# Package 'safestats'

July 23, 2025

```
Type Package
Title Safe Anytime-Valid Inference
Version 0.8.7
Maintainer Alexander Ly <a.ly@jasp-stats.org>
Description Functions to design and apply tests that are anytime valid. The
      functions can be used to design hypothesis tests in the prospective/randomised
      control trial setting or in the observational/retrospective setting. The
      resulting tests remain valid under both optional stopping and optional
      continuation. The current version includes safe t-tests and safe tests of
      two proportions. For details on the theory of safe tests, see
      Grunwald, de Heide and Koolen (2019) ``Safe Testing" <doi:10.48550/arXiv.1906.07801>,
      for details on safe logrank tests see ter Schure, Perez-Ortiz, Ly and Grunwald
      (2020) `The Safe Logrank Test: Error Control under Continuous Monitoring with
      Unlimited Horizon" <doi:10.48550/arXiv.2011.06931v3> and Turner, Ly and Grunwald (2021)
      ``Safe Tests and Always-Valid Confidence Intervals for contingency tables and
      beyond" <doi:10.48550/arXiv.2106.02693> for details on safe contingency table tests.
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Author Rosanne Turner [aut],
      Alexander Ly [cre, aut],
      Muriel Felipe Perez-Ortiz [ctb],
      Judith ter Schure [ctb],
      Peter Grunwald [ctb]
```

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#### $check And Returns Es {\tt MinParameter Side}$

Checks consistency between the sided of the hypothesis and the minimal clinically relevant effect size or safe test defining parameter. Throws an error if the one-sided hypothesis is incongruent with the

### Description

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Checks consistency between the sided of the hypothesis and the minimal clinically relevant effect size or safe test defining parameter. Throws an error if the one-sided hypothesis is incongruent with the

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#### Usage

```
checkAndReturnsEsMinParameterSide(
  paramToCheck,
  alternative = c("twoSided", "greater", "less"),
  esMinName = c("noName", "meanDiffMin", "phiS", "deltaMin", "deltaS", "hrMin", "thetaS",
        "deltaTrue"),
  paramDomain = NULL
)
```

#### **Arguments**

paramToCheck numeric. Either a named safe test defining parameter such as phiS, or thetaS,

or a minimal clinically relevant effect size called with a non-null esMinName

name

alternative a character string specifying the alternative hypothesis must be one of "twoSided"

(default), "greater" or "less".

esMinName provides the name of the effect size. Either "meanDiffMin" for the z-test, "deltaMin"

for the t-test, or "hrMin" for the logrank test

paramDomain Domain of the paramToCheck, typically, positiveNumbers. Default NULL

#### Value

paramToCheck after checking, perhaps with a change in sign

checkAndReturnsNPlan Check consistency between nPlan and the testType for one and twosample z and t-tests

#### **Description**

Check consistency between nPlan and the testType for one and two-sample z and t-tests

#### Usage

```
checkAndReturnsNPlan(
    nPlan,
    ratio = 1,
    testType = c("oneSample", "paired", "twoSample")
)
```

nPlan	optional numeric vector of length at most 2. When provided, it is used to find the safe test defining parameter phiS. Note that if the purpose is to plan based on nPlan alone, then both meanDiffMin and beta should be set to NULL.
ratio	numeric > 0 representing the randomisation ratio of condition 2 over condition 1. If testType is not equal to "twoSample", or if nPlan is of length(1) then ratio=1.
testType	either one of "oneSample", "paired", "twoSample".

#### Value

nPlan a vector of sample sizes of length 1 or 2

check Double Arguments Design Object

Helper function to check whether arguments are specified in a function at a higher level and already provided in the design object.

### Description

Helper function to check whether arguments are specified in a function at a higher level and already provided in the design object.

### Usage

```
checkDoubleArgumentsDesignObject(designObj, ...)
```

### Arguments

```
design0bj an object of class "safeDesign".
... arguments that need checking.
```

### Value

Returns nothing only used for its side-effects to produces warnings if needed.

### **Examples**

```
designObj <- designSafeZ(0.4)
checkDoubleArgumentsDesignObject(designObj, "alpha"=NULL, alternative=NULL)
# Throws a warning
checkDoubleArgumentsDesignObject(designObj, "alpha"=0.4, alternative="d")</pre>
```

computeBetaBatchSafeZ Helper function: Computes the type II error based on the minimal clinically relevant effect size and sample size.

### **Description**

Helper function: Computes the type II error based on the minimal clinically relevant effect size and sample size.

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#### Usage

```
computeBetaBatchSafeZ(
  meanDiffMin,
  nPlan,
  alpha = 0.05,
  sigma = 1,
  kappa = sigma,
  alternative = c("twoSided", "greater", "less"),
  testType = c("oneSample", "paired", "twoSample"),
  parameter = NULL
)
```

#### **Arguments**

meanDiffMin numeric that defines the minimal relevant mean difference, the smallest population mean that we would like to detect. nPlan optional numeric vector of length at most 2. When provided, it is used to find the safe test defining parameter phiS. Note that if the purpose is to plan based on nPlan alone, then both meanDiffMin and beta should be set to NULL. alpha numeric in (0, 1) that specifies the tolerable type I error control –independent on n- that the designed test has to adhere to. Note that it also defines the rejection rule e10 > 1/alpha. sigma numeric > 0 representing the assumed population standard deviation used for the true population standard deviation. Default kappa=sigma. kappa alternative a character string specifying the alternative hypothesis must be one of "twoSided" (default), "greater" or "less". either one of "oneSample", "paired", "twoSample". testType

#### Value

parameter

numeric that represents the type II error

nPlan.	computeBetaSafeT	Helper function: Computes the type II error of the safeTTest based on the minimal clinically relevant standardised mean difference and nPlan.
--------	------------------	---

optional test defining parameter. Default set to NULL.

### **Description**

Helper function: Computes the type II error of the safeTTest based on the minimal clinically relevant standardised mean difference and nPlan.

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#### Usage

```
computeBetaSafeT(
  deltaMin,
  nPlan,
  alpha = 0.05,
  alternative = c("twoSided", "greater", "less"),
  testType = c("oneSample", "paired", "twoSample"),
  seed = NULL,
  parameter = NULL,
  pb = TRUE,
  nSim = 1000L,
  nBoot = 1000L
)
```

#### **Arguments**

deltaMin numeric that defines the minimal relevant standardised effect size, the smallest

effect size that we would the experiment to be able to detect.

nPlan vector of max length 2 representing the planned sample sizes.

alpha numeric in (0, 1) that specifies the tolerable type I error control –independent of

n- that the designed test has to adhere to. Note that it also defines the rejection

rule e10 > 1/alpha.

alternative a character string specifying the alternative hypothesis must be one of "twoSided"

(default), "greater" or "less".

testType either one of "oneSample", "paired", "twoSample".

seed integer, seed number.

parameter optional test defining parameter. Default set to NULL.

pb logical, if TRUE, then show progress bar.

nSim integer > 0, the number of simulations needed to compute power or the number

of samples paths for the safe z test under continuous monitoring.

nBoot integer > 0 representing the number of bootstrap samples to assess the accuracy

of approximation of the power, the number of samples for the safe z test under continuous monitoring, or for the computation of the logarithm of the implied

target.

#### Value

a list which contains at least beta and an adapted bootObject of class boot.

#### **Examples**

```
computeBetaSafeT(deltaMin=0.7, 27, nSim=10)
```

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computeBetaSafeZ

Helper function: Computes the type II error based on the minimal clinically relevant mean difference and nPlan

### Description

Helper function: Computes the type II error based on the minimal clinically relevant mean difference and nPlan

### Usage

```
computeBetaSafeZ(
  meanDiffMin,
  nPlan,
  alpha = 0.05,
  alternative = c("twoSided", "greater", "less"),
  sigma = 1,
  kappa = sigma,
  testType = c("oneSample", "paired", "twoSample"),
  parameter = NULL,
  pb = TRUE,
  nSim = 1000L,
  nBoot = 1000L
)
```

meanDiffMin	numeric that defines the minimal relevant mean difference, the smallest population mean that we would like to detect.
nPlan	optional numeric vector of length at most 2. When provided, it is used to find the safe test defining parameter phiS. Note that if the purpose is to plan based on nPlan alone, then both meanDiffMin and beta should be set to NULL.
alpha	numeric in $(0, 1)$ that specifies the tolerable type I error control –independent on n– that the designed test has to adhere to. Note that it also defines the rejection rule $e^{10} > 1/a$ lpha.
alternative	a character string specifying the alternative hypothesis must be one of "twoSided" (default), "greater" or "less".
sigma	numeric $> 0$ representing the assumed population standard deviation used for the test.
kappa	the true population standard deviation. Default kappa=sigma.
testType	either one of "oneSample", "paired", "twoSample".
parameter	optional test defining parameter. Default set to NULL.
pb	logical, if TRUE, then show progress bar.
nSim	integer $> 0$ , the number of simulations needed to compute power or the number of samples paths for the safe z test under continuous monitoring.

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nBoot

integer > 0 representing the number of bootstrap samples to assess the accuracy of approximation of the power, the number of samples for the safe z test under continuous monitoring, or for the computation of the logarithm of the implied target.

#### Value

a list which contains at least beta and an adapted bootObject of class boot.

### **Examples**

```
computeBetaSafeZ(meanDiffMin=0.7, 20, nSim=10)
```

computeBootObj

Computes the bootObj for sequential sampling procedures regarding nPlan, beta, the implied target

#### **Description**

Computes the bootObj for sequential sampling procedures regarding nPlan, beta, the implied target

### Usage

values	numeric vector. If objType equals "nPlan" or "beta" then values should be stopping times, if objType equals "logImpliedTarget" then values should be eValues.
beta	numeric in (0, 1) that specifies the tolerable type II error control necessary to calculate both "n" and "phiS". Note that 1-beta defines the power.
nPlan	integer > 0 representing the number of planned samples (for the first group).
nBoot	integer > 0 representing the number of bootstrap samples to assess the accuracy of approximation of the power, the planned sample size(s) of the safe test under continuous monitoring.
alpha	numeric in $(0, 1)$ that specifies the tolerable type I error control –independent on n– that the designed test has to adhere to. Note that it also defines the rejection rule $e10 > 1/alpha$ .
objType	character string either "nPlan", "nMean", "beta", "betaFromEValues", "expectedStopTime" or "logImpliedTarget".

### Value

bootObj

### **Examples**

```
computeBootObj(1:100, objType="nPlan", beta=0.3)
```

 $compute {\tt Confidence Bound For Log Odds Two Proportions}$ 

Estimate an upper or lower bound for a safe confidence sequence on the logarithm of the odds ratio for two proportions.

### **Description**

Estimate an upper or lower bound for a safe confidence sequence on the logarithm of the odds ratio for two proportions.

### Usage

```
computeConfidenceBoundForLogOddsTwoProportions(
   ya,
   yb,
   safeDesign,
   bound = c("lower", "upper"),
   deltaStart,
   deltaStop,
   precision
)
```

ya	positive observations/ events per data block in group a: a numeric with integer values between (and including) 0 and na, the number of observations in group a per block.
yb	positive observations/ events per data block in group b: a numeric with integer values between (and including) 0 and nb, the number of observations in group b per block.
safeDesign	a 'safeDesign' object obtained through designSafeTwoProportions
bound	type of bound to calculate; "lower" to get a lower bound on positive delta, "upper" to get an upper bound on negative delta.
deltaStart	starting value of the grid to search over for the bound on the confidence sequence (in practice: the interval). Numeric $>0$ when searching for a lower bound, numeric $<0$ when searching for an upper bound.
deltaStop	end value of the grid to search over for the bound on the confidence sequence (in practice: the interval). Numeric >0 when searching for a lower bound, numeric < 0 when searching for an upper bound.
precision	precision of the grid between deltaStart and deltaStop.

#### Value

numeric: the established lower- or upper bound on the logarithm of the odds ratio between the groups

### Examples

 $\verb|computeConfidenceBoundsForDifferenceTwoProportions|\\$ 

Estimate Lower and Upper Bounds on the Confidence Sequence (Interval) for the Difference Divergence Measure for Two Proportions

### **Description**

Estimate Lower and Upper Bounds on the Confidence Sequence (Interval) for the Difference Divergence Measure for Two Proportions

### Usage

```
computeConfidenceBoundsForDifferenceTwoProportions(
  ya,
  yb,
  precision,
  safeDesign
)
```

#### **Arguments**

ya

positive observations/ events per data block in group a: a numeric with integer values between (and including) 0 and na, the number of observations in group a per block.

positive observations/ events per data block in group b: a numeric with integer values between (and including) 0 and nb, the number of observations in group b per block.

precision precision of the grid of differences to search over for the lower and upper bounds.

safeDesign a 'safeDesign' object obtained through designSafeTwoProportions

#### Value

list with found lower and upper bound.

### **Examples**

```
balancedSafeDesign <- designSafeTwoProportions(na = 1, \\ nb = 1, \\ nBlocksPlan = 10, \\ alpha = 0.05) ya <- c(1,1,1,1,1,1,1,1,1,0,1) yb <- c(0,0,0,0,1,0,0,0,0,0) computeConfidenceBoundsForDifferenceTwoProportions(ya = ya, \\ yb = yb, \\ precision = 20, \\ safeDesign = balancedSafeDesign)
```

computeConfidenceIntervalT

Helper function: Computes the safe confidence sequence for the mean in a t-test

#### **Description**

Helper function: Computes the safe confidence sequence for the mean in a t-test

```
computeConfidenceIntervalT(
  meanObs,
  sdObs,
  nEff,
  nu,
  deltaS,
  ciValue = 0.95,
  g = NULL
)
```

meanObs	numeric, the observed mean. For two sample tests this is difference of the means.
sd0bs	numeric, the observed standard deviation. For a two-sample test this is the root of the pooled variance.
nEff	numeric $> 0$ , the effective sample size. For one sample test this is just n.
nu	numeric > 0, the degrees of freedom.
deltaS	numeric > 0, the safe test defining parameter.
ciValue	numeric is the ciValue-level of the confidence sequence. Default ciValue=0.95.
g	numeric > 0, used as the variance of the normal prior on the population delta Default is NULL in which case g=delta^2.

### Value

numeric vector that contains the upper and lower bound of the safe confidence sequence

### **Examples**

```
computeConfidenceIntervalT(meanObs=0.3, sdObs=2, nEff=12, nu=11, deltaS=0.4)
```

computeConfidenceIntervalZ

Helper function: Computes the safe confidence sequence for a z-test

# Description

Helper function: Computes the safe confidence sequence for a z-test

```
computeConfidenceIntervalZ(
  nEff,
  meanObs,
  phiS,
  sigma = 1,
  ciValue = 0.95,
  alternative = "twoSided",
  a = NULL,
  g = NULL
)
```

nEff	numeric > 0, the effective sample size.
meanObs	numeric, the observed mean. For two sample tests this is difference of the means.
phiS	numeric > 0, the safe test defining parameter.
sigma	numeric $> 0$ representing the assumed population standard deviation used for the test.
ciValue	numeric is the ciValue-level of the confidence sequence. Default ciValue=0.95.
alternative	a character string specifying the alternative hypothesis must be one of "twoSided" (default), "greater" or "less".
a	numeric, the centre of the normal prior on population mean (of the normal data). Default is NULL, which implies the default choice of setting the centre equal to the null hypothesis.
g	numeric > 0, used to define g sigma^2 as the variance of the normal prior on the population (of the normal data). Default is NULL in which case $g=phiS^2/sigma^2$ .

#### Value

numeric vector that contains the upper and lower bound of the safe confidence sequence

#### **Examples**

```
computeConfidenceIntervalZ(nEff=15, meanObs=0.3, phiS=0.2)
```

 ${\tt computeEsMinSafeT}$ 

Helper function: Computes the minimal clinically relevant standardised mean difference for the safe t-test nPlan and beta.

### Description

Helper function: Computes the minimal clinically relevant standardised mean difference for the safe t-test nPlan and beta.

```
computeEsMinSafeT(
   nPlan,
   alpha = 0.05,
   beta = 0.2,
   alternative = c("twoSided", "greater", "less"),
   testType = c("oneSample", "paired", "twoSample"),
   lowN = 3,
   highN = 1e+06,
   ratio = 1
)
```

nPlan	vector of max length 2 representing the planned sample sizes.
alpha	numeric in $(0, 1)$ that specifies the tolerable type I error control –independent of n– that the designed test has to adhere to. Note that it also defines the rejection rule $e10 > 1/alpha$ .
beta	numeric in $(0, 1)$ that specifies the tolerable type II error control necessary to calculate both the sample sizes and deltaS, which defines the test. Note that 1-beta defines the power.
alternative	a character string specifying the alternative hypothesis must be one of "twoSided" (default), "greater" or "less".
testType	either one of "oneSample", "paired", "twoSample".
lowN	integer minimal sample size of the (first) sample when computing the power due to optional stopping. Default lowN is set $1$ .
highN	integer minimal sample size of the (first) sample when computing the power due to optional stopping. Default highN is set 1e6.
ratio	$numeric > 0 \ representing \ the \ randomisation \ ratio \ of \ condition \ 2 \ over \ condition \ 1.$ If testType is not equal to "twoSample", or if nPlan is of length(1) then ratio=1.

