

# Package ‘PwrGSD’

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**Title** Power in a Group Sequential Design

**Version** 2.3.8

**Depends** survival

**Description** Tools for the evaluation of interim analysis plans for sequentially monitored trials on a survival endpoint; tools to construct efficacy and futility boundaries, for deriving power of a sequential design at a specified alternative, template for evaluating the performance of candidate plans at a set of time varying alternatives. See Izmirlian, G. (2014) <[doi:10.4310/SII.2014.v7.n1.a4](https://doi.org/10.4310/SII.2014.v7.n1.a4)>.

**Maintainer** Grant Izmirlian <[izmirlig@mail.nih.gov](mailto:izmirlig@mail.nih.gov)>

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**Author** Grant Izmirlian [aut, cre]

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## Contents

agghaz . . . . .	2
as.boundaries . . . . .	3
CDFOR2LRR . . . . .	4
CondPower . . . . .	4
cpd.PwrGSD . . . . .	5
CRRtoRR . . . . .	10
CY2TOShaz . . . . .	11
detail . . . . .	12
DX . . . . .	12
Elements . . . . .	13
EX1gXK . . . . .	14
GrpSeqBnds . . . . .	15
gsd.dens . . . . .	19
Haybittle . . . . .	21
IntSurvDiff . . . . .	23
LanDemets . . . . .	25

lookup . . . . .	27
lung . . . . .	28
mystack . . . . .	29
mysurvfit . . . . .	30
ObrienFleming . . . . .	31
plot.cpd.PwrGSD . . . . .	32
Pocock . . . . .	33
Pow . . . . .	34
Power . . . . .	36
PwrGSD . . . . .	37
RCM2RR . . . . .	45
RR2RCM . . . . .	46
SC . . . . .	46
SCtoBdry . . . . .	49
SimGSB . . . . .	50
wtdlogrank . . . . .	51

<b>Index</b>	<b>54</b>
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agghaz	<i>Aggregated Hazard</i>
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---

### Description

Computes the MLE for the model that assumes piecewise constant hazards on intervals defined by a grid of points. One applications for example is to calculate monthly hazard rates given numbers of events, numbers at risk and event times reported to the day. Can also handle time to event data stratified on a blocking factor.

### Usage

```
agghaz(t.agg, time, nrisk, nevent)
```

### Arguments

t.agg	Vector defining intervals upon which the user wants constant hazard rates.
time	Event times, possibly stratified on a blocking factor into multiple columns, in units that occur in enough numbers per interval specified above. If there is just a single column then it must be in column form (see example below).
nrisk	Numbers at risk at specified event times
nevent	Numbers of events at specified event times

### Value

time.a	User supplied left-hand endpoints of intervals of hazard constancy
nrisk.a	Numbers at risk on specified intervals
nevent.a	Numbers of events on specified intervals

**Author(s)**

Grant Izmirlian <izmirlian@nih.gov>

**Examples**

```
library(PwrGSD)
data(lung)
fit.msf <- mysurvfit(Surv(time, I(status==2)) ~ sex, data=lung)

## A single stratum:
with(fit.msf$Table, agghaz(30, time, cbind(nrisk.sex1), cbind(nevent.sex1)))

## Multiple strata--pooled and group 1:
with(fit.msf$Table, agghaz(30, time, cbind(nrisk.sex1+nrisk.sex2,nrisk.sex1),
                                         cbind(nevent.sex1+nevent.sex2,nevent.sex1)))
```

---

as.boundaries

*Convert a "PwrGSD" object to a "boundaries" object*

---

**Description**

Convert a PwrGSD object to a boundaries object

**Usage**

```
as.boundaries(object, ...)
```

**Arguments**

object	an object of class PwrGSD
...	if object is of class PwrGSD and there are more than one statistic under investigation, then you may specify an argument stat. The default value is 1, meaning the first one.

**Value**

an object of class boundaries. See the documentation for [GrpSeqBnds](#)

**Author(s)**

Grant Izmirlian <izmirlian@nih.gov>

**See Also**

[GrpSeqBnds](#)

**Examples**

```
## none as yet
```

---

 CDFOR2LRR

*Convert CDF Odds Ratio to Logged Relative Risks*


---

### Description

Given the values of the baseline hazard and odds ratio of the CDF at a grid of time points find the corresponding logged risk ratio.

### Usage

```
CDFOR2LRR(tcut, tmax, h0, CDFOR)
```

### Arguments

tcut	Grid of time points (left endpoints)
tmax	The right endpoint of the last interval
h0	Values of the baseline hazard function on given intervals
CDFOR	Values of the odds ratio of the CDF's on the given intervals

### Value

An m by 2 matrix, where m=length(tcut), having columns 'tcut' and logged RR.

### Author(s)

Grant Izmirlian <izmirlian@nih.gov>

---

 CondPower

*Conditional type I and type II error probabilities given current value of the test statistic*


---

### Description

Computes conditional type I and type II error probabilities given current value of the test statistic for monitoring based upon stochastic curtailment. This is now obsolete and included in the functionality of "GrpSeqBnds" and is here for instructional purposes only.

### Usage

```
CondPower(Z, frac, drift, drift.end, err.I, sided = 1)
```

**Arguments**

Z	Current value of test statistic standardized to unit variance.
frac	Current value of the information fraction (variance fraction).
drift	Current value of the drift, i.e. the expected value of the test statistic normalized to have variance equal to the information fraction. Required if you want to compute conditional type II error, otherwise enter 0.
drift.end	Projected value of the drift at the end of the trial.
err.I	Overall (total) type I error probability
sided	Enter 1 or 2 for sided-ness of the test.

**Value**

A named numeric vector containing the two components “Pr.cond.typeIerr” and “Pr.cond.typeIIerr”

**Author(s)**

Grant Izmirlian <izmirlian@nih.gov>

**References**

A General Theory on Stochastic Curtailment for Censored Survival Data D. Y. Lin, Q. Yao, Zhiliang Ying Journal of the American Statistical Association, Vol. 94, No. 446 (Jun., 1999), pp. 510-521

**See Also**

[GrpSeqBnds](#)

**Examples**

```
## None as yet
```

---

cpd.PwrGSD

*Create a skeleton compound PwrGSD object*

---

**Description**

Given a user defined indexing dataframe as its only argument, creates a skeleton compound PwrGSD object having a component `Elements`, a list of PwrGSD objects, of length equal to the number of rows in the indexing dataframe

**Usage**

```
cpd.PwrGSD(descr)
```

**Arguments**

`descr` A dataframe of a number of rows equal to the length of the resulting list, `Elements`, of `PwrGSD` objects. The user defines the mapping between rows of `descr` and components of `Elements` and uses it to set up a loop over scenarios. There are several S3 classes and methods for example `plot.cpd.PwrGSD`, which exploit this mapping between characteristics of a run and the rows of `descr` for subsetting and constructing conditioned plots. See the example below.

**Value**

An object of class `cpd.PwrGSD` containing elements:

<code>date</code>	the POSIX date that the object was created—its quite useful
<code>Elements</code>	a list of length equal to the number of rows of <code>descr</code> which will later contain objects of class <code>PwrGSD</code>
<code>descr</code>	a copy of the indexing dataframe argument for use in navigating the compound object in subsequent calls to other functions such as the related <code>plot</code> method, and the subset extractor, <code>Elements</code>

**Note**

A `cpd.PwrGSD` object essentially a list of `PwrGSD` objects that a user may set up in order to investigate the space of possible trial scenarios, test statistics, and boundary construction options. One could store a list of results without appealing at all to these internal indexing capabilities. The advantage of setting up a `cpd.PwrGSD` object is the nice summarization functionality provided, for example the `plot` method for the `cpd.PwrGSD` class.

The key ingredient to (i) the construction of the empty object, (ii) and summarizing the results in tabular or plotted form via its manipulation in subsequent function calls, is the indexing dataset, `descr` (for description). The correspondence between rows of `descr` and elements in the list of `PwrGSD` objects is purposely left very loose. In the example outlined below, the user creates a “base case” call to `PwrGSD` and then decides which quantities in this “base case” call to vary in order to navigate the space of possible trial scenarios, monitoring statistics and boundary construction methods. Next, for each one of these settings being varied, a variable with levels that determine each possible setting is created. The dataset `descr` is created with one line corresponding to each combination of the selection variables so created. In order to ensure that there is 1-1 correspondence between the order of the rows in `descr` and the order in the list `Elements` of `PwrGSD` objects, the user carries out the computation in a loop over rows of `descr` in which the values of the selection variables in each given row of `descr` are used to create the corresponding component of `Elements` via an update the “base case” call.

**Author(s)**

Grant Izmirlian <izmirlian@nih.gov>

**See Also**

[Elements](#), [plot.cpd.PwrGSD](#) and [Power](#)

## Examples

```

## don't worry--these examples are guaranteed to work,
## its just inconvenient for the package checker
## Not run:
  library(PwrGSD)

## In order to set up a compound object of class `cpd.PwrGSD'
## we first construct a base case: a two arm trial randomized in just
## under eight years with a maximum of 20 years of follow-up.
## We compute power at a specific alternative, `rhaz', under
## an interim analysis plan with roughly one annual analysis, some
## crossover between intervention and control arms, with Efficacy
## and futility boundaries constructed via the Lan-Demets procedure
## with O'Brien-Fleming spending on the hybrid scale. Investigate
## the behavior of three weighted log-rank statistics.

test.example <-
  PwrGSD(EfficacyBoundary = LanDemets(alpha = 0.05, spending = ObrienFleming),
        FutilityBoundary = LanDemets(alpha = 0.1, spending = ObrienFleming),
        RR.Futility = 0.82, sided="1<",method="A",accru =7.73, accrat =9818.65,
        tlook =c(7.14, 8.14, 9.14, 10.14, 10.64, 11.15, 12.14, 13.14,
                 14.14, 15.14, 16.14, 17.14, 18.14, 19.14, 20.14),
        tcut0 =0:19, h0 =c(rep(3.73e-04, 2), rep(7.45e-04, 3),
                          rep(1.49e-03, 15)),
        tcut1 =0:19, rhaz =c(1, 0.9125, 0.8688, 0.7814, 0.6941,
                             0.6943, 0.6072, 0.5202, 0.4332, 0.6520,
                             0.6524, 0.6527, 0.6530, 0.6534, 0.6537,
                             0.6541, 0.6544, 0.6547, 0.6551, 0.6554),
        tcutc0 =0:19, hc0 =c(rep(1.05e-02, 2), rep(2.09e-02, 3),
                             rep(4.19e-02, 15)),
        tcutc1 =0:19, hc1 =c(rep(1.05e-02, 2), rep(2.09e-02, 3),
                             rep(4.19e-02, 15)),
        tcutd0B =c(0, 13), hd0B =c(0.04777, 0),
        tcutd1B =0:6, hd1B =c(0.1109, 0.1381, 0.1485, 0.1637, 0.2446,
                              0.2497, 0),
        noncompliance =crossover, gradual =TRUE,
        WtFun =c("FH", "SFH", "Ramp"),
        ppar =c(0, 1, 0, 1, 10, 10))

## we will construct a variety of alternate hypotheses relative to the
## base case specified above

rhaz <-
  c(1, 0.9125, 0.8688, 0.7814, 0.6941, 0.6943, 0.6072, 0.5202, 0.4332,
    0.652, 0.6524, 0.6527, 0.653, 0.6534, 0.6537, 0.6541, 0.6544,
    0.6547, 0.6551, 0.6554)

max.effect <- 0.80 + 0.05*(0:8)
n.me <- length(max.effect)

## we will also vary extent of censoring relative to the base case
## specified above

