Package ‘TrialSize’

July 6, 2020

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

Author Ed Zhang ; Vicky Qian Wu ; Shein-Chung Chow ; Harry G.Zhang
(Quality check) <ed.zhang.jr@gmail.com>

Maintainer Vicky Qian Wu <wuqian7@gmail.com>

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

R topics documented:

TrialSize-package ......................................................... 3
AB.withDescalation .................................................... 4
AB.withoutDescalation .................................................. 5
ABE ........................................................................ 6
ANOV A.Repeat.Measure .................................................. 7
Carry.Over ................................................................. 8
Cochran.Armitage.Trend .................................................. 8
Cox.Equality ............................................................... 9
Cox.Equivalence .......................................................... 10
Cox.NIS .................................................................... 11
CrossOver.ISV.Equality .................................................. 12
CrossOver.ISV.Equivalence ............................................. 12
CrossOver.ISV.NIS ...................................................... 13
Dose.Min.Effect .......................................................... 14
Dose.Response.binary ................................................... 15
<table>
<thead>
<tr>
<th>R topics documented:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose.Response.Linear</td>
<td>16</td>
</tr>
<tr>
<td>Dose.Response.time.to.event</td>
<td>17</td>
</tr>
<tr>
<td>gof.Pearson</td>
<td>18</td>
</tr>
<tr>
<td>gof.Pearson.twoway</td>
<td>19</td>
</tr>
<tr>
<td>IBE</td>
<td>19</td>
</tr>
<tr>
<td>InterSV.Equality</td>
<td>20</td>
</tr>
<tr>
<td>InterSV.NIS</td>
<td>21</td>
</tr>
<tr>
<td>ISCV.Equality</td>
<td>22</td>
</tr>
<tr>
<td>ISCV.Equivalence</td>
<td>22</td>
</tr>
<tr>
<td>ISCV.NIS</td>
<td>23</td>
</tr>
<tr>
<td>ISV.Equality</td>
<td>24</td>
</tr>
<tr>
<td>ISV.Equivalence</td>
<td>24</td>
</tr>
<tr>
<td>ISV.NIS</td>
<td>25</td>
</tr>
<tr>
<td>McNemar.Test</td>
<td>26</td>
</tr>
<tr>
<td>MeanWilliamsDesign.Equality</td>
<td>27</td>
</tr>
<tr>
<td>MeanWilliamsDesign.Equivalence</td>
<td>28</td>
</tr>
<tr>
<td>MeanWilliamsDesign.NIS</td>
<td>28</td>
</tr>
<tr>
<td>Multiple.Testing</td>
<td>29</td>
</tr>
<tr>
<td>Nonpara.Independ</td>
<td>30</td>
</tr>
<tr>
<td>Nonpara.One.Sample</td>
<td>31</td>
</tr>
<tr>
<td>Nonpara.Two.Sample</td>
<td>31</td>
</tr>
<tr>
<td>OneSampleMean.Equality</td>
<td>32</td>
</tr>
<tr>
<td>OneSampleMean.Equivalence</td>
<td>33</td>
</tr>
<tr>
<td>OneSampleMean.NIS</td>
<td>34</td>
</tr>
<tr>
<td>OneSampleProportion.Equality</td>
<td>35</td>
</tr>
<tr>
<td>OneSampleProportion.Equivalence</td>
<td>35</td>
</tr>
<tr>
<td>OneSampleProportion.NIS</td>
<td>36</td>
</tr>
<tr>
<td>OneSide.fixEffect</td>
<td>37</td>
</tr>
<tr>
<td>OneSide.varyEffect</td>
<td>38</td>
</tr>
<tr>
<td>OneWayANOVA.pairwise</td>
<td>39</td>
</tr>
<tr>
<td>OneWayANOVA.PairwiseComparison</td>
<td>40</td>
</tr>
<tr>
<td>PBE</td>
<td>41</td>
</tr>
<tr>
<td>Propensity.Score.nostrata</td>
<td>42</td>
</tr>
<tr>
<td>Propensity.Score.strata</td>
<td>43</td>
</tr>
<tr>
<td>QOL</td>
<td>44</td>
</tr>
<tr>
<td>QT.crossover</td>
<td>44</td>
</tr>
<tr>
<td>QT.parallel</td>
<td>45</td>
</tr>
<tr>
<td>QT.PK.crossover</td>
<td>46</td>
</tr>
<tr>
<td>QT.PK.parallel</td>
<td>47</td>
</tr>
<tr>
<td>RelativeRisk.Equality</td>
<td>48</td>
</tr>
<tr>
<td>RelativeRisk.Equivalence</td>
<td>48</td>
</tr>
<tr>
<td>RelativeRisk.NIS</td>
<td>49</td>
</tr>
<tr>
<td>RelativeRiskCrossOver.Equality</td>
<td>50</td>
</tr>
<tr>
<td>RelativeRiskCrossOver.Equivalence</td>
<td>51</td>
</tr>
<tr>
<td>RelativeRiskCrossOver.NIS</td>
<td>51</td>
</tr>
<tr>
<td>Sensitivity.Index</td>
<td>52</td>
</tr>
<tr>
<td>Stuart.Maxwell.Test</td>
<td>53</td>
</tr>
<tr>
<td>TwoSampleCrossOver.Equality</td>
<td>53</td>
</tr>
</tbody>
</table>
**TrialSize-package**

