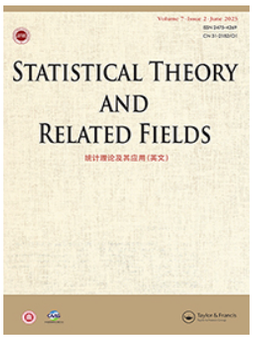

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On the construction of balanced repeated measurements designs with good circular properties

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ABSTRACT
Several fields, such as biological, medical, public health, agricultural sciences, etc., require circular balanced repeated measurement designs with fewer unequal number of repeated measurements than the number of treatments. Also, the availability and high cost of experimental subjects in these fields prefer the design in fewer experimental units. However, balancing the carryover effects of the treatments in minimal experimental subjects is one of the problems in this case. In this paper, several new series of minimal circular nearly strongly balanced RMDs in periods of two and three different sizes are constructed. The proposed construction of designs has high efficiency and, therefore, can save the cost of experimentations due to a fewer experimental subjects. Most of the designs are very useful because of the unavailability of strongly balanced RMDs for these combinations of parameters. A list of sets of shifts for the construction of minimal circular nearly SBRMDs has also been mentioned in the Appendix.

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1. Introduction

Experimental design deals with the arrangement of experimental units and the assignment of treatments to them in such a way that the comparisons among the treatments are unbiased and as precise as possible. The precision of the experiment depends to a large extent on the size of the experiment and the variations present in the experimental units. In designing experiments, keeping in view the limitation on experimental resources, efforts are made to minimize standard errors of estimated contrasts of interest. Mostly error variation arises because of the variation in experimental units under the same treatments. Therefore, it is suggested to use the same experimental unit for different treatments in an experiment but in different periods. This results in a type of design known as repeated measurements design (RMD) which makes them different from other designs presented in the literature which make use of different experimental units for different treatments. Repeated measurements design (RMD) is the type of experimental design in which experimental subjects are repeatedly measured by giving a sequence of treatments. RMDs are a special kind of carryover design in which each subject is influenced by a treatment applied in a current period called treatment effects and treatment applied in a previous period called carryover effects. Cross-over designs are RMDs in which each unit receives the sequence of each treatment over different periods. RMDs in unequal period sizes are very useful if there is a restriction on the total number of treatments, and some experimental units can receive on the total length of time, while some experimental units can remain in the trial which results in RMDs of different or unequal period sizes. RMDs balanced in treatments and carryover effects are useful in several fields such as medicine, pharmacology, animal sciences and psychology where carryover effects are natural.

2. Literature review

Cheng and Wu (1980) proposed the construction of BRMDs and CSBRMDs, especially for unequal block sizes. With the help of advanced technology in computer systems, the uses of block designs of unequal sizes k are beneficial, and hence it is very useful in industrial and agricultural experiments. The utilization of different block sizes in biological experiments was mentioned by Pearce (1964). Afsarinejad (1994) constructed minimal CSBRMDs for different period sizes. Iqbal and Jones (1994) proposed the construction of efficient RMDs and CSBs for two different period sizes. Iqbal and Tahir (2009), Iqbal et al. (2010) and Bashir et al. (2018) constructed CSBs for some classes. Rasheed et al. (2018) recently developed some generators to obtain MCSBs in a period of three different sizes for

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some cases of t, where $2 \leq k_3 < k_2 \leq 10$. However, there do not exist MCSBs for certain combinations of treatments and periods when several treatments are less than the number of periods. Here, minimal circular nearly CSBs are useful. A design is said to be CNBs (Circular nearly strongly balanced repeated measurement designs) if every treatment is immediately followed by every other treatment including itself except the treatment (labelled as $t-1$) which is not preceded by itself. In this article, some generators are developed to construct CNBs in periods of (i) two different sizes and (ii) three different sizes. These designs have their own importance in extended scientific and biological experimentations with different block sizes which consist of clinical experimentations of human and also animal behaviour responses for the comparison of several non-curative treatments for their effectiveness. With the advancement of technological computer systems, block designs with unequal sizes p have become very useful in huge industrial and agricultural experiments. In biological experiments, the utilization of different block sizes has been studied significantly. RCTs become prone to the unravelling of sizes of the block when it remains the same throughout the trial, so investigators use different block sizes, i.e. they randomly vary the block size to lower the chances of unbiasedness (Schulz & Grimes, 2002; Schulz, 1995). There exist different scientific research areas such as animal husbandry and genetic experimentation. RCTs, where these designs are applied as within-subject treatment comparisons, are more efficient than between-subject treatment comparisons. These proposed designs are additions to the literature as they are incorporating different period sizes and also possess good efficiency in estimating direct and residual effects.

Important definitions with abbreviations used that will be discussed throughout the article are discussed below briefly.

