
<sup>π</sup> 30	.804/.935	.804/.935	.303/.391	.334/.402	.493/.728	.606/.810
π <sub>40</sub>	.352/.521	.484/.644	.305/.402	.334/.402	.421/.614	.280/.358
π <sub>50</sub>	.022/.036	.031/.047	.329/.399	.329/.399	.022/.030	.010/.010
.5 1 1.5 1 .5 π <sub>10</sub>	.149/.191	.197/.307	.144/.186	.194/.301	.065/.106	.074/.085
π <sub>20</sub>	.530/.667	.573/.709	.439/.573	.502/.631	.355/.507	.335/.405
π30	.864/.961	.864/.961	.540/.698	.568/.707	.649/.830	.705/.853
π <sub>40</sub>	.534/.668	.574/.712	.541/.706	.568/.707	.429/.589	.335/.410
π <sub>50</sub>	.151/.201	.196/.299	.568/.708	.568/.708	.098/.138	.079/.086
$1.5 \ 1 \ .5 \ 0 \ 0 \ \pi_{10}$	.810/.941	.810/.941	.133/.158	.148/.160	.578/.775	.609/.796
<sup>π</sup> 20	.508/.651	.547/.709	.133/.150	.148/.160	.308/.464	.281/.350
π <sub>30</sub>	.165/.206	.223/.265	.130/.156	.148/.160	.075/.118	.063/.074
π40	.022/.025	.036/.032	.133/.160	.146/.160	.012/.019	010.\900.
<sup>π</sup> 50	.007/.007	.012/.009	.157/.171	.158/.171	.011/.014	.010/.009
1.5 1 1 .5 .5 π <sub>10</sub>	.862/.959	.862/.959	.402/.542	.418/.550	.584/.758	.706/.841
π <sub>20</sub>	.613/.754	.648/.800	.403/.535	.424/.550	.419/.595	.334/.405
π <sub>30</sub>	.484/.619	.566/.702	.401/.541	.427/.552	.346/.497	.335/.401
$\pi_{40}$	.190/.239	.286/.336	.406/.550	.425/.553	.108/.161	.074/.085
π <sub>50</sub>	.093/.115	.167/.218	.454/.574	.454/.574	.066/.097	.079/.083

TABLE IV Comparison-wise power estimates for  $\alpha = .05$ ,  $n_0 = c$  and  $n_1 = ... = n_3 = 5$ (a) Normal

θιο	θ20	θ <sub>30</sub>	с	CW(p)	MCW(p)	S	W	CW(\$s)	D
 0	.5	1	5	.095	.102	.094	.102	.058	.036
			10	.120	.122	.118	.122	.079	.046
.5	1	1	5	.080	.090	.080	.090	.032	.014
			10	.109	.144	.112	.144	.049	.025
.5	1	0	5	.091	.094	.000	.000	.050	.034
			10	.124	.142	.000	.000	.070	.048
.5	1	.5	5	.037	.039	.075	.076	.018	.008
			10	.046	.066	.094	.111	.024	.011
1	.5	0	5	.099	.102	.000	.000	.050	.035
			10	.124	.125	.000	.000	.072	.050
1	.5	.5	5	.063	.064	.101	.108	.028	.008
			10	.079	.091	.142	.146	.040	.012

				(0) 2	"rponontia				
 θιο	θ20	θ30	С	CW(p)	MCW(p)	S	W	CW( $\beta_s$ )	D
 0	.5	1	5	.162	.190	.159	.190	.111	.077
			10	.203	.224	.208	.224	.152	.105
.5	1	1	5	.159	.189	.158	.189	.090	.058
			10	.194	.291	.201	.291	.122	.079
.5	1	0	5	.163	.166	.000	.000	.109	.082
			10	.203	.263	.000	.000	.140	.102
.5	1	.5	5	.094	.120	.172	.177	.056	.038
			10	.103	.185	.204	.260	.065	.040
1	.5	0	5	.168	.187	.000	.000	.102	.075
			10	.212	.229	.000	.000	.143	.107
1	.5	.5	5	.136	.165	.255	.259	.087	.033
			10	.159	.214	.326	.337	.108	.041