#### Value

a list which contains at least nPlan and the phiS the parameter that defines the safe test

computeLogrankBetaFrom

Helper function: Computes the type II error under optional stopping based on the minimal clinically relevant hazard ratio and the maximum number of nEvents.

### **Description**

Helper function: Computes the type II error under optional stopping based on the minimal clinically relevant hazard ratio and the maximum number of nEvents.

```
computeLogrankBetaFrom(
  hrMin,
  nEvents,
  m0 = 50000L,
  m1 = 50000L,
  alpha = 0.05,
  alternative = c("twoSided", "greater", "less"),
  nSim = 1000L,
  nBoot = 10000L,
```

```
groupSizePerTimeFunction = returnOne,
parameter = NULL,
pb = TRUE
)
```

hrMin numeric that defines the minimal relevant hazard ratio, the smallest hazard ratio

that we want to detect.

nEvents numeric > 0, targetted number of events.

m0 Number of subjects in the control group 0/1 at the beginning of the trial, i.e.,

nPlan[1].

m1 Number of subjects in the treatment group 1/2 at the beginning of the trial, i.e.,

nPlan[2].

alpha numeric in (0, 1) that specifies the tolerable type I error control –independent on

n- that the designed test has to adhere to. Note that it also defines the rejection

rule e10 > 1/alpha.

alternative a character string specifying the alternative hypothesis, which must be one of

"twoSided" (default), "greater" or "less". The alternative is pitted against the null hypothesis of equality of the survival distributions. More specifically, let lambda1 be the hazard rate of group 1 (i.e., placebo), and lambda2 the hazard ratio of group 2 (i.e., treatment), then the null hypothesis states that the hazard ratio theta = lambda2/lambda1 = 1. If alternative = "less", the null hypothesis is compared to theta < 1, thus, lambda2 < lambda1, that is, the hazard of group 2 (i.e., treatment) is less than that of group 1 (i.e., placebo), hence, the treatment is beneficial. If alternative = "greater", then the null hypothesis is compared to

theta > 1, thus, lambda2 > lambda1, hence, harm.

nSim integer > 0, the number of simulations needed to compute power or the number

of events for the exact safe logrank test under continuous monitoring

nBoot integer > 0 representing the number of bootstrap samples to assess the accuracy

of the approximation of power or nEvents for the exact safe logrank test under

continuous monitoring

groupSizePerTimeFunction

A function without parameters and integer output. This function provides the number of events at each time step. For instance, if rpois(1, 7) leads to a

random number of events at each time step.

parameter Numeric > 0, represents the safe tests defining thetaS. Default NULL so it's

decided by the algorithm, typically, this equals hrMin, which corresponds to the

GROW choice.

pb logical, if TRUE, then show progress bar.

#### Value

a list which contains at least beta and an adapted bootObject of class boot.

#### Author(s)

Muriel Felipe Perez-Ortiz and Alexander Ly

#### **Examples**

```
computeLogrankBetaFrom(hrMin=0.7, 300, nSim=10)
```

computeLogrankNEvents Helper function: Computes the planned sample size based on the minimal clinical relevant hazard ratio, alpha and beta under optional stopping.

# Description

Helper function: Computes the planned sample size based on the minimal clinical relevant hazard ratio, alpha and beta under optional stopping.

### Usage

```
computeLogrankNEvents(
   hrMin,
   beta,
   m0 = 50000,
   m1 = 50000,
   alpha = 0.05,
   alternative = c("twoSided", "greater", "less"),
   nSim = 1000L,
   nBoot = 1000L,
   groupSizePerTimeFunction = returnOne,
   nMax = Inf,
   parameter = NULL,
   digits = getOption("digits"),
   pb = TRUE
)
```

hrMin	numeric that defines the minimal relevant hazard ratio, the smallest hazard ratio that we want to detect.
beta	numeric in $(0, 1)$ that specifies the tolerable type II error control necessary to calculate both "n" and "phiS". Note that 1-beta defines the power.
mØ	Number of subjects in the control group 0/1 at the beginning of the trial, i.e., nPlan[1].
m1	Number of subjects in the treatment group 1/2 at the beginning of the trial, i.e., nPlan[2].

alpha numeric in (0, 1) that specifies the tolerable type I error control –independent on

n- that the designed test has to adhere to. Note that it also defines the rejection

rule e10 > 1/alpha.

alternative a character string specifying the alternative hypothesis, which must be one of

"twoSided" (default), "greater" or "less". The alternative is pitted against the null hypothesis of equality of the survival distributions. More specifically, let lambda1 be the hazard rate of group 1 (i.e., placebo), and lambda2 the hazard ratio of group 2 (i.e., treatment), then the null hypothesis states that the hazard ratio theta = lambda2/lambda1 = 1. If alternative = "less", the null hypothesis is compared to theta < 1, thus, lambda2 < lambda1, that is, the hazard of group 2 (i.e., treatment) is less than that of group 1 (i.e., placebo), hence, the treatment is beneficial. If alternative = "greater", then the null hypothesis is compared to

theta > 1, thus, lambda2 > lambda1, hence, harm.

nSim integer > 0, the number of simulations needed to compute power or the number

of events for the exact safe logrank test under continuous monitoring

nBoot integer > 0 representing the number of bootstrap samples to assess the accuracy

of the approximation of power or nEvents for the exact safe logrank test under

continuous monitoring

groupSizePerTimeFunction

A function without parameters and integer output. This function provides the number of events at each time step. For instance, if rpois(1, 7) leads to a

random number of events at each time step.

nMax An integer. Once nEvents hits nMax the experiment terminates, if it didn't stop

due to threshold crossing crossing already. Default set to Inf.

parameter Numeric > 0, represents the safe tests defining thetaS. Default NULL so it's

decided by the algorithm, typically, this equals hrMin, which corresponds to the

GROW choice.

digits number of significant digits to be used.

pb logical, if TRUE, then show progress bar.

#### Value

a list which contains at least nEvents and an adapted bootObject of class boot.

#### Author(s)

Muriel Felipe Perez-Ortiz and Alexander Ly

### **Examples**

computeLogrankNEvents(0.7, 0.2, nSim=10)

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computeLogrankZ	Helper function to computes the logrank statistic for 'Surv' objects of
	type "right" and "counting" with the hypergeometric variance.

#### **Description**

This function was created to complement survdiff from the 'survival' package, which is restricted to 'Surv' objects of type "right". Most likely survdiff is much faster

### Usage

```
computeLogrankZ(
   survObj,
   group,
   computeZ = TRUE,
   computeExactE = FALSE,
   theta0 = 1,
   thetaS = NULL,
   ...
)
```

#### **Arguments**

survObj a Surv object that is either of type group a grouping factor with 2 levels computeZ logical. If TRUE computes the logrank z-statistic. Default is TRUE. computeExactE logical. If TRUE computes one-sided exact logrank e-value. Default is FALSE. theta0 numeric > 0 used only for the e-value, i.e., if computeExactE is TRUE. Default is 1. thetaS numeric > 0 used only for the e-value, i.e., if computeExactE is TRUE. Default is NULL. further arguments to be passed to or from methods.

#### Value

Returns a list containing at least the following components:

```
nEvents the number of events.
z the observed logrank statistic.
oMinEVector vector of observed minus expected.
varVector vector of hypergeometric variances.
stopTimeVector vector at which the events occurred.
```

#### **Examples**

computeMinEsBatchSafeZ

Computes the smallest mean difference that is detectable with chance 1-beta, for the provided sample size

### **Description**

Computes the smallest mean difference that is detectable with chance 1-beta, for the provided sample size

#### Usage

```
computeMinEsBatchSafeZ(
   nPlan,
   alpha = 0.05,
   beta = 0.2,
   sigma = 1,
   kappa = sigma,
   alternative = c("twoSided", "greater", "less"),
   testType = c("oneSample", "paired", "twoSample"),
   parameter = NULL,
   maxIter = 10
)
```

### Arguments

nPlan

optional numeric vector of length at most 2. When provided, it is used to find the safe test defining parameter phiS. Note that if the purpose is to plan based on nPlan alone, then both meanDiffMin and beta should be set to NULL.

alpha

numeric in (0, 1) that specifies the tolerable type I error control –independent on n– that the designed test has to adhere to. Note that it also defines the rejection rule e10 > 1/alpha.

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numeric in (0, 1) that specifies the tolerable type II error control necessary to calculate both "n" and "phiS". Note that 1-beta defines the power.

sigma numeric > 0 representing the assumed population standard deviation used for the test.

kappa the true population standard deviation. Default kappa=sigma.

alternative a character string specifying the alternative hypothesis must be one of "twoSided" (default), "greater" or "less".

testType either one of "oneSample", "paired", "twoSample".

parameter optional test defining parameter. Default set to NULL.

maximum number of iterations in the optimisation process for two-sided designs

Value

maxIter

numeric > 0 that represents the minimal detectable mean difference

computeNEff	Help function to compute the effective sample size based on a length 2 vector of samples

### **Description**

Help function to compute the effective sample size based on a length 2 vector of samples

#### Usage

```
computeNEff(n, testType = c("oneSample", "paired", "twoSample"), silent = TRUE)
```

### **Arguments**

n vector of length at most 2 representing the sample sizes of the first and second

group

 $test {\tt Type} \qquad \qquad either \ one \ of \ "one Sample", \ "paired", \ "two Sample".$ 

silent logical, if true, then turn off warnings

#### Value

a numeric that represents the effective sample size.

 ${\tt computeNPlanBatchSafeT}$ 

Helper function: Computes the planned sample size for the safe t-test based on the minimal clinically relevant standardised effect size, alpha and beta.

### Description

Helper function: Computes the planned sample size for the safe t-test based on the minimal clinically relevant standardised effect size, alpha and beta.

### Usage

```
computeNPlanBatchSafeT(
  deltaMin,
  alpha = 0.05,
  beta = 0.2,
  alternative = c("twoSided", "greater", "less"),
  testType = c("oneSample", "paired", "twoSample"),
  lowN = 3,
  highN = 1e+06,
  ratio = 1
)
```

deltaMin	numeric that defines the minimal relevant standardised effect size, the smallest effect size that we would the experiment to be able to detect.
alpha	numeric in $(0, 1)$ that specifies the tolerable type I error control –independent of n– that the designed test has to adhere to. Note that it also defines the rejection rule $e10 > 1/alpha$ .
beta	numeric in (0, 1) that specifies the tolerable type II error control necessary to calculate both the sample sizes and deltaS, which defines the test. Note that 1-beta defines the power.
alternative	a character string specifying the alternative hypothesis must be one of "twoSided" (default), "greater" or "less".
testType	either one of "oneSample", "paired", "twoSample".
lowN	integer minimal sample size of the (first) sample when computing the power due to optional stopping. Default lowN is set 1.
highN	integer minimal sample size of the (first) sample when computing the power due to optional stopping. Default highN is set 1e6.
ratio	numeric > 0 representing the randomisation ratio of condition 2 over condition 1. If testType is not equal to "twoSample", or if nPlan is of length(1) then ratio=1.

### Value

a list which contains at least nPlan and the phiS the parameter that defines the safe test

computeNPlanBatchSafeZ

Helper function: Computes the planned sample size based on the minimal clinical relevant mean difference, alpha and beta.

### Description

Helper function: Computes the planned sample size based on the minimal clinical relevant mean difference, alpha and beta.

### Usage

```
computeNPlanBatchSafeZ(
  meanDiffMin,
  alpha = 0.05,
  beta = 0.2,
  sigma = 1,
  kappa = sigma,
  alternative = c("twoSided", "greater", "less"),
  testType = c("oneSample", "paired", "twoSample"),
  tol = 1e-05,
  highN = 1e+06,
  ratio = 1,
  parameter = NULL,
  grow = TRUE
)
```

meanDiffMin	numeric that defines the minimal relevant mean difference, the smallest population mean that we would like to detect.
alpha	numeric in $(0, 1)$ that specifies the tolerable type I error control –independent on n– that the designed test has to adhere to. Note that it also defines the rejection rule $e10 > 1/alpha$ .
beta	numeric in (0, 1) that specifies the tolerable type II error control necessary to calculate both "n" and "phiS". Note that 1-beta defines the power.
sigma	numeric $> 0$ representing the assumed population standard deviation used for the test.
kappa	the true population standard deviation. Default kappa=sigma.
alternative	a character string specifying the alternative hypothesis must be one of "twoSided" (default), "greater" or "less".
testType	either one of "oneSample", "paired", "twoSample".

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tol	a number that defines the stepsizes between the lowParam and highParam.
highN	integer that defines the largest n of our search space for n. This might be the largest n that we are able to fund.
ratio	numeric > 0 representing the randomisation ratio of condition 2 over condition 1. If testType is not equal to "twoSample", or if nPlan is of length(1) then ratio=1.
parameter	optional test defining parameter. Default set to NULL.
grow	logical, default set to TRUE so the grow safe test is used in the design.

### Value

a list which contains at least nPlan and the phiS, that is, the parameter that defines the safe test.

computeNPlanSafeT Helper function: Computes the planned sample size of the safe t-test based on the minimal clinical relevant standardised mean difference.

#### **Description**

Helper function: Computes the planned sample size of the safe t-test based on the minimal clinical relevant standardised mean difference.

### Usage

```
computeNPlanSafeT(
  deltaMin,
 beta = 0.2,
  alpha = 0.05,
  alternative = c("twoSided", "less", "greater"),
  testType = c("oneSample", "paired", "twoSample"),
  lowN = 3,
  highN = 1e+06,
  ratio = 1,
  nSim = 1000L,
  nBoot = 1000L
  parameter = NULL,
  pb = TRUE,
 nMax = 1e+06,
  seed = NULL
)
```

### Arguments

deltaMin numeric that defines the minimal relevant standardised effect size, the smallest

effect size that we would the experiment to be able to detect.

beta numeric in (0, 1) that specifies the tolerable type II error control necessary to

calculate both the sample sizes and deltaS, which defines the test. Note that

1-beta defines the power.

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alpha	numeric in $(0, 1)$ that specifies the tolerable type I error control –independent of n– that the designed test has to adhere to. Note that it also defines the rejection rule $e10 > 1/alpha$ .
alternative	a character string specifying the alternative hypothesis must be one of "twoSided" (default), "greater" or "less".
testType	either one of "oneSample", "paired", "twoSample".
lowN	integer minimal sample size of the (first) sample when computing the power due to optional stopping. Default lowN is set 1.
highN	integer minimal sample size of the (first) sample when computing the power due to optional stopping. Default highN is set 1e6.
ratio	numeric > 0 representing the randomisation ratio of condition 2 over condition 1. If testType is not equal to "twoSample", or if nPlan is of length(1) then ratio=1.
nSim	integer $> 0$ , the number of simulations needed to compute power or the number of samples paths for the safe z test under continuous monitoring.
nBoot	integer > 0 representing the number of bootstrap samples to assess the accuracy of approximation of the power, the number of samples for the safe z test under continuous monitoring, or for the computation of the logarithm of the implied target.
parameter	optional test defining parameter. Default set to NULL.
pb	logical, if TRUE, then show progress bar.
nMax	integer > 0, maximum sample size of the (first) sample in each sample path.
seed	integer, seed number.

### Value

a list which contains at least nPlan and an adapted bootObject of class boot.

# **Examples**

```
computeNPlanSafeT(0.7, 0.2, nSim=10)
```

computeNPlanSafeZ	Helper function: Computes the planned sample size based on the min-
00pa 00 2a0a. 02	Tresper functions compared the premitted sample size caused on the mini
	imal clinical relevant mean difference, alpha and beta
	imai ciinicai reievani mean aijjerence, aipna ana beia

# Description

Helper function: Computes the planned sample size based on the minimal clinical relevant mean difference, alpha and beta

#### Usage

```
computeNPlanSafeZ(
  meanDiffMin,
  beta = 0.2,
  alpha = 0.05,
  alternative = c("twoSided", "less", "greater"),
  testType = c("oneSample", "paired", "twoSample"),
  sigma = 1,
  kappa = sigma,
  ratio = 1,
  nSim = 1000L,
  nBoot = 1000L,
  parameter = NULL,
  pb = TRUE,
  nMax = 1e+08
)
```

#### **Arguments**

meanDiffMin numeric that defines the minimal relevant mean difference, the smallest popula-

tion mean that we would like to detect.

beta numeric in (0, 1) that specifies the tolerable type II error control necessary to

calculate both "n" and "phiS". Note that 1-beta defines the power.

alpha numeric in (0, 1) that specifies the tolerable type I error control –independent on

n- that the designed test has to adhere to. Note that it also defines the rejection

rule e10 > 1/alpha.

alternative a character string specifying the alternative hypothesis must be one of "twoSided"

(default), "greater" or "less".

testType either one of "oneSample", "paired", "twoSample".

sigma numeric > 0 representing the assumed population standard deviation used for

the test.

kappa the true population standard deviation. Default kappa=sigma.

ratio numeric > 0 representing the randomisation ratio of condition 2 over condition 1.

