Package 'TrialSize'

November 5, 2024

Title R Functions for Chapter 3,4,6,7,9,10,11,12,14,15 of Sample Size Calculation in Clinical Research

Version 1.4.1

Date 2020-07-01

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Description Functions and Examples in Sample Size Calculation in Clinical Research.

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LazyLoad yes

NeedsCompilation yes

Repository CRAN

Date/Publication 2024-11-05 05:38:51 UTC

Contents

`TrialSize-package` *Sample Size calculation in Clinical Research*

Description

More than 80 functions in this package are widely used to calculate sample size in clinical trial research studies.

This package covers the functions in Chapter 3,4,6,7,9,10,11,12,14,15 of the reference book.

Details

Package:	TrialSize
Type:	Package
Version:	1.3
Date:	2013-05-31
License:	GPL (>=2
LazyLoad:	yes

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References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2008

`AB.withDescalation` *A + B Escalation Design with Dose De-escalation*

Description

The general A+B designs with dose de-escalation. There are A patients at dose level i.

(1) If less than C/A patients have dose limiting toxicity (DLTs), then the dose is escalated to the next dose level i+1.

(2)If more than D/A (D $\geq$ C) patients have DLTs, then it will come back to dose i-1.If more than A patients have already been treated at dose level i-1, it will stop here and dose i-1 is the MTD. If there are only A patients treated at dose i-1, then Bmore patients are treated at this dose level i-1. This is dose de-escalation. The de-escalation may continue to the next dose level i-2 and so on if necessary.

(3)If no less than C/A but no more than D/A patients have DLTs, B more patients are treated at this dose level i.

(4)If no more than E (where E $\geq$ D) of the total A+B patients have DLT, then the dose is escalated.

(5)If more than E of the total of A+B patients have DLT, and the similar procedure in (2) will be applied.

Usage

```
AB.withDescalation(A, B, C, D, E, DLT)
```

Arguments

`A`	number of patients for the start A
`B`	number of patients for the continuous B
`C`	number of patients for the first cut off C
`D`	number of patients for the second cut off D, D $\geq$ C
`E`	number of patients for the third cut off D, E $\geq$ D
`DLT`	dose limiting toxicity rate for each dose level.

Note

For this design, the MTD is the dose level at which no more than E/(A+B) patients experience DLTs, and more than D/A or (no less than C/A and no more than D/A) if more than E/(A+B) patients treated with the next higher dose have DLTs.

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
DLT=c(0.01,0.014,0.025,0.056,0.177,0.594,0.963)
Example.11.6.2<-AB.withDescalation(A=3,B=3,C=1,D=1,E=1,DLT=DLT)
Example.11.6.2
# Example.11.6.2[7]=0.2
```

AB.withoutDescalation *A + B Escalation Design without Dose De-escalation*

Description

The general A+B designs without dose de-escalation. There are A patients at dose level i.

(1) If less than C/A patients have dose limiting toxicity (DLTs), then the dose is escalated to the next dose level i+1.

(2)If more than D/A (D $\geq$ C) patients have DLTs, then the previous dose i-1 will be considered the maximum tolerable dose (MTD).

(3)If no less than C/A but no more than D/A patients have DLTs, B more patients are treated at this dose level i.

(4)If no more than E (where E $\geq$ D) of the total A+B patients have DLT, then the dose is escalated.

(5)If more than E of the total of A+B patients have DLT, then the previous dose i-1 will be considered the MTD.

Usage

```
AB.withoutDescalation(A, B, C, D, E, DLT)
```

Arguments

A	number of patients for the start A
B	number of patients for the continuous B
C	number of patients for the first cut off C
D	number of patients for the second cut off D, D $\geq$ C
E	number of patients for the third cut off D, E $\geq$ D
DLT	dose limiting toxicity rate for each dose level.

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
DLT=c(0.01,0.014,0.025,0.056,0.177,0.594,0.963)
Example.11.6.1<-AB.withoutDescalation(A=3,B=3,C=1,D=1,E=1,DLT=DLT)
Example.11.6.1
# Example.11.6.1[1]=3.1
```

ABE *Average Bioequivalence*

Description

The most commonly used design for ABE is a standard two-sequence and two-period crossover design. Ft is the fixed effect of the test formulation and Fr is the fixed effect of the reference formulation.

Ho: Ft-Fr $\leq \delta_L$ or Ft-Fr $\leq \delta_U$

Ha: $\delta_L <$ Ft-Fr $< \delta_U$

Usage

```
ABE(alpha, beta, sigma1.1, delta, epsilon)
```

Arguments

alpha	significance level
beta	power = 1- beta
sigma1.1	$\sigma_{a.b}$ with a=1 and b=1.
delta	delta is the bioequivalence limit. here delta=0.223
epsilon	epsilon=Ft-Fr

Value

$$\sigma^2_{a.b} = \sigma^2_D + a * \sigma^2_{WT} + b * \sigma^2_{WR}$$

.

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.10.2<-ABE(0.05,0.2,0.4,0.223,0.05)
Example.10.2
# 21
```

`ANOVA.Repeat.Measure` *ANOVA with Repeat Measures*

Description

The study has multiple assessments in a parallel-group clinical trial. α_i is the fixed effect for the ith treatment $\sum \alpha_i = 0$.

Ho: $\alpha_i = \alpha_{i'}$

Ha: not equal

Usage

```
ANOVA.Repeat.Measure(alpha, beta, sigma, delta, m)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`sigma`	sigma^2 is the sum of the variance components.
`delta`	a clinically meaningful difference
`m`	Bonferroni adjustment for alpha, totally m pairs comparison.

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.15.3.4<-ANOVA.Repeat.Measure(0.05,0.2,1.25,1.5,3)
Example.15.3.4
# 15
```

Carry.Over *Test the Carry-over effect*

Description

2 by 2 crossover design. Test the treatment-by-period interaction (carry-over effect)

H0: the difference of the two sequence carry-over effects is equal to 0

Ha: not equal to 0

The test is finding whether there is a difference between the carry-over effect for sequence AB and BA.

Usage

```
Carry.Over(alpha, beta, sigma1, sigma2, gamma)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma1	standard deviation of sequence AB
sigma2	standard deviation of sequence BA
gamma	the difference of carry-over effect between sequence AB and BA

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.6.5.2<-Carry.Over(0.025,0.2,2.3,2.4,0.89)
Example.6.5.2 # 110
```

Cochran.Armitage.Trend

Cochran-Armitage's Test for Trend

Description

H0: p0=p1=p2=...=pK

Ha: p0 <= p1 <= p2 <=...<= pK with p0 < pK

Usage

```
Cochran.Armitage.Trend(alpha, beta, pi, di, ni, delta)
```

Arguments

alpha	significance level
beta	power = 1-beta
pi	pi is the response rate in ith group.
di	di is the dose level
ni	ni is the sample size for group i
delta	delta is the clinically meaningful minimal difference

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
pi=c(0.1,0.3,0.5,0.7);
di=c(1,2,3,4);
ni=c(10,10,10,10);

Example.11.5<-Cochran.Armitage.Trend(alpha=0.05,beta=0.2,pi=pi,di=di,ni=ni,delta=1)
Example.11.5
# 7.5 for one group. Total 28-32.
```

Cox.Equality *Test for equality in Cox PH model.*

Description

b is the log hazard ratio for treatment, b0 is the log hazard ratio for the controls

H0: b=b0

Ha: not equal to b0

The test is finding whether there is a difference between the hazard rates of the treatment and control.

Usage

```
Cox.Equality(alpha, beta, loghr, p1,d)
```

Arguments

alpha	significance level
beta	power = 1-beta
loghr	log hazard ratio=log(lamda2/lamda1)=b
p1	the proportion of patients in treatment 1 group
d	the probability of observing an event

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.7.3.4<-Cox.Equality(0.05,0.2,log(2),0.5,0.8)
Example.7.3.4
```

Cox.Equivalence *Test for Equivalence in Cox PH model.*

Description

b is the log hazard ratio for treatment, delta is the margin

Ho: $|b| \geq \delta$

Ha: $|b| < \delta$

Usage

```
Cox.Equivalence(alpha, beta, loghr, p1, d, delta)
```

Arguments

alpha	significance level
beta	power = 1-beta
loghr	log hazard ratio=log(lamda2/lamda1)=b
p1	the proportion of patients in treatment 1 group
d	the probability of observing an event
delta	delta is the true difference of log hazard rates between control group lamda1 and a test drug group lamda2

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.7.3.4<-Cox.Equivalence(0.05,0.2,log(2),0.5,0.8,0.5)
Example.7.3.4
```

Cox.NIS *Test for non-inferiority/superiority in Cox PH model.*

Description

b is the log hazard ratio for treatment, δ is the margin

H0: b $\leq \delta$

Ha: b > δ

Usage

```
Cox.NIS(alpha, beta, loghr, p1, d, delta)
```

Arguments

alpha	significance level
beta	power = 1-beta
loghr	log hazard ratio=log(lamda2/lamda1)=b
p1	the proportion of patients in treatment 1 group
d	the probability of observing an event
delta	margin is the true difference of log hazard rates between control group lamda1 and a test drug group lamda2

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.7.3.4<-Cox.NIS(0.05,0.2,log(2),0.5,0.8,0.5)
Example.7.3.4
```

`CrossOver.ISV.Equality` *Test for Equality of Intra-Subject Variabilities in Crossover Design*

Description

H0: within-subject variance of treatment T is equal to within-subject variance of treatment R

Ha: not equal

The test is finding whether two drug products have the same intra-subject variability in crossover design

Usage

```
CrossOver.ISV.Equality(alpha, beta, sigma1, sigma2, m)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`sigma1`	within-subject variance of treatment 1
`sigma2`	within-subject variance of treatment 2
`m`	for each subject, there are m replicates.

