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# R-optimal Designs for Logistic Regression Model in Two Variables

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### Abstract

This article obtains locally R-optimal designs for a logistic regression model with two explanatory variables. The R-optimality criterion has been proposed in the literature as an alternative to the most frequently used D-optimality criterion when the experimenter wishes to minimize the volume of the confidence region for unknown parameters based on Bonferroni *t*-intervals. The necessary and sufficient conditions of this optimality criterion are confirmed through the equivalence theorem.

*Key words:* R-optimal design; Logistic regression model; D-optimality criterion; Bonferroni *t*-intervals; Equivalence theorem.

# AMS Subject Classifications: 62K05

# 1. Introduction

The Generalized Linear Models (GLMs) are mostly used in those experiments where the responses are categorical type. These models are broadly applied in various types of studies when the experimenter wishes : (i) to estimate individual treatment effects in a multicenter clinical trial (*see* Lee and Nelder, 2002), (ii) to investigate the pattern of distribution of important tree species, and (iii) to identify the relationship between the risk of HIV (Human immunodeficiency virus) infection and the number of contacts with other partners and explanatory variables (*see* Jewell and Shiboski, 1992). McCullagh and Nelder (1989) have provided a detailed discussion on the analysis of data using GLMs and their application in different interdisciplinary areas.

The basic objective of finding an optimal design based on a certain criterion is to discuss statistical inference about the response of interest by selecting the control variable appropriately. The values of the control variables are chosen to minimize the variability of the estimators of the unknown parameters involved with the regression model. The pioneering work on optimal design was laid out by Kiefer (1959) and Kiefer and Wolfowitz (1959). The task of finding the optimal design for the GLM becomes quite challenging as the information matrix depends upon the unknown parameters *i.e.*, to find the best design to estimate the unknown parameters and yet one has to know the parameters to obtain the best design.

Chernoff (1953) proposed an approach that targets obtaining a local optimal design for a best guess value of the parameter.

For a logistic model with two variables, Abdelbasit and Plackett (1983) established that a D-optimal k-point design is a 2-point design when k is even and a 3-point design when k is odd. Minkin (1987) modified the result of the D-optimal design by relaxing the various constraints imposed on the design space. Chaloner and Larntzin (1989) discussed Bayesian D-optimal designs for the logistic regression model. Using a geometric approach, Ford *et al.* (1992) obtained C-optimal and D-optimal designs for the discussed model. Sitter and Wu (1993) obtained D-, A-, and F-optimal designs for the logistic model, while Dette and Haines (1994) found E-optimal designs for the same model. Mathew and Sinha (2002) derived a unified approach of D-, A-, and E- optimal designs for binary data under the logistic model with two parameters. Woods et al. (2006), Dror and Steinberg (2006), and McGree and Eccleston (2008) reported optimal designs for two variable binary logistic models with interaction. These designs were constructed by using numerical methods. In this article, we obtain locally R-optimal designs for a logistic regression model with two explanatory variables. Dette (1997) proposed the R-optimality criterion in the literature as an alternative to the most frequently used D-optimality criterion. He recommended that an experimenter can prefer the R-optimality criterion in comparison to the D-optimality criterion when he/she wishes to minimize the volume of the confidence region for unknown parameters based on the Bonferroni *t*-intervals.

The rest of the article is organized as follows. Section 2 provides the preliminaries. In Section 3, we obtain R-optimal designs for the logistic model with two variables. In Section 4, we discuss the robustness of the proposed optimal design through a simulation study. Finally, the article is concluded with some discussion and conclusions in Section 5.