If testType is not equal to "twoSample", or if nPlan is of length(1) then ratio=1.

nSim integer > 0, the number of simulations needed to compute power or the number

of samples paths for the safe z test under continuous monitoring.

nBoot integer > 0 representing the number of bootstrap samples to assess the accuracy

of approximation of the power, the number of samples for the safe z test under continuous monitoring, or for the computation of the logarithm of the implied

target.

parameter optional test defining parameter. Default set to NULL.

pb logical, if TRUE, then show progress bar.

nMax integer > 0, maximum sample size of the (first) sample in each sample path.

#### Value

a list which contains at least nPlan and an adapted bootObject of class boot.

#### **Examples**

```
computeNPlanSafeZ(0.7, 0.2, nSim=10)
```

computeStatsForLogrank

Computes the sufficient statistics needed to compute 'logrankSingleZ'

### **Description**

Computes the sufficient statistics needed to compute 'logrankSingleZ'

### Usage

```
computeStatsForLogrank(
   survDataFrame,
   y0Index,
   y1Index,
   timeNow,
   timeBefore,
   survType = "right",
   ...
)
```

### **Arguments**

```
survDataFrame a 'Surv' object converted to a matrix, then to a data.frame

y@Index vector of integers corresponding to the control group

y1Index vector of integers corresponding to the treatment group

timeNow numeric, current time

timeBefore numeric, previous time

survType character, either "right" or "counting" (left truncated, right censored)

... further arguments to be passed to or from methods.
```

#### Value

Returns a list containing at least the following components:

```
obs0 number of observations in the control group.
obs1 number of observations in the treatment group.
y0 total number of participants in the control group.
y1 total number of participants in the treatment group.#'
```

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#### **Examples**

```
data <- generateSurvData(nP = 5,</pre>
                           nT = 5,
                           lambdaP = 0.03943723,
                           lambdaT = 0.5 \times 0.03943723,
                           endTime = 40,
                           seed = 2006)
survObj <- survival::Surv(data$time, data$status)</pre>
survDataFrame <- as.data.frame(as.matrix(survObj))</pre>
y0Index <- which(data$group=="P")</pre>
y1Index <- which(data$group=="T")</pre>
timeNow <- 4
timeBefore <- 0
computeStatsForLogrank(survDataFrame, y0Index, y1Index, timeNow, timeBefore)
timeNow <- 13
timeBefore <- 4
computeStatsForLogrank(survDataFrame, y0Index, y1Index, timeNow, timeBefore)
```

defineTTestN

Computes a Sequence of (Effective) Sample Sizes

### Description

Helper function that outputs the sample sizes, effective sample sizes and the degrees of freedom depending on the type of t-test. Also used for z-tests.

### Usage

```
defineTTestN(
  lowN = 3,
  highN = 100,
  ratio = 1,
  testType = c("oneSample", "paired", "twoSample")
)
```

### **Arguments**

lowN integer minimal sample size of the (first) sample when computing the power due

to optional stopping. Default lowN is set 1.

highN integer minimal sample size of the (first) sample when computing the power due

to optional stopping. Default highN is set 1e6.

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ratio	numeric $> 0$ representing the randomisation ratio of condition 2 over condition 1.
	If testType is not equal to "twoSample", or if nPlan is of length(1) then ratio=1.
testType	either one of "oneSample", "paired", "twoSample".

# Value

Returns the sample sizes and degrees of freedom.

designFreqT	Design a Frequentist T-Test	

# Description

Computes the number of samples necessary to reach a tolerable type I and type II error for the frequentist t-test.

# Usage

```
designFreqT(
  deltaMin,
  alpha = 0.05,
  beta = 0.2,
  alternative = c("twoSided", "greater", "less"),
  h0 = 0,
  testType = c("oneSample", "paired", "twoSample"),
  ...
)
```

deltaMin	numeric that defines the minimal relevant standardised effect size, the smallest effect size that we would the experiment to be able to detect.
alpha	numeric in $(0, 1)$ that specifies the tolerable type I error control –independent of n– that the designed test has to adhere to. Note that it also defines the rejection rule $e10 > 1/alpha$ .
beta	numeric in (0, 1) that specifies the tolerable type II error control necessary to calculate both the sample sizes and deltaS, which defines the test. Note that 1-beta defines the power.
alternative	a character string specifying the alternative hypothesis must be one of "twoSided" (default), "greater" or "less".
h0	a number indicating the hypothesised true value of the mean under the null. For the moment $h0=0$ .
testType	either one of "oneSample", "paired", "twoSample".
	further arguments to be passed to or from methods, but mainly to perform do.calls.

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#### Value

Returns an object of class 'freqTDesign'. An object of class 'freqTDesign' is a list containing at least the following components:

```
nPlan the planned sample size(s).
```

esMin the minimal clinically relevant standardised effect size provided by the user.

alpha the tolerable type I error provided by the user.

beta the tolerable type II error provided by the user.

lowN the smallest n of the search space for n provided by the user.

**highN** the largest n of the search space for n provided by the user.

testType any of "oneSample", "paired", "twoSample" provided by the user.

alternative any of "twoSided", "greater", "less" provided by the user.

### **Examples**

```
designFreqT(0.5)
```

designFreqZ

Design a Frequentist Z-Test

### **Description**

Computes the number of samples necessary to reach a tolerable type I and type II error for the frequentist z-test.

```
designFreqZ(
  meanDiffMin,
  alternative = c("twoSided", "greater", "less"),
  alpha = 0.05,
  beta = 0.2,
  testType = c("oneSample", "paired", "twoSample"),
  ratio = 1,
  sigma = 1,
  h0 = 0,
  kappa = sigma,
  lowN = 3L,
  highN = 100L,
  ...
)
```

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#### **Arguments**

meanDiffMin	numeric that defines the minimal relevant mean difference, the smallest population mean that we would like to detect.
alternative	a character string specifying the alternative hypothesis must be one of "twoSided" (default), "greater" or "less".
alpha	numeric in $(0,1)$ that specifies the tolerable type I error control –independent on n– that the designed test has to adhere to. Note that it also defines the rejection rule $e10 > 1/alpha$ .
beta	numeric in $(0, 1)$ that specifies the tolerable type II error control necessary to calculate both "n" and "phiS". Note that 1-beta defines the power.
testType	either one of "oneSample", "paired", "twoSample".
ratio	numeric $> 0$ representing the randomisation ratio of condition 2 over condition 1. If testType is not equal to "twoSample", or if nPlan is of length(1) then ratio=1.
sigma	numeric $> 0$ representing the assumed population standard deviation used for the test.
h0	numeric, represents the null hypothesis, default h0=0.
kappa	the true population standard deviation. Default kappa=sigma.
lowN	integer that defines the smallest n of our search space for n.
highN	integer that defines the largest $n$ of our search space for $n$ . This might be the largest $n$ that we are able to fund.
	further arguments to be passed to or from methods.

### Value

returns a 'freqZDesign' object.

### **Examples**

```
freqDesign <- designFreqZ(meanDiffMin = 0.5, highN = 100)
freqDesign$nPlan
freqDesign2 <- designFreqZ(meanDiffMin = 0.2, lowN = 32, highN = 200)
freqDesign2$nPlan</pre>
```

 ${\tt designPilotSafeT}$ 

Designs a Safe T-Test Based on Planned Samples nPlan

### Description

Designs a safe experiment for a prespecified tolerable type I error based on planned sample size(s), which are fixed ahead of time. Outputs a list that includes the deltaS, i.e., the safe test defining parameter.

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#### Usage

```
designPilotSafeT(
  nPlan = 50,
  alpha = 0.05,
  alternative = c("twoSided", "greater", "less"),
  h0 = 0,
  lowParam = 0.01,
  highParam = 1.2,
  tol = 0.01,
  inverseMethod = TRUE,
  logging = FALSE,
  paired = FALSE,
  maxIter = 10
)
```

#### **Arguments**

nPlan the planned sample size(s).

alpha numeric in (0, 1) that specifies the tolerable type I error control –independent of

n- that the designed test has to adhere to. Note that it also defines the rejection

rule e10 > 1/alpha.

alternative a character string specifying the alternative hypothesis must be one of "twoSided"

(default), "greater" or "less".

h0 a number indicating the hypothesised true value of the mean under the null. For

the moment h0=0.

lowParam numeric defining the smallest delta of the search space for the test-defining

deltaS for scenario 3. Currently not yet in use.

highParam numeric defining the largest delta of the search space for the test-defining deltaS

for scenario 3. Currently not yet in use.

tol a number that defines the stepsizes between the lowParam and highParam.

inverseMethod logical, always TRUE for the moment.

logging logical, if TRUE, then add invSToTThresh to output.

paired logical, if TRUE then paired t-test.

maxIter numeric > 0, the maximum number of iterations of adjustment to the candidate

set from lowParam to highParam, if the minimum is not found.

### Value

Returns an object of class 'safeDesign'. An object of class 'safeDesign' is a list containing at least the following components:

**nPlan** the planned sample size(s).

**parameter** the safe test defining parameter. Here deltaS.

**esMin** the minimal clinically relevant standardised effect size provided by the user.

alpha the tolerable type I error provided by the user.

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**beta** the tolerable type II error provided by the user.

alternative any of "twoSided", "greater", "less" provided by the user.

testType any of "oneSample", "paired", "twoSample" provided by the user.

paired logical, TRUE if "paired", FALSE otherwise.

**h0** the specified hypothesised value of the mean or mean difference depending on whether it was a one-sample or a two-sample test.

ratio default is 1. Different from 1, whenever testType equals "twoSample", then it defines ratio between the planned randomisation of condition 2 over condition 1.

lowN the smallest n of the search space for n provided by the user.

 $\mbox{highN}$  the largest n of the search space for n provided by the user.

lowParam the smallest delta of the search space for delta provided by the user.

highParam the largest delta of the search space for delta provided by the user.

tol the step size between lowParam and highParam provided by the user.

pilot FALSE (default) specified by the user to indicate that the design is not a pilot study.

call the expression with which this function is called.

#### **Examples**

```
designPilotSafeT(nPlan=30)
```

designPilotSafeZ

Designs a Safe Z-Test Based on Planned Samples nPlan

#### Description

Designs a safe experiment for a prespecified tolerable type I error based on planned sample size(s), which are fixed ahead of time. Outputs a list that includes phiS, i.e., the safe test defining parameter.

```
designPilotSafeZ(
   nPlan,
   alternative = c("twoSided", "greater", "less"),
   alpha = 0.05,
   sigma = 1,
   h0 = 0,
   kappa = sigma,
   tol = 1e-05,
   paired = FALSE,
   parameter = NULL
)
```

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#### **Arguments**

nPlan optional numeric vector of length at most 2. When provided, it is used to find

the safe test defining parameter phiS. Note that if the purpose is to plan based

on nPlan alone, then both meanDiffMin and beta should be set to NULL.

alternative a character string specifying the alternative hypothesis must be one of "twoSided"

(default), "greater" or "less".

alpha numeric in (0, 1) that specifies the tolerable type I error control –independent on

n- that the designed test has to adhere to. Note that it also defines the rejection

rule e10 > 1/alpha.

sigma numeric > 0 representing the assumed population standard deviation used for

the test.

h0 numeric, represents the null hypothesis, default h0=0.

kappa the true population standard deviation. Default kappa=sigma.

tol a number that defines the stepsizes between the lowParam and highParam.

paired logical, if TRUE then paired z-test.

parameter optional test defining parameter. Default set to NULL.

#### Value

Returns a 'safeDesign' object

**nPlan** the sample size(s) to plan for. Provided by the user.

**parameter** the safe test defining parameter. Here phiS.

esMin NULL no minimally clinically relevant effect size provided.

alpha the tolerable type I error provided by the user.

beta NULL, no tolerable type II error specified.

alternative any of "twoSided", "greater", "less" provided by the user.

testType any of "oneSample", "paired", "twoSample" effectively provided by the user.

paired logical, TRUE if "paired", FALSE otherwise.

**sigma** the assumed population standard deviation used for the test provided by the user.

**kappa** the true population standard deviation, typically, sigma=kappa.

**ratio** default is 1. Different from 1, whenever testType equals "twoSample", then it defines ratio between the planned randomisation of condition 2 over condition 1.

tol the step size between parameter values in the candidate space.

pilot logical, specifying whether it's a pilot design.

call the expression with which this function is called.

#### **Examples**

designPilotSafeZ(nPlan=30, alpha = 0.05)

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designSafeLogrank

Designs a Safe Logrank Test Experiment

### **Description**

A designed experiment requires (1) an anticipated number of events nEvents, or even better nPlan, the number of participants to be recruited in the study, and (2) the parameter of the safe test, i.e., thetaS. Provided with a clinically relevant minimal hazard ratio hrMin, this function outputs thetaS = hrMin as the safe test defining parameter in accordance to the GROW criterion. If a tolerable type II error beta is provided then nEvents can be sampled. The sampled nEvents is then the smallest nEvents for which hrMin is found with power of at least 1 - beta under optional stopping. If exact equal FALSE, then the computations exploit the local asymptotic normal approximation to sampling distribution of the logrank test derived by Schoenfeld (1981).

### Usage

```
designSafeLogrank(
 hrMin = NULL,
 beta = NULL,
 nEvents = NULL,
 h0 = 1,
  alternative = c("twoSided", "greater", "less"),
  alpha = 0.05,
  ratio = 1,
  exact = TRUE,
  tol = 1e-05,
 m0 = 50000L,
 m1 = 50000L
 nSim = 1000L,
 nBoot = 10000L
 parameter = NULL,
 groupSizePerTimeFunction = returnOne,
 pb = TRUE,
)
```

hrMin	numeric that defines the minimal relevant hazard ratio, the smallest hazard ratio that we want to detect.
beta	numeric in $(0,1)$ that specifies the tolerable type II error control necessary to calculate both "n" and "phiS". Note that 1-beta defines the power.
nEvents	numeric > 0, targetted number of events.
h0	numeric $> 0$ , represents the null hypothesis, default h0=1.

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alternative a character string specifying the alternative hypothesis, which must be one of "twoSided" (default), "greater" or "less". The alternative is pitted against the null hypothesis of equality of the survival distributions. More specifically, let lambda1 be the hazard rate of group 1 (i.e., placebo), and lambda2 the hazard ratio of group 2 (i.e., treatment), then the null hypothesis states that the hazard ratio theta = lambda2/lambda1 = 1. If alternative = "less", the null hypothesis is compared to theta < 1, thus, lambda2 < lambda1, that is, the hazard of group 2 (i.e., treatment) is less than that of group 1 (i.e., placebo), hence, the treatment is beneficial. If alternative = "greater", then the null hypothesis is compared to theta > 1, thus, lambda2 > lambda1, hence, harm. alpha numeric in (0, 1) that specifies the tolerable type I error control –independent on n- that the designed test has to adhere to. Note that it also defines the rejection rule e10 > 1/alpha. ratio numeric > 0 representing the randomisation ratio of condition 2 (Treatment) over condition 1 (Placebo), thus, m1/m0. Note that m1 and m0 are not used to specify ratio. Ratio is only used when zApprox=TRUE, which ignores m1 and exact a logical indicating whether the design should be based on the exact safe logrank test based on the hypergeometric likelihood. Default is TRUE, if FALSE then the design is based on a safe z-test. tol a number that defines the stepsizes between the lowParam and highParam. m0 Number of subjects in the control group 0/1 at the beginning of the trial, i.e., nPlan[1]. Number of subjects in the treatment group 1/2 at the beginning of the trial, i.e., m1 nPlan[2]. nSim integer > 0, the number of simulations needed to compute power or the number of events for the exact safe logrank test under continuous monitoring nBoot integer > 0 representing the number of bootstrap samples to assess the accuracy of the approximation of power or nEvents for the exact safe logrank test under continuous monitoring Numeric > 0, represents the safe tests defining thetaS. Default NULL so it's parameter decided by the algorithm, typically, this equals hrMin, which corresponds to the GROW choice. groupSizePerTimeFunction A function without parameters and integer output. This function provides the number of events at each time step. For instance, if rpois(1, 7) leads to a random number of events at each time step.

pb logical, if TRUE, then show progress bar.