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

`CrossOver.ISV.Equivalence` *Test for Similarity of Intra-Subject Variabilities in Crossover Design*

Description

the ratio = within-subject variance of treatment T / within-subject variance of treatment R

H0: the ratio $\geq \delta$ or the ratio $\leq \frac{1}{\delta}$

Ha: $\frac{1}{\delta}$ < the ratio < δ

Usage

```
CrossOver.ISV.Equivalence(alpha, beta, sigma1, sigma2, m, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma1	within-subject variance of treatment 1
sigma2	within-subject variance of treatment 2
m	for each subject, there are m replicates.
margin	margin= δ, the true ratio of sigma1/sigma2

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

CrossOver.ISV.NIS *Test for Non-Inferiority/Superiority of Intra-Subject Variabilitie in Crossover Design*

Description

H0: the ratio that within-subject variance of treatment T / within-subject variance of treatment R $\geq \delta$

Ha: the ratio < δ

if $\delta < 1$, the rejection of Null Hypothesis indicates the superiority of the test drug over the reference for the intra-subject variability;

if $\delta > 1$, the rejection of the null hypothesis implies the non-inferiority of the test drug against the reference for the intra-subject variability; .

Usage

```
CrossOver.ISV.NIS(alpha, beta, sigma1, sigma2, m, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma1	within-subject variance of treatment 1
sigma2	within-subject variance of treatment 2
m	for each subject, there are m replicates.
margin	margin=δ, the true ratio of sigma1/sigma2

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.9.1.1<-CrossOver.ISV.NIS(0.05,0.2,0.3^2,0.45^2,2,1.1)
Example.9.1.1
```

`Dose.Min.Effect` *Williams' Test for Minimum effective dose (MED)*

Description

Ho: $\mu_1 = \mu_2 = ... = \mu_K$ Ha: $\mu_1 = \mu_2 = ... = \mu_{i-1} < \mu_i < \mu_{i+1} < \mu_K$

Usage

```
Dose.Min.Effect(alpha, beta, qt, sigma, delta)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`qt`	the critical value tk(alpha)
`sigma`	standard deviation
`delta`	δ is the clinically meaningful minimal difference

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.11.4.1<-Dose.Min.Effect(0.05,0.2,1.75,0.22,0.11)
Example.11.4.1
#54
```

`Dose.Response.binary` *Linear Contrast Test for Binary Dose Response Study*

Description

pi is the proportion of response in the ith group.

Ho: p1=p2=...=pk

Ha: L(p)= $\sum ci \times pi = \epsilon$, not equal to 0

Usage

```
Dose.Response.binary(alpha, beta, pi, ci, fi)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`pi`	pi is the proportion of response in the ith group.
`ci`	a linear contrast coefficients ci with $\sum ci = 0$.
`fi`	fi=ni/n is the sample size fraction for the ith group

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
pi=c(0.05,0.12,0.14,0.16);
ci=c(-6,1,2,3);

Example.11.2<-Dose.Response.binary(alpha=0.05,beta=0.2,pi=pi,ci=ci,fi=1/4)
Example.11.2
#382
```

`Dose.Response.Linear` *Linear Contrast Test for Dose Response Study*

Description

For a multi-arm dose response design, we use a linear contrast coefficients ci with $\sum ci = 0$.

H0: L(mu)=$\sum ci \times \mu_i = 0$

Ha: L(mu)=$\sum ci \times \mu_i = \epsilon$, not equal to 0

Usage

```
Dose.Response.Linear(alpha, beta, sigma, mui, ci, fi)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`sigma`	standard deviation for the population
`mui`	mui is the population mean for group i.
`ci`	a linear contrast coefficients ci with $\sum ci = 0$.
`fi`	fi=ni/n is the sample size fraction for the ith group

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
mui=c(0.05,0.12,0.14,0.16);
ci=c(-6,1,2,3);

Example.11.1<-Dose.Response.Linear(alpha=0.05,beta=0.2,sigma=0.22,mui=mui,ci=ci,fi=1/4)
Example.11.1
#178
```

`Dose.Response.time.to.event` *Linear Contrast Test for Time-to-Event Endpoint in dose response study*

Description

Under the exponential survival model, let lambdai be the proportion hazard rate for group i.

$\sum ci = 0$.

Ho: $L(\mu) = \sum ci \times \lambda_i = 0$

Ha: $L(p) = \sum ci \times \lambda_i = \epsilon > 0$

Usage

```
Dose.Response.time.to.event(alpha, beta, T0, T, Ti, ci, fi)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`T0`	T0 is the accrual time period
`T`	T is the total trial duration
`Ti`	$\lambda_i = log(2)/Ti$, Ti is the estimated median time for each group.
`ci`	a linear contrast coefficients ci with sum(ci)=0.
`fi`	fi=ni/n is the sample size fraction for the ith group

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Ti=c(14,20,22,24);
ci=c(-6,1,2,3);

Example.11.3.1<-Dose.Response.time.to.event(alpha=0.05,beta=0.2,T0=9,T=16,Ti=Ti,ci=ci,fi=1/4)
Example.11.3.1
#412

fi1=c(1/9,2/9,2/9,2/9);
Example.11.3.2<-Dose.Response.time.to.event(alpha=0.05,beta=0.2,T0=9,T=16,Ti=Ti,ci=ci,fi=fi1)
Example.11.3.2
#814
```

```
fi2=c(1/2.919,0.711/2.919,0.634/2.919,0.574/2.919);
Example.11.3.3<-Dose.Response.time.to.event(alpha=0.05,beta=0.2,T0=9,T=16,Ti=Ti,ci=ci,fi=fi2)
Example.11.3.3
#349
```

`gof.Pearson` *Test Goodness of Fit by Pearson's Test*

Description

Test the goodness of fit and the primary study endpoint is non-binary categorical response. pk=nk/n, nk is the frequency count of the subjects with response value k. pk,0 is a reference value.

H0: pk=pk,0 for all k

Ha: not equal

Usage

```
gof.Pearson(alpha, beta, pk, pk0, r)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`pk`	pk is the proportion of each subject in treatment group.
`pk0`	pk0 is a reference value.
`r`	degree of freedom=r-1

Details

(*) is $\chi^2_{r-1}(\chi^2_{\alpha,r-1}|noncen) = \beta$

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

gof.Pearson.twoway *Test Goodness of Fit by Pearson's Test for two-way table*

Description

H0: pk=pk,0 for all k

Ha: not equal

Usage

```
gof.Pearson.twoway(alpha, beta, trt, ctl, r, c)
```

Arguments

alpha	significance level
beta	power = 1-beta
trt	proportion of each subject in treatment group
ctl	proportion of each subject in control group
r	number of rows in the two-way table
c	number of column in the two-way table

Details

(*) is $\chi^2_{r-1}(\chi^2_{\alpha,r-1}|noncen) = \beta$

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

IBE *Individual Bioequivalence*

Description

Consider 2 by 2 crossover design. $\gamma = \delta^2 + \sigma^2_D + \sigma^2_{WT} - \sigma^2_{WR} - \theta_{IBE} * max(\sigma^2_0, \sigma^2_{WR})$

Ho: $\gamma \geq 0$

Ha: $\gamma < 0$

Usage

```
IBE(alpha, beta, delta, sigmaD, sigmaWT, sigmaWR, a, b, thetaIBE)
```

Arguments

alpha	significance level
beta	power = 1-beta
delta	delta is the mean difference
sigmaD	sigmaD^2=sigmaBT^2+sigmaBR^2-2*rho*sigmaBT*sigmaBR, sigmaBT^2 is the between-subjects variance in test formulation, sigmaBR^2 is the between-subjects variance in reference formulation
sigmaWT	sigmaWT^2 is the within-subjects variance in test formulation
sigmaWR	sigmaWR^2 is the within-subjects variance in reference formulation
a	Sigma(a,b)=sigmaD^2+a*sigmaWT^2+b*sigmaWR^2 a=0.5 here
b	b=0.5 here
thetaIBE	thetaIBE=2.5

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.10.4<-IBE(0.05, 0.2, 0, 0.2,0.3,0.3,0.5,0.5,2.5)
Example.10.4

# n=22 IBE reach 0
```

`InterSV.Equality` *Test for Equality of Inter-Subject Variabilities*

Description

H0: between-subject variance of treatment T is equal to between-subject variance of treatment R

Ha: not equal

The test is finding whether two drug products have the same inter-subject variability.

Usage

