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calogrank

Survival curves analysis of covariance

Description

Logrank test to compare survival curves adjusting for covariates

Usage

```r
calogrank(ftime, fstatus, grp, cvt, strat=NULL)
```

Arguments

- `ftime`: failure times
- `fstatus`: status indicator
- `grp`: group indicator
- `cvt`: continuous covariates used for adjusted analysis
- `strat`: stratification variable

Details

calogrank is the covariate adjusted version of k-sample survdiff. The function in its current form only does basic error checking.

References


Examples

```r
## Not run:  library(survival)
data(pbc)
pbc1 <- pbc
pbc1$trt[pbc1$trt == -9] <- NA
pbc1$copper[pbc1$copper == -9] <- NA
calogrank(pbc1$time, pbc1$status, pbc1$trt, pbc1[,c("copper")])
calogrank(pbc1$time, pbc1$status, pbc1$trt, pbc1[,c("copper")])

## End(Not run)
```
**Description**
Calculates the Concordance Probability Estimate for a Cox model.

**Usage**
```r
coxphCPE(phfit)
```

**Arguments**
- `phfit`: output from a proportional hazards fit.

**Value**
coxphCPE returns a vector with CPE, smooth.CPE & se.CPE which are the estimate, the smoothed estimate and its standard error respectively.

**References**

**Examples**
```r
## Not run: library(survival)
data(pbc)
pbcfit <- coxph(Surv(time, status==2) ~ trt + log(copper), pbc, subset=(trt>0 & copper>0))
coxphCPE(pbcfit)
## End(Not run)
```

---

**Description**
Calculates the contribution of a subset of covariates to the explained relative risk derived from the full Cox proportional hazards model.

**Usage**
```r
coxphERR(phfit, ngamma=NULL)
```
### coxphQuantile

**Survival time quantile as a function of covariate**

**Description**

Draws a quantile curve of survival distribution as a function of covariate.

**Usage**

```r
coxphQuantile(phfit, xrange, p=0.5, whichx=1, otherx=NULL, ...)
```

**Arguments**

- `phfit`: The output from a proportional hazards fit.
- `ngamma`: A vector of indices corresponding to covariates of interest. If missing (default), the explained relative risk is computed for the full model.

**Details**

The object `phfit` should be the result of a call to `coxph` with the option `x=TRUE`.

**Value**

The function `coxphERR` returns the vector `(ERR, se.ERR)`. The first component `ERR` represents the contribution of a subset of covariates to the explained relative risk estimate of the full model. If a set of covariates is not provided, then it computes the estimate of the full model. The second component `se.ERR` is the standard error of the estimate.

**References**

Heller G. (2012) A measure of explained risk in the proportional hazards model. *Biostatistics*

**Examples**

```r
## Not run:
library(survival)
ovarianfit <- coxph(Surv(futime, fustat) ~ age + resid.ds + rx +
                     ecog.ps, data=ovarian, x=T)

# Compute the explained relative risk (ERR) and its standard error (se.ERR) for the full model.
coxphERR(ovarianfit)
# Compute the contribution of age and ECOG performance status to the explained relative risk. Age and ECOG performance status are the first and fourth covariates in the model.
coxphERR(ovarianfit, c(1,4))

## End(Not run)
```
Arguments

- **phfit**: output from a proportional hazards fit.
- **xrange**: the range of covariate values for which the quantiles of survival times are computed.
- **p**: the probability level for the quantile (default is median).
- **whichx**: if there are more than one covariates in the Cox model, the one chosen for the quantile plot.
- **otherx**: the values for other covariates in the Cox model. If missing uses their average values.
- **...**: additional parameters to be passed on to the lines command.

Details

This function is used to draw quantile curves. It requires a plot of the data (time & covariate of interest) to be present. See example.

It invisibly returns the observed failure times and the covariate values at which the estimated survival probability is (exactly) \( p \).

