Package ‘ph2bye’

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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.
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The ph2bye package provides three categories of important functions: PostP.design, PredP.design and MultPostP.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.

Posterior probability criterion function for multiple outcomes
The posterior probability criterion functions include MultPostP and MultPostP.design functions.

Whole design function with double thresholds showing futility and efficacy boundary together
The criterion function DT.design.

Prior calculation function
The function prior calculating Beta prior parameters according to different prior information.

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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 significant level to determine the credible interval, set 0.05 by default.
p0  the prespecified response 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


Examples

# Using Multiple Myeloma (MM) data example
MM.r = rep(0,6); 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(0,1,0,1,1); 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 significant 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


Examples

# Using APL data
r=rep(0,6)
BB.aniplot(a=1,b=1,r=r, alpha=0.05, seed=1234)
# Simulate binomial data
B <- 10; N=1; p=0.3
DT.design

r <- rbinom(n = N, size = N, prob = p)
BB aniplot(a=1,b=1,r=r,time.interval = 0.2,output = FALSE)

DT.design
The whole design with double thresholds showing futility and efficacy boundary together

Description
The design function to sequentially monitor sample size and stopping boundary for both futility and efficacy

Usage
DT.design(type, a, b, nmin, nmax, p0, p1, theta0, theta1, theta_t, optimize)

Arguments
- type: type of stopping criterion: "PostP" or "PredP".
- a: the hyperparameter (shape1) of the Beta prior for the experimental drug.
- b: the hyperparameter (shape2) of the Beta prior for the experimental drug.
- nmin: the minimum number of patients treated by the experimental drug.
- nmax: the maximum number of patients treated by the experimental drug.
- p0: the pre-specified response rate.
- p1: the pre-specified response rate.
- theta0: the cutoff probability for futility: typically, \( \theta_0 = [0.01, 0.1] \).
- theta1: the cutoff probability for efficacy: typically, \( \theta_1 = [0.9, 0.99] \).
- theta_t: the cutoff probability for efficacy including future patients; typically, \( \theta_T = [0.85, 0.95] \). Set 0.9 by default.
- optimize: logical value, if optimize=TRUE, then only output the minimal sample size for the same number of futility and efficacy boundaries.

Value
- boundsets: the boundaries sets: \( U_n \) and \( L_n \)

References


Examples

```r
## Using vague prior Unif(0,1), sequential monitor
DT.design(type = "PostP", a=1, b=1, nmin=20, nmax=60, p0=0.4, p1=0.3, theta0 = 0.05, theta1 = 0.9)
DT.design(type = "PredP", a=1, b=1, nmin=20, nmax=60, p0=0.4, p1=0.3, theta0 = 0.05, theta1 = 0.9, theta_t = 0.9)
## Or using Jeffery prior with Beta(0.5,0.5), multi-stage monitor when sample size is
## 10, 20, ... , 80
DT.design(type = "PostP", a=0.5, b=0.5, nmin=1, nmax=85, p0=0.3, p1=0.3, theta0 = 0.05, theta1 = 0.9)[(1:8)*10,]
DT.design(type = "PredP", a=0.5, b=0.5, nmin=1, nmax=85, p0=0.3, p1=0.3, theta0 = 0.05, theta1 = 0.9, theta_t = 0.9)[(1:8)*10,]
```

---

**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**

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

**Arguments**

- `x`: the value of observed data. It can be \( x_E = y_{ET} + y_{EC_T} \) i.e. number of responses for efficacy among \( n \) patients treated by the experimental drug, or \( x_T = y_{ET} + y_{E_T C} \) i.e. number of responses for toxicity among \( n \) patients treated by the experimental drug, where \( y = (y_{ET}, y_{ECT}, y_{ETC}, y_{ECTC}) \), that is, among \( n \) patients treated by the experimental drug, \( y_{ET} \) of them have experienced both toxicity and efficacy, \( y_{ECT} \) have experienced toxicity only, \( y_{ETC} \) have experienced efficacy only, \( y_{ECTC} \) have neither experienced toxicity nor efficacy.

- `n`: the number of patients treated by the experimental drug at a certain stage of the trial.


