

# Package ‘EQUIVNONINF’

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## Description

Making available in R the complete set of programs accompanying S. Wellek's (2010) monograph "Testing Statistical Hypotheses of Equivalence and Noninferiority. Second Edition" (Chapman&Hall/CRC).

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EQUIVNONINF-package      *Testing for equivalence and noninferiority*

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## Description

The package makes available in R the complete set of programs accompanying S. Wellek's (2010) monograph "Testing Statistical Hypotheses of Equivalence and Noninferiority. Second Edition" (Chapman&Hall/CRC).

## Note

In order to keep execution time of all examples below the limit set by the CRAN administration, in a number of cases the function calls shown in the documentation contain specifications which are insufficient for real applications. This holds in particular true for the width `sw` of search grids, which should be chosen to be `.001` or smaller. Similarly, the maximum number of interval halving steps to be carried out in finding maximally admissible significance levels should be set to values  $\geq 10$ .

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**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2015.

**Examples**

```
bi2ste1(397, 397, 0.0, 0.025, 0.511, 0.384)
bi2ste2(0.0, 0.025, 0.95, 0.8, 0.80, 1.0)
```

---

bi1st	<i>Critical constants and power of the UMP test for equivalence of a single binomial proportion to some given reference value</i>
-------	---

---

**Description**

The function computes the critical constants defining the uniformly most powerful (randomized) test for the problem  $p \leq p_1$  or  $p \geq p_2$  versus  $p_1 < p < p_2$ , with  $p$  denoting the parameter of a binomial distribution from which a single sample of size  $n$  is available. In the output, one also finds the power against the alternative that the true value of  $p$  falls on the midpoint of the hypothetical equivalence interval  $(p_1, p_2)$ .

**Usage**

```
bi1st(alpha, n, P1, P2)
```

**Arguments**

alpha	significance level
n	sample size
P1	lower limit of the hypothetical equivalence range for the binomial parameter $p$
P2	upper limit of the hypothetical equivalence range for $p$

**Value**

alpha	significance level
n	sample size
P1	lower limit of the hypothetical equivalence range for the binomial parameter $p$
P2	upper limit of the hypothetical equivalence range for $p$

C1	left-hand limit of the critical interval for the observed number $X$ of successes
C2	right-hand limit of the critical interval for $X$
GAM1	probability of rejecting the null hypothesis when it turns out that $X = C_1$
GAM2	probability of rejecting the null hypothesis for $X = C_2$
POWNONRD	Power of the nonrandomized version of the test against the alternative $p = (p_1 + p_2)/2$
POW	Power of the randomized UMP test against the alternative $p = (p_1 + p_2)/2$

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**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 4.3.

**Examples**

```
bi1st(.05,273,.65,.75)
```

---

 bi2aeq1

---

*Power of the exact Fisher type test for equivalence*


---

**Description**

The function computes exact values of the power of the randomized UMPU test for equivalence in the strict (i.e. two-sided) sense of two binomial distributions and the conservative nonrandomized version of that test. It is assumed that the samples being available from both distributions are independent.

**Usage**

```
bi2aeq1(m,n,rho1,rho2,alpha,p1,p2)
```

**Arguments**

m	size of Sample 1
n	size of Sample 2
rho1	lower limit of the hypothetical equivalence range for the odds ratio
rho2	upper limit of the hypothetical equivalence range for the odds ratio
alpha	significance level
p1	true success rate in Population 1
p2	true success rate in Population 2

**Value**

m	size of Sample 1
n	size of Sample 2
rho1	lower limit of the hypothetical equivalence range for the odds ratio
rho2	upper limit of the hypothetical equivalence range for the odds ratio
alpha	significance level
p1	true success rate in Population 1
p2	true success rate in Population 2
POWNR	Power of the nonrandomized version of the test
POW	Power of the randomized UMPU test

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**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 6.6.4.

**Examples**

```
bi2aeq1(302,302,0.6667,1.5,0.05,0.5,0.5)
```

---

 bi2aeq2

*Sample sizes for the exact Fisher type test for equivalence*

---

**Description**

The function computes minimum sample sizes required in the randomized UMPU test for equivalence of two binomial distributions with respect to the odds ratio. Computation is done under the side condition that the ratio  $m/n$  has some predefined value  $\lambda$ .

**Usage**

```
bi2aeq2(rho1, rho2, alpha, p1, p2, beta, qlambda)
```

**Arguments**

rho1	lower limit of the hypothetical equivalence range for the odds ratio
rho2	upper limit of the hypothetical equivalence range for the odds ratio
alpha	significance level
p1	true success rate in Population 1
p2	true success rate in Population 2
beta	target value of power
qlambda	sample size ratio $m/n$

**Value**

rho1	lower limit of the hypothetical equivalence range for the odds ratio
rho2	upper limit of the hypothetical equivalence range for the odds ratio
alpha	significance level
p1	true success rate in Population 1
p2	true success rate in Population 2
beta	target value of power
qlambda	sample size ratio $m/n$
M	minimum size of Sample 1
N	minimum size of Sample 2
POW	Power of the randomized UMPU test attained with the computed values of $m,n$

**Author(s)**

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**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 6.6.4.

**Examples**

```
bi2aeq2(0.5, 2.0, 0.05, 0.5, 0.5, 0.60, 1.0)
```

---

bi2aeq3	<i>Determination of a maximally raised nominal significance level for the nonrandomized version of the exact Fisher type test for equivalence</i>
---------	---

---

### Description

The objective is to raise the nominal significance level as far as possible without exceeding the target significance level in the nonrandomized version of the test. The approach goes back to R.D. Boschloo (1970) who used the same technique for reducing the conservatism of the traditional nonrandomized Fisher test for superiority.

### Usage

```
bi2aeq3(m,n,rho1,rho2,alpha,sw,tolrd,tol,maxh)
```

### Arguments

m	size of Sample 1
n	size of Sample 2
rho1	lower limit of the hypothetical equivalence range for the odds ratio
rho2	upper limit of the hypothetical equivalence range for the odds ratio
alpha	significance level
sw	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
tolrd	horizontal distance from 0 and 1, respectively of the left- and right-most boundary point to be included in the search grid
tol	upper bound to the absolute difference between size and target level below which the search for a corrected nominal level terminates
maxh	maximum number of interval halving steps to be carried out in finding the maximally raised nominal level

### Details

It should be noted that, as the function of the nominal level, the size of the nonrandomized test is piecewise constant. Accordingly, there is a nondegenerate interval of "candidate" nominal levels serving the purpose. The limits of such an interval can be read from the output. In terms of execution time, bi2aeq3 is the most demanding program of the whole package.