#### 2. Preliminaries

Let us consider a binary response variable Y which follows a Bernoulli distribution and takes two values *i.e.* it takes value 1 for a success/positive response and 0 for a failure/negative response. If the response variable Y is related to the explanatory variables  $x_1$ and  $x_2$  through the two-variable binary logistic model, then the probability of success, p, can be expressed in terms of the logit

$$\mu = logit(p) = ln \frac{p}{1-p} = \beta_0 + \beta_1 x_1 + \beta_2 x_2 \tag{1}$$

where  $x_1$  and  $x_2$  are considered to be concentrations of the doses of two drugs with  $x_1 \ge 0$ , and  $x_2 \ge 0$ . In addition, the probability of a positive response is expected to increase with dose concentrations for both drugs, and thus  $\beta_1$  and  $\beta_2$  can be considered a strictly positive value [see Haines et al. (2007), and Haines et al. (2018)]. Due to practical considerations, the values of the parameter  $\beta_0$  may be chosen as negative values in different experiments. Based on the scaled doses *i.e.*  $z_1 = \beta_1 x_1$  and  $z_2 = \beta_2 x_2$ , the model Equations (1) can be expressed as

$$logit(p) = \beta_0 + z_1 + z_2$$
  $z_1 \ge 0 \text{ and } z_2 \ge 0.$  (2)

Consider an approximate design  $\xi$  that assigns weights  $w_i$  on the distinct points  $\mathbf{z}_i = (z_{1i}, z_{2i})$  for i = 1, 2, ..., r is denoted by

$$\xi = \left\{ \begin{pmatrix} z_{11}, z_{21} \end{pmatrix} \dots \begin{pmatrix} z_{1r}, z_{2r} \end{pmatrix} \right\}, \text{ where } 0 < w_i < 1 \text{ and } \sum_{i=1}^r w_i = 1.$$

The information matrix for the model Equation (2) based on the above design is given by

$$\boldsymbol{M}(\xi) = \sum_{i=1}^{r} w_i \boldsymbol{f}(\boldsymbol{z}_i) \boldsymbol{f}'(\boldsymbol{z}_i)$$
(3)

where

$$f(z)f'(z) = k \begin{bmatrix} 1 & z_1 & z_2 \\ z_1 & z_1^2 & z_1z_2 \\ z_2 & z_1z_2 & z_2^2 \end{bmatrix}$$

with 
$$k = \frac{e^{\mu}}{(1+e^{\mu})^2}$$
,  $f(z) = \frac{e^{\mu/2}}{(1+e^{\mu})}(1,z_1,z_2)$  and  $\mu = \beta_0 + z_1 + z_2$ 

**Selection of initial designs:** To obtain the R-optimal design for the model Equation (2) we consider the support points of 3-point and 4-point D-optimal designs (*see* Haines, 2007) and define them as follows:

3-point design : 
$$\xi = \begin{cases} (0,0) & (\mu - \beta_0, 0) & (0, \mu - \beta_0) \\ 1 - w & \frac{w}{2} & \frac{w}{2} \end{cases}$$
 (4)

4-point design : 
$$\xi_1 = \begin{cases} (-\mu - \beta_0, 0) & (0, -\mu - \beta_0) & (\mu - \beta_0, 0) & (0, \mu - \beta_0) \\ w & w & \frac{1}{2} - w & \frac{1}{2} - w \end{cases}$$
 (5)

respectively. The support points of the design  $\xi_1$  are having complimentary  $\mu$ -values. These points are located on the boundary of the design space on lines of constant. Further, the weights allocated to these points are based on the symmetric position of the support points.

**R-optimal design:** A design  $\xi^* \in \Omega$  with a non-singular matrix  $M(\xi^*)$  is called R-optimal for the model equation (3) if it minimizes

$$\Psi(\xi) = \prod_{i=1}^{q} (\boldsymbol{M}^{-1}(\xi))_{ii} = \prod_{i=1}^{q} \boldsymbol{e}'_{i} \boldsymbol{M}^{-1}(\xi) \boldsymbol{e}_{i}$$
(6)

for all  $\xi \in \Omega$ , where  $e_i$  denotes the ith unit vector in  $\mathbb{R}^q$  where q is the number of parameters associated with the model Equation (2). The necessary and sufficient conditions for the R-optimality can be verified using the following equivalence theorem. For further details, one can refer to the article of Dette (1997).

