

## GENERAL RANKED SET SAMPLING FOR EFFICIENT TREATMENT COMPARISONS

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*Abstract:* In treatment comparison experiments, the treatment responses are often correlated with some concomitant variables which can be measured before or at the beginning of the experiments. In this article, we propose schemes for the assignment of experimental units that may greatly improve the efficiency of the comparison in such situations. The proposed schemes are based on general ranked set sampling. The relative efficiency and cost-effectiveness of the proposed schemes are studied and compared. It is found that some proposed schemes are always more efficient than the traditional simple random assignment scheme when the total cost is the same. Numerical studies show promising results using the proposed schemes.

*Key words and phrases:* Correlation, cost-effectiveness, ranked set sampling, relative precision, treatment comparison.

### 1. Introduction

Ranked set sampling (RSS) was first proposed by McIntyre (1952) and has been extensively studied in recent years. This is a methodology for improving cost-effectiveness in certain situations. For an introduction to RSS, the reader is referred to Chen, Bai and Sinha (2004). In the context of experiments for treatment comparisons, experimental units are usually associated with certain concomitant variables that are correlated with the treatment responses and can be measured before the experiment starts. For example in certain clinical trials, baseline variables are often measured before treatment assignment, are correlated with the treatment responses, and can be taken as the concomitant variables. A clinical trial example will be discussed later. In such situations, the methodology of RSS can be used to devise assignment schemes for improving the efficiency of the comparisons (cf., Chen and Wang (2004)).

The RSS is a two-stage sampling procedure. At the first stage, a simple random sample of sampling units (referred to as a set in RSS) is taken without measuring the variable of interest, and the units in the set are ranked by some other means. At the second stage, only the unit in the set with a pre-specified rank is taken for the measurement of the variable of interest. By taking into

account the cost involved in sampling and ranking the units, Wang, Chen and Liu (2004) proposed general ranked set sampling (GRSS): at the second stage of RSS, more than one unit are taken for the measurement of the variable of interest.

In this article, the idea of GRSS is applied to devise assignment schemes for treatment comparisons. For clarity, we focus on two treatments. However the proposed schemes can be easily extended to the case of multiple-treatment comparison. We refer to a scheme devised this way as a GRSS scheme. In the case of two treatments, a typical GRSS scheme goes as follows. At the second stage of the GRSS, an even number of units with pre-specified ranks are taken and divided into two subsets of equal size, the units in one subset are assigned to one treatment and the units in the other subset are assigned to the other treatment. The principle here is very closely related to matched-pair designs and stratified sampling. To ensure the unbiasedness of the estimation for the treatment effect means, the ranks are pre-specified in such a way that the scheme results in a balanced GRSS sample for each treatment.

Suppose the responses from the two treatments (1 and 2) using a balanced design can be described as follows.

$$Y_i = \gamma_1 + \beta_1 X_{1i} + \epsilon_{1i}, \quad Z_i = \gamma_2 + \beta_2 X_{2i} + \epsilon_{2i}, \quad i = 1, \dots, n,$$

where the  $X_{li}$  is the value of the concomitant variable of the  $i$ th unit with treatment  $l$ , and the  $\epsilon_{li}$ 's are independent and identically distributed with mean zero and variance  $\sigma_l^2$ ,  $l = 1, 2$ . Here the  $\epsilon_{li}$ 's are independent of the  $X_{li}$ 's. The treatment comparison is made by a test based on the sample mean difference  $\bar{Y} - \bar{Z}$ . The power of the test depends on the variance of this difference. In a GRSS scheme, experiment units are ranked according to the values of the concomitant variable. The lack of complete mutual dependence in each of the GRSS samples and the positive correlation between the two GRSS samples will greatly reduce the variance of the sample mean difference.

The article is arranged as follows. In Section 2, various GRSS schemes are proposed. In Section 3, the variances of the sample mean difference under the proposed GRSS schemes are displayed. In Section 4, we consider the efficiency and cost-effectiveness of these GRSS schemes. Some technical details are given in the Appendix.

## 2. General Ranked Set Sampling Schemes

Let  $k$  be the set size in RSS and  $\tau$  an even number smaller than or equal to  $k$ . A GRSS scheme can be described as follows. At the first step,  $k$  experimental units are taken at random and ranked according to their values of the concomitant variable  $X$ . Let  $\tau$  numbers (ranks) be chosen from  $\{1, \dots, k\}$  according to some rule and then divided into subsets 1 and 2 of equal size. The units with ranks

in the first subset are assigned to treatment 1 and the units with ranks in the second subset are assigned to treatment 2. The units whose ranks are not among the  $\tau$  chosen ranks are discarded. At the second step, a new sample is taken and the same process as in the first step is repeated. The same subsets of ranks are considered, but this time the units with ranks in the first subset are assigned to treatment 2 and the units with ranks in the second subset are assigned to treatment 1. These two steps are repeated for different sets of ranks. The sets of ranks are chosen in such a way that each rank is assigned the same number of times as others to each treatment. We refer to such an assignment as a first-order balanced GRSS scheme. The requirement of first-order balancedness is necessary for the resultant treatment sample means to be unbiased estimates of the expected treatment means. A first-order balanced assignment can be achieved in various ways, some specific methods will be introduced later.