BRMDs	Balanced repeated measurement designs
CSBs	Circular strongly balanced repeated measurement designs
CNBs	Circular nearly strongly balanced repeated measurement designs

2.1. BRMDs

In an RMD each experimental subject or unit receives a series of several treatments in successive periods.

2.2. CSBs

If every treatment is directly preceded by every other treatment (including itself) then it is called CSBs.

2.3. CNBs

In this type of design, every treatment is immediately followed by every other treatment exactly once as well as with itself except the treatment labelled as $v-1$, which is not preceded by itself.

In Section 3, the model and information matrix are described along with the formula for the computation of the efficiency for CNBs. In Section 4, the Method of Cyclic Shifts (MOCS) is described to generate CNBs in different period sizes. A series of generators is proposed in Section 5 to obtain CNBs in two different sizes of periods. Also, a series of generators for the construction of CNBs in three different sizes of periods are proposed in Section 6. Section 7 contains the concluding remarks about the proposed designs. A list of sets of shifts for the construction of CNBs in two and three different sizes of periods with many treatments smaller than thirty is provided in the Appendix.

3. Model and efficiency for CNBs

The model used for repeated measurements designs in the literature is the conventional model proposed by Magda (1980)

$$y_{ijk} = \mu + \tau_{d(k,\,j)} + \gamma_{d(k-1,\,j)} + \pi_k + \xi_{ij} + \varepsilon_{ijk}, \tag{1}$$

where y_{ijk} is the ith observation from the subject jth with the sequence i in period k for which treatment $d(k, j)$ is given.

μ = Overall mean, $\tau_{d(k,\,j)}$ = treatment $d(k, j)$ effect, $\gamma_{d(k-1,\,j)}$ = treatment $d(k-1, j)$ effect in the period k which was applied in the period $k-1$ to the same experimental subject, π_k = kth period effect, ξ_{ij} = jth subject effect of sequence i, and ε_{ijk} is i.i.d normally distributed residual term having mean 0 and fixed variance σ^2.

The joint information matrix of treatment and carryover effects for the CNB is expressed by

$$A_{(\tau,\gamma)} = \begin{pmatrix} A_{11} & A_{12} \\ A'_{12} & A_{22} \end{pmatrix},$$

where A_{11}, A_{12} and A_{22} in two different period sizes are expressed by

$$A_{11} = R - M - \frac{1}{k_1}N_1N_1' - \frac{1}{k_2}N_2N_2' + \frac{\underline{r}\underline{r}'}{n_1k_1 + n_2k_2}J,$$

$$M = \begin{bmatrix} \left(\dfrac{s^2(k_2-1)+(s-1)^2}{n_1+n_2} + \dfrac{(k_1-k_2)}{n_1}\right)J_{t-1} & \dfrac{(t-1)(s-1)}{n_1+n_2}\underline{1}_{t-1} \\ \dfrac{(t-1)(s-1)}{n_1+n_2}\underline{1}'_{t-1} & \dfrac{(t-1)^2}{n_1+n_2} \end{bmatrix},$$

$$A_{12} = Z - \overline{M} - \frac{1}{k_1}N_1\overline{N}_1' - \frac{1}{k_2}N_2\overline{N}_2' + \frac{\underline{r}\underline{\bar{r}}'}{n_1k_1 + n_2k_2}J,$$

$$\overline{M} = \begin{bmatrix} \left(\dfrac{s^2(k_2-2)+2s(s-1)}{n_1+n_2} + \dfrac{(k_1-k_2)}{n_1}\right)J_{t-1} & \dfrac{s(t-1)}{n_1+n_2}\underline{1}_{t-1} \\ \dfrac{s(t-1)}{n_1+n_2}\underline{1}_{t-1} & 0 \end{bmatrix},$$

$$A_{22} = \overline{R} - M - \frac{1}{k_1}\overline{N}_1\overline{N}_1' - \frac{1}{k_2}\overline{N}_2\overline{N}_2' + \frac{\underline{\bar{r}}\underline{\bar{r}}'}{n_1k_1 + n_2k_2}J,$$

and A_{11}, A_{12} and A_{22} in periods of three different sizes are expressed by

$$A_{11} = R - M - \frac{1}{k_1}N_1N_1' - \frac{1}{k_2}N_2N_2' - \frac{1}{k_3}N_3N_3' + \frac{\underline{r}\underline{r}'}{n_1k_1 + n_2k_2 + n_3k_3}J,$$

