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Optimal Crossover Designs for Generalized Linear Models: An Application to Work Environment Experiment

Jeevan Jankar[1] **and Abhyuday Mandal**[1]
[1]*Department of Statistics*
University of Georgia, Athens, USA

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Abstract

We consider locally D-optimal crossover designs for generalized linear models. Three different types of responses were recorded in a work environment experiment conducted at Booking.com. These responses follow Poisson, beta and gamma distributions. The responses from the same subjects are naturally correlated. To capture the dependence among these observations, we use six different types of correlation structures. The optimal allocations of subjects to each treatment sequence are obtained by minimizing the objective function, which is the variance of direct treatment effect estimates. We show that optimal allocations are reasonably robust to a different choice of correlation structures. Although uniform allocations are widely used in practice, we establish these designs are sub-optimal under certain conditions.

Key words: D-Optimality; Generalized Linear Models; Generalized estimating Equations; Latin Square Design.

1. Introduction

Crossover designs, also known as repeated measurements designs or change-over designs, have been used extensively in pharmaceutical and agriculture research. Most of the present work focuses on optimal crossover designs for normal responses. But, there are ample examples where responses are non-normal and needed to be described by generalized linear models (GLMs). The optimal designs obtained for normal responses can be quite inefficient for GLMs. The goal of this manuscript is to bridge this gap in the literature and obtain efficient designs for crossover experiments with responses under GLMs, including Poisson, beta, gamma responses, *etc.*

In crossover experiments, every subject is exposed to a sequence of treatments over different time periods, *i.e.*, subjects crossover from one treatment to another. Among different types of experiments available for treatment comparisons with multiple periods, the crossover designs are among the most important ones. We can get the same number of observations but with fewer subjects. The time at which the subject receives the treatment is known as a *period* and the order in which the particular subject receives treatments is known as a *sequence*. Each subject receives one treatment in each period, and the corresponding

Corresponding Author: Abhyuday Mandal
Email: amandal@stat.uga.edu

response is recorded. Naturally, crossover designs also provide within-subject information about treatment differences.

Most of the current literature in the crossover design deal with the continuous responses (see, for example, Kershner and Federer (1981), Laska and Meisner (1985), Matthews (1987), Carriere and Huang (2000), and the references therein). The problem of determining optimal crossover designs for continuous responses has been studied extensively (see, for example, Bose and Dey (2009) for a review of results). For examples of practical cases where the responses are discrete, such as binary responses, one may refer to Jones and Kenward (2014) and Senn (2003).

Different fixed effects models have been proposed in the literature, but the following linear model is used extensively to formulate crossover designs. For an experiment involving n subjects and p periods, the response is modeled as

$$Y_{ij} = \lambda + \beta_i + \alpha_j + \tau_{d(i,j)} + \rho_{d(i-1,j)} + \epsilon_{ij}, \tag{1}$$

where Y_{ij} is the observation from the jth subject in the ith time period, with $i = 1, \ldots, p$ and $j = 1, \ldots, n$. Here $d(i, j)$ stands for the treatment assigned to the jth subject at time period i and $\lambda, \beta_i, \alpha_j, \tau_{d(i,j)}, \rho_{d(i-1,j)}$ are the corresponding overall mean, the ith period effect, the jth subject effect, the direct treatment effect and the carryover treatment effect respectively. We define $\rho_{d(0,j)} = 0$. Here $\epsilon_{ij}s$ are the uncorrelated error terms which follow a normal distribution with zero mean and constant variance. Model (1) is commonly referred to as the traditional model due to its extensive use in the literature.

Note that the Fisher information matrix, for the linear model (1), is independent of model parameters because all the effects are fixed. Various optimality criteria such as A-, D-, E-optimality depend on this information matrix (see, for example, Pukelsheim (1993)). The optimality of crossover designs for linear models has been studied extensively in the literature. Hedayat and Afsarinejad (1978), Cheng and Wu (1980) and Kunert (1984b) considered the optimality of balanced, uniform designs. Optimality of designs when $p \leq t$ were first formulated in Dey *et al.* (1983). However, these results are not directly applicable to non-normal responses. In the case of GLMs Fisher information matrix depends on the model parameters (McCullagh and Nelder (1989), Stufken and Yang (2012)); hence the results on the optimality of crossover designs for linear models cannot be readily extended to other types of responses.

2. Preliminary Setup: Crossover Design for GLM

Most of the results available on optimal crossover designs deal with normal responses, so the results on crossover designs under GLMs are limited. Before presenting the results for optimal crossover designs, we formally introduce the associated generalized linear models for crossover designs.

Consider a crossover experiment with t treatments, n subjects, and p periods. The response from the jth subject is $Y_j = (Y_{1j}, \ldots, Y_{pj})'$ and the overall response for these n subjects are denoted as $Y_1, \ldots, Y_n$. The marginal distribution of Y_{ij} is described using GLMs as mentioned in Liang and Zeger (1986). Then the marginal mean μ_{ij} of Y_{ij} for crossover

trial is modeled as

$$\mathrm{g}(\mu_{ij}) = \eta_{ij} = \lambda + \beta_i + \tau_{d(i,j)} + \rho_{d(i-1,j)}, \tag{2}$$

where $i = 1, \ldots, p; j = 1, \ldots, n$; λ is the overall mean, β_i represents the effect of the ith period, τ_s is the direct effect due to treatment s assigned to subject j in period i, ρ_s is the carryover effect due to treatment s assigned to subject j in period $(i-1)$, where $s = 1, \ldots, t$ and g is a link function. We define $\rho_{d(0,j)} = 0$. For example, $\mu_{1,j}$ is modeled as $g(\mu_{1,j}) = \eta_{1,j} = \lambda + \tau_{d(1,j)}$.

In many situations interest lies mainly in the estimation of direct treatment effects, so we treat carryover effects as nuisance parameter. To ensure the estimability of the parameters, we set the baseline constraints as $\beta_1 = \tau_1 = \rho_1 = 0$.

Consider $\beta = (\beta_2, \ldots, \beta_p)'$, $\tau = (\tau_2, \ldots, \tau_t)'$ and $\rho = (\rho_2, \ldots, \rho_t)'$, which define the parameter vector $\theta = (\lambda, \beta, \tau, \rho)'$. Then the linear predictor corresponding to the jth subject, $\eta_j = (\eta_{1j}, \ldots, \eta_{pj})'$ can be written as

$$\eta_j \quad = \quad X_j\theta.$$

The corresponding design matrix X_j can be written as $X_j = [1_p, P_j, T_j, F_j]$, where P_j is $p \times (p-1)$ matrix such that $P_j = [0_{(p-1)1}, I_{p-1}]'$; T_j is a $p \times (t-1)$ matrix with its $(i,s)th$ entry equal to 1 if subject j receives the direct effect of the treatment s in the ith period and zero otherwise; F_j is a $p \times (t-1)$ matrix with its $(i,s)th$ entry equal to 1 if subject j receives the carryover effect of the treatment s in the ith period and zero otherwise. The columns of T_j and F_j are indexed by $2, \ldots, t$. Note that T_j and F_j have $t-1$ columns instead of t, because of the baseline constraints $\tau_1 = \rho_1 = 0$.