```

```

hc <- c(rep(0.0105, 2), rep(0.0209, 3), rep(0.0419, 15))

cens.amt <- 0.75 + 0.25*(0:2)
n.ca <- length(cens.amt)

## we may also wish to compare the Lan-Demets/O'Brien-Fleming efficacy
## boundary with a Lan-Demets/linear spending boundary

Eff.bound.choice <- 1:2
ebc.nms <- c("LanDemets(alpha=0.05, spending=ObrienFleming)",
            "LanDemets(alpha=0.05, spending=Pow(1))")
n.ec <- length(Eff.bound.choice)

## The following line creates the indexing dataframe, `descr`, with one
## line for each possible combination of the selection variables we've
## created.

descr <- as.data.frame(
  cbind(Eff.bound.choice=rep(Eff.bound.choice, each=n.ca*n.me),
        cens.amt=rep(rep(cens.amt, each=n.me), n.ec),
        max.effect=rep(max.effect, n.ec*n.ca))

descr$Eff.bound.choice <- ebc.nms[descr$Eff.bound.choice]

## Now descr contains one row for each combination of the levels of
## the user defined selection variables, `Eff.bound.choice`,
## `max.effect` and `cens.amt`. Keep in mind that the names and number
## of these variables is arbitrary. Next we create a skeleton
## `cpd.PwrGSD` object with a call to the function `cpd.PwrGSD` with
## argument `descr`

test.example.set <- cpd.PwrGSD(descr)

## Now, the newly created object, of class `cpd.PwrGSD`, contains
## an element `descr`, a component `date`, the date created
## and a component `Elements`, an empty list of length equal
## to the number of rows in `descr`. Next we do the computation in
## a loop over the rows of `descr`.

n.descr <- nrow(descr)

for(k in 1:n.descr){

  ## First, we copy the original call to the current call,
  ## `Elements[[k]]$call`

  test.example.set$Elements[[k]]$call <- test.example$call

  ## Use the efficacy boundary choice in the kth row of `descr`
  ## to set the efficacy boundary choice in the current call

```

```

test.example.set$Elements[[k]]$call$EfficacyBoundary <-
  parse(text=as.character(descr[k,"Eff.bound.choice"]))[[1]]

## Derive the `rhaz` defined by the selection variable "max.effect"
## in the kth row of `descr` and use this to set the `rhaz`
## components of the current call

test.example.set$Elements[[k]]$call$rhaz <-
  exp(descr[k,"max.effect"] * log(rhaz))

## Derive the censoring components from the selection variable
## "cens.amt" in the kth row of `descr` and place that result
## into the current call

test.example.set$Elements[[k]]$call$hc0 <-
test.example.set$Elements[[k]]$call$hc1 <- descr[k, "cens.amt"] * hc

## Now the current call corresponds exactly to the selection
## variable values in row `k` of `descr`. The computation is
## done by calling `update`

test.example.set$Elements[[k]] <- update(test.example.set$Elements[[k]])
cat(k/n.descr, "\r")
}

## We can create a new `cpd.PwrGSD` object by subsetting on
## the selection variables in `descr`:

Elements(test.example.set,
  subset=(substring(Eff.bound.choice, 32, 34)=="Obr" &
    max.effect >= 1))

## or we can plot the results -- see the help under `plot.cpd.PwrGSD`

plot(test.example.set, formula = ~ max.effect | stat * cens.amt,
  subset=(substring(Eff.bound.choice, 32, 34)=="Obr"))

plot(test.example.set, formula = ~ max.effect | stat * cens.amt,
  subset=(substring(Eff.bound.choice, 32, 34)=="Pow"))

## Notice the appearance of the selection variable `stat` which was
## not defined in the dataset `descr`.

## Recall that each single "PwrGSD" object can contain results
## for a list of test statistics, as in the example shown here where
## we have results on three statistics per component of `Elements`.
## For this reason the variable `stat` can be also be referenced in
## the `subset` or `formula` arguments of calls to this `plot` method,
## and in the `subset` argument of the function `Power` shown below.

## The function `Power` is used to convert the `cpd.PwrGSD` object
## into a dataframe, stacked by rows of `descr` and by `stat`

```

```

## (there are three statistics being profiled per each component of
## `Elements'), for generating tables or performing other
## computations.

Power(test.example.set,
      subset=(substring(Eff.bound.choice, 32, 34)=="Pow" & stat %in% c(1,3)))

## End(Not run)

```

---

CRRtoRR

*Cumulative-risk ratios to risk ratios*


---

### Description

Given a vector of cumulative-risk ratios, computes risk ratios

### Usage

```
CRRtoRR(CRR, DT, h = NULL)
```

### Arguments

CRR	vector of cumulative risk ratios of length $m$
DT	vector of time increments upon which the cumulative ratios represent. For example if the hazard takes values $h_1, h_2, \dots, h_m$ on the intervals $[t_1, t_2), [t_2, t_3), \dots, [t_m, t_{\{m+1\}})$ then DT will be $c(t_2-t_1, t_3-t_2, \dots, t_{\{m+1\}}-t_m)$
h	The hazard in the reference arm, of length $m$

### Value

The vector of risk ratios at the  $m$  time points

### Author(s)

Grant Izmirlian <izmirlian@nih.gov>

### Examples

```
## none as yet
```

---

`CY2TOShaz`*Calender year rates to Study Year Rates*

---

**Description**

Given the cutpoints at which the hazard is to be constant, the values taken by the calender year rates and the calender time offset from the start of the trial at which randomization ended, this function converts to time on study rates, assuming uniform accrual.

**Usage**

```
CY2TOShaz(tcut, t.eor, m, verbose = FALSE)
```

**Arguments**

<code>tcut</code>	Left hand endpoints of intervals on which time on study hazard is taken to be constant
<code>t.eor</code>	Time offsest from the beginning of the trial at which randomization ended
<code>m</code>	Annual calender time rates
<code>verbose</code>	do you want to see alot of debugging info—defaults to FALSE

**Value**

```
hazard = h, table = attr(obj., "tbl")
```

`hazard` time on study hazard values taken on intervals specified by the argument `tcut`

`table` a table containg the observed and fitted values

**Author(s)**

Grant Izmirlian <izmirlian@nih.gov>

**Examples**

```
## none as yet
```

---

detail	<i>Function to extract the 'detail' component from a PwrGSD object</i>
--------	--

---

**Description**

Extracts the 'detail' component from an object of class PwrGSD

**Usage**

detail(obj)

**Arguments**

obj	An object of class PwrGSD returned from the function PwrGSD or a component of the list returned by the function cpd.PwrGSD
-----	--

**Value**

The 'detail' component of the object. For the Asymptotic method, this will be most of the quantities involved in the computation, the input parameters such as the various incidence rates, cross over rates etc, as well as intermediate computations such as the drift function variance function as well. For the simulation method, some of these are returned in addition, the simulated event histories.

**Author(s)**

Grant Izmirlian <izmirlian at nih dot gov>

---

DX	<i>A utility function for forming differences</i>
----	---

---

**Description**

DX(x) returns c(x[1], diff(x))

**Usage**

DX(x)

**Arguments**

x	A grid of time points (increasing)
---	------------------------------------

**Value**

DX(x) returns c(x[1], diff(x))

**Author(s)**

Grant Izmirlian <izmirlian@nih.gov>

---

Elements

*Create a subset of a "cpd.PwrGSD" object*

---

**Description**

Create a subset of a cpd.PwrGSD object

**Usage**

```
Elements(object, subset, na.action = na.pass)
```

**Arguments**

object	an object of class cpd.PwrGSD
subset	you may extract a subset via a logical expression in the variables of the index dataframe, descr
na.action	a method for handling NA values in the variables in the subset expression.

**Value**

an object of class cpd.PwrGSD. See help on that topic for details.

**Author(s)**

Grant Izmirlian <izmirlian@nih.gov>

**See Also**

[cpd.PwrGSD](#) and [PwrGSD](#)

**Examples**

```
## See the `cpd.PwrGSD` example
```

---

EX1gXK                      *A function for computing the bias adjusted point estimate for a statistic observed to cross the efficacy boundary.*

---

**Description**

A function for computing the bias adjusted point estimate for a statistic, on the Brownian scale, observed to cross the efficacy boundary.

**Usage**

```
EX1gXK(xk, b.eff, frac)
```

**Arguments**

xk	The observed value of the statistic, on the “Brownian” scale.
b.eff	Efficacy boundary points at current and prior analyses
frac	Information fraction at current and prior analyses

**Value**

Returns the expected value of  $X_1$  given  $X_K$ , which is the bias adjusted point estimate

**Note**

This works for the unweighted, proportional hazards case, but also works in the case of the weighted log-rank statistic when we assume the chosen weights are proportional to the true shape.

**Author(s)**

Grant Izmirlian <izmirlig@mail.nih.gov>

**References**

Emerson, S. S. (1993). Computation of the uniform minimum variance unbiased estimator of a normal mean following a group sequential trial discrete sequential boundaries for clinical trials. *Computers and Biomedical Research* 26 68–73.

Izmirlian, G. (2014). Estimation of the relative risk following group sequential procedure based upon the weighted log-rank statistic. *Statistics and its Interface* 00 00–00

**See Also**

[gsd.dens](#)

**Examples**

```

# if  $Z.K = U_K/V_K^{0.5}$  is the log-rank statistic on the standard normal
# scale, then we obtain an estimate of the logged relative risk as follows
# Suppose we've stopped at analysis number  $K=4$ , and  $Z.K = 2.5$ 
# suppose the end of trial variance of the log-rank statistic
# (specified in design and used to compute 'frac') is  $V.end = 100$ 

K <- 4
Z.K <- 2.5
V.end <- 100

# Information fraction
frac <- c(0.15, 0.37, 0.64, 0.76)

# Efficacy Boundary
gsb <- GrpSeqBnds(frac=frac, EfficacyBoundary=LanDemets(spending=ObrienFleming, alpha=0.05))

# Efficacy boundary points
be <- gsb$table[,"b.e"]

# Brownian scale
X.K <- Z.K*frac[K]

# expected value of  $X_1$  given  $X_K$ 
ex1gxk <- EX1gXK(X.K, be, frac)

# Crude estimate of logged relative risk
X.K/(frac[K]*V.end^0.5)

# Bias adjusted estimate of logged relative risk
ex1gxk/(frac[1]*V.end^0.5)

```

---

GrpSeqBnds

*Computes efficacy and futility boundaries*


---

**Description**

This computes efficacy and futility boundaries for interim analysis and sequential designs. Two sided symmetric efficacy boundaries can be computed by specifying half of the intended total type I error probability in the argument, Alpha.Efficacy. Otherwise, especially in the case of efficacy and futility bounds only one sided boundaries are currently computed. The computation allows for two different time scales—one must be the variance ratio, and the second can be a user chosen increasing scale beginning with 0 that takes the value 1 at the conclusion of the trial.

**Usage**

```

GrpSeqBnds(EfficacyBoundary = LanDemets(alpha = 0.05, spending = ObrienFleming),
           FutilityBoundary = LanDemets(alpha = 0.1, spending = ObrienFleming),
           NonBindingFutility = TRUE, frac, frac.ii = NULL, drift = NULL)

```

**Arguments**

## EfficacyBoundary

This specifies the method used to construct the efficacy boundary. The available choices are:

‘(i) ’Lan-Demets(alpha=<total type I error>, spending=<spending function>). The Lan-Demets method is based upon a error probability spending approach. The spending function can be set to ObrienFleming, Pocock, or Power(rho), where rho is the the power argument for the power spending function: rho=3 is roughly equivalent to the O’Brien-Fleming spending function and smaller powers result in a less conservative spending function.

‘(ii) ’Haybittle(alpha=<total type I error>, b.Haybittle=<user specified boundary point>). The Haybittle approach is conceptually the simplest of all methods for efficacy boundary construction. However, as it spends nearly no alpha until the end, is for all practical purposes equivalent to a single analysis design and to be considered overly conservative. This method sets all the boundary points equal to b.Haybittle, a user specified value (try 3) for all analyses except the last, which is calculated so as to result in the total type I error, set with the argument alpha.

‘(iii) ’SC(be.end=<efficacy boundary point at trial end>, prob=<threshold for conditional type I error for efficacy stopping>). The stochastic curtailment method is based upon the conditional probability of type I error given the current value of the statistic. Under this method, a sequence of boundary points on the standard normal scale (as are boundary points under all other methods) is calculated so that the total probability of type I error is maintained. This is done by considering the joint probabilities of continuing to the current analysis and then exceeding the threshold at the current analysis. A good value for the threshold value for the conditional type I error, prob is 0.90 or greater.

