Package 'earlygating'

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Type Package

Title Properties of Bayesian Early Gating Designs

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Description Computes the most important properties of four 'Bayesian' early gating designs (two single arm and two randomized controlled designs), such as minimum required number of successes in the experimental group to make a GO decision, operating characteristics and average operating characteristics with respect to the sample size.
These might aid in deciding what design to use for the early phase trial.

Depends R (>= 3.3.0)

License GPL-3

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Contents

avg_oc_wr_ne *Single Arm Average Operating Characteristics*

Description

Function for calculating the average operating characteristics of two single arm bayesian designs for early gating with respect to the sample size in the experimental group and possible historical data.

Usage

```
avg_oc_wr_ne(
  N_e,
  true_RR_c = NULL,
  delta,
  delta_power,
  confidence,
  e_a = 0.5,
  e_b = 0.5,
  h_a = 0.5,
  h_b = 0.5,
  RR_h = NULL,
  N_h = NULL,
  hist_RR_c = NULL,
  alpha_c,
  beta_c,
  trues = seq(0, 1, 0.001),
  adapt = 1,
  plot = T,
  coresnum = NULL,
  legend = T,
  legend.pos = "topleft"
)
```

Arguments

N_e	Sample Size in the experimental group. Can be either a single value or a vector.
true_RR_c	Default value is NULL. If specified, will be used in the generated plots, indicating the true achieved decision power and decision type 1 error. If not specified, will be set to either RR_h or hist_RR_c, depending on which was specified by the user.
delta	Required superiority to make a "GO" decision. Corresponds to δ.
delta_power	Superiority, at which decision power will be evaluated. Corresponds to $\bar{\delta}$.
confidence	Required confidence to make "GO" decision. Corresponds to γ.
e_a	Alpha parameter of Beta Prior Distribution for the experimental response rate. Corresponds to α_e. Default is $\frac{1}{2}$.

e_b	Beta parameter of Beta Prior Distribution for the experimental response rate. Corresponds to β_e. Default is $\frac{1}{2}$.
h_a	Alpha parameter of Beta Prior Distribution for the historical control response rate. Corresponds to α_h. Only needs to be specified, if RR_h and N_h are also specified. Default is $\frac{1}{2}$.
h_b	Beta parameter of Beta Prior Distribution for the historical control response rate. Corresponds to β_h. Only needs to be specified, if RR_h and N_h are also specified. Default is $\frac{1}{2}$.
RR_h	Historical control response rate. Corresponds to p_h. If specified together with N_h, function will use setting 2 from pdf.
N_h	Historical control sample size. Corresponds to n_h. If specified together with RR_h, function will use setting 2 from pdf.
hist_RR_c	Point estimate of historical control repsonse rate. Corresponds to $\hat{p_h}$. If specified, while RR_h and N_h are not specified, function will use setting 1 from pdf.
alpha_c	Alpha parameter of Beta Distribution for the control response rate used to calculate average operating characteristics. Corresponds to α_c.
beta_c	Beta parameter of Beta Distribution for the control response rate used to calculate average operating characteristics. Corresponds to β_c.
trues	Sequence of true control response rates and experimental response rates, at which the Probability to Go will be computed. Default is seq(0,1,0.01) to ensure continuous plots and accurate results.
adapt	Level of adapting of experimental control rate to account for patient selection bias from phase II to phase III. Corresponds to ξ. Default is 1, so no adapting.
plot	Plots yes or no. Default is TRUE.
coresnum	Number of cores used for parallel computing, in case N_e is a vector. Default is the number of total cores - 1.
legend	Logical; whether or not to include legend in plot. Default is TRUE.
legend.pos	Position of legend. Default is "topleft".

Value

Either a vector containing the average decision power and average alpha (if N_e has length 1), or a matrix containing the average decision power and average decision alpha (if N_e has length > 1), where every row corresponds to one value of N_e.