- `p0`: the prespecified response rate for efficacy, futility or toxicity.

**Value**

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


Examples
```r
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, theta, optimize)
```

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 response rate for efficacy or toxicity.
- **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.
- **optimize** logical value, if optimize=TRUE, then only output the minimal sample size for the same number of futility boundaries and maximal sample size for the same number efficacy boundaries.

Value
- **boundset** the boundaries set: \( U_n \) or \( L_n \) for the experimental drug efficacy or futility; \( T_n \) for the experimental drug toxicity.
**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 response rate.

**Value**

- `prob`: the posterior probability: \( P_r(p > p_0 | X = x) \)

**References**


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, theta, optimize)

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.
theta the cutoff probability: typically, \( \theta = [0.9, 0.99] \) for efficacy, \( \theta = [0.01, 0.1] \) for futility.
optimize logical value, if optimize=TRUE, then only output the minimal sample size for the same number of futility and efficacy boundaries.

Value

boundset the boundaries set: \( U_n \) or \( L_n \)

References


Examples

```r
# Using vague prior Unif(0,1)
PostP.design(type = "futility", nmax=100, a=1, b=1, p0=0.3, theta=0.05)
PostP.design(type = "efficacy", nmax=100, a=1, b=1, p0=0.3, 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=0.3, theta=0.05)
PostP.design(type = "efficacy", nmax=100, a=0.5, b=0.5, p0=0.3, theta=0.9)
```
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**

\[
\text{PredP}(x, n, n_{\text{max}}, a, b, p_0, \theta_{T})
\]

**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.
- \(n_{\text{max}}\): 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.
- \(p_0\): the response rate for the standard drug.
- \(\theta_{T}\): the cutoff probability for efficacy including future patients; typically, \(\theta_T = [0.85, 0.95]\). Set 0.9 by default.

**Value**

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

**References**


**Examples**

```r
# Using vague prior Uniform(0,1), i.e. Beta(1,1)
PredP(16, 23, 40, 1, 1, 0.5, 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**

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

**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 response rate for the standard drug.
- `theta_t`: the cutoff probability for efficacy including future patients; typically, \( \theta_T = [0.85, 0.95] \). Set 0.9 by default.
- `theta`: the cutoff probability: typically, \( \theta = [0.9, 0.99] \) for efficacy, \( \theta = [0.01, 0.1] \) for futility.
- `optimize`: logical value, if `optimize=TRUE`, then only output the minimal sample size for the same number of futility and efficacy boundaries.

**Value**

- `boundset`: the boundaries set: \( U_n \) or \( L_n \)

**References**


**Examples**

```r
PredP.design(type = "futility", nmax=40, a=1, b=1, p0=0.3, theta=0.05)
PredP.design(type = "efficacy", nmax=40, a=1, b=1, p0=0.3, theta=0.9)
```
Description

The prior function to calculate the Beta prior parameters

Usage

\texttt{prior(type, mu, v, N, W, init)}

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>\texttt{type}</td>
<td>type of prior information: &quot;MeanVar&quot; uses mean and variance, &quot;Optimist&quot; uses (ORR) mean, &quot;ORRN&quot; uses ORR and sample size, &quot;ORRW&quot; uses ORR and CI width.</td>
</tr>
<tr>
<td>\texttt{mu}</td>
<td>prior(ORR) mean.</td>
</tr>
<tr>
<td>\texttt{v}</td>
<td>prior variance</td>
</tr>
<tr>
<td>\texttt{N}</td>
<td>prior sample size.</td>
</tr>
<tr>
<td>\texttt{W}</td>
<td>prior confidence interval width.</td>
</tr>
<tr>
<td>\texttt{init}</td>
<td>initial value to solve the nonlinear equations for &quot;ORRW&quot; type.</td>
</tr>
</tbody>
</table>

Value

the vector of Beta parameters: \(a\) and \(b\)

References


Examples

\texttt{prior(type = "MeanVar", mu=0.2, v=0.025)}
\texttt{prior(type = "Optimist", mu = 0.2)}
\texttt{prior(type = "ORRN", mu = 0.2, N = 10)}
\texttt{prior(type = "ORRW", mu = 0.2, W = 0.5)}
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