References


Examples

```r
# Not run: library(survival)
data(pbc)
pbcfit <- coxph(Surv(time, status==2) ~ trt + log(copper), pbc, subset=(trt>0 & copper>0))
plot(log(pbc$copper[pbc$trt>0 & pbc$copper>0]), pbc$time[pbc$trt>0 & pbc$copper>0], pch=c("o","x")[1+pbc$status[pbc$trt>0 & pbc$copper>0]], xlab="log Copper", ylab="Survival time")
coxphQuantile(pbcfit, c(2.5,6), whichx=2, otherx=1)
coxphQuantile(pbcfit, c(2.5,6), p=0.75, whichx=2, otherx=2, col=2)
# End(Not run)
```

Description

Calculates sample size, effect size and power based on Fisher's exact test.
Usage

fe.ssize(p1, p2, alpha=0.05, power=0.8, r=1, npm=5, mmax=1000)
CPS.ssize(p1, p2, alpha=0.05, power=0.8, r=1)
fe.mdoor(ncase, ncontrol, pcontrol, alpha=0.05, power=0.8)
mdrr(n, cprob, presp, alpha=0.05, power=0.8, niter=15)
fe.power(d, n1, n2, p1, alpha = 0.05)
or2pcase(pcontrol, OR)

Arguments

p1 response rate of standard treatment
p2 response rate of experimental treatment
d difference = p2-p1
pcontrol control group probability
n1 sample size for the standard treatment group
n2 sample size for the standard treatment group
ncontrol control group sample size
ncase case group sample size
alpha size of the test (default 5%)
power power of the test (default 80%)
r treatments are randomized in 1:r ratio (default r=1)
npm the sample size program searches for sample sizes in a range (+/- npm) to get the exact power
mmax the maximum group size for which exact power is calculated
n total number of subjects
cprob proportion of patients who are marker positive
presp probability of response in all subjects
niter number of iterations in binary search
OR odds-ratio

Details

CPS.ssize returns Casagrande, Pike, Smith sample size which is a very close to the exact. Use this for small differences p2-p1 (hence large sample sizes) to get the result instantaneously.
fe.ssize return a 2x3 matrix with CPS and Fisher’s exact sample sizes with power.
fe.mdoor return a 3x2 matrix with Schlesselman, CPS and Fisher’s exact minimum detectable odds ratios and the corresponding power.
fe.power returns a Kx2 matrix with probabilities (p2) and exact power.
mdrr computes the minimum detectable P(resp|marker+) and P(resp|marker-) configurations when total sample size (n), P(response) (presp) and proportion of subjects who are marker positive (cprob) are specified.
or2pcase give the probability of disease among the cases for a given probability of disease in controls (pcontrol) and odds-ratio (OR).
gsdesign

References

---

**gsdesign**

*Group Sequential Designs*

**Description**

Functions to calculate sample size for group sequential designs

**Usage**

```r
gsdesign.binomial(ifrac, pC, pE, sig.level = 0.05, power = 0.8,
delta.eb=0.5, delta.fb = NULL, alternative = c("two.sided",
"one.sided"), pooled.variance = FALSE, CPS = TRUE, tol=0.00001, ...)
```

```r
gsdesign.normal(ifrac, delta, sd = 1, sig.level = 0.05,
power = 0.8, delta.eb = 0.5, delta.fb = NULL, alternative =
c("two.sided", "one.sided"), tol=0.00001, ...)
```

```r
gsdesign.survival(ifrac, haz.ratio, sig.level = 0.05,
power = 0.8, delta.eb = 0.5, delta.fb = NULL, alternative =
c("two.sided", "one.sided"), tol=0.00001, ...)
```