```
InterSV.Equality(alpha, beta, vbt, vwt, vbr, vwr, m)
```

Arguments

alpha	significance level
beta	power = 1-beta
vbt	between-subject variance of treatment T
vwt	within-subject variance of treatment T
vbr	between-subject variance of treatment R
vwr	within-subject variance of treatment R
m	for each subject, there are m replicates.

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

InterSV.NIS *Test for Equality of Inter-Subject Variabilities*

Description

H0: between-subject variance of treatment T is equal to between-subject variance of treatment R

Ha: not equal

The test is finding whether two drug products have the same inter-subject variability.

Usage

```
InterSV.NIS(alpha, beta, vbt, vwt, vbr, vwr, m,margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
vbt	between-subject variance of treatment T
vwt	within-subject variance of treatment T
vbr	between-subject variance of treatment R
vwr	within-subject variance of treatment R
m	for each subject, there are m replicates.
margin	margin=delta, the true ratio of sigma1/sigma2

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

ISCV.Equality *Test for Equality of Intra-Subject CVs*

Description

H0: CVr = CVt

Ha: not equal

The test is finding whether two drug products have the same intra-subject CVs

Usage

```
ISCV.Equality(alpha, beta, CVt, CVr, m)
```

Arguments

alpha	significance level
beta	power = 1-beta
CVt	Coefficient Of Variation for treatment T
CVr	Coefficient Of Variation for treatment R
m	for each subject, there are m replicates.

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

ISCV.Equivalence *Test for Equivalence of Intra-Subject CVs*

Description

H0: |CVr - CVt| $\geq \delta$

Ha: |CVr - CVt| < δ

Usage

```
ISCV.Equivalence(alpha, beta, CVt, CVr, m, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
CVt	Coefficient Of Variation for treatment T
CVr	Coefficient Of Variation for treatment R
m	for each subject, there are m replicates.
margin	margin=delta,

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

ISCV.NIS *Test for Non-Inferiority/Superiority of Intra-Subject CVs*

Description

H0: CVr - CVt < δ

Ha: CVr - CVt $\geq \delta$

if $\delta > 0$, the rejection of Null Hypothesis indicates the superiority of the test drug over the reference;

if $\delta < 0$, the rejection of the null hypothesis implies the non-inferiority of the test drug against the reference.

Usage

```
ISCV.NIS(alpha, beta, CVt, CVr, m, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
CVt	Coefficient Of Variation for treatment T
CVr	Coefficient Of Variation for treatment R
m	for each subject, there are m replicates.
margin	margin=delta,

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.9.2.1<-ISCV.NIS(0.05,0.2,0.7,0.5,2,0.1)
Example.9.2.1
```

`ISV.Equality` *Test for Equality of Intra-Subject Variabilities*

Description

H0: within-subject variance of treatment T is equal to within-subject variance of treatment R

Ha: not equal

The test is finding whether two drug products have the same intra-subject variability.

Usage

```
ISV.Equality(alpha, beta, sigma1, sigma2, m)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`sigma1`	within-subject variance of treatment 1
`sigma2`	within-subject variance of treatment 2
`m`	for each subject, there are m replicates.

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

`ISV.Equivalence` *Test for Similarity of Intra-Subject Variabilities*

Description

the ratio = within-subject variance of treatment T / within-subject variance of treatment R

Ho: the ratio $\geq \delta$ or the ratio $\leq \frac{1}{\delta}$

Ha: $\leq \frac{1}{\delta}$ < the ratio < δ

Usage

```
ISV.Equivalence(alpha, beta, sigma1, sigma2, m, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma1	within-subject variance of treatment 1
sigma2	within-subject variance of treatment 2
m	for each subject, there are m replicates.
margin	margin=delta, the true ratio of sigma1/sigma2

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

ISV.NIS *Test for Non-Inferiority/Superiority of Intra-Subject Variabilities*

Description

the ratio = within-subject variance of treatment T / within-subject variance of treatment R

H0: the ratio $\geq \delta$

Ha: the ratio < δ

if $\delta < 1$, the rejection of Null Hypothesis indicates the superiority of the test drug over the reference for the intra-subject variability;

if $\delta > 1$, the rejection of the null hypothesis implies the non-inferiority of the test drug against the reference for the intra-subject variability; .

Usage

```
ISV.NIS(alpha, beta, sigma1, sigma2, m, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma1	within-subject variance of treatment 1
sigma2	within-subject variance of treatment 2
m	for each subject, there are m replicates.
margin	margin=delta, the true ratio of sigma1/sigma2

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.9.1.1<-ISV.NIS(0.05,0.2,0.3^2,0.45^2,3,1.1)
Example.9.1.1
```

McNemar.Test *McNemar Test in 2 by 2 table*

Description

2 by 2 table. Test either a shift from 0 to 1 or a shift from 1 to 0 before treatment and after treatment.

$p_{1+} = P_{10} + P_{11}, p_{+1} = P_{01} + P_{11}$

Ho: $p_{1+} = p_{+1}$

Ha: not equal

The test is finding whether there is a categorical shift after treatment.

Usage

```
McNemar.Test(alpha, beta, psai, paid)
```

Arguments

alpha	significance level
beta	power = 1-beta
psai	the ratio of p01/p10
paid	the sum p10+p01

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.6.4.3<-McNemar.Test(0.05,0.2,0.2/0.5,.7)
Example.6.4.3
# 59
```

`MeanWilliamsDesign.Equality` *Test for Equality in Multiple-Sample William Design*

Description

Compare more than two treatment under a crossover design.

H0: margin is equal to 0 Ha: margin is not equal to 0

The test is finding whether there is a difference between treatment i and treatment j

Usage

```
MeanWilliamsDesign.Equality(alpha, beta, sigma, k, margin)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`sigma`	standard deviation
`k`	Total k treatments in the design
`margin`	$margin = \mu_i - \mu_j$ the difference between the true mean response of group i μ_i and group j μ_j

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.3.5.4<-MeanWilliamsDesign.Equality(0.025,0.2,0.1,6,0.05)
Example.3.5.4 # 6
Example.3.5.4<-MeanWilliamsDesign.Equality(0.025,0.2,0.1,6,-0.05)
Example.3.5.4 # 6
Example.3.5.4<-MeanWilliamsDesign.Equality(0.025,0.2,0.1,6,-0.1)
Example.3.5.4 # 2
```

`MeanWilliamsDesign.Equivalence` *Test for Equivalence in Multiple-Sample William Design*

Description

Compare more than two treatment under a crossover design.

H0: |margin| $\geq \delta$ Ha: |margin| < δ

This test is whether the test drug is equivalent to the control in average if the null hypothesis is rejected at significant level alpha

Usage

```
MeanWilliamsDesign.Equivalence(alpha, beta, sigma, k, delta, margin)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`sigma`	standard deviation
`k`	Total k treatments in the design
`delta`	the superiority or non-inferiority margin
`margin`	$margin = \mu_i - \mu_j$ the difference between the true mean response of group i μ_i and group j μ_j

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

`MeanWilliamsDesign.NIS` *Test for Non-Inferiority/Superiority in Multiple-Sample William Design*

Description

Compare more than two treatment under a crossover design.

H0: margin $\leq \delta$ Ha: margin > δ

if δ >0, the rejection of Null Hypothesis indicates the superiority of the test over the control;

if δ <0, the rejection of the null hypothesis implies the non-inferiority of the test against the control.

Usage

```
MeanWilliamsDesign.NIS(alpha, beta, sigma, k, delta, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma	standard deviation
k	Total k treatments in the design
delta	the superiority or non-inferiority margin
margin	$margin = \mu_i - \mu_j$ the difference between the true mean response of group i μ_i and group j μ_j

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

`Multiple.Testing` *Multiple Testing procedures*

Description

Ho: $\mu_{1j} - \mu_{2j} = 0$

Ha: $\mu_{1j} - \mu_{2j} > 0$

Usage

```
Multiple.Testing(s1, s2, m, p, D, delta, BCS, pho, K, alpha, beta)
```

Arguments

s1	We use bisection method to find the sample size, which let the equation h(n)=0. Here s1 and s2 are the initial value, 0 < s1 < s2. h(s1) should be smaller than 0.
s2	s2 is also the initial value, which is larger than s1 and h(s2) should be larger than 0.
m	m is the total number of multiple tests
p	p=n1/n. n1 is the sample size for group 1, n2 is the sample size for group 2, n=n1+n2.
D	D is the number of predictive genes.
delta	δ_j is the fix effect size among the predictive genes. We assume $\delta_j = delta, j = 1, ..., D$ and $\delta_j = 0, j = D+1, ..., m$.
BCS	BCS means block compound symmetry, which is the length of each blocks. If we only have one block, BCS=m, which is refer to compound symmetry(CS).

pho	pho is the correlation parameter. If j and j' in the same block, $\rho_{jj'} = pho$; otherwise $\rho_{jj'} = 0$.
K	K is the number of replicates for the simulation.
alpha	here alpha is the adjusted Familywise error rate (FWER)
beta	here power is a global power. power=1-beta