### Value

m	size of Sample 1
n	size of Sample 2
rho1	lower limit of the hypothetical equivalence range for the odds ratio
rho2	upper limit of the hypothetical equivalence range for the odds ratio

alpha	significance level
sw	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
tolrd	horizontal distance from 0 and 1, respectively of the left- and right-most boundary point to be included in the search grid
tol	upper bound to the absolute difference between size and target level below which the search for a corrected nominal level terminates
maxh	maximum number of interval halving steps to be carried out in finding the maximally raised nominal level
ALPH_0	current trial value of the raised nominal level searched for
NHST	number of interval-halving steps performed up to now
SIZE	size of the critical region corresponding to $\alpha_0$

### Author(s)

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### References

Boschloo RD: Raised conditional level of significance for the 2 x 2- table when testing the equality of two probabilities. *Statistica Neerlandica* 24 (1970), 1-35.

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 6.6.5.

### Examples

```
bi2aeq3(50,50,0.6667,1.5000,0.05,0.01,0.000001,0.0001,5)
```

---

bi2by_ni_del	<i>Objective Bayesian test for noninferiority in the two-sample setting with binary data and the difference of the two proportions as the parameter of interest</i>
--------------	---

---

### Description

Implementation of the construction described on pp. 185-6 of Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition.

### Usage

```
bi2by_ni_del(N1, N2, EPS, SW, NSUB, ALPHA, MAXH)
```



**Arguments**

N1	size of Sample 1
N2	size of sample 2
EPS	noninferiority margin to the difference of success probabilities
SW	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
NSUB	number of subintervals for partitioning the range of integration
ALPHA	target significance level
MAXH	maximum number of interval halving steps to be carried out in finding the maximally admissible nominal level

**Details**

The program uses 96-point Gauss-Legendre quadrature on each of the NSUB intervals into which the range of integration is partitioned.

**Value**

N1	size of Sample 1
N2	size of sample 2
EPS	noninferiority margin to the difference of success probabilities
NSUB	number of subintervals for partitioning the range of integration
SW	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
ALPHA0	result of the search for the largest admissible nominal level
SIZE0	size of the critical region corresponding to $\alpha_0$
SIZE_UNC	size of the critical region of the test at uncorrected nominal level

**Author(s)**

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**References**

Wellek S: Statistical methods for the analysis of two-armed non-inferiority trials with binary outcomes. *Biometrical Journal* 47 (2005), 48–61.

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 6.6.3.

**Examples**

```
bi2by_ni_del(20,20,.10,.01,10,.05,5)
```

---

 bi2by\_ni\_OR

*Objective Bayesian test for noninferiority in the two-sample setting with binary data and the odds ratio as the parameter of interest*

---

### Description

Implementation of the construction described on pp. 179–181 of Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition.

### Usage

```
bi2by_ni_OR(N1 , N2 , EPS , SW , NSUB , ALPHA , MAXH)
```

### Arguments

N1	size of sample 1
N2	size of sample 2
EPS	noninferiority margin to the deviation of the odds ratio from unity
SW	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
NSUB	number of subintervals for partitioning the range of integration
ALPHA	target significance level
MAXH	maximum number of interval halving steps to be carried out in finding the maximally admissible nominal level

### Details

The program uses 96-point Gauss-Legendre quadrature on each of the NSUB intervals into which the range of integration is partitioned.

### Value

N1	size of sample 1
N2	size of sample 2
EPS	noninferiority margin to the deviation of the odds ratio from unity
NSUB	number of subintervals for partitioning the range of integration
SW	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
ALPHA0	result of the search for the largest admissible nominal level
SIZE0	size of the critical region corresponding to $\alpha_0$
SIZE_UNC	size of the critical region of the test at uncorrected nominal level

**Author(s)**

Stefan Wellek <stefan.wellek@zi-mannheim.de>  
 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Statistical methods for the analysis of two-arm non-inferiority trials with binary outcomes. *Biometrical Journal* 47 (2005), 48–61.  
 Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 6.6.2.

**Examples**

```
bi2by_ni_OR(10,10,1/3,.0005,10,.05,12)
```

---

bi2diffac	<i>Determination of a corrected nominal significance level for the asymptotic test for equivalence of two unrelated binomial proportions with respect to the difference <math>\delta</math> of their population counterparts</i>
-----------	--

---

**Description**

The program computes the largest nominal significance level which can be substituted for the target level  $\alpha$  without making the exact size of the asymptotic testing procedure larger than  $\alpha$ .

**Usage**

```
bi2diffac(alpha,m,n,del1,del2,sw,tolrd,tol,maxh)
```

**Arguments**

alpha	significance level
m	size of Sample 1
n	size of Sample 2
del1	absolute value of the lower limit of the hypothetical equivalence range for $p_1 - p_2$
del2	upper limit of the hypothetical equivalence range for $p_1 - p_2$
sw	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
tolrd	horizontal distance of the left- and right-most boundary point to be included in the search grid
tol	upper bound to the absolute difference between size and target level below which the search for a corrected nominal level terminates
maxh	maximum number of interval halving steps to be carried out in finding the maximally raised nominal level

**Value**

alpha	significance level
m	size of Sample 1
n	size of Sample 2
de11	absolute value of the lower limit of the hypothetical equivalence range for $p_1 - p_2$
de12	upper limit of the hypothetical equivalence range for $p_1 - p_2$
sw	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
tolrd	horizontal distance of the left- and right-most boundary point to be included in the search grid
tol	upper bound to the absolute difference between size and target level below which the search for a corrected nominal level terminates
maxh	maximum number of interval halving steps to be carried out in finding the maximally raised nominal level
NH	number of interval-halving steps actually performed
ALPH_0	value of the raised nominal level obtained after NH steps
SIZE0	size of the critical region corresponding to $\alpha_0$
ERROR	error indicator answering the question of whether or not the sufficient condition for the correctness of the result output by the program, was satisfied

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**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 6.6.6.

**Examples**

```
bi2diffac(0.05,20,20,0.40,0.40,0.1,1e-6,1e-4,3)
```

---

bi2dipow	<i>Exact rejection probability of the asymptotic test for equivalence of two unrelated binomial proportions with respect to the difference of their expectations at any nominal level under an arbitrary parameter configuration</i>
----------	--

---

**Description**

The program computes exact values of the rejection probability of the asymptotic test for equivalence in the sense of  $-\delta_1 < p_1 - p_2 < \delta_2$ , at any nominal level  $\alpha_0$ . [The largest  $\alpha_0$  for which the test is valid in terms of the significance level, can be computed by means of the program bi2diffac.]

