

Package ‘TrialSize’

October 12, 2022

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

Date 2020-07-01

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

License GPL (>= 2.15.1)

LazyLoad yes

NeedsCompilation yes

Repository CRAN

Date/Publication 2020-07-06 21:40:03 UTC

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TrialSize-package	<i>Sample Size calculation in Clinical Research</i>
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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 B more 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: $F_t - F_r \leq \delta_L$ or $F_t - F_r \leq \delta_U$

Ha: $\delta_L < F_t - F_r < \delta_U$

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

$$\sigma_{a,b}^2 = \sigma_D^2 + a * \sigma_{WT}^2 + b * \sigma_{WR}^2$$

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 i th 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: $p_0=p_1=p_2=\dots=p_K$

Ha: $p_0 \leq p_1 \leq p_2 \leq \dots \leq p_K$ with $p_0 < p_K$

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= $\log(\lambda_2/\lambda_1)=b$
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= $\log(\lambda_2/\lambda_1)=b$
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 λ_1 and a test drug group λ_2

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: $b > \delta$

Usage

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

Arguments

alpha	significance level
beta	power = 1-beta
loghr	log hazard ratio= $\log(\lambda_2/\lambda_1)=b$
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 λ_1 and a test drug group λ_2

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: $\frac{1}{\delta} < \text{the ratio} < \delta$

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	<i>Test for Non-Inferiority/Superiority of Intra-Subject Variability in Crossover Design</i>
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Description