. . . further arguments to be passed to or from methods.

#### Value

Returns a safeDesign object that includes:

**nEvents** the anticipated number of events, either (1) specified by the user, or (2) computed based on beta and thetaMin.

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```
parameter the parameter that defines the safe test. Here log(thetaS).
esMin the minimally clinically relevant hazard ratio specified by the user.
alpha the tolerable type I error provided by the user.
beta the tolerable type II error provided by the user.
alternative any of "twoSided", "greater", "less" provided by the user.
testType "logrank".
ratio default is 1. It defines the ratio between the planned randomisation of condition 2 over condition 1.
pilot FALSE to indicate that the design is not a pilot study.
call the expression with which this function is called.
```

#### References

Schoenfeld, D. (1981). The asymptotic properties of nonparametric tests for comparing survival distributions. Biometrika, 68(1), 316-319.

### **Examples**

```
designSafeLogrank(hrMin=0.7)
designSafeLogrank(hrMin=0.7, zApprox=TRUE)
designSafeLogrank(hrMin=0.7, beta=0.3, nSim=10)
designSafeLogrank(hrMin=0.7, nEvents=190, nSim=10)
```

designSafeT

Designs a Safe Experiment to Test Means with a T Test

### Description

A designed experiment requires (1) a sample size nPlan to plan for, and (2) the parameter of the safe test, i.e., deltaS. If nPlan is provided, then only the safe test defining parameter deltaS needs to determined. That resulting deltaS leads to an (approximately) most powerful safe test. Typically, nPlan is unknown and the user has to specify (i) a tolerable type II error beta, and (ii) a clinically relevant minimal population standardised effect size deltaMin. The procedure finds the smallest nPlan for which deltaMin is found with power of at least 1 - beta.

### Usage

```
designSafeT(
  deltaMin = NULL,
  beta = NULL,
  nPlan = NULL,
  alpha = 0.05,
  h0 = 0,
  alternative = c("twoSided", "greater", "less"),
  lowN = 3L,
```

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```
highN = 1000000L,
lowParam = 0.01,
highParam = 1.5,
tol = 0.01,
testType = c("oneSample", "paired", "twoSample"),
ratio = 1,
nSim = 1000L,
nBoot = 1000L,
parameter = NULL,
pb = TRUE,
seed = NULL,
...
)
```

#### **Arguments**

deltaMin numeric that defines the minimal relevant standardised effect size, the smallest

effect size that we would the experiment to be able to detect.

beta numeric in (0, 1) that specifies the tolerable type II error control necessary to

calculate both the sample sizes and deltaS, which defines the test. Note that

1-beta defines the power.

nPlan vector of max length 2 representing the planned sample sizes.

alpha numeric in (0, 1) that specifies the tolerable type I error control –independent of

n- that the designed test has to adhere to. Note that it also defines the rejection

rule e10 > 1/alpha.

h0 a number indicating the hypothesised true value of the mean under the null. For

the moment h0=0.

alternative a character string specifying the alternative hypothesis must be one of "twoSided"

(default), "greater" or "less".

lowN integer minimal sample size of the (first) sample when computing the power due

to optional stopping. Default lowN is set 1.

highN integer minimal sample size of the (first) sample when computing the power due

to optional stopping. Default highN is set 1e6.

lowParam numeric defining the smallest delta of the search space for the test-defining

deltaS for scenario 3. Currently not yet in use.

highParam numeric defining the largest delta of the search space for the test-defining deltaS

for scenario 3. Currently not yet in use.

tol a number that defines the stepsizes between the lowParam and highParam.

testType either one of "oneSample", "paired", "twoSample".

ratio numeric > 0 representing the randomisation ratio of condition 2 over condition 1.

If testType is not equal to "twoSample", or if nPlan is of length(1) then ratio=1.

nSim integer > 0, the number of simulations needed to compute power or the number

of samples paths for the safe z test under continuous monitoring.

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nBoot integer > 0 representing the number of bootstrap samples to assess the accuracy

of approximation of the power, the number of samples for the safe z test under continuous monitoring, or for the computation of the logarithm of the implied

target.

parameter optional test defining parameter. Default set to NULL.

pb logical, if TRUE, then show progress bar.

seed integer, seed number.

... further arguments to be passed to or from methods, but mainly to perform

do.calls.

### Value

Returns an object of class 'safeDesign'. An object of class 'safeDesign' is a list containing at least the following components:

**nPlan** the planned sample size(s).

parameter the safe test defining parameter. Here deltaS.

esMin the minimal clinically relevant standardised effect size provided by the user.

**alpha** the tolerable type I error provided by the user.

beta the tolerable type II error provided by the user.

alternative any of "twoSided", "greater", "less" provided by the user.

testType any of "oneSample", "paired", "twoSample" provided by the user.

paired logical, TRUE if "paired", FALSE otherwise.

**h0** the specified hypothesised value of the mean or mean difference depending on whether it was a one-sample or a two-sample test.

**ratio** default is 1. Different from 1, whenever testType equals "twoSample", then it defines ratio between the planned randomisation of condition 2 over condition 1.

lowN the smallest n of the search space for n provided by the user.

**highN** the largest n of the search space for n provided by the user.

lowParam the smallest delta of the search space for delta provided by the user.

**highParam** the largest delta of the search space for delta provided by the user.

tol the step size between lowParam and highParam provided by the user.

pilot FALSE (default) specified by the user to indicate that the design is not a pilot study.

call the expression with which this function is called.

```
designObj <- designSafeT(deltaMin=0.8, alpha=0.03, alternative="greater")
designObj

# "Scenario 1.a": Minimal clinically relevant standarised mean difference and tolerable type
# II error also known. Goal: find nPlan.
designObj <- designSafeT(deltaMin=0.8, alpha=0.03, beta=0.4, nSim=10, alternative="greater")
designObj</pre>
```

```
# "Scenario 2": Minimal clinically relevant standarised mean difference and nPlan known.
# Goal: find the power, hence, the type II error of the procedure under optional stopping.
designObj <- designSafeT(deltaMin=0.8, alpha=0.03, nPlan=16, nSim=10, alternative="greater")
designObj</pre>
```

designSafeTwoProportions

Designs a Safe Experiment to Test Two Proportions in Stream Data

### **Description**

The design requires the number of observations one expects to collect in each group in each data block. I.e., when one expects balanced data, one could choose na = nb = 1 and would be allowed to analyse the data stream each time a new observation in both groups has come in. The best results in terms of power are achieved when the data blocks are chosen as small as possible, as this allows for analysing and updating the safe test as often as possible, to fit the data best. Further, the design requires two out of the following three parameters to be known:

- the power one aims to achieve (1 beta),
- the minimal relevant difference between the groups (delta)
- the number of blocks planned (nBlocksPlan),

where the unknown out of the three will be estimated. In the case of an exploratory "pilot" analysis, one can also only provide the number of blocks planned.

## Usage

```
designSafeTwoProportions(
   na,
   nb,
   nBlocksPlan = NULL,
   beta = NULL,
   delta = NULL,
   alternativeRestriction = c("none", "difference", "logOddsRatio"),
   alpha = 0.05,
   pilot = "FALSE",
   hyperParameterValues = NULL,
   previousSafeTestResult = NULL,
   M = 1000,
   simThetaAMin = NULL,
   simThetaAMax = NULL
)
```

### **Arguments**

na number of observations in group a per data block
nb number of observations in group b per data block

nBlocksPlan planned number of data blocks collected

numeric in (0, 1) that specifies the tolerable type II error control necessary to

calculate both "nBlocksPlan" and "delta". Note that 1-beta defines the power.

delta a priori minimal relevant divergence between group means b and a, either a

numeric between -1 and 1 for no alternative restriction or a restriction on differ-

ence, or a real for a restriction on the log odds ratio.

alternativeRestriction

a character string specifying an optional restriction on the alternative hypothesis; must be one of "none" (default), "difference" (difference group mean b minus group b) or "logOddsRatio" (the log odds ratio between group means b and a).

alpha numeric in (0, 1) that specifies the tolerable type I error control –independent on

n- that the designed test has to adhere to. Note that it also defines the rejection

rule e10 > 1/alpha.

pilot logical, specifying whether it's a pilot design.

hyperParameterValues

named list containing numeric values for hyperparameters betaA1, betaA2, betaB1 and betaB2, with betaA1 and betaB1 specifying the parameter equivalent to shape1 in stats::dbeta for groups A and B, respectively, and betaA2 and betaB2 equivalent to shape2. By default chosen to optimize evidence collected over subsequent experiments (REGRET). Pass in the following format: list(betaA1 = numeric1, betaA2 = numeric2, betaB1 = numeric3, betaB2 =

numeric4).

previousSafeTestResult

optionally, a previous safe test result can be provided. The posterior of the hyperparameters of this test is then used for the hyperparameter settings. Default

NULL.

M number of simulations used to estimate power or nBlocksPlan. Default 1000.

simThetaAMin minimal event rate in control group to simulate nPlan or power for. Can be

specified when specifically interested in planning studies for specific event rates. Default NULL, then the entire parameter space (possibly restricted by delta) is

used for simulation.

simThetaAMax maximal event rate in control group to simulate nPlan or power for. Default

NULL.

#### Value

Returns a 'safeDesign' object that includes:

**nPlan** the sample size(s) to plan for. Computed based on beta and meanDiffMin, or provided by the user if known.

**parameter** the safe test defining parameter: here the hyperparameters.

esMin the minimally clinically relevant effect size provided by the user.

alpha the tolerable type I error provided by the user.

beta the tolerable type II error specified by the user.

alternative any of "twoSided", "greater", "less" based on the alternativeRestriction provided
 by the user.

testType here 2x2

pilot logical, specifying whether it's a pilot design.

call the expression with which this function is called.

```
#plan for an experiment to detect minimal difference of 0.6 with a balanced design
set.seed(3152021)
designSafeTwoProportions(na = 1,
                         alpha = 0.1,
                         beta = 0.20,
                         delta = 0.6,
                         alternativeRestriction = "none",
                         M = 75
#safe analysis of a pilot: number of samples already known
designSafeTwoProportions(na = 1,
                          nb = 1,
                          nBlocksPlan = 20,
                          pilot = TRUE)
#specify own hyperparameters
hyperParameterValues <- list(betaA1 = 10, betaA2 = 1, betaB1 = 1, betaB2 = 10)
designSafeTwoProportions(na = 1,
                         nb = 1,
                         alpha = 0.1,
                         beta = 0.20,
                         delta = 0.6,
                         hyperParameterValues = hyperParameterValues,
                         alternativeRestriction = "none",
                         M = 75
#restrict range of proportions for estimating nPlan in the control group
designSafeTwoProportions(na = 1,
                         nb = 1,
                         beta = 0.20,
                         delta = 0.3,
                         alternativeRestriction = "none",
                         M = 75,
                         simThetaAMin = 0.1, simThetaAMax = 0.2)
```

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designSafeZ

Designs a Safe Z Experiment

## **Description**

A designed experiment requires (1) a sample size nPlan to plan for, and (2) the parameter of the safe test, i.e., phiS. Provided with a clinically relevant minimal mean difference meanDiffMin, this function outputs phiS = meanDiffMin as the safe test defining parameter in accordance to the GROW criterion. If a tolerable type II error, i.e., beta, is provided then nPlan can be sampled. The sampled nPlan is then the smallest nPlan for which meanDiffMin can be found with power at least 1 - beta under optional stopping.

# Usage

```
designSafeZ(
 meanDiffMin = NULL,
 beta = NULL,
  nPlan = NULL,
  alpha = 0.05,
 h0 = 0,
  alternative = c("twoSided", "greater", "less"),
  sigma = 1,
  kappa = sigma,
  tol = 1e-05,
  testType = c("oneSample", "paired", "twoSample"),
  ratio = 1,
  parameter = NULL,
 nSim = 1000L,
  nBoot = 1000L
 pb = TRUE,
 grow = TRUE,
)
```

## **Arguments**

meanDiffMin	numeric that defines the minimal relevant mean difference, the smallest population mean that we would like to detect.
beta	numeric in (0, 1) that specifies the tolerable type II error control necessary to calculate both "n" and "phiS". Note that 1-beta defines the power.
nPlan	optional numeric vector of length at most 2. When provided, it is used to find the safe test defining parameter phiS. Note that if the purpose is to plan based on nPlan alone, then both meanDiffMin and beta should be set to NULL.
alpha	numeric in $(0, 1)$ that specifies the tolerable type I error control –independent on n– that the designed test has to adhere to. Note that it also defines the rejection rule $e^{10} > 1/a$ lpha.

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h0 numeric, represents the null hypothesis, default h0=0.

alternative a character string specifying the alternative hypothesis must be one of "twoSided"

(default), "greater" or "less".

sigma numeric > 0 representing the assumed population standard deviation used for

the test.

kappa the true population standard deviation. Default kappa=sigma.

tol a number that defines the stepsizes between the lowParam and highParam.

testType either one of "oneSample", "paired", "twoSample".

ratio numeric > 0 representing the randomisation ratio of condition 2 over condition 1.

If testType is not equal to "twoSample", or if nPlan is of length(1) then ratio=1.

parameter optional test defining parameter. Default set to NULL.

nSim integer > 0, the number of simulations needed to compute power or the number

of samples paths for the safe z test under continuous monitoring.

nBoot integer > 0 representing the number of bootstrap samples to assess the accuracy

of approximation of the power, the number of samples for the safe z test under continuous monitoring, or for the computation of the logarithm of the implied

target.

pb logical, if TRUE, then show progress bar.

grow logical, default set to TRUE so the grow safe test is used in the design.

... further arguments to be passed to or from methods.

#### Value

Returns a safeDesign object that includes:

**nPlan** the sample size(s) to plan for. Computed based on beta and meanDiffMin, or provided by the user if known.

parameter the safe test defining parameter. Here phiS.

esMin the minimally clinically relevant effect size provided by the user.

**alpha** the tolerable type I error provided by the user.

beta the tolerable type II error specified by the user.

alternative any of "twoSided", "greater", "less" provided by the user.

testType any of "oneSample", "paired", "twoSample" effectively provided by the user.

paired logical, TRUE if "paired", FALSE otherwise.

sigma the assumed population standard deviation used for the test provided by the user.

**kappa** the true population standard deviation, typically, sigma=kappa.

**ratio** default is 1. Different from 1, whenever testType equals "twoSample", then it defines ratio between the planned randomisation of condition 2 over condition 1.

tol the step size between parameter values in the candidate space.

pilot logical, specifying whether it's a pilot design.

**call** the expression with which this function is called.

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### References

Grunwald, de Heide and Koolen (2019) "Safe Testing" <arXiv:1906.07801>

## **Examples**

```
designObj <- designSafeZ(meanDiffMin=0.8, alpha=0.08, beta=0.01, alternative="greater")
#nPlan known:
designObj <- designSafeZ(nPlan = 100, alpha=0.05)</pre>
```

extractNameFromArgs

Helper function: Get all names as entered by the user

# Description

Helper function: Get all names as entered by the user

### Usage

```
extractNameFromArgs(list, name)
```

# Arguments

list from which the element needs retrieving

name character string, name of the item that need retrieving

### Value

returns a character string

generateNormalData

Generates Normally Distributed Data Depending on the Design

# Description

The designs supported are "oneSample", "paired", "twoSample".