**Usage**

```
bi2dipow(alpha0,m,n,de11,de12,p1,p2)
```

**Arguments**

alpha0	nominal significance level
m	size of Sample 1
n	size of Sample 2
de11	absolute value of the lower limit of the hypothetical equivalence range for $p_1 - p_2$
de12	upper limit of the hypothetical equivalence range for $p_1 - p_2$
p1	true value of the success probability in Population 1
p2	true value of the success probability in Population 2

**Value**

alpha0	nominal significance level
m	size of Sample 1
n	size of Sample 2
de11	absolute value of the lower limit of the hypothetical equivalence range for $p_1 - p_2$
de12	upper limit of the hypothetical equivalence range for $p_1 - p_2$
p1	true value of the success probability in Population 1
p2	true value of the success probability in Population 2
POWEX0	exact rejection probability under $(p_1, p_2)$ of the test at nominal level $\alpha_0$ for equivalence of two binomial distributions with respect to the difference of the success probabilities
ERROR	error indicator answering the question of whether or not the sufficient condition for the correctness of the result output by the program, was satisfied

**Author(s)**

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Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 6.6.6.

**Examples**

```
bi2dipow(0.0228,50,50,0.20,0.20,0.50,0.50)
```

---

 bi2rlv1

*Power of the exact Fisher type test for relevant differences*


---

**Description**

The function computes exact values of the power of the randomized UMPU test for relevant differences between two binomial distributions and the conservative nonrandomized version of that test. It is assumed that the samples being available from both distributions are independent.

**Usage**

```
bi2rlv1(m,n,rho1,rho2,alpha,p1,p2)
```

**Arguments**

m	size of Sample 1
n	size of Sample 2
rho1	lower limit of the hypothetical equivalence range for the odds ratio
rho2	upper limit of the hypothetical equivalence range for the odds ratio
alpha	significance level
p1	true success rate in Population 1
p2	true success rate in Population 2

**Value**

m	size of Sample 1
n	size of Sample 2
rho1	lower limit of the hypothetical equivalence range for the odds ratio
rho2	upper limit of the hypothetical equivalence range for the odds ratio
alpha	significance level
p1	true success rate in Population 1
p2	true success rate in Population 2
POWNR	power of the nonrandomized version of the test
POW	power of the randomized UMPU test

**Author(s)**

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 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 11.3.3.

**Examples**

```
bi2rlv1(200,300,.6667,1.5,.05,.25,.10)
```

---

 bi2rlv2
 

---



---

*Sample sizes for the exact Fisher type test for relevant differences*


---

**Description**

The function computes minimum sample sizes required in the randomized UMPU test for relevant differences between two binomial distributions with respect to the odds ratio. Computation is done under the side condition that the ratio  $m/n$  has some predefined value  $\lambda$ .

**Usage**

```
bi2rlv2(rho1, rho2, alpha, p1, p2, beta, qlambda)
```

**Arguments**

rho1	lower limit of the hypothetical equivalence range for the odds ratio
rho2	upper limit of the hypothetical equivalence range for the odds ratio
alpha	significance level
p1	true success rate in Population 1
p2	true success rate in Population 2
beta	target value of power
qlambda	sample size ratio $m/n$

**Value**

rho1	lower limit of the hypothetical equivalence range for the odds ratio
rho2	upper limit of the hypothetical equivalence range for the odds ratio
alpha	significance level
p1	true success rate in Population 1
p2	true success rate in Population 2
beta	target value of power
qlambda	sample size ratio $m/n$
M	minimum size of Sample 1
N	minimum size of Sample 2
POW	power of the randomized UMPU test attained with the computed values of m, n

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**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 11.3.3.

**Examples**

```
bi2rlv2(.6667,1.5,.05,.70,.50,.80,2.0)
```

---

bi2st	<i>Critical constants for the exact Fisher type UMPU test for equivalence of two binomial distributions with respect to the odds ratio</i>
-------	--

---

**Description**

The function computes the critical constants defining the uniformly most powerful unbiased test for equivalence of two binomial distributions with parameters  $p_1$  and  $p_2$  in terms of the odds ratio. Like the ordinary Fisher type test of the null hypothesis  $p_1 = p_2$ , the test is conditional on the total number  $S$  of successes in the pooled sample.

**Usage**

```
bi2st(alpha,m,n,s,rho1,rho2)
```

**Arguments**

alpha	significance level
m	size of Sample 1
n	size of Sample 2
s	observed total count of successes
rho1	lower limit of the hypothetical equivalence range for the odds ratio $\varrho = \frac{p_1(1-p_2)}{p_2(1-p_1)}$
rho2	upper limit of the hypothetical equivalence range for $\varrho$

**Value**

alpha	significance level
m	size of Sample 1
n	size of Sample 2
s	observed total count of successes
rho1	lower limit of the hypothetical equivalence range for the odds ratio $\varrho = \frac{p_1(1-p_2)}{p_2(1-p_1)}$
rho2	upper limit of the hypothetical equivalence range for $\varrho$
C1	left-hand limit of the critical interval for the number $X$ of successes observed in Sample 1
C2	right-hand limit of the critical interval for $X$
GAM1	probability of rejecting the null hypothesis when it turns out that $X = C_1$
GAM2	probability of rejecting the null hypothesis for $X = C_2$



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**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 6.6.4.

**Examples**

```
bi2st(.05,225,119,171, 2/3, 3/2)
```

---

bi2ste1	<i>Power of the exact Fisher type test for noninferiority</i>
---------	---

---

**Description**

The function computes exact values of the power of the randomized UMPU test for one-sided equivalence of two binomial distributions and its conservative nonrandomized version. It is assumed that the samples being available from both distributions are independent.

**Usage**

```
bi2ste1(m, n, eps, alpha, p1, p2)
```

**Arguments**

m	size of Sample 1
n	size of Sample 2
eps	noninferiority margin to the odds ratio $\varrho$ , defined to be the maximum acceptable deviation of the true value of $\varrho$ from unity
alpha	significance level
p1	success rate in Population 1
p2	success rate in Population 2

**Value**

m	size of Sample 1
n	size of Sample 2
eps	noninferiority margin to the odds ratio $\varrho$ , defined to be the maximum acceptable deviation of the true value of $\varrho$ from unity
alpha	significance level
p1	success rate in Population 1
p2	success rate in Population 2
POWNR	power of the nonrandomized version of the test
POW	power of the randomized UMPU test

**Author(s)**

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 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, 6.6.1.