**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
AB.withDescalation

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 ≥ 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 ≥ 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 ≥ C
E number of patients for the third cut off D, E ≥ 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


Examples

```r
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 ≥ 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 ≥ 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

```r
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 ≥ C
- E: number of patients for the third cut off D, E ≥ D
- DLT: dose limiting toxicity rate for each dose level.
References


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. \(F_t\) is the fixed effect of the test formulation and \(F_r\) 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**

\[
\text{ABE}(\alpha, \beta, \sigma_{1.1}, \delta, \epsilon)
\]

**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 = \(F_t - F_r\)

**Value**

\[
\sigma_{a,b}^2 = \sigma_D^2 + a \ast \sigma_{WT}^2 + b \ast \sigma_{WR}^2
\]

**References**

ANOVA.Repeat.Measure

Examples

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

Description

The study has multiple assessments in a parallel-group clinical trial. $\alpha_i$ 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


Examples

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

**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**

```r
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**


**Examples**

```r
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
Cox.Equality

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


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)
Cox.Equivalence

Arguments

- **alpha**: significance level
- **beta**: power = 1-beta
- **loghr**: log hazard ratio = \log(\text{lambda}_2/\text{lambda}_1) = b
- **p1**: the proportion of patients in treatment 1 group
- **d**: the probability of observing an event

References


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| ≥ δ
- Ha: |b| < δ

Usage

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

Arguments

- **alpha**: significance level
- **beta**: power = 1-beta
- **loghr**: log hazard ratio = \log(\text{lambda}_2/\text{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 \text{lambda}_1 and a test drug group \text{lambda}_2

References

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 ≤ δ
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


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


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)
CrossOver.ISV.NIS

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


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 ≥ δ
Ha: the ratio < δ
if δ < 1, the rejection of Null Hypothesis indicates the superiority of the test drug over the reference for the intra-subject variability;
if δ > 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

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  \( \delta \) is the clinically meaningful minimal difference

References


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 \( i \)th group.

\( H_0: p_1=p_2=...=p_k \)

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

Usage

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

Arguments

\( \alpha \)  
significance level

\( \beta \)  
power = 1-\( \beta \)

\( \pi \)  
\( \pi \) is the proportion of response in the \( i \)th group.

\( c_i \)  
a linear contrast coefficients \( c_i \) with \( \sum c_i = 0 \).

\( f_i \)  
\( f_i=n_i/n \) is the sample size fraction for the \( i \)th group

References


Examples

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

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

\[
\text{Dose.Response.Linear}(\alpha, \beta, \sigma, mui, ci, fi)
\]

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 \( i \)th group

References


Examples

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

\[
\text{Example.11.1} <- \text{Dose.Response.Linear}(\alpha = 0.05, \beta = 0.2, \sigma = 0.22, mui = mui, ci = ci, fi = 1/4)
\]

\[
\text{Example.11.1}
\]

#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 \( \lambda_i \) be the proportion hazard rate for group i.
\[ \sum c_i = 0. \]

**Ho:** \( L(\mu) = \sum c_i \times \lambda_i = 0 \)

**Ha:** \( L(p) = \sum c_i \times \lambda_i = \epsilon > 0 \)

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**  
  \( \lambda_i = \frac{\log(2)}{Ti} \), Ti is the estimated median time for each group.
- **ci**  
  a linear contrast coefficients ci with sum(ci)=0.
- **fi**  
  fi=n_i/n is the sample size fraction for the ith group

References


Examples

```r
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
```
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

---

**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.

\( H_0: pk=pk,0 \) for all \( k \)

\( Ha: \) not equal

**Usage**

\[
gof.Pearson(\alpha, \beta, \text{pk}, \text{pk0}, r)
\]

**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**

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

**References**

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

References


IBE

Individual Bioequivalence

Description

Consider 2 by 2 crossover design. $\gamma = \delta^2 + \sigma_D^2 + \sigma_{WT}^2 - \sigma_{WR}^2 - \theta_{IBE} \ast \max(\sigma_D^2, \sigma_{WR}^2)$

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  
  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