Examples

```
# Setting 1
avg_oc_wr_ne(
  N_e = 50, delta = 0.08, delta_power = 0.13,
  confidence = 0.6, hist_RR_c = 0.5,
  alpha_c = 15, beta_c = 13
)

# Setting 2
```

```
avg_oc_wr_ne(
  N_e = 50, delta = 0.08, delta_power = 0.13,
  confidence = 0.6, RR_h = 0.5, N_h = 50,
  alpha_c = 15, beta_c = 13
)
```

`avg_oc_wr_ne_rct` *RCT Average Operating Characteristics*

Description

Function for calculating the average operating characteristics of two RCT bayesian designs for early gating with respect to the sample size in the experimental group, the sample size in the control group and possible historical data.

Usage

```
avg_oc_wr_ne_rct(
  N_c,
  N_e,
  delta,
  delta_power,
  confidence,
  e_a = 0.5,
  e_b = 0.5,
  c_a = 0.5,
  c_b = 0.5,
  h_a = 0.5,
  h_b = 0.5,
  N_h = NULL,
  RR_h = NULL,
  w = NULL,
  alpha_c,
  beta_c,
  trues = seq(0, 1, 0.01),
  plot = T,
  coresnum = NULL,
  legend = T,
  legend.pos = "topleft"
)
```

Arguments

`N_c`	Sample Size in the control group. Can be either a single value or a vector, but needs to be the same length as N_e.
`N_e`	Sample Size in the experimental group. Can be either a single value or a vector, but needs to be the same length as N_c.

delta	Required superiority to make a "GO" decision. Corresponds to δ.
delta_power	Superiority, at which decision power will be evaluated. Corresponds to $\bar{\delta}$.
confidence	Required confidence to make "GO" decision. Corresponds to γ.
e_a	Alpha parameter of Beta Prior Distribution for the experimental response rate. Corresponds to α_e. Default is $\frac{1}{2}$.
e_b	Beta parameter of Beta Prior Distribution for the experimental response rate. Corresponds to β_e. Default is $\frac{1}{2}$.
c_a	Alpha parameter of Beta Prior Distribution for the control response rate. Corresponds to α_c. Default is $\frac{1}{2}$.
c_b	Beta parameter of Beta Prior Distribution for the control response rate. Corresponds to β_c. Default is $\frac{1}{2}$.
h_a	Alpha parameter of Beta Prior Distribution for the historical control response rate. Corresponds to α_h. Only needs to be specified, if RR_h, N_h and w are also specified. Default is $\frac{1}{2}$.
h_b	Beta parameter of Beta Prior Distribution for the historical control response rate. Corresponds to β_h. Only needs to be specified, if RR_h, N_h and w are also specified. Default is $\frac{1}{2}$.
N_h	Historical control sample size. Corresponds to n_h. If specified together with RR_h and w, function will use setting 4 from pdf.
RR_h	Historical control response rate. Corresponds to p_h. If specified together with N_h and w, function will use setting 4 from pdf.
w	Level of dynmaic borrowing. Corresponds to w.
alpha_c	Alpha parameter of Beta Distribution for the control response rate used to calculate average operating characteristics. Corresponds to α_c.
beta_c	Beta parameter of Beta Distribution for the control response rate used to calculate average operating characteristics. Corresponds to β_c.
trues	Sequence of true control response rates and experimental response rates, at which the Probability to Go will be computed. Default is seq(0,1,0.01) to ensure continuous plots and accurate results.
plot	Plots yes or no. Default is TRUE.
coresnum	Number of cores used for parallel computing, in case N_e is a vector. Default is the number of total cores - 1.
legend	Logical; whether or not to include legend in plot. Default is TRUE.
legend.pos	Position of legend. Default is "topleft".

Value

Either a vector containing the average decision power and average alpha (if N_e has length 1) or a matrix containing the average decision power and average decision alpha (if N_e has length > 1), where every row corresponds to one value of N_e.