(b) Exponential

sample, and a variety of umbrella pattern treatment effects. The designated configurations of treatment effects correspond to values of  $\theta_{10} = \theta_1 - \theta_0$ , ...,  $\theta_{k0} = \theta_k - \theta_0$ . For each of these settings, the International Mathematical and Statistical Libraries (IMSL) routine RNUN was used to generate uniformly distributed random numbers in (0,1]. Routines RNNOR and RNEXP were employed to generate appropriate normal and exponential deviates according to the pertinent treatment effects. In each case, we used 10,000 replications to obtain the various power estimates. Simulated critical values corresponding to level  $\alpha$ =0.05 were

					(a	) Normai				
$\overline{\theta_{lo}}$	θ20	θ30	θ40	с	CW(p)	MCW(p)	S	W	CW(∮ <sub>s</sub> )	D
0	0	.5	I	5	.097	.101	.090	.101	.056	.030
				10	.130	.131	.128	.131	.066	.037
.5	1	1	1.5	5	.060	.090	.063	.090	.021	.004
			•	10	.093	.139	.092	.139	.033	.010
0	.5	1	0	5	.081	.083	.000	.000	.048	.031
				10	.110	.130	.000	.000	.060	.037
.5	1	1.5	.5	5	.021	.040	.068	.082	.007	.001
				10	.034	.060	.098	.136	.011	.005
0	1	.5	0	5	.082	.089	.000	.000	.059	.031
				10	.110	.136	.000	.000	.077	.035
1	1.5	.5	.5	5	.028	.063	.153	.151	.015	.002
				10	.041	.075	.222	.244	.020	.004
1	.5	0	0	5	.091	.098	.000	.000	.045	.027
				10	.132	.140	.000	.000	.052	.037
1.5	1	1	.5	5	.060	.113	.249	.246	.025	.004
				10	.100	.143	.367	.382	.042	.008

TABLE V Comparison-wise power estimates for  $\alpha$ =.05,  $n_0$ = c and  $n_1$ = ... = $n_4$ =5 (a) Normal

θιο	θ20	θ30	θ40	с	CW(p)	MCW(p)	S	W	CW(\$)	D
0	0	.5	1	5	.156	.185	.160	.185	.102	.063
				10		.231	.221	.231	.127	.085
.5	1	1	1.5	5	.108	.191	.116	.191	.055	.016
				10	.159	.297	.160	.297	.078	.030
0	.5	1	0	5	.137	.166	.000	.000	.086	.063
				10	.200	.217	.000	.000	.110	.077
.5	1	1.5	.5	5	.046	.117	.143	.183	.020	.007
				10	.068	.185	.186	.293	.027	.014
0	1	.5	0	5	.135	.160	.000	.000	.121	.061
				10	.201	.225	.000	.000	.156	.080
1	1.5	.5	.5	5	.072	.150	.328	.329	.044	.005
				10	.096	.212	.451	.504	.062	.015
1	.5	0	0	5	.157	.180	.000	.000	.088	.060
				10	.221	.233	.000	.000	.105	.078
1.5	1	1	.5	5	.112	.190	.445	.446	.059	.015
				10	.167	.293	.616	.636	.089	.033

# (b) Exponential

TABLE VI Comparison-wise power estimates for  $\alpha$ =.05,  $n_0$ = c and  $n_1$ = ... = $n_5$ =5 (a) Normal

θιοθ	20 θ	30 <sup>θ</sup>	40	θ50	с	CW(p)	MCW(p)	S	W	CW(∲ <sub>s</sub> )	D
0.0	.5	1		1.5	5	.079	.093	.071	.093	.027	.016
					10	.112	.131	.111	.131	.052	.020
.5.5	1		1	1.5	5	.042	.065	.038	.065	.006	.001
					10	.052	.081	.051	.081	.016	.001
0.5	1	5	1	0	5	.051	.073	.000	.000	.022	.015
					10	.080	.085	.000	.000	.042	.019
.5 1	1	.5	1	.5	5	.019	.037	.070	.090	.003	.001
					10	.029	.053	.096	.133	.008	.001
1.5	1	.5	0	0	5	.080	.097	.000	.000	.016	.015
					10	.115	.129	.000	.000	.050	.019
1.5	1	1	.5	.5	5	.043	.065	.195	.196	.009	.002
					10	.056	.084	.286	.294	.027	.002