**Theorem 1:** For model Equation (2) let

$$\varphi(\boldsymbol{z},\xi) = \boldsymbol{f}(\boldsymbol{z})\boldsymbol{M}^{-1}(\xi) \left(\sum_{i=1}^{q} \frac{\boldsymbol{e}_{i}\boldsymbol{e}_{i}'}{\boldsymbol{e}_{i}'\boldsymbol{M}^{-1}(\xi)\boldsymbol{e}_{i}}\right)\boldsymbol{M}^{-1}(\xi)\boldsymbol{f}'(\boldsymbol{z}).$$
(7)

A design  $\xi^* \in \Omega$  is R-optimal if and only if

$$\sup_{z \in \Delta} \varphi(z, \xi^*) = q$$

with equality holds at the support points of  $\xi^*$ . Here  $\Delta$  is the experimental region of interest.

#### 3. R-optimal designs

In this section, we obtain locally R-optimal designs which minimize the product of the diagonal elements of the information matrix at best guesses of the unknown parameters  $\beta_0$ ,  $\beta_1$ , and  $\beta_2$ .

#### 3.1. Designs based on 3 points

Consider a 3-point design  $\xi$  of the form given by Equation (4) and assume that  $\mu > \beta_0$  whenever  $\beta_0 < 0$  and  $\mu < \beta_0$  whenever  $\beta_0 > 0$ . Then we have the following theorem.

**Theorem 2:** The design  $\xi^*$  that assigns a weight of 0.2324 to the point  $(\mu - \beta_0, 0)$ , 0.5352 to the point (0, 0), and 0.2324 to the point  $(0, \mu - \beta_0)$  in  $\Delta$  is an R-optimal design where

$$\Delta = \{ (z_1, z_2) : z_1 \ge 0, z_2 \ge 0, z_1 + z_2 \le 3.7422 \}$$

**Proof:** The information matrix for the model Equation (2) at the three-point design  $\xi$  defined in Equation (4) is given by

$$\boldsymbol{M}(\xi) = \begin{bmatrix} \frac{e^{\mu}}{(1+e^{\mu})^2} & \frac{e^{\mu}w(\mu-\beta_0)}{2(1+e^{\mu})^2} & \frac{e^{\mu}w(\mu-\beta_0)}{2(1+e^{\mu})^2} \\ \frac{e^{\mu}w(\mu-\beta_0)}{2(1+e^{\mu})^2} & \frac{e^{\mu}w(\mu-\beta_0)^2}{2(1+e^{\mu})^2} & 0 \\ \frac{e^{\mu}w(\mu-\beta_0)}{2(1+e^{\mu})^2} & 0 & \frac{e^{\mu}w(\mu-\beta_0)^2}{2(1+e^{\mu})^2} \end{bmatrix}$$

The inverse of the above information matrix is given by

$$\boldsymbol{M}^{-1}(\boldsymbol{\xi}) = \begin{bmatrix} a & b & b \\ b & c & d \\ b & d & c \end{bmatrix}$$
(8)

with

$$a = \frac{-2(1 + \cosh(\mu))}{-1 + w}, \quad c = \frac{2(-2 + w)(1 + \cosh(\mu))}{(\beta_0 - \mu)^2(-1 + w)w},$$

$$b = \frac{-2(1 + \cosh(\mu))}{(\beta_0 - \mu)(-1 + w)}, \text{ and } d = \frac{-2(1 + \cosh(\mu))}{(\beta_0 - \mu)^2(-1 + w)}.$$

Using Equation (8), we obtain the function

$$\Psi(\xi) = \frac{-8(-2+w)^2(1+\cosh(\mu))^3}{(\beta_0-\mu)^4(-1+w)^3w^2}.$$
(9)