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)
**InterSV.NIS**

**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**


---

**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**

**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**


---

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

**Description**

H0: |CVr - CVt| ≥ δ  
Ha: |CVr - CVt| < δ

**Usage**

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

**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**


---

**ISCV.NIS**

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

**Description**

H0: CVr - CVt < δ  
Ha: CVr - CVt ≥ δ

if δ > 0, the rejection of Null Hypothesis indicates the superiority of the test drug over the reference;
if δ < 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**

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**


---

**ISV.Equivalence**

*Test for Similarity of Intra-Subject Variabilities*

**Description**

the ratio = within-subject variance of treatment T / within-subject variance of treatment R  
H0: the ratio ≥ δ or the ratio ≤ 1/3  
Ha: ≤ 1/3 < the ratio < δ

**Usage**

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

**Description**

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

H0: the ratio ≥ δ

H1: the ratio < δ

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

if δ > 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**

McNemar.Test

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


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

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>alpha</td>
<td>significance level</td>
</tr>
<tr>
<td>beta</td>
<td>power = 1-beta</td>
</tr>
<tr>
<td>sigma</td>
<td>standard deviation</td>
</tr>
<tr>
<td>k</td>
<td>Total k treatments in the design</td>
</tr>
<tr>
<td>margin</td>
<td>margin = $\mu_i - \mu_j$ the difference between the true mean response of group i $\mu_i$ and group j $\mu_j$</td>
</tr>
</tbody>
</table>

References


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 \(\mu_i\) and group j \(\mu_j\)

References


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

\texttt{MeanWilliamsDesign.NIS(\textalpha{}, \textbeta{}, \textsigma{}, k, \textdelta{}, \textmargin{})}

Arguments

\begin{itemize}
  \item \textalpha{}  \quad \text{significance level}
  \item \textbeta{}  \quad \text{power = 1-\beta} \text{a}
  \item \textsigma{}  \quad \text{standard deviation}
  \item k  \quad \text{Total k treatments in the design}
  \item \textdelta{}  \quad \text{the superiority or non-inferiority margin}
  \item \textmargin{}  \quad \text{\textit{margin} = } \mu_i - \mu_j \text{ the difference between the true mean response of group } i \mu_i \text{ and group } j \mu_j
\end{itemize}

References


---

Multiple.Testing  \quad \textit{Multiple Testing procedures}

Description

\begin{itemize}
  \item Ho: \mu_{1j} - \mu_{2j} = 0
  \item Ha: \mu_{1j} - \mu_{2j} > 0
\end{itemize}

Usage

\texttt{Multiple.Testing(s1, s2, m, p, D, \textdelta{}, \textBCS{}, \textpho{}, K, \textalpha{}, \textbeta{})}

Arguments

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

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


---

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

\( p1 = P((x_1 - x_2)(y_1 - y_2) > 0) \)

p2

\( p2 = P((x_1 - x_2)(y_1 - y_2)(x_1 - x_3)(y_1 - y_3) > 0) \)

References


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     \( p_2 = P(|z_i| \geq |z_j|, z_i > 0) \)
p3     \( p_3 = P(|z_i| \geq |z_{j1}|, |z_i| \geq |z_{j2}|, z_i > 0) \)
p4     \( p_4 = P(|z_{j1}| \geq |z_i| \geq |z_{j2}|, z_{j1} > 0, z_i > 0) \)

References


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)
OneSampleMean.Equality

Arguments

- alpha: significance level
- beta: power = 1-beta
- k: k=n1/n2
- p1: \( p_1 = P(y_i \geq x_j) \)
- p2: \( p_2 = P(y_i \geq x_{j1} \text{ and } y_i \geq x_{j2}) \)
- p3: \( p_3 = P(y_{i1} \geq x_j \text{ and } y_{i2} \geq x_j) \)

References


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 \( \mu_0 \)

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 \( \mu_0 \)
OneSampleMean.Equivalence

References

Examples
OneSampleMean.Equivalence(0.05,0.2,1,0.5)
# 32

OneSampleMean.Equivalence

One Sample Mean Test for Equivalence

Description
Ho: \(|\text{margin}| \geq \delta\) Ha: \(|\text{margin}| < \delta\)
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 \(\mu_0\)
delta                the superiority or non-inferiority margin

References

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 \( \mu_0 \); 
if delta < 0, the rejection of the null hypothesis implies the true mean is non-inferior against the reference value \( \mu_0 \).

