Package ‘ldbounds’

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bounds

Group Sequential Boundaries Using Spending Functions

Description
'bounds' determines group sequential boundaries for interim analyses of accumulating data in clinical trials using the Lan-DeMets alpha spending function method. These can be used as guidelines for early stopping of the trial.

Usage
bounds(t, t2 = t, iuse = 1, asf = NULL, alpha = 0.05,
   phi = rep(1, length(alpha)), ztrun = rep(8, length(alpha)))

Arguments
  t        the vector of analysis times, which must be increasing and in (0,1].
  t2       the second time scale, usually in terms of amount of accumulating information. By default, same as t.
  iuse     a vector of the type of alpha spending function(s) to use for lower and upper bounds, respectively (in the two-sided case). Details of specification are given below.
  asf      a list of one or two functions to be used as alpha spending function(s). Used with iuse=5 (See below).
  alpha    a vector of type I errors. In two-sided situations, these correspond to the amount allocated to the lower and upper boundaries, respectively. The total alpha must be greater than 0 and less than or equal to 1.
  phi      a vector of values used when iuse=3 or 4 (See below).
  ztrun    a vector of values specifying where to truncate lower and upper boundaries, respectively. Default is c(-8,8) (or just 8 for one-sided), which is essentially no truncation.

Details
This is based on a Fortran program, 'ld98', by Reboussin, DeMets, Kim, and Lan. It has some advantages, like making use of probability distributions in R and the ability to specify any valid spending function without changing the program.

iuse values of 1 and 2 correspond to alpha spending functions which give O'Brien Fleming and Pocock type boundaries, respectively. A value of 3 is the power family. Here, the spending function is \( \alpha t^\phi \), where \( \phi \) must be greater than 0. A value of 4 is the Hwang-Shih-DeCani family, with spending function \( \alpha(1 - e^{-\phi t})/(1 - e^{-\phi}) \), where \( \phi \) cannot be 0.

iuse and alpha must have the same length. If alpha has length 2 and phi has length 1, the same value of phi will be used for the upper and the lower boundaries.

With iuse=5, the user will specify any alpha spending function as asf. Such a function asf() must be of class 'function' and must satisfy \( asf(0)=0 \) and \( asf(1)=1 \) and must be strictly increasing.
Currently, this option cannot be used for one side of the boundary with one of the other options for the other side. In other words, the user may define one spending function for a one-sided boundary or two for a two-sided boundary, symmetric or asymmetric, but cannot define one spending function and select the other from iuse 1 through 4.

Value

'bounds' returns an object of 'class' "bounds".

An object of class "bounds" is a list containing the following components:

bounds.type the type of bounds: 1 is 'one-sided', 2 is 'two-sided symmetric', and 3 is 'two-sided asymmetric'.

spending.type the type(s) of spending function. A descriptive version of the value(s) used for iuse

time the original time scale.

time2 the second (information) time scale.

alpha the alpha(s) used.

overall.alpha if two-sided, the sum of the two alphas. If one-sided, just alpha.

lower.bounds the vector of lower boundaries calculated. Should be ignored if one-sided.

upper.bounds the vector of upper boundaries calculated.

exit.pr the vector of cumulative exit probabilities at each analysis.

diff.pr the vector of exit probabilities accumulated at each analysis.

Author(s)

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References


Fortran program 'ld98' by the same authors as above.


See Also

Generic functions *summary.bounds* and *plot.bounds*.

drift for exit probabilities given boundaries or drift (effect) or confidence interval given power.
**Examples**

```r
## From Reboussin, et al. (2000)

t <- seq(0,1,length=5)
obf.bd <- bounds(t,iuse=c(1,1),alpha=c(0.025,0.025))
summary(obf.bd)
plot(obf.bd)

t <- c(0.294,0.3333,0.4375,0.5833,0.7083,0.8333)
t2 <- c(0.294,0.3333,0.4375,0.5833,0.7083,0.8333)
power.fam <- bounds(t,t2,iuse=c(3,3),alpha=c(0.025,0.025))
summary(power.fam)
```

---

**drift**

*Drift and Probabilities for Group Sequential Boundaries*

**Description**

'drift' calculates drift (effect), confidence interval for drift, or power and other probabilities given drift for specified group sequential boundaries for interim analyses of accumulating data in clinical trials.

**Usage**

```r
drift(za = -zb, zb, t, t2 = t, pow = NULL, drft = NULL,
     conf = NULL, zval = zb[length(zb)])
```

**Arguments**

- **za** the vector of lower boundaries. Symmetric to zb by default.
- **zb** the vector of upper boundaries.
- **t** the vector of analysis times, which must be increasing and in (0,1].
- **t2** the second time scale, usually in terms of amount of accumulating information. By default, same as t.
- **pow** the desired power when drift is not specified.
- **drft** the true drift (i.e. treatment effect when t=1).
- **conf** the confidence level when a confidence interval for drift is wanted.
- **zval** the final observed Z statistic (i.e. when trial is stopped). Used for confidence interval.

**Details**

This is based on a Fortran program, 'ld98', by Reboussin, DeMets, Kim, and Lan. It has some advantages, like making use of probability distributions in R. Only one of pow, drft, and conf is to be specified and zval is only used in the last case.
drift

Value

'drift' returns an object of 'class' "'drift'".

