

# Package ‘BAR’

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**Type** Package

**Title** Bayesian Adaptive Randomization

**Version** 0.1.1

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**Description** Bayesian adaptive randomization is also called outcome adaptive randomization, which is increasingly used in clinical trials.

**License** GPL-2

**Encoding** UTF-8

**Suggests** knitr, rmarkdown

**VignetteBuilder** knitr

**NeedsCompilation** no

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**Repository** CRAN

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get_oc_BAR	<i>Generate operating characteristics for Bayesian adaptive randomization</i>
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## Description

Randomization is the established method for obtaining scientifically valid comparisons of competing treatments in clinical trials and other experiments. Bayesian adaptive randomization (BAR) allows changes to be made to the randomization probabilities to treatments during the trial. The aim of the procedure is to allocate a greater proportion of patients to treatments that have so far demonstrated evidence of a better performance than other arms. Binary outcomes are considered in this package

## Usage

```
get_oc_BAR(success_prob, n_burn_in, tot_num, block_size,
           power_c = "n/2N", lower_bound = .05, reptime,
           control_arm = "", output = "", seed = 100)
```

## Arguments

success_prob	the successful probability for each arm (the first slot refers to the control arm)
n_burn_in	the number of burn-in for each arm
tot_num	the total number of patients enrolled for the trial
block_size	the block size
power_c	the power correction of allocation probability. The default value is power_c = "n/2N" and can also be numeric, e.g., power_c = .5
lower_bound	the lower bound of the allocation probability. It must between 0 and $\frac{1}{K}$ . The default value is lower_bound = .05; K indicates total number of arms (including control arm)
reptime	the number of simulated trials
control_arm	if this argument is "fixed", then allocation probability of control arm (the first slot) will be fixed to $\frac{1}{K}$ . The default of this argument will return unfixed results; K indicates total number of arms (including control arm)
output	if this argument is "raw", then the function will return updated allocation probability path after burn-in for each arm for each simulated trial. The default of this argument will return the average allocation probability and the average number of patients assigned to each arm
seed	the seed. The default value is seed = 100

## Details

We show how the updated allocation probabilities for each arm are calculated.

Treatments are denoted by  $k = 1, \dots, K$ .  $N$  is the total sample size. If no burn-in(s), the BAR will be initiated start of a study, that is, for each enrolled patient,  $n = 1, \dots, N$ , the BAR will be used to assign each patient. Denoting the true unknown response rates of  $K$  treatments by  $\pi_1, \dots, \pi_K$ , we can compute  $K$  posterior probabilities:  $r_{k,n} = Pr(\pi_k = \max\{\pi_1, \dots, \pi_K\} \mid Data_n)$ , here,  $n$  refers to the  $n$ -th patient and  $k$  refers to the  $k$ -th arm. We calculate the updated probabilities of the BAR algorithm according to the following steps.

Step 1: (Normalization) Normalize  $r_{k,n}$  as  $r_{k,n}^{(c)} = \frac{(r_{k,n})^c}{\sum_{j=1}^K (r_{j,n})^c}$ , here  $c = \frac{n}{2N}$ .

Step 2: (Restriction) To avoid the BAR sticking to very low/high probabilities, a restriction rule to the posterior probability  $r_{k,n}^{(c)}$  will be applied:

$$\text{Lower Bound} \leq r_{k,n}^{(c)} \leq 1 - (K - 1) \times \text{Lower Bound},$$

$$0 \leq \text{Lower Bound} \leq \frac{1}{K}$$

After restriction, the posterior probability is denoted as  $r_{k,n}^{(c, re)}$ .

Step 3: (Re-normalization) Then, we can have the updated allocation probabilities by the BAR denoted as:

$$r_{k,n}^{(f)} = \frac{r_{k,n}^{(c, re)} \times \left(\frac{r_{k,n}^{(c, re)}}{n_k}\right)^2}{\sum_{j=1}^K \{r_{j,n}^{(c, re)} \times \left(\frac{r_{j,n}^{(c, re)}}{n_j}\right)^2\}}$$

where  $n_k$  is the number of patients enrolled on arm  $k$  up-to-now.

Step 4: (Re-restriction) Finally, restricts again by using

$$\text{Lower Bound} \leq r_{k,n}^{(f)} \leq 1 - (K - 1) \times \text{Lower Bound},$$

$$0 \leq \text{Lower Bound} \leq \frac{1}{K}$$

and denote  $r_{k,n}^{(ff)}$  as the allocation probability used in the BAR package.

## Value

get\_oc\_BAR() depending on the argument "output", it returns:

default: (1) the average allocation probability (2) the average number of patients assigned to each arm

raw: (1) updated allocation probability path after burn-in for each arm for each simulated trial

## Author(s)

Chia-Wei Hsu, Haitao Pan

## References

Wathen JK, Thall PF. A simulation study of outcome adaptive randomization in multi-arm clinical trials. Clin Trials. 2017 Oct; 14(5): 432-440. doi: 10.1177/1740774517692302.

Xiao, Y., Liu, Z. & Hu, F. Bayesian doubly adaptive randomization in clinical trials. Sci. China Math. 60, 2503-2514 (2017). doi: 10.1007/s11425-016-0056-1.

