Package 'ph2bye'

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Type Package

Title Phase II Clinical Trial Design Using Bayesian Methods

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Description Calculate the Bayesian posterior/predictive probability and
determine the sample size and stopping boundaries for single-arm Phase II design.

License GPL (>= 2)

LazyData TRUE

Depends stats,
graphics,
animation

Imports base,
ph2bayes,
VGAM

Suggests clinfun,
gsDesign,
survival,
testthat

RoxygenNote 5.0.1

R topics documented:

bayes.design *Bayesian design method for sequentially monitoring patients using Beta-Binomial posterior probability based on observing data*

Description

Make animation plots to present sequential monitor stopping rule using Beta-Binomial Bayesian model

Usage

```
bayes.design(a,b,r=0, stop.rule="futility", add.size=5, alpha=0.05,
p0 ,delta=0.2,tau1=0.9,tau2=0.9,tau3=0.9,tau4=0.9, time.interval =1)
```

Arguments

a	the hyperparameter (shape1) of the Beta prior for the experimental drug.
b	the hyperparameter (shape2) of the Beta prior for the experimental drug.
r	the maximum number of patients treated by the experimental drug.
stop.rule	the hyperparameter (shape1) of the Beta prior for the experimental drug.
add.size	a single integer value, random number generator (RNG) state for random number generation.
alpha	the siginificant level to determine the credible interval, set 0.05 by default.
p0	the prespecified reseponse rate.
delta	the minimally acceptable increment of the response rate.
tau1	threshold for stopping rule 1.
tau2	threshold for stopping rule 2.
tau3	threshold for stopping rule 3.
tau4	threshold for stopping rule 4.
time.interval	a positive number to set the time interval of the animation (unit in seconds); default to be 1.

Value

animation plot of determination of stopping boundaries.

References

Yin, G. (2012). *Clinical Trial Design: Bayesian and Frequentist Adaptive Methods.* New York: Wiley.

Examples

```
# Using Multiple Myeloma (MM) data example
MM.r = rep(0,12); MM.mean = 0.1; MM.var = 0.0225
a <- MM.mean^2*(1-MM.mean)/MM.var - MM.mean; b <- MM.mean*(1-MM.mean)^2/MM.var - (1-MM.mean)
bayes.design(a=a,b=b,r=MM.r,stop.rule="futility",p0=0.1)

# Using Acute Promyelocytic Leukaemia (APL) data example
APL.r <- c(0,1,0,0,1,1,1,1,0,1,1,1,0,1,1,1,1,1,1); APL.mean = 0.3; APL.var = 0.0191
a <- APL.mean^2*(1-APL.mean)/APL.var - APL.mean; b <- APL.mean*(1-APL.mean)^2/APL.var - (1-APL.mean)
bayes.design(a=a,b=b,r=APL.r,stop.rule="efficacy",p0=0.1)
```

`BB.aniplot` *Sequentially monitor patients using Beta-Binomial posterior probability*

Description

Make animation plots to present sequential monitor the patients using Beta-Binomial Bayesian model

Usage

```
BB.aniplot(a, b, r, N=1, alpha=0.05, seed=1234, time.interval=1, output=TRUE)
```

Arguments

`a`	the hyperparameter (shape1) of the Beta prior for the experimental drug.
`b`	the hyperparameter (shape2) of the Beta prior for the experimental drug.
`r`	vector of number of response in each cohort, the value of each element should not exceed N
`N`	the number of patients treated by the experimental drug at a certain stage of the trial.
`alpha`	the siginificant level to determine the credible interval, set 0.05 by default.
`seed`	a single integer value, random number generator (RNG) state for random number generation.
`time.interval`	a positive number to set the time interval of the animation (unit in seconds); default to be 1.
`output`	a logical value, whether to output the inference results of posterior distribution and mean, observed data and credible interval.

Value

animation plot of updating posterior as prior, and output the inference information of prior and posterior distribution if `output=TRUE`.

References

Yin, G. (2012). *Clinical Trial Design: Bayesian and Frequentist Adaptive Methods.* New York: Wiley.

Examples

```
# Using APL data
r=rep(0,12)
BB.aniplot(a=1,b=1,r=r, alpha=0.05, seed=1234)
# Simulate binomial data
B <- 50; N=1; p=0.3
r <- rbinom(n = B,size = N,prob = p)
BB.aniplot(a=1,b=1,r=r,time.interval = 0.2,output = FALSE)
```

`MultPostP` *The posterior probability criterion function for Phase II single-arm design*

Description

Thall, Simon and Estey's criterion function for determining the trial decision boundaries for efficacy (futility) and safety (toxicity).

