

# Package ‘ldbounds’

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**Type** Package

**Title** Lan-DeMets Method for Group Sequential Boundaries

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**Imports** lattice

**Description** Computations related to group sequential boundaries. Includes calculation of bounds using the Lan-DeMets alpha spending function approach.

**License** GPL ( $\geq 2$ )

**NeedsCompilation** no

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 bounds

*Group Sequential Boundaries Using Spending Functions*


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### 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:

<code>bounds.type</code>	the type of bounds: 1 is 'one-sided', 2 is 'two-sided symmetric', and 3 is 'two-sided asymmetric'.
<code>spending.type</code>	the type(s) of spending function. A descriptive version of the value(s) used for <code>iuse</code>
<code>time</code>	the original time scale.
<code>time2</code>	the second (information) time scale.
<code>alpha</code>	the alpha(s) used.
<code>overall.alpha</code>	if two-sided, the sum of the two alphas. If one-sided, just alpha.
<code>lower.bounds</code>	the vector of lower boundaries calculated. Should be ignored if one-sided.
<code>upper.bounds</code>	the vector of upper boundaries calculated.
<code>exit.pr</code>	the vector of cumulative exit probabilities at each analysis.
<code>diff.pr</code>	the vector of exit probabilities accumulated at each analysis.

### Author(s)

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### References

Reboussin, D. M., DeMets, D. L., Kim, K. M., and Lan, K. K. G. (2000) Computations for group sequential boundaries using the Lan-DeMets spending function method. *Controlled Clinical Trials*, 21:190-207.

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

DeMets, D. L. and Lan, K. K. G. (1995) *Recent Advances in Clinical Trial Design and Analysis*, Thall, P. F. (ed.). Boston: Kluwer Academic Publishers.

Lan, K. K. G. and DeMets, D. L. (1983) Discrete sequential boundaries for clinical trials. *Biometrika*, 70:659-63.

### See Also

Generic functions [summary.bounds](#) and [plot.bounds](#).

[drift](#) for exit probabilities given boundaries or drift (effect) or confidence interval given power.

**Examples**

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

t <- seq(0.2,1,length=5)
obf.bd <- bounds(t,iuse=c(1,1),alpha=c(0.025,0.025))
summary(obf.bd)
plot(obf.bd)

t <- c(0.2292,0.3333,0.4375,0.5833,0.7083,0.8333)
t2 <- c(56,77,126,177,247,318)
power.fam <- bounds(t,t2,iuse=c(3,3),alpha=c(0.025,0.025))
summary(power.fam)
```

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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**

```
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.

**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**

- Reboussin, D. M., DeMets, D. L., Kim, K. M., and Lan, K. K. G. (2000) Computations for group sequential boundaries using the Lan-DeMets spending function method. *Controlled Clinical Trials*, 21:190-207.
- Fortran program 'ld98' by the same authors as above.
- DeMets, D. L. and Lan, K. K. G. (1995) *Recent Advances in Clinical Trial Design and Analysis*, Thall, P. F. (ed.). Boston: Kluwer Academic Publishers.
- Lan, K. K. G. and DeMets, D. L. (1983) Discrete sequential boundaries for clinical trials. *Biometrika*, 70:659-63.

**See Also**

Generic functions [summary.drift](#) and [plot.drift](#).

[bounds](#) for computation of boundaries using alpha spending function method.

**Examples**

```
## 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)

t <- c(0.2292,0.3333,0.4375,0.5833,0.7083,0.8333)
upper <- c(2.53,2.61,2.57,2.47,2.43,2.38)
drift.ci <- drift(zb=upper,t=t,conf=0.95,zval=2.82)
summary(drift.ci)
plot(drift.ci)

## 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**

```
## 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**

<code>x</code>	an object of class <code>"bounds"</code> or <code>"drift"</code> .
<code>main</code>	an overall title for the plot: see <code>title</code> .
<code>xlab</code>	a title for the x axis: see <code>title</code> .
<code>ylab</code>	a title for the y axis: see <code>title</code> .
<code>...</code>	graphical parameters can be given as arguments to <code>plot</code> .

**Author(s)**

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**References**

Reboussin, D. M., DeMets, D. L., Kim, K. M., and Lan, K. K. G. (2000) Computations for group sequential boundaries using the Lan-DeMets spending function method. *Controlled Clinical Trials*, 21:190-207.

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

DeMets, D. L. and Lan, K. K. G. (1995) *Recent Advances in Clinical Trial Design and Analysis*, Thall, P. F. (ed.). Boston: Kluwer Academic Publishers.

Lan, K. K. G. and DeMets, D. L. (1983) Discrete sequential boundaries for clinical trials. *Biometrika*, 70:659-63.

**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**

```
## See 'bounds' or 'drift'.
```

---

summary.bounds

*Summary for Group Sequential Boundaries*

---

**Description**

'summary' method for class '"bounds"'.

**Usage**

```
## 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)**

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**References**

Reboussin, D. M., DeMets, D. L., Kim, K. M., and Lan, K. K. G. (2000) Computations for group sequential boundaries using the Lan-DeMets spending function method. *Controlled Clinical Trials*, 21:190-207.

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

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Lan, K. K. G. and DeMets, D. L. (1983) Discrete sequential boundaries for clinical trials. *Biometrika*, 70:659-63.

**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**

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

---

summary.drift

*Summary for Computations Related to Group Sequential Boundaries*

---

**Description**

'summary' method for class '"drift"'.

**Usage**

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



**Arguments**

object	an object of class <code>"drift"</code> , a result of a call to <code>drift</code> .
x	an object of class <code>"summary.drift"</code> , a result of a call to <code>summary.drift</code> .
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)**

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**References**

Reboussin, D. M., DeMets, D. L., Kim, K. M., and Lan, K. K. G. (2000) Computations for group sequential boundaries using the Lan-DeMets spending function method. *Controlled Clinical Trials*, 21:190-207.

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**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**

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

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