Now we define second-order balance. A second-order balanced assignment satisfies the following two requirements: (i) all  $\binom{k}{\tau}$   $\tau$ -tuples of ranks are chosen the same number of times, and (ii) for a given  $\tau$ -tuple, all  $\binom{\tau}{\tau/2}$  subsets of the  $\tau$ -tuple of size  $\tau/2$  are assigned the same number of times to each treatment. A second-order balanced assignment is also a first-order balanced one. To distinguish, we reserve the terminology “first-order balanced” for the schemes which are first-order balanced but not second-order balanced. A second-order balanced assignment may not be statistically desirable, as will be illustrated later. However, for the completeness, we include second-order balance to make comparisons with first-order balance.

In the remainder of this section, we give details for second-order balanced GRSS schemes with  $\tau = 2$  and 4, and two special first-order balanced GRSS schemes.

*Second-order balanced GRSS scheme with  $\tau = 2$ .* The procedure is carried out in cycles. In each cycle, each of  $\binom{k}{2}$  pairs of ranks  $(i, j)$ ,  $1 \leq i < j \leq k$ , is specified once. For each pair  $(i, j)$ , two sets of experimental units, each of size  $k$ , are taken at random and ranked according to their  $X$ -values within each set. Then, in the first set, the unit with rank  $i$  is assigned to treatment 1, the unit with rank  $j$  is assigned to treatment 2 and the others are discarded. In the second set, the unit with rank  $i$  is assigned to treatment 2, the unit with rank  $j$  is assigned to treatment 1 and the others are discarded.

*Second-order balanced GRSS scheme with  $\tau = 4$ .* Again, the procedure is carried out in cycles. In every cycle, each of the  $\binom{k}{4}$  4-tuples of ranks is specified for six ranked sets. For a given 4-tuple, say  $(i_1, i_2, i_3, i_4)$ , the units with these ranks in the six ranked sets are assigned to treatments 1 or 2 according to Table 1. The units with ranks other than  $i_1, i_2, i_3$  and  $i_4$  are discarded.

Table 1. Assignment of prespecified ranks to treatments in a second-order balanced GRSS scheme with  $\tau = 4$ .

Set number	Ranks of units assigned to treatment 1	Ranks of units assigned to treatment 2
1	$(i_1, i_2)$	$(i_3, i_4)$
2	$(i_1, i_3)$	$(i_2, i_4)$
3	$(i_1, i_4)$	$(i_2, i_3)$
4	$(i_2, i_3)$	$(i_1, i_4)$
5	$(i_2, i_4)$	$(i_1, i_3)$
6	$(i_3, i_4)$	$(i_1, i_2)$

We now turn to first-order balanced GRSS schemes. As mentioned earlier, first-order balanced GRSS schemes are not unique. It is desirable to devise a first-order balanced scheme that would result in the most efficient comparison. An understanding of why GRSS schemes can lead to more efficiency is helpful. The ranked set schemes achieve more efficiency by (i) breaking off the correlations among the induced order statistics within each treatment, and (ii) introducing positive correlations among the induced order statistics between the two treatments. It is well known that order statistics are more correlated when their ranks are closer to each other. Therefore, as a rule of thumb, units with ranks close to each other should be assigned to different treatments, units assigned to the same treatment should have ranks as far apart as possible. In the following, we present two rules reflecting this consideration.

*Symmetric rule for first-order balanced GRSS schemes with  $\tau = k$ .* The ranked sets are processed two at a time. For the first set, units with odd ranks are assigned to treatment 1 and units with even ranks are assigned to treatment 2. For the second set, units with odd ranks are assigned to treatment 2 and units with even ranks are assigned to treatment 1.

*Circular rule for first-order balanced GRSS schemes with  $\tau < k$ .* The circular rule is a natural extension of the symmetric rule. The pre-specified ranks for the ranked sets circulate in the following order:

$$(1, 2, \dots, \tau - 1, \tau), (2, 3, \dots, \tau, \tau + 1), \dots, (k, 1, \dots, \tau - 2, \tau - 1).$$

For each of the above  $\tau$ -tuples of ranks, two ranked sets are considered. The selected units with the specified ranks are assigned as follows: for the units selected from the first set, units with ranks in the odd positions are assigned to treatment 1 and units with ranks in the even positions are assigned to treatment 2; for the units selected from the second set, units with ranks in the odd positions are assigned to treatment 2 and units with ranks in the even positions are assigned to treatment 1.