‘(iv) ’User supplied boundary points in the form c(b1, b2, b3, . . . , b\_m), where m is the number of looks.

## FutilityBoundary

This specifies the method used to construct the futility boundary. The available choices are:

‘(i) ’Lan-Demets(alpha=<total type II error>, spending=<spending function>). The Lan-Demets method is based upon a error probability spending approach. The spending function can be set to ObrienFleming, Pocock, or Power(rho), where rho is the the power argument for the power spending function: rho=3 is roughly equivalent to the O’Brien-Fleming spending function and smaller powers result in a less conservative spending function.

‘NOTE: ’there is no implementation of the Haybittle method for futility boundary construction. Given that the futility boundary depends upon values of the drift function, this method doesn’t apply.

‘(ii) ’SC(be.end=<efficacy boundary point at trial end>, prob=<threshold for conditional type II error for futility stopping>, drift.end=<projected drift at end of trial>). The stochastic curtailment method is based upon the conditional probability of type II error given the current value of the statistic. Under this method, a sequence of boundary points on the standard normal scale (as are boundary points under all other methods) is calculated so that the total proba-

bility of type II error, is maintained. This is done by considering the joint probabilities of continuing to the current analysis and then exceeding the threshold at the current analysis. A good value for the threshold value for the conditional type I error, `prob` is 0.90 or greater.

‘(iii) ’User supplied boundary points in the form `c(b1, b2, b3, . . . , b_m)`, where `m` is the number of looks.

#### NonBindingFutility

When using a futility boundary and this is set to ‘TRUE’, the efficacy boundary will be constructed in the absence of the futility boundary, and then the futility boundary will be constructed given the resulting efficacy boundary. This results in a more conservative efficacy boundary with true type I error less than the nominal level. This is recommended due to the fact that futility crossings are viewed by DSMB’s with much less gravity than an efficacy crossing and as such, the consensus is that efficacy bounds should not be discounted towards the null hypothesis because of paths which cross a futility boundary. Default value is ‘TRUE’.

<code>frac</code>	The variance ratio. If the end of trial variance is unknown then normalize all previous variances by the current variance. In this case you must specify a second scale that is monotone increasing from 0 to 1 at the end of the trial. Required.
<code>frac.ii</code>	The second information scale that is used for type I and type II error probability spending. Optional (see above)
<code>drift</code>	The drift function of the underlying brownian motion, which is the expected value under the design alternative of the un-normalized weighted log-rank statistic, then normalized to have variance one when the variance ratio equals 1. See the examples below.

#### Value

An object of class `boundaries` with components: `"table" "frac" "frac.ii" "drift" "call"`

<code>call</code>	The call that produced the returned results.
<code>frac</code>	The vector of variance ratios.
<code>frac.ii</code>	The vector of information ratios for type I and type II error probability spending, which differs from the above if the user sets the argument <code>frac.ii</code> to a second scale as mentioned above.
<code>drift</code>	The drift vector that is required as an argument when futility boundaries are calculated.
<code>table</code>	A matrix with components ‘ <code>frac</code> ’ The information ratio for type I and type II error probability spending. ‘ <code>b.f</code> ’ The calculated futility boundary (if requested). ‘ <code>alpha.f</code> ’ The type II error probability spent at that analysis (if doing futility bounds). ‘ <code>cum-alpha.f</code> ’ Cumulative sum of <code>alpha.f</code> (if doing futility bounds). ‘ <code>b.e</code> ’ The calculated efficacy boundary. ‘ <code>alpha.e</code> ’ The type I error probability spent at that analysis. ‘ <code>cum-alpha.e</code> ’ Cumulative sum of <code>alpha.e</code> .

**Author(s)**

Grant Izmirlian <izmirlian@nih.gov>

**References**

- Gu, M.-G. and Lai, T.-L. "Determination of power and sample size in the design of clinical trials with failure-time endpoints and interim analyses." *Controlled Clinical Trials* 20 (5): 423-438. 1999
- Izmirlian, G. "The PwrGSD package." NCI Div. of Cancer Prevention Technical Report. 2004
- Jennison, C. and Turnbull, B.W. (1999) *Group Sequential Methods: Applications to Clinical Trials* Chapman & Hall/Crc, Boca Raton FL
- Proschan, M.A., Lan, K.K.G., Wittes, J.T. (2006), corr 2nd printing (2008) *Statistical Monitoring of Clinical Trials A Unified Approach* Springer Verlag, New York
- Izmirlian G. (2014). Estimation of the relative risk following group sequential procedure based upon the weighted log-rank statistic. *Statistics and its Interface* 7(1), 27-42

**See Also**

[PwrGSD](#)

**Examples**

```
## NOTE: In an unweighted analysis, the variance ratios and event ratios
## are the same, whereas in a weighted analysis, they are quite different.
##
## For example, in a trial with 7 or so years of accrual and maximum follow-up of 20 years
## using the stopped Fleming-Harrington weights, `WtFun' = "SFH", with paramaters
## `ppar' = c(0, 1, 10) we might get the following vector of variance ratios:

frac <- c(0.006995655, 0.01444565, 0.02682463, 0.04641363, 0.0585665,
          0.07614902, 0.1135391, 0.168252, 0.2336901, 0.3186155, 0.4164776,
          0.5352199, 0.670739, 0.8246061, 1)

## and the following vector of event ratios:

frac.ii <- c(0.1494354, 0.1972965, 0.2625075, 0.3274323, 0.3519184, 0.40231,
            0.4673037, 0.5579035, 0.6080742, 0.6982293, 0.7671917, 0.8195019,
            0.9045182, 0.9515884, 1)

## and the following drift under a given alternative hypothesis

drift <- c(0.06214444, 0.1061856, 0.1731267, 0.2641265, 0.3105231, 0.3836636,
          0.5117394, 0.6918584, 0.8657705, 1.091984, 1.311094, 1.538582,
          1.818346, 2.081775, 2.345386)

## JUST ONE SIDED EFFICACY BOUNDARY
## In this call, we calculate a one sided efficacy boundary at each of 15 analyses
## which will occur at the given (known) variance ratios, and we use the variance
## ratio for type I error probability spending, with a total type I error probability
## of 0.05, using the Lan-Demets method with O'Brien-Fleming spending (the default).
```

```

gsb.all.just.eff <- GrpSeqBnds(frac=frac,
                             EfficacyBoundary=LanDemets(alpha=0.05, spending=ObrienFleming))

## ONE SIDED EFFICACY AND FUTILITY BOUNDARIES
## In this call, we calculate a one sided efficacy boundary at each of 15 analyses
## which will occur at the given (known) variance ratios, and we use the variance
## ratio for type I and type II error probability spending, with a total type I error
## probability of 0.05 and a total type II error probability of 0.10, using the Lan-Demets
## method with Obrien-Fleming spending (the default) for both efficacy and futility.

gsb.all.eff.fut <- GrpSeqBnds(frac=frac,
                             EfficacyBoundary=LanDemets(alpha=0.05, spending=ObrienFleming),
                             FutilityBoundary=LanDemets(alpha=0.10, spending=ObrienFleming),
                             drift=drift)

## Now suppose that we are performing the 7th interim analysis. We don't know what the variance
## will be at the end of the trial, so we normalize variances of the current and previous
## statistics by the variance of the current statistic. This is equivalent to the following
## length 7 vector of variance ratios:

frac7 <- frac[1:7]/frac[7]

## To proceed under the "unknown variance at end of trial" case, we must use a second
## scale for spending type I and II error probability. Unlike the above scale
## which is renormalized at each analysis to have value 1 at the current analysis, the
## alpha spending scale must be monotone increasing and attain the value 1 only at the
## end of the trial. A natural choice is the event ratio, which is known in advance if
## the trial is run until a required number of events is obtained, a so called
## maximum information trial:

frac7.ii <- frac.ii[1:7]

## the first seven values of the drift function

drift7 <- drift[1:7]/frac[7]^0.5

gsb.1st7.eff.fut <- GrpSeqBnds(frac=frac7, frac.ii=frac7.ii,
                             EfficacyBoundary=LanDemets(alpha=0.05, spending=ObrienFleming),
                             FutilityBoundary=LanDemets(alpha=0.10, spending=ObrienFleming),
                             drift=drift7)

## Of course there are other options not covered in these examples but this should get you
## started

```

**Description**

A function for computing the probability density for a sequentially monitored test. This is the joint density, in the rejection region, of  $(X_K, K)$ , where  $X_K$  is the observed value of the test statistic upon efficacy boundary crossing, and  $K$  is the analysis number at which the efficacy boundary was crossed.

**Usage**

```
gsd.dens(x, frac = NULL, scale="Standard")
```

**Arguments**

<code>x</code>	The main argument, <code>x</code> , is either a object of class “boundaries” or a numeric vector. If it is of class “boundaries” then no other arguments are required. If it is a numeric vector then the <code>frac</code> argument must be specified. See below. In this case, <code>x</code> will be the observed values of the statistic at the current and all prior analyses, either on the standard normal scale (the default) or on the “Brownian” scale. For “Brownian” scale, set argument <code>scale</code> to “Brownian”.
<code>frac</code>	Required only when the main argument, <code>x</code> , is a numeric vector, and must be a vector of the same length. In this case, <code>frac</code> will be the information at the current and all prior interim analyses.
<code>scale</code>	Required only when the main argument, <code>x</code> , is a numeric vector. A switch indicating whether the elements of the numeric vector, <code>x</code> , are specified on the standard normal scale, <code>x</code> ="Standard", or on the Brownian scale, <code>x</code> ="Brownian".

**Value**

A list with elements `x`, `dF`, `x1c`, and `dF1c`:

<code>x</code>	Node points used in Gaussian quadrature. See examples below.
<code>dF</code>	Probability mass at each node point. See examples below.
<code>x1c</code>	Node points in the continuation region at the first analysis.
<code>dF1c</code>	Probability mass at each node point in the continuation region at the first analysis.

**Note**

Also used in computation of Rao-Blackwell-ized bias adjusted point estimate for statistic observed to cross the efficacy boundary.

**Author(s)**

Grant Izmirlian <izmirlig@mail.nih.gov>

## References

Emerson, S. S. (1993). Computation of the uniform minimum variance unbiased estimator of a normal mean following a group sequential trial discrete sequential boundaries for clinical trials. *Computers and Biomedical Research* 26 68–73.

Izmirlan, G. (2014). Estimation of the relative risk following group sequential procedure based upon the weighted log-rank statistic. *Statistics and its Interface* 00 00–00

## See Also

[EX1gXK](#)

## Examples

```
# Information fraction
frac <- c(0.15, 0.37, 0.64, 0.76)

# Efficacy Boundary
gsb <- GrpSeqBnds(frac=frac, EfficacyBoundary=LanDemets(spending=ObrienFleming, alpha=0.05))

# To compute the p-value under the stagewise ordering, for an observed
# value of the monitoring statistic 2.1, crossing the efficacy
# boundary at the 4th analysis, we do the following

be <- gsb$table[,"b.e"]
be[4] <- 2.1

sum(gsd.dens(be, frac, scale="Standard")$dF)
```

---

Haybittle

*The Haybittle method of Boundary Construction*

---

## Description

The function `Haybittle` is used in calls to the functions `GrpSeqBnds` and `PwrGSD` as a possible setting for the argument `EfficacyBoundary`. NOTE: the `Haybittle` method is not implemented as a futility boundary method. The `Haybittle` method is one of four currently available choices (efficacy only), the others being `LanDemets`, `SC` (stochastic curtailment), and user specified.

## Usage

```
Haybittle(alpha, b.Haybittle, from = NULL, to = NULL)
```

**Arguments**

alpha	The total probability of type I error.
b.Haybittle	User specified efficacy boundary at all but the last analysis.
from	WARNING EXPERIMENTAL: See the documentation under LanDemets or SC. I'm not quite sure if this works or even makes sense. Don't use it, ok?
to	See above.

