

Package: cobenrich (via r-universe)

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Type Package

Title Using Multiple Continuous Biomarkers for Patient Enrichment in Two-Stage Clinical Designs

Version 1.0.1

Description Enrichment strategies play a critical role in modern clinical trial design, especially as precision medicine advances the focus on patient-specific efficacy. Recent developments in enrichment design have introduced biomarker randomness and accounted for the correlation structure between treatment effect and biomarker, resulting in a two-stage threshold enrichment design. We propose novel two-stage enrichment designs capable of handling two or more continuous biomarkers. See Zhang, F. and Gou, J. (2025). Using multiple biomarkers for patient enrichment in two-stage clinical designs. Technical Report.

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Encoding UTF-8

Depends R (>= 4.2.0)

Imports tmvtnorm (>= 1.2), stats (>= 4.0.0)

RoxygenNote 7.3.2

NeedsCompilation no

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Contents

avetrteff2	2
findATE2	3
findSATE2	4
targetDel	5
targetLam	6
Index	7

avetrteff2	<i>Compute the average subpopulation treatment effect and the standardized average subpopulation treatment effect when two biomarkers are involved</i>
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Description

Compute the average subpopulation treatment effect and the standardized average subpopulation treatment effect when two biomarkers are involved

Usage

```
avetrteff2(z1z2, kappa, rhovec, sigma, muminusmu0)
```

Arguments

z1z2	a numeric vector of two numbers that are standardized biomarker values
kappa	a number of the correlation coefficient between two biomarkers
rhovec	a numeric vector of two correlation coefficients between the output and two biomarkers
sigma	a number of the standard deviation of outcome
muminusmu0	a number of the difference between the mean of outcome and the minimal clinically important treatment effect

Value

a list of three numbers: delta is the average subpopulation treatment effect, lambda is the standardized average subpopulation treatment effect, and cVar is the variance with respect to the truncated distribution with specified cutoff values

Author(s)

Jiangtao Gou

References

Zhang, F. and Gou, J. (2025). Using multiple biomarkers for patient enrichment in two-stage clinical designs. Technical Report.

Examples

```

x1x2 <- c(2, 1)
nu1nu2 <- c(0,0)
tau1tau2 <- c(1,1)
z1z2 <- (x1x2 - nu1nu2)/tau1tau2
muminusmu0 <- 1.8
kappa <- 0.1
sigma <- 1
rhovec <- c(0.1, 0.2)
avetrtteff2(z1z2, kappa, rhovec, sigma, muminusmu0)

```

findATE2

Find the cutoff values of biomarkers based on the average subpopulation treatment effect

Description

Find the cutoff values of biomarkers based on the average subpopulation treatment effect

Usage

```
findATE2(z2interval, kkk, muminusmu0, kappa, rhovec, sigma, cDel)
```

Arguments

z2interval	a numeric vector of two values, including the lower and upper limits of the initial interval for z2
kkk	the researchers' weighting preference between the two biomarkers
muminusmu0	a number of the difference between the mean of outcome and the minimal clinically important treatment effect
kappa	a number of the correlation coefficient between two biomarkers
rhovec	a numeric vector of two correlation coefficients between the output and two biomarkers
sigma	a number of the standard deviation of outcome
cDel	the desired average subpopulation treatment effect

Value

a numeric vector of two values which are the cutoff values for z1 and z2

Author(s)

Jiangtao Gou
Fengqing Zhang

References

Zhang, F. and Gou, J. (2025). Using multiple biomarkers for patient enrichment in two-stage clinical designs. Technical Report.

Examples

```
z2interval <- c(-5, 5)
kkk <- 1
muminusmu0 <- 1.8
kappa <- 0.1
rhovec <- c(0.1, 0.2)
sigma <- 1
cDel <- 2.5
findATE2(z2interval, kkk, muminusmu0, kappa, rhovec, sigma, cDel)
```

findSATE2

Find the cutoff values of biomarkers based on the standardized average subpopulation treatment effect

Description

Find the cutoff values of biomarkers based on the standardized average subpopulation treatment effect

Usage

```
findSATE2(z2interval, kkk, muminusmu0, kappa, rhovec, sigma, cLam)
```

Arguments

z2interval	a numeric vector of two values, including the lower and upper limits of the initial interval for z2
kkk	the researchers' weighting preference between the two biomarkers
muminusmu0	a number of the difference between the mean of outcome and the minimal clinically important treatment effect
kappa	a number of the correlation coefficient between two biomarkers
rhovec	a numeric vector of two correlation coefficients between the output and two biomarkers
sigma	a number of the standard deviation of outcome
cLam	the desired standardized average subpopulation treatment effect

Value

a numeric vector of two values which are the cutoff values for z1 and z2

Author(s)

Jiangtao Gou
Fengqing Zhang

References

Zhang, F. and Gou, J. (2025). Using multiple biomarkers for patient enrichment in two-stage clinical designs. Technical Report.

Examples

```
z2interval <- c(-4, 4)
kkk <- 1
muminusmu0 <- 1.8
kappa <- 0.1
rhoVec <- c(0.1, 0.2)
sigma <- 1
cLam <- 2.5
findSATE2(z2interval, kkk, muminusmu0, kappa, rhoVec, sigma, cLam)
```

targetDel	<i>Find the difference between the average subpopulation treatment effect and the desired one</i>
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Description

Find the difference between the average subpopulation treatment effect and the desired one

Usage

```
targetDel(z2, kkk, muminusmu0, kappa, rhoVec, sigma, cDel)
```

Arguments

z2	the standardized biomarker value of the second biomarker
kkk	the researchers' weighting preference between the two biomarkers
muminusmu0	a number of the difference between the mean of outcome and the minimal clinically important treatment effect
kappa	a number of the correlation coefficient between two biomarkers
rhoVec	a numeric vector of two correlation coefficients between the output and two biomarkers
sigma	a number of the standard deviation of outcome
cDel	the desired average subpopulation treatment effect

Value

the difference between the average subpopulation treatment effect and the desired one

targetLam	<i>Find the difference between the standardized average subpopulation treatment effect and the desired one</i>
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Description

Find the difference between the standardized average subpopulation treatment effect and the desired one

Usage

```
targetLam(z2, kkk, muminusmu0, kappa, rhoVec, sigma, cLam)
```

Arguments

z2	the standardized biomarker value of the second biomarker
kkk	the researchers' weighting preference between the two biomarkers
muminusmu0	a number of the difference between the mean of outcome and the minimal clinically important treatment effect
kappa	a number of the correlation coefficient between two biomarkers
rhoVec	a numeric vector of two correlation coefficients between the output and two biomarkers
sigma	a number of the standard deviation of outcome
cLam	the desired standardized average subpopulation treatment effect

Value

the difference between the standardized average subpopulation treatment effect and the desired one

Index

avetrteff2, 2

findATE2, 3

findSATE2, 4

targetDel, 5

targetLam, 6