Next, we wish to minimize  $\Psi(\xi)$  w.r.t.  $\mu$  and w for that we obtain the partial derivatives of Equation (9) w.r.t.  $\mu$  and w and set them equal to 0. Then we get

$$\frac{d}{d\mu}\Psi(\xi) = \frac{-8(-2+w)^2(1+\cosh(\mu))^2(4+4\cosh(\mu)+3(\beta_0-\mu)\sinh(\mu))}{(\beta_0-\mu)^5(-1+w)^3w^2} = 0, \quad (10)$$

$$\frac{d}{dw}\Psi(\xi) = \frac{64(-2+w)(4+w(-10+3w))\cosh\left(\frac{\mu}{2}\right)^6}{(3+\mu)^4(-1+w)^4w^3} = 0.$$
 (11)

Here  $cosh(\mu)$  and  $sinh(\mu)$  are defined as the cosine and sine hyperbolic functions evaluated at  $\mu$ . Next, Equation (10) leads to the following cases:

= 0,

(i) 
$$w = 2$$
,  
(ii)  $cosh(\mu) = -1$ ,  
(iii)  $4 + 4cosh(\mu) + 3(\beta_0 - \mu)sinh(\mu)$ 

and Equation (11) leads to the following cases:

(iv) 
$$w = 2$$
,  
(v)  $\cosh\left(\frac{\mu}{2}\right) = 0$ ,

and (vi) 4+w(-10+3w) = 0.

Out of these above-mentioned cases, the four cases *i.e.* (i), (ii), (iv), and (v) are the absurd cases. Therefore, we need to consider cases (iii) and (vi) only. Case (iii) implies

$$4 + 4\cosh(\mu) + 3(\beta_0 - \mu)\sinh(\mu) = 0$$
  

$$\Rightarrow \beta_0 - \mu = \frac{-4}{3\sinh(\mu)} - \frac{4\coth(\mu)}{3}$$
  

$$\Rightarrow \beta_0 - \mu = \frac{-4\operatorname{cosech}(\mu)}{3} - \frac{4\coth(\mu)}{3}$$
  

$$\Rightarrow \beta_0 = \mu - \frac{4}{3}[\operatorname{cosech}(\mu) - \coth(\mu)], \qquad (12)$$

where the functions  $cosech(\mu)$  and  $coth(\mu)$  are the cosecant and cotangent hyperbolic functions evaluated at  $\mu$ . Further, considering the first four terms of the Taylor series expansion of  $cosech(\mu)$ , and  $coth(\mu)$  in Equation (12), we get the following

$$\beta_0 = \mu - \frac{4}{3} \left[ \frac{1}{\mu} - \frac{\mu}{6} + \frac{7\mu^3}{360} - \frac{31\mu^5}{15120} + \dots \right] - \frac{4}{3} \left[ \frac{1}{\mu} + \frac{\mu}{3} - \frac{\mu^3}{45} + \frac{2\mu^5}{45} + \dots \right]$$
$$\Rightarrow \beta_0 = \frac{703\mu^5}{11340} + \frac{\mu^3}{270} + \frac{7\mu}{9} - \frac{8}{3\mu} \,. \tag{13}$$

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Next considering case (vi), we get two values of w out of which one value is feasible *i.e.*, the optimal value of w denoted by

$$w^* = \frac{5 - \sqrt{13}}{3} = 0.4648.$$
<sup>(14)</sup>

Here the optimal value  $\mu$  should satisfy Equation (13). From the numerical solutions obtained for Equation (13), we see that there is a unique solution exists for all values  $\mu > \beta_0$ . Let us denote the solution by  $\mu^*$ . As the solution can not be represented in an explicit form thus we provide the optimal values  $\mu^*$  for some selected values of  $\beta_0$  in Table 1.