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

Ha: the ratio $< \delta$

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

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
```

Description

p_i is the proportion of response in the i th group.

Ho: $p_1=p_2=\dots=p_k$

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

Usage

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

Arguments

alpha	significance level
beta	power = 1-beta
pi	p_i is the proportion of response in the i th group.
ci	a linear contrast coefficients c_i with $\sum c_i = 0$.
fi	$f_i=n_i/n$ is the sample size fraction for the i th 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 c_i with $\sum c_i = 0$.

$$H_0: L(\mu) = \sum c_i \times \mu_i = 0$$

$$H_a: L(\mu) = \sum c_i \times \mu_i = \epsilon, \text{ not equal to } 0$$

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 c_i with $\sum c_i = 0$.
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 λ_i be the proportion hazard rate for group i .

$$\sum c_i = 0.$$

$$H_0: L(\mu) = \sum c_i \times \lambda_i = 0$$

$$H_a: L(p) = \sum c_i \times \lambda_i = \epsilon > 0$$

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	$\lambda_i = \log(2)/T_i$, T_i is the estimated median time for each group.
ci	a linear contrast coefficients c_i with $\sum(c_i)=0$.
fi	$f_i=n_i/n$ is the sample size fraction for the i th 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. $p_k = nk/n$, n_k is the frequency count of the subjects with response value k . $p_{k,0}$ is a reference value.

H_0 : $p_k = p_{k,0}$ for all k

H_a : not equal

Usage

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

Arguments

alpha	significance level
beta	power = 1-beta
pk	p_k is the proportion of each subject in treatment group.
pk0	$p_{k,0}$ 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: $p_k = p_{k,0}$ 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. $\gamma = \delta^2 + \sigma_D^2 + \sigma_{WT}^2 - \sigma_{WR}^2 - \theta_{IBE} * \max(\sigma_0^2, \sigma_{WR}^2)$

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	$\sigma_D^2 = \sigma_{BT}^2 + \sigma_{BR}^2 - 2\rho\sigma_{BT}\sigma_{BR}$, σ_{BT}^2 is the between-subjects variance in test formulation, σ_{BR}^2 is the between-subjects variance in reference formulation
sigmaWT	σ_{WT}^2 is the within-subjects variance in test formulation
sigmaWR	σ_{WR}^2 is the within-subjects variance in reference formulation
a	$\Sigma(a,b) = \sigma_D^2 + a\sigma_{WT}^2 + b\sigma_{WR}^2$ 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 σ_1/σ_2

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: $CV_r = CV_t$

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: $|CV_r - CV_t| \geq \delta$

Ha: $|CV_r - CV_t| < \delta$

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: $CVr - CVt < \delta$

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: $\frac{1}{\delta} < \text{the ratio} < \delta$

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 $< \delta$

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: $|\text{margin}| \geq \delta$ Ha: $|\text{margin}| < \delta$

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

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	$\text{margin} = \mu_i - \mu_j$ 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: $\text{margin} \leq \delta$ Ha: $\text{margin} > \delta$

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

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 $\delta_j = delta, j = 1, \dots, D$ and $\delta_j = 0, j = D + 1, \dots, m$.
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).

rho	rho is the correlation parameter. If j and j' in the same block, $\rho_{jj'} = rho$; 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: $P(x \leq a \text{ and } y \leq b) = P(x \leq a)P(y \leq b)$ 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: θ is not equal to 0.

Usage

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

Arguments

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

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: θ 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	$p2 = P(y_i \geq x_{j1} \text{ and } y_i \geq x_{j2})$
p3	$p3 = P(y_{i1} \geq x_j \text{ and } y_{i2} \geq x_j)$

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 μ_0 ;

if $\delta < 0$, the rejection of the null hypothesis implies the true mean is non-inferior against the reference value μ_0 .

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: $p=p_0$

Ha: not equal

The test is finding whether there is a difference between the true rate of the test drug and reference value p_0

Usage

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

Arguments

alpha	significance level
beta	power = 1-beta
p	the true response rate
differ	differ= $p-p_0$ the difference between the true response rate of a test drug and a reference value p_0

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: $|p - p_0| \geq margin$

Ha: $|p-p_0| < margin$

The proportion of response is equivalent to the reference p_0 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: $p - p_0 \leq \text{margin}$

Ha: $p - p_0 > \text{margin}$

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. $\delta_j = (E(X_j) - E(Y_j))/\sigma_j$. $X_{ij}(Y_{ij})$ 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 $\delta_j = 0, j \text{ in } M0$ and $\delta_j > 0, j \text{ in } M1$ =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. $\delta_j = (E(X_j) - E(Y_j))/\sigma_j$. $X_{ij}(Y_{ij})$ 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

$\alpha_{\text{star}} = r1 * \text{fdr} / ((m-1) * (1-\text{fdr}))$, which is the marginal type I error level for r1 true rejection with the FDR controlled at f.

$\beta_{\text{star}} = 1 - r1/m1$, 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 $\text{margin} = \mu_i - \mu_j$
 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	$\text{delta} = p_i - p_j$

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

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	$\sigma_{a.b}^2 = \sigma_D^2 + a\sigma_{WT}^2 + b\sigma_{WR}^2$. Here a=b=1.
sigmatt	$\sigma_{tt}^2 = \sigma_{BT}^2 + \sigma_{WT}^2$, σ_{wt}^2 is the within-subjects variance in test formulation