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 \( \mu_0 \)

References


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: \( \text{differ} = p - p_0 \)
  the difference between the true response rate of a test drug and a reference value \( p_0 \)

References


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: \( |p - p_0| \geq \text{margin} \)
Ha: \( |p-p_0| < \text{margin} \)

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

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>alpha</td>
<td>significance level</td>
</tr>
<tr>
<td>beta</td>
<td>power = 1-beta</td>
</tr>
<tr>
<td>p</td>
<td>the true response rate</td>
</tr>
<tr>
<td>delta</td>
<td>delta=p-p0</td>
</tr>
<tr>
<td>differ</td>
<td>the difference between the true response rate of a test drug and a reference value p0</td>
</tr>
<tr>
<td></td>
<td>the superiority or non-inferiority margin</td>
</tr>
</tbody>
</table>

References


Examples

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

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


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**: $\delta_j$ 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 $\sigma^2_j$. 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

\[ \alpha_{\text{star}} = r_1 \cdot \text{fdr} / ((m-m_1) \cdot (1-\text{fdr})) , \] which is the marginal type I error level for \( r_1 \) true rejection with the FDR controlled at \( f \).

\[ \beta_{\text{star}} = 1 - r_1 / m_1 , \] which is equal to 1-power.

References


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 \( s_1 \) and \( s_2 \) are the initial value, \( 0 < s_1 < s_2 \). \( h(s_1) \) should be smaller than 0.

- **s2**
  
  \( s_2 \) is also the initial value, which is larger than \( s_1 \) and \( h(s_2) \) should be larger than 0.

- **m**
  
  \( m \) is the total number of multiple tested

- **m1**
  
  \( m_1 = m - m_0 \). \( m_0 \) is the number of tests which the null hypotheses are true; \( m_1 \) is the number of tests which the alternative hypotheses are true. (or \( m_1 \) is the number of prognostic genes)

- **delta**
  
  \( \delta_j \) 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 \( \sigma_j^2 \). We assume \( \delta_j = 0 \), \( j \) in \( M_0 \) and \( \delta_j > 0 \), \( j \) in \( M_1 \)=effect size for prognostic genes.
a1 is the allocation proportion for group 1. a2=1-a1.

r1 is the number of true rejection

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


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
References


---

OneWayANOVA.PairwiseComparison

*One-way ANOVA pairwise comparison*

**Description**

Ho: \( p_i = p_j \) Ha: not all equal

**Usage**

OneWayANOVA.PairwiseComparison(\( \alpha \), \( \beta \), \( \tau \), \( p_1 \), \( p_2 \), \( \delta \))

**Arguments**

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>alpha</td>
<td>significance level</td>
</tr>
<tr>
<td>beta</td>
<td>power = 1-beta</td>
</tr>
<tr>
<td>tau</td>
<td>there are ( \tau ) comparisons here</td>
</tr>
<tr>
<td>( p_1 )</td>
<td>the mean response rate for test drug</td>
</tr>
<tr>
<td>( p_2 )</td>
<td>the rate for reference drug</td>
</tr>
<tr>
<td>( \delta )</td>
<td>( \delta = p_i - p_j )</td>
</tr>
</tbody>
</table>

**References**


**Examples**

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

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

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

Consider 2 by 2 crossover design.

H0: lamda >= 0
Ha: lamda < 0

Usage

\( \text{PBE}(\alpha, \beta, \sigma_{1.1}, \sigma_{tt}, \sigma_{tr}, \sigma_{bt}, \rho, a, \delta, \lambda) \)

Arguments

- alpha: significance level
- beta: power = 1-beta
- \( \sigma_{1.1}^2 = \sigma_D^2 + a\sigma_{WT}^2 + b\sigma_{WR}^2 \). Here a=b=1.
- \( \sigma_{tt}^2 = \sigma_{BT}^2 + \sigma_{WT}^2 \), \( \sigma_{wt}^2 \) is the within-subjects variance in test formulation
- \( \sigma_{tr}^2 = \sigma_{BR}^2 + \sigma_{WR}^2 \), \( \sigma_{wr}^2 \) is the within-subjects variance in reference formulation
- \( \sigma_{bt}^2 \) is the between-subjects variance in test formulation
- \( \sigma_{br}^2 \) is the between-subjects variance in reference formulation
- rho: rho is the inter-subject correlation coefficient.
- a: \( a = \theta_{PBE} = 1.74 \)
- delta: delta is the mean difference of AUC
- lamda: \( \lambda = \delta^2 + \sigma^2 - \sigma_{TR}^2 - \theta_{PBE} \max(\sigma_0^2, \sigma_{TR}^2) \)

References


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
Description


Ho: \( p_{j1} = p_{j2} \),

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

Usage

\texttt{Propensity.Score.nostrata(alpha, beta, J, a, b, p1, phi)}

Arguments

\begin{itemize}
  \item \texttt{alpha} \hspace{1cm} \text{significance level}
  \item \texttt{beta} \hspace{1cm} \text{power = 1-beta}
  \item \texttt{J} \hspace{1cm} \text{There are totally J stratas.}
  \item \texttt{a} \hspace{1cm} \text{a=c(a1,a2,...,aJ), \( aj=nj/n \) denote the allocation proportion for stratum j (\( \sum(aj)=1 \))}
  \item \texttt{b} \hspace{1cm} \text{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.}
  \item \texttt{p1} \hspace{1cm} \text{p1=c(p11,p21,.....,pj1), pjk denote the response probability for group k in stratum j. qjk=1-pjk.}
  \item \texttt{phi} \hspace{1cm} \text{\( p_{j2}q_{j1}/(p_{j1}q_{j2})=\phi \), so that \( p_{j2} = \phi p_{j1}/(q_{j1} + \phi p_{j1}) \)}
\end{itemize}