Examples

```
# Setting 3
avg_oc_wr_ne_rct(
N_c = 25, N_e = 25, delta = 0.08,
delta_power = 0.13, confidence = 0.6,
alpha_c = 15, beta_c = 13
)



# Setting 4
avg_oc_wr_ne_rct(
N_c = 25, N_e = 25, delta = 0.08,
delta_power = 0.13, confidence = 0.6,
alpha_c = 15, beta_c = 13,
RR_h = 0.5, N_h = 100, w = 0.3
)
```

---

avg_oc_wr_ph *Average operating characteristics with respect to historic target*

Description

Function for calculating the average operating characteristics of a single arm Bayesian designs for early gating with respect to the historic target.

Usage

```
avg_oc_wr_ph(
  N_e,
  delta,
  delta_power,
  confidence,
  e_a = 0.5,
  e_b = 0.5,
  alpha_c,
  beta_c,
  trues = seq(0, 1, 0.01),
  adapt = 1,
  plot = T,
  legend = T,
  legend.pos = "topleft"
)
```

Arguments

N_e	Sample Size in the experimental group. Can be either a single value or a vector.
delta	Required superiority to make a "GO" decision. Corresponds to δ.
delta_power	Superiority, at which decision power will be evaluated. Corresponds to $\bar{\delta}$.
confidence	Required confidence to make "GO" decision. Corresponds to γ.
e_a	Alpha parameter of Beta Prior Distribution for the experimental response rate. Corresponds to α_e. Default is $\frac{1}{2}$.
e_b	Beta parameter of Beta Prior Distribution for the experimental response rate. Corresponds to β_e. Default is $\frac{1}{2}$.
alpha_c	Alpha parameter of Beta Distribution for the control response rate used to calculate average operating characteristics. Corresponds to α_c.
beta_c	Beta parameter of Beta Distribution for the control response rate used to calculate average operating characteristics. Corresponds to β_c.
trues	Sequence of true control response rates and experimental response rates, at which the Probability to Go will be computed. Default is seq(0,1,0.01) to ensure continuous plots and accurate results.
adapt	Level of adapting of experimental control rate to account for patient selection bias from phase II to phase III. Corresponds to ξ. Default is 1, so no adapting.
plot	Plots yes or no. Default is TRUE.
legend	Logical; whether or not to include legend in plot. Default is TRUE.
legend.pos	Position of legend. Default is "topleft".

Value

A matrix containing information about the decision power and the decision alpha with respect to p_h.

Examples

```
avg_oc_wr_ph(
  N_e = 50, delta = 0.08, delta_power = 0.13,
  confidence = 0.6, alpha_c = 15, beta_c = 13
)
```

---

beta_par *Parameters of Beta distribution given Historical Data*

Description

Function for calculating the parameters of the beta distribution used to average the operating characteristics, given historical data.

Usage

```
beta_par(
  mu_cov,
  phi_cov = NULL,
  orr,
  data,
  newdata,
  link = NULL,
  weights = NULL,
  plot = T
)
```

Arguments

mu_cov	A character vector containing the names of covariates in data that should be used to model the parameter μ in the pdf.
phi_cov	A character vector containing the names of covariates in data that should be used to model the parameter ϕ in the pdf. Default is NULL, so ϕ will not be modelled with respect to the covariates.
orr	Character containing the name of the variable in data that represents the objective response rate.
data	Data frame containing all the covariates and the ORR.
newdata	Data frame containing a single value for each of the specified covariates that will be used to estimate the parameters of the Beta distribution.
link	Link function for μ. Corresponds to g. Default is NULL, which means the link function will be automatically chosen as the one yielding the highest log-likelihood for the given data and covariates.
weights	Weights that should be used for regression. Default is NULL, so no weights.
plot	Plots yes or no. Default is TRUE.