The symmetric GRSS scheme is especially appealing in clinical trials where patients cannot be discarded once recruited. We briefly discuss here an example to explain the application of the symmetric GRSS scheme. In a clinical trial referred to as ACTG 320, the effect of the three-drug combination, IDV+ZDV+3TC and of the two-drug combination, ZDV+3TC on an AIDS-defining event were compared. For the background and details of the trial, we refer the reader to, e.g., Hammer et al. (1997) and Marschner et al. (1999). The patients accrued for the trial were stratified by CD4 cell count ( $\leq 50$  versus  $> 50$  cells/mm<sup>3</sup>). In this trial, the patients were randomly assigned to the two drug-combinations within each stratum. The effect of a drug combination on a patient was measured by the HIV-1 RNA change of the patient from his or her baseline HIV-1 RNA level. In the following, we discuss how the symmetric GRSS scheme could have been used to increase the efficiency of the trial. The results of the trial showed that the HIV-1 RNA change is reasonably correlated with the baseline HIV-I RNA level in both treatments. The correlation coefficients in the two treatments are roughly as 0.61 and 0.43, so the baseline HIV-I RNA level can be used as the concomitant variable in the symmetric GRSS scheme. The scheme can be applied to each stratum in a sequential manner. In each stratum, when the recruited patients accrue to the number  $k$  (the set size in RSS), the patients are ranked according to their HIV-1 RNA levels at the time of ranking, and the two treatments are assigned to them according to the symmetric rule. There is a practical problem here: a patient cannot wait without treatment until the time that ranking is done. A strategy to overcome this is initially to randomly assign treatments to patients. At the time of ranking, if the initial treatment of a patient happens to be the same as the treatment assigned to him or her by the GRSS scheme, the patient remains in the initial treatment. Otherwise, the patient switches to the other treatment. To reduce the adverse effect of this strategy, the set size  $k$  cannot be too large;  $k = 2$  or  $4$  is practical. The choice of  $k$  can of course be determined by the average waiting time to recruit a new patient. If the symmetric GRSS scheme were applied in this particular trial, a relative precision around 1.21 and 1.29 compared with random assignment could have been achieved without additional cost were  $k$  taken as 2 and 4, respectively. The relative precision in general is discussed in the subsequent sections.

### 3. Some Variance Expressions

To facilitate the comparison among different schemes, we first introduce the concept of the variance per pair of observations as follows. Let  $(Y_i, Z_i), i = 1, \dots, n$ , be  $n$  pairs of observed responses of  $2n$  units from a complete cycle of a scheme. The variance per pair of observations of the scheme is defined as

$\text{Var}[\sum_{i=1}^n (Y_i - Z_i)]/n$ . We denote the variance per pair of observations of the schemes discussed in the last section as

- $\sigma_{\text{SRS}}^2$  — simple random assignment,
- $\sigma_{k,\tau,1}^2$  — first-order balanced GRSS scheme with set size  $k$  and number of selected units  $\tau$ ,
- $\sigma_{k,\tau,2}^2$  — second-order balanced GRSS scheme with set size  $k$  and number of selected units  $\tau$ .

It is to be understood that, for first-order balanced GRSS schemes, the symmetric rule is assumed if  $\tau = k$ , and the circular rule is assumed if  $\tau < k$ . Let  $\sigma_x^2$  denote the variance of  $X$ . Let  $\sigma_{\text{XRSS};k}^2 = (1/k) \sum_{r=1}^k \text{Var}(X_{(r)})$  and  $\sigma_{(r,s;k)} = \text{Cov}(X_{(r)}, X_{(s)})$  where  $X_{(r)}$  and  $X_{(s)}$  are the  $r$ th and  $s$ th order statistics of the same simple random sample of size  $k$  from the population of  $X$ . Again,  $\sigma_1^2$  and  $\sigma_2^2$  denote the error variances associated with treatment 1 and 2 respectively. We have the following results:

$$\begin{aligned} \sigma_{\text{SRS}}^2 &= \sigma_1^2 + \sigma_2^2 + (\beta_1^2 + \beta_2^2)\sigma_x^2, \\ \sigma_{k,2,2}^2 &= \sigma_{\text{SRS}}^2 - \left( \beta_1^2 + \beta_2^2 + \frac{2\beta_1\beta_2}{k-1} \right) (\sigma_x^2 - \sigma_{\text{XRSS};k}^2), \\ \sigma_{k,4,2}^2 &= \sigma_{\text{SRS}}^2 - \frac{1}{k-1} [(k-2)(\beta_1^2 + \beta_2^2) + 4\beta_1\beta_2] (\sigma_x^2 - \sigma_{\text{XRSS};k}^2), \\ \sigma_{k,2,1}^2 &= \sigma_{\text{SRS}}^2 - \frac{2}{k} (\beta_1^2 + \beta_2^2 + \beta_1\beta_2) \sum_{r=1}^k \sigma_{(r,\overline{r+1};k)} \\ &\quad - \frac{2}{k} (\beta_1^2 + \beta_2^2) \left( \sum_{r+1 < s} \sigma_{(r,s;k)} - \sigma_{(1,k;k)} \right), \\ \sigma_{k,4,1}^2 &= \sigma_{\text{SRS}}^2 - \frac{(\beta_1 + \beta_2)^2}{2k} \sum_{r=1}^k (3\sigma_{(r,\overline{r+1};k)} + \sigma_{(r,\overline{r+3};k)}) \\ &\quad - \frac{\beta_1^2 + \beta_2^2}{2k} \left[ 4 \sum_{r < s} \sigma_{(r,s;k)} - \sum_{r=1}^k (3\sigma_{(r,\overline{r+1};k)} + 2\sigma_{(r,\overline{r+2};k)} + \sigma_{(r,\overline{r+3};k)}) \right]. \end{aligned}$$

Here the meaning of  $\overline{s}$  is that  $\overline{s} = s$  if  $s \leq k$ ,  $\overline{s} = s - k$  otherwise. It is worth noting that  $\sigma_{\text{SRS}}^2 - \sigma_{k,\tau,j}^2 > 0$  for all  $k, \tau, j$  and any values of  $\beta_1$  and  $\beta_2$ . The derivation of these results is given in the Appendix.