**Examples**

```
bi2ste1(106,107,0.5,0.05,0.9245,0.9065)
```

---

 bi2ste2

---

*Sample sizes for the exact Fisher type test for noninferiority*


---

**Description**

Sample sizes for the exact Fisher type test for noninferiority

**Usage**

```
bi2ste2(eps, alpha, p1, p2, bet, qlambda)
```

**Arguments**

eps	noninferiority margin to the odds ratio
alpha	significance level
p1	success rate in Population 1
p2	success rate in Population 2
bet	target power value
qlambda	sample size ratio $m/n$

**Details**

The program computes the smallest sample sizes  $m, n$  satisfying  $m/n = \lambda$  required for ensuring that the power of the randomized UMPU test does not fall below  $\beta$ .

**Value**

eps	noninferiority margin to the odds ratio
alpha	significance level
p1	success rate in Population 1
p2	success rate in Population 2
bet	target power value
qlambda	sample size ratio $m/n$
M	minimum size of Sample 1
N	minimum size of Sample 2
POW	power of the randomized UMPU test attained with the computed values of m, n

**Author(s)**

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 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, 6.6.1.

**Examples**

```
bi2ste2(0.5,0.05,0.9245,0.9065,0.80,1.00)
```

---

bi2ste3	<i>Determination of a maximally raised nominal significance level for the nonrandomized version of the exact Fisher type test for noninferiority</i>
---------	--

---

**Description**

The objective is to raise the nominal significance level as far as possible without exceeding the target significance level in the nonrandomized version of the test. The approach goes back to R.D. Boschloo (1970) who used the same technique for reducing the conservatism of the traditional nonrandomized Fisher test for superiority.

**Usage**

```
bi2ste3(m, n, eps, alpha, sw, tolrd, tol, maxh)
```

**Arguments**

m	size of Sample 1
n	size of Sample 2
eps	noninferiority margin to the odds ratio $\varrho$ , defined to be the maximum acceptable deviation of the true value of $\varrho$ from unity
alpha	target significance level
sw	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
tolrd	horizontal distance from 0 and 1, respectively, of the left- and right-most boundary point to be included in the search grid
tol	upper bound to the absolute difference between size and target level below which the search for a corrected nominal level terminates
maxh	maximum number of interval-halving steps to be carried out in finding the maximally raised nominal level

**Details**

It should be noted that, as the function of the nominal level, the size of the nonrandomized test is piecewise constant. Accordingly, there is a nondegenerate interval of "candidate" nominal levels serving the purpose. The limits of such an interval can be read from the output.

**Value**

m	size of Sample 1
n	size of Sample 2
eps	noninferiority margin to the odds ratio $\varrho$ , defined to be the maximum acceptable deviation of the true value of $\varrho$ from unity
alpha	target significance level
sw	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
tolrd	horizontal distance from 0 and 1, respectively, of the left- and right-most boundary point to be included in the search grid
tol	upper bound to the absolute difference between size and target level below which the search for a corrected nominal level terminates
maxh	maximum number of interval-halving steps to be carried out in finding the maximally raised nominal level
ALPH_0	current trial value of the raised nominal level searched for
NHST	number of interval-halving steps performed up to now
SIZE	size of the critical region corresponding to $\alpha_0$

**Author(s)**

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 Peter Ziegler <peter.ziegler@zi-mannheim.de>

## References

Boschloo RD: Raised conditional level of significance for the 2 x 2- table when testing the equality of two probabilities. *Statistica Neerlandica* 24 (1970), 1-35.

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, §6.6.2.

## Examples

```
bi2ste3(50, 50, 1/3, 0.05, 0.05, 1e-10, 1e-8, 10)
```

---

bi2wld_ni_del	<i>Function to compute corrected nominal levels for the Wald type (asymptotic) test for one-sided equivalence of two binomial distributions with respect to the difference of success rates</i>
---------------	---

---

## Description

Implementation of the construction described on pp. 183-5 of Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition.

## Usage

```
bi2wld_ni_del(N1, N2, EPS, SW, ALPHA, MAXH)
```

## Arguments

N1	size of Sample 1
N2	size of Sample 2
EPS	noninferiority margin to the difference of success probabilities
SW	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
ALPHA	target significance level
MAXH	maximum number of interval-halving steps

## Details

The program computes the largest nominal significance level to be used for determining the critical lower bound to the Wald-type statistic for the problem of testing  $H : p_1 \leq p_2 - \varepsilon$  versus  $K : p_1 < p_2 - \varepsilon$ .

**Value**

N1	size of Sample 1
N2	size of Sample 2
EPS	noninferiority margin to the difference of success probabilities
SW	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
ALPHA	target significance level
MAXH	maximum number of interval-halving steps
ALPHA0	corrected nominal level
SIZE0	size of the critical region of the test at nominal level ALPHA0
SIZE_UNC	size of the test at uncorrected nominal level ALPHA
ERR_IND	indicator taking value 1 when it occurs that the sufficient condition allowing one to restrict the search for the maximum of the rejection probability under the null hypothesis to its boundary, fails to be satisfied; otherwise the indicator retains its default value 0.

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 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 6.6.3.

**Examples**

```
bi2wld_ni_del(25,25,.10,.01,.05,10)
```

---

cf_reh_exact	<i>Exact confidence bounds to the relative excess heterozygosity (REH) exhibited by a SNP genotype distribution</i>
--------------	---

---

**Description**

Implementation of the interval estimation procedure described on pp. 305-6 of Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition.

**Usage**

```
cf_reh_exact(X1,X2,X3,alpha,SW,TOL,ITMAX)
```

**Arguments**

X1	count of homozygotes of the first kind [ $\leftrightarrow$ genotype AA]
X2	count of heterozygotes [ $\leftrightarrow$ genotype AB]
X3	count of homozygotes of the second kind [ $\leftrightarrow$ genotype BB]
alpha	1 - confidence level
SW	width of the search grid for determining an interval covering the parameter point at which the conditional distribution function takes value $\alpha$ and $1 - \alpha$ , respectively
TOL	numerical tolerance to the deviation between the computed confidence limits and their exact values
ITMAX	maximum number of interval-halving steps

**Details**

The program exploits the structure of the family of all genotype distributions, which is 2-parameter exponential with  $\log(REH)$  as one of these parameters.

