

# Package: RABR (via r-universe)

August 30, 2024

**Title** Simulations for Response Adaptive Block Randomization Design

**Version** 0.1.1

**Description** Conduct simulations of the Response Adaptive Block Randomization (RABR) design to evaluate its type I error rate, power and operating characteristics for binary and continuous endpoints. For more details of the proposed method, please refer to Zhan et al. (2021) <<https://doi.org/10.1002/sim.9104>>.

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**Encoding** UTF-8

**LazyData** true

**Roxygen** list(markdown = TRUE)

**RoxygenNote** 7.2.1

**Imports** asd, cubature, data.table, doParallel, foreach, ggplot2, multcomp, multxpert, parallel, survival

**Suggests** rmarkdown, knitr, testthat (>= 3.0.0)

**Config/testthat/edition** 3

**VignetteBuilder** knitr

**URL** <https://github.com/tian-yu-zhan/RABR>

**BugReports** <https://github.com/tian-yu-zhan/RABR/issues>

**Repository** <https://tian-yu-zhan.r-universe.dev>

**RemoteUrl** <https://github.com/tian-yu-zhan/rabr>

**RemoteRef** HEAD

**RemoteSha** f129bb8e97f43c9c655bccd5fed1de68d847646f

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RABRbinary	<i>Simulate RABR for binary endpoints to evaluate operating characteristics</i>
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### Description

Simulate RABR for binary endpoints to evaluate operating characteristics

### Usage

```
RABRbinary(
  RateVec,
  M,
  N,
  R,
  Nitt,
  Alpha,
  Ncluster = 1,
  Seed = 12345,
  MultiMethod
)
```

### Arguments

RateVec	Vector of response rate for placebo and active treatment groups.
M	Total sample size of burn-in period.
N	Total sample size of RABR. Must be larger than M.
R	Randomization vector for placebo and active treatment groups.
Nitt	Number of simulation iterations.
Alpha	One-sided significance level.
Ncluster	Number of clusters for parallel computing.
Seed	Random seed.
MultiMethod	Multiplicity adjustment method. Must be one of the following values "holm", "hochberg", "hommel", "bonferroni", or "dunnett".

### Details

The RateVec is a vector of response rate for placebo and active treatment groups. The current package supports 2 or 3 active treatment groups. Note that a larger response corresponds to a better outcome.

The M is the total sample size of burn-in period with equal randomization. The total sample size N should be larger than N. The choice of M can be selected by comparing simulations from several candidate values. The R is a pre-specified randomization vector, where the first element is for placebo, and the next one for the best performing group, up to the worst performing group.

The Alpha is the one-sided significance level. The MultiMethod can be set at "holm" for Holm, "hochberg" for Hochberg, "hommel" for Hommel, "bonferroni" for Bonferroni, or "dunnett" for Dunnett procedures.

### Value

ProbUnadj: Probability of rejecting each elementary null hypothesis without multiplicity adjustment

ProbAdj: Probability of rejecting each elementary null hypothesis with multiplicity adjustment

ProbAdjSelected: Probability of selecting and confirming the efficacy of each active treatment group

ProbAdjOverall: Probability of rejecting at least one elementary null hypothesis with multiplicity adjustment

ASN: Average sample size of placebo and active treatment groups

### Author(s)

Tianyu Zhan (tianyu.zhan.stats@gmail.com)

### References

Zhan, T., Cui, L., Geng, Z., Zhang, L., Gu, Y., & Chan, I. S. (2021). A practical response adaptive block randomization (RABR) design with analytic type I error protection. *Statistics in Medicine*, 40(23), 4947-4960.

Cui, L., Zhan, T., Zhang, L., Geng, Z., Gu, Y., & Chan, I. S. (2021). An automation-based adaptive seamless design for dose selection and confirmation with improved power and efficiency. *Statistical Methods in Medical Research*, 30(4), 1013-1025.

### Examples

```
## Consider an example with two active treatment
## groups and a placebo. Suppose that the response
## rate of placebo is 0.15, 0.28 and 0.4 for
## two active treatment groups. The total sample
## size is N = 180 with a burn-in period M = 90. We
## use the randomization vector of (7, 7, 1),
## which means that placebo, the better performing
## group, and the worse group have randomization
## probabilities 7/15, 7/15, 1/15 respectively.
## The one-sided significance level is 2.5%.
## Nitt = 100 is for demonstration, and should be
## increased to 10^5 in practice.
##
library(parallel)
library(doParallel)
RABR.fit = RABRbinary(
  RateVec = c(0.15, 0.28, 0.4),
  M = 90,
  N = 180,
```

```

      R = c(7, 7, 1),
      Nitt = 100,
      Alpha = 0.025,
      Ncluster = 2,
      Seed = 12345,
      MultiMethod = "bonferroni")
##
## Probability of rejecting each elementary null
## hypothesis without multiplicity adjustment
print(RABR.fit$ProbUnadj)
##
## Probability of rejecting each elementary null
## hypothesis with multiplicity adjustment
print(RABR.fit$ProbAdj)
##
## Probability of selecting and confirming the
## efficacy of each active treatment group
print(RABR.fit$ProbAdjSelected)
##
## ProbAdjOverall Probability of rejecting at
## least one elementary null hypothesis
## with multiplicity adjustment
print(RABR.fit$ProbAdjOverall)
##
## ASN Average sample size of placebo and active
## treatment groups
print(RABR.fit$ASN)