If the number of subjects is fixed to n and the number of periods is p, then we determine the proportion of subjects assigned to a particular treatment sequence. As the number of periods is fixed to p, each treatment sequence will be of length p and a typical sequence can be written as $\omega = (t_1, \ldots, t_p)'$ where $t_i \in \{1, \ldots, t\}$. Now, let Ω be the set of all such sequences and n_ω denote the number of subjects assigned to sequence ω. Then, the total number of subjects n can be written as $n = \Sigma_{\omega \in \Omega} n_\omega$, with $n_\omega \geq 0$. A crossover design ζ in approximate theory is specified by the set $\{p_\omega, \omega \in \Omega\}$, where $p_\omega = n_\omega/n$ is the proportion of subjects assigned to treatment sequence ω. Such a crossover design ζ can be denoted as follows:

$$\zeta = \left\{ \begin{array}{cccc} \omega_1 & \omega_2 & \ldots & \omega_k \\ p_{\omega_1} & p_{\omega_2} & \ldots & p_{\omega_k} \end{array} \right\},$$

where k is the number of treatment sequences involved, such that $\sum_{i=1}^{k} p_{\omega_i} = 1$. From the definitions of matrices T_j and F_j it can be noted that they depend only on the treatments sequence ω that subject j receives. Let T_ω be the matrix T and F_ω be the matrix F when subject receives sequence ω. Then it can be inferred that all the subjects receiving sequence ω have same T and F matrices. This implies, all the subjects receiving sequence ω have same design matrix *i.e.* $X_j = X_\omega$ as $P_j = [0_{(p-1)1}, I_{p-1}]'$.

Following Jankar *et al.* (2020), we use generalized estimating equations (GEEs) to estimate quasi-likelihood estimates of the model parameters. As mentioned in Zeger *et al.* (1988, equation (3.1)), it can be shown that for repeated measurement model, the GEEs are

$$\sum_{j=1}^{n} \frac{\partial \mu_j'}{\partial \theta} W_j^{-1} (Y_j - \mu_j) = 0,$$

where $\mu_j = (\mu_{1j}, \ldots, \mu_{pj})'$ and the asymptotic variance for the GEE estimator $\hat{\theta}$ (see Zeger *et al.*, 1988, equation (3.2)) is

$$\text{Var}(\hat{\theta}) = \left[\sum_{j=1}^{n} \frac{\partial \mu_j'}{\partial \theta} W_j^{-1} \frac{\partial \mu_j}{\partial \theta} \right]^{-1},$$

where $W_j = Cov(Y_j)$.

We can write the above equation in the form of approximate designs as follows,

$$\text{Var}(\hat{\theta}) = \sum_{\omega \epsilon \Omega} n p_\omega \frac{\partial \mu_\omega'}{\partial \theta} W_\omega^{-1} \frac{\partial \mu_\omega}{\partial \theta},$$

where W_ω corresponds to the covariance matrix of response Y_j when subject j receives treatment sequence ω.

Main interest usually lies in estimating the direct treatment effect contrasts. So, instead of working with the full variance-covariance matrix of parameter estimator $\hat{\theta}$, we concentrate only on the variance of the estimator of treatment effect $\text{Var}(\hat{\tau})$. Here

$$\text{Var}(\hat{\tau}) \quad = \quad H \text{Var}(\hat{\theta}) H', \tag{3}$$

where H is a $(t-1) \times m$ matrix given by $[0_{(t-1)1}, 0_{(t-1)(p-1)}, I_{t-1}, 0_{(t-1)(t-1)}]$, where $m = p + 2t - 2$ is the total number of parameters in θ and $0_{(t-1)(p-1)}$ is a $(t-1) \times (p-1)$ matrix of zeros.

Optimal proportions for crossover designs are obtained by minimizing the variances of estimators of treatment effect. We use the D-optimality criterion and use the determinant of $\text{Var}(\hat{\tau})$ as our objective function. Then an optimal design ζ^* minimizes the determinant of $\text{Var}(\hat{\tau})$ in equation (3) with respect to p_ω, such that $\sum_{w \in \Omega} p_w = 1$.

Note that the baseline constraints $\tau_1 = 0$ we set earlier results in the estimators for $\tau_i - \tau_1$ for $i \geq 2$. In the case of a D-optimality criterion, it is okay to use an above baseline constraint, but we must use different constraints in other optimality criteria. The above method has been discussed in detail in Jankar *et al.* (2020).

3. The Work Environment Experiment

We considered the data obtained from the work environment experiment conducted at Booking.com (Pitchforth *et al.* (2020)). In recent years, most corporate offices and organizations are adopting open office spaces over the traditional cubical office spaces. Since there

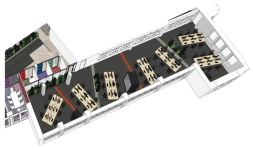
were no previous studies to examine the effects of office designs in workspaces, Booking.com conducted an experiment to assess different office spacing efficiency.

In the work environment experiment, there were a total of $n = 288$ participants. These participants were divided into four groups G_1, G_2, G_3, G_4 with each group having an equal number of (72) individual participants. This experiment is essentially an uniform crossover design with $p = 4$ periods and $t = 4$ treatments. Periods were named Wave1, Wave2, Wave3 and Wave4, where each Wave had a duration of 2 weeks. The four treatments involved in this experiment are office designs named as A (Activity-Based), B (Open Plan), C (Team Offices), and D (Zoned Open Plan), as shown in the figure below:

$A-$ ACT

$B-$ OPEN

$C-$ TEAM



$D-$ ZONE.

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During the experiment, each group is exposed to different treatments over different periods depending on the treatment sequence. At a given particular period, there was no interaction between subjects from different groups. A Latin square design (Wu and Hamada, 2009) of order four has been used to decide the sequence of exposure so that no group was exposed to the conditions in the same order as any other group. The design is shown below in Table 1. A total of $m = 23$ covariates was involved in the experiment, but we consider only the most important ones in our fitted model.

Table 1: Latin square design

Groups ⇒ Period ⇓	G_1	G_2	G_3	G_3
Wave 1	OPEN	TEAM	ZONE	ACT
Wave 2	ACT	ZONE	OPEN	TEAM
Wave 3	ZONE	ACT	TEAM	OPEN
Wave 4	TEAM	OPEN	ACT	ZONE

In the following analysis, we consider three different responses that were recorded during the experiment. We discuss these responses in more detail in the following sections.