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

`Nonpara.Independ` *Test for independence for nonparametric study*

Description

Ho: $P(x \leq a \; and \; y \leq b) = P(x \leq a)P(y \leq b)$ for all a and b. Ha: not equal

Usage

```
Nonpara.Independ(alpha, beta, p1, p2)
```

Arguments

alpha	significance level
beta	power = 1-beta
p1	$p1 = P((x1 - x2)(y1 - y2) > 0)$
p2	$p2 = P((x1 - x2)(y1 - y2)(x1 - x3)(y1 - y3) > 0)$

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.14.4<-Nonpara.Independ(0.05,0.2,0.6,0.7)
Example.14.4
# 135
```

Nonpara.One.Sample *One Sample Location problem in Nonparametric*

Description

Ho: theta=0

Ha: theta is not equal to 0.

Usage

```
Nonpara.One.Sample(alpha, beta, p2, p3, p4)
```

Arguments

alpha	significance level
beta	power = 1-beta
p2	$p2 = P(\|z_i\| >= \|z_j\|, z_i > 0)$
p3	$p3 = P(\|z_i\| >= \|z_{j1}\|, \|z_i\| >= \|z_{j2}\|, z_i > 0)$
p4	$p4 = P(\|z_{j1}\| >= \|z_i\| >= \|z_{j2}\|, z_{j1} > 0, z_i > 0)$

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.14.2<-Nonpara.One.Sample(0.05,0.2,0.3,0.4,0.05)
Example.14.2
# 383
```

Nonpara.Two.Sample *Two sample location problem for Nonparametric*

Description

Ho: theta=0;

Ha: theta is not equal to 0.

Usage

```
Nonpara.Two.Sample(alpha, beta, k, p1, p2, p3)
```

Arguments

alpha	significance level
beta	power = 1-beta
k	k=n1/n2
p1	$p1 = P(y_i \geq x_j)$
p2	$p2 = P(y_i \geq x_{j1}\ and\ y_i \geq x_{j2})$
p3	$p3 = P(y_{i1} \geq x_j\ and\ y_{i2} \geq x_j)$

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.14.3<-Nonpara.Two.Sample(0.05,0.2,1,0.7,0.8,0.8)
Example.14.3
#54
```

OneSampleMean.Equality

One Sample Mean Test for Equality

Description

H0: margin is equal to 0 Ha: margin is not equal to 0

The test is finding whether there is a difference between the mean response of the test $\bar{x}$ and the reference value μ_0

Usage

```
OneSampleMean.Equality(alpha, beta, sigma, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma	standard deviation
margin	$margin = \bar{x} - \mu_0$ the difference between the true mean response of a test $\bar{x}$ and a reference value μ_0

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
OneSampleMean.Equality(0.05,0.2,1,0.5)
# 32
```

`OneSampleMean.Equivalence`

One Sample Mean Test for Equivalence

Description

Ho: $|margin| \geq delta$ Ha: |margin| < delta

The test is concluded to be equivalent to a gold standard on average if the null hypothesis is rejected at significance level alpha

Usage

```
OneSampleMean.Equivalence(alpha, beta, sigma,margin, delta)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`sigma`	standard deviation
`margin`	$margin = \bar{x} - \mu_0$ the difference between the true mean response of a test $\bar{x}$ and a reference value μ_0
`delta`	the superiority or non-inferiority margin

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
OneSampleMean.Equivalence(0.05,0.2,0.1,0.05,0)
# 35
```

`OneSampleMean.NIS` *One Sample Mean Test for Non-Inferiority/Superiority*

Description

Ho: $margin \leq delta$ Ha: margin > delta

if delta >0, the rejection of Null Hypothesis indicates the true mean is superior over the reference value mu0;

if delta <0, the rejection of the null hypothesis implies the true mean is non-inferior against the reference value mu0.

Usage

```
OneSampleMean.NIS(alpha, beta, sigma, margin, delta)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`sigma`	standard deviation
`delta`	the superiority or non-inferiority margin
`margin`	$margin = \bar{x} - \mu_0$ the difference between the true mean response of a test $\bar{x}$ and a reference value μ_0

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
OneSampleMean.NIS(0.05,0.2,1,0.5,-0.5)
# 7
```

OneSampleProportion.Equality

One sample proportion test for equality

Description

Ho: p=p0

Ha: not equal

The test is finding whether there is a difference between the true rate of the test drug and reference value p0

Usage

```
OneSampleProportion.Equality(alpha, beta, p, differ)
```

Arguments

alpha	significance level
beta	power = 1-beta
p	the true response rate
differ	differ=p-p0 the difference between the true response rate of a test drug and a reference value p0

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.4.1.4<-OneSampleProportion.Equality(0.05,0.2,0.5,0.2)
Example.4.1.4
```

OneSampleProportion.Equivalence

One sample proportion test for equivalence

Description

Ho: $|p - p0| \geq margin$

Ha: |p-p0| < margin

The proportion of response is equivalent to the reference p0 is the null hypothesis is rejected

Usage

```
OneSampleProportion.Equivalence(alpha, beta, p, delta, differ)
```

Arguments

alpha	significance level
beta	power = 1-beta
p	the true response rate
delta	delta=p-p0 the difference between the true response rate of a test drug and a reference value p0
differ	the superiority or non-inferiority margin

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.4.1.4<-OneSampleProportion.Equivalence(0.05,0.2,0.6,0.05,.2)
Example.4.1.4
```

OneSampleProportion.NIS

One sample proportion test for Non-inferiority/Superiority

Description

Ho: $p - p0 \leq margin$

Ha: p-p0 > margin

if margin >0, the rejection of Null Hypothesis indicates the true rate is superior over the reference value p0;

if margin <0, the rejection of the null hypothesis implies the true rate is non-inferior against the reference value p0.

Usage

```
OneSampleProportion.NIS(alpha, beta, p, delta, differ)
```

Arguments

alpha	significance level
beta	power = 1-beta
p	the true response rate
delta	delta=p-p0 the difference between the true response rate of a test drug and a reference value p0
differ	the superiority or non-inferiority margin

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.4.1.4<-OneSampleProportion.NIS(0.025,0.2,0.5,0.2,-0.1)
Example.4.1.4
```

OneSide.fixEffect *One-Sided Tests with fixed effect sizes*

Description

One-sided tests

Ho: $\delta_j = 0$

Ha: $\delta_j > 0$

Usage

```
OneSide.fixEffect(m, m1, delta, a1, r1, fdr)
```

Arguments

m	m is the total number of multiple tests
m1	m1 = m - m0. m0 is the number of tests which the null hypotheses are true ; m1 is the number of tests which the alternative hypotheses are true. (or m1 is the number of prognostic genes)
delta	δ_j is the constant effect size for jth test. $\delta_j = (E(Xj) - E(Yj))/\sigma_j$. $X_{ij}(Y_{ij})$ denote the expression level of gene j for subject i in group 1(and group 2, respectively) with common variance σ_j^2. We assume $\delta_j = 0,\ j\ in\ M0$ and $\delta_j > 0,\ j\ in\ M1$=effect size for prognostic genes.
a1	a1 is the allocation proportion for group 1. a2=1-a1.
r1	r1 is the number of true rejection
fdr	fdr is the FDR level.

Details

alpha_star=r1*fdr/((m-m1)*(1-fdr)), which is the marginal type I error level for r1 true rejection with the FDR controlled at f.

beta_star=1-r1/m1, which is equal to 1-power.

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.12.2.1<-OneSide.fixEffect(m=4000,m1=40,delta=1,a1=0.5,r1=24,fdr=0.01)
Example.12.2.1
# n=68; n1=34=n2
```

`OneSide.varyEffect` *One-Sided Tests with varying effect sizes*

Description

One-sided tests

Ho: $\delta_j = 0$

Ha: $\delta_j > 0$

Usage

```
OneSide.varyEffect(s1, s2, m, m1, delta, a1, r1, fdr)
```

Arguments

`s1`	We use bisection method to find the sample size, which let the equation h(n)=0. Here s1 and s2 are the initial value, 0<s1<s2. h(s1) should be smaller than 0.
`s2`	s2 is also the initial value, which is larger than s1 and h(s2) should be larger than 0.
`m`	m is the total number of multiple tests
`m1`	m1 = m - m0. m0 is the number of tests which the null hypotheses are true ; m1 is the number of tests which the alternative hypotheses are true. (or m1 is the number of prognostic genes)
`delta`	δ_j is the constant effect size for jth test. $\delta_j = (E(Xj) - E(Yj))/\sigma_j$. $X_{ij}(Y_{ij})$ denote the expression level of gene j for subject i in group 1(and group 2, respectively) with common variance σ_j^2. We assume $\delta_j = 0,\ j\ in\ M0$ and $\delta_j > 0,\ j\ in\ M1$=effect size for prognostic genes.
`a1`	a1 is the allocation proportion for group 1. a2=1-a1.
`r1`	r1 is the number of true rejection
`fdr`	fdr is the FDR level.

Details

alpha_star=r1*fdr/((m-m1)*(1-fdr)), which is the marginal type I error level for r1 true rejection with the FDR controlled at f.

beta_star=1-r1/m1, which is equal to 1-power.

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
delta=c(rep(1,40/2),rep(1/2,40/2));

Example.12.2.2 <- OneSide.varyEffect(100,150,4000,40,delta,0.5,24,0.01)
Example.12.2.2
# n=148 s1<n<s2, h(s1)<0,h(s2)<0
```