#### 4. Relative Precision and Cost-Effectiveness

In this section, the variances per pair of observations are used to investigate the efficiency and cost of the various GRSS schemes. The efficiency of a scheme can be measured by the variance of the treatment sample mean difference that

results. The schemes can be compared on two different bases: the same number of units assigned to the treatments; the same cost. If the cost involved in recruiting and discarding an experimental unit is relatively negligible compared with the cost of observing the treatment effect on the unit, the comparison based on the same number of units is appropriate. However, if the cost involved in recruiting and discarding a unit cannot be neglected, which is usually the case in practice, the comparison should be based on cost.

We define the *relative precision* of a GRSS scheme with respect to simple random assignment as the ratio of their variances per pair of observations,

$$r_{k,\tau,j} = \frac{\sigma_{\text{SRS}}^2}{\sigma_{k,\tau,j}^2}.$$

In fact, this is the ratio of the variances of the corresponding treatment sample mean differences when the number of units is the same for both schemes. It is easy to see that the variance of the treatment sample mean difference can be obtained as the variance per pair of observations divided by the sample size of the treatment samples. Since the variance per pair of observation of a GRSS scheme is always smaller than that of the simple random assignment, the relative precision  $r_{k,\tau,j}$  is always bigger than 1. In other words, if the cost involved in recruiting and discarding experiment units is negligible, the GRSS plans are always preferable to simple random assignment. To demonstrate how big the relative precision can be, we present the relative precision in the following setting:  $\sigma_1^2 = \sigma_2^2 = 1$ ,  $X$  follows a standard normal distribution,  $\beta_1$  and  $\beta_2$  are determined by  $\beta_l^2 = [\rho_l^2 / (1 - \rho_l^2)](\sigma_l^2 / \sigma_X^2)$  for given  $\rho_l$ . For various combinations of  $\rho_1$  and  $\rho_2$  in the above setting, the relative precision of the second-order balanced GRSS schemes and those of the first-order balanced GRSS schemes are presented in Table 2 and Table 3, respectively.

Table 2. Relative precision of second-order balanced GRSS schemes with  $\tau = 2$  and 4.

$k$	2		3		4		5	
$(\rho_1, \rho_2)$	$\tau = 2$	$\tau = 2$	$\tau = 2$	$\tau = 2$	$\tau = 4$	$\tau = 4$	$\tau = 2$	$\tau = 4$
(0.9,0.9)	2.0646	2.3816	2.6304	2.6304	2.8329	2.8329	2.8329	2.8329
(0.9,0.7)	1.6907	1.9195	2.0930	1.9649	2.2303	2.1080	2.2303	2.1080
(0.9,0.5)	1.5080	1.7212	1.8835	1.6804	2.0122	1.8164	2.0122	1.8164
(0.9,0.3)	1.3951	1.6028	1.7623	1.5162	1.8895	1.6497	1.8895	1.6497
(0.7,0.7)	1.4534	1.5407	1.5999	1.5999	1.6431	1.6431	1.6431	1.6431
(0.7,0.5)	1.3062	1.3691	1.4109	1.3923	1.4408	1.4246	1.4408	1.4246
(0.7,0.3)	1.2112	1.2714	1.3112	1.2652	1.3396	1.2993	1.3396	1.2993
(0.5,0.5)	1.1893	1.2181	1.2366	1.2366	1.2496	1.2496	1.2496	1.2496
(0.5,0.3)	1.1162	1.1370	1.1502	1.1430	1.1593	1.1532	1.1593	1.1532
(0.3,0.3)	1.0608	1.0689	1.0740	1.0740	1.0775	1.0775	1.0775	1.0775

Table 3. Relative precision of first-order balanced GRSS schemes with  $\tau = 2$  and 4, where the symmetric rule is used when  $\tau = k$  and the circular rule is used when  $\tau < k$ .

$k$	2		3		4		5	
$(\rho_1, \rho_2)$	$\tau = 2$	$\tau = 2$	$\tau = 2$	$\tau = 2$	$\tau = 4$	$\tau = 4$	$\tau = 2$	$\tau = 4$
(0.9,0.9)	2.0646	2.3816	2.7273	3.0656	3.0290	3.2541		
(0.9,0.7)	1.6907	1.9195	2.1347	2.1451	2.3117	2.2820		
(0.9,0.5)	1.5080	1.7212	1.9051	1.7862	2.0543	1.9205		
(0.9,0.3)	1.3951	1.6028	1.7729	1.5875	1.9103	1.7209		
(0.7,0.7)	1.4534	1.5407	1.6211	1.6880	1.6813	1.7213		
(0.7,0.5)	1.3062	1.3691	1.4223	1.4416	1.4612	1.4681		
(0.7,0.3)	1.2112	1.2714	1.3170	1.2951	1.3499	1.3259		
(0.5,0.5)	1.1893	1.2181	1.2430	1.2626	1.2607	1.2720		
(0.5,0.3)	1.1162	1.1370	1.1535	1.1574	1.1650	1.1657		
(0.3,0.3)	1.0608	1.0689	1.0757	1.0809	1.0804	1.0834		