These three responses follow three different types of distributions. We make an extra assumption that the responses from a particular subject are mutually correlated, while the responses from different subjects are uncorrelated. To capture the dependency among the observations coming from the same subject, we calculate optimal proportions for these different responses using six different correlation structures proposed in Section 2.3 of Jankar *et al.* (2020) and shown in the Appendix. For each correlation matrix that we consider, an optimal design ζ^* is the one minimizing the determinant of $\text{Var}(\hat{\tau})$ in equation (3) with respect to p_ω such that $\sum_{w\in\Omega} p_w = 1$.

We use different colors to represent different correlation structures. The color scheme that we use is as follows:

Correlation Structure	Color
Corr(1)	
Corr(2)	
Corr(3)	
Corr(4)	
Corr(5)	
Corr(6)	

4. Poisson Regression

In the case of Poisson response we calculate locally optimal design for the above example under the model,

$$\log(\mu_{ij}) = \eta_{ij} = \lambda + \beta_i + \tau_{d(i,j)} + \rho_{d(i-1,j)},$$

where notations have the same meaning as in equation (2). In the above experiment, there were many different types of responses recorded. We consider the response *commit count* to illustrate the optimal crossover design for the Poisson response. The commit counts were the number of commits submitted to the main git repository.

4.1. Analysis of data

We consider the three main predictors in the model, which are *area*, *wave* and *carryover* where *area* corresponds to the direct treatment effect, *wave* corresponds to the period effect, and *carryover* corresponds to the carryover effect of a treatment given in previous period. We use different kinds of correlation matrices and calculate the optimal proportions. As mentioned earlier we consider baseline constraints as $\beta_1 = \tau_1 = \rho_1 = 0$, so that all the parameters are estimable.

We fit the Poisson regression model to the commit data by using the `glm` function in **R** and calculate the parameter estimates. We use these parameter estimates to make a guess for values of unknown parameters. Our nominal guess for the parameter values is $\theta_1 = [2,$

0.3, 0.8, −0.1, −0.2, 0.04, −0.2, −0.6, 0.15, −0.4]. It is interesting to note that carryover effects are larger than direct effects even though θ_1 is calculated using experimental data. Now, we calculate the optimal designs for different correlation structures by minimizing the objective function. We also calculate optimal proportions for another parameter θ_2 = [2, 0.3, 0.8, −0.1, −2.0, 0.40, −2.0, −1.0, 0.30, −1.0], which is significantly different from θ_1.

4.2. Optimal designs

In the Table 2, we present the optimal proportions corresponding to Poisson response for six different choices of the correlation matrix.

Table 2: Optimal proportions in case of Poisson response

Correlation	θ_1				θ_2			
Structure	$BADC$	$CDAB$	$DBCA$	$ACBD$	$BADC$	$CDAB$	$DBCA$	$ACBD$
$Corr(1)$	0.2500	0.2500	0.2500	0.2500	0.2500	0.2500	0.2500	0.2500
$Corr(2)$	0.2500	0.2500	0.2500	0.2500	0.2747	0.3113	0.1841	0.2299
$Corr(3)$	0.2500	0.2500	0.2500	0.2500	0.2795	0.3074	0.1798	0.2333
$Corr(4)$	0.2500	0.2500	0.2500	0.2500	0.2562	0.3168	0.1860	0.2410
$Corr(5)$	0.2500	0.2500	0.2500	0.2500	0.2736	0.3138	0.1922	0.2204
$Corr(6)$	0.2500	0.2500	0.2500	0.2500	0.2537	0.3190	0.1844	0.2429

As seen from Table 2, in case of Poisson response the optimal proportions that we obtain using θ_1 are nearly uniform and that using θ_2 are non-uniform.

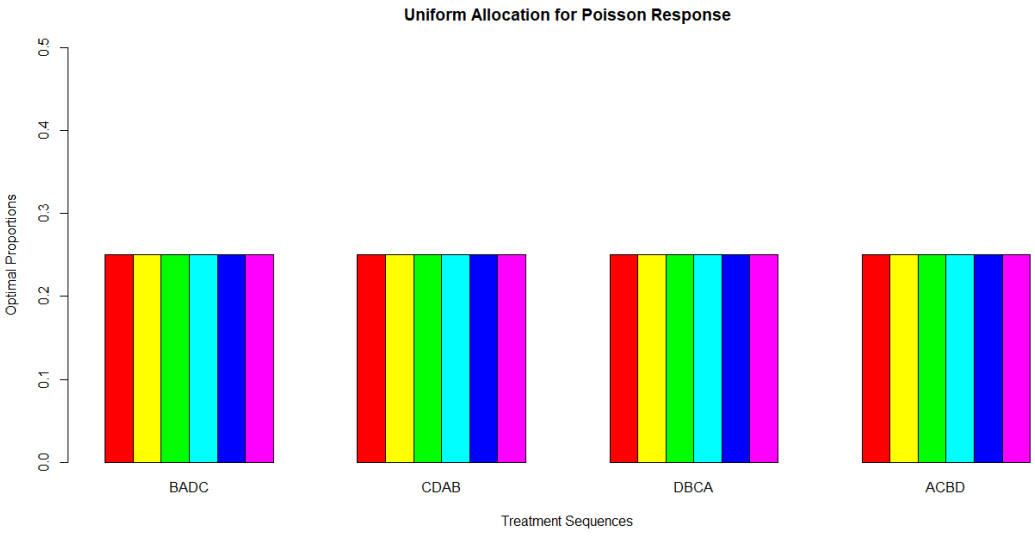

Figure 1: Uniform optimal proportions for Poisson response under θ_1

The plots in Figures 1 and 2 represent the optimal proportions for Poisson response under θ_1 and θ_2 respectively. It can be seen from these plots that the optimal proportions do not vary much when we use different correlation structures under θ_1 and θ_2. In most situations in practice, uniform, optimal designs (the same proportion for each treatment sequence) are used. It is clear from the above analysis that those uniform designs are sub-optimal under θ_2.

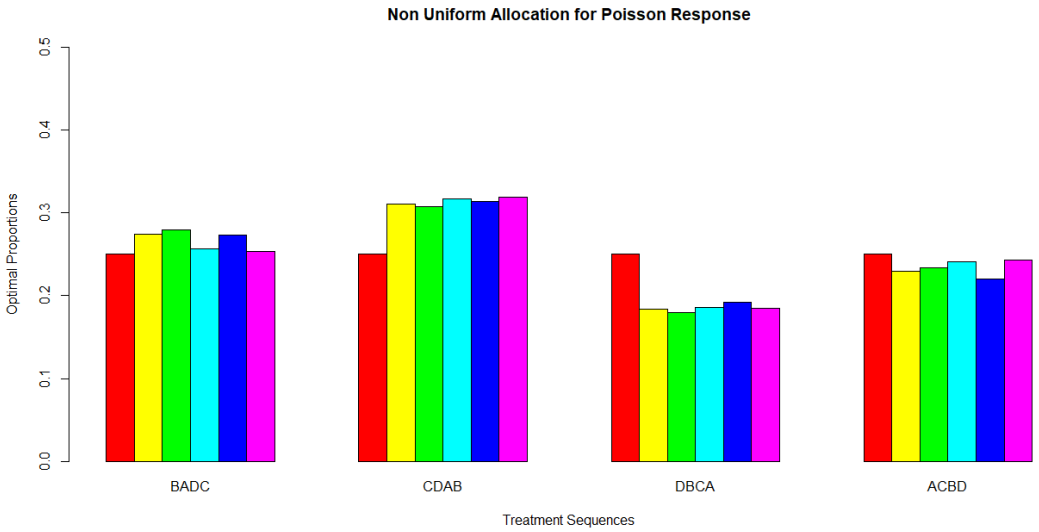

Figure 2: Non-uniform optimal proportions for Poisson response under θ_2

5. Beta Regression

In the beta response case, we calculate the locally optimal design for the response from the Booking.com example under two different models. We consider two different link functions to model the marginal mean of the response as follows:

$$\text{logit}(\mu_{ij}) = \log(\frac{\mu_{ij}}{1-\mu_{ij}}) = \eta_{ij} = \lambda + \beta_i + \tau_{d(i,j)} + \rho_{d(i-1,j)},$$

and,

$$\log(\mu_{ij}) = \eta_{ij} = \lambda + \beta_i + \tau_{d(i,j)} + \rho_{d(i-1,j)},$$

where notations have the same meaning as in equation (2).

To illustrate the optimal proportions in the beta response case, we consider the normalized response *engagement* from the work environment experiment. In the case of this experiment, *engagement* is a measure of the extent to which participants felt focused on and excited to complete regular work tasks.

5.1. Analysis of data

Similar to the Poisson response analysis, we consider three main predictors in the model for a beta response which are *area*, *wave* and *carryover*. We use six different kinds of correlation matrices as mentioned above and calculate optimal proportions under two different models with different link functions. As mentioned earlier, we consider baseline constraints so that all the parameters are estimable.

We get the initial estimates of parameters by fitting the beta regression model to the response. For two different link functions we need to guess two different sets of parameter values for θ_1 and θ_2. In case of *logit* link function, our nominal guess for the parameter values is $\theta_1 = [1.24, -0.035, 0.17, 0.078, -0.2, -0.3, 0.01, -0.35, -0.62, -0.329]$ and $\theta_2 = [1.24, -0.035, 0.17, 0.078, -4, -6, 2, -3.5, -3.1, -1.28]$. In case of *log* link function, our nominal guess for the parameter values is $\theta_1 = [-0.25, -0.01, 0.04, 0.02, -0.05, -0.08, -0.004, -0.088, -0.172, -0.08]$ and $\theta_2 = [-0.25, -0.01, 0.04, 0.02, -5, -8, -0.4, -2.2, -4.3, -2]$. Note that, as before, θ_1 is an educated guess based on the data at hand, whereas θ_2 has significantly different values for the parameters of interest than that of θ_1.

5.2. Optimal designs

In the Table 3, we present the optimal proportions corresponding to *logit* link case for six different choices of correlation matrix. As seen from Table 3, in case of beta response (*logit* link) the optimal proportions that we obtain using θ_1 are nearly uniform and that using θ_2 are non-uniform.

Table 3: Optimal proportions in case of beta response (*logit* link).

Correlation	θ_1				θ_2			
Structure	$BADC$	$CDAB$	$DBCA$	$ACBD$	$BADC$	$CDAB$	$DBCA$	$ACBD$
$Corr(1)$	0.2518	0.2563	0.2465	0.2454	0.3418	0.2085	0.1643	0.2854
$Corr(2)$	0.2525	0.2572	0.2453	0.2450	0.3316	0.2066	0.1690	0.2928
$Corr(3)$	0.2515	0.2568	0.2462	0.2455	0.3363	0.2058	0.1682	0.2897
$Corr(4)$	0.2405	0.2539	0.2419	0.2637	0.3205	0.2043	0.1739	0.3013
$Corr(5)$	0.2595	0.2542	0.2467	0.2396	0.3250	0.2070	0.1711	0.2969
$Corr(6)$	0.2366	0.2562	0.2423	0.2649	0.3218	0.2088	0.1668	0.3026

In Table 4, we present the optimal proportions corresponding to the *log* link case for six different choices of the correlation matrix. As before, in the beta response (*log* link) case, the optimal proportions that we obtain using θ_1 are nearly uniform and that using θ_2 are non-uniform.

The plots in Figures 3, 4 and Figures 5, 6 represent the optimal proportions for beta response under θ_1 and θ_2 for two different choices of link functions respectively.