**Details**

The Haybittle approach is conceptually the simplest of all methods for efficacy boundary construction. However, as it spends nearly no alpha until the end, is for all practical purposes equivalent to a single analysis design and to be considered overly conservative. This method sets all the boundary points equal to b.Haybittle, a user specified value (try 3) for all analyses except the last, which is calculated so as to result in the total type I error, set with the argument alpha.

**Value**

An object of class `boundary.construction.method` which is really a list with the following components. The print method displays the original call.

type	Gives the boundary construction method type, which is the character string "Haybittle"
alpha	The numeric value passed to the argument 'alpha' which is the total probability of type I error.
b.Haybittle	The numeric value passed to the argument 'b.Haybittle' which is the user specified efficacy boundary at all but the last analysis.
from	Description of 'comp2'
to	You're not using this, right?
call	see above.

**Note**

The print method returns the call by default

**Author(s)**

Grant Izmirlian

**References**

see references under [PwrGSD](#)

**See Also**

[LanDemets](#), [SC](#), [GrpSeqBnds](#), and [PwrGSD](#)

**Examples**

```
## example 1: what is the result of calling a Boundary Construction Method function
## A call to 'Haybittle' just returns the call
Haybittle(alpha=0.05, b.Haybittle=3)

## It does argument checking...this results in an error
## Not run:
Haybittle(alpha=0.05)

## End(Not run)

## but really its value is a list with the a component containing
## the boundary method type, "LanDems", and components for each
## of the arguments.
names(Haybittle(alpha=0.05, b.Haybittle=3))

Haybittle(alpha=0.05, b.Haybittle=3)$type
Haybittle(alpha=0.05, b.Haybittle=3)$alpha
Haybittle(alpha=0.05, b.Haybittle=3)$b.Haybittle
Haybittle(alpha=0.05, b.Haybittle=3)$call

## example 2: ...But the intended purpose of the spending functions
## is in constructing calls to 'GrpSeqBnds' and to 'PwrGSD':

frac <- c(0.07614902,0.1135391,0.168252,0.2336901,0.3186155,
          0.4164776,0.5352199,0.670739,0.8246061,1)

test <- GrpSeqBnds(frac=frac, EfficacyBoundary=Haybittle(alpha=0.025, b.Haybittle=3))
```

---

IntSurvDiff

*Weighted Integrated Survival function test*


---

**Description**

Computes a two sample weighted integrated survival function log-rank statistic with events weighted according to one of the available weighting function choices

**Usage**

```
IntSurvDiff(formula =formula(data), data =parent.frame(), WtFun =c("FH", "SFH", "Ramp"),
            param = c(0, 0), sided = c(2, 1), subset, na.action, w = FALSE)
```

**Arguments**

formula	a formula of the form $\text{Surv}(\text{Time}, \text{Event}) \sim \text{arm}$ where arm is a dichotomous variable with values 0 and 1.
data	a dataframe

WtFun	a selection from the available list: “FH” (Fleming-Harrington), “SFH” (stopped Fleming-Harrington) or “Ramp”. See param in the following line.
param	Weight function parameters. Length and interpretation depends upon the selected value of WtFun: If WtFun==“FH” then param is a length 2 vector specifying the power of the pooled (across arms) kaplan meier estimate and its complement. If WtFun==“SFH” then param is a length 3 vector with first two components as in the “FH” case, and third component the time (in the same units as the time to event) at which the “FH” weight function is capped off at its current value. If WtFun==SFH then param is of length 1 specifying the time (same units as time to event) at which events begin to get equal weight. The “Ramp” weight function is a linearly increasing deterministic weight function which is capped off at 1 at the user specified time.
sided	One or Two sided test? Set to 1 or 2
subset	Analysis can be applied to a subset of the dataframe based upon a logical expression in its variables
na.action	Method for handling NA values in the covariate, arm
w	currently no effect

### Value

An object of class `survtest` containing components

pn	sample size
wtyp	internal representation of the WtFun argument
par	internal representation of the param argument
time	unique times of events accross all arms
nrisk	number at risk accross all arms at each event time
nrisk1	Number at risk in the experimental arm at each event time
nevent	Number of events accross all arms at each event time
nevent1	Number of events in the experimental arm at each event time
wt	Values of the weight function at each event time
pntimes	Number of event times
stat	The un-normalized weighted log-rank statistic, i.e. the summed weighted observed minus expected differences at each event time
var	Variance estimate for the above
pu0	person units of follow-up time in the control arm
pu1	person units of follow-up time in the intervention arm
n0	events in the control arm
n1	events in the intervention arm
n	sample size, same as pn
call	the call that created the object

**Author(s)**

Grant Izmirlian <izmirlian@nih.gov>

**References**

Weiland S, Gail MH, James BR, James KL. (1989). A family of nonparametric statistics for comparing diagnostic makers with paired or unpaired data. *Biometrika* **76**, 585-592.

**See Also**

[wtdlogrank](#)

**Examples**

```
library(PwrGSD)
data(lung)
fit.isd<-IntSurvDiff(Surv(time,I(status==2))~I(sex==2), data=lung, WtFun="SFH", param=c(0,1,300))
```

---

LanDemets

*The Lan-Demets method of Boundary Construction*

---

**Description**

The function LanDemets is used in calls to the functions GrpSeqBnds and PwrGSD as a possible setting for the arguments EfficacyBoundary and FutilityBoundary, in specification of the method whereby efficacy and or futility boundaries are to be constructed. The Lan-Demets method is one of four currently available choices, the others being SC (stochastic curtailment), Haybittle (efficacy only) and user specified.

**Usage**

```
LanDemets(alpha,
  spending, from = NULL, to = NULL)
```

**Arguments**

alpha	If LanDemets is used to specify the EfficacyBoundary then the argument alpha is the total probability of type I error. If LanDemets is used to specify the FutilityBoundary then the argument alpha is the total probability of type II error.
spending	Specify the alpha spending function. Set this to O'BrienFleming, Pow(rho=<x>), or Pocock. See help files for these spending functions.
from	<b>WARNING EXPERIMENTAL:</b> you can actually construct boundaries via a hybrid of the 3 boundary construction methods, LanDemets, SC, and 'user specified'. When using a hybrid boundary, set the argument EfficacyBoundary or FutilityBoundary respectively, to a list with components LanDemets, SC, or user specified numbers. In the former two cases, from and to are used in

LanDemets and also in SC to stipulate how many interim analyses they are in effect. See the help for GrpSeqBnds and PwrGSD

to See above.

### Details

The cornerstone of the Lan-Demets method is that the amount of alpha (type I or II error probability) that is "spent" at a given interim analysis is determined via a user specified "spending function". A spending function is a monotone increasing mapping on (0,1) with range (0,alpha). The 'alpha' spent at a given analysis is determined by the increment in the values of the spending function at the current and at the most recent information fractions.

### Value

An object of class `boundary.construction.method` which is really a list with the following components. The `print` method displays the original call.

type	Gives the boundary construction method type, which is the character string "LanDemets"
alpha	The numeric value passed to the argument 'alpha' which is the total probability of type I (efficacy) or type II (futility) error.
spending	The spending function that was passed to the argument 'spending'. Note that this will be of class 'name' for 'ObrienFleming' and 'Pocock', but will be of class 'function' for 'Pow'
from	The numeric value passed to the argument 'from'. See above.
to	The numeric value passed to the argument 'to'. See above.
call	returns the call

### Note

The `print` method returns the call by default

### Author(s)

Grant Izmirlian

### References

see references under [PwrGSD](#)

### See Also

[SC](#), [ObrienFleming](#), [Pow](#), [Pocock](#), [GrpSeqBnds](#), and [PwrGSD](#)

**Examples**

```
## example 1: what is the result of calling a Boundary Construction Method function
## A call to 'LanDemets' just returns the call
LanDemets(alpha=0.05, spending=ObrienFleming)

## It does arguement checking...this results in an error
## Not run:
LanDemets(alpha=0.05)

## End(Not run)

## but really its value is a list with the a component containing
## the boundary method type, "LanDemets", and components for each
## of the arguments.
names(LanDemets(alpha=0.05, spending=ObrienFleming))

LanDemets(alpha=0.05, spending=ObrienFleming)$type
LanDemets(alpha=0.05, spending=ObrienFleming)$alpha
LanDemets(alpha=0.05, spending=ObrienFleming)$spending
class(LanDemets(alpha=0.05, spending=ObrienFleming)$spending)
LanDemets(alpha=0.05, spending=Pow(2))$spending
class(LanDemets(alpha=0.05, spending=Pow(2))$spending)
LanDemets(alpha=0.05, spending=ObrienFleming)$call

## example 2: ...But the intended purpose of the spending functions is
## in constructing calls to 'GrpSeqBnds' and to 'PwrGSD':

frac <- c(0.07614902,0.1135391,0.168252,0.2336901,0.3186155,
          0.4164776,0.5352199,0.670739,0.8246061,1)
drift <- c(0.3836636,0.5117394,0.6918584,0.8657705,1.091984,
           1.311094,1.538582,1.818346,2.081775,2.345386)

test <- GrpSeqBnds(frac=frac, EfficacyBoundary=LanDemets(alpha=0.05, spending=ObrienFleming),
                  FutilityBoundary=LanDemets(alpha=0.10, spending=Pocock),
                  drift=drift)
```

---

lookup

*Lookup values for a piecewise constant function*


---

**Description**

Given the values and lefthand endpoints for intervals of constancy, lookup values of the function at arbitrary values of the independent variable.

**Usage**

```
lookup(xgrid, ygrid, x, y0 = 0)
```

**Arguments**

xgrid	Lefthand endpoints of intervals of constancy
ygrid	Values on these intervals, of same length as xgrid
x	Input vector of arbitrary independent variables.
y0	Value to be returned for values of x that are smaller than min(xgrid).

**Value**

~Describe the value returned If it is a LIST, use

comp1	Description of 'comp1'
comp2	Description of 'comp2'

**Author(s)**

Grant Izmirlian <izmirlian@nih.gov>

**Examples**

```
## none as yet
```

---

lung

*Mayo Clinic Lung Cancer Data*

---

**Description**

Survival in patients with lung cancer at Mayo Clinic. Performance scores rate how well the patient can perform usual daily activities.

**Usage**

```
data(lung)
```

**Format**

inst:	Institution code
time:	Survival time in days
status:	censoring status 1=censored, 2=dead
age:	Age in years
sex:	Male=1 Female=2
ph.ecog:	ECOG performance score (0=good 5=dead)
ph.karno:	Karnofsky performance score (bad=0-good=100) rated by physician
pat.karno:	Karnofsky performance score rated by patient
meal.cal:	Calories consumed at meals
wt.loss:	Weight loss in last six months

**Source**

Terry Therneau

---

`mystack`*Stack a dataset*

---

**Description**

Given a dataframe containing one or more variables named with a common prefix, this function creates a stacked dataset with one set of observed values of the variables (in order of occurrence) per line.

**Usage**

```
mystack(object, fu.vars, create.idvar = FALSE)
```

**Arguments**

<code>object</code>	a dataframe containing one or more variables named with a common prefix
<code>fu.vars</code>	a list of the unique prefixes
<code>create.idvar</code>	Do you want to add an ID variable with a common value given to all records resulting from a given input record? Default is FALSE

**Value**

A stacked dataframe

**Author(s)**

Grant Izmirlian &lt;izmirlian@nih.gov&gt;

**Examples**

```
## none as yet
```

---

 mysurvfit

*My Survfit*


---

**Description**

Computes numbers at risk, numbers of events at each unique event time within levels of a blocking factor

**Usage**

```
mysurvfit(formula = formula(data), data = parent.frame(), subset, na.action = na.fail)
```

**Arguments**

formula	Should be a formula of the form $\text{Surv}(ti, ev) \sim \text{block}$ where block is the blocking factor. It need not be a factor per se but should have relatively few discrete levels. Sorry, no staggered entry allowed at present
data	a dataframe
subset	you can subset the analysis via logical expression in variables in the dataframe
na.action	pass a method for handling NA values in block such as <code>na.omit</code> , or <code>na.fail</code>

**Value**

A dataframe of  $2 * \text{NLEV} + 1$  columns where NLEV is the number of levels of the factor block.

time	The sorted vector of unique event times from all blocks
nrisk1	The number at risk in block level 1 at each event time
nevent1	The number of events in block level 1 at each event time
...	
nriskNLEV	The number at risk in block level NLEV at each event time
neventNLEV	The number of events in block level NLEV at each event time

**Author(s)**

Grant Izmirlian <izmirlian@nih.gov>

**Examples**

```
library(PwrGSD)
data(lung)

fit.msf <- mysurvfit(Surv(time, I(status==2)) ~ sex, data=lung)

fit.msf
## Not run:
plot(fit.msf)

## End(Not run)
```

---

 ObrienFleming

*The O'Brien-Fleming Alpha Spending Function*


---

**Description**

Stipulates alpha spending according to the O'Brien-Fleming spending function in the Lan-Demets boundary construction method. Its intended purpose is in constructing calls to GrpSeqBnds and PwrGSD.