The relative precision of the GRSS schemes are quite significant, as can be seen from Tables 2 and 3. Some features manifested in the two tables are summarized here. (i) For fixed  $k$ ,  $\tau$  and  $\rho$ 's, first-order balance is more efficient than second-order balance; (ii) for fixed  $k$ , second-order balance with  $\tau = 2$  is more efficient than second-order balance with  $\tau = 4$ ; (iii) for fixed  $k$ , when the  $\rho$ 's are the same, first-order balance with  $\tau = 4$  is more efficient than first-order balance with  $\tau = 2$ , though the efficiency with  $\tau = 4$  over  $\tau = 2$  diminishes as the  $\rho$ 's diverge and eventually it becomes less efficient; (iv) the relative precision is larger for larger set size  $k$  or for stronger correlation between the treatment effects and the concomitant variable.

We now turn to the comparison based on cost. The issue of cost in RSS has been considered by several authors, see Bohn and Wolfe (1994), Kaur et al. (1996) and Nahhas, Wolfe and Chen (2002). Here we take a similar approach in taking into account cost. The following notations are to be used:

- $c_i$  — cost of recruiting one experimental unit;
- $c_{qx}$  — cost of taking the measurement of  $X$  on one experimental unit;
- $c_{qyz}$  — cost of obtaining the treatment effect on one experimental unit.

Let  $N_{k,\tau,j}$  be the number of experimental units employed under the  $j$ th-order balanced GRSS scheme with set size  $k$  and number of selected units  $\tau$ . The total cost for such a scheme is  $C_{k,\tau,j} = N_{k,\tau,j}[k(c_i + c_{qx}) + \tau c_{qyz}]/\tau$ . The cost for the simple random assignment with  $N_{\text{SRS}}$  experimental units is  $C_{\text{SRS}} = N_{\text{SRS}}(c_i + c_{qyz})$ . Let  $C_{k,\tau,j} = C_{\text{SRS}}$ , and then

$$\frac{N_{k,\tau,j}}{N_{\text{SRS}}} = \frac{\tau(c_i + c_{qyz})}{k(c_i + c_{qx}) + \tau c_{qyz}}.$$

Note that this ratio does not depend on the balance order. In fact, the cost is the same for both first and second-order balanced schemes with the same  $k$  and  $\tau$  to assign the same number of units to the treatments.

Now we define the *relative cost-effectiveness* of the  $j$ th-order balanced GRSS scheme with set size  $k$  and number of selected units  $\tau$ , with respect to simple random assignment, as

$$\begin{aligned} \kappa_{k,\tau,j} &= r_{k,\tau,j} \frac{N_{k,\tau,j}}{N_{\text{SRS}}} \\ &= r_{k,\tau,j} \frac{\tau(c_i + c_{qyz})}{k(c_i + c_{qx}) + \tau c_{qyz}} \\ &= r_{k,\tau,j} \frac{\tau(1 + \alpha_2)}{k(1 + \alpha_1) + \tau\alpha_2}, \end{aligned}$$

where  $\alpha_1$  and  $\alpha_2$  are the cost ratios:  $\alpha_1 = c_{qx}/c_i$  and  $\alpha_2 = c_{qyz}/c_i$ .

We have  $\kappa_{k,\tau,1} > \kappa_{k,\tau,2}$  no matter what the cost ratios are, since  $r_{k,\tau,1} > r_{k,\tau,2}$  and the first and second-order balanced GRSS schemes with the same  $k$  and  $\tau$  bear the same cost. In what follows we only consider the relative cost-effectiveness of the first-order balanced GRSS schemes. Under the same setting for the computation of relative precision, the relative cost-effectiveness of the first-order balanced GRSS schemes are computed for  $\alpha_1 = 0.1$  and  $\alpha_2 = 10$ . The relative cost-effectiveness are presented in Table 4.

Table 4. Relative cost-effectiveness of first-order balanced GRSS schemes with  $\tau = 2$  and 4,  $\alpha_1 = 0.1, \alpha_2 = 10$ .

$k$	2		3		4		5	
$(\rho_1, \rho_2)$	$\tau = 2$	$\tau = 2$	$\tau = 2$	$\tau = 2$	$\tau = 4$	$\tau = 2$	$\tau = 4$	
(0.9,0.9)	2.0460	2.2487	2.4590	3.0379	2.6133	3.1469		
(0.9,0.7)	1.6755	1.8124	1.9248	2.1257	1.9944	2.2068		
(0.9,0.5)	1.4944	1.6252	1.7177	1.7701	1.7724	1.8571		
(0.9,0.3)	1.3826	1.5134	1.5986	1.5732	1.6481	1.6642		
(0.7,0.7)	1.4403	1.4547	1.4616	1.6728	1.4505	1.6645		
(0.7,0.5)	1.2944	1.2928	1.2824	1.4286	1.2606	1.4197		
(0.7,0.3)	1.2003	1.2005	1.1874	1.2834	1.1646	1.2822		
(0.5,0.5)	1.1786	1.1502	1.1207	1.2512	1.0876	1.2300		
(0.5,0.3)	1.1061	1.0736	1.0400	1.1470	1.0051	1.1272		
(0.3,0.3)	1.0512	1.0093	0.9699	1.0712	0.9321	1.0477		

It can be seen from Table 4 that, with the given cost ratios, for fixed  $k$  the schemes that select four units per set are generally more cost-effective than the schemes that select two units per set. However, this statement depends on the given cost ratios, and especially on  $\alpha_2$ . In general, we can expect that as  $\alpha_2$

becomes smaller, the schemes that select four units per set will become even more cost-effective than the schemes that select two units per set, but the selection of two units per set becomes more cost-effective for large  $\alpha_2$ .