Examples

```
mu_cov <- c("date", "Phase")
orr <- "ORR"
newdata <- data.frame(
  "date" = 2017,
  "Phase" = factor(3)
  )
studs <- data.frame(
  "ORR"= c(0.693, 0.580, 0.693, 0.477, 0.609,
           0.727, 0.727, 0.591, 0.362, 0.593,
           0.792, 0.620, 0.550, 0.690, 0.776),
  "date" = c(2011, 2008.5, 2009, 1996, 2001,
             2003.5, 2002.5, 2008, 2000,
             2006, 2005, 2007.5, 2009.5,
             2010.5, 2010),
   "Phase" = factor(c(3, 2, 3, 3, 2, 2, 3, 3,
                      3, 3, 2, 3, 3, 3, 2)),
```

```
   "N" = c(293, 69, 336, 235, 92, 110, 131,
           208, 94, 123, 53, 182, 267, 239, 237)
 )

beta_par(
  mu_cov = mu_cov,
  orr = orr,
  data = studs,
  newdata = newdata,
  weights = studs$N/mean(studs$N)
)
```

---

oc *Single Arm Operating Characteristics*

Description

Function for calculating the operating characteristics of the single arm Bayesian designs in setting 1 and 2 for early gating.

Usage

```
oc(
  N_e,
  delta,
  delta_power,
  confidence,
  e_a = 0.5,
  e_b = 0.5,
  h_a = 0.5,
  h_b = 0.5,
  RR_h = NULL,
  N_h = NULL,
  hist_RR_c = NULL,
  trues = seq(0, 1, 0.01),
  adapt = 1,
  plot = T,
  legend = T,
  legend.pos = "topleft"
)
```

Arguments

N_e	Sample Size in the experimental group. Can be either a single value or a vector.
delta	Required superiority to make a "GO" decision. Corresponds to δ.
delta_power	Superiority, at which decision power will be evaluated. Corresponds to $\bar{\delta}$.

confidence	Required confidence to make "GO" decision. Corresponds to γ.
e_a	Alpha parameter of Beta Prior Distribution for the experimental response rate. Corresponds to α_e. Default is $\frac{1}{2}$.
e_b	Beta parameter of Beta Prior Distribution for the experimental response rate. Corresponds to β_e. Default is $\frac{1}{2}$.
h_a	Alpha parameter of Beta Prior Distribution for the historical control response rate. Corresponds to α_h. Only needs to be specified, if RR_h and N_h are also specified. Default is $\frac{1}{2}$.
h_b	Beta parameter of Beta Prior Distribution for the historical control response rate. Corresponds to β_h. Only needs to be specified, if RR_h and N_h are also specified. Default is $\frac{1}{2}$.
RR_h	Historical control response rate. Corresponds to p_h. If specified together with N_h, function will use setting 2 from pdf.
N_h	Historical control sample size. Corresponds to n_h. If specified together with RR_h, function will use setting 2 from pdf.
hist_RR_c	Point estimate of historical control repsonse rate. Corresponds to $\hat{p_h}$. If specified, while RR_h and N_h are not specified, function will use setting 1 from pdf.
trues	Sequence of true control response rates and experimental response rates, at which the Probability to Go will be computed. Default is seq(0,1,0.01) to ensure continuous plots and accurate results.
adapt	Level of adapting of experimental control rate to account for patient selection bias from phase II to phase III. Corresponds to ξ. Default is 1, so no adapting.
plot	Plots yes or no. Default is TRUE.
legend	Logical; whether or not to include legend in plot. Default is TRUE.
legend.pos	Position of legend. Default is "topleft".

Value

A matrix containing the decision power and decision alpha with respect to the true control response rate.

Examples

```
# Setting 1
oc(
  N_e = 50, delta = 0.08, delta_power = 0.13,
  confidence = 0.6, hist_RR_c = 0.5
)

# Setting 2
oc(
  N_e = 50, delta = 0.08, delta_power = 0.13,
  confidence = 0.6, RR_h = 0.5, N_h = 50
)
```

`oc_rct` *RCT Operating Characteristics*

Description

Function for calculating the operating characteristics of the RCT Bayesian designs in setting 3 and 4 for early gating.