The necessary and sufficient condition of the locally R-optimal design *i.e.*  $\sup_{z \in \Delta} \varphi(z, \xi^*) = q$  is confirmed by using the equivalence theorem which is as follows:

$$\varphi(\mathbf{z},\xi^*) = k \left\{ a + bz_1 + bz_2 - \frac{(\beta_0 - \mu)w(b + cz_1 + dz_2)}{-2 + w} - \frac{(\beta_0 - \mu)w(b + dz_1 + cz_2)}{-2 + w} + z_2 \left( b + dz_1 + cz_2 - \frac{w(b + cz_1 + dz_2)}{-2 + w} + \frac{a + bz_1 + bz_2}{\beta_0 - \mu} \right) + z_1 \left( b + cz_1 + dz_2 + \frac{a + bz_1 + bz_2}{\beta_0 - \mu} - \frac{w(b + dz_1 + cz_2)}{-2 + w} \right) \right\}.$$
(15)

Next, we provide the values of  $\varphi(\boldsymbol{z}, \xi^*)$  for some selected values of  $z_1$  and  $z_2$  in Table 2. We verify equivalence theorem for locally R-optimal design  $\xi^*$  by plotting a 3-dimensional plot of  $\varphi(\boldsymbol{z}, \xi^*)$  against  $z_1 \geq 0$  and  $z_2 \geq 0$  within the region  $\Delta$  (see Figure 1). This proves Theorem 2.

Ta	ble 1: Va	alues of $\mu^*$	for	selected $\beta_0$	for 3-pe	oint design	s
Bo	-3	-2.5	-2	-1.5	-1	-0.5	0

$ ho_{0}$	-0	-2.0	-2	-1.0	-1	-0.5	0
$\mu^*$	0.7422	0.8386	0.9543	1.0896	1.2392	1.3917	1.5355

$z_1$	$z_2$	$arphi(oldsymbol{z},\xi^*)$
0	0	3
0	3.742231	3
3.742231	0	3
3.5	0.5	2.88382
3	1	2.34827
2.5	1.5	2.02694
1.87112	1.87112	1.5
2	1	0.774831
0.5	2	0.663202
1.25	1.45	0.494252

Table 2: Values of $\varphi(\boldsymbol{z}, \boldsymbol{z})$	$\xi^*$ ) for different	values of $z_1$ and $z_2$
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Figure 1: Plot of the  $\varphi(\boldsymbol{z}, \xi^*)$  against  $z_1$  and  $z_2$ 

#### 3.2. Designs based on 4 points

In this section, we consider a 4-point design  $\xi_1$  of the form given by Equation (5) and assume that  $0 \le \mu \le -\beta_0$ . Then we have the following theorem.

**Theorem 3:** For the model Equation (2), there exists no mass-symmetric design of the form  $\xi_1$  based on the four support points given by Equation (5).

**Proof:** The information matrix for the model Equation (2) at the four-point design  $\xi_1$  is given by

$$\boldsymbol{M}(\xi_1) = \begin{bmatrix} M_{11} & M_{12} & M_{13} \\ M_{21} & M_{22} & M_{23} \\ M_{31} & M_{32} & M_{33} \end{bmatrix}$$

where

$$M_{11} = \frac{e^{\mu}}{(1+e^{\mu})^2},$$

$$M_{12} = M_{21} = M_{13} = M_{31} = \frac{e^{\mu}}{(1+e^{\mu})^2} \Big\{ \frac{\mu}{2} - \frac{\beta_0}{2} - 2\mu w \Big\},$$

$$M_{22} = M_{33} = \frac{e^{\mu}}{(1+e^{\mu})^2} \Big\{ -2\mu^2 w - 2w\beta_0^2 + 4w\mu\beta_0 + \frac{\mu^2}{2} + \frac{\beta_0^2}{2} - \mu\beta_0 \Big\},$$

and  $M_{23} = M_{32} = 0.$ 

The inverse of the above information matrix is

$$\boldsymbol{M}^{-1}(\xi_1) = \begin{bmatrix} M_{11}^+ & M_{12}^+ & M_{13}^+ \\ M_{21}^+ & M_{22}^+ & M_{23}^+ \\ M_{31}^+ & M_{32}^+ & M_{33}^+ \end{bmatrix}$$
(16)