$$M = \begin{bmatrix} \left(\dfrac{s^2(k_3-1)+(s-1)^2}{n_1+n_2+n_3} + \dfrac{(s-1)^2(k_2-k_3)}{n_1+n_2} + \dfrac{(s-2)^2(k_1-k_2)}{n_1}\right)J_{t-1} & \dfrac{n_3(s-1)}{n_1+n_2+n_3}\underline{1}_{t-1} \\ \dfrac{n_3(s-1)}{n_1+n_2+n_3}\underline{1}'_{t-1} & \dfrac{n_3^2}{n_1+n_2+n_3} \end{bmatrix},$$

$$A_{12} = Z - \overline{M} - \frac{1}{k_1}N_1\overline{N}_1' - \frac{1}{k_2}N_2\overline{N}_2' - \frac{1}{k_3}N_3\overline{N}_3' + \frac{\underline{r}\underline{\bar{r}}'}{n_1k_1 + n_2k_2 + n_3k_3}J,$$

$$\overline{M} = \begin{bmatrix} \left(\dfrac{s^2(k_3-2)+2s(s-1)}{n_1+n_2+n_3} + \dfrac{(s-1)^2(k_2-k_3)}{n_1+n_2} + \dfrac{(s-2)^2(k_1-pk_2)}{n_1}\right)J_{t-1} & \dfrac{sn_3}{n_1+n_2+n_3}\underline{1}_{t-1} \\ \dfrac{sn_3}{n_1+n_2+n_3}\underline{1}'_{t-1} & 0 \end{bmatrix},$$

$$A_{22} = \overline{R} - M - \frac{1}{k_1}\overline{N}_1\overline{N}_1' - \frac{1}{k_2}\overline{N}_2\overline{N}_2' - \frac{1}{k_3}\overline{N}_3\overline{N}_3' + \frac{\underline{\bar{r}}\underline{\bar{r}}'}{n_1k_1 + n_2k_2 + n_3k_3}J.$$

Here,

n_1	subjects measured repeatedly up to k_1 size
n_3	subjects measured repeatedly up to k_3 size
s	number of sets of shifts
N_1	t incidence matrix vs 1 to n_1
N_2	t incidence matrix vs $n_1 + 1$ to $n_1 + n_2$
N_3	t incidence matrix vs $n_1 + n_2 + 1$ to $n_1 + n_2 + n_3$
$\overline{N}_1$	residual incidence matrix vs 1 to n_1
$\overline{N}_2$	residual incidence matrix vs $n_1 + 1$ to $n_1 + n_2$
$\overline{N}_3$	residual incidence matrix vs $n_1 + n_2 + 1$ to $n_1 + n_2 + n_3$
$\underline{r}$	vector of replication of treatments
$\underline{\bar{r}}$	vector of replication of residual
R	diagonal matrix of replication of t
$\overline{R}$	diagonal matrix of replication of residual
J	matrix of 1s

Then the information matrix of the treatment and carryover effects are $A_\tau = A_{11} - A_{12}A_{22}^{-}A_{21}$ and $A_\gamma = A_{22} - A_{21}A_{11}^{-}A_{12}$, respectively.

RMDs should be analysed for their capability of discriminating the effects of treatment from carryover effects. Hanford (2005) has given the criteria to compare the RMDs based on this ability. Divecha and Gondaliya (2014) gave a convenient method for calculating the efficiency of separability (ES) for the BRMDs. This formula considering the provided constraints of our proposed type of RMDs is given by

$$\mathrm{ES} = \left[\frac{t\sqrt{t-1}-1}{t\sqrt{t-1}}\right] \times 100\%. \tag{2}$$

4. Construction methodology

Construction of CNBs from all the series of generators requires an understanding of rule II of an MOCS which was proposed by Iqbal and Jones (1994). MOCS (Rule II) is defined here briefly for constructing CNBs in periods of different sizes.

Let $S_1 = [q_{11}, q_{12}, \dots, q_{p_1-1}]$, $S_2 = [q_{21}, q_{22}, \dots, q_{p_2-1}]$ and $S_3 = [q_{31}, q_{32}, \dots, q_{p_3-2}]t$ be the sets of shifts, where $0 \le q_{ij} \le v-2$. If every element $0, 1, \dots, v-2$ appears exactly once in $S*$, it is CNB in periods of sizes p_1, p_2 and p_3, where $S* = [q_{11}, q_{12}, \dots, q_{p_1-1}, q_{21}, q_{22}, \dots, q_{p_2-1}, q_{31}, q_{32}, \dots, q_{p_3-1}, v-1-(q_{11}+q_{12}+\cdots+q_{p_1-1}) \bmod (v-1), v-1-(q_{21}+q_{22}+\cdots+q_{p_2-1}) \bmod (v-1)]$. In these sets of shifts, the sum of any $2, 3, \dots$, or $(p-3)$ successive elements should not be $0 \bmod (v-1)$. If so, rearrange them.