`OneWayANOVA.pairwise` *Pairwise Comparison for Multiple-Sample One-Way ANOVA*

Description

Ho: μ_i is equal to μ_j Ha: μ_i is not equal to μ_j

The test is comparing the means among treatments. There are tau pair comparisons of interested. Adjusted the multiple comparison by Bonferroni method,

Usage

```
OneWayANOVA.pairwise(alpha, beta, tau, sigma, margin)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`tau`	there are tau pair comparisons
`sigma`	standard deviation
`margin`	$margin = \mu_i - \mu_j$ the difference between the true mean response of group i μ_i and group j μ_j

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

OneWayANOVA.PairwiseComparison *One-way ANOVA pairwise comparison*

Description

Ho: $p_i = p_j$ Ha: not all equal

Usage

```
OneWayANOVA.PairwiseComparison(alpha, beta, tau, p1, p2, delta)
```

Arguments

alpha	significance level
beta	power = 1-beta
tau	there are tau comparisons here
p1	the mean response rate for test drug
p2	the rate for reference drug
delta	delta=$p_i - p_j$

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.4.4.2<-OneWayANOVA.PairwiseComparison(0.05,0.2,2,0.2,0.4,-0.2)
Example.4.4.2

Example.4.4.2<-OneWayANOVA.PairwiseComparison(0.05,0.2,2,0.2,0.5,-0.3)
Example.4.4.2
```

PBE *Population Bioequivalence*

Description

Consider 2 by 2 crossover design.

H0: lamda >= 0

Ha: lamda < 0

Usage

```
PBE(alpha, beta, sigma1.1, sigmatt, sigmatr, sigmabt, sigmabr, rho, a, delta, lamda)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma1.1	$\sigma^2_{a.b} = \sigma^2_D + a\sigma^2_{WT} + b\sigma^2_{WR}$. Here a=b=1.
sigmatt	$\sigma^2_{tt} = \sigma^2_{BT} + \sigma^2_{WT}$, σ^2_{wt} is the within-subjects variance in test formulation
sigmatr	$\sigma^2_{tr} = \sigma^2_{BR} + \sigma^2_{WR}$, σ^2_{wr} is the within-subjects variance in reference formulation
sigmabt	σ^2_{bt} is the between-subjects variance in test formulation
sigmabr	σ^2_{br} is the between-subjects variance in reference formulation
rho	rho is the inter-subject correlation coefficient.
a	a= thetaPBE =1.74
delta	delta is the mean difference of AUC
lamda	$lamda = delta^2 + \sigma^2 - \sigma^2_{TR} - thetaPBE * max(\sigma^2_0, \sigma^2_{TR})$

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.10.3<-PBE(0.05,0.2,0.2,sqrt(0.17),sqrt(0.17),0.4,0.4,0.75,1.74,0.00,-0.2966)
Example.10.3
# 12
```

Propensity.Score.nostrata

Propensity Score ignoring strata

Description

Combining data across J strata. Still use weighted Mantel_Haenszel test.

Ho: $p_{j1} = p_{j2}$,

Ha: $p_{j2}q_{j1}/(p_{j1}q_{j2})$=phi, which is not equal to 1

Usage

```
Propensity.Score.nostrata(alpha, beta, J, a, b, p1, phi)
```

Arguments

alpha	significance level
beta	power = 1-beta
J	There are totally J stratas.
a	a=c(a1,a2,...,aJ), aj=nj/n denote the allocation proportion for stratuum j (sum(aj)=1)
b	b=c(b11,b21,...,bJ1), bjk=njk/nj, k=1,2 denote the allocation proportion for group k within stratum j (bj1+bj2=1). Assume group 1 is the control.
p1	p1=c(p11,p21,....,pj1), pjk denote the response probability for group k in stratum j. qjk=1-pjk.
phi	$p_{j2}q_{j1}/(p_{j1}q_{j2})$=phi, so that $p_{j2} = phip_{j1}/(q_{j1} + phip_{j1})$

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
a=c(0.15,0.15,0.2,0.25,0.25);
b=c(0.4,0.4,0.5,0.6,0.6);
p1=c(0.5,0.6,0.7,0.8,0.9);

Example.15.2.3.2<-Propensity.Score.nostrata(alpha=0.05,beta=0.2,J=5,a,b,p1,phi=2)
Example.15.2.3.2
# 1151
```

Propensity.Score.strata

Propensity Score with Stratas

Description

Using weighted Mantel_Haenszel test in propensity analysis with stratas.

Ho: $p_{j1} = p_{j2}$,

Ha: $p_{j2}q_{j1}/(p_{j1}q_{j2})$=phi, which is not equal to 1

Usage

```
Propensity.Score.strata(alpha, beta, J, a, b, p1, phi)
```

Arguments

alpha	significance level
beta	power = 1-beta
J	There are totally J stratas.
a	a=c(a1,a2,...,aJ), aj=nj/n denote the allocation proportion for stratuum j (sum(aj)=1)
b	b=c(b11,b21,...,bJ1), bjk=njk/nj, k=1,2 denote the allocation proportion for group k within stratum j (bj1+bj2=1). Assume group 1 is the control.
p1	p1=c(p11,p21,....,pj1), pjk denote the response probability for group k in stratum j. qjk=1-pjk.
phi	$p_{j2}q_{j1}/(p_{j1}q_{j2})$=phi, so that $p_{j2} = phip_{j1}/(q_{j1} + phip_{j1})$

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
a=c(0.15,0.15,0.2,0.25,0.25);
b=c(0.4,0.4,0.5,0.6,0.6);
p1=c(0.5,0.6,0.7,0.8,0.9);

Example.15.2.3.1<-Propensity.Score.strata(alpha=0.05,beta=0.2,J=5,a,b,p1,phi=2)
Example.15.2.3.1
# 447
```

QOL *Quality of life*

Description

Under the time series model, determine sample size based on normal approximation.

Usage

```
QOL(alpha, beta, c, epsilon)
```

Arguments

alpha	significance level
beta	power = 1-beta
c	constant c=0.5
epsilon	a meaningful difference epsilon. If the chosen acceptable limits are $(-\delta, \delta)$. $epsilon = \delta - \eta$, η is the measure for detecting an equivalence when the true difference in treatment means is less than a small constant η.

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.15.4.3<-QOL(0.05,0.1,0.5,0.25)
Example.15.4.3
```

`QT.crossover` *Crossover Design in QT/QTc Studies without covariates*

Description

Ho: $\mu_1 - \mu_2 = 0$

Ha: $\mu_1 - \mu_2 = d$

The test is finding the treatment difference in QT interval for crossover design . d is not equal to 0, which is the difference of clinically importance.

Usage

```
QT.crossover(alpha, beta, pho, K, delta, gamma)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`pho`	pho=between subject variance σ_s^2/(between subject variance σ_s^2+within subject variance σ_e^2)
`K`	There are K recording replicates for each subject.
`delta`	$\sigma^2 = \sigma_s^2 + \sigma_e^2$. d is the difference of clinically importance. $\delta = d/\sigma$
`gamma`	σ_p^2 is the extra variance from the random period effect for the crossover design. $\gamma = \sigma_p^2/\sigma^2$

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.15.1.3<-QT.crossover(0.05,0.2,0.8,3,0.5,0.002)
Example.15.1.3
# 29
```

QT.parallel *Parallel Group Design in QT/QTc Studies without covariates*

Description

Ho: $\mu_1 - \mu_2 = 0$

Ha: $\mu_1 - \mu_2 = d$

The test is finding the treatment difference in QT interval. d is not equal to 0, which is the difference of clinically importance.

Usage

```
QT.parallel(alpha, beta, pho, K, delta)
```

Arguments

alpha	significance level
beta	power = 1-beta
pho	pho=between subject variance σ_s^2/(between subject variance σ_s^2+within subject variance σ_e^2)
K	There are K recording replicates for each subject.
delta	$\sigma^2 = \sigma_s^2 + \sigma_e^2$. d is the difference of clinically importance. $\delta = d/\sigma$

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.15.1.2<-QT.parallel(0.05,0.2,0.8,3,0.5)
Example.15.1.2
# 54
```

QT.PK.crossover *Crossover Design in QT/QTc Studies with PK response as covariate*

Description

Ho: $\mu_1 - \mu_2 = 0$

Ha: $\mu_1 - \mu_2 = d$

The test is finding the treatment difference in QT interval for crossover design. d is not equal to 0, which is the difference of clinically importance.