(b) Exponential

$\overline{\theta_{10}} \theta_2$	<sub>20</sub> θ <sub>3</sub>	θ	40	θ50	с	CW(p)	MCW(p)	S	W	CW(\$s)	D
00	.5	1		1.5	5	.139	.186	.126	.186	.056	.038
					10	.174	.231	.172	.231	.093	.040
.5.5	1		1	1.5	5	.092	.169	.085	.169	.020	.003
					10	.110	.218	.107	.218	.043	.006
0.5	1.	5	1	0	5	.099	.157	.000	.000	.050	.037
					10	.115	.189	.000	.000	.076	.040
.5 1	1	.5	1	.5	5	.049	.122	.145	.194	.009	.004
					10	.061	.187	.183	.300	.024	.007
1.5	1	.5	0	0	5	.142	.187	.000	.000	.058	.037
					10	.181	.233	.000	.000	.095	.040
1.5	1	1	.5	.5	5	.093	.167	.400	.415	.036	.004
					10	.115	.218	.530	.550	.066	.007

used. The simulated pairwise and comparison-wise power estimates for the six procedures considered in this paper are then presented in Tables I - V I.

We observe from the simulation results that Williams' procedure, W, is generally better than Shirley's procedure, S, for comparing ordered treatment effects with a control. Likewise, the procedure MCW(p) provides an improvement over CW(p) for comparing peak known umbrella pattern treatment effects with a control. Although W or S is better than the other competing procedures in terms of comparison-wise power when the treatments are all better than the control, both W

and S perform poorly when the kth treatment is the same as the control. In these cases, the procedures CW(p), MCW(p),  $CW(p_s)$  and D all do better than W and S.

For comparing unknown peak umbrella pattern treatment effects with a control, the Chen-Wolfe procedure,  $CW(p_s)$ , is superior to Dunn's procedure, D, with respective to comparison-wise power. In terms of pairwise power, however,  $CW(p_s)$  may not be as powerful as D when the peak group is relatively far from the kth population.

As a consequence of the simulation results, we, therefore, have several recommendations. When the prior information about the umbrella pattern treatment effects is available, the procedure MCW(p) should be used if one is relatively confident of the location of the peak group. The procedure  $CW(p'_s)$  is recommended if the peak group of the the umbrella is unknown, but is believed to be relatively close to the kth population. For the setting where no information about the location of the peak group is available, Dunn's procedure, D, is then suggested.

#### ACKNOWLEDGEMENTS

The author is grateful to the associate editor for helpful comments and suggestions which led to improvements in the presentation of the material in this manuscript.

#### BIBLIOGRAPHY

- Chen, Y. I. and Wolfe, D. A. (1990). A study of distribution-free tests for umbrella alternatives. *Biometrical Journal* 32, 47-57.
- Chen, Y. I. and Wolfe, D. A. (1993). Nonparametric procedures for comparing umbrella pattern treatment effects with a control in a one-way layout. To appear in *Biometrics*.
- Dunn, O. J. (1964). Multiple comparisons using rank sums. Technometrics 6, 241-252.
- Mack, G. A. and Wolfe, D. A. (1981). K-sample rank tests for umbrella alternatives. *Journal of the American Statistical Association* **76**, 175-181.

Puri, P. S. and Singh, H. (1990). On recursive formulas for isotonic regression useful for statistical inference under order restrictions. *Journal of Statistical Planning and Inference* 24, 1-11.

Shirley, E. (1977). A non-parametric equivalent of Williams' test for contrasting increasing dose levels of a treatment. *Biometrics* 33, 386-389.

- 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.
- Williams, D. A. (1975). Correction to "A test for differences between treatment means when several dose levels are compared with a zero dose control," by Williams, D. A. (1971), *Biometrics* 27, 103-17, and "The comparison of several dose levels with a zero dose control," by Williams, D. A. (1972), *Biometrics* 28, 519-31. *Biometrics* 31, 1019.
- Williams, D. A. (1986). A note on Shirley's nonparametric test for comparing several dose levels with a zero-dose control. *Biometrics* 42, 183-186.

Received April 1992; Revised February 1993