Consider here the Rule II of an MOCS briefly for the construction of CNBs with the help of an example as $t = 13$, $S_1 = [3, 4, 5, 9, 8]$ and $S_2 = [6]t$.

Take $t-1$ experimental subjects for one set of shifts [3,4,9,5,8]. Write $0, 1, \dots, t-2$ in the first period of $t-1$ experimental subjects, respectively. For the second period of every subject, add $3 \bmod (t-1)$ to every element of the first period of each subject. Then add $4 \bmod (t-1)$ to every element of the second period which gives the treatment number of the third period in each subject. Similarly add 9, 5 and 8, respectively.

	Experimental Subjects											
Periods	1	2	3	4	5	6	7	8	9	10	11	12
1	0	1	2	3	4	5	6	7	8	9	10	11
2	3	4	5	6	7	8	9	10	11	0	1	2
3	7	8	9	10	11	0	1	2	3	4	5	6
4	4	5	6	7	8	9	10	11	0	1	2	3
5	9	10	11	0	1	2	3	4	5	6	7	8
6	5	6	7	8	9	10	11	0	1	2	3	4

Take $t-1$ more subjects for the second set of shifts $[6]t$. Allocate $0, 1, \dots, t-2$ to every subject in the first period, respectively. To obtain the elements of the second period for every subject, add $6 \bmod (t-1)$ to every element of the first period for all subjects. Then insert $t-1$ (i.e. 12) in each element of the third period.

	Subjects											
Periods	13	14	15	16	17	18	19	20	21	22	23	24
1	0	1	2	3	4	5	6	7	8	9	10	11
2	6	7	8	9	10	11	0	1	2	3	4	5
3	12	12	12	12	12	12	12	12	12	12	12	12

The above design is CNB in $t = 13$, $k_1 = 6$, $k_2 = 3$, $n_1 = 12$, $n_2 = 12$ and $\mathrm{ES} = 98\%$.

5. Generators to obtain CNBs in two different sizes of periods

Let $S_1 = [e_{11}, e_{12}, \dots, e_{p_1-1}]$ and $S_2 = [e_{21}, e_{22}, \dots, e_{p_2-2}]t$ be two sets of shifts, where $0 \le e_{ij} \le t-2$. Define, $S* = [e_{11}, e_{12}, \dots, e_{p_1-1}, e_{21}, e_{22}, \dots, e_{p_2-2}, t-1-(e_{11}+e_{12}+\cdots+e_{p_1-1}) \bmod (t-1)]$. If every element $0, 1, \dots, t-2$ appears exactly once in the new set of shifts S∗, then the design from the set of shifts will be CNB in periods of sizes k_1 and k_2. The sum of any $2, 3, \dots, (k-3)$ successive elements of any set of shifts should not be $0 \bmod (t-1)$. If so, rearrange the elements.

Example: Sets of shifts $S_1 = [1, 7, 4, 3, 9, 6]$ and $S_2 = [2, 5, 8]t$ give following CNB for $t = 11$ in $k_1 = 7$ and $k_2 = 5$ with $\mathrm{ES} = 97\%$.

Subjects									
1	2	3	4	5	6	7	8	9	10
0_0	1_1	2_2	3_3	4_4	5_5	6_6	7_7	8_8	9_9
1_0	2_1	3_2	4_3	5_4	6_5	7_6	8_7	9_8	0_9
8_1	9_2	0_3	1_4	2_5	3_6	4_7	5_8	6_9	7_0
2_8	3_9	4_0	5_1	6_2	7_3	8_4	9_5	0_6	1_7
5_2	6_3	7_4	8_5	9_6	0_7	1_8	2_9	3_0	4_1
4_5	5_6	6_7	7_8	8_9	9_0	0_1	1_2	2_3	3_4
0_4	1_5	2_6	3_7	4_8	5_9	6_0	7_1	8_2	9_3

Subjects									
1	2	3	4	5	6	7	8	9	10
0_{10}	1_{10}	2_{10}	3_{10}	4_{10}	5_{10}	6_{10}	7_{10}	8_{10}	9_{10}
2_0	3_1	4_2	5_3	6_4	7_5	8_6	9_7	0_8	1_9
7_2	8_3	9_4	0_5	1_6	2_7	3_8	4_9	5_0	6_1
5_7	6_8	7_9	8_0	9_1	0_2	1_3	2_4	3_5	4_6
10_5	10_6	10_7	10_8	10_9	10_0	10_1	10_2	10_3	10_4

Here, 10_6 means that treatment 10 was applied in the current period, while the subscript '6' is the treatment applied in the previous period.