Usage

```
QT.PK.crossover(alpha, beta, pho, K, delta, gamma, v1, v2, tau1, tau2)
```

Arguments

alpha	significance level
beta	power = 1-beta
pho	pho=between subject variance σ_s^2/(between subject variance σ_s^2+within subject variance σ_e^2)
K	There are K recording replicates for each subject.
delta	$\sigma^2 = \sigma_s^2 + \sigma_e^2$. d is the difference of clinically importance. $\delta = d/\sigma$
gamma	σ_p^2 is the extra variance from the random period effect for the crossover design. $\gamma = \sigma_p^2/\sigma^2$
v1	sample mean for group 1
v2	sample mean for group 2
tau1	sample variance for group 1
tau2	sample variance for group 2

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.15.1.4.2<-QT.PK.crossover(0.05,0.2,0.8,3,0.5,0.002,1,1,4,5)
Example.15.1.4.2
# 29
```

QT.PK.parallel *Parallel Group Design in QT/QTc Studies with PK response as covariate*

Description

Ho: $\mu_1 - \mu_2 = 0$

Ha: $\mu_1 - \mu_2 = d$

The test is finding the treatment difference in QT interval. d is not equal to 0, which is the difference of clinically importance.

Usage

```
QT.PK.parallel(alpha, beta, pho, K, delta, v1, v2, tau1, tau2)
```

Arguments

alpha	significance level
beta	power = 1-beta
pho	pho=between subject variance σ_s^2/(between subject variance σ_s^2+within subject variance σ_e^2)
K	There are K recording replicates for each subject.
delta	$\sigma^2 = \sigma_s^2 + \sigma_e^2$. d is the difference of clinically importance. $\delta = d/\sigma$
v1	sample mean for group 1
v2	sample mean for group 2
tau1	sample variance for group 1
tau2	sample variance for group 2

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.15.1.4.1<-QT.PK.parallel(0.05,0.2,0.8,3,0.5,1,1,4,5)
Example.15.1.4.1
# 54
```

RelativeRisk.Equality *Relative Risk in Parallel Design test for Equality*

Description

Ho: OR=1

Ha: not equal to 1

Usage

```
RelativeRisk.Equality(alpha, beta, or, k, pt, pc)
```

Arguments

alpha	significance level
beta	power = 1-beta
or	or=pt(1-pc)/pc(1-pt)
k	k=nT/nC
pt	the probability of observing an outcome of interest for a patient treatment by a test treatment
pc	the probability of observing an outcome of interest for a patient treatment by a control

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.4.6.4<-RelativeRisk.Equality(0.05,0.2,2,1,0.4,0.25)
Example.4.6.4
```

RelativeRisk.Equivalence *Relative Risk in Parallel Design test for Equivalence*

Description

Ho: $|log(OR)| \geq margin$

Ha: |log(OR)| < margin

Usage

```
RelativeRisk.Equivalence(alpha, beta, or, k, pt, pc, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
or	or=pt(1-pc)/pc(1-pt)
k	k=nT/nC
pt	the probability of observing an outcome of interest for a patient treatment by a test treatment
pc	the probability of observing an outcome of interest for a patient treatment by a control
margin	the superiority or non-inferiority margin

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.4.6.4<-RelativeRisk.Equivalence(0.05,0.2,2,1,0.25,0.25,.5)
Example.4.6.4
```

RelativeRisk.NIS *Relative Risk in Parallel Design test for Non-inferiority/Superiority*

Description

Ho: $OR \leq margin$

Ha: OR > margin

Usage

```
RelativeRisk.NIS(alpha, beta, or, k, pt, pc, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
or	or=pt(1-pc)/pc(1-pt)
k	k=nT/nC
pt	the probability of observing an outcome of interest for a patient treatment by a test treatment
pc	the probability of observing an outcome of interest for a patient treatment by a control
margin	the superiority or non-inferiority margin

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.4.6.4<-RelativeRisk.NIS(0.05,0.2,2,1,0.4,0.25,.2)
Example.4.6.4
```

RelativeRiskCrossOver.Equality

Relative Risk in Crossover Design test for Equality

Description

Ho: log(OR)=0

Ha: not equal to 0

Usage

```
RelativeRiskCrossOver.Equality(alpha, beta, sigma, or)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma	standard deviation in crossover design
or	or=pt(1-pc)/pc(1-pt)

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

`RelativeRiskCrossOver.Equivalence`
Relative Risk in Crossover Design test for Equivalence

Description

Ho: $|log(OR)| \geq margin$

Ha: |log(OR)| < margin

Usage

```
RelativeRiskCrossOver.Equivalence(alpha, beta, sigma, or, margin)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`sigma`	standard deviation in crossover design
`or`	or=pt(1-pc)/pc(1-pt)
`margin`	the superiority or non-inferiority margin

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

`RelativeRiskCrossOver.NIS`
Relative Risk in Crossover Design test for Non-inferiority/Superiority

Description

Ho: $log(OR) \leq margin$

Ha: log(OR) > margin

Usage

```
RelativeRiskCrossOver.NIS(alpha, beta, sigma, or, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma	standard deviation in crossover design
or	or=pt(1-pc)/pc(1-pt)
margin	the superiority or non-inferiority margin

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Sensitivity.Index *Calculate the power for Sensitivity Index*

Description

Ho: $\mu_1 = \mu_2$

Ha: μ_1 is not equal to μ_2

The test is finding the treatment difference in QT interval.

d is not equal to 0, which is the difference of clinically importance.

Usage

```
Sensitivity.Index(alpha, n, deltaT)
```

Arguments

alpha	significance level
n	sample size n
deltaT	a measure of change in the signal-to-noise ratio for the population difference, which is the sensitivity index of population difference between regions.

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.15.5.1<-Sensitivity.Index(0.05,30,2.92)
Example.15.5.1
# power=0.805
```

Stuart.Maxwell.Test *Stuart-Maxwell Test*

Description

Extention from McNemar test to r by r table (r>2).

Ho: $p_{ij} = p_{ji}$ for all different i,j.

Ha: not equal

The test is finding whether there is a categorical shift from i pre-treatment to j post-treatment.

Usage

```
Stuart.Maxwell.Test(noncen, p.ij, p.ji, r)
```

Arguments

noncen	the solution of the equation, which is non-central parameter of non-central chisquare distribtuion .
p.ij	the probability of shift from i pre-treatment to j post-treatment
p.ji	the probability of shift from j pre-treatment to i post-treatment
r	r by r tables, r is df

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

TwoSampleCrossOver.Equality *Two Sample Crossover Design Test for Equality*

Description

Ho: margin is equal to 0 Ha: margin is unequal to 0

The test is finding whether there is a difference between the mean responses of the test group and control group.

Usage

```
TwoSampleCrossOver.Equality(alpha, beta, sigma, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma	standard deviation in crossover design
margin	$margin = \mu_2 - \mu_1$ the true mean difference between a test mu2 and a control mu1

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

TwoSampleCrossOver.Equivalence

Two Sample Crossover Design Test for Equivalence

Description

Ho: $|margin| \geq delta$ Ha: |margin| < delta

This test is whether the test drug is equivalent to the control in average if the null hypothesis is rejected at significant level alpha

Usage

```
TwoSampleCrossOver.Equivalence(alpha, beta, sigma, delta, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma	standard deviation in crossover design
delta	the superiority or non-inferiority margin
margin	$margin = \mu_2 - \mu_1$ the true mean difference between a test mu2 and a control mu1

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.3.3.4<-TwoSampleCrossOver.Equivalence(0.05,0.1,0.2,0.25,-0.1)
Example.3.3.4 # 8
```

TwoSampleCrossOver.NIS

Two Sample Crossover Design Test for Non-Inferiority/Superiority

Description

Ho: $|margin| \geq delta$ Ha: |margin| < delta

if delta >0, the rejection of Null Hypothesis indicates the superiority of the test over the control;

if delta <0, the rejection of the null hypothesis implies the non-inferiority of the test against the control.

Usage

```
TwoSampleCrossOver.NIS(alpha, beta, sigma, delta, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma	standard deviation in crossover design
delta	the superiority or non-inferiority margin
margin	$margin = \mu_2 - \mu_1$ the true mean difference between a test mu2 and a control mu1

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.3.3.4<-TwoSampleCrossOver.NIS(0.05,0.2,0.2,-0.2,-0.1)
Example.3.3.4 # 13
```

TwoSampleMean.Equality

Two Sample Mean Test for Equality

Description

H0: margin is equal to 0 Ha: margin is unequal to 0

The test is finding whether there is a difference between the mean responses of the test group and control group.

