Package 'RABR'

October 12, 2022

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) <doi:10.1002/sim.9104>.

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Encoding UTF-8

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

NeedsCompilation no

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R topics documented:

RABRbinary *Simulate RABR for binary endpoints to evaluate operating characteristics*

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)

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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)
```

RABRcontinuous *Simulate RABR for continuous endpoints to evaluate operating characteristics*

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)

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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)
```

Index