**Usage**

```
ObrienFleming()
```

**Value**

An object of class spending.function which is really a list with the following components. The print method displays the original call.

type	Gives the spending function type, which is the character string "ObrienFleming"
call	returns the call

**Note**

The print method returns the call by default

**Author(s)**

Grant Izmirlian

**References**

see references under [PwrGSD](#)

**See Also**

[LanDemets](#), [Pow](#), [Pocock](#), [GrpSeqBnds](#), [PwrGSD](#)

**Examples**

```
## example 1: what is the result of calling a spending function
## A call to 'ObrienFleming' just returns the call
ObrienFleming()

## but really its value is a list with a component named
## 'type' equal to "ObrienFleming" and a component named
## 'call' equal to the call.
names(ObrienFleming)

ObrienFleming()$type
```

```

O'BrienFleming()$call

## example 2: ...But the intended purpose of the spending functions is
## in constructing calls to 'GrpSeqBnds' and to 'PwrGSD':

frac <- c(0.07614902,0.1135391,0.168252,0.2336901,0.3186155,
          0.4164776,0.5352199,0.670739,0.8246061,1)
drift <- c(0.3836636,0.5117394,0.6918584,0.8657705,1.091984,
           1.311094,1.538582,1.818346,2.081775,2.345386)

test <- GrpSeqBnds(frac=frac, EfficacyBoundary=LanDemets(alpha=0.05, spending=O'BrienFleming),
                  FutilityBoundary=LanDemets(alpha=0.10, spending=Pocock),
                  drift=drift)

```

---

plot.cpd.PwrGSD

*Plot Method for cpd.PwrGSD objects*


---

### Description

Creates a trellis plot of type II error probability and power at each interim analysis, stacked, versus an effect size variable, conditioned upon levels of up to two factors.

### Usage

```

## S3 method for class 'cpd.PwrGSD'
plot(x, formula, subset, na.action,...)

```

### Arguments

x	an object of class cpd.PwrGSD
formula	a one sided formula of the form $\sim$ effect   f1 or $\sim$ effect   f1 * f2 where effect, f1, and f2 are variables in the indexing dataframe descr, or the special variable stat which may be used when there are multiple test statistics per component of Elements. See the example in the documentation for cpd.PwrGSD
.	
subset	the plot can be applied to a subset of rows of descr via a logical expression on its variables in combination with the special variable, stat when applicable.
na.action	a na.action method for handling NA values
...	other parameters to pass to the R function coplot usually not necessary

### Value

Returns the object, x, invisibly

**Note**

This processes the `cpd.PwrGSD` object into a dataframe, stacked on interim looks and then passes the results to the R function `coplot`

**Author(s)**

Abovementioned `cpd.PwrGSD` processing done by Grant Izmirlian <izmirlian@nih.gov>

**References**

Chambers, J. M. (1992) *Data for models*. Chapter 3 of *Statistical Models in S* eds J. M. Chambers and T. J. Hastie, Wadsworth and Brooks/Cole.

Cleveland, W. S. (1993) *Visualizing Data*. New Jersey: Summit Press.

**See Also**

[cpd.PwrGSD Power](#) and [Elements](#)

**Examples**

```
## See the example in the 'cpd.PwrGSD' documentation
```

---

Pocock

*The Pocock Alpha Spending Function*

---

**Description**

Stipulates alpha spending according to the Pocock spending function in the Lan-Demets boundary construction method. Its intended purpose is in constructing calls to `GrpSeqBnds` and `PwrGSD`.

**Usage**

```
Pocock()
```

**Value**

An object of class `spending.function`

`type` Gives the spending function type, which is the character string "Pocock"

`call` returns the call

**Note**

The print method returns the call by default

**Author(s)**

Grant Izmirlian

**References**

see references under [PwrGSD](#)

**See Also**

[LanDemets](#), [ObrienFleming](#), [Pow](#), [GrpSeqBnds](#), [PwrGSD](#)

**Examples**

```
## example 1: what is the result of calling a spending function

## A call to 'Pocock' just returns the call
Pocock()

## but really its value is a list with a component named
## 'type' equal to "Pocock" and a component named
## 'call' equal to the call.
names(Pocock)

Pocock()$type

Pocock()$call

## example 2: ...But the intended purpose of the spending functions is
## in constructing calls to 'GrpSeqBnds' and to 'PwrGSD':

frac <- c(0.07614902,0.1135391,0.168252,0.2336901,0.3186155,
          0.4164776,0.5352199,0.670739,0.8246061,1)
drift <- c(0.3836636,0.5117394,0.6918584,0.8657705,1.091984,
          1.311094,1.538582,1.818346,2.081775,2.345386)

test <- GrpSeqBnds(frac=frac, EfficacyBoundary=LanDemets(alpha=0.05, spending=Pocock),
                  FutilityBoundary=LanDemets(alpha=0.10, spending=ObrienFleming),
                  drift=drift)
```

---

Pow

*The Wang-Tsiatis Power Alpha Spending Function*

---

**Description**

Stipulates alpha spending according to the Wang-Tsiatis Power function in the Lan-Demets boundary construction method. Its intended purpose is in constructing calls to `GrpSeqBnds` and `PwrGSD`.

**Usage**

`Pow(rho)`

**Arguments**

rho                    The exponent for the Wang-Tsiatis power spending function

**Details**

Larger rho results in more conservative boundaries. rho=3 is roughly equivalent to Obrien-Fleming spending. rho=1 spends alpha linearly in the information fraction

**Value**

An object of class `spending.function` which is really a list with the following components. The print method displays the original call.

type                    Gives the spending function type, which is the character string "Pow"  
rho                      the numeric value passed to the single argument, rho  
call                     returns the call

**Note**

The print method returns the call by default

**Author(s)**

Grant Izmirlian

**References**

see references under [PwrGSD](#)

**See Also**

[LanDemets](#), [ObrienFleming](#), [Pocock](#), [GrpSeqBnds](#), [PwrGSD](#)

**Examples**

```
## example 1: what is the result of calling a spending function
## A call to 'Pow' just returns the call
Pow(rho=2)

## It does argument checking...the following results in an error:
## Not run:
Pow()

## End(Not run)

## it doesn't matter whether the argument is named or not,
## either produces the same result
Pow(2)

## but really its value is a list with a component named
```

```

## 'type' equal to "Pow", a component named 'rho' equal
## to the numeric value passed to the single argument 'rho'
## and a component named 'call' equal to the call.
names(Pow(rho=2))

names(Pow(2))

Pow(rho=2)$type
Pow(rho=2)$rho
Pow(rho=2)$call

## example 2: ...But the intended purpose of the spending functions is
## in constructing calls to 'GrpSeqBnds' and to 'PwrGSD':

frac <- c(0.07614902,0.1135391,0.168252,0.2336901,0.3186155,
          0.4164776,0.5352199,0.670739,0.8246061,1)
drift <- c(0.3836636,0.5117394,0.6918584,0.8657705,1.091984,
           1.311094,1.538582,1.818346,2.081775,2.345386)

test <- GrpSeqBnds(frac=frac, EfficacyBoundary=LanDemets(alpha=0.05, spending=Pow(2)),
                  FutilityBoundary=LanDemets(alpha=0.10, spending=ObrienFleming),
                  drift=drift)

```

---

Power

---

*Extract the Power results*


---

## Description

The function 'Power' is used to summarize the 'cpd.PwrGSD' object into a dataframe containing power and type II error, summed over analysis times. The data frame is stacked by rows of 'descr' and by 'stat' (if there are multiple statistics being profiled per each component of 'Elements'), for generating tables or performing other computations.

## Usage

```
Power(object, subset, nlook.ind = NULL)
```

## Arguments

object	an object of class cpd.PwrGSD
subset	you may extract a subset via a logical expression in the variables of the index dataframe, descr
nlook.ind	(optional) a vector containing a subset of the indices of analysis times over which the sum is formed. Use this for example if you want to know the probability of stopping by the kth analysis under an unfavorable alternative. Set nlook.ind to 1:k

**Value**

a dataframe, stacked by rows of ‘descr’ and then by choices of ‘stat’

**Author(s)**

Grant Izmirlian <izmirlian@nih.gov>

**See Also**

[cpd.PwrGSD](#) and [PwrGSD](#)

**Examples**

```
## See the `cpd.PwrGSD` example
```

---

PwrGSD

*Calculate Power in a Group Sequential Design*

---

**Description**

Derives power in a two arm clinical trial under a group sequential design. Allows for arbitrary number of interim analyses, arbitrary specification of arm-0/arm-1 time to event distributions (via survival or hazard), arm-0/arm-1 censoring distribution, provisions for two types of continuous time non-compliance according to arm-0/arm-1 rate followed by switch to new hazard rate. Allows for analyses using (I) weighted log-rank statistic, with weighting function (a) a member of the Fleming-Harrington G-Rho class, or (b) a stopped version thereof, or (c) the ramp-plateau deterministic weights, or (II) the integrated survival distance (currently under method=="S" without futility only). Stopping boundaries are computed via the Lan-Demets method, Haybittle method, converted from the stochastic curtailment procedure, or be completely specified by the user. The Lan-Demets boundaries can be constructed using either O'Brien-Flemming, Pocock or Wang-Tsiatis power alpha-spending. The C kernel is readily extensible, and further options will become available in the near future.

**Usage**

```
PwrGSD(EfficacyBoundary = LanDemets(alpha = 0.05, spending = ObrienFleming),
       FutilityBoundary = LanDemets(alpha = 0.1, spending = ObrienFleming),
       NonBindingFutility = TRUE, sided = c(">", "<", ">", "<"),
       method = c("S", "A"), accru, accrat, tlook,
       tcut0 = NULL, h0 = NULL, s0 = NULL, tcut1 = NULL,
       rhaz = NULL, h1 = NULL, s1 = NULL, tcutc0 = NULL, hc0 = NULL,
       sc0 = NULL, tcutc1 = NULL, hc1 = NULL, sc1 = NULL, tcutd0A = NULL,
       hd0A = NULL, sd0A = NULL, tcutd0B = NULL, hd0B = NULL, sd0B = NULL,
       tcutd1A = NULL, hd1A = NULL, sd1A = NULL, tcutd1B = NULL,
       hd1B = NULL, sd1B = NULL, tcutx0A = NULL, hx0A = NULL, sx0A = NULL,
       tcutx0B = NULL, hx0B = NULL, sx0B = NULL, tcutx1A = NULL,
       hx1A = NULL, sx1A = NULL, tcutx1B = NULL, hx1B = NULL, sx1B = NULL,
```

```

noncompliance = c("none", "crossover", "mixed", "user"),
gradual = FALSE, WtFun = c("FH", "SFH", "Ramp"), ppar = cbind(c(0, 0)),
Spend.Info = c("Variance", "Events", "Hybrid(k)", "Calendar"), RR.Futility = NULL,
qProp.one.or.Q = c("one", "Q"), Nsim = NULL, detail = FALSE, StatType = c("WLR",
"ISD"), doProj=FALSE)

```

## Arguments

### EfficacyBoundary

This specifies the method used to construct the efficacy boundary. The available choices are:

‘(i) ’Lan-Demets(alpha=<total type I error>, spending =<spending function>). The Lan-Demets method is based upon a error probability spending approach. The spending function can be set to ObrienFleming, Pocock, or Power(rho), where rho is the the power argument for the power spending function: rho=3 is roughly equivalent to the O’Brien-Fleming spending function and smaller powers result in a less conservative spending function.