**Arguments**

- **ifrac**: information fraction or the ratio of current sample size or number of events to the total sample size or number of events. This should be an increasing vector of numbers from 0 to 1 with the last one being 1. If just 1 is given a fixed sample design is derived.
- **pC**: prob of success of the standard therapy (for binomial data)
- **pE**: prob of success of the experimental therapy (for binomial data)
- **delta**: true difference in means (for normal data)
- **sd**: standard deviation (for normal data)
- **haz.ratio**: hazard ratio (for survival comparison)
- **sig.level**: significance level (type I error probability)
- **power**: power of test (1 minus type II error probability)
- **delta.eb**: power for efficacy boundary in the Pocock (=0) to O’Brien-Fleming (=0.5) family (default is 0.5)
- **delta.fb**: power for futility boundary in the Pocock (=0) to O’Brien-Fleming (=0.5) family (default is NULL i.e. no futility boundary is requested.)
alternative one- or two-sided test.
pooled.variance whether the test statistic is standardized by pooled \(2\times pE\times(1-pE)\) or unpooled variance \(pC\times(1-pC) + pE\times(1-pE)\). Default is unpooled variance.
PNS whether continuity correction is used for sample size calculation as in Casagrande, Pike & Smith. Default is to use it.
tol tolerance level for multivariate normal probability computation.
... additional options passed on the pmvnorm function.

Details

The futility boundary is not returned when delta.fb is not specified i.e. stopping for futility is not requested. The futility boundary is non-binding. That is the significance level is not adjusted to account for early stopping for utility. This makes the test a bit conservative in that the true size is less than the nominal level.

The Casagrande-Pike-Smith type continuity correction is obtained using the formula \(n^{*}1 + \sqrt{1+4/abs(pC-pE)}\times n^{*2}\) where \(n\) is the uncorrected sample size.

Value

a list with ifrac, sig.level, power, alternative, delta.eb, delta.fb and:

- efbdry the critical value to use at the different looks.
- futbdry the critical value to use at the different looks.
- sample.size the sample size per arm for binomial/normal data.
- num.events the total number of failures which should be converted to number of subjects using censoring proportion.

 jonckheere.test  

 jonckheere.terpstra.test

Description

Jonckheere-Terpstra test to test for ordered differences among classes

Usage

```r
jonckheere.test(x, g, alternative = c("two.sided", "increasing", "decreasing"), nperm=NULL)
```

Arguments

- `x`, `g` data and group vector
- `alternative` means are monotonic (two.sided), increasing, or decreasing
- `nperm` number of permutations for the reference distribution. The default is null in which case the permutation p-value is not computed. Recommend that the user set nperm to be 1000 or higher if permutation p-value is desired.
Details

jonckheere.test is the exact (permutation) version of the Jonckheere-Terpstra test. It uses the statistic

\[ \sum_{k \neq l} \sum_{k < l} I(X_{ik} < X_{jl}) + 0.5I(X_{ik} = X_{jl}), \]

where \( i, j \) are observations in groups \( k \) and \( l \) respectively. The asymptotic version is equivalent to cor.test(x, g, method="k"). The exact calculation requires that there be no ties and that the sample size is less than 100. When data are tied and sample size is at most 100 permutation p-value is returned.

References

Terpstra, T. J. (1952). The asymptotic normality and consistency of Kendall’s test against trend, when ties are present in one ranking. *Indagationes Mathematicae* 14:327-333.

Examples

```r
set.seed(1234)
g <- rep(1:5, rep(10,5))
x <- rnorm(50)
jonckheere.test(x+0.3*g, g)
x[1:2] <- mean(x[1:2]) # tied data
jonckheere.test(x+0.3*g, g)
jonckheere.test(x+0.3*g, g, nperm=5000)
```

ktau

*Kendall’s tau-b estimate*

Description

Calculates the Kendall’s tau-b.

Usage

```r
ktau(x, y)
```

Arguments

- `x`: first variable
- `y`: second variable

Details

ktau computes the same quantity as cor(x, y, method="kendall"). It uses a faster algorithm than pairwise comparisons used by cor.
Value

\texttt{ktau} returns Kendall’s tau-b.