with

$$\begin{split} M_{11}^{+} &= -\frac{((\beta_0 - \mu)^2 + 8\beta_0\mu w)(1 + \cosh(\mu))}{4\mu^2 w(-1 + 2w)}, \\ M_{12}^{+} &= M_{21}^{+} = M_{13}^{+} = M_{31}^{+} = -\frac{(\beta_0 + \mu(-1 + 4w))(1 + \cosh(\mu))}{4\mu^2 w(-1 + 2w)}, \\ M_{22}^{+} &= M_{33}^{+} = -\frac{e^{-\mu}(1 + e^{\mu})^2((\beta_0 - \mu)^2 + 8\mu(\beta_0 - \mu)w - 16\mu^2 w^2)}{8\mu^2 w(-1 + 2w)((\beta_0 - \mu)^2 + 8\beta_0\mu w)}, \end{split}$$

and  $M_{23}^+ = M_{32}^+ = -\frac{(\beta_0 + \mu(-1 + 4w)^2)(1 + \cosh(\mu))}{4\mu^2 w(-1 + 2w)((\beta_0 - \mu)^2 + 8\beta_0 \mu w)}.$ 

Using Equation (6), we obtain the function

$$\Psi(\xi_1) = \frac{e^{-3\mu}(1+e^{\mu})^6((\beta_0-\mu)^2+8\mu(\beta_0+\mu)w-16\mu^2w^2)^2}{512\mu^2w^2(-1+2w)^3((\beta_0-\mu)^2+8\beta_0\mu w)}.$$
(17)

Next, we wish to minimize  $\Psi(\xi_1)$  w.r.t.  $\mu$  and w for that we obtain the partial derivatives of Equation (17) w.r.t.  $\mu$  and w and set them equal to 0. Here we also replace the functions  $\sinh(\mu/2)$  and  $\cosh(\mu/2)$  by the first three terms of their Taylor series expansion respectively. Then, we get

$$\frac{d}{d\mu}\Psi(\xi_1) = -\frac{\kappa_1(\mu,\beta_0,w)}{\kappa_2(\mu,\beta_0,w)} = 0 , \qquad (18)$$

$$\frac{d}{dw}\Psi(\xi_1) = -\frac{\lambda_1(\mu,\beta_0,w)}{\lambda_2(\mu,\beta_0,w)} = 0$$
(19)

where

$$\begin{aligned} \kappa_1(\mu,\beta_0,w) = & \left( e^{\frac{-5\mu}{2}} (1+e^{\mu})^5 ((-\beta_0-\mu)^2 - 8\mu(\beta_0+\mu)w + 16\mu^2 w^2) \right) \\ & \left( 2((3\beta_0-2\mu)(\beta_0-\mu)^3 + 4(\beta_0-\mu)^2\mu(11\beta_0+4\mu)w + 16\mu^2(9\beta_0^2+9\beta_0\mu-2\mu^2)w^2 - 192\beta_0\mu^3w^3)\cosh(\frac{\mu}{2}) + 3\mu((\beta_0-\mu)^2 + 8\beta_0\mu w)(-(\beta_0-\mu)^2 - 8\mu(\beta_0+\mu)w + 16\mu^2 w^2)\sinh(\frac{\mu}{2}) \right) \right), \end{aligned}$$

$$\kappa_2(\mu,\beta_0,w) = 256\mu^7 w^3 (-1+2w)^3 ((\beta_0-\mu)^2 + 8\beta_0\mu w)^2,$$

$$\lambda_{1}(\mu,\beta_{0},w) = e^{-3\mu}(1+e^{\mu})^{6}((-\beta_{0}-\mu)^{2}+8\mu(\beta_{0}+\mu)w-16\mu^{2}w^{2})$$

$$(3\beta_{0}^{4}(-1+4w)-12\beta_{0}\mu^{3}(1-4w)^{2}(-1-2w+4w^{2})$$

$$+18\beta_{0}^{2}\mu^{2}(-1+4w)(1-4w+8w^{2})+4\beta_{0}^{3}\mu(3)$$

$$+22w(-1+2w)+\mu^{4}(-3+4w(1+4(3-4w)w))),$$

and 
$$\lambda_2(\mu, \beta_0, w) = 512\mu^6(-1+2w)^4w^4((\beta_0-\mu)^2+8\beta_0\mu w)^2.$$