If $t = 2zi + 2a - 1$, i is an integer, $k_1 = 2z$, $k_2 = 2a$, $a \neq z$ and $a, z > 1$, then CNBs can be obtained from the sets given below where $j = 0, 1, \ldots, i-1$.

$$S_{j+1} = [zj+1, zj+2, \ldots, zj+z, t-1-(zj+1), t-1-(zj+2), \ldots, t-1-(zj+z-1)];$$
$$S_{i+1} = [zi+1, zi+2, \ldots, zi+a-1, t-1-(zi+1), t-1-(zi+2), \ldots, t-1-(zi+a-2),\ 0]t.$$

Example 5.1: CNBs for $t = 13$, $k_1 = 8$ and $k_2 = 6$ are constructed from the sets of shifts given below with 98% efficiency.

$$S_1 = [1,\ 2,\ 3,\ 4,\ 11,\ 10,\ 9], S_2 = [5,\ 6,\ 7,\ 0]t.$$

If $t = 2zi + 2a$, i is an integer, $k_1 = 2z$, $k_2 = 2a + 1$ and $a, z > 1$, then CNBs can be obtained from the sets given below where $j = 0, 1, \ldots, i-1$.

$$S_{j+1} = [zj+1, zj+2, \ldots, zj+z, t-1-(zj+1), t-1-(zj+2), \ldots, t-1-(zj+z-1)];$$
$$S_{i+1} = [zi+1, zi+2, \ldots, zi+a-1, t-1-(zi+1), t-1-(zi+2), \ldots, t-1-(zi+a-1),\ 0]t.$$

Example 5.2: CNBs for $t = 16$, $k_1 = 10$ and $k_2 = 7$ are constructed from the sets given below with 98% efficiency.

$$S_1 = [1, 2, 3, 4, 14, 5, 13, 11, 12], S_2 = [6, 7, 9, 8, 0]t.$$

If $t = 2zi + 4a - 1$, i is an integer, $k_1 = 2z$, $k_2 = 2a$ and $a \neq z$, $a, z > 1$, then CNBs can be obtained from the sets given below.

$$S_{j+1} = [zj+1, zj+2, \ldots, zj+z, t-1-(zj+1), t-1-(zj+2), \ldots, t-1-(zj+z-1)];$$
$$S_{i+1} = [zi+1, zi+2, \ldots, zi+a-1, t-1-(zi+a-1), t-1-(zi+a-2), \ldots, t-1-(zi+1)];$$
$$S_{i+2} = [zi+a+1, zi+a+2, \ldots, zi+2a-1, t-1-(zi+a+1), t-1-(zi+a+2),$$
$$\ldots, t-1-(zi+2a-2),\ 0]t.$$

Example 5.3: CNBs for $t = 25$, $k_1 = 10$ and $k_2 = 8$ are constructed from the sets given below with 99% efficiency.

$$S_1 = [1, 2, 3, 4, 5, 23, 22, 21, 20], S_2 = [6, 7, 8, 17, 9, 18, 16], S_3 = [10, 11, 12, 14, 13, 0]t.$$

If $t = 2zi + 4a + 1$, i is an integer, $k_1 = 2z$, $k_2 = 2a + 1$ and $a, z > 1$, then CNBs can be obtained from the sets given below.

$$S_{j+1} = [zj+1, zj+2, \ldots, zj+z, t-1-(zj+1), t-1-(zj+2), \ldots, t-1-(zj+z-1)];$$
$$S_{i+1} = [zi+1, zi+2, \ldots, zi+a, t-1-(zi+1), t-1-(zi+2), \ldots, t-1-(zi+a)];$$

$$S_{i+2} = [zi + a + 1, zi + a + 2, \\ \ldots, zi + 2a, t - 1 - (zi + a + 1), t - 1 - (zi + a + 2), \ldots, t - 1 - (zi + 2a - 1)]t.$$

Example 5.4: CNBs for $t = 21$, $k_1 = 8$ and $k_2 = 7$ are constructed from the sets given below with 99% efficiency.

$$S_1 = [1, 2, 3, 4, 19, 18, 17], S_2 = [5, 6, 7, 15, 14, 13], S_3 = [8, 9, 10, 12, 11]t.$$

6. Generators to obtain CNBs in three different sizes of periods

Let $S_1 = [e_{11}, e_{12}, \ldots, e_{p_1-1}]$, $S_2 = [e_{21}, e, \ldots, e_{p_2-1}]$ and $S_3 = [e_{31}, e_{32}, \ldots, e_{p_3-2}]t$ be the sets of shifts, where $0 \le e_{ij} \le t - 2$. Define, $S* = [e_{11}, e_{12}, \ldots, e_{p_1-1}, q_{21}, e_{22}, \ldots, e_{p_2-1}, e_{31}, e_{32}, \ldots, e_{p_3-1}, t - 1 - (e_{11} + e_{12} + \cdots + e_{p_1-1})$ mod $(t - 1)$, $t - 1 - (e_{21} + e_{22} + \cdots + e_{p_2-1})$ mod $(t - 1)]$. If every element $0, 1, \ldots, t - 2$ appears exactly once in the new set of shifts $S*$, then the design from the set of shifts will be CNB in periods of sizes k_1, k_2 and k_3. The sum of any $2, 3, \ldots, (k - 3)$ successive elements of the set of shifts S_{i+1} should not be 0 mod $(t - 1)$. If so rearrange the elements.