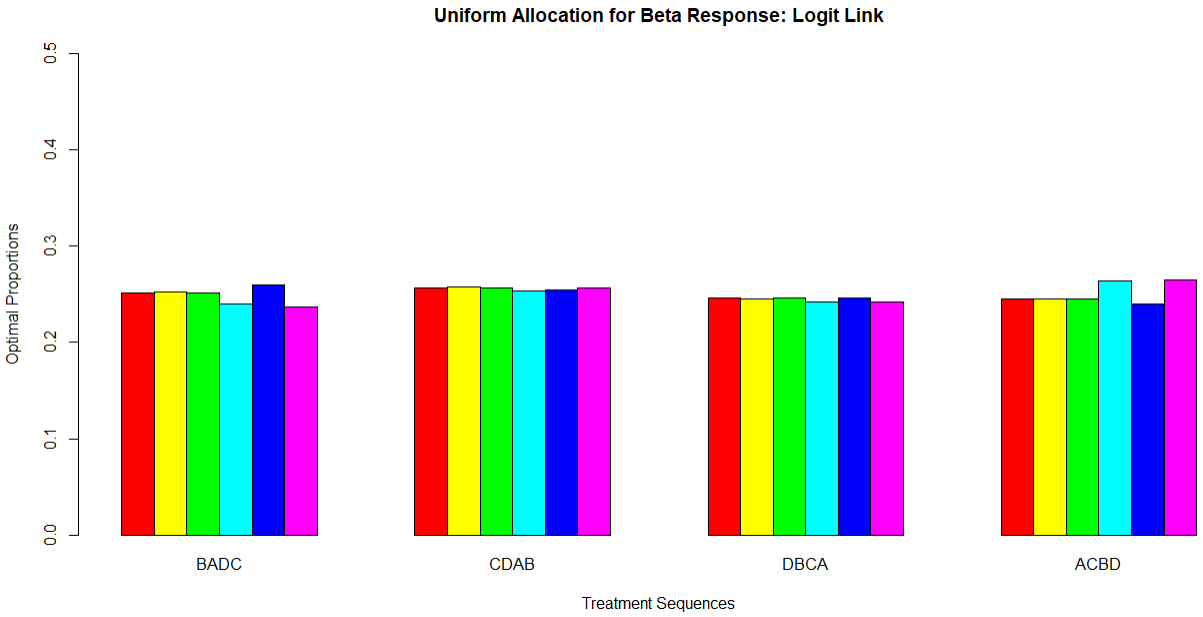

Figure 3: Uniform optimal proportions for beta response (*logit* link) under θ_1

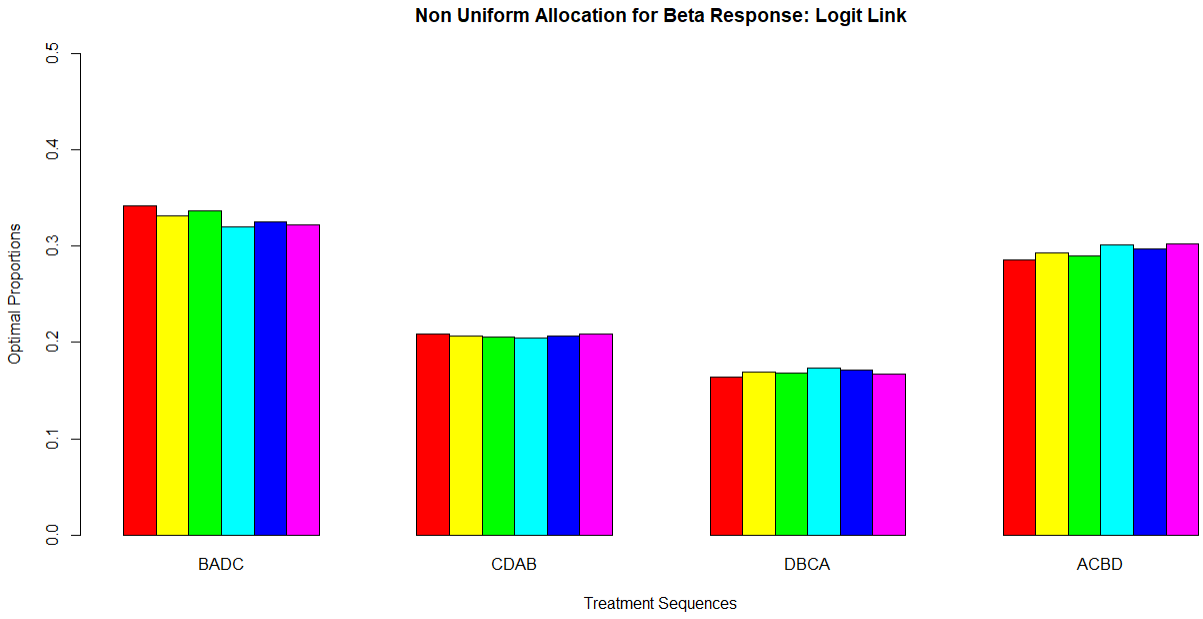

Figure 4: Non-uniform optimal proportions for beta response (*logit* link) under θ_2

Table 4: Optimal proportions in case of beta response (*log* link).

Correlation Structure	θ_1				θ_2			
	$BADC$	$CDAB$	$DBCA$	$ACBD$	$BADC$	$CDAB$	$DBCA$	$ACBD$
$Corr(1)$	0.2522	0.2560	0.2470	0.2448	0.3305	0.1470	0.1930	0.3295
$Corr(2)$	0.2529	0.2569	0.2458	0.2444	0.3270	0.1200	0.2084	0.3446
$Corr(3)$	0.2520	0.2564	0.2466	0.2450	0.3290	0.1210	0.2050	0.3450
$Corr(4)$	0.2410	0.2535	0.2425	0.2630	0.3271	0.1060	0.2137	0.3532
$Corr(5)$	0.2600	0.2540	0.2460	0.2400	0.3245	0.1101	0.2102	0.3552
$Corr(6)$	0.2371	0.2558	0.2428	0.2643	0.3272	0.1096	0.2120	0.3512

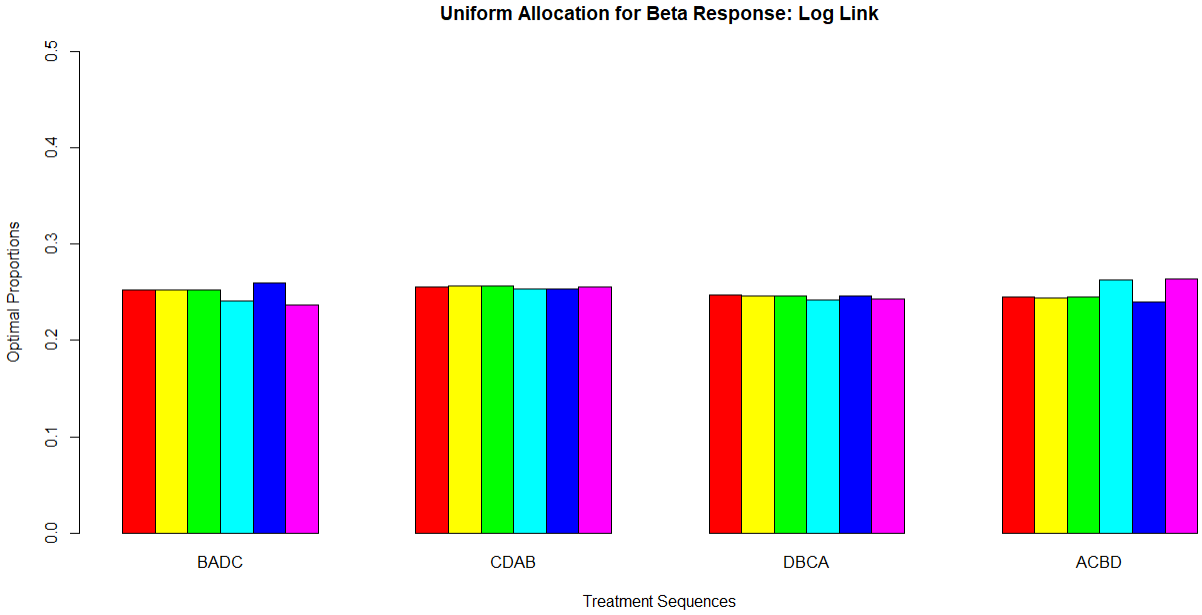

Figure 5: Uniform optimal proportions for beta response (*log* link) under θ_1

It can be seen from these plots that optimal proportions do not vary much when we use different correlation structures under θ_1 and θ_2. In most of the situations in practice uniform optimal designs are used. The above analysis shows that those uniform designs are sub-optimal under θ_2 irrespective of what link function is used.