An object of class "'drift'" is a list containing the following components:

- **type**: Type of computation performed: 1 is drift given power, 2 is exit probabilities given drift, and 3 is confidence interval for drift given final Z statistic.
- **time**: the original time scale.
- **time2**: the second (information) time scale.
- **lower.bounds**: the vector of lower boundaries given.
- **upper.bounds**: the vector of upper boundaries given.
- **power**: the power. If power is given, it is returned here. If drift is given, the resulting power is calculated.
- **drift**: the drift. If drift is given, it is returned here. If power is given, the drift resulting in given power is calculated.
- **lower.probs**: the vector of exit probabilities across the lower boundary. Returned if power or drift is given.
- **upper.probs**: the same for upper boundary.
- **exit.probs**: the probability at each analysis of crossing the boundary. The sum of lower.probs and upper.probs.
- **cum.exit**: the cumulative probability of crossing.
- **conf.level**: the desired confidence level, if given.
- **final.zvalue**: the final Z statistic, if given.
- **conf.interval**: the confidence interval for drift, if conf and zval are given.

Author(s)

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References


Fortran program 'ld98' by the same authors as above.


See Also

Generic functions *summary.drift* and *plot.drift*.

*bounds* for computation of boundaries using alpha spending function method.
Examples

```r
## From Reboussin, et al. (2000)

t <- c(0.13, 0.4, 0.69, 0.9, 0.98, 1)
upper <- c(5.3666, 3.7102, 2.9728, 2.5365, 2.2154, 1.9668)
drift.pr <- drift(zb=upper, t=t, drft=3.242)
summary(drift.pr)

## using output from 'bounds'
t <- seq(0.2, 1, length=5)
obf.bd <- bounds(t, iuse=c(1,1), alpha=c(0.025, 0.025))
drift.dr <- drift(obf.bd$lower.bounds, obf.bd$upper.bounds, t, pow=0.9)
summary(drift.dr)
```

---

**plot.bounds**

Plot for Group Sequential Boundaries

Description

Plot of the sequential boundaries for objects of class ""bounds"" or ""drift"".

Usage

```r
## S3 method for class 'bounds'
plot(x, main = NULL, xlab = NULL, ylab = NULL, ...)
## S3 method for class 'drift'
plot(x, main = NULL, xlab = NULL, ylab = NULL, ...)
```

Arguments

- `x`: an object of class ""bounds"" or ""drift"".
- `main`: an overall title for the plot: see `title`.
- `xlab`: a title for the x axis: see `title`.
- `ylab`: a title for the y axis: see `title`.
- `...`: graphical parameters can be given as arguments to `plot`.
Author(s)

Charlie Casper <charlie.casper@hsc.utah.edu> and Oscar A. Perez

References


Fortran program 'ld98' by the same authors as above.


See Also

Generic functions `summary.bounds` and `summary.drift.bounds` to calculate sequential boundaries, `drift` for exit probabilities given boundaries or drift (effect) or confidence interval given power.

Examples

```r
## see 'bounds' or 'drift'.
```

---

**summary.bounds**

*Summary for Group Sequential Boundaries*

**Description**

'summary' method for class "bounds".

**Usage**

```r
## S3 method for class 'bounds'
summary(object, ...)
## S3 method for class 'summary.bounds'
print(x, digit = 5, ...)
```

**Arguments**

- `object` an object of class "bounds", a result of a call to bounds.
- `x` an object of class "summary.bounds", a result of a call to summary.bounds.
- `digit` the number of significant digits to use when printing.
- `...` further arguments passed to or from other methods.
Value

The function 'summary.bounds' returns a list of summary values of the group sequential boundary calculations given in 'object'.

Author(s)

Oscar A. Perez and T. Charles Casper <charlie.casper@hsc.utah.edu>

References


Fortran program 'ld98' by the same authors as above.


See Also

bounds for computation of boundaries using alpha spending function method. drift for exit probabilities given boundaries or drift (effect) or confidence interval given power.

Examples

```r
## See function 'bounds'
```

summary.drift  

**Summary for Computations Related to Group Sequential Boundaries**

Description

'summary' method for class "drift".

Usage

```r
## S3 method for class 'drift'
summary(object, ...)  
## S3 method for class 'summary.drift'
print(x, digit = 5, ...)
```
**summary.drift**

**Arguments**

- **object**
  - an object of class ""drift"", a result of a call to `drift`.
- **x**
  - an object of class ""summary.drift"", a result of a call to `summary.drift`.
- **digit**
  - the number of significant digits to use when printing.
- **...**
  - further arguments passed to or from other methods.

**Value**

The function 'summary.drift' returns a list of summary values of the group sequential boundary calculations given in 'object'.

**Author(s)**

Oscar A. Perez and T. Charles Casper <charlie.casper@hs.c.utah.edu>

**References**


Fortran program 'ld98' by the same authors as above.


**See Also**

- `bounds` for computation of boundaries using alpha spending function method. `drift` for exit probabilities given boundaries or drift (effect) or confidence interval given power.

**Examples**

```r
# See function 'drift'
```
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