Example: Sets of shifts $S_1 = [3, 4, 9, 5, 8]$, $S_2 = [1, 2, 11, 10]$ and $S_3 = [6]t$ give the following CNBs for $t = 13$ in $k_1 = 6$, $k_2 = 5$ and $k_3 = 3$ with ES = 98%.

Subjects											
1	2	3	4	5	6	7	8	9	10	11	12
0_5	1_6	2_7	3_8	4_9	5_{10}	6_{11}	7_0	8_1	9_2	10_3	11_4
3_0	4_1	5_2	6_3	7_4	8_5	9_6	10_7	11_8	0_9	1_{10}	2_{11}
7_3	8_4	9_5	10_6	11_7	0_8	1_9	2_{10}	3_{11}	4_0	5_1	6_2
4_7	5_8	6_9	7_{10}	8_{11}	9_0	10_1	11_2	0_3	1_4	2_5	3_6
9_4	10_5	11_6	0_7	1_8	2_9	3_{10}	4_{11}	5_0	6_1	7_2	8_3
5_9	6_{10}	7_{11}	8_0	9_1	10_2	11_3	0_4	1_5	2_6	3_7	4_8

Subjects											
13	14	15	16	17	18	19	20	21	22	23	24
0_0	1_1	2_2	3_3	4_4	5_5	6_6	7_7	8_8	9_9	10_{10}	11_{11}
1_0	2_1	3_2	4_3	5_4	6_5	7_6	8_7	9_8	10_9	11_{10}	0_{11}
3_1	4_2	5_3	6_4	7_5	8_6	9_7	10_8	11_9	0_{10}	1_{11}	2_0
2_3	3_4	4_5	5_6	6_7	7_8	8_9	9_{10}	10_{11}	11_0	0_1	1_2
0_2	1_3	2_4	3_5	4_6	5_7	6_8	7_9	8_{10}	9_{11}	10_0	11_1

Subjects											
25	26	27	28	29	30	31	32	33	34	35	36
0_{12}	1_{12}	2_{12}	3_{12}	4_{12}	5_{12}	6_{12}	7_{12}	8_{12}	9_{12}	10_{12}	11_{12}
6_0	7_1	8_2	9_3	10_4	11_5	0_6	1_7	2_8	3_9	4_{10}	5_{11}
12_6	12_7	12_8	12_9	12_{10}	12_{11}	12_0	12_1	12_2	12_3	12_4	12_5

Here, 11_6 is the treatment 11 applied in the present period, while the subscript '6' is the treatment applied in the previous period.

If $t = 2zi + 2a + 2b$, i is an integer, $k_1 = 2a$, $z \neq a$, z, a, $b > 1$, $k_2 = 2a + 1$ and $k_3 = 2b$, then CNBs can be obtained from the sets given below where $j = 0, 1, \ldots, i - 1$.

$$S_{j+1} = [zj + 1, zj + 2, \ldots, zj + z, t - 1 - (zj + 1), t - 1 - (zj + 2), \ldots, t - 1 - (zj + z - 1)];$$

$$S_{i+1} = [zi + 1, zi + 2, \ldots, zi + a, t - 1 - (zi + 1), t - 1 - (zi + 2), \ldots, t - 1 - (zi + a)];$$

$$S_{i+2} = [zi + a + 1, zi + a + 2, \ldots, zi + a + b - 1, t - 1 - (zi + a + 1), t - 1 - (zi + a + 2), \\ \ldots, t - 1 - (zi + a + b - 1)]t.$$

Example 6.1: CNBs for $t = 13$, $k_1 = 8$, $k_2 = 7$ and $k_3 = 4$ are constructed from the sets given below with 98% efficiency.

$$S_1 = [1, 2, 3, 4, 16, 15, 14], S_2 = [5, 6, 7, 12, 11, 10] \text{ and } S_3 = [8, 9]t.$$

If $t = 2zi + 2a + 2b - 1$, i is an integer, $k_1 = 2z$, $z \neq a \neq b > 1$, $k_2 = 2a$ and $k_3 = 2b$, then CNBs can be constructed from the sets given below where $j = 0, 1, \ldots, i-2$.