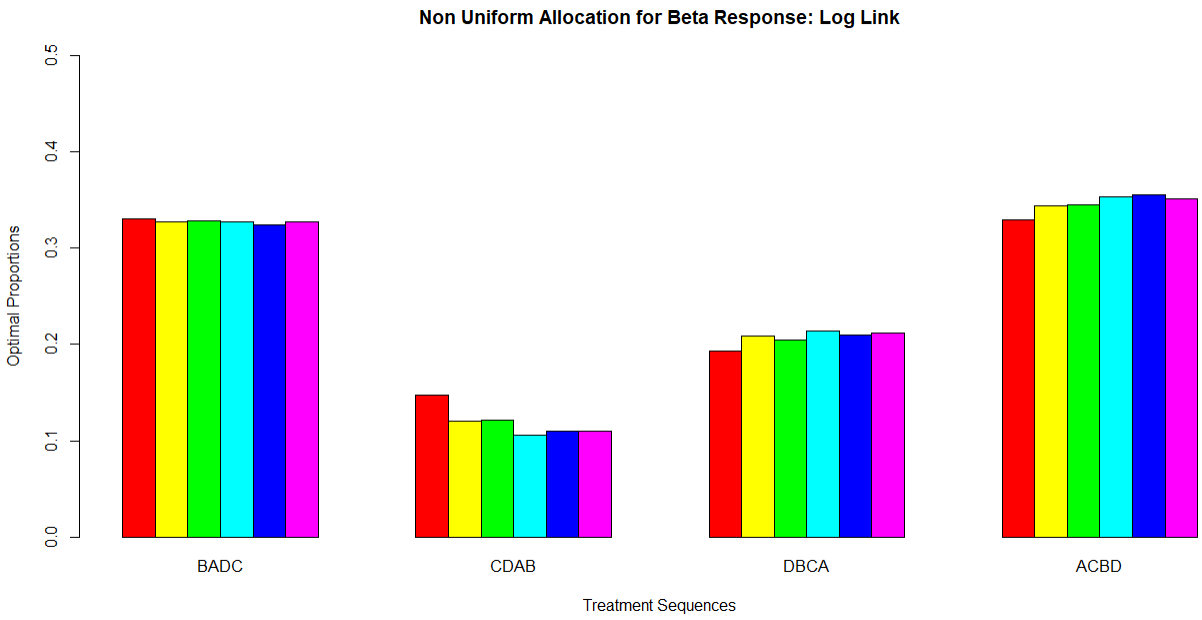

Figure 6: Non-uniform optimal proportions for beta response (*log* link) under θ_2

6. Gamma Regression

In the case of Gamma response, we calculate locally D-optimal design for the response from the same Booking.com example under two different models. Similar to the beta response, we consider two different link functions to model the marginal mean of the response. We use the *log*, and *inverse* link functions, and the two models are as follows:

$$\log(\mu_{ij}) = \eta_{ij} = \lambda + \beta_i + \tau_{d(i,j)} + \rho_{d(i-1,j)},$$

and,

$$inv(\mu_{ij}) = \frac{1}{\mu_{ij}} = \eta_{ij} = \lambda + \beta_i + \tau_{d(i,j)} + \rho_{d(i-1,j)},$$

where, as before, notations have the same meaning as in equation (2).

From the work environment experiment, we consider the response $satisfaction$. Satisfaction is an essential concept for organisational and office design research, and it is usually used to measure employees' sentiments. In the work environment experiment, the Leesman satisfaction index was used, which is useful for many benchmark purposes. Since the response is right-skewed, it is safe to assume that the response follows a gamma distribution.

6.1. Analysis of data

Similar to previous two cases, we consider three main predictors in the model for gamma response which are *area*, *wave* and *carryover*. As before, we consider six different kinds of correlation matrices and calculate optimal proportions under two different models with different link functions. We consider same baseline constraints as mentioned earlier. We fit the gamma regression model to the data with $satisfaction$ as response by using the `glm` function in **R** and calculate the parameter estimates.

In case of *log* link function, our nominal guess for the parameter values is $\theta_1 = [2.1, -0.19, -0.04, -0.04, -0.16, -0.4, -0.06, 0.05, 0.005, -0.05]$ and $\theta_2 = [2.1, -0.19, -0.04, -0.04, -1.6, -4.0, -0.6, 0.5, 0.05, -0.5]$. In case of *inverse* link function, our nominal guess for the parameter values is $\theta_1 = [0.13, 0.03, 0.003, 0.003, 0.025, 0.07, 0.008, -0.007, -0.0001, -0.01]$ and $\theta_2 = [0.13, 0.03, 0.003, 0.003, 2.5, 7, 0.8, -0.7, -0.01, -1]$. As before, θ_1 was motivated by the data provided by Pitchforth *et al.* (20202) and θ_2 is significantly different from θ_1.

6.2. Optimal designs

In the Table 5, we present the optimal proportions corresponding to *log* link case for six different choices of correlation matrix. As seen from Table 5, in case of gamma response (*log* link) the optimal proportions that we obtain using θ_1 are nearly uniform and that using θ_2 are non-uniform.

Table 5: Optimal proportions in case of gamma response (*log* link).

Correlation	θ_1				θ_2			
Structure	$BADC$	$CDAB$	$DBCA$	$ACBD$	$BADC$	$CDAB$	$DBCA$	$ACBD$
$Corr(1)$	0.2500	0.2500	0.2500	0.2500	0.1328	0.2775	0.3336	0.2561
$Corr(2)$	0.2500	0.2500	0.2500	0.2500	0.1248	0.2639	0.3527	0.2586
$Corr(3)$	0.2500	0.2500	0.2500	0.2500	0.1258	0.2582	0.3596	0.2564
$Corr(4)$	0.2500	0.2500	0.2500	0.2500	0.1206	0.2671	0.3451	0.2672
$Corr(5)$	0.2500	0.2500	0.2500	0.2500	0.1225	0.2770	0.3354	0.2656
$Corr(6)$	0.2500	0.2500	0.2500	0.2500	0.1195	0.2685	0.3416	0.2704

In Table 6, we present the optimal proportions corresponding to *inverse* link case for six different choices of correlation matrix. As before, Table 6 indicates that the optimal proportions that we obtain using θ_1 are nearly uniform and that using θ_2 are non-uniform in case of gamma response (*inverse* link).

The plots in Figures 7, 8 and Figures 9, 10 represent the optimal proportions for gamma response under θ_1 and θ_2 for two different choices of link functions respectively.