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### Usage

```
generateNormalData(
    nPlan,
    nSim = 1000L,
    deltaTrue = NULL,
    muGlobal = 0,
    sigmaTrue = 1,
    paired = FALSE,
    seed = NULL,
    muTrue = NULL
)
```

### **Arguments**

nPlan vector of max length 2 representing the planned sample sizes.

nSim the number of replications, that is, experiments with max samples nPlan.

numeric, the value of the true standardised effect size (test-relevant parameter).

numeric, the true global mean of a paired or two-sample t-test. Its value should

not matter for the test. This parameter is treated as a nuisance.

not matter for the test. This parameter is treated as a nuisance.

sigmaTrue numeric > 0,the true standard deviation of the data. Its value should not matter

for the test. This parameter treated is treated as a nuisance.

paired logical, if TRUE then paired t-test.

seed To set the seed for the simulated data.

muTrue numeric representing the true mean for simulations with a z-test. Default NULL

### Value

Returns a list of two data matrices contains at least the following components:

```
dataGroup1 a matrix of data dimension nSim by nPlan[1].dataGroup2 a matrix of data dimension nSim by nPlan[2].
```

### **Examples**

```
generateNormalData(20, 15, deltaTrue=0.3)
```

generateSurvData	Generate Survival Data which Can Be Analysed With the 'survival'
	Package

## Description

Generate Survival Data which Can Be Analysed With the 'survival' Package

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## Usage

```
generateSurvData(
    nP,
    nT,
    alpha = 1,
    lambdaP,
    lambdaT,
    seed = NULL,
    nDigits = 0,
    startTime = 1,
    endTime = 180,
    orderTime = TRUE,
    competeRatio = 0
)
```

# Arguments

nP	integer > 0 representing the number of of patients in the placebo group.
nT	integer $> 0$ representing the number of of patients in the treatment group.
alpha	numeric $> 0$ , representing the shape parameter of the Weibull distribution. If alpha=1, then data are generated from the exponential, i.e., constant hazard. For alpha $> 1$ the hazard increases, if alpha $< 1$ , the hazard decreases.
lambdaP	The (relative) hazard of the placebo group.
lambdaT	The (relative) hazard of the treatment group.
seed	A seed number.
nDigits	numeric, the number of digits to round of the random time to
startTime	numeric, adds this to the random times. Default 1, so the startTime is not 0, which is the start time of rweibull.
endTime	The endtime of the experiment.

logical, if TRUE then put the data set in increasing order

The ratio of the data that is due to competing risk.

## Value

orderTime

competeRatio

A data set with time, status and group.

```
generateSurvData(800, 800, alpha=1, lambdaP=0.008, lambdaT=0.008/2)
```

48 getNameAlternative

getArgs

Helper function: Get all arguments as entered by the user

## **Description**

Helper function: Get all arguments as entered by the user

## Usage

```
getArgs()
```

### Value

a list of variable names of class "call" that can be changed into names

getNameAlternative

Gets the Label of the Alternative Hypothesis

## **Description**

Helper function that outputs the alternative hypothesis of the analysis.

# Usage

```
getNameAlternative(
  alternative = c("twoSided", "greater", "less"),
  testType,
  h0 = 0
)
```

# Arguments

alternative A character string. "twoSided", "greater", "less".

testType A character string either "oneSample", "paired", "twoSample", "gLogrank", or

"eLogrank".

h0 the value of the null hypothesis

# Value

Returns a character string with the name of the analysis.

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getNameTestType

Gets the Label of the Test

# Description

Helper function that outputs the name of the analysis.

# Usage

```
getNameTestType(testType, parameterName)
```

## **Arguments**

testType A character string. For the t-tests: "oneSample", "paired", "twoSample".

parameterName The name of the parameter to identify test performed

#### Value

Returns a character string with the name of the analysis.

isTryError

Checks Whether a Vector of Object Inherits from the Class 'try-error'

## Description

Checks whether any of the provided objects contains a try error.

### Usage

```
isTryError(...)
```

# **Arguments**

... objects that need testing.

### Value

Returns TRUE if there's some object that's a try-error, FALSE when all objects are not try-errors.

```
x <- 1
y <- "a"
z <- try(integrate(exp, -Inf, Inf))
isTryError(x, y)
isTryError(x, y, z)</pre>
```

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logrankSingleEExact	Helper function computes single component of the exact logrank e-
	value

## **Description**

Helper function computes single component of the exact logrank e-value

### Usage

```
logrankSingleEExact(obs0, obs1, y0, y1, thetaS, theta0 = 1, ...)
```

# Arguments

obs0	integer, number of observations in the control group.
obs1	integer, number of observations in the treatment group.
y0	integer, total number of participants in the control group.
y1	integer, total number of participants in the treatment group.
thetaS	numeric $> 0$ represents the safe test defining (GROW) alternative hypothesis obtained from designSafeLogrank().
theta0	numeric > 0 represents the null hypothesis. Default theta0=1.
	further arguments to be passed to or from methods.

# Value

Returns a list containing at least the following components:

logP0 Log likelihood of Fisher's hypergeometric at the nulllogEValueLess Log likelihood of Fisher's hypergeometric at the alternativelogEValueGreater Log likelihood of Fisher's hypergeometric at 1/alternative

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```
logEValueGreater[i] <- tempResult[["logEValueGreater"]]
}
eValueLess <- exp(sum(logEValueLess))
eValueLess #1.116161
eValueGreater <- exp(sum(logEValueGreater))
eValueGreater # 0.7665818
eValue <- 1/2*eValueLess + 1/2*eValueGreater
eValue # 0.9413714</pre>
```

logrankSingleZ

Helper function computes single component of the logrank statistic

# Description

Helper function computes single component of the logrank statistic

### Usage

```
logrankSingleZ(obs0, obs1, y0, y1, ...)
```

## **Arguments**

obs0	integer, number of observations in the control group
obs1	integer, number of observations in the treatment group
y0	integer, total number of participants in the control group
y1	integer, total number of participants in the treatment group
	further arguments to be passed to or from methods.

## Value

Returns a list containing at least the following components:

oMinE observed minus expected.

v hypergeometric variance.

```
y0Vector <- c(6, 4, 4, 1, 0)
y1Vector <- c(6, 6, 5, 2, 2)
obs0Vector <- c(1, 0, 2, 1, 0)
obs1Vector <- c(0, 1, 1, 0, 1)

varVector <- oMinEVector <-y0Vector

for (i in seq_along(y0Vector)) {
   tempResult <- logrankSingleZ(obs0=obs0Vector[i], obs1=obs1Vector[i],</pre>
```

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```
y0=y0Vector[i], y1=y1Vector[i])
oMinEVector[i] <- tempResult[["oMinE"]]
varVector[i] <- tempResult[["v"]]
}
sum(oMinEVector)/sqrt(sum(varVector))</pre>
```

plot.safe2x2Sim

Plots Results of Simulations for Comparing Hyperparameters for Safe Tests of Two Proportions

## **Description**

Plots Results of Simulations for Comparing Hyperparameters for Safe Tests of Two Proportions

### Usage

```
## S3 method for class 'safe2x2Sim'
plot(x, ...)
```

### **Arguments**

x a result object obtained through simulateTwoProportions().

... further arguments to be passed to or from methods.

### Value

Plot data, mainly called for side effects, the plot of simulation results.

```
priorList1 <- list(betaA1 = 10, betaA2 = 1, betaB1 = 1, betaB2 = 10)
priorList2 <- list(betaA1 = 0.18, betaA2 = 0.18, betaB1 = 0.18, betaB2 = 0.18)
priorList3 <- list(betaA1 = 1, betaA2 = 1, betaB1 = 1, betaB2 = 1)

simResult <- simulateTwoProportions(
    hyperparameterList = list(priorList1, priorList2, priorList3),
    alternativeRestriction = "none",
    alpha = 0.1, beta = 0.2, na = 1, nb = 1,
    deltamax = -0.4, deltamin = -0.9, deltaGridSize = 3,
    M = 10
    )

plot(simResult)</pre>
```

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plot.safeTSim

Plots a 'safeTSim' Object

## **Description**

```
Plots a 'safeTSim' Object
```

## Usage

```
## S3 method for class 'safeTSim'
plot(x, y = NULL, showOnlyNRejected = FALSE, nBin = 25, ...)
```

### **Arguments**

```
x a 'safeDesign' object acquired from designSafeT().

y NULL.

showOnlyNRejected
logical, when TRUE discards the cases that did not reject.

nBin numeric > 0, the minimum number of bins in the histogram.

further arguments to be passed to or from methods.
```

### Value

a histogram object, and called for its side-effect to plot the histogram.

```
# Design safe test
alpha <- 0.05
beta <- 0.20
designObj <- designSafeT(1, alpha=alpha, beta=beta)

# Design frequentist test
freqObj <- designFreqT(1, alpha=alpha, beta=beta)

# Simulate under the alternative with deltaTrue=deltaMin
simResults <- simulate(designObj, nSim=100)

plot(simResults)

plot(simResults, showOnlyNRejected=TRUE)</pre>
```

plotConfidenceSequenceTwoProportions

Plot bounds of a safe confidence sequence of the difference or log odds ratio for two proportions against the number of data blocks in two data streams ya and yb.

## **Description**

Plot bounds of a safe confidence sequence of the difference or log odds ratio for two proportions against the number of data blocks in two data streams ya and yb.

## Usage

```
plotConfidenceSequenceTwoProportions(
   ya,
   yb,
   safeDesign,
   differenceMeasure = c("difference", "odds"),
   precision = 100,
   deltaStart = 0.001,
   deltaStop = 3,
   trueDifference = NA
)
```

## **Arguments**

ya	positive observations/ events per data block in group a: a numeric with integer values between (and including) 0 and na, the number of observations in group a per block.
yb	positive observations/ events per data block in group b: a numeric with integer values between (and including) 0 and nb, the number of observations in group b per block.
safeDesign	a safe test design for two proportions retrieved through $designSafeTwoProportions()$ .
differenceMeasu	ire
	the difference measure to construct the confidence interval for: one of "difference" and "odds".
precision	precision of the grid to search over for the confidence sequence bounds.
deltaStart	for the odds difference measure: the (absolute value of the) smallest log odds ratio to assess for in- or exclusion in the confidence sequence. Default 0.001.
deltaStop	for the odds difference measure: the (absolute value of the) highest log odds ratio to assess for in- or exclusion in the confidence sequence. Default 3.
${\tt true Difference}$	true difference or log odds ratio in groups A and B: added to the plot.

## Value

no return value; called for its side effects, a plot of the confidence sequence.

### **Examples**

```
set.seed(39413)
ya < - rbinom(n = 30, size = 1, prob = 0.1)
yb \leftarrow rbinom(n = 30, size = 1, prob = 0.8)
balancedSafeDesign <- designSafeTwoProportions(na = 1,</pre>
                                                nb = 1,
                                                nBlocksPlan = 30)
plotConfidenceSequenceTwoProportions(ya = ya,
                                      yb = yb,
                                      safeDesign = balancedSafeDesign,
                                      differenceMeasure = "difference",
                                      precision = 15,
                                      trueDifference = 0.7)
#log odds ratio difference measure
plotConfidenceSequenceTwoProportions(ya = ya,
                                      yb = yb,
                                      safeDesign = balancedSafeDesign,
                                      differenceMeasure = "odds",
                                      precision = 15,
                                      deltaStop = 5,
                                      trueDifference = log(36))
#switch ya and yb: observe negative log odds ratio in the data, plot mirrored in x-axis
plotConfidenceSequenceTwoProportions(ya = yb,
                                      yb = ya,
                                      safeDesign = balancedSafeDesign,
                                      differenceMeasure = "odds",
                                      precision = 15,
                                      deltaStop = 5,
                                      trueDifference = -log(36))
```

plotHistogramDistributionStoppingTimes

Plots the Histogram of Stopping Times

## **Description**

Helper function to display the histogram of stopping times.

# Usage

```
plotHistogramDistributionStoppingTimes(
  safeSim,
  nPlan,
  deltaTrue,
  showOnlyNRejected = FALSE,
  nBin = 25L,
```

```
)
```

### **Arguments**

safeSim A safeSim object, returned from replicateTTests.

nPlan numeric > 0, the planned sample size(s).

deltaTrue numeric, that represents the true underlying standardised effect size delta. showOnlyNRejected logical, when TRUE discards the cases that did not reject.

nBin numeric > 0, the minimum number of bins in the histogram.

... further arguments to be passed to or from methods.

#### Value

a histogram object, and called for its side-effect to plot the histogram.

### **Examples**

```
# Design safe test
alpha <- 0.05
beta <- 0.20
designObj <- designSafeT(1, alpha=alpha, beta=beta)

# Design frequentist test
freqObj <- designFreqT(1, alpha=alpha, beta=beta)

# Simulate under the alternative with deltaTrue=deltaMin
simResults <- replicateTTests(nPlan=designObj$nPlan, deltaTrue=1, parameter=designObj$parameter,
nPlanFreq=freqObj$nPlan)

plotHistogramDistributionStoppingTimes(
    simResults$safeSim, nPlan = simResults$nPlan,
    deltaTrue = simResults$deltaTrue)</pre>
```

plotSafeTDesignSampleSizeProfile

Plots the Sample Sizes Necessary for a Tolerable Alpha and Beta as a Function of deltaMin

### **Description**

For given tolerable alpha and beta, (1) the planned sample sizes to using a safe test, (2) the frequentist test, and (3) the average sample size necessary due to optional stopping are plotted as a function of the minimal clinically relevant standardised effect size deltaMin.

### Usage

```
plotSafeTDesignSampleSizeProfile(
  alpha = 0.05,
  beta = 0.2,
  nMax = 100,
  lowDeltaMin = 0.1,
  highDeltaMin = 1,
  stepDeltaMin = 0.1,
  testType = c("oneSample", "paired", "twoSample"),
  alternative = c("twoSided", "greater", "less"),
  ratio = 1,
  nSim = 1000L,
  nBoot = 1000L
  seed = NULL,
  pb = TRUE,
  freqPlot = FALSE,
)
```

### **Arguments**

alpha	numeric in (0, 1	) that specifies	the tolerable type	error control –	independent of

n- that the designed test has to adhere to. Note that it also defines the rejection

rule e10 > 1/alpha.

beta numeric in (0, 1) that specifies the tolerable type II error control necessary to

calculate both the sample sizes and deltaS, which defines the test. Note that

1-beta defines the power.

nMax numeric, the maximum number of samples one has budget for to collect data.

lowDeltaMin numeric, lowest value for deltaMin of interest highDeltaMin numeric, largest value for deltaMin of interest

stepDeltaMin numeric, step size between lowDeltaMin and highDeltaMin

testType either one of "oneSample", "paired", "twoSample".

alternative a character string specifying the alternative hypothesis must be one of "twoSided"

(default), "greater" or "less".

ratio numeric > 0 representing the randomisation ratio of condition 2 over condition 1.

If testType is not equal to "twoSample", or if nPlan is of length(1) then ratio=1.

nSim integer > 0, the number of simulations needed to compute power or the number

of samples paths for the safe z test under continuous monitoring.

nBoot integer > 0 representing the number of bootstrap samples to assess the accuracy

of approximation of the power, the number of samples for the safe z test under continuous monitoring, or for the computation of the logarithm of the implied

target.

seed integer, seed number.

pb logical, if TRUE, then show progress bar.

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freqPlot logical, if TRUE plot frequentist sample size profiles.

... further arguments to be passed to or from methods, but mainly to perform

do.calls.

### Value

Returns a list that contains the planned sample size needed for the frequentist and safe tests as a function of the minimal clinically relevant effect sizes. The returned list contains at least the following components:

**alpha** the tolerable type I error provided by the user.

beta the tolerable type II error provided by the user.

maxN the largest number of samples provided by the user.

deltaDomain vector of the domain of deltaMin.

**allN1PlanFreq** vector of the planned sample sizes needed for the frequentist test corresponding to alpha and beta.

**allN1PlanSafe** vector of the planned sample sizes needed for the safe test corresponding to alpha and beta.

allDeltaS vector of safe test defining deltaS.

### **Examples**

```
plotSafeTDesignSampleSizeProfile(nSim=1e2L)
```

print.safe2x2Sim

Prints Results of Simulations for Comparing Hyperparameters for Safe Tests of Two Proportions

### **Description**

Prints Results of Simulations for Comparing Hyperparameters for Safe Tests of Two Proportions

### Usage

```
## S3 method for class 'safe2x2Sim'
print(x, ...)
```

### Arguments

x a result object obtained through simulateTwoProportions().

... further arguments to be passed to or from methods.

### Value

The data frame with simulation results, called for side effects to pretty print the simulation results.

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### **Examples**

```
priorList1 <- list(betaA1 = 10, betaA2 = 1, betaB1 = 1, betaB2 = 10)
priorList2 <- list(betaA1 = 0.18, betaA2 = 0.18, betaB1 = 0.18, betaB2 = 0.18)
priorList3 <- list(betaA1 = 1, betaA2 = 1, betaB1 = 1, betaB2 = 1)

simResult <- simulateTwoProportions(
   hyperparameterList = list(priorList1, priorList2, priorList3),
   alternativeRestriction = "none",
   alpha = 0.1, beta = 0.2, na = 1, nb = 1,
   deltamax = -0.4, deltamin = -0.9, deltaGridSize = 3,
   M = 10
   )</pre>
```

print.safeDesign

Print Method for Safe Tests

## **Description**

Printing objects of class 'safeTest' modelled after print.power.htest().