$$\begin{aligned}
S_{j+1} &= [zj+1, zj+2, \ldots, zj+z, t-1-(zj+1), t-1-(zj+2), \ldots, t-1-(zj+z-1)];\\
S_{i+1} &= [zi+1, zi+2, \ldots, zi+a, t-1-(zi+1), t-1-(zi+2), \ldots, t-1-(zi+a-1)];\\
S_{i+2} &= [zi+a+1, zi+a+2, \ldots, zi+a+b-1, t-1-(zi+a+1), t-1-(zi+a+2),\\
&\quad \ldots, t-1-(zi+a+b-2), 0]t, \text{for } b > 2;\\
S_{i+2} &= [(t-1)/2,\ 0]t, \text{for } b = 2.
\end{aligned}$$

Example 6.2: CNBs for $t = 23$, $k_1 = 10$, $k_2 = 8$ and $k_3 = 6$ are constructed from the sets given below with 99% efficiency.

$$S_1 = [1, 2, 3, 4, 5, 21, 20, 19, 18], \quad S_2 = [6, 7, 8, 9, 16, 15, 14] \text{ and } S_3 = [10, 11, 12, 0]t.$$

If $t = 2zi + 2a + 2b + 1$, $k_1 = 2z$, i is an integer, $k_2 = 2a + 1$, $k_3 = 2b + 1$, $a \neq b > 1$ and $z > 1$, then CNBs can be obtained from the sets given below where $j = 0, 1, \ldots, i-1$.

$$\begin{aligned}
S_{j+1} &= [zj+1, zj+2, \ldots, zj+z, t-1-(zj+1), t-1-(zj+2), \ldots, t-1-(zj+z-1)];\\
S_{i+1} &= [zi+1, zi+2, \ldots, zi+a, t-1-(zi+1), t-1-(zi+2), \ldots, t-1-(zi+a)];\\
S_{i+2} &= [zi+a+1, zi+a+2, \ldots, zi+a+b, t-1-(zi+a+1),\\
&\quad t-1-(zi+a+2), \ldots, t-1-(zi+a+b-1)]t.
\end{aligned}$$

Example 6.3: CNBs for $t = 19$, $k_1 = 8$, $k_2 = 7$ and $k_3 = 5$ are constructed from the sets given below with 99% efficiency.

$$S_1 = [1, 2, 3, 4, 17, 16, 15], S_2 = [5, 6, 13, 7, 12, 11], S_3 = [8, 9, 10]t.$$

7. Concluding remarks

CSBs help in estimating direct and carryover effects independently and providing high efficiency of separability. Despite the importance of RMDs, there is no sufficient literature available on the construction of the CSBs and CNBs with high efficiency of separability for unequal period sizes. In situations where CSBs cannot be constructed, they are preferable as they give efficiencies close to CSBs. Through well-known MOCS Rule II, these designs have been constructed for unequal period sizes with high efficiency of separability which covers the lack of designs for unequal period sizes. The experimenters now have more choices when dealing with different period sizes. All the proposed designs possess an efficiency close to 100% and, therefore, they should be a better alternative to CSBs.

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Appendix

Table A1. List of sets of shifts for CNBs in two different sizes of periods and treatments smaller than 30.