References


Examples

\begin{verbatim}
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
\end{verbatim}
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

\[ \text{Propensity.Score.strata}(\alpha, \beta, J, a, b, p1, \phi) \]

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 stratum \( j \) (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 \( p_{j2} = \phi p_{j1}/(q_{j1} + \phi p_{j1}) \)

References


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 \((-\delta, \delta)\).

\[ \epsilon = \delta - \eta \]
\eta is the measure for detecting an equivalence when the true difference in treatment means is less than a small constant \eta.

**References**

**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 \( \sigma^2_s/(\text{between subject variance } \sigma^2_s + \text{within subject variance } \sigma^2_e) \)
K  
  There are K recording replicates for each subject.
delta  
  \( \sigma^2 = \sigma^2_s + \sigma^2_e \). d is the difference of clinically importance. \( \delta = d/\sigma \)
gamma  
  \( \sigma^2_p \) is the extra variance from the random period effect for the crossover design. \( \gamma = \sigma^2_p/\sigma^2 \)

References


Examples

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

---

**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 \( \sigma^2_s/(\text{between subject variance } \sigma^2_s + \text{within subject variance } \sigma^2_e) \)
K  
  There are K recording replicates for each subject.
delta  
  \( \sigma^2 = \sigma^2_s + \sigma^2_e \). d is the difference of clinically importance. \( \delta = d/\sigma \)
References


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  signification level
beta   power = 1-beta
pho    pho=between subject variance $\sigma^2_s/(\text{between subject variance } \sigma^2_s + \text{within subject variance } \sigma^2_e)$
K      There are K recording replicates for each subject.
delta  $\sigma^2 = \sigma^2_s + \sigma^2_c$. $d$ is the difference of clinically importance. $\delta = d/\sigma$
gamma $\sigma^2_p$ is the extra variance from the random period effect for the crossover design. $\gamma = \sigma^2_p/\sigma^2$
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

Examples

Example.15.1.4.2<-QT.PK.parallel(0.05,0.2,0.8,3,0.5,0.002,1,1,4,5)
Example.15.1.4.1

# 29

\[
\text{Example.15.1.4.1} <- \text{QT.PK.parallel}(0.05, 0.2, 0.8, 3, 0.5, 0.002, 1, 1, 4, 5)
\]

\[
\text{Example.15.1.4.1}
\]

# 54

---

**QT.PK.parallel**

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

**Description**

H0: \( \mu_1 - \mu_2 = 0 \)

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**

\[
\text{QT.PK.parallel}(\alpha, \beta, \phi, K, \delta, v_1, v_2, \tau_1, \tau_2)
\]

**Arguments**

- **alpha**: significance level
- **beta**: power = 1-beta
- **phi**: \( \phi = \text{between subject variance } \sigma_s^2 / (\text{between subject variance } \sigma_s^2 + \text{within subject variance } \sigma_e^2) \)
- **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**


**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

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)| ≥ margin
Ha: |log(OR)| < margin
RelativeRisk.NIS

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


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


Examples

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

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

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: or=pt(1-pc)/pc(1-pt)
margin: the superiority or non-inferiority margin

References


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)
Sensitivity.Index

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>alpha</td>
<td>significance level</td>
</tr>
<tr>
<td>beta</td>
<td>power = 1-beta</td>
</tr>
<tr>
<td>sigma</td>
<td>standard deviation in crossover design</td>
</tr>
<tr>
<td>or</td>
<td>or=pt(1-pc)/pc(1-pf)</td>
</tr>
<tr>
<td>margin</td>
<td>the superiority or non-inferiority margin</td>
</tr>
</tbody>
</table>

References


Sensitivity.Index Calculate the power for Sensitivity Index

Description

Ho: \( \mu_1 = \mu_2 \)
Ha: \( \mu_1 \) is not equal to \( \mu_2 \)
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

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>alpha</td>
<td>significance level</td>
</tr>
<tr>
<td>n</td>
<td>sample size n</td>
</tr>
<tr>
<td>deltaT</td>
<td>a measure of change in the signal-to-noise ratio for the population difference, which is the sensitivity index of population difference between regions.</td>
</tr>
</tbody>
</table>

References


Examples

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

**Description**

Extension 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 distribution.
- **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**


---

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  
\text{significance level}

beta  
\text{power} = 1 - \text{beta}

sigma  
\text{standard deviation in crossover design}

margin  
margin = \mu_2 - \mu_1
\text{the true mean difference between a test mu2 and a control mu1}