**Value**

X1	count of homozygotes of the first kind [ $\leftrightarrow$ genotype AA]
X2	count of heterozygotes [ $\leftrightarrow$ genotype AB]
X3	count of homozygotes of the second kind [ $\leftrightarrow$ genotype BB]
alpha	1 - confidence level
SW	width of the search grid for determining an interval covering the parameter point at which the conditional distribution function takes value $\alpha$ and $1 - \alpha$ , respectively
TOL	numerical tolerance to the deviation between the computed confidence limits and their exact values
ITMAX	maximum number of interval-halving steps
C_l_exact	exact conditional lower $(1 - \alpha)$ -confidence bound to REH
C_r_exact	exact conditional upper $(1 - \alpha)$ -confidence bound to REH

**Author(s)**

Stefan Wellek <stefan.wellek@zi-mannheim.de>  
 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

- Wellek S, Goddard KAB, Ziegler A: A confidence-limit-based approach to the assessment of Hardy-Weinberg equilibrium. *Biometrical Journal* 52 (2010), 253-270.
- Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 9.4.3.

**Examples**

```
cf_reh_exact(34,118,96,.05,.1,1E-4,25)
```

---

cf_reh_midp	<i>Mid-p-value - based confidence bounds to the relative excess heterozygosity (REH) exhibited by a SNP genotype distribution</i>
-------------	---

---

**Description**

Implementation of the interval estimation procedure described on pp. 306-7 of Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition.

**Usage**

```
cf_reh_midp(X1,X2,X3,alpha,SW,TOL,ITMAX)
```

**Arguments**

X1	count of homozygotes of the first kind [ $\leftrightarrow$ genotype AA]
X2	count of heterozygotes [ $\leftrightarrow$ genotype AB]
X3	count of homozygotes of the second kind [ $\leftrightarrow$ genotype BB]
alpha	1 - confidence level
SW	width of the search grid for determining an interval covering the parameter point at which the conditional distribution function takes value $\alpha$ and $1 - \alpha$ , respectively
TOL	numerical tolerance to the deviation between the computed confidence limits and their exact values
ITMAX	maximum number of interval-halving steps

**Details**

The mid-p algorithm serves as a device for reducing the conservatism inherent in exact confidence estimation procedures for parameters of discrete distributions.

**Value**

X1	count of homozygotes of the first kind [ $\leftrightarrow$ genotype AA]
X2	count of heterozygotes [ $\leftrightarrow$ genotype AB]
X3	count of homozygotes of the second kind [ $\leftrightarrow$ genotype BB]
alpha	1 - confidence level
SW	width of the search grid for determining an interval covering the parameter point at which the conditional distribution function takes value $\alpha$ and $1 - \alpha$ , respectively



TOL	numerical tolerance to the deviation between the computed confidence limits and their exact values
ITMAX	maximum number of interval-halving steps
C_l_midp	lower $(1 - \alpha)$ -confidence bound to REH based on conditional mid-p-values
C_r_midp	upper $(1 - \alpha)$ -confidence bound to REH based on conditional mid-p-values

**Author(s)**

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 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Agresti A: Categorical data Analysis (2nd edn). Hoboken, NJ: Wiley, Inc., 2002, Section 1.4.5.  
 Wellek S, Goddard KAB, Ziegler A: A confidence-limit-based approach to the assessment of Hardy-Weinberg equilibrium. *Biometrical Journal* 52 (2010), 253-270.  
 Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 9.4.3.

**Examples**

```
cf_reh_midp(137,34,8,.05,.1,1E-4,25)
```

---

exp1st	<i>Critical constants and power against the null alternative of the UMP test for equivalence of the hazard rate of a single exponential distribution to some given reference value</i>
--------	--

---

**Description**

The function computes the critical constants defining the uniformly most powerful test for the problem  $\sigma \leq 1/(1 + \varepsilon)$  or  $\sigma \geq (1 + \varepsilon)$  versus  $1/(1 + \varepsilon) < \sigma < (1 + \varepsilon)$ , with  $\sigma$  denoting the scale parameter [ $\equiv$  reciprocal hazard rate] of an exponential distribution.

**Usage**

```
exp1st(alpha, tol, itmax, n, eps)
```

**Arguments**

alpha	significance level
tol	tolerable deviation from $\alpha$ of the rejection probability at either boundary of the hypothetical equivalence interval
itmax	maximum number of iteration steps
n	sample size
eps	margin determining the hypothetical equivalence range symmetrically on the log-scale

**Value**

alpha	significance level
tol	tolerable deviation from $\alpha$ of the rejection probability at either boundary of the hypothetical equivalence interval
itmax	maximum number of iteration steps
n	sample size
eps	margin determining the hypothetical equivalence range symmetrically on the log-scale
IT	number of iteration steps performed until reaching the stopping criterion corresponding to TOL
C1	left-hand limit of the critical interval for $T = \sum_{i=1}^n X_i$
C2	right-hand limit of the critical interval for $T = \sum_{i=1}^n X_i$
ERR1	deviation of the rejection probability from $\alpha$ under $\sigma = 1/(1 + \varepsilon)$
POW0	power of the randomized UMP test against the alternative $\sigma = 1$

**Author(s)**

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 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 4.2.

**Examples**

```
exp1st(0.05, 1.0e-10, 100, 80, 0.3)
```

---

fstretch	<i>Critical constants and power of the UMPI (uniformly most powerful invariant) test for dispersion equivalence of two Gaussian distributions</i>
----------	---

---

**Description**

The function computes the critical constants defining the optimal test for the problem  $\sigma^2/\tau^2 \leq \varrho_1$  or  $\sigma^2/\tau^2 \geq \varrho_2$  versus  $\varrho_1 < \sigma^2/\tau^2 < \varrho_2$ , with  $(\varrho_1, \varrho_2)$  as a fixed nonempty interval around unity.

**Usage**

```
fstretch(alpha, tol, itmax, ny1, ny2, rho1, rho2)
```

**Arguments**

alpha	significance level
tol	tolerable deviation from $\alpha$ of the rejection probability at either boundary of the hypothetical equivalence interval
itmax	maximum number of iteration steps
ny1	number of degrees of freedom of the estimator of $\sigma^2$
ny2	number of degrees of freedom of the estimator of $\tau^2$
rho1	lower equivalence limit to $\sigma^2/\tau^2$
rho2	upper equivalence limit to $\sigma^2/\tau^2$

**Value**

alpha	significance level
tol	tolerable deviation from $\alpha$ of the rejection probability at either boundary of the hypothetical equivalence interval
itmax	maximum number of iteration steps
ny1	number of degrees of freedom of the estimator of $\sigma^2$
ny2	number of degrees of freedom of the estimator of $\tau^2$
rho1	lower equivalence limit to $\sigma^2/\tau^2$
rho2	upper equivalence limit to $\sigma^2/\tau^2$
IT	number of iteration steps performed until reaching the stopping criterion corresponding to TOL
C1	left-hand limit of the critical interval for

$$T = \frac{n-1}{m-1} \sum_{i=1}^m (X_i - \bar{X})^2 / \sum_{j=1}^{n-1} (Y_j - \bar{Y})^2$$

C2	right-hand limit of the critical interval for
----	---

$$T = \frac{n-1}{m-1} \sum_{i=1}^m (X_i - \bar{X})^2 / \sum_{j=1}^{n-1} (Y_j - \bar{Y})^2$$

ERR	deviation of the rejection probability from $\alpha$ under $\sigma^2/\tau^2 = \varrho_1$
POW0	power of the UMPI test against the alternative $\sigma^2/\tau^2 = 1$

**Note**

If the two independent samples under analysis are from exponential rather than Gaussian distributions, the critical constants computed by means of fstretch with  $\nu_1 = 2m$ ,  $\nu_2 = 2n$ , can be used for testing for equivalence with respect to the ratio of hazard rates. The only difference is that the ratio of sample means rather than variances has to be used as the test statistic then.