Usage

```
TwoSampleMean.Equality(alpha, beta, sigma, k, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma	pooled standard deviation of two groups
k	k=n1/n2 Example: k=2 indicates a 1 to 2 test-control allocation.
margin	$margin = \mu_2 - \mu_1$ the true mean difference between a test mu2 and a control mu1

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.3.2.4<-TwoSampleMean.Equality(0.05,0.2,0.1,1,0.05)
Example.3.2.4 # 63
```

TwoSampleMean.Equivalence

Two Sample Mean Test for Equivalence

Description

Ho: $|margin| \geq delta$ Ha: |margin| < delta

This test is whether the test drug is equivalent to the control in average if the null hypothesis is rejected at significant level alpha

Usage

```
TwoSampleMean.Equivalence(alpha, beta, sigma, k, delta, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma	pooled standard deviation of two groups
k	k=n1/n2 Example: k=2 indicates a 1 to 2 test-control allocation.

delta	the superiority or non-inferiority margin
margin	$margin = \mu_2 - \mu_1$ the true mean difference between a test mu2 and a control mu1

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.3.2.4<-TwoSampleMean.Equivalence(0.1,0.1,0.1,1,0.05,0.01)
Example.3.2.4 #107
```

TwoSampleMean.NIS *Two Sample Mean Test for Non-Inferiority/Superiority*

Description

Ho: $margin \leq delta$ Ha: margin > delta

if delta >0, the rejection of Null Hypothesis indicates the superiority of the test over the control;

if delta <0, the rejection of the null hypothesis implies the non-inferiority of the test against the control.

Usage

```
TwoSampleMean.NIS(alpha, beta, sigma, k, delta, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma	pooled standard deviation of two groups
k	k=n1/n2 Example: k=2 indicates a 1 to 2 test-control allocation.
delta	the superiority or non-inferiority margin
margin	$margin = \mu_2 - \mu_1$ the true mean difference between a test mu2 and a control mu1

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.3.2.4<-TwoSampleMean.NIS(0.05,0.2,0.1,1,-0.05,0)
Example.3.2.4 # 50
```

`TwoSampleProportion.Equality`
Two sample proportion test for equality

Description

H0: p1=p2

Ha: not equal

The test is finding whether there is a difference between the mean response rates of the test drug and reference drug

Usage

```
TwoSampleProportion.Equality(alpha, beta, p1, p2, k)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`p1`	the mean response rate for test drug
`p2`	the rate for reference drug
`k`	k=n1/n2

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.4.2.4<-TwoSampleProportion.Equality(0.05,0.2,0.65,0.85,1)
Example.4.2.4
```

`TwoSampleProportion.Equivalence` *Two sample proportion test for equivalence*

Description

Ho: $|p1 - p2| \geq margin$

Ha: |p1-p2| < margin

The proportion of response p1 is equivalent to the reference drug p2 is the null hypothesis is rejected

Usage

```
TwoSampleProportion.Equivalence(alpha, beta, p1, p2, k, delta, margin)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`p1`	the mean response rate for test drug
`p2`	the rate for reference drug
`k`	k=n1/n2
`delta`	delta=p1-p2
`margin`	the superiority or non-inferiority margin

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.4.2.4<-TwoSampleProportion.Equivalence(0.05,0.2,0.75,0.8,1,0.2,0.05)
Example.4.2.4
```

`TwoSampleProportion.NIS` *Two sample proportion test for Non-Inferiority/Superiority*

Description

Ho: $p1 - p2 \leq margin$ Ha: p1-p2 > margin

if margin >0, the rejection of Null Hypothesis indicates the true rate p1 is superior over the reference value p2;

if margin <0, the rejection of the null hypothesis implies the true rate p1 is non-inferior against the reference value p2.

Usage

```
TwoSampleProportion.NIS(alpha, beta, p1, p2, k, delta, margin)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`p1`	the mean response rate for test drug
`p2`	the rate for reference drug
`k`	k=n1/n2
`delta`	delta=p1-p2
`margin`	the superiority or non-inferiority margin

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.4.2.4<-TwoSampleProportion.NIS(0.05,0.2,0.65,0.85,1,0.2,0.05)
Example.4.2.4
```

TwoSampleSeqCrossOver.Equality

Two sample proportion Crossover design test for equality

Description

H0: p2-p1 = 0 Ha: not equal to 0

Usage

```
TwoSampleSeqCrossOver.Equality(alpha, beta, sigma, sequence, delta)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma	standard deviation in crossover design
sequence	total sequence number
delta	delta=p2-p1

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.4.3.4<-TwoSampleSeqCrossOver.Equality(0.05,0.2,0.25,2,0.2)
Example.4.3.4
```

TwoSampleSeqCrossOver.Equivalence

Two sample proportion Crossover design test for equivalence

Description

Ho: $|p1 - p2| \geq margin$

Ha: |p1-p2| < margin

Usage

```
TwoSampleSeqCrossOver.Equivalence(alpha, beta, sigma, sequence, delta, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma	standard deviation in crossover design
sequence	total sequence number
delta	the superiority or non-inferiority margin
margin	margin=p2-p1

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.4.3.4<-TwoSampleSeqCrossOver.Equivalence(0.05,0.2,0.25,2,0,0.2)
Example.4.3.4
```

TwoSampleSeqCrossOver.NIS

Two sample proportion Crossover design for Non-inferiority/Superiority

---

Description

H0: p2-p1 <= margin

Ha: p2-p1 > margin

Usage

```
TwoSampleSeqCrossOver.NIS(alpha, beta, sigma, sequence, delta, margin)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma	standard deviation in crossover design
sequence	total sequence number
delta	the superiority or non-inferiority margin
margin	margin=p2-p1

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.4.3.4<-TwoSampleSeqCrossOver.NIS(0.05,0.2,0.25,2,0,-0.2)
Example.4.3.4
```

TwoSampleSurvival.Conditional

Test for two sample conditional data in exponential model for survival data

---

Description

unconditional versus conditional

Usage

```
TwoSampleSurvival.Conditional(alpha,beta,lam1,lam2,eta1,eta2,k,ttotal,taccrual,g1,g2)
```

Arguments

alpha	significance level
beta	power = 1-beta
lam1	the hazard rates of control group
lam2	the hazard rates of a test drug
eta1	in control group, the losses are exponentially distributed with loss hazard rate eta1
eta2	in treatment group, the losses are exponentially distributed with loss hazard rate eta2
k	k=n1/n2 sample size ratio
ttotal	Total trial time
taccrual	accrual time period
g1	parameter for the entry distribution of control group, which is uniform patient entry with gamma1=0.
g2	parameter for the entry distribution of treatment group, which is uniform patient entry with gamma2=0.

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

`TwoSampleSurvival.Equality` *Test for two sample equality in exponential model for survival data*

Description

H0: the difference between the hazard rates of two samples is equal to

Ha: not equal to 0

The test is finding whether there is a difference between the hazard rates of the test drug and the reference drug.

Usage

```
TwoSampleSurvival.Equality(alpha, beta, lam1, lam2, k, ttotal, taccrual, gamma)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`lam1`	the hazard rates of control group
`lam2`	the hazard rates of a test drug
`k`	k=n1/n2 sample size ratio
`ttotal`	Total trial time
`taccrual`	accrual time period
`gamma`	parameter for exponential distribution. Assume Uniform patient entry if gamma =0

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.7.2.4<-TwoSampleSurvival.Equality(0.05,0.2,1,2,1,3,1,0.00001)
Example.7.2.4
```

`TwoSampleSurvival.Equivalence` *Test for two sample equivalence in exponential model for survival data*

Description

margin=lamda1-lamda2, the true difference of hazard rates between control group lamda1 and a test drug group lamda2

H0: |margin| >= delta

Ha: |margin| < delta

This test is whether the test drug is equivalent to the control in average if the null hypothesis is rejected at significant level alpha

Usage

```
TwoSampleSurvival.Equivalence(alpha, beta, lam1, lam2, k, ttotal, taccrual, gamma, margin)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`lam1`	the hazard rates of control group
`lam2`	the hazard rates of a test drug
`k`	k=n1/n2 sample size ratio
`ttotal`	Total trial time
`taccrual`	accrual time period
`gamma`	parameter for exponential distribution. Assume Uniform patient entry if gamma =0
`margin`	margin=lamda1-lamda2, the true difference of hazard rates between control group lamda1 and a test drug group lamda2

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.7.2.4<-TwoSampleSurvival.Equivalence(0.05,0.2,1,1,1,3,1,0.00001,0.5)
Example.7.2.4
```

`TwoSampleSurvival.NIS` *Test for two sample Non-Inferiority/Superiority in exponential model for survival data*

Description

margin=lamda1-lamda2, the true difference of hazard rates between control group lamda1 and a test drug group lamda2

H0: margin <= delta

Ha: margin > delta

if delta >0, the rejection of Null Hypothesis indicates the superiority of the test drug over the control;

if delta <0, the rejection of the null hypothesis implies the non-inferiority of the test test drug against the control.