# Usage

```
## S3 method for class 'safeDesign'
print(x, digits = getOption("digits"), prefix = "\t", ...)
```

## **Arguments**

```
    x a safeTest object.
    digits number of significant digits to be used.
    prefix string, passed to strwrap for displaying the method components.
    ... further arguments to be passed to or from methods.
```

## Value

No returned value, called for side effects.

```
designSafeZ(meanDiffMin=0.5)
designSafeT(deltaMin=0.5)
designSafeLogrank(hrMin=0.7)
```

print.safeTSim

print.safeTest

Print Method for Safe Tests

## **Description**

Printing objects of class 'safeTest' modelled after print.htest().

## Usage

```
## S3 method for class 'safeTest'
print(x, digits = getOption("digits"), prefix = "\t", ...)
```

## **Arguments**

x a safeTest object.

digits number of significant digits to be used.

prefix string, passed to strwrap for displaying the method components.

... further arguments to be passed to or from methods.

### Value

No returned value, called for side effects.

# **Examples**

```
safeTTest(rnorm(19), pilot=TRUE)
safeZTest(rnorm(19), pilot=TRUE)
```

print.safeTSim

Prints a safeTSim Object

## **Description**

Prints a safeTSim Object

## Usage

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

# Arguments

x a 'safeTSim' object.

. . . further arguments to be passed to or from methods.

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## Value

No returned value, called for side effects.

### **Examples**

```
designObj <- designSafeT(1, beta=0.2, nSim=10)
# Data under deltaTrue=deltaMin
simObj <- simulate(designObj, nSim=10)
print(simObj)</pre>
```

replicateTTests

Simulate Early Stopping Experiments

## **Description**

Simulate multiple data sets to show the effects of optional testing for safe (and frequentist) tests.

# Usage

```
replicateTTests(
  nPlan,
  deltaTrue,
 muGlobal = 0,
  sigmaTrue = 1,
  paired = FALSE,
  alternative = c("twoSided", "greater", "less"),
  lowN = 3,
  nSim = 1000L,
  alpha = 0.05,
 beta = 0.2,
  safeOptioStop = TRUE,
  parameter = NULL,
  freqOptioStop = FALSE,
  nPlanFreq = NULL,
  logging = TRUE,
  seed = NULL,
  pb = TRUE,
)
```

## **Arguments**

nPlan vector of max length 2 representing the planned sample sizes.

deltaTrue numeric, the value of the true standardised effect size (test-relevant parameter).

muGlobal numeric, the true global mean of a paired or two-sample t-test. Its value should not matter for the test. This parameter is treated as a nuisance.

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sigmaTrue numeric > 0,the true standard deviation of the data. Its value should not matter

for the test. This parameter treated is treated as a nuisance.

paired logical, if TRUE then paired t-test.

alternative a character string specifying the alternative hypothesis must be one of "twoSided"

(default), "greater" or "less".

lowN integer that defines the smallest n of our search space for n.

nSim the number of replications, that is, experiments with max samples nPlan.

alpha numeric in (0, 1) that specifies the tolerable type I error control –independent of

n- that the designed test has to adhere to. Note that it also defines the rejection

rule e10 > 1/alpha.

beta numeric in (0, 1) that specifies the tolerable type II error control necessary to

calculate both the sample sizes and deltaS, which defines the test. Note that

1-beta defines the power.

safeOptioStop logical, TRUE implies that optional stopping simulation is performed for the safe

test.

parameter numeric, the safe test defining parameter, i.e., deltaS (use designSafeT to find

this).

freqOptioStop logical, TRUE implies that optional stopping simulation is performed for the fre-

quentist test.

nPlanFreq the frequentist sample size(s) to plan for. Acquired from designFreqT().

logging logical, if TRUE, then return the simulated data.

seed To set the seed for the simulated data.

pb logical, if TRUE, then show progress bar.

... further arguments to be passed to or from methods.

#### Value

Returns an object of class "safeTSim". An object of class "safeTSim" is a list containing at least the following components:

**nPlan** the planned sample size(s).

**deltaTrue** the value of the true standardised effect size (test-relevant parameter) provided by the user.

muGlobal the true global mean of a paired or two-sample t-test (nuisance parameter) provided by the user.

paired if TRUE then paired t-test.

alternative any of "twoSided", "greater", "less" provided by the user.

lowN the smallest number of samples (first group) at which monitoring of the tests begins.

**nSim** the number of replications of the experiment.

**alpha** the tolerable type I error provided by the user.

**beta** the tolerable type II error provided by the user.

testType any of "oneSample", "paired", "twoSample" provided by the user.

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parameter the parameter (point prior) used in the safe test derived from the design. Acquired from designSafeT().

**nPlanFreq** the frequentist planned sample size(s). Acquired from designFreqT() safeSim list with the simulation results of the safe test under optional stopping. freqSim list with the simulation results of the frequentist test under optional stopping.

```
# Design safe test
alpha <- 0.05
beta <- 0.20
designObj <- designSafeT(1, alpha=alpha, beta=beta)</pre>
# Design frequentist test
freqObj <- designFreqT(1, alpha=alpha, beta=beta)</pre>
# Simulate under the alternative with deltaTrue=deltaMin
simResults <- replicateTTests(nPlan=designObj$nPlan, deltaTrue=1, parameter=designObj$parameter,</pre>
                              nPlanFreq=freqObj$nPlan, beta=beta, nSim=250)
# Should be about 1-beta
simResults$safeSim$powerAtN1Plan
# This is higher due to optional stopping
simResults$safeSim$powerOptioStop
# Optional stopping allows us to do better than n1PlanFreq once in a while
simResults$safeSim$probLegN1PlanFreq
graphics::hist(simResults$safeSim$allN, main="Histogram of stopping times", xlab="n1",
               breaks=seq.int(designObj$nPlan[1]))
# Simulate under the alternative with deltaTrue > deltaMin
simResults <- replicateTTests(nPlan=designObj$nPlan, deltaTrue=1.5, parameter=designObj$parameter,</pre>
                               nPlanFreq=freqObj$nPlan, beta=beta, nSim=250)
# Should be larger than 1-beta
simResults$safeSim$powerAtN1Plan
# This is even higher due to optional stopping
simResults$safeSim$powerOptioStop
# Optional stopping allows us to do better than n1PlanFreq once in a while
simResults$safeSim$probLeqN1PlanFreq
graphics::hist(simResults$safeSim$allN, main="Histogram of stopping times", xlab="n1",
               breaks=seq.int(designObj$nPlan[1]))
# Under the null deltaTrue=0
simResults <- replicateTTests(nPlan=designObj$nPlan, deltaTrue=0, parameter=designObj$parameter,</pre>
                        nPlanFreq=freqObj$nPlan, freqOptioStop=TRUE, beta=beta, nSim=250)
# Should be lower than alpha, because if the null is true, P(S > 1/alpha) < alpha for all n
simResults$safeSim$powerAtN1Plan
```

rLogrank

```
# This is a bit higher due to optional stopping, but if the null is true,
# then still P(S > 1/alpha) < alpha for all n
simResults$safeSim$powerOptioStop

# Should be lowr than alpha, as the experiment is performed as was planned
simResults$freqSim$powerAtN1Plan

# This is larger than alpha, due to optional stopping.
simResults$freqSim$powerOptioStop
simResults$freqSim$powerOptioStop > alpha
```

return0ne

Auxiliary function for sampling of the logrank simulations to return the integer 1 event per time.

# Description

Auxiliary function for sampling of the logrank simulations to return the integer 1 event per time.

### Usage

returnOne()

# Value

1

### **Examples**

returnOne()

rLogrank

Randomly samples from a logrank distribution

## Description

Draws a number of occurrences in group 1 (treatment) out of obsTotal number of occurrences.

### Usage

```
rLogrank(n = 1, y0, y1, obsTotal, theta)
```

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## **Arguments**

n	integer, number of observations to be sampled.
y0	Size of the risk set of group 0 (Placebo).
y1	Size of the risk set of group 1 (Treatment).
obsTotal	Total number of observations.
theta	Odds of group 1 over group 0 (treatment over placebo).

### Value

integer representing the number of occurrences in group 1 out of obsTotal number of occurrences.

## Author(s)

Muriel Felipe Perez-Ortiz and Alexander Ly

## **Examples**

```
rLogrank(y0=360, y1=89, obsTotal=12, theta=3.14)
```

safeLogrankTest Safe Logrank Test

## **Description**

A safe test to test whether there is a difference between two survival curves. This function builds on the Mantel-Cox version of the logrank test.

## Usage

```
safeLogrankTest(
  formula,
  designObj = NULL,
  ciValue = NULL,
  data = NULL,
  survTime = NULL,
  group = NULL,
  pilot = FALSE,
  exact = TRUE,
  computeZ = TRUE,
  ...
)
safeLogrankTestStat(
  z,
  nEvents,
```

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```
designObj,
  ciValue = NULL,
  dataNull = 1,
  sigma = 1
)
```

### **Arguments**

formula a formula expression as for other survival models, of the form Surv(time, status)

~ grouping Variable, see Surv for more details.

designObj a safe logrank design obtained from designSafeLogrank.

ciValue numeric, represents the ciValue-level of the confidence sequence. Default ciValue=NULL,

and ciValue = 1 - alpha, where alpha is taken from the design object.

data an optional data frame in which to interpret the variables occurring in survTime

and group.

survTime an optional survival time object of class 'Surv' created with Surv, or a name of

a column in the data set of class 'Surv'. Does not need specifying if a formula

is provided, therefore set to NULL by default.

group an optional factor, a grouping variable. Currently, only two levels allowed. Does

not need specifying if a formula is provided, therefore set to NULL by default.

pilot a logical indicating whether a pilot study is run. If TRUE, it is assumed that

the number of samples is exactly as planned. The default null h0=1 is used, alpha=0.05, and alternative="twoSided" is used. To change these default values,

please use designSafeLogrank.

exact a logical indicating whether the exact safe logrank test needs to be performed

based on the hypergeometric likelihood. Default is TRUE, if FALSE then the safe

z-test (for Gaussian data) applied to the logrank z-statistic is used instead.

computeZ logical. If TRUE computes the logrank z-statistic. Default is TRUE.

... further arguments to be passed to or from methods.

z numeric representing the observed logrank z statistic.

nEvents numeric > 0, observed number of events.

dataNull numeric > 0, the null hypothesis corresponding to the z statistics. By default

dataNull = 1 representing equality of the hazard ratio.

sigma numeric > 0, scaling in the data.

#### Value

Returns an object of class 'safeTest'. An object of class 'safeTest' is a list containing at least the following components:

**statistic** the value of the summary, i.e., z-statistic or the e-value.

**nEvents** The number of observed events.

eValue the e-value of the safe test.

**confSeq** An anytime-valid confidence sequence.

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```
estimate To be implemented: An estimate of the hazard ratio.
testType "logrank".
dataName a character string giving the name(s) of the data.
designObj an object of class "safeDesign" obtained from designSafeLogrank.
sumStats a list containing the time of events, the progression of the risk sets and events.
call the expression with which this function is called.
```

#### **Functions**

• safeLogrankTestStat(): Safe Logrank Test based on Summary Statistic Z All provided data (i.e., z-scores) are assumed to be centred on a hazard ratio = 1, thus, log(hr) = 0, and the proper (e.g., hypergeometric) scaling is applied to the data, so sigma = 1. The null hypothesis in the design object pertains to the population and is allowed to differ from log(theta) = 0.

```
# Example taken from survival::survdiff
designObj <- designSafeLogrank(hrMin=1/2)</pre>
ovData <- survival::ovarian
ovData$survTime <- survival::Surv(ovData$futime, ovData$fustat)</pre>
safeLogrankTest(formula=survTime~ rx, data=ovData, designObj=designObj)
safeLogrankTest(survTime=survTime, group=rx, data=ovData, designObj=designObj)
# Examples taken from coin::logrank_test
## Example data (Callaert, 2003, Tab. 1)
callaert <- data.frame(</pre>
 time = c(1, 1, 5, 6, 6, 6, 6, 2, 2, 2, 3, 4, 4, 5, 5),
 group = factor(rep(0:1, c(7, 8)))
designObj <- designSafeLogrank(hrMin=1/2)</pre>
safeLogrankTest(survival::Surv(callaert$time)~callaert$group,
                designObj = designObj)
safeLogrankTest(survTime=survival::Surv(callaert$time),
                group=callaert$group, designObj = designObj)
result <- safeLogrankTest(survTime=survival::Surv(callaert$time),</pre>
                group=callaert$group, designObj = designObj)
result
## Sequentially
# Greater
```

safeTTest

```
eValueGreater <- exp(cumsum(result$sumStats$logEValueGreater))</pre>
eValueLess <- exp(cumsum(result$sumStats$logEValueLess))</pre>
# twoSided
eValueTwoSided <- 1/2*eValueGreater+1/2*eValueLess
eValueTwoSided
result$eValue
###### Example switching between safe exact and safe Gaussian logrank test
designObj <- designSafeLogrank(0.8, alternative="less")</pre>
dat <- safestats::generateSurvData(300, 300, 2, 0.0065, 0.0065*0.8, seed=1)</pre>
survTime <- survival::Surv(dat$time, dat$status)</pre>
resultE <- safeLogrankTest(survTime ~ dat$group,</pre>
                            designObj = designObj)
resultG <- safeLogrankTest(survTime ~ dat$group,</pre>
                            designObj = designObj, exact=FALSE)
resultE
resultG
###### Example switching between safe exact and safe Gaussian logrank test other side
designObj <- designSafeLogrank(1/0.8, alternative="greater")</pre>
resultE <- safeLogrankTest(survTime ~ dat$group,</pre>
                             designObj = designObj)
resultG <- safeLogrankTest(survTime ~ dat$group,</pre>
                            designObj = designObj, exact=FALSE)
if (log(resultE$eValue) >= 0 && log(resultG$eValue) >= 0 )
  stop("one-sided wrong")
```

safeTTest

Safe Student's T-Test.

### **Description**

A safe t-test adapted from t.test() to perform one and two sample t-tests on vectors of data.

### Usage

```
safeTTest(
```

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```
Х,
 y = NULL,
 designObj = NULL,
 paired = FALSE,
 varEqual = TRUE,
 pilot = FALSE,
 alpha = NULL,
 alternative = NULL,
 ciValue = NULL,
 na.rm = FALSE,
)
safe.t.test(
 Х,
 y = NULL,
 designObj = NULL,
 paired = FALSE,
 var.equal = TRUE,
 pilot = FALSE,
 alpha = NULL,
 alternative = NULL,
)
```

# Arguments

X	a (non-empty) numeric vector of data values.
у	an optional (non-empty) numeric vector of data values.
designObj	an object obtained from designSafeT(), or NULL, when pilot equals TRUE.
paired	a logical indicating whether you want a paired t-test.
varEqual	a logical variable indicating whether to treat the two variances as being equal. For the moment, this is always $TRUE$ .
pilot	a logical indicating whether a pilot study is run. If TRUE, it is assumed that the number of samples is exactly as planned.
alpha	numeric > 0 only used if pilot equals TRUE. If pilot equals FALSE, then the alpha of the design object is used instead in constructing the decision rule $S > 1/alpha$ .
alternative	a character only used if pilot equals TRUE. If pilot equals FALSE, then the alternative specified by the design object is used instead.
ciValue	numeric is the ciValue-level of the confidence sequence. Default ciValue=NULL, and ciValue = $1$ - alpha
na.rm	a logical value indicating whether NA values should be stripped before the computation proceeds.
	further arguments to be passed to or from methods.
var.equal	a logical variable indicating whether to treat the two variances as being equal. For the moment, this is always TRUE.

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#### Value

Returns an object of class "safeTest". An object of class "safeTest" is a list containing at least the following components:

statistic the value of the t-statistic.

**n** The realised sample size(s).

eValue the realised e-value from the safe test.

**confSeq** A safe confidence interval for the mean appropriate to the specific alternative hypothesis.

**estimate** the estimated mean or difference in means or mean difference depending on whether it a one- sample test or a two-sample test was conducted.

stderr the standard error of the mean (difference), used as denominator in the t-statistic formula.

testType any of "oneSample", "paired", "twoSample" provided by the user.

dataName a character string giving the name(s) of the data.

designObj an object of class "safeTDesign" obtained from designSafeT().

call the expression with which this function is called.

### **Examples**

```
designObj <- designSafeT(deltaMin=0.6, alpha=0.008, alternative="greater",</pre>
                          testType="twoSample", ratio=1.2)
set.seed(1)
x <- rnorm(100)
y <- rnorm(100)
safeTTest(x, y, designObj=designObj)
                                            #0.2959334
safeTTest(1:10, y = c(7:20), pilot=TRUE)
                                                \# s = 658.69 > 1/alpha
designObj <- designSafeT(deltaMin=0.6, alpha=0.008, alternative="greater",</pre>
                          testType="twoSample", ratio=1.2)
set.seed(1)
x <- rnorm(100)
y <- rnorm(100)
safe.t.test(x,\ y,\ alternative="greater",\ designObj=designObj)
                                                                      #0.2959334
safe.t.test(1:10, y = c(7:20), pilot=TRUE)
                                                  \# s = 658.69 > 1/alpha
```

safeTTestStat

Computes E-Values Based on the T-Statistic

### **Description**

A summary stats version of safeTTest() with the data replaced by t, n1 and n2, and the design object by deltaS.

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# Usage