t	k_1	k_2	Sets of shifts	ES
9	6	4	[1,3,2,7,6] + [4,0]t	96
10	6	5	[1,3,2,8,7] + [4,5,0]t	97
11	8	4	[1,3,2,4,9,8,7] + [5,0]t	97
13	6	4	[1,3,2,11,10] + [4,5,8] + [6,0]t	98
13	8	6	[1,3,2,4,11,10,9] + [5,6,7,0]t	98
13	10	4	[1,3,2,4,5,11,10,9,8] + [6,0]t	98
14	8	7	[1,3,2,4,12,11,10] + [5,6,7,8,0]t	98
15	6	4	[1,3,2,13,12] + [4,5,6,10,9] + [7,0]t	98
15	6	5	[1,2,3,13,12] + [4,5,10,9] + [6,7,8]t	98
15	8	4	[1,3,2,4,13,12,11] + [5,6,9] + [7,0]t	98
16	6	5	[1,3,2,14,13] + [4,5,6,11,10] + [7,8,0]t	98
17	10	4	[1,3,2,4,5,15,14,13] + [6,7,10] + [8,0]t	99
17	10	8	[1,3,2,4,5,15,14,13,12] + [6,7,8,10,9,0]t	99
18	10	9	[1,3,2,4,5,16,15,14,13] + [6,7,8,9,10,11,0]t	99
19	6	4	[1,3,2,17,16] + [4,5,6,14,13] + [7,8,11] + [9,0]t	99
19	8	4	[1,3,2,4,17,16,15] + [5,6,7,8,13,12,11] + [9,0]t	99
21	6	4	[1,3,2,19,18] + [4,5,6,16,15] + [7,8,9,13,12] + [10,0]t	99
21	6	5	[1,2,3,19,18] + [4,5,6,16,15] + [7,8,13,12] + [9,10,11]t	99
21	8	6	[1,3,2,4,19,18,17] + [5,6,7,8,15,14,13] + [9,11,10,0]t	99
21	8	7	[1,2,3,4,19,18,17] + [5,6,7,15,14,13] + [8,9,10,12,11]t	99
22	6	5	[1,3,2,20,19] + [4,5,6,17,16] + [7,8,9,14,13] + [10,11,0]t	99
22	8	7	[1,3,2,4,20,19,18] + [5,6,7,8,16,15,14] + [9,10,11,12,0]t	99
23	8	4	[1,3,2,4,21,20,19] + [5,6,7,8,17,16,15] + [9,10,13] + [11,0]t	99
23	10	4	[1,3,2,4,5,21,20,19,18] + [6,7,8,9,10,16,15,14,13] + [11,0]t	99
25	6	4	[1,3,2,23,22] + [4,5,6,20,19] + [7,8,9,17,16] + [10,11,14] + [12,0]t	99
27	6	4	[1,3,2,25,24] + [4,5,6,22,21] + [7,8,9,19,18] + [10,11,12,16,15] + [13,0]t	99
27	6	5	[1,2,3,25,24] + [4,5,6,22,21] + [7,8,9,19,18] + [10,11,16,15] + [12,13,14]t	99
27	8	4	[1,3,2,4,25,24,23] + [5,6,7,8,21,20,19] + [9,10,11,12,17,16,15] + [13,0]t	99
27	10	4	[1,3,2,4,5,25,24,23,22] + [6,7,8,9,10,20,19,18,17] + [11,12,15] + [13,0]t	99
27	10	8	[1,3,2,4,5,25,24,23,22] + [6,7,8,9,10,20,19,18,17] + [11,12,13,15,14,0]t	99
27	10	9	[1,2,3,4,5,25,24,23,22] + [6,7,8,9,20,19,18,17] + [10,11,12,16,15,14,13]t	99
28	6	5	[1,3,2,26,25] + [4,5,6,23,22] + [7,8,9,20,19] + [10,11,12,17,16] + [13,14,0]t	99
28	10	9	[1,3,2,4,5,26,25,24,23] + [6,7,8,9,10,21,20,19,18] + [11,12,13,14,15,16,0]t	99
29	8	6	[1,3,2,4,27,26,25] + [5,6,7,8,23,22,21] + [9,10,11,12,19,18,17] + [13,15,14,0]t	99
29	8	7	[1,2,3,4,27,26,25] + [5,6,7,8,23,22,21] + [9,10,11,19,18,17] + [12,13,14,16,15]t	99

Table A2. List of sets of shifts for CNBs in three different sizes of periods and treatments smaller than 30.

t	k_1	k_2	k_3	Sets of shifts	ES
14	6	5	4	[1,2,3,12,11] + [4,5,9,8] + [6,7]t	98
17	8	6	4	[1,2,3,4,15,14,13] + [5,6,7,11,10] + [8,0]t	99
19	8	7	5	[1,2,3,4,17,16,15] + [5,6,7,13,12,11] + [8,9,10]t	99
20	6	5	4	[1,2,3,18,17] + [4,5,6,15,14] + [7,8,12,11] + [9,10]t	99
20	8	7	6	[1,2,3,4,18,17,16] + [5,6,7,14,13,12] + [8,9,11,10]t	99
23	10	8	6	[1,2,3,4,5,21,20,19,18] + [6,7,8,9,16,15,14] + [10,11,12,0]t	99
25	8	6	4	[1,2,3,4,23,22,21] + [5,6,7,8,19,18,17] + [9,10,11,15,14] + [12,0]t	99
25	10	9	7	[1,2,3,4,5,23,22,21,20] + [6,7,8,9,18,17,16,15] + [10,11,12,13,14]t	99
26	6	5	4	[1,2,3,24,23] + [4,5,6,21,20,19] + [7,8,9,18,17,16] + [10,11,15,14] + [12,13]t	99
26	10	9	8	[1,2,3,4,5,24,23,22,21] + [6,7,8,9,19,18,17,16] + [10,11,12,15,14,13]t	99
27	8	7	5	[1,2,3,4,25,24,23] + [5,6,7,8,21,20,19] + [9,10,11,17,16,15] + [12,13,14]t	99
28	8	7	6	[1,2,3,4,26,25,24] + [5,6,7,8,22,21,20] + [9,10,11,18,17,16] + [12,13,15,14]t	99