References


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  
\text{significance level}

beta  
\text{power} = 1 - \text{beta}

sigma  
\text{standard deviation in crossover design}

delta  
\text{the superiority or non-inferiority margin}

margin  
margin = \mu_2 - \mu_1
\text{the true mean difference between a test mu2 and a control mu1}

References


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

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**: $\text{margin} = \mu_2 - \mu_1$  
the true mean difference between a test mu2 and a control mu1

**References**


**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.
TwoSampleMean.Equivalence

Usage

TwoSampleMean.Equivalence(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 = μ2 - μ1
       the true mean difference between a test μ2 and a control μ1

References


Examples

Example.3.2.4<-TwoSampleMean.Equivalence(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| ≥ 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)
TwoSampleMean.NIS

Arguments

- **alpha**: significance level
- **beta**: power = 1-beta
- **sigma**: pooled standard deviation of two groups
- **k**: \(k=\frac{n_1}{n_2}\)
  - Example: \(k=2\) indicates a 1 to 2 test-control allocation.
- **delta**: the superiority or non-inferiority margin
- **margin**: \(\text{margin} = \mu_2 - \mu_1\)
  - the true mean difference between a test \(\mu_2\) and a control \(\mu_1\)

References


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: \(\text{margin} \leq \text{delta}\) Ha: \(\text{margin} > \text{delta}\)
- if \(\text{delta} > 0\), the rejection of Null Hypothesis indicates the superiority of the test over the control;
- if \(\text{delta} < 0\), 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**: \(k=\frac{n_1}{n_2}\)
  - Example: \(k=2\) indicates a 1 to 2 test-control allocation.
- **delta**: the superiority or non-inferiority margin
- **margin**: \(\text{margin} = \mu_2 - \mu_1\)
  - the true mean difference between a test \(\mu_2\) and a control \(\mu_1\)
References

Examples
Example.3.2.4<-TwoSampleProportion.Equality(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

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: \(|p_1 - p_2| \geq margin\)
Ha: \(|p_1 - p_2| < margin\)