**Author(s)**

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**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 6.5.

**Examples**

```
fstretch(0.05, 1.0e-10, 50,40,45,0.5625,1.7689)
```

---

gofhwex

*Critical constants of the exact UMPU test for approximate compatibility of a SNP genotype distribution with the Hardy-Weinberg model*

---

**Description**

The function computes the critical constants defining the uniformly most powerful unbiased test for equivalence of the population distribution of the three genotypes distinguishable in terms of a single nucleotide polymorphism (SNP), to a distribution being in Hardy-Weinberg equilibrium (HWE).

The test is conditional on the total count  $S$  of alleles of the kind of interest, and the parameter  $\theta$ , in terms of which equivalence shall be established, is defined by  $\theta = \frac{\pi_2^2}{\pi_1(1-\pi_1-\pi_2)}$ , with  $\pi_1$  and  $\pi_2$  denoting the population frequency of homozygotes of the 1st kind and heterozygotes, respectively.

**Usage**

```
gofhwex(alpha,n,s,de11,de12)
```

**Arguments**

alpha	significance level
n	number of genotyped individuals
s	observed count of alleles of the kind of interest
de11	absolute value of the lower equivalence limit to $\theta/4 - 1$
de12	upper equivalence limit to $\theta/4 - 1$

**Value**

alpha	significance level
n	number of genotyped individuals
s	observed count of alleles of the kind of interest
de11	absolute value of the lower equivalence limit to $\theta/4 - 1$
de12	upper equivalence limit to $\theta/4 - 1$

C1	left-hand limit of the critical interval for the observed number $X_2$ of heterozygotes
C2	right-hand limit of the critical interval for the observed number $X_2$
GAM1	probability of rejecting the null hypothesis when it turns out that $X_2 = C_1$
GAM2	probability of rejecting the null hypothesis for $X_2 = C_2$

**Author(s)**

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 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

- Wellek S: Tests for establishing compatibility of an observed genotype distribution with Hardy-Weinberg equilibrium in the case of a biallelic locus. *Biometrics* 60 (2004), 694-703.
- Goddard KAB, Ziegler A, Wellek S: Adapting the logical basis of tests for Hardy-Weinberg equilibrium to the real needs of association studies in human and medical genetics. *Genetic Epidemiology* 33 (2009), 569-580.
- Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 9.4.2.

**Examples**

```
gofhwex(0.05, 475, 429, 1-1/1.96, 0.96)
```

---

gofhwex_1s	<i>Critical constants of the exact UMPU test for absence of a substantial deficit of heterozygotes as compared with a HWE-compliant SNP genotype distribution [noninferiority version of the test implemented by means of gofhwex]</i>
------------	--

---

**Description**

The function computes the critical constants defining the UMPU test for one-sided equivalence of the population distribution of a SNP, to a distribution being in Hardy-Weinberg equilibrium (HWE). A substantial deficit of heterozygotes is defined to occur when the true value of the parametric function  $\omega = \frac{\pi_2/2}{\sqrt{\pi_1\pi_3}}$  [called relative excess heterozygosity (REH)] falls below unity by more than some given margin  $\delta_0$ .

Like its two-sided counterpart [see the description of the R function gofhwex], the test is conditional on the total count  $S$  of alleles of the kind of interest.

**Usage**

```
gofhwex_1s(alpha, n, s, del0)
```

**Arguments**

alpha	significance level
n	number of genotyped individuals
s	observed count of alleles of the kind of interest
de10	noninferiority margin for $\omega$ , which has to satisfy $\omega > 1 - \delta_0$ under the alternative hypothesis to be established

**Value**

alpha	significance level
n	number of genotyped individuals
s	observed count of alleles of the kind of interest
de10	noninferiority margin for $\omega$ , which has to satisfy $\omega > 1 - \delta_0$ under the alternative hypothesis to be established
C	left-hand limit of the critical interval for the observed number $X_2$ of heterozygotes
GAM	probability of rejecting the null hypothesis when it turns out that $X_2 = C$

**Author(s)**

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 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, pp. 300-302.

**Examples**

```
gofhwex_1s(0.05, 133, 65, 1-1/1.96)
```

---

gofind_t	<i>Establishing approximate independence in a two-way contingency table: Test statistic and critical bound</i>
----------	--

---

**Description**

The function computes all quantities required for carrying out the asymptotic test for approximate independence of two categorical variables derived in § 9.2 of Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition.

**Usage**

```
gofind_t(alpha, r, s, eps, xv)
```

**Arguments**

alpha	significance level
r	number of rows of the contingency table under analysis
s	number of columns of the contingency table under analysis
eps	margin to the Euclidean distance between the vector $\pi$ of true cell probabilities and the associated vector of products of marginal totals
xv	row vector of length $r \cdot s$ whose $(i - 1)s + j$ -th component is the entry in cell $(i, j)$ of the $r \times s$ contingency table under analysis $i = 1, \dots, r, j = 1, \dots, s$ .

**Value**

n	size of the sample to which the input table relates
alpha	significance level
r	number of rows of the contingency table under analysis
s	number of columns of the contingency table under analysis
eps	margin to the Euclidean distance between the vector $\pi$ of true cell probabilities and the associated vector of products of marginal totals
$X(r, s)$	observed cell counts
DSQ_OBS	observed value of the squared Euclidean distance
VN	square root of the estimated asymptotic variance of $\sqrt{n}DSQ\_OBS$
CRIT	upper critical bound to $\sqrt{n}DSQ\_OBS$
REJ	indicator of a positive [=1] vs negative [=0] rejection decision to be taken with the data under analysis

**Author(s)**

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 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 9.2.