```
safeTTestStat(
   t,
   parameter,
   n1,
   n2 = NULL,
   alternative = c("twoSided", "less", "greater"),
   tDensity = FALSE,
   paired = FALSE,
   ...
)
```

# Arguments

t	numeric that represents the observed t-statistic.
parameter	numeric this defines the safe test S, i.e., a likelihood ratio of t distributions with in the denominator the likelihood with delta = 0 and in the numerator an average likelihood defined by $1/2$ time the likelihood at the non-centrality parameter $sqrt(nEff)$ *parameter and $1/2$ times the likelihood at the non-centrality parameter $-sqrt(nEff)$ *parameter.
n1	integer that represents the size in a one-sample t-test, (n2=NULL). When n2 is not NULL, this specifies the size of the first sample for a two-sample test.
n2	an optional integer that specifies the size of the second sample. If it's left unspecified, thus, NULL it implies that the t-statistic is based on one-sample.
alternative	a character only used if pilot equals TRUE. If pilot equals FALSE, then the alternative specified by the design object is used instead.
tDensity	Uses the the representation of the safe t-test as the likelihood ratio of t densities.
paired	a logical indicating whether you want a paired t-test.
	further arguments to be passed to or from methods.

## Value

Returns a numeric that represent the e10, that is, the e-value in favour of the alternative over the null

```
safeTTestStat(t=1, n1=100, 0.4)
safeTTestStat(t=3, n1=100, parameter=0.3)
```

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safeTTestStatAlpha

safeTTestStat() Subtracted with 1/alpha.

## **Description**

This is basically just safeTTestStat() - 1/alpha. This function is used for root finding for pilot designs.

# Usage

```
safeTTestStatAlpha(
   t,
   parameter,
   n1,
   n2 = NULL,
   alpha,
   alternative = c("twoSided", "greater", "less"),
   tDensity = FALSE
)
```

# Arguments

t	numeric that represents the observed t-statistic.
parameter	numeric this defines the safe test S, i.e., a likelihood ratio of t distributions with in the denominator the likelihood with delta = $0$ and in the numerator an average likelihood defined by $1/2$ time the likelihood at the non-centrality parameter sqrt(nEff)*parameter and $1/2$ times the likelihood at the non-centrality parameter -sqrt(nEff)*parameter.
n1	integer that represents the size in a one-sample t-test, (n2=NULL). When n2 is not NULL, this specifies the size of the first sample for a two-sample test.
n2	an optional integer that specifies the size of the second sample. If it's left unspecified, thus, NULL it implies that the t-statistic is based on one-sample.
alpha	numeric $> 0$ only used if pilot equals TRUE. If pilot equals FALSE, then the alpha of the design object is used instead in constructing the decision rule $S > 1/alpha$ .
alternative	a character only used if pilot equals TRUE. If pilot equals FALSE, then the alternative specified by the design object is used instead.
tDensity	Uses the the representation of the safe t-test as the likelihood ratio of t densities.

## Value

Returns a numeric that represent the e10 - 1/alpha, that is, the e-value in favour of the alternative over the null - 1/alpha.

```
safeTTestStat(t=1, n1=100, 0.4)
safeTTestStat(t=3, n1=100, parameter=0.3)
```

safeTTestStatTDensity 73

```
safeTTestStat()\ based\ on\ t\text{-}densities
```

# Description

This is basically just safeTTestStat() - 1/alpha. This function is used for root finding for pilot designs.

# Usage

```
safeTTestStatTDensity(
    t,
    parameter,
    nu,
    nEff,
    alternative = c("twoSided", "less", "greater"),
    paired = FALSE,
    ...
)
```

# Arguments

t	numeric that represents the observed t-statistic.
parameter	numeric this defines the safe test S, i.e., a likelihood ratio of t distributions with in the denominator the likelihood with delta = 0 and in the numerator an average likelihood defined by $1/2$ time the likelihood at the non-centrality parameter $sqrt(nEff)*parameter$ and $1/2$ times the likelihood at the non-centrality parameter $-sqrt(nEff)*parameter$ .
nu	numeric > 0 representing the degrees of freedom.
nEff	numeric > 0 representing the effective sample size in a two-sample problem. For one-sample problems this is equal to the sample size.
alternative	a character only used if pilot equals TRUE. If pilot equals FALSE, then the alternative specified by the design object is used instead.
paired	a logical indicating whether you want a paired t-test.
	further arguments to be passed to or from methods.

## Value

Returns a numeric that represent the e10, that is, the e-value in favour of the alternative over the null.

```
safeTTestStat(t=1, n1=100, 0.4)
safeTTestStat(t=3, n1=100, parameter=0.3)
```

safeTwoProportionsTest

Perform a Safe Test for Two Proportions with Stream Data

#### **Description**

Perform a safe test for two proportions (a 2x2 contingency table test) with a result object retrieved through the design function for planning an experiment to compare two proportions in this package, designSafeTwoProportions().

## Usage

```
safeTwoProportionsTest(
 ya,
 yb,
  designObj = NULL,
 wantConfidenceSequence = FALSE,
  ciValue = NULL,
  confidenceBoundGridPrecision = 20,
  logOddsConfidenceSearchBounds = c(0.01, 5),
  pilot = FALSE
)
safe.prop.test(
  ya,
 yb,
 designObj = NULL,
 wantConfidenceSequence = FALSE,
  ciValue = NULL,
  confidenceBoundGridPrecision = 20,
 logOddsConfidenceSearchBounds = c(0.01, 5),
  pilot = FALSE
)
```

# Arguments

ya positive observations/ events per data block in group a: a numeric with integer values between (and including) 0 and na, the number of observations in group a

per block.

yb positive observations/ events per data block in group b: a numeric with integer

values between (and including) 0 and nb, the number of observations in group b

per block.

designObj a safe test design for two proportions retrieved through designSafeTwoProportions().

wantConfidenceSequence

logical that can be set to true when the user wants a safe confidence sequence to be estimated.

ciValue coverage of the safe confidence sequence; default NULL, if NULL calculated as 1 - designObj[["alpha"]].

confidenceBoundGridPrecision

integer specifying the grid precision used to search for the confidence bounds. Default 20.

logOddsConfidenceSearchBounds

vector of to positive doubles specifying the upper and lower bound of the grid to search over for finding the confidence bound for the logOddsRatio restriction. Default (0.01, 5).

pilot

logical that can be set to true when performing an exploratory analysis without a designObj; only allows for na = nb = 1.

#### Value

Returns an object of class 'safeTest'. An object of class 'safeTest' is a list containing at least the following components:

**n** The realised sample size(s).

eValue the e-value of the safe test.

dataName a character string giving the name(s) of the data.

designObj an object of class "safeDesign" described in designSafeTwoProportions().

```
#balanced design
yb <- c(1,0,1,1,1,0,1)
ya <- c(1,0,1,0,0,0,1)
safeDesign <- designSafeTwoProportions(na = 1,</pre>
                                        nb = 1,
                                        beta = 0.20,
                                        delta = 0.6,
                                        alternativeRestriction = "none",
                                        M = 1e1
safeTwoProportionsTest(ya = ya, yb = yb, designObj = safeDesign)
safeTwoProportionsTest(ya = ya, yb = yb, pilot = TRUE)
#unbalanced design
yb <- c(1,0,1,1,1,0,1)
ya <- c(2,2,1,2,0,2,2)
safeDesign <- designSafeTwoProportions(na = 2,</pre>
                                        nb = 1,
                                        beta = 0.20,
                                        delta = 0.6,
                                        alternativeRestriction = "none",
                                        M = 1e1
safeTwoProportionsTest(ya = ya, yb = yb, designObj = safeDesign)
```

76 safeZTest

safeZ10Inverse Computes the Inverse of the Two-Sided Safe Z-Test	safeZ10Inverse	Computes the Inverse of the Two-Sided Safe Z-Test	
--	----------------	---	--

#### **Description**

This helper function is used in designSafeZ() to find parameter. The function is the (two-sided) inverse of 'safeZTestStat'.

# Usage

```
safeZ10Inverse(parameter, nEff, sigma = 1, alpha = 0.05)
```

# **Arguments**

parameter optional test defining parameter. Default set to NULL.

nEff numeric > 0, the effective sample size.

sigma numeric, the assumed known standard deviation, default 1.

alpha numeric in (0, 1) that specifies the tolerable type I error control –independent on

n- that the designed test has to adhere to. Note that it also defines the rejection

rule e10 > 1/alpha.

# Value

A number that represents a z-value. The function's domain is the positive real line and the range is the real line, i.e., the outcome space of the z-statistic.

# **Examples**

```
safeZ10Inverse(0.4, n=13)
```

safeZTest	Safe Z-Test

# **Description**

Safe one and two sample z-tests on vectors of data. The function is modelled after t.test().

safeZTest 77

# Usage

```
safeZTest(
 Х,
 y = NULL,
 paired = FALSE,
 designObj = NULL,
 pilot = FALSE,
 ciValue = NULL,
  tol = 1e-05,
 na.rm = FALSE,
)
safe.z.test(
 Х,
 y = NULL,
 paired = FALSE,
 designObj = NULL,
 pilot = FALSE,
  tol = 1e-05,
)
```

# Arguments

x	a (non-empty) numeric vector of data values.
У	an optional (non-empty) numeric vector of data values.
paired	a logical indicating whether you want the paired z-test.
designObj	an object obtained from designSafeZ(), or NULL, when pilot is set to TRUE.
pilot	a logical indicating whether a pilot study is run. If TRUE, it is assumed that the number of samples is exactly as planned. The default null h0=1 is used, alpha=0.05, and alternative="twoSided" is used. To change these default values, please use designSafeZ().
ciValue	numeric is the ciValue-level of the confidence sequence. Default ciValue=NULL, and ciValue = $1$ - alpha
tol	numeric > 0, only used if pilot equals TRUE, as it then specifies the mesh used to find the test defining parameter to construct a pilot design object.
na.rm	a logical value indicating whether NA values should be stripped before the computation proceeds.
	further arguments to be passed to or from methods.

# Value

Returns an object of class 'safeTest'. An object of class 'safeTest' is a list containing at least the following components:

78 safeZTestStat

statistic the value of the test statistic. Here the z-statistic.

**n** The realised sample size(s).

eValue the e-value of the safe test.

**confInt** To be implemented: a safe confidence interval for the mean appropriate to the specific alternative hypothesis.

**estimate** the estimated mean or difference in means or mean difference depending on whether it was a one- sample test or a two-sample test.

**h0** the specified hypothesised value of the mean or mean difference depending on whether it was a one-sample or a two-sample test.

testType any of "oneSample", "paired", "twoSample" effectively provided by the user.

dataName a character string giving the name(s) of the data.

designObj an object of class "safeDesign" described in designSafeZ().

call the expression with which this function is called.

## **Examples**

safeZTestStat

Computes E-Values Based on the Z-Statistic

# **Description**

Computes e-values using the z-statistic and the sample sizes only based on the test defining parameter phiS.

#### **Usage**

```
safeZTestStat(
   z,
   phiS,
   n1,
   n2 = NULL,
   alternative = c("twoSided", "less", "greater"),
   paired = FALSE,
   sigma = 1,
   ...
)
```

# **Arguments**

Z	numeric that represents the observed z-statistic.
phiS	numeric this defines the safe test $S$ , i.e., a likelihood ratio of $z$ distributions with in the denominator the likelihood with mean difference $0$ and in the numerator an average likelihood defined by the likelihood at the parameter value. For the two sided case $1/2$ at the parameter value and $1/2$ at minus the parameter value.
n1	integer that represents the size in a one-sample z-test, (n2=NULL). When n2 is not NULL, this specifies the size of the first sample for a two-sample test.
n2	an optional integer that specifies the size of the second sample. If it's left unspecified, thus, NULL it implies that the z-statistic is based on one-sample.
alternative	a character string specifying the alternative hypothesis must be one of "twoSided" (default), "greater" or "less".
paired	a logical, if TRUE ignores n2, and indicates that a paired z-test is performed.
sigma	numeric, the assumed known standard deviation, default 1.
• • •	further arguments to be passed to or from methods.

#### Value

Returns an e-value.

# **Examples**

```
safeZTestStat(z=1,\ n1=100,\ phiS=0.4)\\ safeZTestStat(z=3,\ n1=100,\ phiS=0.3)
```

 ${\tt sampleLogrankStoppingTimes}$ 

Simulate stopping times for the exact safe logrank test

# Description

Simulate stopping times for the exact safe logrank test

# Usage

```
sampleLogrankStoppingTimes(
  hazardRatio,
  alpha = 0.05,
  alternative = c("twoSided", "less", "greater"),
  m0 = 50000L,
  m1 = 50000L,
  nSim = 1000L,
  groupSizePerTimeFunction = returnOne,
  parameter = NULL,
  nMax = Inf,
  pb = TRUE
)
```

#### **Arguments**

hazardRatio numeric that defines the data generating hazard ratio with which data are sam-

pled.

alpha numeric in (0, 1) that specifies the tolerable type I error control –independent on

n- that the designed test has to adhere to. Note that it also defines the rejection

rule e10 > 1/alpha.

alternative a character string specifying the alternative hypothesis, which must be one of

"twoSided" (default), "greater" or "less". The alternative is pitted against the null hypothesis of equality of the survival distributions. More specifically, let lambda1 be the hazard rate of group 1 (i.e., placebo), and lambda2 the hazard ratio of group 2 (i.e., treatment), then the null hypothesis states that the hazard ratio theta = lambda2/lambda1 = 1. If alternative = "less", the null hypothesis is compared to theta < 1, thus, lambda2 < lambda1, that is, the hazard of group 2 (i.e., treatment) is less than that of group 1 (i.e., placebo), hence, the treatment is beneficial. If alternative = "greater", then the null hypothesis is compared to

theta > 1, thus, lambda2 > lambda1, hence, harm.

Mumber of subjects in the control group 0/1 at the beginning of the trial, i.e.,

nPlan[1].

m1 Number of subjects in the treatment group 1/2 at the beginning of the trial, i.e.,

nPlan[2].

nSim integer > 0, the number of simulations needed to compute power or the number

of events for the exact safe logrank test under continuous monitoring

groupSizePerTimeFunction

A function without parameters and integer output. This function provides the number of events at each time step. For instance, if rpois(1, 7) leads to a

random number of events at each time step.

parameter Numeric > 0, represents the safe tests defining thetaS. Default NULL so it's

decided by the algorithm, typically, this equals hrMin, which corresponds to the

GROW choice.

nMax An integer. Once nEvents hits nMax the experiment terminates, if it didn't stop

due to threshold crossing crossing already. Default set to Inf.

pb logical, if TRUE, then show progress bar.

#### Value

a list with stopping Times and break Vector. Entries of break Vector are 0, 1. A 1 represents stopping due to exceeding nMax, and 0 due to 1/alpha threshold crossing, or running out of participants, which implies that the corresponding stopping time is Inf.

#### Author(s)

Muriel Felipe Perez-Ortiz and Alexander Ly

#### **Examples**

sampleLogrankStoppingTimes(0.7, nSim=10)

```
{\tt sampleStoppingTimesSafeT}
```

Simulate stopping times for the safe z-test

# Description

Simulate stopping times for the safe z-test

# Usage

```
sampleStoppingTimesSafeT(
  deltaTrue,
  alpha = 0.05,
  alternative = c("twoSided", "less", "greater"),
  testType = c("oneSample", "paired", "twoSample"),
  nSim = 1000L,
  nMax = 1000,
  ratio = 1,
  lowN = 3L,
  parameter = NULL,
  seed = NULL,
  wantEValuesAtNMax = FALSE,
  pb = TRUE
)
```

# Arguments

deltaTrue	numeric, the value of the true standardised effect size (test-relevant parameter). This argument is used by 'designSafeT()' with 'deltaTrue <- deltaMin'
alpha	numeric in $(0, 1)$ that specifies the tolerable type I error control –independent of n– that the designed test has to adhere to. Note that it also defines the rejection rule e10 > 1/alpha.
alternative	a character string specifying the alternative hypothesis must be one of "twoSided" (default), "greater" or "less".
testType	either one of "oneSample", "paired", "twoSample".
nSim	integer $> 0$ , the number of simulations needed to compute power or the number of samples paths for the safe z test under continuous monitoring.
nMax	integer > 0, maximum sample size of the (first) sample in each sample path.
ratio	numeric > 0 representing the randomisation ratio of condition 2 over condition 1. If testType is not equal to "twoSample", or if nPlan is of length(1) then ratio=1.
lowN	integer minimal sample size of the (first) sample when computing the power due to optional stopping. Default lowN is set 1.
parameter	optional test defining parameter. Default set to NULL.
seed	integer, seed number.

wantEValuesAtNMax

logical. If TRUE then compute eValues at nMax. Default FALSE.

pb

logical, if TRUE, then show progress bar.

#### Value

a list with stopping Times and break Vector. Entries of break Vector are 0, 1. A 1 represents stopping due to exceeding nMax, and 0 due to 1/alpha threshold crossing, which implies that in corresponding stopping time is Inf.

# **Examples**