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


Examples

```r
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

\[ \text{Ho: } p_1 - p_2 \leq \text{margin} \quad \text{Ha: } p_1 - p_2 > \text{margin} \]

if margin > 0, the rejection of Null Hypothesis indicates the true rate \( p_1 \) is superior over the reference value \( p_2 \);

if margin < 0, the rejection of the null hypothesis implies the true rate \( p_1 \) is non-inferior against the reference value \( p_2 \).

Usage

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

Arguments

- \( \alpha \): significance level
- \( \beta \): power = 1 - \( \beta \)
- \( p_1 \): the mean response rate for test drug
- \( p_2 \): the rate for reference drug
- \( k \): \( k = n_1/n_2 \)
- \( \delta \): \( \delta = p_1 - p_2 \)
- \( \text{margin} \): the superiority or non-inferiority margin

References


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

Description

\[ H_0: p_2 - p_1 = 0 \]  \[ Ha: \text{not equal to } 0 \]

Usage

\[ \text{TwoSampleSeqCrossOver.Equality}(\alpha, \beta, \sigma, \text{sequence}, \delta) \]

Arguments

- \( \alpha \): significance level
- \( \beta \): power = 1 - \( \beta \)
- \( \sigma \): standard deviation in crossover design
- \( \text{sequence} \): total sequence number
- \( \delta \): \( \delta = p_2 - p_1 \)

References


Examples

\[ \text{Example.4.3.4}\leftarrow \text{TwoSampleSeqCrossOver.Equality}(0.05, 0.2, 0.25, 2, 0.2) \]
\[ \text{Example.4.3.4} \]

TwoSampleSeqCrossOver.Equivalence

Description

\[ H_0: |p_1 - p_2| \geq \text{margin} \]
\[ Ha: |p_1 - p_2| < \text{margin} \]

Usage

\[ \text{TwoSampleSeqCrossOver.Equivalence}(\alpha, \beta, \sigma, \text{sequence}, \delta, \text{margin}) \]
TwoSampleSeqCrossOver.NIS

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


Examples

Example.4.3.4<-TwoSampleSeqCrossOver.Equivalence(0.0,0.2,0.25,2,0,0.2)
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
TwoSampleSurvival.Conditional

References

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

TwoSampleSurvival.Conditional

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

Description
unconditional versus conditional

Usage
TwoSampleSurvival.Conditional(alpha,beta,lambda1,lambda2,eta1,eta2,k,totalk,accrual,g1,g2)

Arguments

alpha  significance level
beta   power = 1-beta
lambda1 the hazard rates of control group
lambda2 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
totalk Total trial time
accrual 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
TwoSampleSurvival.Equality

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


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

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

References


Examples

Example.7.2.4 <- TwoSampleSurvival.Equivalence(0.05, 0.2, 1, 1, 1, 3, 1, 0.00001, 0.5)
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 \lambda_1 and a test drug group \lambda_2

H_0: margin \leq delta
H_a: 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 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=\lambda_1-\lambda_2, the true difference of hazard rates between control group \lambda_1 and a test drug group \lambda_2

References


Examples

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

Ho: \( \delta_j = 0 \)

Ha: \( \delta_j \) is not equal to 0

Usage

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

Arguments

- \( m \) is the total number of multiple tests
- \( m1 = m - m0 \). \( m0 \) 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)
- \( \delta_j \) is the constant effect size for \( j \)th test. \( \delta_j = (E(X_{ij}) - E(Y_{ij}))/\sigma_j \). \( X_{ij} \) (and \( Y_{ij} \)) denote the expression level of gene \( j \) for subject \( i \) in group 1 and 2, respectively) with common variance \( \sigma^2_j \). We assume \( \delta_j = 0 \), \( j \) in \( m0 \) and \( \delta_j > 0 \), \( j \) in \( m1 \)=effect size for prognostic genes.
- \( a1 \) is the allocation proportion for group 1. \( a2 = 1-a1 \).
- \( r1 \) is the number of true rejection
- \( fdr \) is the FDR level.

Details

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

\( \beta_{\text{star}} = 1-r1/m1 \), which is equal to \( 1\)-power.

References


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

\(H_0: \delta_j = 0\)

\(H_a: \delta_j \neq 0\)

### Usage

\[
\text{TwoSide.varyEffect}(s1, s2, m, m1, \delta_j, a1, r1, fdr)
\]

### 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)
- **\(\delta_j\)**: \(\delta_j\) is the constant effect size for \(j\)th test, \(\delta_j = \frac{(E(X_j) - E(Y_j))/\sigma_j}{X_{ij}(Y_{ij})}\) denote the expression level of gene \(j\) for subject \(i\) in group 1 (and group 2, respectively) with common variance \(\sigma_j^2\). 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

\[
\alpha_{\text{star}}=r1\cdot fdr/((m-m1)*((1-fdr)))\]

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

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 jth case in the ith 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 $\mu_T$ is not equal to $\mu_C$

Usage

\[
\text{Vaccine.CEM}(\alpha, \beta, \mu_t, \mu_c, \sigma_t, \sigma_c, pt, pc)
\]

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


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.

\[ H_0: \theta \geq \theta_0 \]