**Examples**

```
xv <- c(8, 13, 15, 6, 19, 21, 31, 7)
gofind_t(0.05, 2, 4, 0.15, xv)
```

gofsimpt

*Establishing goodness of fit of an observed to a fully specified multinomial distribution: test statistic and critical bound*

### Description

The function computes all quantities required for carrying out the asymptotic test for goodness rather than lack of fit of an observed to a fully specified multinomial distribution derived in § 9.1 of Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition.

### Usage

```
gofsimpt(alpha,n,k,eps,x,pio)
```

### Arguments

alpha	significance level
n	sample size
k	number of categories
eps	margin to the Euclidean distance between the vectors $\pi$ and $\pi_0$ of true and hypothesized cell probabilities
x	vector of length $k$ with the observed cell counts as components
pio	prespecified vector of cell probabilities

### Value

alpha	significance level
n	sample size
k	number of categories
eps	margin to the Euclidean distance between the vectors $\pi$ and $\pi_0$ of true and hypothesized cell probabilities
X(1,K)	observed cell counts
PI0(1,K)	hypothesized cell probabilities
DSQPIH_0	observed value of the squared Euclidean distance
VN_N	square root of the estimated asymptotic variance of $\sqrt{n}DSQPIH_0$
CRIT	upper critical bound to $\sqrt{n}DSQPIH_0$
REJ	indicator of a positive [=1] vs negative [=0] rejection decision to be taken with the data under analysis

### Author(s)

Stefan Wellek <stefan.wellek@zi-mannheim.de>  
 Peter Ziegler <peter.ziegler@zi-mannheim.de>



## References

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 9.1.

## Examples

```
x<- c(17,16,25,9,16,17)
pio <- rep(1,6)/6
gofsimpt(0.05,100,6,0.15,x,pio)
```

---

mawi

*Mann-Whitney test for equivalence of two continuous distributions of arbitrary shape: test statistic and critical upper bound*

---

## Description

Implementation of the asymptotically distribution-free test for equivalence of two continuous distributions in terms of the Mann-Whitney-Wilcoxon functional. For details see Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition, § 6.2.

## Usage

```
mawi(alpha,m,n,eps1_,eps2_,x,y)
```

## Arguments

alpha	significance level
m	size of Sample 1
n	size of Sample 2
eps1_	absolute value of the left-hand limit of the hypothetical equivalence range for $\pi_+ - 1/2$
eps2_	right-hand limit of the hypothetical equivalence range for $\pi_+ - 1/2$
x	row vector with the $m$ observations making up Sample1 as components
y	row vector with the $n$ observations making up Sample2 as components

## Details

Notation:  $\pi_+$  stands for the Mann-Whitney functional defined by  $\pi_+ = P[X > Y]$ , with  $X \sim F \equiv$  cdf of Population 1 being independent of  $Y \sim G \equiv$  cdf of Population 2.

**Value**

alpha	significance level
m	size of Sample 1
n	size of Sample 2
eps1_	absolute value of the left-hand limit of the hypothetical equivalence range for $\pi_+ - 1/2$
eps2_	right-hand limit of the hypothetical equivalence range for $\pi_+ - 1/2$
W+	observed value of the $U$ -statistics estimator of $\pi_+$
SIGMAH	square root of the estimated asymptotic variance of $W_+$
CRIT	upper critical bound to $ W_+ - 1/2 - (\varepsilon'_2 - \varepsilon'_1)/2 /\hat{\sigma}$
REJ	indicator of a positive [=1] vs negative [=0] rejection decision to be taken with the data under analysis

**Author(s)**

Stefan Wellek <stefan.wellek@zi-mannheim.de>  
 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: A new approach to equivalence assessment in standard comparative bioavailability trials by means of the Mann-Whitney statistic. *Biometrical Journal* 38 (1996), 695-710.

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 6.2.

**Examples**

```
x <- c(10.3, 11.3, 2.0, -6.1, 6.2, 6.8, 3.7, -3.3, -3.6, -3.5, 13.7, 12.6)
y <- c(3.3, 17.7, 6.7, 11.1, -5.8, 6.9, 5.8, 3.0, 6.0, 3.5, 18.7, 9.6)
mawi(0.05, 12, 12, 0.1382, 0.2602, x, y)
```

---

 mcnasc\_ni

*Determination of a corrected nominal significance level for the asymptotic test for noninferiority in the McNemar setting*

---

**Description**

The program computes the largest nominal significance level which can be substituted for the target level  $\alpha$  without making the exact size of the asymptotic testing procedure larger than  $\alpha$ .

**Usage**

```
mcnasc_ni(alpha, n, del0, sw, tol, maxh)
```

**Arguments**

alpha	significance level
n	sample size
de10	absolute value of the noninferiority margin for $\delta := p_{10} - p_{01}$ , with $p_{10}$ and $p_{01}$ denoting the probabilities of discordant pairs of both kinds
sw	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
tol	upper bound to the absolute difference between size and target level below which the search for a corrected nominal level terminates
maxh	maximum number of interval halving steps to be carried out in finding the maximally raised nominal level

**Value**

alpha	significance level
n	sample size
de10	absolute value of the noninferiority margin for $\delta := p_{10} - p_{01}$ , with $p_{10}$ and $p_{01}$ denoting the probabilities of discordant pairs of both kinds
sw	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
ALPH_0	value of the corrected nominal level obtained after nh steps
SIZE_UNC	exact size of the rejection region of the test at uncorrected nominal level $\alpha$
SIZE0	exact size of the rejection region of the test at nominal level $\alpha_0$
NH	number of interval-halving steps actually performed

**Author(s)**

Stefan Wellek <stefan.wellek@zi-mannheim.de>  
 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 5.2.3.

**Examples**

```
mcnasc_ni(0.05, 50, 0.05, 0.05, 0.0001, 5)
```

---

mcnby_ni	<i>Bayesian test for noninferiority in the McNemar setting with the difference of proportions as the parameter of interest</i>
----------	--

---

### Description

The program determines through iteration the largest nominal level  $\alpha_0$  such that comparing the posterior probability of the alternative hypothesis  $K_1 : \delta > -\delta_0$  to the lower bound  $1 - \alpha_0$  generates a critical region whose size does not exceed the target significance level  $\alpha$ . In addition, exact values of the power against specific parameter configurations with  $\delta = 0$  are output.