Examples

\begin{verbatim}
set.seed(1234)
x <- rnorm(10000); y <- x+rnorm(10000)
cor(x, y, method="k")
clinfun::ktau(x, y)
\end{verbatim}

\texttt{oc.twostage.bdry} \hspace{1cm} \textit{Two-stage boundary operating characteristics}

Description

Calculates the operating characteristics of a two-stage boundary.

Usage

\texttt{oc.twostage.bdry(pu, pa, r1, n1, r, n)}

Arguments

- \texttt{pu} \hspace{1cm} unacceptable response rate
- \texttt{pa} \hspace{1cm} response rate that is desirable
- \texttt{r1} \hspace{1cm} first stage threshold to declare treatment undesirable
- \texttt{n1} \hspace{1cm} first stage sample size
- \texttt{r} \hspace{1cm} overall threshold to declare treatment undesirable
- \texttt{n} \hspace{1cm} total sample size

Value

\texttt{oc.twostage.bdry} returns the type I and II error rates as well as the probability of early termination and expected sample size under \texttt{pu} for a specific boundary.
permlogrank

**Description**

Small sample survdiff using permutation reference distributions.

**Usage**

```r
permlogrank(formula, data, subset, na.action, rho=0, nperm=5000)
```

**Arguments**

- `nperm`: number of permutations for the reference distribution
- `formula`, `data`, `subset`, `na.action`, `rho`
  
  see `survdiff` for details

**Details**

permlogrank is the permutation version of k-sample survdiff. see `survdiff` in survival package for details.

**References**


---

ph2simon

**Description**

Calculates Optimal and Minimax 2-stage Phase II designs given by Richard Simon

**Usage**

```r
ph2simon(pu, pa, ep1, ep2, nmax=100)
```

---
Arguments

- **pu**: unacceptable response rate
- **pa**: response rate that is desirable
- **ep1**: threshold for the probability of declaring drug desirable under p0
- **ep2**: threshold for the probability of rejecting the drug under p1
- **nmax**: maximum total sample size (default 100; can be at most 500)
- **x**: object returned by ph2simon
- **...**: arguments to be passed onto plot and print commands called within

Value

ph2simon returns a list with pu, pa, alpha, beta and nmax as above and:

- **out**: matrix of best 2 stage designs for each value of total sample size n. the 6 columns are: r1, n1, r, n, EN(p0), PET(p0)

The "print" method formats and returns the minimax and optimal designs. The "plot" plots the expected sample size against the maximum sample size as in Jung et al., 2001

References


See Also

two-stage.inference, oc.two-stage.bdry

Examples

```r
ph2simon(0.2, 0.4, 0.1, 0.1)
ph2simon(0.2, 0.35, 0.05, 0.05)
ph2simon(0.2, 0.35, 0.05, 0.05, nmax=150)
```

---

**ph2single**

*Exact single stage Phase II design*

Description

Calculates the exact one stage Phase II design

Usage

```
ph2single(pu, pa, ep1, ep2, nsohn=5)
```
### power.ladesign

**Power of k-sample rank test under Lehmann alternative**

#### Description

Functions to calculate the power of rank tests for animal studies.

#### Usage

```r
power.ladesign(gsize, odds.ratio, sig.level = 0.05, statistic =
  c("Kruskal-Wallis", "Jonckheere-Terpstra"), alternative =
  c("two.sided", "one.sided"), nrep=1e+6)
```

```r
## S3 method for class 'ladesign'
print(x,...)
```

#### Arguments

- `gsize`: sample size of the k (= length of vector) groups.
- `odds.ratio`: odds ratio parameters for the k-1 groups. The first group is considered the control.
- `sig.level`: the significance level of the test (default = 0.05)
- `statistic`: the test statistic for the k-group comparison. Is one of Kruskal-Wallis (default) or Jonckheere-Terpstra.
- `alternative`: one- or two-sided test. Valid only for the Jonckheere-Terpstra test.
- `nrep`: number of reps (default 1 million) for Monte Carlo.
- `x`: object of class ladesign returned by power.ladesign
- `...`: arguments to be passed on left for S3 method consistency.