Usage

```
oc_rct(
  N_c,
  N_e,
  delta,
  delta_power,
  confidence,
  e_a = 0.5,
  e_b = 0.5,
  c_a = 0.5,
  c_b = 0.5,
  h_a = 0.5,
  h_b = 0.5,
  RR_h = NULL,
  N_h = NULL,
  w = NULL,
  trues = seq(0, 1, 0.01),
  plot = T,
  legend = T,
  legend.pos = "topleft"
)
```

Arguments

`N_c`	Sample Size in the control group. Can be either a single value or a vector, but needs to be the same length as N_e.
`N_e`	Sample Size in the experimental group. Can be either a single value or a vector, but needs to be the same length as N_c.
`delta`	Required superiority to make a "GO" decision. Corresponds to δ.
`delta_power`	Superiority, at which decision power will be evaluated. Corresponds to $\bar{\delta}$.
`confidence`	Required confidence to make "GO" decision. Corresponds to γ.
`e_a`	Alpha parameter of Beta Prior Distribution for the experimental response rate. Corresponds to α_e. Default is $\frac{1}{2}$.
`e_b`	Beta parameter of Beta Prior Distribution for the experimental response rate. Corresponds to β_e. Default is $\frac{1}{2}$.

c_a	Alpha parameter of Beta Prior Distribution for the control response rate. Corresponds to α_c. Default is $\frac{1}{2}$.
c_b	Beta parameter of Beta Prior Distribution for the control response rate. Corresponds to β_c. Default is $\frac{1}{2}$.
h_a	Alpha parameter of Beta Prior Distribution for the historical control response rate. Corresponds to α_h. Only needs to be specified, if RR_h, N_h and w are also specified. Default is $\frac{1}{2}$.
h_b	Beta parameter of Beta Prior Distribution for the historical control response rate. Corresponds to β_h. Only needs to be specified, if RR_h, N_h and w are also specified. Default is $\frac{1}{2}$.
RR_h	Historical control response rate. Corresponds to p_h. If specified together with N_h and w, function will use setting 4 from pdf.
N_h	Historical control sample size. Corresponds to n_h. If specified together with RR_h and w, function will use setting 4 from pdf.
w	Level of dynmaic borrowing. Corresponds to w.
trues	Sequence of true control response rates and experimental response rates, at which the Probability to Go will be computed. Default is seq(0,1,0.01) to ensure continuous plots and accurate results.
plot	Plots yes or no. Default is TRUE.
legend	Logical; whether or not to include legend in plot. Default is TRUE.
legend.pos	Position of legend. Default is "topleft".

Value

A matrix containing the decision power and decision alpha with respect to the true control response rate.

Examples

```
# Setting 3
oc_rct(
  N_c = 25, N_e = 25, delta = 0.08,
  delta_power = 0.13, confidence = 0.6
)

# Setting 4
oc_rct(
  N_c = 25, N_e = 25, delta = 0.08,
  delta_power = 0.13, confidence = 0.6,
  RR_h = 0.5, N_h = 50, w = 0.3
)
```

req_resp *Required Responders for GO decision Single Arm*

Description

Function for calculating the minimum required number of responders in the experimental group to make a GO decision in Settings 1 and 2.

Usage

```
req_resp(
  N_e,
  delta,
  confidence,
  e_a = 0.5,
  e_b = 0.5,
  h_a = 0.5,
  h_b = 0.5,
  RR_h = NULL,
  N_h = NULL,
  hist_RR_c = NULL,
  adapt = 1
)
```