‘(ii) ’Haybittle(alpha=<total type I error>, b.Haybittle=<user specified boundary point>). The Haybittle approach is conceptually the simplest of all methods for efficacy boundary construction. However, as it spends nearly no alpha until the end, is for all practical purposes equivalent to a single analysis design and to be considered overly conservative. This method sets all the boundary points equal to b.Haybittle, a user specified value (try 3) for all analyses except the last, which is calculated so as to result in the total type I error, set with the argument alpha.

‘(iii) ’SC(be.end=<efficacy boundary point at trial end>, prob=<threshold for conditional type I error for efficacy stopping>). The stochastic curtailment method is based upon the conditional probability of type I error given the current value of the statistic. Under this method, a sequence of boundary points on the standard normal scale (as are boundary points under all other methods) is calculated so that the total probability of type I error is maintained. This is done by considering the joint probabilities of continuing to the current analysis and then exceeding the threshold at the current analysis. A good value for the threshold value for the conditional type I error, prob is 0.90 or greater.

‘(iv) ’User supplied boundary points in the form c(b1, b2, b3, . . . , b\_m), where m is the number of looks.

### FutilityBoundary

This specifies the method used to construct the futility boundary. The available choices are:

‘(i) ’Lan-Demets(alpha=<total type II error>, spending= <spending function>). The Lan-Demets method is based upon a error probability spending approach. The spending function can be set to ObrienFleming, Pocock, or Power(rho), where rho is the the power argument for the power spending function: rho=3 is roughly equivalent to the O’Brien-Fleming spending function and smaller powers result in a less conservative spending function.

‘NOTE: ’there is no implementation of the Haybittle method for futility boundary construction. Given that the futility boundary depends upon values of the drift function, this method doesn’t apply.

‘(ii) ’SC(be.end=<efficacy boundary point at trial end>, prob=<threshold for conditional type II error for futility stopping>, drift.end=<projected drift at end of trial>). The stochastic curtailment method is based upon the conditional probability of type II error given the current value of the statistic. Under this method, a sequence of boundary points on the standard normal scale (as are boundary points under all other methods) is calculated so that the total probability of type II error, is maintained. This is done by considering the joint probabilities of continuing to the current analysis and then exceeding the threshold at the current analysis. A good value for the threshold value for the conditional type I error, prob is 0.90 or greater.

‘(iii) ’User supplied boundary points in the form c(b1, b2, b3, . . . , b\_m), where m is the number of looks.

#### NonBindingFutility

When using a futility boundary and this is set to 'TRUE', the efficacy boundary will be constructed in the absence of the futility boundary, and then the futility boundary will be constructed given the resulting efficacy boundary. This results in a more conservative efficacy boundary with true type I error less than the nominal level. This is recommended due to the fact that futility crossings are viewed by DSMB's with much less gravity than an efficacy crossing and as such, the consensus is that efficacy bounds should not be discounted towards the null hypothesis because of paths which cross a futility boundary. Default value is 'TRUE'.

sided	Set to “2>” (quoted) for two sided tests of the null hypothesis when a positive drift corresponds to efficacy. Set to “2<” (quoted) for two sided tests of the null hypothesis when a negative drift corresponds to efficacy. Set to “1>” or “1<” for one sided tests of H0 when efficacy corresponds to a positive or negative drift, respectively. If method==“S” then this must be of the same length as StatType because the interpretation of sided is different depending upon whether StatType==“WLR” (negative is benefit) or StatType==“ISD” (positive is benefit)
method	Determines how to calculate the power. Set to “A” (Asymptotic method, the default) or “S” (Simulation method)
accru	The upper endpoint of the accrual period beginning with time 0.
accrat	The rate of accrual per unit of time.
tlook	The times of planned interim analyses.
tcut0	Left hand endpoints for intervals upon which the arm-0 specific mortality is constant. The last given component is the left hand endpoint of the interval having right hand endpoint infinity.
h0	A vector of the same length as tcut0 which specifies the piecewise constant arm-0 mortality rate.
s0	Alternatively, the arm-0 mortality distribution can be supplied via this argument, in terms of of the corresponding survival function values at the times given in the vector tcut0. If s0 is supplied, then h0is derived internally, assuming the piecewise exponential distrubiton. If you specify s0, the first element must be 1, and correspondingly, the first component of tcut0 will be the lower support point of the distribution. You must supply either h0 or s0 but not both.

tcut1	Left hand endpoints for intervals upon which the arm-1 specific mortality is constant. The last given component is the left hand endpoint of the interval having right hand endpoint infinity.
rhaz	A vector of piecewise constant arm-1 versus arm-0 mortality rate ratios. If tcut1 and tcut0 are not identical, then tcut1, h0, and rhaz are internally rederived at the union of the sequences tcut0 and tcut1. In all cases the arm-1 mortality rate is then derived at the time cutpoints tcut1 as rhaz times h0.
h1	Alternatively, the arm-1 mortality distribution can be supplied via this argument by specifying the piecewise constant arm-1 mortality rate. See the comments above.
s1	Alternatively, the arm-1 mortality distribution can be supplied via this argument, in terms of of the corresponding survival function values at the times given in the vector tcut1. Comments regarding s0 above apply here as well. You must supply exactly one of the following: h1, rhaz, or s1.
tcutc0	Left hand endpoints for intervals upon which the arm-0 specific censoring distribution hazard function is constant. The last given component is the left hand endpoint of the interval having right hand endpoint infinity.
hc0	A vector of the same length as tcutc0 which specifies the arm-0 censoring distribution in terms of a piecewise constant hazard function.
sc0	Alternatively, the arm-0 censoring distribution can be supplied via this argument, in terms of of the corresponding survival function values at the times given in the vector tcutc0. See comments above. You must supply either hc0 or sc0 but not both.
tcutc1	Left hand endpoints for intervals upon which the arm-1 specific censoring distribution hazard function is constant. The last given component is the left hand endpoint of the interval having right hand endpoint infinity.
hc1	A vector of the same length as tcutc1 which specifies the arm-1 censoring distribution in terms of a piecewise constant hazard function.
sc1	Alternatively, the arm-1 censoring distribution can be supplied via this argument, in terms of of the corresponding survival function values at the times given in the vector tcutc1. See comments above. You must supply either hc1 or sc1 but not both.
noncompliance	(i) Setting noncompliance to “none” for no non-compliance will automatically set the non-compliance arguments, below, to appropriate values for no compliance. This requires no additional user specification of non-compliance parameters. (ii) Setting noncompliance to “crossover” will automatically set crossover values in the arm 0/1 specific <i>post-cause-B-delay-mortality</i> for cross-over, i.e. simple interchange of the arm 0 and arm 1 mortalities. The user is required to specify all parameters corresponding to the arm 0/1 specific <i>cause-B-delay</i> distributions. The <i>cause-A-delay</i> and <i>post-cause-A-delay-mortality</i> are automatically set so as not to influence the calculations. Setting noncompliance to “mixed” will set the arm 0/1 specific <i>post-cause-B-delay-mortality</i> distributions for crossover as defined above. The user specifies the arm 0/1 specific <i>cause-B-delay</i> distribution as above, and in addition, all parameters related to the arm 0/1 specific <i>cause-A-delay</i> distributions and corresponding arm 0/1 specific <i>post-cause-A-delay-mortality</i> distributions. (iii) Setting noncompliance to “user” requires the user to specify all non-compliance distribution parameters.

tcutd0A	Left hand endpoints for intervals upon which the arm-0 specific <i>cause-A delay</i> distribution hazard function is constant. The last given component is the left hand endpoint of the interval having right hand endpoint infinity. Required only when noncompliance is set to “mixed” or “user”.
hd0A	A vector of the same length as tcutd0A containing peicewise constant hazard rates for the arm-0 <i>cause-A delay</i> distribution. Required only when noncompliance is set to “mixed” or “user”.
sd0A	When required, the arm-0 <i>cause-A-delay</i> distribution is alternately specified via a survival function. A vector of the same length as tcutd0A.
tcutd0B	Left hand endpoints for intervals upon which the arm-0 specific <i>cause-B delay</i> distribution hazard function is constant. The last given component is the left hand endpoint of the interval having right hand endpoint infinity. Always required when noncompliance is set to any value other than “none”.
hd0B	A vector of the same length as tcutd0B containing peicewise constant hazard rates for the arm-0 <i>cause-B delay</i> distribution. Always required when noncompliance is set to any value other than “none”.
sd0B	When required, the arm-0 <i>cause-B-delay</i> distribution is alternately specified via a survival function. A vector of the same length as tcutd0B.
tcutd1A	Left hand endpoints for intervals upon which the arm-1 specific <i>cause-A delay</i> distribution hazard function is constant. The last given component is the left hand endpoint of the interval having right hand endpoint infinity. Required only when noncompliance is set to “mixed” or “user”.
hd1A	A vector of the same length as tcutd1A containing peicewise constant hazard rates for the arm-1 <i>cause-A delay</i> distribution. Required only when noncompliance is set to “mixed” or “user”.
sd1A	When required, the arm-1 <i>cause-A-delay</i> distribution is alternately specified via a survival function. A vector of the same length as tcutd1A.
tcutd1B	Left hand endpoints for intervals upon which the arm-1 specific <i>cause-B delay</i> distribution hazard function is constant. The last given component is the left hand endpoint of the interval having right hand endpoint infinity. Always required when noncompliance is set to any value other than “none”.
hd1B	A vector of the same length as tcutd1B containing peicewise constant hazard rates for the arm-1 <i>cause-B delay</i> distribution. Always required when noncompliance is set to any value other than “none”.
sd1B	When required, the arm-1 <i>cause-A-delay</i> distribution is alternately specified via a survival function. A vector of the same length as tcutd1A.
tcutx0A	Left hand endpoints for intervals upon which the arm-0 specific <i>post-cause-A-delay-mortality</i> rate is constant. The last given component is the left hand endpoint of the interval having right hand endpoint infinity. Required only when noncompliance is set to “mixed” or “user”.
hx0A	A vector of the same length as tcutx0A containing the arm-0 <i>post-cause-A-delay mortality</i> rates. Required only when noncompliance is set to “mixed” or “user”.
sx0A	When required, the arm-0 <i>post-cause-A-delay mortality</i> distribution is alternately specified via a survival function. A vector of the same length as tcutx0A.

