Package 'ph2hetero'

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Type Package

Title Stratified Adaptive Designs for Two-Stage Phase II Studies

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Description Implementation of Jones (2007) <doi:10.1016/j.cct.2007.02.008> , Tournoux-Facon (2011) <doi:10.1002/sim.4148> and Parashar (2016) <doi:10.1002/pst.1742> designs.

Depends mvtnorm, clinfun, R (>= 3.0.3)

License GPL

SystemRequirements GNU make

LazyLoad yes

Author Patrick Sfumato [aut, cre],
Thomas Filleron [aut],
Bastien Cabarrou [aut],
Andrew D. Martin [cph],
Kevin M. Quinn [cph],
Daniel Pemstein [cph],
Ross Ihaka [cph],
The R Development Core Team [cph],
The R Foundation [cph],
Pierre L'Ecuyer [cph],
Makoto Matsumoto [cph],
Takuji Nishimura [cph]

Maintainer Patrick Sfumato <sfumatop@gmail.com>

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`design.jones` *Jones 2-stage Phase II design*

Description

Calculates Optimal 2-stage Phase II designs given by Cheryl L. Jones (2007).

Usage

```
design.jones(alpha=0.05,beta=0.2,p0,p1n,p1p,Nmax=100,Ppos=0.5,NumThreads=1)
```

Arguments

`alpha`	Type I error.
`beta`	Type II error.
`p0`	Max unacceptable response rate.
`p1n`	Min acceptable response rate for "negative" subgroup.
`p1p`	Min acceptable response rate for "positive" subgroup.
`Nmax`	Maximum sample size.
`Ppos`	Prevalence of "biomarker-positive" subjects.
`NumThreads`	Number of threads used for parallel compilation.

Value

Returns a data.frame object which components are :

`alpha`	Type I error probability of the optimal design.
`power`	Power of the optimal design.
`p0`	Max unacceptable response rate.
`p1n`	Min acceptable response rate for "negative" subgroup.
`p1p`	Min acceptable response rate for "positive" subgroup.
`PET`	Overall probability of early termination.
`EN`	Expected sample size.
`k1n`	Minimum number of responses in marker negative subjects to go into the unselected population during stage 2.
`k1p`	Minimum number of responses in the marker positive subjects.
`N1n`	Number of marker negative subjects enrolled during the first stage.
`N1p`	Number of marker positive subjects enrolled during the first stage.
`k2p`	Total number of response required during stage 1 and stage 2 combined in the amplified when preliminary efficacity is in the amplified subgroup.

N2p	Number of amplified subjects enrolled during the second stage if preliminary evidence of efficacy leads to this path.
kn	Total number of response required during stage 1 and stage 2 combined in the negative sample to conclude efficacy in the unselected population.
kp	Total number of response required during stage 1 and stage 2 combined in the amplified sample to conclude efficacy in this population when preliminary efficacy is unselected.
N2un	Number of unselected subjects enrolled during the second stage if preliminary evidence of efficacy leads to this path.

Author(s)

Patrick Sfumato and Bastien Cabarrou.

References

Jones CL, Holmgren E (2007).*An adaptive Simon Two-Stage Design for Phase 2 studies of targeted therapies.* Contemporary Clinical Trials 28 654-661.

Examples

```
out.jones<-design.jones(alpha=0.05,
                        beta=0.2,
                        p0=0.03,
                        p1n=0.10,
                        p1p=0.15,
                        Nmax=150,
                        Ppos=0.40)
```

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design.parashar *Parashar's 2-stage Phase II design*

Description

Calculates Optimal 2-stage Phase II designs given by Deepak Parashar (2016).

Usage

```
design.parashar(alpha=0.05,beta=0.2,p0,p1n,p1p,Nmax=100,NumThreads=1)
```

Arguments

alpha	Type I error.
beta	Type II error.
p0	Max unacceptable response rate.
p1n	Min acceptable response rate for "negative" subgroup.

p1p	Min acceptable response rate for "positive" subgroup.
Nmax	Maximum sample size.
NumThreads	Number of threads used for parallel compilation.

Value

Returns a data.frame object which components are :

alpha	Type I error probability of the optimal design.
power	Power of the optimal design.
p0	Max unacceptable response rate.
p1n	Min acceptable response rate for "negative" subgroup.
p1p	Min acceptable response rate for "positive" subgroup.
PET	Overall probability of early termination.
EN	Expected sample size.
k1n	Minimum number of responses in marker negative subjects to go into the unselected population during stage 2.
k1p	Minimum number of responses in the marker positive subjects.
N1n	Number of marker negative subjects enrolled during the first stage.
N1p	Number of marker positive subjects enrolled during the first stage.
kep	Minimum number of responses in the enrichment population.
Nep	Number of subjects in the enrichment population.
kn	Total number of response required during stage 1 and stage 2 combined in the negative sample to conclude efficacy in the unselected population.
kp	Total number of response required during stage 1 and stage 2 combined in the amplified sample to conclude efficacy in this population when preliminary efficacy is unselected.
Nn	Number of marker negative subjects enrolled during the first stage and the second stage.
N2p	Number of marker positive subjects enrolled during the first stage and the second stage.

Author(s)

Patrick Sfumato and Bastien Cabarrou.

References

Parashar D, Bowden J, Starr C, Wernisch L and Mander A (2016).*An optimal stratified Simon two-stage design.* Pharmaceutical statistics 15(4) 333-40.

Examples

```
out.parashar<-design.parashar(alpha=0.05,
                              beta=0.2,
                              p0=0.03,
                              p1n=0.25,
                              p1p=0.40,
                              Nmax=30)
```

`design.tournoux` *Tournoux 2-stage Phase II design*

Description

Calculates Optimal 2-stage Phase II designs given by Caroline Tournoux-Facon (2011).

Usage

```
design.tournoux(alpha=0.05,beta=0.2,p0n,p0p,p1n,p1p,w=1,gamma=0.6)
```

Arguments

`alpha`	Type I error.
`beta`	Type II error.
`p0n`	Max unacceptable response rate for "negative" subgroup.
`p0p`	Max unacceptable response rate for "positive" subgroup.
`p1n`	Min acceptable response rate for "negative" subgroup.
`p1p`	Min acceptable response rate for "positive" subgroup.
`w`	Ratio between the two subgroups $\frac{N_{pos}}{N_{neg}}$.
`gamma`	Level of the heterogeneity test.

Value

Returns a data.frame object which components are number of patients, error-rates and power-levels for each stage. The first line of the data.frame corresponds to the arguments for an One-stage Fleming design and the others are two-stages Fleming designs with :

- Non-stratified heterogeneous Fleming two-stage design when psi=0.

- Stratified adaptive Fleming two-stage with identification of heterogeneity of responses in favour of "negative" subgroup when psi=1.

- Stratified adaptive Fleming two-stage with identification of heterogeneity of responses in favour of "positive" subgroup when psi=2.

Author(s)

Patrick Sfumato and Bastien Cabarrou.

References

Tournoux-Facon C, De Rycke Y and Tubert-Bitter P (2011).*Targeting population entering phase III trials: A new stratified adaptive phase II design.* Statistics in Medecine 30(8) 801-11.

Tournoux-Facon C, De Rycke Y and Tubert-Bitter P (2011).*How a new stratified adaptive phase II design could improve targeting population.* Statistics in Medecine 30(13) 1555-62.

Examples

```
out.tournoux<-design.tournoux(p0n=0.15,
                              p0p=0.15,
                              p1n=0.30,
                              p1p=0.25,
                              w=2,
                              gamma=0.6,
                              alpha=0.05,
                              beta=0.1)
```

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