In certain practical problems, the situation might not allow experimental units to be discarded because of the difficulty of the recruitment, or other reasons. Therefore, we can only consider GRSS assignments with  $k = \tau$  against simple random assignment. It is desirable to compare such schemes with different  $k$ 's. Since the cost is the same for all schemes, the relative precision and the relative cost-effectiveness of a scheme with respect to simple random assignment are the same. Because all GRSS schemes are more efficient than simple random assignment when compared based on the same number of units, we only need to consider GRSS schemes. The relative precision of first-order balance with  $k = \tau = 4$  with respect to  $k = \tau = 2$  is

$$r_{4:2} = \frac{r_{4,4,1}}{r_{2,2,1}} = \frac{\sigma_{2,2,1}^2}{\sigma_{4,4,1}^2}.$$

This is computed under the same setting as that for Tables 2 and 3, and is presented in Table 5. It is obvious from Table 5 that the first-order balanced scheme with  $k = \tau = 4$  is more efficient than the GRSS scheme with  $k = \tau = 2$ . When the correlations between treatment effects and the concomitant variable become stronger, the relative precision becomes larger.

Table 5. Relative precision of the first-order balanced scheme with  $k = \tau = 4$  with respect to the scheme with  $k = \tau = 2$ .

$\rho_1$	$\rho_2$						
	0.9	0.8	0.7	0.6	0.5	0.4	0.3
0.9	1.4848	1.3480	1.2688	1.2190	1.1845	1.1585	1.1379
0.8		1.2671	1.2079	1.1671	1.1374	1.1147	1.0965
0.7			1.1614	1.1282	1.1037	1.0845	1.0693
0.6				1.1003	1.0795	1.0634	1.0505
0.5					1.0616	1.0479	1.0369
0.4						1.0360	1.0268
0.3							1.0189

## Appendix

The technical details for the derivation of the variances per pair of observations for the various GRSS schemes are given in this appendix.

*The variance per pair of observations of the second-order balanced GRSS scheme with  $\tau = 2$ .* The treatment effects observed on the units assigned in one cycle of the scheme can be represented by  $Y_{ij}^{[i]1}, Z_{ij}^{[j]1}; Y_{ij}^{[j]2}, Z_{ij}^{[i]2}; 1 \leq i < j \leq k$ .

We adopt the following convention for notation: the subscripts denote the pre-specified ranks selected for the ranked sets, the bracketed superscript indicates the rank of the unit, the un-bracketed superscript indicates the set from which the unit is taken. The observations are dependent if they have common un-bracketed superscript and common subscripts, and are independent otherwise. Thus, we have

$$\begin{aligned}
 \sigma_{k,2,2}^2 &= \frac{1}{k(k-1)} \text{Var} \left( \sum_{1 \leq i < j \leq k} [(Y_{ij}^{[i]1} - Z_{ij}^{[j]1}) + (Y_{ij}^{[j]2} - Z_{ij}^{[i]2})] \right) \\
 &= \frac{1}{k(k-1)} \sum_{1 \leq i \neq j \leq k} [\text{Var}(Y^{[i]}) + \text{Var}(Z^{[j]}) - 2 \text{Cov}(Y^{[i]}, Z^{[j]})] \\
 &= \frac{1}{k} \sum_{r=1}^k [\text{Var}(Y^{[r]}) + \text{Var}(Z^{[r]})] - \frac{4}{k(k-1)} \sum_{1 \leq i < j \leq k} \text{Cov}(Y^{[i]}, Z^{[j]}) \\
 &= \sigma_1^2 + \sigma_2^2 + (\beta_1^2 + \beta_2^2) \sigma_{\text{XRSS};k}^2 - \frac{4\beta_1\beta_2}{k(k-1)} \sum_{1 \leq i < j \leq k} \sigma_{(i,j;k)} \\
 &= \sigma_{\text{SRS}}^2 - \left( \beta_1^2 + \beta_2^2 + \frac{2\beta_1\beta_2}{k-1} \right) (\sigma_x^2 - \sigma_{\text{XRSS};k}^2),
 \end{aligned}$$

where the last equality holds since  $(2/k) \sum_{1 \leq i < j \leq k} \sigma_{(i,j;k)} = \sigma_x^2 - \sigma_{\text{XRSS};k}^2$ .