Usage

```
MultPostP(x, n, a.vec, p0)
```

Arguments

`x`	the value of observed data. It can be $x_E = y_{ET} + y_{ET^C}$ i.e. number of responses for efficacy among n patients treated by the experimental drug, or $x_T = y_{ET} + y_{E^CT}$ i.e. number of responses for toxicity among n patients treated by the experimental drug, where $y = (y_{ET}, y_{E^CT}, y_{ET^C}, y_{E^CT^C})$, that is, among n patients treated by the experimental drug, y_{ET} of them have experienced both toxicity and efficacy, y_{E^CT} have experienced toxicity only, y_{ET^C} have experienced efficacy only, $y_{E^CT^C}$ have neither experienced toxicity nor efficacy.
`n`	the number of patients treated by the experimental drug at a certain stage of the trial.
`a.vec`	the hyperparameter vector of the Dirichlet prior for the experimental drug.
`p0`	the prespecified reseponse rate for efficacy, futility or toxicity.

Value

`prob`	the posterior probability: $Pr(p_E > p_0 \mid X = x_E)$ or $Pr(p_T > p_0 \mid X = x_T)$

References

Berry, S. M., Carlin, B. P., Lee, J. J., & Muller, P. (2010). *Bayesian adaptive methods for clinical trials.* CRC press.

Thall, Peter F., Richard M. Simon, and Elihu H. Estey. (1995). *Bayesian sequential monitoring designs for single-arm clinical trials with multiple outcomes. Statistics in medicine* **14.4**: 357-379.

Yin, G. (2013). *Clinical Trial Design: Bayesian and Frequentist Adaptive Methods.* New York: Wiley.

Examples

```
n <- 30; x.eff <- 5; x.tox <- 8; param <- c(1,1,1,1); p0.eff <- 0.9; p0.tox <- 0.95
MultPostP(x=x.eff, n=n, a.vec=param, p0=p0.eff)
MultPostP(x=x.tox, n=n, a.vec=param, p0=p0.tox)
```

MultPostP.design *The stopping boundaries based on the multiple outcomes criterion*

Description

The design function to sequentially monitor sample size and boundary based on Thall, Simon and Estey's criterion.

Usage

```
MultPostP.design(type, nmax, a.vec, p0, delta, theta)
```

Arguments

type	type of boundaries: "efficacy" or "futility" or "toxicity".
nmax	the maximum number of patients treated by the experimental drug.
a.vec	the hyperparameter vector of the Dirichlet prior for the experimental drug.
p0	the prespecified reseponse rate for efficacy or toxicity.
delta	the minimally acceptable increment of the response rate for the experimental drug compared with the pre-specific rate.
theta	the cutoff probability: typically, $\theta = [0.9, 0.99]$ for efficacy, $\theta = [0.01, 0.1]$ for futility, and $\theta = [0.95, 1]$ for toxicity.

Value

boundset	the boundaries set: U_n or L_n for the experimental drug efficacy or futility; T_n for the experimental drug toxicity.

References

Thall, Peter F., Richard M. Simon, and Elihu H. Estey. (1995). *Bayesian sequential monitoring designs for single-arm clinical trials with multiple outcomes. Statistics in medicine* **14.4**: 357-379.

Yin, G. (2012). *Clinical Trial Design: Bayesian and Frequentist Adaptive Methods.* New York: Wiley.

Examples

```
## Using vague prior Unif(0,1)
MultPostP.design(type="futility",nmax = 30,a.vec = c(1,1,1,1),p0 = 0.15, theta = 0.05)
MultPostP.design(type="efficacy",nmax = 30,a.vec = c(1,1,1,1),p0 = 0.15, theta = 0.9)
MultPostP.design(type="toxicity",nmax = 30,a.vec = c(1,1,1,1),p0 = 0.15, theta = 0.95)
```

ph2bye *ph2bye: A package for Phase II single-arm Bayesian design.*

Description

The ph2bye package provides two categories of important functions: PostP.design and PredP.design.

Posterior probability criterion functions

The posterior probability criterion functions include PostP and PostP.design functions.

Predictive probability criterion functions

The predictive probability criterion functions include PredP and PredP.design functions.

Author(s)

Yalin Zhu <yalin.zhu@outlook.com>

PostP *The posterior probability criterion function for Phase II single-arm design*

Description

Thall and Simon's criterion function for determining the trial decision boundaries based on the posterior probability.

Usage

```
PostP(x, n, a, b, p0)
```

Arguments

x	the number of responses among n patients treated by the experimental drug.
n	the number of patients treated by the experimental drug.
a	the hyperparameter (shape1) of the Beta prior for the experimental drug.
b	the hyperparameter (shape2) of the Beta prior for the experimental drug.
p0	the prespecified reseponse rate.

Value

prob	the posterior probability: $Pr(p > p_0 \mid X = x)$

References

Berry, S. M., Carlin, B. P., Lee, J. J., & Muller, P. (2010). *Bayesian adaptive methods for clinical trials.* CRC press.

Thall, P. F., Simon, R. (1994). Practical Bayesian guidelines for phase IIB clinical trials. *Biometrics* **50**: 337-349.