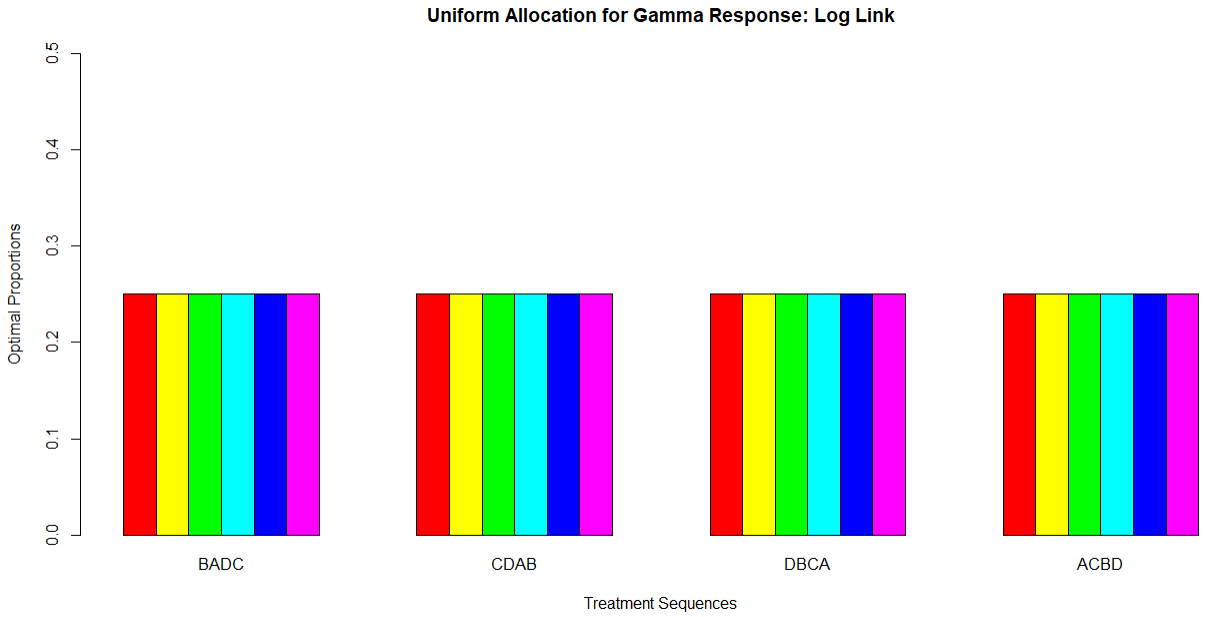

Figure 7: Uniform optimal proportions for gamma response (log link) under θ_1

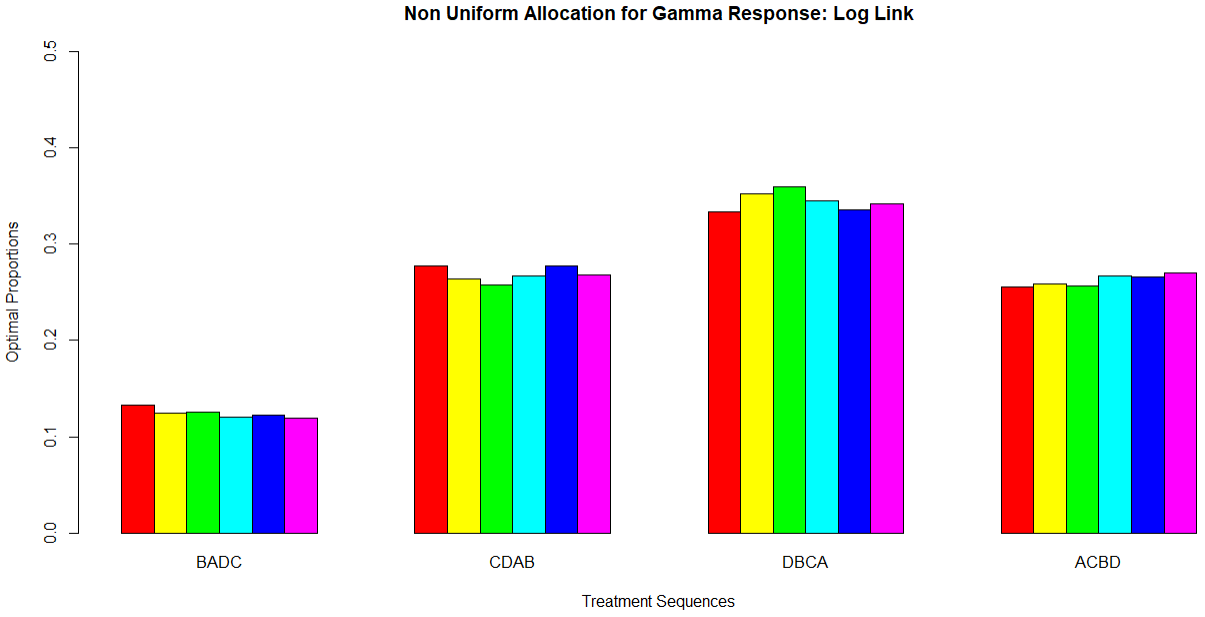

Figure 8: Non-uniform optimal proportions for gamma response (log link) under θ_2

Table 6: Optimal proportions in case of gamma response (*inverse* link).

Correlation Structure	θ_1				θ_2			
	$BADC$	$CDAB$	$DBCA$	$ACBD$	$BADC$	$CDAB$	$DBCA$	$ACBD$
$Corr(1)$	0.2500	0.2500	0.2500	0.2500	0.2650	0.3093	0.1828	0.2429
$Corr(2)$	0.2500	0.2500	0.2500	0.2500	0.2486	0.3031	0.1911	0.2572
$Corr(3)$	0.2500	0.2500	0.2500	0.2500	0.2588	0.3051	0.1879	0.2482
$Corr(4)$	0.2500	0.2500	0.2500	0.2500	0.2389	0.3087	0.1784	0.2740
$Corr(5)$	0.2500	0.2500	0.2500	0.2500	0.2406	0.3112	0.1762	0.2720
$Corr(6)$	0.2500	0.2500	0.2500	0.2500	0.2421	0.3146	0.1740	0.2729