```

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RABRcontinuous

*Simulate RABR for continuous endpoints to evaluate operating characteristics*


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## Description

Simulate RABR for continuous endpoints to evaluate operating characteristics

## Usage

```

RABRcontinuous(
  MeanVec,
  SdVec,
  M,
  N,
  R,
  Nitt,
  Alpha,

```

```

Ncluster = 1,
Seed = 12345,
MultiMethod
)

```

### Arguments

MeanVec	Vector of response mean for placebo and active treatment groups.
SdVec	Vector of standard deviation for placebo and active treatment groups.
M	Total sample size of burn-in period.
N	Total sample size of RABR. Must be larger than M.
R	Randomization vector for placebo and active treatment groups.
Nitt	Number of simulation iterations.
Alpha	One-sided significance level.
Ncluster	Number of clusters for parallel computing.
Seed	Random seed.
MultiMethod	Multiplicity adjustment method. Must be one of the following values "holm", "hochberg", "hommel", "bonferroni", or "dunnett".

### Details

The MeanVec is a vector of response mean for placebo and active treatment groups, while SdVec is for standard deviation. They should be with the same length. The current package supports 2 or 3 active treatment groups. Note that a larger response corresponds to a better outcome.

The M is the total sample size of burn-in period with equal randomization. The total sample size N should be larger than N. The choice of M can be selected by comparing simulations from several candidate values. The R is a pre-specified randomization vector, where the first element is for placebo, and the next one for the best performing group, up to the worst performing group.

The Alpha is the one-sided significance level. The MultiMethod can be set at "holm" for Holm, "hochberg" for Hochberg, "hommel" for Hommel, "bonferroni" for Bonferroni, or "dunnett" for Dunnett procedures.

### Value

ProbUnadj: Probability of rejecting each elementary null hypothesis without multiplicity adjustment

ProbAdj: Probability of rejecting each elementary null hypothesis with multiplicity adjustment

ProbAdjSelected: Probability of selecting and confirming the efficacy of each active treatment group

ProbAdjOverall: Probability of rejecting at least one elementary null hypothesis with multiplicity adjustment

ASN: Average sample size of placebo and active treatment groups

### Author(s)

Tianyu Zhan (tianyu.zhan.stats@gmail.com)

## References

Zhan, T., Cui, L., Geng, Z., Zhang, L., Gu, Y., & Chan, I. S. (2021). A practical response adaptive block randomization (RABR) design with analytic type I error protection. *Statistics in Medicine*, 40(23), 4947-4960.

Cui, L., Zhan, T., Zhang, L., Geng, Z., Gu, Y., & Chan, I. S. (2021). An automation-based adaptive seamless design for dose selection and confirmation with improved power and efficiency. *Statistical Methods in Medical Research*, 30(4), 1013-1025.

## Examples

```
## Consider an example with three active treatment
## groups and a placebo. Suppose that the response
## mean for placebo is 0.43 and 0.48, 0.63, and 1.2
## for three active treatment groups. The standard
## deviation is 1 for all groups. The total sample
## size is N = 120 with a burn-in period M = 60. We
## use the randomization vector of (8, 9, 2, 1),
## which means that placebo, the best performing
## group, the second-best group, and the worst group
## have randomization probabilities 8/20, 9/20, 2/20
## 1/20, respectively. The one-sided significance
## level is considered at 2.5%. Nitt = 100 is for
## demonstration, and should be increased to 10^5
## in practice.
##
library(parallel)
library(doParallel)
RABR.fit = RABRcontinuous(
  MeanVec = c(0.43, 0.48, 0.63, 1.2),
  SdVec = c(1, 1, 1, 1),
  M = 60,
  N = 120,
  R = c(8, 9, 2, 1),
  Nitt = 100,
  Alpha = 0.025,
  Ncluster = 2,
  Seed = 12345,
  MultiMethod = "dunnett")
##
## Probability of rejecting each elementary null
## hypothesis without multiplicity adjustment
print(RABR.fit$ProbUnadj)
##
## Probability of rejecting each elementary null
## hypothesis with multiplicity adjustment
print(RABR.fit$ProbAdj)
##
## Probability of selecting and confirming the
## efficacy of each active treatment group
print(RABR.fit$ProbAdjSelected)
##
```

```
## ProbAdjOverall Probability of rejecting at
## least one elementary null hypothesis
## with multiplicity adjustment
  print(RABR.fit$ProbAdjOverall)
##
## ASN Average sample size of placebo and active
## treatment groups
  print(RABR.fit$ASN)
```

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