#### Details

Although the power for Jonckheere-Terpstra test is calculated for any set of odds ratio, the test is meant for monotone alternative. Thus it is preferable to specify odds ratios that are monotonically increasing with all values larger than 1 or decreasing with all values smaller than 1.
pselect

Value
returns a list with objects group.size, odds.ratio, statistic, sig.level and power. The "print" method formats the output.

References

Examples

```r
power.ladesign(c(9,7), 4, statistic="K")
power.ladesign(c(9,7,9), c(2,4), statistic="J")
power.ladesign(c(9,7,9), c(2,4), statistic="J", alt="o")
```

---

**pselect**

*Probability of selection under pick the winner rule*

Description
Calculates the probability of selecting the treatment with the higher response rate under the pick the winner rule.

Usage

```r
pselect(n, p, min.diff=NULL, min.resp=NULL)
```

Arguments

- **n** sample size for each treatment arm. This is either a single integer or a vector of two integers for the special case of comparing two treatments with unequal sample sizes.
- **p** vector of response rates for the treatments.
- **min.diff** this is the number of responses or the rate by which the best treatment should be superior to the others to be chosen. This must be a positive integer or a rate between 0 and 1. If missing it defaults to 1 for the equal sample size case but quits with a warning for the unequal sample size case.
- **min.resp** the minimum number of responses in each treatment arm for it to be considered further. If missing defaults to 0.
Value

the function returns a list with:

prob.none.worthy
is the probability that no treatment has the minimum number of responses specified in min.resp. this element is present only if min.resp is greater than 0 for at least one arm.

prob.inconclusive
this is the probability that the best treatment has the requisite min.resp responses but exceeds the second best by less than min.diff responses (rate) provided the second best also has at least min.resp responses.

prob.selection
this is a matrix which for each treatment gives the response probability and the probability of selecting it i.e. the number of responses in the chosen arm is at least min.resp and either none of the remaining arms exceed the min.resp threshold or the chosen (best) arm is better than the second best by at least min.diff responses (rate).

References


Examples

# selection when no difference i.e. type I error
pselect(18, c(0.2, 0.2, 0.2))
# selection probability
pselect(18, c(0.2, 0.2, 0.4))
pselect(26, c(0.2, 0.2, 0.4), min.diff=2, min.resp=3)
# unequal sample size case
pselect(c(27,54), c(0.5, 0.65), min.diff=0.05)
# unequal sample size case
pselect(c(27,54), c(0.5, 0.65), min.diff=0.05, min.resp=c(14,27))

roc.area.test          Nonparametric area under the ROC curve

Description

Computes the nonparametric area under the ROC curve and its variance based on U-statistic theory (DDCP).

Usage

roc.area.test(markers, status)
    ## S3 method for class 'roc.area.test'
print(x, ...)

roc.area.test
Arguments

- `markers`: The marker values for each subject. If there are more than one markers then this should be a matrix.
- `status`: binary disease status indicator
- `x`: object of class `roc.area.test` output from this function.
- `...`: optional arguments to the print function.

Details

It calculates the area and its variance. For more than one marker it calculates the statistic to test for the equality of all AUCs. This statistic has a standard normal reference distribution for two variables and chi-square with number of variables minus 1.

Value

A list with the following elements:

- `area`: estimated area.
- `var`: estimated variance (matrix).
- `stat`: test statistic for equality of AUCs. Is not returned when only one diagnostic marker is present.
- `p.value`: the p-value for the test of equality (2-sided).
- `df`: the degrees of freedom of the chi-square.

The "print" method formats and returns the output.