Equation (17) leads to the following cases:

(a) 
$$e^{\frac{-5\mu}{2}} = 0,$$
  
(b)  $1 + e^{\mu} = 0,$   
(c)  $-(\beta_0 - \mu)^2 - 8\mu(\beta_0 + \mu)w + 16\mu^2w^2 = 0,$   
(d)  $\left(2((3\beta_0 - 2\mu)(\beta_0 - \mu)^3 + 4(\beta_0 - \mu)^2\mu(11\beta_0 + 4\mu)w + 16\mu^2(9\beta_0^2 + 9\beta_0\mu - 2\mu^2)w^2 - 192\beta_0\mu^3w^3)\cosh(\frac{\mu}{2}) + 3\mu((\beta_0 - \mu)^2 + 8\beta_0\mu w)(-(\beta_0 - \mu)^2 - 8\mu(\beta_0 + \mu)w + 16\mu^2w^2)\sinh(\frac{\mu}{2})\right) = 0,$ 

and Equation (18) leads to the following cases:

(e) 
$$e^{-3\mu} = 0$$
,  
(f)  $(1 + e^{\mu})^6 = 0$ ,

(g) 
$$(-\beta_0 - \mu)^2 + 8\mu(\beta_0 + \mu)w - 16\mu^2w^2) = 0,$$

(h)  $(3\beta_0^4(-1+4w) - 12\beta_0\mu^3(1-4w)^2(-1-2w+4w^2) + 18\beta_0^2\mu^2(-1+4w)(-1-4w+8w^2) + 4\beta_0^3\mu(3+22w(-1+2w) + \mu^4(-3+4w(1+4(3-4w)w))) = 0.$ 

Out of the above-mentioned cases (a), (b), (e), and (f) are the absurd cases. Case (c) leads to two possible values of  $\mu$  *i.e.* 

$$\mu = \frac{-\beta_0 + 4\beta_0 w \pm 4\sqrt{-\beta_0^2 w + 2\beta_0^2 w^2}}{16w^2 - 8w - 1} \,. \tag{20}$$

However, the values given in Equation (19) will be real provided  $w \ge 1/2$  which is again meaningless. Further, by solving the pair of Equations corresponding to cases (c) and (g) we get w = 1/2 which is not permissible. Next, we observe that the solutions of Equations corresponding to cases (d) and (h) (for different values of  $\beta_0$ ) do not satisfy the restrictions 0 < w < 1/2, and  $0 < \mu < -\beta_0$ . This indicates that there does not exist a four-point mass symmetric R-optimal design of the form  $\xi_1$  for the model Equation (2).

#### 4. Robustness and simulation study

In this section, we examine the robustness of the proposed optimal design through a simulation study. First of all, we generate a sample of 50 observations of the unknown parameter  $\beta_0$  from the U(-10, 10) distribution and obtain the corresponding value of  $\mu$  using Equation (13) by considering the assumptions about the parameter  $\beta_0$  and  $\mu$  as discussed in section 3.1. Next, for the pair of values of ( $\beta_0$ ,  $\mu$ ) we find the supremum value of  $\varphi(z, \xi^*)$  over the set  $\Delta$  using Equation (2.7). The values of  $\beta_0$ ,  $\mu$  and  $\sup_{z \in \Delta} \varphi(z, \xi^*)$  are shown in Table 3 (Appendix I). From Table 3, we observe that the value of  $\sup_{z \in \Delta} \varphi(z, \xi^*)$  is equal to 3 and it exists at all the support points of optimal design  $\xi^*$  as defined in Equation (4). This shows that the necessary and sufficient condition of the locally R-optimal design *i.e.* the equivalence theorem is satisfied for different values of  $\beta_0$ . Thus, it can be concluded that the proposed optimum design is robust or insensitive toward variation in parameter values.