The variance per pair of observations of the second-order balanced GRSS scheme with  $\tau = 4$ . We represent the observed treatment effects on the units from one cycle of this scheme as follows:

$$\begin{aligned}
 &Y_{i_1 i_2 i_3 i_4}^{[i_1]1}, Y_{i_1 i_2 i_3 i_4}^{[i_2]1}, Z_{i_1 i_2 i_3 i_4}^{[i_3]1}, Z_{i_1 i_2 i_3 i_4}^{[i_4]1}; \\
 &Y_{i_1 i_2 i_3 i_4}^{[i_1]2}, Y_{i_1 i_2 i_3 i_4}^{[i_3]2}, Z_{i_1 i_2 i_3 i_4}^{[i_2]2}, Z_{i_1 i_2 i_3 i_4}^{[i_4]2}; \\
 &Y_{i_1 i_2 i_3 i_4}^{[i_1]3}, Y_{i_1 i_2 i_3 i_4}^{[i_4]3}, Z_{i_1 i_2 i_3 i_4}^{[i_2]3}, Z_{i_1 i_2 i_3 i_4}^{[i_3]3}; \\
 &Y_{i_1 i_2 i_3 i_4}^{[i_2]4}, Y_{i_1 i_2 i_3 i_4}^{[i_3]4}, Z_{i_1 i_2 i_3 i_4}^{[i_1]4}, Z_{i_1 i_2 i_3 i_4}^{[i_4]4}; \\
 &Y_{i_1 i_2 i_3 i_4}^{[i_2]5}, Y_{i_1 i_2 i_3 i_4}^{[i_4]5}, Z_{i_1 i_2 i_3 i_4}^{[i_1]5}, Z_{i_1 i_2 i_3 i_4}^{[i_3]5}; \\
 &Y_{i_1 i_2 i_3 i_4}^{[i_3]6}, Y_{i_1 i_2 i_3 i_4}^{[i_4]6}, Z_{i_1 i_2 i_3 i_4}^{[i_1]6}, Z_{i_1 i_2 i_3 i_4}^{[i_2]6};
 \end{aligned} \quad 1 \leq i_1 < i_2 < i_3 < i_4 \leq k.$$

Let  $N = \binom{k}{4} \binom{4}{2}$ . We have

$$\begin{aligned}
 \sigma_{k,4,2}^2 &= \frac{1}{N} \text{Var} \left( \sum_{1 \leq i_1 < i_2 < i_3 < i_4 \leq k} \sum_{s=1}^6 [(Y_{i_1 i_2 i_3 i_4}^{[i_{s_1}]s} + Y_{i_1 i_2 i_3 i_4}^{[i_{s_2}]s}) - (Z_{i_1 i_2 i_3 i_4}^{[i_{s_3}]s} + Z_{i_1 i_2 i_3 i_4}^{[i_{s_4}]s})] \right) \\
 &= \frac{1}{N} \sum_{1 \leq i_1 < i_2 < i_3 < i_4 \leq k} \sum_{j=1}^4 \binom{3}{1} [\text{Var}(Y^{[i_j]}) + \text{Var}(Z^{[i_j]})]
 \end{aligned}$$

$$\begin{aligned}
& + \frac{2}{N} \sum_{1 \leq i_1 < i_2 < i_3 < i_4 \leq k} \sum_{1 \leq r < s \leq 4} \left[ \text{Cov}(Y^{[i_r]}, Y^{[i_s]}) + \text{Cov}(Z^{[i_r]}, Z^{[i_s]}) \right] \\
& - \frac{4}{N} \sum_{1 \leq i_1 < i_2 < i_3 < i_4 \leq k} \sum_{1 \leq r < s \leq 4} \left[ \text{Cov}(Y^{[i_r]}, Z^{[i_s]}) + \text{Cov}(Z^{[i_r]}, Y^{[i_s]}) \right] \\
& = \frac{3}{N} \sum_{r=1}^k \binom{k-1}{3} [\text{Var}(Y^{[r]}) + \text{Var}(Z^{[r]})] \\
& + \frac{2}{N} \sum_{1 \leq r < s \leq k} \binom{k-2}{2} [\text{Cov}(Y^{[r]}, Y^{[s]}) + \text{Cov}(Z^{[r]}, Z^{[s]})] \\
& - \frac{4}{N} \sum_{1 \leq r < s \leq k} \binom{k-2}{2} [\text{Cov}(Y^{[r]}, Z^{[s]}) + \text{Cov}(Z^{[r]}, Y^{[s]})] \\
& = \sigma_1^2 + \sigma_2^2 + (\beta_1^2 + \beta_2^2) \sigma_{\text{XRSS};k}^2 - \frac{(4\beta_1\beta_2 - \beta_1^2 - \beta_2^2)}{k-1} (\sigma_x^2 - \sigma_{\text{XRSS};k}^2) \\
& = \sigma_{\text{SRS}}^2 - \frac{1}{k-1} [(k-2)(\beta_1^2 + \beta_2^2) + 4\beta_1\beta_2] (\sigma_x^2 - \sigma_{\text{XRSS};k}^2).
\end{aligned}$$

The observed treatment effects on the units assigned from a whole cycle of the first order GRSS scheme using the circular rule can be represented as

$$\begin{aligned}
& Y_{j \cdots j + \tau - 1}^{[\overline{j+2r}]1}, Z_{j \cdots j + \tau - 1}^{[\overline{j+2r+1}]1}, \\
& Y_{j \cdots j + \tau - 1}^{[\overline{j+2r+1}]2}, Z_{j \cdots j + \tau - 1}^{[\overline{j+2r}]2}, \quad j = 1, \dots, k; r = 0, \dots, \frac{\tau}{2} - 1.
\end{aligned}$$

For the case of symmetric rule with  $\tau = k$ , the data can be represented in the same form, but  $j$  only takes the value 1. The cases  $\tau = 2$  and  $\tau = 4$  are treated separately.