Hu F, Zhang L X. Asymptotic properties of doubly adaptive biased coin designs for multi-treatment clinical trials. Ann Statist, 2004, 30: 268–301.

**Examples**

```
## power_c = "n/2N"
get_oc_BAR(success_prob = c(.1, .5, .8), n_burn_in = 10,
            tot_num = 150, block_size = 1, reptime = 5)

## power_c = .5
get_oc_BAR(success_prob = c(.1, .5, .8), n_burn_in = 10,
            tot_num = 150, block_size = 1, power_c = .5,
            reptime = 5)
```

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```
next_allocation_rate_BAR
```

*Calculate the allocation probability for the next block of new patients using Bayesian adaptive randomization*

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**Description**

Calculate updated allocation probability for each arm based on the accumulative data with binary outcomes

**Usage**

```
next_allocation_rate_BAR(n, success_count, tot_num,
                        power_c = "n/2N",
                        lower_bound = .05,
                        control_arm = "",
                        seed = 100)
```

**Arguments**

n	the number of patients enrolled for each arm
success_count	the number of responders for each arm
tot_num	the total number of patients enrolled for the trial. If this number cannot be pre-planned, the user can choose argument "power_c" to be numeric instead of "n/2N". In this case, even if the "tot_num" is given a number, this number will not be used
power_c	the power correction of allocation probability. The default value is power_c = "n/2N" and can also be numeric, e.g., power_c = .5
lower_bound	the lower bound of the allocation probability. It must be between 0 and $\frac{1}{K}$ . The default value is lower_bound = .05; K indicates total number of arms (including control arm)
control_arm	if this argument is "fixed", then allocation probability of control arm (the first slot) will be fixed to $\frac{1}{K}$ . The default of this argument will return unfixed results; K indicates total number of arms (including control arm)
seed	the seed. The default value is seed = 100

## Details

We show how the updated allocation probabilities for each arm are calculated.

Treatments are denoted by  $k = 1, \dots, K$ .  $N$  is the total sample size. If no burn-in(s), the BAR will be initiated start of a study, that is, for each enrolled patient,  $n = 1, \dots, N$ , the BAR will be used to assign each patient. Denoting the true unknown response rates of  $K$  treatments by  $\pi_1, \dots, \pi_K$ , we can compute  $K$  posterior probabilities:  $r_{k,n} = Pr(\pi_k = \max\{\pi_1, \dots, \pi_K\} \mid Data_n)$ , here,  $n$  refers to the  $n$ -th patient and  $k$  refers to the  $k$ -th arm. We calculate the updated probabilities of the BAR algorithm according to the following steps.

Step 1: (Normalization) Normalize  $r_{k,n}$  as  $r_{k,n}^{(c)} = \frac{(r_{k,n})^c}{\sum_{j=1}^K (r_{j,n})^c}$ , here  $c = \frac{n}{2N}$ .

Step 2: (Restriction) To avoid the BAR sticking to very low/high probabilities, a restriction rule to the posterior probability  $r_{k,n}^{(c)}$  will be applied:

$$Lower\ Bound \leq r_{k,n}^{(c)} \leq 1 - (K - 1) \times Lower\ Bound,$$

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After restriction, the posterior probability is denoted as  $r_{k,n}^{(c, re)}$ .

Step 3: (Re-normalization) Then, we can have the updated allocation probabilities by the BAR denoted as:

$$r_{k,n}^{(f)} = \frac{r_{k,n}^{(c, re)} \times \left(\frac{r_{k,n}^{(c, re)}}{n_k}\right)^2}{\sum_{j=1}^K \{r_{j,n}^{(c, re)} \times \left(\frac{r_{j,n}^{(c, re)}}{n_j}\right)^2\}}$$

where  $n_k$  is the number of patients enrolled on arm  $k$  up-to-now.

Step 4: (Re-restriction) Finally, restricts again by using

$$Lower\ Bound \leq r_{k,n}^{(f)} \leq 1 - (K - 1) \times Lower\ Bound,$$

$$0 \leq Lower\ Bound \leq \frac{1}{K}$$

and denote  $r_{k,n}^{(ff)}$  as the allocation probability used in the BAR package.

## Value

next\_allocation\_rate\_BAR() returns the updated allocation probability for each arm

## Author(s)

Chia-Wei Hsu, Haitao Pan

**References**

Wathen JK, Thall PF. A simulation study of outcome adaptive randomization in multi-arm clinical trials. *Clin Trials*. 2017 Oct; 14(5): 432-440. doi: 10.1177/1740774517692302.

Xiao, Y., Liu, Z. & Hu, F. Bayesian doubly adaptive randomization in clinical trials. *Sci. China Math*. 60, 2503-2514 (2017). doi: 10.1007/s11425-016-0056-1.

Hu F, Zhang L X. Asymptotic properties of doubly adaptive biased coin designs for multi-treatment clinical trials. *Ann Statist*, 2004, 30: 268–301.

**Examples**

```
## power_c = "n/2N"  
next_allocation_rate_BAR(n = c(30, 30, 30),  
                        success_count = c(5, 6, 12),  
                        tot_num = 150)  
  
## power_c = .5  
next_allocation_rate_BAR(n = c(30, 30, 30),  
                        success_count = c(5, 6, 12),  
                        tot_num = 150, power_c = .5)
```

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