#### 5. Discussion and conclusions

In the literature on the construction of optimal designs, the widely used optimality criterion is the D-optimality criterion. An experimenter decides to consider the D-optimality criterion when he/she is interested in the confidence ellipsoid of the estimators of the unknown parameters However, if the experimenter wishes to construct a rectangular confidence region then he/she should prefer an R-optimal design instead of a D-optimal design.

This present article obtains locally R-optimal designs for the logistic regression model in two variables subject to the constraint that the values of the variables are greater than or equal to zero. It is observed that the constructed designs depend upon the two unknown parameters through a scaled transformation of the explanatory variables whereas the intercept parameter  $\beta_0$  provides the basic structure of the design.

Haines *et al.* (2018) have obtained D-optimal designs for the two-variable binary logistic regression model with interaction where the design points consist of an origin, two axial points, and a ray point, which lies within the design space that accommodates interaction. In this article, it is assumed that equal weights are assigned to each of the design points. An interesting research problem is to investigate locally R-optimal designs for the same model. For this purpose, the design points proposed by Haines *et al.* (2018) can be used. This shall be an interesting and challenging research problem as the weights assigned to each design point in the case of locally R-optimal designs may not be the same. We look forward to exploring this open problem in future research.

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#### Conflict of interest

The authors do not have any financial or non-financial conflict of interest to declare for the research work included in this article.

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# Appendix-I

Table 3: Values  $\beta_0$ ,  $\mu$  and  $\sup_{z \in \Delta} \varphi(z, \xi^*)$ 

S.N.	$\beta_0$	$\mu$	$\sup_{oldsymbol{z}\in\Delta} arphi(oldsymbol{z},\xi^*)$	S.N.	$\beta_0$	$\mu$	$\sup_{oldsymbol{z}\in\Delta} arphi(oldsymbol{z},\xi^*)$
1	-5.6013	0.448	3	26	6.5924	2.4696	3
2	-3.1882	0.7104	3	27	-8.9667	2.6341	3
3	-4.7036	0.5216	3	28	1.3853	1.854	3
4	-3.9974	0.5969	3	29	-5.1861	0.4795	3
5	-6.5366	0.3898	3	30	-1.4474	1.1048	3
6	-9.3569	0.2785	3	31	-1.7531	1.0188	3
7	8.5955	2.6108	3	32	-9.2929	0.2803	3
8	-9.9134	0.2635	3	33	-3.2952	0.6934	3
9	-4.1403	0.5801	3	34	-8.1109	0.319	3
10	-5.7407	0.4383	3	35	8.8737	2.6283	3
11	9.2823	2.6534	3	36	-0.41	1.4185	3
12	5.6955	2.3958	3	37	9.629	2.674	3
13	-4.7861	0.5139	3	38	9.036	2.6384	3
14	-0.4474	1.4074	3	39	7.3492	2.5263	3
15	7.1903	2.5148	3	40	-0.4009	1.4212	3
16	-2.9595	0.7493	3	41	-4.3566	0.5563	3
17	6.2333	2.441	3	42	-3.2532	0.7	3
18	-3.0336	0.7363	3	43	-8.1627	0.317	3
19	7.5542	2.5409	3	44	-0.1417	1.4961	3
20	-2.4755	0.8437	3	45	-0.0297	1.5273	3
21	1.822	1.9327	3	46	-1.8701	0.9876	3
22	6.2163	2.4396	3	47	-9.2231	0.2823	3
23	3.6757	2.1933	3	48	-7.3585	0.3494	3
24	1.4215	1.8608	3	49	-3.5446	0.6562	3
25	1.675	1.9071	3	50	-1.4147	1.1143	3