Yin, G. (2013). *Clinical Trial Design: Bayesian and Frequentist Adaptive Methods.* New York: Wiley.

Examples

```
PostP(8,15,1,1,0.8)
```

`PostP.design` *The stopping boundaries based on the posterior probability criterion*

Description

The design function to sequentially monitor sample size and boundary based on Thall and Simon's criterion.

Usage

```
PostP.design(type, nmax, a, b, p0, delta, theta)
```

Arguments

`type`	type of boundaries: "efficacy" or "futility".
`nmax`	the maximum number of patients treated by the experimental drug.
`a`	the hyperparameter (shape1) of the Beta prior for the experimental drug.
`b`	the hyperparameter (shape2) of the Beta prior for the experimental drug.
`p0`	the pre-specified reseponse rate.
`delta`	the minimally acceptable increment of the response rate for the experimental drug compared with the standard drug.
`theta`	the cutoff probability: typically, $\theta = [0.9, 0.99]$ for efficacy, $\theta = [0.01, 0.1]$ for futility.

Value

`boundset`	the boundaries set; U_n or L_n

References

Thall, P. F., Simon, R. (1994). Practical Bayesian guidelines for phase IIB clinical trials. *Biometrics* **50**: 337-349.

Yin, G. (2012). *Clinical Trial Design: Bayesian and Frequentist Adaptive Methods.* New York: Wiley.

Examples

```
## Using vague prior Unif(0,1)
PostP.design(type = "futility", nmax=100, a=1, b=1, p0=0.15, delta=0.15, theta=0.05)
PostP.design(type = "efficacy", nmax=100, a=1, b=1, p0=0.15, delta=0.15, theta=0.9)
## Or using Jeffery prior with Beta(0.5,0.5)
PostP.design(type = "futility", nmax=100, a=0.5, b=0.5, p0=0.15, delta=0.15, theta=0.05)
PostP.design(type = "efficacy", nmax=100, a=0.5, b=0.5, p0=0.15, delta=0.15, theta=0.9)
```

PredP *The predictive probability criterion function for Phase II single-arm design*

Description

Lee and Liu's criterion function for determining the trial decision cutoffs based on the predictive probability.

Usage

```
PredP(x, n, nmax, a, b, p0, theta_t)
```

Arguments

x	the number of responses among n patients treated by the experimental drug at a certain stage of the trial.
n	the number of patients treated by the experimental drug at a certain stage of the trial.
nmax	the maximum number of patients treated by the experimental drug.
a	the hyperparameter (shape1) of the Beta prior for the experimental drug.
b	the hyperparameter (shape2) of the Beta prior for the experimental drug.
p0	the the response rate for the standard drug.
theta_t	the prespecified target probability; tipically, $\theta_T = [0.85, 0.95]$.

Value

prob	the predictive probability: $PP = \sum_{y=0}^{n_{max}-n} Pr(Y = y\|x) I(\Pr(p > p_0\|Y = y, x) \geq \theta_T)$

References

Lee, J. J., Liu, D. D. (2008). A predictive probability design for phase II cancer clinical trials. *Clinical Trials* **5**: 93-106.

Yin, G. (2012). *Clinical Trial Design: Bayesian and Frequentist Adaptive Methods.* New York: Wiley.

Examples

```
# Using vague prior Uniform(0,1), i.e. Beta(1,1)
PredP(16, 23, 40, 1, 1, 0.15, 0.9)
```

PredP.design *The stopping boundaries based on the predictive probability criterion*

Description

The design function to sequentially monitor sample size and boundary based on Lee and Liu's criterion.

Usage

```
PredP.design(type, nmax, a, b, p0, theta_t, delta, theta)
```

Arguments

type	type of boundaries: "efficacy" or "futility".
nmax	the maximum number of patients treated by the experimental drug.
a	the hyperparameter (shape1) of the Beta prior for the experimental drug.
b	the hyperparameter (shape2) of the Beta prior for the experimental drug.
p0	the the response rate for the standard drug.
theta_t	the prespecified target probability; tipically, $\theta_T = [0.85, 0.95]$. Set 0.9 by default.
delta	the minimally acceptable increment of the response rate for the experimental drug compared with the standard drug
theta	the cutoff probability: typically, $\theta = [0.9, 0.99]$ for efficacy, $\theta = [0.01, 0.1]$ for futility.

Value

boundset	the boundaries set: U_n or L_n

References

Lee, J. J., Liu, D. D. (2008). A predictive probability design for phase II cancer clinical trials. *Clinical Trials* **5**: 93-106.

Yin, G. (2012). *Clinical Trial Design: Bayesian and Frequentist Adaptive Methods.* New York: Wiley.

Examples

```
PredP.design(type = "futility", nmax=40, a=1, b=1, p0=0.15, delta=0.15, theta=0.05)
PredP.design(type = "efficacy", nmax=40, a=1, b=1, p0=0.15, delta=0.15, theta=0.9)
```

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