References


Examples

```r
  g <- rep(0:1, 50)
  x <- rnorm(100) + g
  y <- rnorm(100) + g
  z <- rnorm(100) + g
  roc.area.test(cbind(x, y), g)
  roc.area.test(cbind(x, y, z), g)
  y1 <- y + 0.75*g
  roc.area.test(cbind(x, y1), g)
```
Description

Computes the empirical ROC curve for a diagnostic tool.

Usage

roc.curve(marker, status, method=c("empirical"))
## S3 method for class 'roc.curve'
print(x, ...)
## S3 method for class 'roc.curve'
plot(x, ...)
## S3 method for class 'roc.curve'
lines(x, ...)

Arguments

marker the marker values for each subject.
status binary disease status indicator
method the method for estimating the ROC curve. Currently only the empirical curve is implemented.
x object of class roc.area.test output from this function.
... optional arguments to the print, plot and lines functions.

Details

The computation is based on assuming that larger values of the marker is indicative of the disease. So for a given threshold \(x_0\), TPR is \(P(\text{marker} \geq x_0 | \text{status} = 1)\) and FPR is \(P(\text{marker} \geq x_0 | \text{status} = 0)\). This function computes the empirical estimates of TPR and FPR.

Value

a list with the following elements

- tpr true positive rates for all thresholds.
- fpr true positive rates for all thresholds.
- marker the diagnostic marker being studied.
- status binary disease

The "print" method returns the nonparametric AUC and its s.e.
The "plot" and "lines" methods can be used to draw a new plot and add to an existing plot of ROC curve.
Examples

```r
g <- rep(0:1, 50)
x <- rnorm(100) + g
y <- rnorm(100) + 1.5*g
o <- roc.curve(x, g)
plot(o)
lines(roc.curve(y, g), col=2)
```

**Description**

Computes the test statistic and permutation reference distribution for comparing paired or unpaired ROC curves.

**Usage**

```r
roc.perm.test(marker, status, marker2=NULL, group=NULL, nperm=2500, mp=NULL)
## S3 method for class 'roc.perm.test'
print(x, ...)
## S3 method for class 'roc.perm.test'
plot(x, ...)
```

**Arguments**

- `marker`: marker values for each subject.
- `status`: binary disease status indicator.
- `marker2`: second diagnostic marker for the same subjects (paired).
- `group`: indicator of which diagnostic test was used (unpaired).
- `nperm`: number of permutations for the reference distribution.
- `mp`: mixing proportion for the unpaired case when proportion of diseased subjects can differ.
- `x`: object of class roc.perm.test output from this function.
- `...`: optional arguments to print and plot functions.

**Details**

This function implements the permutation method described in the Venkatraman and Begg (1996) paper for the paired case and the Venkatraman (2000) paper for the unpaired case.

The function detects whether the data are paired or unpaired by testing which of the options marker2 and group is specified. If both are missing it will stop with an error message. At present exactly one should be missing.
Value

an object of class roc.perm.test with the following elements

- `ostat` test statistic from the observed data.
- `pstat` test statistic from permuted data.
- `p.value` the p-value for the test of equality (2-sided).

The "print" method formats and returns the statistic and p-value. The "plot" method plots the density from the permutation reference distribution and marks the location of the observed statistic.

References


Examples

```r
d <- rep(0:1, 50)
x <- rnorm(100) + 1.2*d
y <- rnorm(100) + 1.2*d
oo <- roc.perm.test(x, d, marker2=y)
plot(oo)
oo <- roc.perm.test(c(x,y), c(d,d), group=rep(1:2,each=100))
plot(oo)
```

---

**ROCAnalysis**

*Functions to plot and compare ROC curves.*

**Description**

These functions can be used for nonparametric analysis of ROC curves.

**Details**

The relevant functions are `roc.curve`, `roc.area.test` and `roc.perm.test`. See the individual functions for usage details.
Stopping rule for toxicity monitoring

Description
Computes a stopping rule and its operating characteristics for toxicity monitoring based repeated significance testing.