Usage

```
TwoSampleSurvival.NIS(alpha, beta, lam1, lam2, k, ttotal, taccrual, gamma,margin)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`lam1`	the hazard rates of control group
`lam2`	the hazard rates of a test drug
`k`	k=n1/n2 sample size ratio
`ttotal`	Total trial time
`taccrual`	accrual time period
`gamma`	parameter for exponential distribution. Assume Uniform patient entry if gamma =0
`margin`	margin=lamda1-lamda2, the true difference of hazard rates between control group lamda1 and a test drug group lamda2

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.7.2.4<-TwoSampleSurvival.NIS(0.05,0.2,1,2,1,3,1,0.00001,0.2)
Example.7.2.4
```

`TwoSide.fixEffect` *Two-Sided Tests with fixed effect sizes*

Description

Two-sided tests

Ho: $\delta_j = 0$

Ha: δ_j is not equal to 0

Usage

```
TwoSide.fixEffect(m, m1, delta, a1, r1, fdr)
```

Arguments

`m`	m is the total number of multiple tests
`m1`	m1 = m - m0. m0 is the number of tests which the null hypotheses are true ; m1 is the number of tests which the alternative hypotheses are true. (or m1 is the number of prognostic genes)
`delta`	δ_j is the constant effect size for jth test. $\delta_j = (E(Xj) - E(Yj))/\sigma_j$. $X_{ij}(Y_{ij})$ denote the expression level of gene j for subject i in group 1(and group 2, respectively) with common variance σ_j^2. We assume $\delta_j = 0,\ j\ in\ M0$ and $\delta_j > 0,\ j\ in\ M1$=effect size for prognostic genes.
`a1`	a1 is the allocation proportion for group 1. a2=1-a1.
`r1`	r1 is the number of true rejection
`fdr`	fdr is the FDR level.

Details

alpha_star=r1*fdr/((m-m1)*(1-fdr)), which is the marginal type I error level for r1 true rejection with the FDR controlled at f.

beta_star=1-r1/m1, which is equal to 1-power.

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.12.2.3<-TwoSide.fixEffect(m=4000,m1=40,delta=1,a1=0.5,r1=24,fdr=0.01)
Example.12.2.3
# n=73
```

`TwoSide.varyEffect` *Two-Sided Tests with varying effect sizes*

Description

Two-sided tests

Ho: $\delta_j = 0$

Ha: δ_j is not equal to 0

Usage

```
TwoSide.varyEffect(s1, s2, m, m1, delta, a1, r1, fdr)
```

Arguments

`s1`	We use bisection method to find the sample size, which let the equation h(n)=0. Here s1 and s2 are the initial value, 0<s1<s2. h(s1) should be smaller than 0.
`s2`	s2 is also the initial value, which is larger than s1 and h(s2) should be larger than 0.
`m`	m is the total number of multiple tests
`m1`	m1 = m - m0. m0 is the number of tests which the null hypotheses are true ; m1 is the number of tests which the alternative hypotheses are true. (or m1 is the number of prognostic genes)
`delta`	δ_j is the constant effect size for jth test. $\delta_j = (E(Xj) - E(Yj))/\sigma_j$. $X_{ij}(Y_{ij})$ denote the expression level of gene j for subject i in group 1(and group 2, respectively) with common variance σ_j^2. We assume $\delta_j = 0,\ j\ in\ M0$ and $\delta_j > 0,\ j\ in\ M1$=effect size for prognostic genes.
`a1`	a1 is the allocation proportion for group 1. a2=1-a1.
`r1`	r1 is the number of true rejection
`fdr`	fdr is the FDR level.

Details

alpha_star=r1*fdr/((m-m1)*(1-fdr)), which is the marginal type I error level for r1 true rejection with the FDR controlled at f.

beta_star=1-r1/m1, which is equal to 1-power.

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
delta=c(rep(1,40/2),rep(1/2,40/2));
Example.12.2.4<-TwoSide.varyEffect(s1=100,s2=200,m=4000,m1=40,delta=delta,a1=0.5,r1=24,fdr=0.01)
Example.12.2.4
# n=164 s1<n<s2, h(s1)<0,h(s2)<0
```

`Vaccine.CEM` *Composite Efficacy Measure(CEM) for Vaccine clinical trials.*

Description

Let sij be the severity score associated with the jth case in the ith treatment group. $\mu_i = mean(s_{ij})$, $\sigma_i^2 = var(s_{ij})$.

H0: pT=pC and muT=muC

Ha: pT is not equal to pC and muT is not equal to muC

Usage

```
Vaccine.CEM(alpha, beta, mu_t, mu_c, sigma_t, sigma_c, pt, pc)
```

Arguments

`alpha`	significance level
`beta`	power=1-beta
`mu_t`	mean of treatment group
`mu_c`	mean of control group
`sigma_t`	standard deviation of treatment group
`sigma_c`	standard deviation of control group
`pt`	the true disease incidence rates of the nt vaccines
`pc`	the true disease incidence rates of the nc controls

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.15.6.4<-Vaccine.CEM(0.05,0.2,0.2,0.3,sqrt(0.15),sqrt(0.15),0.1,0.2)
Example.15.6.4
```

Vaccine.ELDI *The evaluation of vaccine efficacy with Extremely Low Disease Incidence(ELDI)*

Description

If the disease incidence rate is extremely low, the number of cases in the vaccine group given the total number of cases is distributed as a binomial random variable with parameter theta.

Ho: $\theta \geq \theta_0$

Ha: $\theta < \theta_0$

Usage

```
Vaccine.ELDI(alpha, beta, theta0, theta, pt, pc)
```

Arguments

alpha	significance level
beta	power=1-beta
theta0	the true parameter for binomial distribution. Theta0 is usually equal to 0.5
theta	theta=disease rate for treatment group/(disease rate for treatment group + for control group)
pt	the true disease incidence rates of the nt vaccines
pc	the true disease incidence rates of the nc controls

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.15.6.2<-Vaccine.ELDI(0.05,0.2,0.5,1/3,0.001,0.002)
Example.15.6.2
# 17837
```

Vaccine.RDI *Reduction in Disease Incidence(RDI) for Vaccine clinical trials.*

Description

The test is to find whether the vaccine can prevent the disease or reduce the incidence of the disease in the target population. Usually use prospective, randomized, placebo-controlled trials.

Usage

```
Vaccine.RDI(alpha, d, pt, pc)
```

Arguments

alpha	significance level
d	the half length of the confidence interval of pt/pc
pt	the true disease incidence rates of the nt vaccines
pc	the true disease incidence rates of the nc controls

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.15.6.1<-Vaccine.RDI(0.05,0.2,0.01,0.02)
Example.15.6.1
# 14214
```

Vitro.BE *In Vitro Bioequivalence*

Description

Consider 2 by 2 crossover design. $\zeta = \delta^2 + sT^2 + sR^2 - thetaBE * max(\sigma_0^2, sR^2)$. $sT^2 = \sigma_{BT}^2 + \sigma_{WT}^2$, $sR^2 = \sigma_{BR}^2 + \sigma_{WR}^2$

Ho: $\zeta \geq 0$

Ha: $\zeta < 0$

Usage

```
Vitro.BE(alpha, beta, delta, sigmaBT, sigmaBR, sigmaWT, sigmaWR, thetaBE)
```

Arguments

alpha	significance level
beta	power = 1-beta
delta	delta is the mean difference
sigmaBT	σ^2_{BT} is the between-subjects variance in test formulation
sigmaBR	σ^2_{BR} is the between-subjects variance in reference formulation
sigmaWT	σ^2_{WT} is the within-subjects variance in test formulation
sigmaWR	σ^2_{WR} is the within-subjects variance in reference formulation
thetaBE	here thetaBE=1

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.10.5<-Vitro.BE(0.05,0.2,0,0.5,0.5,0.5,0.5,1)
Example.10.5

# n=43 Vitro.BE reach 0
```

WilliamsDesign.Equality

William Design test for equality

Description

Ho: $\mu_1 - \mu_2 = 0$

Ha: not equal to 0

Usage

```
WilliamsDesign.Equality(alpha, beta, sigma, sequence, delta)
```

Arguments

alpha	significance level
beta	power = 1-beta
sigma	standard deviation in crossover design
sequence	total sequence number
delta	delta=$\mu_1 - \mu_2$

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.4.5.4<-WilliamsDesign.Equality(0.05,0.2,0.75^2,6,0.2)
Example.4.5.4
```

`WilliamsDesign.Equivalence`

Williams Design test for equivalence

Description

Ho: $|\mu_2 - \mu_1| \geq margin$

Ha: $|\mu_2 - \mu_1| < margin$

Usage

```
WilliamsDesign.Equivalence(alpha, beta, sigma, sequence, delta, margin)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`sigma`	standard deviation in crossover design
`sequence`	total sequence number
`delta`	the superiority or non-inferiority margin
`margin`	margin=$\mu_1 - \mu_2$

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.4.5.4<-WilliamsDesign.Equivalence(0.05,0.2,0.75^2,6,0.2,0.3)
Example.4.5.4
```

`WilliamsDesign.NIS` *Williams Design test for Non-inferiority/Superiority*

Description

H0: $\mu_1 - \mu_2 \leq margin$

Ha: $\mu_1 - \mu_2 > margin$

Usage

```
WilliamsDesign.NIS(alpha, beta, sigma, sequence, delta, margin)
```

Arguments

`alpha`	significance level
`beta`	power = 1-beta
`sigma`	standard deviation in crossover design
`sequence`	total sequence number
`delta`	the superiority or non-inferiority margin
`margin`	margin=$\mu_1 - \mu_2$

References

Chow SC, Shao J, Wang H. Sample Size Calculation in Clinical Research. New York: Marcel Dekker, 2003

Examples

```
Example.4.5.4<-WilliamsDesign.NIS(0.05,0.2,0.75^2,6,0.2,0.05)
Example.4.5.4
```

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