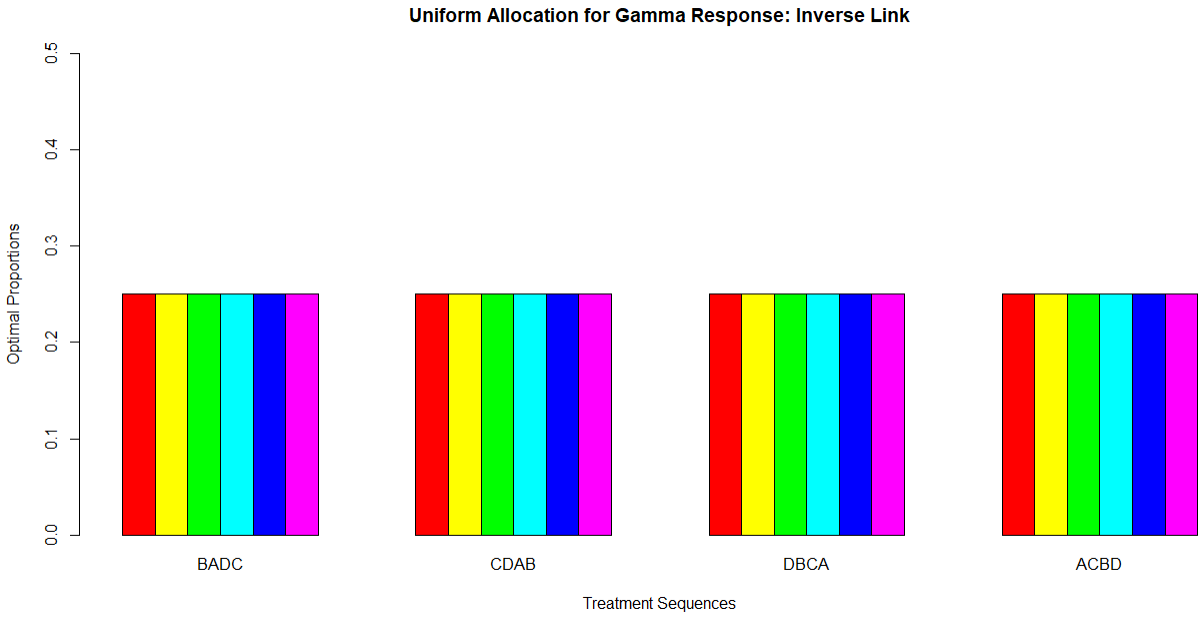

Figure 9: Uniform optimal proportions for gamma response (*inv* link) under θ_1

It can be seen from these plots that optimal proportions do not vary much when we use different correlation structures under θ_1 and θ_2. In most of the situations in practice uniform optimal designs are used. The above analysis shows that those uniform designs are sub-optimal under θ_2 irrespective of what link function is used.

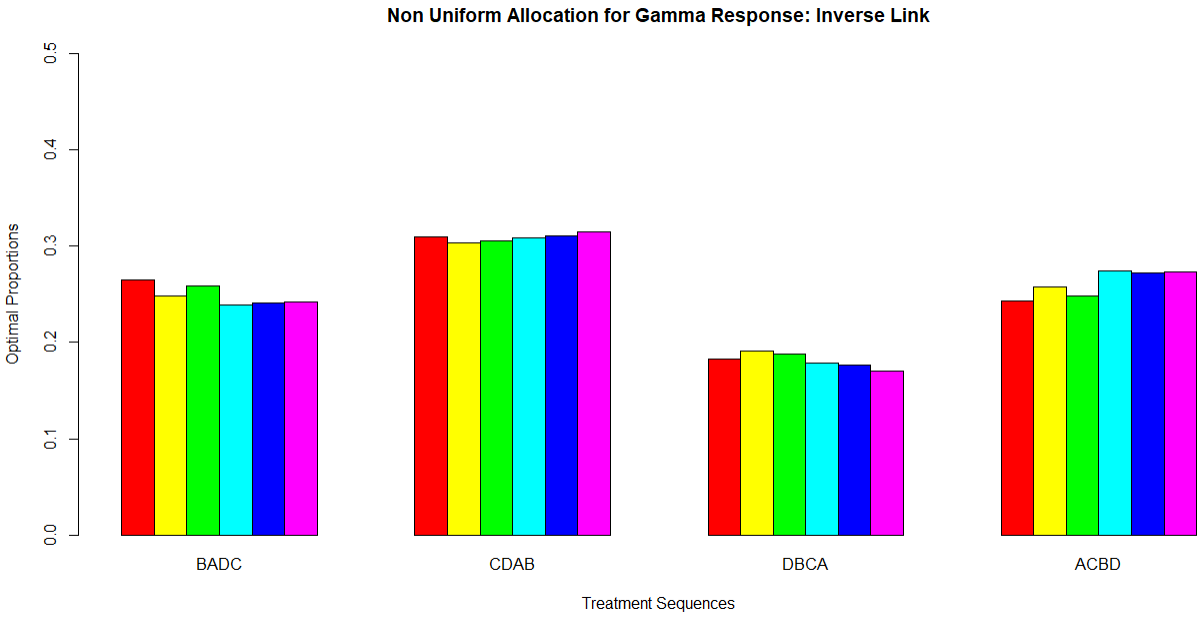

Figure 10: Non-uniform optimal proportions for gamma response (*inv* link) under θ_2

7. Summary and Conclusion

In many experiments in real life, uniform designs are often used. Uniform designs are those in which the same number of subjects are assigned to each treatment sequence. These uniform designs are optimal in the linear model case, *i.e.* when the response is normally distributed. But, in situations where responses are non-normal, the obtained optimal proportions are not necessarily uniform. In this paper's analysis, we identify locally optimal designs for responses belonging to Poisson, beta and gamma distributions. Two different link functions were considered in the case of beta and gamma responses. Tables 2 to 6 and plots in Figures 1 to 10 suggest that obtained optimal proportions are robust for different choice of correlations structures. These results also suggest that uniform designs are sub-optimal under θ_2 irrespective of the link function used or the response's distribution. Note that we are using the local optimality approach of Chernoff (1953). In real experiments, it is not always possible to guess the values of parameter estimates from prior knowledge. In that case, it is not easy to obtain locally optimal designs. In this paper we consider approximate designs in terms of optimal proportions. While conducting real life experiments, the practitioners must use exact designs where these proportions are to be converted into integers for determining the replication numbers of the sequences. The rounding off error might be significant unless the total number of observations is large. The Work Environment Experiment had 288 subjects and hence such issues do not arise.

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APPENDIX

Six Different Correlation Structures

The first correlation structure is a compound symmetric correlation structure, *i.e.*,

$$Corr(1) = (1-\rho)I_p + \rho J_p,$$

where I_p is the identity matrix of order p, and J_p is a $p \times p$ matrix with all elements unity.

The second correlation structure is the AR(1) correlation structure, *i.e.*,

$$Corr(2) = \left(\rho^{|i-i'|}\right),$$

so that the correlation between responses decreases as the time gap between responses increases.

The third correlation structure is as follows:

$$Corr(3) = \begin{pmatrix} 1 & \rho & 0 & \dots & 0 & 0 & 0 \\ \rho & 1 & \rho & \dots & 0 & 0 & 0 \\ \vdots & & & \vdots & & & \vdots \\ 0 & 0 & 0 & \dots & \rho & 1 & \rho \\ 0 & 0 & 0 & \dots & 0 & \rho & 1 \end{pmatrix}.$$

For each correlation structure different correlation matrices using different ρ values are considered.

To understand the other three correlation structures, we denote the correlation coefficient between the response when a subject receives treatment A first and the response when the same subject receives treatment B afterwards as ρ_{AB} and ρ_{BA} when the subject receives B first and A afterwards. Note that in general, ρ_{AB} is not necessarily the same as ρ_{BA}. In a similar manner we define ρ_{AA} and ρ_{BB}. To define the fourth type of correlation structure, we will use the same structure as $Corr(3)$ but with different values of the correlation coefficient for different treatment sequences.

To define the fifth and sixth type of correlation structures, we use AR(1) correlation structure with correlation coefficient depending on treatment sequence. For the fifth type, we use the same values for ρ_{AB} and ρ_{BA}, and for the sixth type of correlation structure, we use different values for ρ_{AB} and ρ_{BA}. For both fifth and sixth type of correlation structure we keep $\rho_{AA} = \rho_{BB}$. These values might vary from example to example and depend on what treatments A and B are. As the correlation matrix entries depend on which treatment the subject receives in a particular period, these correlation matrices are different for different treatment sequences.