\[ H_a: \theta < \theta_0 \]

Usage

\[ \text{Vaccine.ELDI}(\alpha, \beta, \theta_0, \theta, p_t, p_c) \]

Arguments

\begin{itemize}
  \item \texttt{alpha} \hspace{1cm} \text{significance level}
  \item \texttt{beta} \hspace{1cm} \text{power=}1-\beta
  \item \texttt{theta0} \hspace{1cm} \text{the true parameter for binomial distribution. Theta0 is usually equal to 0.5}
  \item \texttt{theta} \hspace{1cm} \text{theta=disease rate for treatment group}/(\text{disease rate for treatment group} + \text{for control group})
  \item \texttt{pt} \hspace{1cm} \text{the true disease incidence rates of the nt vaccines}
  \item \texttt{pc} \hspace{1cm} \text{the true disease incidence rates of the nc controls}
\end{itemize}

References


Examples

\texttt{Example.15.6.2}\leftarrow \text{Vaccine.ELDI}(0.05,0.2,0.5,1/3,0.001,0.002)
\texttt{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

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. \( \zeta = \delta^2 + sT^2 + sR^2 - \text{thetaBE} \ast \max(\sigma_0^2, sR^2) \). \( sT^2 = \sigma_{BT}^2 + \sigma_{WT}^2 \), \( sR^2 = \sigma_{BR}^2 + \sigma_{WR}^2 \)
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 $\sigma^2_{BT}$ is the between-subjects variance in test formulation
sigmaBR $\sigma^2_{BR}$ is the between-subjects variance in reference formulation
sigmaWT $\sigma^2_{WT}$ is the within-subjects variance in test formulation
sigmaWR $\sigma^2_{WR}$ is the within-subjects variance in reference formulation
thetaBE here thetaBE=1

References


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  $\delta = \mu_1 - \mu_2$
WilliamsDesign.Equivalence

References


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: $|\mu_2 - \mu_1| \geq \text{margin}$
Ha: $|\mu_2 - \mu_1| < \text{margin}$

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


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: $\mu_1 - \mu_2 \leq \text{margin}$
Ha: $\mu_1 - \mu_2 > \text{margin}$

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


Examples

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

* package

  TrialSize-package, 3
  Nonpara.Indep, 30
  Nonpara.One.Sample, 31
  Nonpara.Two.Sample, 31
  OneSampleMean.Equality, 32
  OneSampleMean.Equivalence, 33
  OneSampleMean.NIS, 34
  OneSampleProportion.Equality, 35
  OneSampleProportion.Equivalence, 35
  OneSampleProportion.NIS, 36
  OneSide.fixEffect, 37
  OneSide.varyEffect, 38
  OneWayANOVA.pairwise, 39
  OneWayANOVA.PairwiseComparison, 40
  PBE, 41
  Propensity.Score.nostrata, 42
  Propensity.Score.strata, 43
  QOL, 44
  QT.crossover, 44
  QT.parallel, 45
  QT.PK.crossover, 46
  QT.PK.parallel, 47
  RelativeRisk.Equality, 48
  RelativeRisk.Equivalence, 48
  RelativeRisk.NIS, 49
  RelativeRiskCrossOver.Equality, 50
  RelativeRiskCrossOver.Equivalence, 51
  RelativeRiskCrossOver.NIS, 51
  Sensitivity.Index, 52
  Stuart.Maxwell.Test, 53
  TrialSize(TrialSize-package), 3
  TrialSize-package, 3
  TwoSampleCrossOver.Equality, 53
  TwoSampleCrossOver.Equivalence, 54
  TwoSampleCrossOver.NIS, 55
  TwoSampleMean.Equality, 55

  AB.withDescalation, 4
  AB.withoutDescalation, 5
  ABE, 6
  ANOVA.Repeat.Measure, 7
  Carry.Over, 8
  Cochran.Armitage.Trend, 8
  Cox.Equality, 9
  Cox.Equivalence, 10
  Cox.NIS, 11
  CrossOver.ISV.Equality, 12
  CrossOver.ISV.Equivalence, 12
  CrossOver.ISV.NIS, 13
  Dose.Min.Effect, 14
  Dose.Response.binary, 15
  Dose.Response.Linear, 16
  Dose.Response.time.to.event, 17
  gof.Pearson, 18
  gof.Pearson.twoway, 19
  IBE, 19
  InterSV.Equality, 20
  InterSV.NIS, 21
  ISCV.Equality, 22
  ISCV.Equivalence, 22
  ISCV.NIS, 23
  ISV.Equality, 24
  ISV.Equivalence, 24
  ISV.NIS, 25
  McNemar.Test, 26
  MeanWilliamsDesign.Equality, 27
  MeanWilliamsDesign.Equivalence, 28
  MeanWilliamsDesign.NIS, 28
  Multiple.Testing, 29
  Nonpara.One.Sample, 31
  Nonpara.Two.Sample, 31
  OneSampleMean.Equality, 32
  OneSampleMean.Equivalence, 33
  OneSampleMean.NIS, 34
  OneSampleProportion.Equality, 35
  OneSampleProportion.Equivalence, 35
  OneSampleProportion.NIS, 36
  OneSide.fixEffect, 37
  OneSide.varyEffect, 38
  OneWayANOVA.pairwise, 39
  OneWayANOVA.PairwiseComparison, 40
  PBE, 41
  Propensity.Score.nostrata, 42
  Propensity.Score.strata, 43
  QOL, 44
  QT.crossover, 44
  QT.parallel, 45
  QT.PK.crossover, 46
  QT.PK.parallel, 47
  RelativeRisk.Equality, 48
  RelativeRisk.Equivalence, 48
  RelativeRisk.NIS, 49
  RelativeRiskCrossOver.Equality, 50
  RelativeRiskCrossOver.Equivalence, 51
  RelativeRiskCrossOver.NIS, 51
  Sensitivity.Index, 52
  Stuart.Maxwell.Test, 53
  TrialSize(TrialSize-package), 3
  TrialSize-package, 3
  TwoSampleCrossOver.Equality, 53
  TwoSampleCrossOver.Equivalence, 54
  TwoSampleCrossOver.NIS, 55
  TwoSampleMean.Equality, 55
TwoSampleMean.Equivalence, 56
TwoSampleMean.NIS, 57
TwoSampleProportion.Equality, 58
TwoSampleProportion.Equivalence, 59
TwoSampleProportion.NIS, 60
TwoSampleSeqCrossOver.Equality, 61
TwoSampleSeqCrossOver.Equivalence, 61
TwoSampleSeqCrossOver.NIS, 62
TwoSampleSurvival.Conditional, 63
TwoSampleSurvival.Equality, 64
TwoSampleSurvival.Equivalence, 65
TwoSampleSurvival.NIS, 66
TwoSide.fixEffect, 67
TwoSide.varyEffect, 68
Vaccine.CEM, 69
Vaccine.ELDI, 70
Vaccine.RDI, 71
Vitro.BE, 71
WilliamsDesign.Equality, 72
WilliamsDesign.Equivalence, 73
WilliamsDesign.NIS, 74