sigmatr	$\sigma_{tr}^2 = \sigma_{BR}^2 + \sigma_{WR}^2$, σ_{wr}^2 is the within-subjects variance in reference formulation
sigmabt	σ_{bt}^2 is the between-subjects variance in test formulation
sigmabr	σ_{br}^2 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	$lamda = delta^2 + \sigma^2 - \sigma_{TR}^2 - thetaPBE * max(\sigma_0^2, \sigma_{TR}^2)$

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	$a=c(a_1, a_2, \dots, a_J)$, $a_j=n_j/n$ denote the allocation proportion for stratum j ($\sum(a_j)=1$)
b	$b=c(b_{11}, b_{21}, \dots, b_{J1})$, $b_{jk}=n_{jk}/n_j$, $k=1,2$ denote the allocation proportion for group k within stratum j ($b_{j1}+b_{j2}=1$). Assume group 1 is the control.
p1	$p1=c(p_{11}, p_{21}, \dots, p_{J1})$, p_{jk} denote the response probability for group k in stratum j. $q_{jk}=1-p_{jk}$.
phi	$p_{j2}q_{j1}/(p_{j1}q_{j2})=\phi$, so that $p_{j2} = \phi p_{j1}/(q_{j1} + \phi p_{j1})$

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	$a=c(a_1,a_2,\dots,a_J)$, $a_j=n_j/n$ denote the allocation proportion for stratum j ($\sum(a_j)=1$)
b	$b=c(b_{11},b_{21},\dots,b_{J1})$, $b_{jk}=n_{jk}/n_j$, $k=1,2$ denote the allocation proportion for group k within stratum j ($b_{j1}+b_{j2}=1$). Assume group 1 is the control.
p1	$p_1=c(p_{11},p_{21},\dots,p_{J1})$, p_{jk} denote the response probability for group k in stratum j. $q_{jk}=1-p_{jk}$.
phi	$p_{j2}q_{j1}/(p_{j1}q_{j2})=\phi$, so that $p_{j2} = \phi p_{j1}/(q_{j1} + \phi p_{j1})$

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	<i>Parallel Group Design in QT/QTc Studies with PK response as covariate</i>
----------------	--

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	$or = \frac{pt(1-pc)}{pc(1-pt)}$
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: $|\log(OR)| \geq \text{margin}$

Ha: $|\log(OR)| < \text{margin}$

Usage

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

Arguments

alpha	significance level
beta	power = 1-beta
sigma	standard deviation in crossover design
or	$\text{or} = \text{pt}(1-\text{pc})/\text{pc}(1-\text{pt})$
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: $\log(OR) \leq \text{margin}$

Ha: $\log(OR) > \text{margin}$

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 μ_2 and a control μ_1

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 μ_2 and a control μ_1

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

$H_0: |margin| \geq \delta$ $H_a: |margin| < \delta$

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 μ_2 and a control μ_1

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

$H_0: \text{margin is equal to } 0$ $H_a: \text{margin is unequal to } 0$

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 μ_2 and a control μ_1

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 μ_2 and a control μ_1

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 μ_2 and a control μ_1

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: $p_1=p_2$

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	$k=n_1/n_2$

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*

DescriptionHo: $|p_1 - p_2| \geq \text{margin}$ Ha: $|p_1 - p_2| < \text{margin}$ The proportion of response p_1 is equivalent to the reference drug p_2 if the null hypothesis is rejected**Usage**`TwoSampleProportion.Equivalence(alpha, beta, p1, p2, k, delta, margin)`**Arguments**

<code>alpha</code>	significance level
<code>beta</code>	power = 1-beta
<code>p1</code>	the mean response rate for test drug
<code>p2</code>	the rate for reference drug
<code>k</code>	$k = n_1/n_2$
<code>delta</code>	$\text{delta} = p_1 - p_2$
<code>margin</code>	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: $p_1 - p_2 \leq \text{margin}$ Ha: $p_1 - p_2 > \text{margin}$

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	$k = n_1/n_2$
delta	$\text{delta} = p_1 - p_2$
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: $p_2 - p_1 = 0$ 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= $p_2 - p_1$

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: $|p_1 - p_2| \geq margin$

Ha: $|p_1 - p_2| < margin$

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: $p_2 - p_1 \leq \text{margin}$

Ha: $p_2 - p_1 > \text{margin}$

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= $\lambda_1 - \lambda_2$, the true difference of hazard rates between control group λ_1 and a test drug group λ_2

H0: $|\text{margin}| \geq \delta$

Ha: $|\text{margin}| < \delta$

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

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	$k = n_1/n_2$ 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= $\lambda_1 - \lambda_2$, the true difference of hazard rates between control group λ_1 and a test drug group λ_2

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= $\lambda_1 - \lambda_2$, the true difference of hazard rates between control group λ_1 and a test drug group λ_2

H0: margin \leq 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	$k = n_1/n_2$ 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= $\lambda_1 - \lambda_2$, the true difference of hazard rates between control group λ_1 and a test drug group λ_2

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. $\delta_j = (E(X_j) - E(Y_j))/\sigma_j$. $X_{ij}(Y_{ij})$ 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. $\delta_j = (E(X_j) - E(Y_j))/\sigma_j$. $X_{ij}(Y_{ij})$ 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 s_{ij} be the severity score associated with the j th case in the i th treatment group. $\mu_i = \text{mean}(s_{ij})$, $\sigma_i^2 = \text{var}(s_{ij})$.

H0: $p_T = p_C$ and $\mu_T = \mu_C$

Ha: p_T is not equal to p_C and μ_T is not equal to μ_C

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	<i>The evaluation of vaccine efficacy with Extremely Low Disease Incidence(ELDI)</i>
--------------	--

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

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_{BT}^2 is the between-subjects variance in test formulation
sigmaBR	σ_{BR}^2 is the between-subjects variance in reference formulation
sigmaWT	σ_{WT}^2 is the within-subjects variance in test formulation
sigmaWR	σ_{WR}^2 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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