The variance per pair of observations of the first-order balanced GRSS scheme with  $\tau = 2$  is

$$\begin{aligned}
\sigma_{k,2,1}^2 & = \frac{1}{2k} \text{Var} \left( \sum_{j=1}^k \left[ (Y_{jj+1}^{[j]1} - Z_{jj+1}^{[\overline{j+1}]1}) + (Y_{jj+1}^{[\overline{j+1}]2} - Z_{jj+1}^{[j]2}) \right] \right) \\
& = \sigma_1^2 + \sigma_2^2 + (\beta_1^2 + \beta_2^2) \sigma_{\text{XRSS};k}^2 - \frac{2\beta_1\beta_2}{k} \sum_{j=1}^k \sigma_{(j, \overline{j+1}; k)} \\
& = \sigma_{\text{SRS}}^2 - \frac{2}{k} (\beta_1^2 + \beta_2^2 + \beta_1\beta_2) \sum_{r=1}^k \sigma_{(r, \overline{r+1}; k)} \\
& \quad - \frac{2}{k} (\beta_1^2 + \beta_2^2) \left[ \sum_{r+1 < s} \sigma_{(r, s; k)} - \sigma_{(1, k; k)} \right].
\end{aligned}$$

The variance per pair of observations of the first-order balanced GRSS scheme with  $\tau = 4$  is

$$\begin{aligned}
 \sigma_{k,4,1}^2 &= \frac{1}{4k} \text{Var} \left( \sum_{j=1}^k \left[ (Y_{j \dots j+3}^{[j]1} + Y_{j \dots j+3}^{[\overline{j+2}]1}) - (Z_{j \dots j+3}^{[\overline{j+1}]1} + Z_{j \dots j+3}^{[\overline{j+3}]1}) \right. \right. \\
 &\quad \left. \left. + (Y_{j \dots j+3}^{[\overline{j+1}]2} + Y_{j \dots j+3}^{[\overline{j+3}]2}) - (Z_{j \dots j+3}^{[j]2} + Z_{j \dots j+3}^{[\overline{j+2}]2}) \right] \right) \\
 &= \frac{1}{k} \sum_{r=1}^k (\text{Var } Y^{[r]} + \text{Var } Z^{[r]}) \\
 &\quad + \frac{2}{4k} \sum_{j=1}^k \sum_{i=0}^1 \left[ \text{Cov} (Y^{[\overline{j+i}]}, Y^{[\overline{j+i+2}]} ) + \text{Cov} (Z^{[\overline{j+i}]}, Z^{[\overline{j+i+2}]} ) \right] \\
 &\quad - \frac{2}{4k} \sum_{j=1}^k \left[ \sum_{i=0}^2 \text{Cov} (Y^{[\overline{j+i}]}, Z^{[\overline{j+i+1}]} ) + \text{Cov} (Y^{[\overline{j+3}]}, Z^{[j]}) \right. \\
 &\quad \left. + \sum_{i=0}^2 \text{Cov} (Z^{[\overline{j+i}]}, Y^{[\overline{j+i+1}]} ) + \text{Cov} (Z^{[\overline{j+3}]}, Y^{[j]}) \right] \\
 &= \sigma_1^2 + \sigma_2^2 + (\beta_1^2 + \beta_2^2) \sigma_{\text{XRSS};k}^2 + \frac{\beta_1^2 + \beta_2^2}{2k} \sum_{j=1}^k (\sigma_{(j, \overline{j+2};k)} + \sigma_{(\overline{j+1}, \overline{j+3};k)}) \\
 &\quad - \frac{\beta_1 \beta_2}{k} \sum_{j=1}^k \left[ \sum_{i=j}^{j+2} \sigma_{(\overline{i}, \overline{i+1};k)} + \sigma_{(\overline{j+3}, j;k)} \right] \\
 &= \sigma_{\text{SRS}}^2 - \frac{\beta_1^2 + \beta_2^2}{k} \left[ 2 \sum_{r < s} \sigma_{(r,s;k)} - \sum_{r=1}^k \sigma_{(r, \overline{r+2};k)} \right] \\
 &\quad - \frac{\beta_1 \beta_2}{k} \sum_{r=1}^k (3\sigma_{(r, \overline{r+1};k)} + \sigma_{(r, \overline{r+3};k)}) \\
 &= \sigma_{\text{SRS}}^2 - \frac{(\beta_1 + \beta_2)^2}{2k} \sum_{r=1}^k (3\sigma_{(r, \overline{r+1};k)} + \sigma_{(r, \overline{r+3};k)}) \\
 &\quad - \frac{\beta_1^2 + \beta_2^2}{2k} \left[ 4 \sum_{r < s} \sigma_{(r,s;k)} - \sum_{r=1}^k (3\sigma_{(r, \overline{r+1};k)} + 2\sigma_{(r, \overline{r+2};k)} + \sigma_{(r, \overline{r+3};k)}) \right].
 \end{aligned}$$

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