```
sampleStoppingTimesSafeT(0.7, nSim=10)
```

sampleStoppingTimesSafeZ

Simulate stopping times for the safe z-test

#### **Description**

Simulate stopping times for the safe z-test

#### Usage

```
sampleStoppingTimesSafeZ(
  meanDiffMin,
  alpha = 0.05,
  alternative = c("twoSided", "less", "greater"),
  sigma = 1,
  kappa = sigma,
  nSim = 1000L,
  nMax = 1000,
  ratio = 1,
  testType = c("oneSample", "paired", "twoSample"),
  parameter = NULL,
  wantEValuesAtNMax = FALSE,
  pb = TRUE
)
```

## **Arguments**

meanDiffMin

numeric that defines the minimal relevant mean difference, the smallest population mean that we would like to detect.

alpha

numeric in (0,1) that specifies the tolerable type I error control –independent on n- that the designed test has to adhere to. Note that it also defines the rejection

rule e10 > 1/alpha.

alternative	a character string specifying the alternative hypothesis must be one of "twoSided" (default), "greater" or "less".
sigma	numeric $> 0$ representing the assumed population standard deviation used for the test.
kappa	the true population standard deviation. Default kappa=sigma.
nSim	integer $> 0$ , the number of simulations needed to compute power or the number of samples paths for the safe z test under continuous monitoring.
nMax	integer > 0, maximum sample size of the (first) sample in each sample path.
ratio	numeric > 0 representing the randomisation ratio of condition 2 over condition 1. If testType is not equal to "twoSample", or if nPlan is of length(1) then ratio=1.
testType	either one of "oneSample", "paired", "twoSample".
parameter	optional test defining parameter. Default set to NULL.
wantEValuesAtNMax	
	logical. If TRUE then compute eValues at nMax. Default FALSE.
pb	logical, if TRUE, then show progress bar.

#### Value

a list with stopping Times and break Vector. Entries of break Vector are 0, 1. A 1 represents stopping due to exceeding nMax, and 0 due to 1/alpha threshold crossing, which implies that in corresponding stopping time is Inf.

# **Examples**

```
sampleStoppingTimesSafeZ(0.7, nSim=10)
```

 ${\tt selectivelyContinueTTestCombineData}$ 

Selectively Continue Experiments that Did Not Lead to a Null Rejection for a (Safe) T-Test

# Description

Helper function used in the vignette.

# Usage

```
selectivelyContinueTTestCombineData(
  oldValues,
  valuesType = c("eValues", "pValues"),
  designObj = NULL,
  alternative = c("twoSided", "greater", "less"),
  oldData,
  deltaTrue,
  alpha = NULL,
```

```
n1Extra = NULL,
n2Extra = NULL,
seed = NULL,
paired = FALSE,
muGlobal = 0,
sigmaTrue = 1,
moreMainText = ""
)
```

# Arguments

vector of e-values or p-values.
character string either "eValues" or "pValues".
a safeDesign object obtained from designSafeT, or NULL if valuesType equal "pValues".
a character string specifying the alternative hypothesis must be one of "twoSided" (default), "greater" or "less".
a list of matrices with names "dataGroup1" and "dataGroup2".
numeric, the value of the true standardised effect size (test-relevant parameter).
numeric in $(0, 1)$ that specifies the tolerable type I error control –independent of n– that the designed test has to adhere to. Note that it also defines the rejection rule $e10 > 1/alpha$ .
integer, that defines the additional number of samples of the first group. If NULL and valuesType equals "eValues", then n1Extra equals designObj\$nPlan[1].
optional integer, that defines the additional number of samples of the second group. If NULL, and values Type equals "eValues", then n2Extra equals design0bj\$nPlan[2].
To set the seed for the simulated data.
logical, if TRUE then paired t-test.
numeric, the true global mean of a paired or two-sample t-test. Its value should not matter for the test. This parameter is treated as a nuisance.
numeric > 0,the true standard deviation of the data. Its value should not matter for the test. This parameter treated is treated as a nuisance.
character, additional remarks in the title of the histogram.

## Value

a list that includes the continued s or p-values based on the combined data, and a list of the combined data.

```
alpha <- 0.05
mIter <- 1000L

designObj <- designSafeT(deltaMin=1, alpha=alpha, beta=0.2, nSim=100)</pre>
```

```
oldData <- generateNormalData(nPlan=designObj$nPlan, deltaTrue=0, nSim=mIter, seed=1)
eValues <- vector("numeric", length=mIter)
for (i in seq_along(eValues)) {
 eValues[i] <- safeTTest(x=oldData$dataGroup1[i, ], designObj=designObj)$eValue
# First run: 8 false null rejections
sum(eValues > 1/alpha)
continuedSafe <- selectivelyContinueTTestCombineData(</pre>
 oldValues=eValues, designObj=designObj, oldData=oldData,
 deltaTrue=0, seed=2)
# Second run: 1 false null rejections
sum(continuedSafe$newValues > 1/alpha)
# Third run: 0 false null rejections
eValues <- continuedSafe$newValues
oldData <- continuedSafe$combinedData</pre>
continuedSafe <- selectivelyContinueTTestCombineData(</pre>
 oldValues=eValues, designObj=designObj, oldData=oldData,
 deltaTrue=0, seed=3)
sum(continuedSafe$newValues > 1/alpha)
```

 ${\tt setSafeStatsPlotOptionsAndReturnOldOnes}$ 

Sets 'safestats' Plot Options and Returns the Current Plot Options.

## Description

Sets 'safestats' Plot Options and Returns the Current Plot Options.

## Usage

```
setSafeStatsPlotOptionsAndReturnOldOnes(...)
```

#### **Arguments**

... further arguments to be passed to or from methods.

#### Value

Returns a list with the user specified plot options.

```
oldPar <- setSafeStatsPlotOptionsAndReturnOldOnes()
graphics::plot(1:10, 1:10)
setPar <- graphics::par(oldPar)</pre>
```

86 simulate.safeDesign

simulate.safeDesign Simulate Early Stopping Experiments for the T Test

# Description

Applied to a 'safeDesign' object this function empirically shows the performance of safe experiments under optional stopping.

# Usage

```
## S3 method for class 'safeDesign'
simulate(
 object,
 nsim = nSim,
 seed = NULL,
 deltaTrue = NULL,
 muGlobal = 0,
  sigmaTrue = 1,
  lowN = 3,
  safeOptioStop = TRUE,
  freqOptioStop = FALSE,
  nPlanFreq = NULL,
  logging = TRUE,
  pb = TRUE,
 nSim = 1,
)
```

quentist test.

# Arguments

object	A safeDesign obtained obtained from designSafeT().
nsim	integer, formally the number of iterations, but by default nsim=nSim
seed	integer, seed number.
deltaTrue	numeric, if NULL, then the minimally clinically relevant standardised effect size is used as the true data generating effect size deltaTrue.
muGlobal	numeric, the true global mean of a paired or two-sample t-test. Its value should not matter for the test. This parameter is treated as a nuisance.
sigmaTrue	numeric > 0,the true standard deviation of the data. Its value should not matter for the test. This parameter treated is treated as a nuisance.
lowN	integer that defines the smallest n of our search space for n.
safeOptioStop	logical, TRUE implies that optional stopping simulation is performed for the safe test. $ \\$
freqOptioStop	logical, TRUE implies that optional stopping simulation is performed for the fre-

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nPlanFreq the frequentist sample size(s) to plan for. Acquired from designFreqT().

logging logical, if TRUE, then return the simulated data.

pb logical, if TRUE, then show progress bar.

nSim integer, number of iterations.

further arguments to be passed to or from methods.

#### Value

Returns an object of class "safeTSim". An object of class "safeTSim" is a list containing at least the following components:

**nPlan** the planned sample size(s).

**deltaTrue** the value of the true standardised effect size (test-relevant parameter) provided by the user.

**muGlobal** the true global mean of a paired or two-sample t-test (nuisance parameter) provided by the user.

paired if TRUE then paired t-test.

alternative any of "twoSided", "greater", "less" provided by the user.

lowN the smallest number of samples (first group) at which monitoring of the tests begins.

**nSim** the number of replications of the experiment.

**alpha** the tolerable type I error provided by the user.

**beta** the tolerable type II error provided by the user.

testType any of "oneSample", "paired", "twoSample" provided by the user.

parameter the parameter (point prior) used in the safe test derived from the design. Acquired from designSafeT().

**nPlanFreq** the frequentist planned sample size(s). Acquired from designFreqT()

safeSim list with the simulation results of the safe test under optional stopping.

freqSim list with the simulation results of the frequentist test under optional stopping.

```
# Design safe test
alpha <- 0.05
beta <- 0.20
deltaMin <- 1
designObj <- designSafeT(deltaMin, alpha=alpha, beta=beta, nSim=100)

# Design frequentist test
freqObj <- designFreqT(deltaMin, alpha=alpha, beta=beta)

# Simulate based on deltaTrue=deltaMin
simResultsDeltaTrueIsDeltaMin <- simulate(object=designObj, nSim=100)

# Simulate based on deltaTrue > deltaMin
simResultsDeltaTrueIsLargerThanDeltaMin <- simulate(</pre>
```

simulateCoverageDifferenceTwoProportions

Simulate the coverage of a safe confidence sequence for differences between proportions for a given distribution and safe design.

# **Description**

Simulate the coverage of a safe confidence sequence for differences between proportions for a given distribution and safe design.

# Usage

```
simulateCoverageDifferenceTwoProportions(
  successProbabilityA,
  trueDelta,
  safeDesign,
  precision = 100,
  M = 1000,
  numberForSeed = NA
)
```

#### **Arguments**

successProbabilityA

probability of observing a success in group A.

trueDelta difference in probability between group A and B.

safeDesign a safe test design for two proportions retrieved through designSafeTwoProportions().

precision precision of the grid to search over for the confidence sequence bounds. Default

100.

M number of simulations to carry out. Default 1000.

numberForSeed number for seed to set, default NA.

#### Value

the proportion of simulations where the trueDelta was included in the confidence sequence.

#### **Examples**

simulateIncorrectStoppingTimesFisher

Simulate incorrect optional stopping with fisher's exact test's p-value as the stopping rule.

# **Description**

Simulate incorrect optional stopping with fisher's exact test's p-value as the stopping rule.

# Usage

```
simulateIncorrectStoppingTimesFisher(
  thetaA,
  thetaB,
  alpha,
  na,
  nb,
  maxSimStoptime = 10000,
  M = 1000,
  numberForSeed = NULL
)
```

# **Arguments**

thetaA Bernoulli distribution parameter in group A thetaB Bernoulli distribution parameter in group B

alpha Significance level

na number of observations in group a per data block
nb number of observations in group b per data block

maxSimStoptime maximal number of blocks to sample in each experiment

M Number of simulations to carry out, default 1e3.

numberForSeed number for seed to set, default NULL.

#### Value

list with stopping times and rejection decisions.

## **Examples**

 ${\it simulate Optional Stopping Scenario Two Proportions}$ 

Simulate an optional stopping scenario according to a safe design for two proportions

## Description

Simulate an optional stopping scenario according to a safe design for two proportions

#### Usage

```
simulateOptionalStoppingScenarioTwoProportions(safeDesign, M, thetaA, thetaB)
```

## Arguments

 $safe Design \\ a 's afe Design' object obtained through \\ design Safe Two Proportions ().$ 

M integer, the number of data streams to sample.
thetaA Bernoulli distribution parameter in group A
thetaB Bernoulli distribution parameter in group B

#### Value

list with the simulation results of the safe test under optional stopping with the following components:

powerOptioStop Proportion of sequences where H0 was rejected

nMean Mean stopping time

probLessNDesign Proportion of experiments stopped before nBlocksPlan was reached

lowN Minimum stopping time

eValues All achieved E values

allN All stopping times

allSafeDecisions Decisions on rejecting H0 for each M

allRejectedN Stopping times of experiments where H0 was rejected

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## **Examples**

simulateTwoProportions

Compare Different Hyperparameter Settings for Safe Tests of Two Proportions.

# **Description**

Simulates for a range of divergence parameter values (differences or log odds ratios) the worst-case stopping times (i.e., number of data blocks collected) and expected stopping times needed to achieve the desired power for each hyperparameter setting provided.

## Usage

```
simulateTwoProportions(
  hyperparameterList,
  alternativeRestriction = c("none", "difference", "logOddsRatio"),
  deltaDesign = NULL,
  alpha,
  beta,
  na,
  nb,
  deltamax = 0.9,
  deltamin = 0.1,
  deltaGridSize = 8,
  M = 100,
  maxSimStoptime = 10000,
  thetaAgridSize = 8
```

#### **Arguments**

hyperparameterList

list object, its components hyperparameter lists with a format as described in designSafeTwoProportions().

alternativeRestriction

a character string specifying an optional restriction on the alternative hypothesis; must be one of "none" (default), "difference" (difference group mean b minus group b) or "logOddsRatio" (the log odds ratio between group means b and a).

deltaDesign optional; when using a restricted alternative, the value of the divergence measure

used. Either a numeric between -1 and 1 for a restriction on difference, or a real

for a restriction on the log odds ratio.

alpha numeric in (0, 1) that specifies the tolerable type I error control –independent on

n- that the designed test has to adhere to. Note that it also defines the rejection

rule e10 > 1/alpha.

beta numeric in (0, 1) that specifies the tolerable type II error control in the study.

Necessary to calculate the worst case stopping time.

na number of observations in group a per data block
nb number of observations in group b per data block

deltamax maximal effect size to calculate power for; between -1 and 1 for designs without

restriction or a restriction on difference; real number for a restriction on the log

odds ratio. Default 0.9.

deltamin minimal effect size to calculate power for; between -1 and 1 for designs without

restriction or a restriction on difference; real number for a restriction on the log

odds ratio. Default 0.1.

deltaGridSize numeric, positive integer: size of grid of delta values worst case and expected

sample sizes are simulated for.

M number of simulations used to estimate sample sizes. Default 100.

maxSimStoptime maximal stream length in simulations; when the e value does not reach the re-

jection threshold before the end of the stream, the maximal stream length is

returned as the stopping time. Default 1e4.

thetaAgridSize numeric, positive integer: size of the grid of probability distributions examined

for each delta value to find the worst case sample size over.

#### Value

Returns an object of class "safe2x2Sim". An object of class "safe2x2Sim" is a list containing at least the following components:

**simData** A data frame containing simulation results with worst case and expected stopping times for each hyperparameter setting, for the specified or default range of effect sizes.

alpha the significance threshold used in the simulations

**beta** the type-II error control used in the simulations

**deltaDesign** the value of restriction on the alternative hypothesis parameter space used for the E variables in the simulations

restriction the type of restriction used for the E variables in the simulation

hyperparameters list of the hyperparameters tested in the simulation

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#### **Examples**

```
priorList1 <- list(betaA1 = 10, betaA2 = 1, betaB1 = 1, betaB2 = 10)
priorList2 <- list(betaA1 = 0.18, betaA2 = 0.18, betaB1 = 0.18, betaB2 = 0.18)
priorList3 <- list(betaA1 = 1, betaA2 = 1, betaB1 = 1, betaB2 = 1)

simResult <- simulateTwoProportions(
    hyperparameterList = list(priorList1, priorList2, priorList3),
    alternativeRestriction = "none",
    alpha = 0.1, beta = 0.2, na = 1, nb = 1,
    deltamax = -0.4, deltamin = -0.9, deltaGridSize = 3,
    M = 10
    )

print(simResult)
plot(simResult)</pre>
```

tryOrFailWithNA

Tries to Evaluate an Expression and Fails with NA

## **Description**

The evaluation fails with NA by default, but it is also able to fail with other values.

#### **Usage**

```
tryOrFailWithNA(expr, value = NA_real_)
```

# Arguments

expr Expression to be evaluated.

value Return value if there is an error, default is NA\_real\_.

# Value

Returns the evaluation of the expression, or value if it doesn't work out.

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