Arguments

N_e	Sample Size in the experimental group.
delta	Required superiority to make a "GO" decision. Corresponds to δ.
confidence	Required confidence to make "GO" decision. Corresponds to γ.
e_a	Alpha parameter of Beta Prior Distribution for the experimental response rate. Corresponds to α_e. Default is $\frac{1}{2}$.
e_b	Beta parameter of Beta Prior Distribution for the experimental response rate. Corresponds to β_e. Default is $\frac{1}{2}$.
h_a	Alpha parameter of Beta Prior Distribution for the historical control response rate. Corresponds to α_h. Only needs to be specified, if RR_h and N_h are also specified. Default is $\frac{1}{2}$.
h_b	Beta parameter of Beta Prior Distribution for the historical control response rate. Corresponds to β_h. Only needs to be specified, if RR_h and N_h are also specified. Default is $\frac{1}{2}$.
RR_h	Historical control response rate. Corresponds to p_h. If specified together with N_h, function will use setting 2 from pdf.
N_h	Historical control sample size. Corresponds to n_h. If specified together with RR_h, function will use setting 2 from pdf.

hist_RR_c	Point estimate of historical control repsonse rate. Corresponds to $\hat{p_h}$. If specified, while RR_h and N_h are not specified, function will use setting 1 from pdf.
adapt	Level of adapting of experimental control rate to account for patient selection bias from phase II to phase III. Corresponds to ξ. Default is 1, so no adapting.

Value

Integer.

Examples

```
# Setting 1
req_resp(
  N_e = 50, delta = 0.08,
  confidence = 0.6, hist_RR_c = 0.5
)

# Setting 2
req_resp(
  N_e = 50, delta = 0.08,
  confidence = 0.6, RR_h = 0.5, N_h = 50
)
```

---

req_resp_rct *Required Responders for GO decision RCT*

Description

Function for calculating the minimum required number of responders in the experimental group to make a GO decision in Settings 3 and 4.

Usage

```
req_resp_rct(
  N_c,
  N_e,
  delta,
  confidence,
  e_a = 0.5,
  e_b = 0.5,
  c_a = 0.5,
  c_b = 0.5,
  h_a = 0.5,
  h_b = 0.5,
  RR_h = NULL,
  N_h = NULL,
```

```
  w = NULL,
  plot = T
)
```

Arguments

N_c	Sample Size in the control group.
N_e	Sample Size in the experimental group.
delta	Required superiority to make a "GO" decision. Corresponds to δ.
confidence	Required confidence to make "GO" decision. Corresponds to γ.
e_a	Alpha parameter of Beta Prior Distribution for the experimental response rate. Corresponds to α_e. Default is $\frac{1}{2}$.
e_b	Beta parameter of Beta Prior Distribution for the experimental response rate. Corresponds to β_e. Default is $\frac{1}{2}$.
c_a	Alpha parameter of Beta Prior Distribution for the control response rate. Corresponds to α_c. Default is $\frac{1}{2}$.
c_b	Beta parameter of Beta Prior Distribution for the control response rate. Corresponds to β_c. Default is $\frac{1}{2}$.
h_a	Alpha parameter of Beta Prior Distribution for the historical control response rate. Corresponds to α_h. Only needs to be specified, if RR_h, N_h and w are also specified. Default is $\frac{1}{2}$.
h_b	Beta parameter of Beta Prior Distribution for the historical control response rate. Corresponds to β_h. Only needs to be specified, if RR_h, N_h and w are also specified. Default is $\frac{1}{2}$.
RR_h	Historical control response rate. Corresponds to p_h. If specified together with N_h and w, function will use setting 4 from pdf.
N_h	Historical control sample size. Corresponds to n_h. If specified together with RR_h and w, function will use setting 4 from pdf.
w	Level of dynmaic borrowing. Corresponds to w.
plot	Plots yes or no. Default is TRUE.

Value

Matrix containing pairs of successes in control group and respective required successes in experimental group.

Examples

```
# Setting 3
req_resp_rct(
  N_c = 25, N_e = 25,
  delta = 0.08, confidence = 0.6
)

# Setting 4
req_resp_rct(
```

```
  N_c = 25, N_e = 25,
  delta = 0.08, confidence = 0.6,
  RR_h = 0.5, N_h = 50, w = 0.3
)
```

Index