tcutx0B	Left hand endpoints for intervals upon which the arm-0 specific <i>post-cause-B-delay-mortality</i> rate is constant. The last given component is the left hand endpoint of the interval having right hand endpoint infinity. Always required when noncompliance is set to any value other than “none”.
hx0B	A vector of the same length as tcutx0B containing the arm-0 <i>post-cause-B-delay mortality</i> rates. Always required when noncompliance is set to any value other than “none”.
sx0B	When required, the arm-0 <i>post-cause-B-delay mortality</i> distribution is alternately specified via a survival function. A vector of the same length as tcutx0B.
tcutx1A	Left hand endpoints for intervals upon which the arm-1 specific <i>post-cause-A-delay-mortality</i> rate is constant. The last given component is the left hand endpoint of the interval having right hand endpoint infinity. Required only when noncompliance is set to “mixed” or “user”.
hx1A	A vector of the same length as tcutx1A containing the arm-1 <i>post-cause-A-delay mortality</i> rates. Required only when noncompliance is set to “mixed” or “user”.
sx1A	When required, the arm-1 <i>post-cause-A-delay mortality</i> distribution is alternately specified via a survival function. A vector of the same length as tcutx1A.
tcutx1B	Left hand endpoints for intervals upon which the arm-1 specific <i>post-cause-B-delay-mortality</i> rate is constant. The last given component is the left hand endpoint of the interval having right hand endpoint infinity. Always required when noncompliance is set to any value other than “none”.
hx1B	A vector of the same length as tcutx1B containing the arm-1 <i>post-cause-B-delay mortality</i> rates. Always required when noncompliance is set to any value other than “none”.
sx1B	When required, the arm-1 <i>post-cause-B-delay mortality</i> distribution is alternately specified via a survival function. A vector of the same length as tcutx1B.
gradual	Should the conversion to post-noncompliance mortality be gradual. Under the default behavior, gradual=FALSE, there is an immediate conversion to the post-noncompliance mortality rate function. If gradual is set to TRUE then this conversion is done “gradually”. In truth, at the individual level what is done is that the new mortality rate function is a convex combination of the pre-noncompliance mortality and the post-noncompliance mortality, with the weighting in proportion to the time spent in compliance with the study arm protocol.
WtFun	Specifies the name of a weighting function (of time) for assigning relative weights to events according to the times at which they occur. The default, “FH”, a two parameter weight function, specifies the ‘Fleming-Harrington’ $g$ - $\rho$ family of weighting functions defined as the pooled arm survival function (Kaplan-Meier estimate) raised to the $g$ times its complement raised to the $\rho$ . Note that $g=\rho=0$ corresponds to the unweighted log-rank statistic. A second choice is the “SFH” function, (for ‘Stopped Fleming-Harrington’), meaning that the “FH” weights are capped at their value at a user specified time, which has a total of 3 parameters. A third choice is Ramp(tcut). Under this choice, weights are assigned in a linearly manner from time 0 until a user specified cut-off time, tcut, after which events are weighted equally. It is possible to conduct computations on nstat candidate statistics within a single run. In this case, WtFun should

	be a character vector of length <code>nstat</code> having components set from among the available choices.
<code>ppar</code>	A vector containing all the weight function parameters, in the order determined by that of <code>"WtFun"</code> . For example, if <code>WtFun</code> is set to <code>c("FH", "SFH", "Ramp")</code> then <code>ppar</code> should be a vector of length six, with the <code>"FH"</code> parameters in the first two elements, <code>"SFH"</code> parameters in the next 3 elements, and <code>"Ramp"</code> parameter in the last element.
<code>RR.Futility</code>	The relative risk corresponding to the alternative alternative hypothesis that is required in the construction of the futility boundary. Required if <code>Boundary.Futility</code> is set to a non-null value.
<code>Spend.Info</code>	When the test statistic is something other than the unweighted log-rank statistic, the variance information, i.e. the ratio of variance at interim analysis to variance at the end of trial, is something other than the ratio of events at interim analysis to the events at trial end. The problem is that in practice one doesn't necessarily have a good idea what the end of trial variance should be. In this case the user may wish to spend the type I and type II error probabilities according to a different time scale. Possible choices are <code>"Variance"</code> , (default), which just uses the variance ratio scale, <code>"Events"</code> , which uses the events ratio scale, <code>"Hybrid(k)"</code> , which makes a linear transition from the <code>"Variance"</code> scale to the <code>"Events"</code> scale beginning with analysis number <code>k</code> . The last choice, <code>"Calendar"</code> , uses the calendar time scale
<code>qProp.one.or.Q</code>	If a futility boundary is specified, what assumption should be made about the drift function (the mean value of the weighted log-rank statistic at analysis <code>j</code> normalized by the square root of the variance function at analysis <code>k</code> ). In practice we don't presume to know the shape of the drift function. Set to <code>"one"</code> or <code>"Q"</code> . The choice <code>"one"</code> results in a more conservative boundary.
<code>Nsim</code>	If you specify <code>method=="S"</code> , then you must specify the number of simulations. 1000 should be sufficient.
<code>detail</code>	If you specify <code>method=="S"</code> , and want to see the full level of detail regarding arguments returned from the C level code, specify <code>detail==TRUE</code>
<code>StatType</code>	If you specify <code>method=="S"</code> , then the available choices are <code>"WLR"</code> (weighted log-rank) and <code>"ISD"</code> (integrated survival difference).
<code>doProj</code>	Works only when <code>method=="S"</code> . If a weighted log-rank statistic is specified without maximum information having been stipulated in the design then certain functionals, the Q first and second moments, must be projected. Setting this argument to <code>TRUE</code> includes this projection into the simulation runs.

### Value

Returns a value of class `PwrGSD` which has components listed below. Note that the print method will display a summary table of estimated powers and type I errors as a `nstat` by 2 matrix. The summary method returns the same object invisibly, but after computing the summary table mentioned above, and it is included in the returned value as a component `TBL`. See examples below.

<code>dPower</code>	A <code>length(tlook)</code> by <code>nstat</code> matrix containing in each column, an increment in power that resulted at that analysis time for the given statistic.
---------------------	---

dErrorI	A length(tlook) by nstat matrix containing in each column, an increment in type I error that resulted at that analysis time for the given statistic. Always sums to the total alpha specified in alphas
detail	A list with components equal to the arguments of the C-call, which correspond in a natural way to the arguments specified in the R call, along with the computed results in palphas, palpha1vec, inffrac, and mu. The first two are identical to dErrorI and dPower, explained above. The last two are length(tlook) by nstat matrices. For each statistic specified in par, the corresponding columns of pinffrac and mu contain the information fraction and drift at each of the analysis times.
call	the call

**Author(s)**

Grant Izmirlian <izmirlian@nih.gov>

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- Jennison, C. and Turnbull, B.W. (1999) *Group Sequential Methods: Applications to Clinical Trials* Chapman & Hall/Crc, Boca Raton FL
- Proschan, M.A., Lan, K.K.G., Wittes, J.T. (2006), corr 2nd printing (2008) *Statistical Monitoring of Clinical Trials A Unified Approach* Springer Verlag, New York
- Izmirlian G. (2014). Estimation of the relative risk following group sequential procedure based upon the weighted log-rank statistic. *Statistics and its Interface* 7(1), 27-42

**See Also**

[cpd.PwrGSD](#)

**Examples**

```
library(PwrGSD)

test.example <-
  PwrGSD(EfficacyBoundary = LanDemets(alpha = 0.05, spending = ObrienFleming),
         FutilityBoundary = LanDemets(alpha = 0.1, spending = ObrienFleming),
         RR.Futility = 0.82, sided="1<",method="A",accru =7.73, accrat =9818.65,
         tlook =c(7.14, 8.14, 9.14, 10.14, 10.64, 11.15, 12.14, 13.14,
                 14.14, 15.14, 16.14, 17.14, 18.14, 19.14, 20.14),
         tcut0 =0:19, h0 =c(rep(3.73e-04, 2), rep(7.45e-04, 3),
                          rep(1.49e-03, 15)),
         tcut1 =0:19, rhaz =c(1, 0.9125, 0.8688, 0.7814, 0.6941,
                             0.6943, 0.6072, 0.5202, 0.4332, 0.6520,
                             0.6524, 0.6527, 0.6530, 0.6534, 0.6537,
                             0.6541, 0.6544, 0.6547, 0.6551, 0.6554),
         tcutc0 =0:19, hc0 =c(rep(1.05e-02, 2), rep(2.09e-02, 3),
```

```

                                rep(4.19e-02, 15)),
tcutc1 =0:19, hc1 =c(rep(1.05e-02, 2), rep(2.09e-02, 3),
                                rep(4.19e-02, 15)),
tcutd0B =c(0, 13), hd0B =c(0.04777, 0),
tcutd1B =0:6, hd1B =c(0.1109, 0.1381, 0.1485, 0.1637, 0.2446,
                                0.2497, 0),
noncompliance =crossover, gradual =TRUE,
WtFun =c("FH", "SFH", "Ramp"),
ppar =c(0, 1, 0, 1, 10, 10))

```

RCM2RR

*Relative cumulative mortality to Relative Risk***Description**

Given the relative cumulative mortality (ratio of CDFs), the baseline hazard and censoring hazard at a grid of time points, calculates the corresponding risk ratio at a second specified grid of time points.

**Usage**

```
RCM2RR(tlook, tcut.i, h.i, h0th, accru, rcm)
```

**Arguments**

tlook	Second grid of time points at which you desire risk ratios
tcut.i	First grid of time points at which baseline hazard, censoring hazard and relative cumulative mortality are specified (left hand endpoints of intervals)
h.i	Values of baseline hazard on intervals given by tcut.i
h0th	Values of censoring hazard on intervals given by tcut.i
accru	Time at which uniform accrual is completed (starts at 0)
rcm	Values of relative cumulative mortality (ratio of CDFs) on intervals given by tcut.i

**Value**

Values of risk ratio on intervals given by tlook

**Author(s)**

Grant Izmirlian <izmirlian@nih.gov>

RR2RCM

*Relative risk to Relative Cumulative Mortality***Description**

Relative risk to Relative Cumulative Mortality

**Usage**

```
RR2RCM(tlook, tcut.i, tcut.ii, h, rr, h0th, accru)
```

**Arguments**

tlook	Grid of time points at which you desire cumulative relative mortality
tcut.i	Grid of time points at which baseline hazard, censoring hazard and relative cumulative mortality are specified (left hand endpoints of intervals)
tcut.ii	Grid of time points at which study arm hazard is specified (left hand endpoints of intervals)
h	Values of baseline hazard on intervals given by tcut.i
rr	Values of risk ratio on intervals given by tcut.i
h0th	Values of censoring hazard on intervals given by tcut.i
accru	Time at which uniform accrual is completed (starts at 0)

**Value**

Values of relative cumulative mortality (ratio of CDFs) on intervals given by tlook

**Author(s)**

Grant Izmirlian <izmirlian@nih.gov>

SC

*The Stochastic Curtailment method of Boundary Construction***Description**

The function SC is used in calls to the functions GrpSeqBnds and PwrGSD as a possible setting for the arguments EfficacyBoundary and FutilityBoundary, in specification of the method whereby efficacy and or futility boundaries are to be constructed. The Stochastic Curtailment method is one of four currently available choices, the others being LanDemets, Haybittle (efficacy only) and user specified.

**Usage**

```
SC(be.end, prob, drift.end = NULL, from = NULL, to = NULL)
```

**Arguments**

be.end	The value of the efficacy criterion in the scale of a standardized normal. This should be set to something further from the null than the single test $Z_{\alpha}$ . For example if the total type I error probability is 0.05 in a two sided test of the null than set be.end to 2.10 or larger (instead of 1.96).
prob	The criterion, a probability to be exceeded in order to stop. 0.90 or above is a good choice. See detail below.
drift.end	Required only if you are using SC to set the FutilityBoundary. In this case, set drift.end to the value of the drift function anticipated at the end of the trial. See detail below.
from	<b>WARNING EXPERIMENTAL:</b> you can actually construct boundaries via a hybrid of the 3 boundary construction methods, LanDemets, SC, and 'user specified'. When using a hybrid boundry, set the argument EfficacyBoundary or FutilityBoundary respectively, to a list with components LanDemets, SC, or user specified numbers. In the former two cases, from and to are used in LanDemets and also in SC to stipulate how many interim analyses they are in effect. See the help for GrpSeqBnds and PwrGSD
to	See above.

**Details**

When the stochastic curtailment procedure is used to construct the efficacy boundary, i.e.  $\text{EfficacyBoundary}=\text{SC}(\dots)$ , the efficacy criterion is reached when the conditional probability, under the null hypothesis, that the last analysis results in statistical significance, given the present value of the statistic, exceeds 'prob'. In of itself, this doesn't produce a boundary on the scale of a standard normal, but it is easily converted to one as is done here. When this is used to construct a futility boundary, i.e.  $\text{FutilityBoundary}=\text{SC}(\dots)$ , the futility criterion is reached when the conditional probability, under the design alternative hypothesis, that the last analysis does not result in statistical significance, given the present value of the statistic, exceeds 'prob'. The design alternative corresponds to a drift function, which is the expected value of the statistic normalized to have variance equal to the information fraction at each interim analysis. For the unweighted log-rank statistic, the drift function is  $(V_T)^{1/2} B f$ , where B is the logged relative risk,  $V_T$  is the variance at the end of the trial and f is the information fraction. If the two trial arms are balanced and the number at risk is roughly constant throughout the trial then  $V_T = \pi (1-\pi) N_T$ , where  $\pi$  is the constant proportion at risk in one of the trial arms and  $N_T$  is the anticipated number of events.

