Package 'SEARS'

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Type Package

Title Seamless Dose Escalation/Expansion with Adaptive Randomization Scheme

Version 0.1.0

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Description A seamless design that combines phase I dose escalation based on toxicity with phase II dose expansion and dose comparison based on efficacy.

License GPL-2

Encoding UTF-8

Depends BOIN

Suggests knitr, rmarkdown

VignetteBuilder knitr

NeedsCompilation no

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R topics documented:

SEARS *A randomized distributed phase I-II seamless dose escalation/expansion schema for dose optimization and selection in early oncology clinical development*

Description

Implements seamless randomized phase I-II SEARS design for finding the optimal design. Practitioners can use a rich set of parameters to explore various real scenarios for their studies. The function can generate operating characteristics via simulation for practitioners to examine the design's properties

Usage

```
SEARS(p.p, p.d, p.tox, k1, k2, pi_t, pi_e, pT, eff_a = 0.5, eff_b = 0.5,
      plac_a = 0.5, plac_b = 0.5, tox_a = 1, tox_b = 1, csize, csize2,
      p.star = 0.2, q.star = 0.6, f.star = 0.06, p.star2 = 0.2,
      q.star2 = 0.98, d.cs, p.cs, phase1_size, n_earlystop,
      extrasafe_BOIN = FALSE, offset_BOIN = 0.05, Nsim, n_catchup,
      control_arm = "", power_c = 0.5, lower_bound = 0.05, weight1,
      weight2, seed = 100)
```

Arguments

p.p	the true placebo response rate
p.d	the true dose response rate vector
p.tox	the true dose toxicity rate vector
k1	the safety rule cutoff value in phase I
k2	the safety rule cutoff value in phase II
pi_t	the physician-specified upper toxicity rate threshold
pi_e	the physician-specified lower response rate threshold
pT	the target toxicity rate
eff_a	the hyperparameter "a" for priors of the response rate for experimental doses. The default value is eff_a = 0.5
eff_b	the hyperparameter "b" for priors of the response rate for experimental doses. The default value is eff_b = 0.5
plac_a	the hyperparameter "a" for prior of the response rate for the control arm. The default value is plac_a = 0.5
plac_b	the hyperparameter "b" for prior of the response rate for the control arm. The default value is plac_b = 0.5
tox_a	the hyperparameter "a" for priors of the toxicity rates. The default value is tox_a = 1

tox_b	the hyperparameter "b" for priors of the toxicity rates. The default value is tox_b = 1
csize	the cohort size in phase I
csize2	the cohort size in phase II
p.star	the fixed cutoff probability for toxicity in phase I. The default value is p.star = 0.2
q.star	the fixed cutoff probability for efficacy in phase I. The default value is q.star = 0.6
f.star	the small probability cutoff. It will be used for futility dose exclusion. The default value is f.star = 0.06
p.star2	the fixed cutoff probability for toxicity in phase II. The default value is p.star2 = 0.2
q.star2	the fixed cutoff probability for efficacy in phase II. The default value is q.star2 = 0.98
d.cs	the prespecified maximum allowable number of patients enrolled for each dose
p.cs	the prespecified maximum allowable number of patients enrolled for the placebo
phase1_size	the prespecified maximum sample size of phase I trial
n_earlystop	the cutoff number in phase I. When the number of patients enrolled at a certain dose reaches this value in phase I, this dose will be graduated to phase II
extrasafe_BOIN	the logical value which indicates whether a more stringent stopping rule will be applied to phase I BOIN design. The default value is extrasafe_BOIN = FALSE
offset_BOIN	the small positive number (between 0 and 0.5) to control how strict the stopping rule is when extrasafe_BOIN = TRUE. The default value is offset_BOIN = 0.05
Nsim	the number of simulated trials
n_catchup	the catch-up cutoff when employing the adaptive randomization in phase II
control_arm	the argument is for phase II design only. If this argument is "fixed", then allocation probability of control arm (the first component of the allocation probability vector) will be fixed to $\frac{1}{K}$. The default of this argument will return unfixed results; K indicates total number of arms (including control arm)
power_c	the power correction parameter of the allocation probability. The default value is power_c = 0.5
lower_bound	the lower bound of the allocation probability in phase II design. It must be a value between 0 and $\frac{1}{K}$. The default value is lower_bound = 0.05; K indicates total number of arms (including the control arm)
weight1	the penalized weight in the utility function for the toxicity
weight2	the additional penalized weight in utility function for dose(s) which has (have) the toxicity probability greater than the pre-specified DLT rate
seed	the seed. The default value is seed = 100

Value

SEARS() returns a list with following elements (1) type I error (2) average sample size for the trial (3) average sample size for each dose (4) average sample size for placebo (5) selection percentage for each dose (6) average toxicity events for each dose

Author(s)

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Examples

```
SEARS(p.p = 0.2, p.d = c(0.2, 0.2, 0.2, 0.2, 0.2), p.tox = c(0.03, 0.06, 0.17, 0.3, 0.5),
      k1 = 0.95, k2 = 0.8, pi_t = 0.17, pi_e = 0.2, pT = 0.17, eff_a = 0.5, eff_b = 0.5,
      plac_a = 0.5, plac_b = 0.5, tox_a = 1, tox_b = 1, csize = 3, csize2 = 3,
      p.star = 0.2, q.star = 0.6, f.star = 0.06, p.star2 = 0.2, q.star2 = 0.98,
      d.cs = 36, p.cs = 36, phase1_size = 30, n_earlystop = 100, extrasafe_BOIN = FALSE,
      offset_BOIN = 0.05, Nsim = 10, n_catchup = 3, control_arm = "fixed", power_c = 0.5,
      lower_bound = 0.05, weight1 = 0.5, weight2 = 0.5, seed = 100)
```

Index