Usage
toxbdry(pLo, pHi, n, cP0=0.1, cP1=0.9, ngrid=6, niter=10, delta=0,
priority=c("null","alt"))
bdrycross.prob(n, r, ptox)
## S3 method for class 'toxbdry'
print(x, ...)

Arguments
- **pLo**: the toxicity rate that is acceptable.
- **pHi**: the toxicity rate that is too high and hence unacceptable.
- **n**: vector of times (sample size) when toxicity is monitored.
- **r**: vector of maximum acceptable toxicities corresponding to n.
- **ptoxt**: the toxicity rates for which the operating characteristics are calculated.
- **cP0**: boundary crossing probability under pLo i.e. type I error or the probability of declaring a treatment with toxicity rate pLo unacceptable.
- **cP1**: boundary crossing probability under pHi i.e. power or the probability of declaring a treatment with toxicity rate pHi unacceptable.
- **ngrid**: the number of toxicity rates from pLo to pHi for which the operating characteristics are computed.
- **niter**: the number of iterations run to obtain the boundary.
- **delta**: power determining the shape of the boundary. Should be between 0 (default) and 0.5.
- **priority**: the error threshold to prioritize when the max sample size is too small to have both error thresholds satisfied. Default is the null i.e. error under pLo.
- **x**: object returned by the function toxbdry.
- **...**: additional arguments to print.

Details
Default value of boundary shape corresponds to the Pocock boundary where the same significance level is used for all looks. For a more conservative stopping rule use delta greater than 0 where 0.5 corresponds to the O’Brien-Fleming boundary which is extremely conservative in the early looks. Value between 0.1 and 0.2 is a reasonable compromise.

The exact calculations in this function are done along the lines of the method in Chapter 12 of Jennison and Turnbull (2000). Ivanova, Qaqish and Schell (2005) have an illustrative paper.
twostage.inference

Value

the function returns a list with:

- looks
  when toxicity is monitored - same as input n.
- lo.bdry
  lower boundary is a vector of maximum acceptable number of toxicities corresponding the number of subjects in n. The boundary crossing probability for this is slightly above cP0.
- hi.bdry
  upper boundary is a vector of maximum acceptable number of toxicities corresponding the number of subjects in n. The boundary crossing probability for this is slightly below cP0.
- bdry.oc
  the operating characteristics i.e the toxicity rate, the probability of crossing, stopping (i.e. cross before the last observation) and the expected sample size for both the low (lo) and high (hi) boundaries.
- bdry.alpha
  the alpha levels for testing at each look for the two boundaries.

stopping for toxicity is done when the number of toxicities exceeda the boundary i.e. the boundary gives the maximum acceptable number.

References


Examples

toxbdry(0.2, 0.35, c(20, 40, 60, 75))
toxbdry(0.2, 0.3, c(20, 40, 60, 75), cP0=0.15, cP1=0.8)
  # continuous monitoring
toxbdry(0.1, 0.3, 2:30)
  # prioritize cP1 error threshold
toxbdry(0.1, 0.3, 2:25, priority="alt")

twostage.inference

Inference following a two-stage design for binary response

Description

Calculates the p-value, UMVUE and CI for the data from a study using a two stage design for response.

Usage

twostage.inference(x, r1, n1, n, pu, alpha=0.05)
Arguments

- x: number of responses observed at the end of the study
- r1: first stage threshold to declare treatment undesirable
- n1: first stage sample size
- n: total sample size
- pu: unacceptable response rate (null hypothesis)
- alpha: the confidence level. For consistency with the design use the same value from the design. (default is 0.05)

Value

twostage.inference returns the UMVUE (Jung & Kim, 2004), p-value and CI (Koyama & Chen, 2008). The CI has confidence level 1-2*alpha and the one-sided (1-alpha) interval consistent with the design is obtained by changing the upper confidence limit (UCL) to 1.

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