**Value**

An object of class boundary.construction.method which is really a list with the following components. The print method displays the original call.

type	Gives the boundary construction method type, which is the character string "SC"
be.end	The numeric value passed to the argument 'be.end', which is the value of the efficacy criterion in the scale of a standardized normal.
prob	The numeric value passed to the argument 'prob', which is the probability to be exceeded in order to stop.

<code>drift.end</code>	The numeric value passed to the argument 'drift.end', which is the value of the drift function at the end of the trial. See details.
<code>from</code>	The numeric value passed to the argument 'from'. See above.
<code>to</code>	The numeric value passed to the argument 'to'. See above.
<code>call</code>	returns the call

**Note**

The print method returns the call by default

**Author(s)**

Grant Izmirlian

**References**

see references under [PwrGSD](#)

**See Also**

[LanDemets](#), [GrpSeqBnds](#), [PwrGSD](#)

**Examples**

```
## example 1: what is the result of calling a Boundary Construction Method function
## A call to 'SC' just returns the call
SC(be.end=2.10, prob=0.90)

## It does argument checking...this results in an error
## Not run:
SC(be.end=2.10)

## End(Not run)

## but really its value is a list with the a component containing
## the boundary method type, "LanDemets", and components for each
## of the arguments.
names(SC(be.end=2.10, prob=0.90))

SC(be.end=2.10, prob=0.90, drift.end=2.34)$type
SC(be.end=2.10, prob=0.90, drift.end=2.34)$be.end
SC(be.end=2.10, prob=0.90, drift.end=2.34)$prob
SC(be.end=2.10, prob=0.90, drift.end=2.34)$drift.end

## example 2: ...But the intended purpose of the spending functions is
## in constructing calls to 'GrpSeqBnds' and to 'PwrGSD':

frac <- c(0.07614902,0.1135391,0.168252,0.2336901,0.3186155,
          0.4164776,0.5352199,0.670739,0.8246061,1)
drift <- c(0.3836636,0.5117394,0.6918584,0.8657705,1.091984,
```

```

1.311094,1.538582,1.818346,2.081775,2.345386)

test <- GrpSeqBnds(frac=frac, EfficacyBoundary=LanDemets(alpha=0.05, spending=ObrienFleming),
                  FutilityBoundary=SC(be.end=2.10, prob=0.90, drift.end=drift[10]),
                  drift=drift)

```

---

SCtoBdry	<i>Converts a stochastic curtailment boundary (conditional type I or II error probability) into a (efficacy or futility) boundary on the standardized Z scale</i>
----------	---

---

### Description

Converts a stochastic curtailment boundary (conditional type I or II error probability) into a (efficacy or futility) boundary on the standardized Z scale

### Usage

```
SCtoBdry(prob, frac, be.end, drift = NULL, drift.end = NULL)
```

### Arguments

prob	The stochastic curtailment thresh-hold probability, which is the complement of the type I (efficacy) or II (futility) error. We typically use 0.90 which will stop for efficacy if the probability under the null that the final analysis results in an efficacious decision given the data so far exceeds 0.90, and stops for futility of the probability under the alternative corresponding to the drift arguments, that the final analysis results in a futility decision given the data so far, exceeds 0.90.
frac	The variance ratio. See the <a href="#">GrpSeqBnds</a> documentation for details.
be.end	Value of efficacy (futility) boundary at the final analysis
drift	The drift function. See the <a href="#">GrpSeqBnds</a> documentation for details.
drift.end	Required if using a futility boundary. This is the value of the drift function at the final analysis. Must be projected using the trial design.

### Value

A efficacy or futility boundary on the standard normal scale

### Author(s)

Grant Izmirlian

## Examples

```
## Here we show how to convert a stochastic curtailment procedure for
## futility into a futility boundary on the standard normal scale
library(PwrGSD)

## Values of the information fraction at interim analyses --
## the sequence does not have to include the last analysis
frac <- c(0.16, 0.32, 0.54, 0.83, 1.0)

## values drift at interim analyses corresponding to values of
## frac given above
drift <- c(0.69, 1.09, 1.54, 2.08, 2.35)

## value of the drift at the final analysis (from the design or
## projected
drift.end <- drift[5]

## value of the efficacy boundary at the final analysis
be.end <- 1.69

## stochastic curtailment threshold probability -- if the probability of rejecting the
## null hypothesis by the scheduled end of the trial, under the alternative hypothesis,
## and conditional upon the current value of the statistic, is not greater than
## prob.thresh, then stop for futility.
prob.thresh <- 0.90

## computes equivalent futility boundary points on the standard normal scale
SctoBdry(prob.thresh, frac=frac, be.end=be.end, drift=drift, drift.end=drift.end)
```

---

SimGSB

*Verifies the results of "GrpSeqBnds" via simulation*

---

## Description

Verifies the results of GrpSeqBnds via simulation

## Usage

```
SimGSB(object, nsim = 1e+05, ...)
```

## Arguments

object	an object of class either boundaries or PwrGSD
nsim	number of simulations to do
...	if object is of class PwrGSD and there are more than one statistic under investigation, then you may specify an argument stat. The default value is 1, meaning the first one.

**Value**

A tabulation of the results

**Author(s)**

Grant Izmirlian <izmirlian@nih.gov>

**See Also**

[GrpSeqBnds](#)

**Examples**

```
## none as yet
```

---

wtdlogrank

*Weighted log-rank test*

---

**Description**

Computes a two sample weighted log-rank statistic with events weighted according to one of the available weighting function choices

**Usage**

```
wtdlogrank(formula = formula(data), data = parent.frame(), WtFun = c("FH", "SFH", "Ramp"),
  param = c(0, 0), sided = c(2, 1), subset, na.action, w = FALSE)
```

**Arguments**

formula	a formula of the form <code>Surv(Time, Event) ~ arm</code> where <code>arm</code> is a dichotomous variable with values 0 and 1.
data	a dataframe
WtFun	a selection from the available list: "FH" (Fleming-Harrington), "SFH" (stopped Fleming-Harrington) or "Ramp". See <code>param</code> in the following line.
param	Weight function parameters. Length and interpretation depends upon the selected value of <code>WtFun</code> : If <code>WtFun=="FH"</code> then <code>param</code> is a length 2 vector specifying the power of the pooled (across arms) kaplan meier estimate and its complement. If <code>WtFun=="SFH"</code> then <code>param</code> is a length 3 vector with first two components as in the "FH" case, and third component the time (in the same units as the time to event) at which the "FH" weight function is capped off at its current value. If <code>WtFun=="Ramp"</code> then <code>param</code> is of length 1 specifying the time (same units as time to event) at which events begin to get equal weight. The "Ramp" weight function is a linearly increasing deterministic weight function which is capped off at 1 at the user specified time.

sided	One or Two sided test? Set to 1 or 2
subset	Analysis can be applied to a subset of the dataframe based upon a logical expression in its variables
na.action	Method for handling NA values in the covariate, arm
w	currently no effect

### Value

An object of class `survtest` containing components

pn	sample size
wtyp	internal representation of the <code>WtFun</code> argument
par	internal representation of the <code>param</code> argument
time	unique times of events accross all arms
nrisk	number at risk accross all arms at each event time
nrisk1	Number at risk in the experimental arm at each event time
nevent	Number of events accross all arms at each event time
nevent1	Number of events in the experimental arm at each event time
wt	Values of the weight function at each event time
pntimes	Number of event times
stat	The un-normalized weighted log-rank statistic, i.e. the summed weighted observed minus expected differences at each event time
var	Variance estimate for the above
Uqt	Cumulative sum of increments in the sum resulting in <code>stat</code> above
varQt	Cumulative sum of increments in the sum resulting in <code>var</code> above
var1t	Cumulative sum of increments in the sum resulting in the variance of an un-weighted version of the statistic
pu0	person units of follow-up time in the control arm
pu1	person units of follow-up time in the intervention arm
n0	events in the control arm
n1	events in the intervention arm
n	sample size, same as <code>pn</code>
call	the call that created the object

### Author(s)

Grant Izmirlian <izmirlian@nih.gov>

### References

Harrington, D. P. and Fleming, T. R. (1982). A class of rank test procedures for censored survival data. *Biometrika* **69**, 553-566.

**See Also**

[IntSurvDiff](#)

**Examples**

```
library(PwrGSD)
data(lung)
fit.wlr <- wtdlogrank(Surv(time, I(status==2))~I(sex==2), data=lung, WtFun="SFH", param=c(0,1,300))
```

# Index

- \* **Bias Adjusted point estimate**
    - EX1gXK, [14](#)
  - \* **Sequential Design**
    - EX1gXK, [14](#)
  - \* **Stage-wise P-value**
    - gsd.dens, [19](#)
  - \* **datasets**
    - lung, [28](#)
  - \* **data**
    - cpd.PwrGSD, [5](#)
    - Elements, [13](#)
    - mystack, [29](#)
    - Power, [36](#)
  - \* **design**
    - as.boundaries, [3](#)
    - CondPower, [4](#)
    - GrpSeqBnds, [15](#)
    - Haybittle, [21](#)
    - LanDemets, [25](#)
    - ObrienFleming, [31](#)
    - Pocock, [33](#)
    - Pow, [34](#)
    - PwrGSD, [37](#)
    - SC, [46](#)
    - SCtoBdry, [49](#)
  - \* **hplot**
    - plot.cpd.PwrGSD, [32](#)
  - \* **htest**
    - as.boundaries, [3](#)
    - CondPower, [4](#)
    - GrpSeqBnds, [15](#)
    - Haybittle, [21](#)
    - LanDemets, [25](#)
    - ObrienFleming, [31](#)
    - Pocock, [33](#)
    - Pow, [34](#)
    - PwrGSD, [37](#)
    - SC, [46](#)
    - SCtoBdry, [49](#)
  - \* **manip**
    - agghaz, [2](#)
  - \* **misc**
    - DX, [12](#)
    - lookup, [27](#)
    - SimGSB, [50](#)
  - \* **sequential statistic pdf**
    - gsd.dens, [19](#)
  - \* **survival**
    - agghaz, [2](#)
    - CDFOR2LRR, [4](#)
    - CRRtoRR, [10](#)
    - CY2TOShaz, [11](#)
    - IntSurvDiff, [23](#)
    - mysurvfit, [30](#)
    - plot.cpd.PwrGSD, [32](#)
    - PwrGSD, [37](#)
    - RCM2RR, [45](#)
    - RR2RCM, [46](#)
    - wtdlogrank, [51](#)
- agghaz, [2](#)
- as.boundaries, [3](#)
- CDFOR2LRR, [4](#)
- CondPower, [4](#)
- cpd.PwrGSD, [5](#), [13](#), [33](#), [37](#), [44](#)
- CRRtoRR, [10](#)
- CY2TOShaz, [11](#)
- detail, [12](#)
- DX, [12](#)
- Elements, [6](#), [13](#), [33](#)
- EX1gXK, [14](#), [21](#)
- GrpSeqBnds, [3](#), [5](#), [15](#), [22](#), [26](#), [31](#), [34](#), [35](#), [48](#), [49](#), [51](#)
- gsd.dens, [14](#), [19](#)
- Haybittle, [21](#)

IntSurvDiff, [23](#), [53](#)

LanDemets, [22](#), [25](#), [31](#), [34](#), [35](#), [48](#)

lookup, [27](#)

lung, [28](#)

mystack, [29](#)

mysurvfit, [30](#)

ObrienFleming, [26](#), [31](#), [34](#), [35](#)

plot.cpd.PwrGSD, [6](#), [32](#)

Pocock, [26](#), [31](#), [33](#), [35](#)

Pow, [26](#), [31](#), [34](#), [34](#)

Power, [6](#), [33](#), [36](#)

PwrGSD, [13](#), [18](#), [22](#), [26](#), [31](#), [34](#), [35](#), [37](#), [37](#), [48](#)

RCM2RR, [45](#)

RR2RCM, [46](#)

SC, [22](#), [26](#), [46](#)

SCtoBdry, [49](#)

SimGSB, [50](#)

wtdlogrank, [25](#), [51](#)