### Usage

```
mcnby_ni(N,DEL0,K1,K2,K3,NSUB,SW,ALPHA,MAXH)
```

### Arguments

N	sample size
DEL0	noninferiority margin to the difference of the parameters of the marginal binomial distributions under comparison
K1	Parameter 1 of the Dirichlet prior for the family of trinomial distributions
K2	Parameter 2 of the Dirichlet prior for the family of trinomial distributions
K3	Parameter 3 of the Dirichlet prior for the family of trinomial distributions
NSUB	number of subintervals for partitioning the range of integration
SW	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
ALPHA	target significance level
MAXH	maximum number of interval halving steps to be carried out in finding the maximally raised nominal level

### Details

The program uses 96-point Gauss-Legendre quadrature on each of the NSUB intervals into which the range of integration is partitioned.

### Value

N	sample size
DEL0	noninferiority margin to the difference of the parameters of the marginal binomial distributions under comparison
K1	Parameter 1 of the Dirichlet prior for the family of trinomial distributions
K2	Parameter 2 of the Dirichlet prior for the family of trinomial distributions
K3	Parameter 3 of the Dirichlet prior for the family of trinomial distributions

NSUB	number of subintervals for partitioning the range of integration
SW	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
ALPHA	target significance level
MAXH	maximum number of interval halving steps to be carried out in finding the maximally raised nominal level
ALPHA0	result of the search for the largest admissible nominal level
SIZE0	size of the critical region corresponding to $\alpha_0$
SIZE_UNC	size of the critical region of test at uncorrected nominal level $\alpha$
POW	power against 7 different parameter configurations with $\delta = 0$

**Author(s)**

Stefan Wellek <stefan.wellek@zi-mannheim.de>  
 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 5.2.3.

**Examples**

```
mcnby_ni(25, .10, .5, .5, .5, 10, .05, .05, 5)
```

---

mcnby_ni_pp	<i>Computation of the posterior probability of the alternative hypothesis of noninferiority in the McNemar setting, given a specific point in the sample space</i>
-------------	--

---

**Description**

Evaluation of the integral on the right-hand side of Equation (5.24) on p. 88 of Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition.

**Usage**

```
mcnby_ni_pp(N, DEL0, N10, N01)
```

**Arguments**

N	sample size
DEL0	noninferiority margin to the difference of the parameters of the marginal binomial distributions under comparison
N10	count of pairs with $(X, Y) = (1, 0)$
N01	count of pairs with $(X, Y) = (0, 1)$

**Details**

The program uses 96-point Gauss-Legendre quadrature on each of 10 subintervals into which the range of integration is partitioned.

**Value**

N	sample size
DEL0	noninferiority margin to the difference of the parameters of the marginal binomial distributions under comparison
N10	count of pairs with $(X, Y) = (1, 0)$
N01	count of pairs with $(X, Y) = (0, 1)$
PPOST	posterior probability of the alternative hypothesis $K_1 : \delta > -\delta_0$ with respect to the noninformative prior determined according to Jeffrey's rule

**Note**

The program uses Equation (5.24) of Wellek S (2010) corrected for a typo in the middle line which must read

$$\int_{\delta_0}^{(1+\delta_0)/2} \left[ B(n_{01} + 1/2, n - n_{01} + 1) p_{01}^{n_{01}-1/2} (1 - p_{01})^{n-n_{01}} \right]$$

**Author(s)**

Stefan Wellek <stefan.wellek@zi-mannheim.de>  
 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 5.2.3.

**Examples**

```
mcnby_ni_pp(72, 0.05, 4, 5)
```

---

 mcnemasc

*Determination of a corrected nominal significance level for the asymptotic test for equivalence of two paired binomial proportions with respect to the difference of their expectations (McNemar setting)*

---

**Description**

The program computes the largest nominal significance level which can be substituted for the target level  $\alpha$  without making the exact size of the asymptotic testing procedure larger than  $\alpha$ .

**Usage**

```
mcnemasc(alpha,n,de10,sw,tol,maxh)
```

**Arguments**

alpha	significance level
n	sample size
de10	upper limit set to $ p_{10} - p_{01} $ under the alternative hypothesis of equivalence, with $p_{10}$ and $p_{01}$ denoting the probabilities of discordant pairs of both kinds
sw	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
tol	upper bound to the absolute difference between size and target level below which the search for a corrected nominal level terminates
maxh	maximum number of interval halving steps to be carried out in finding the maximally raised nominal level

**Value**

alpha	significance level
n	sample size
de10	upper limit set to $ p_{10} - p_{01} $ under the alternative hypothesis of equivalence, with $p_{10}$ and $p_{01}$ denoting the probabilities of discordant pairs of both kinds
sw	width of the search grid for determining the maximum of the rejection probability on the common boundary of the hypotheses
ALPH_0	value of the corrected nominal level obtained after nh steps
NH	number of interval-halving steps actually performed
ERROR	error indicator messaging "!!!!!" if the sufficient condition for the correctness of the result output by the program was found violated

**Author(s)**

Stefan Wellek <stefan.wellek@zi-mannheim.de>

Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 5.2.2.

**Examples**

```
mcnemasc(0.05,50,0.20,0.05,0.0005,5)
```

---

mcnempow	<i>Exact rejection probability of the asymptotic test for equivalence of two paired binomial proportions with respect to the difference of their expectations (McNemar setting)</i>
----------	---

---

### Description

The program computes exact values of the rejection probability of the asymptotic test for equivalence in the sense of  $-\delta_0 < p_{10} - p_{01} < \delta_0$ , at any nominal level  $\alpha$ . [The largest  $\alpha$  for which the test is valid in terms of the significance level, can be computed by means of the program mcnemasc.]

### Usage

```
mcnempow(alpha, n, del0, p10, p01)
```

### Arguments

alpha	nominal significance level
n	sample size
del0	upper limit set to $ \delta $ under the alternative hypothesis of equivalence
p10	true value of $P[X = 1, Y = 0]$
p01	true value of $P[X = 0, Y = 1]$

### Value

alpha	nominal significance level
n	sample size
del0	upper limit set to $ \delta $ under the alternative hypothesis of equivalence
p10	true value of $P[X = 1, Y = 0]$
p01	true value of $P[X = 0, Y = 1]$
POW	exact rejection probability of the asymptotic McNemar test for equivalence at nominal level $\alpha$
ERROR	error indicator messaging "!!!!!" if the sufficient condition for the correctness of the result output by the program was found violated

### Author(s)

Stefan Wellek <stefan.wellek@zi-mannheim.de>  
 Peter Ziegler <peter.ziegler@zi-mannheim.de>

### References

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, p.84.



**Examples**

```
mcnempow(0.024902, 50, 0.20, 0.30, 0.30)
```

---

mwtie\_fr

---

*Analogue of mwtie\_xy for settings with grouped data*


---

**Description**

Implementation of the asymptotically distribution-free test for equivalence of discrete distributions from which grouped data are obtained. Hypothesis formulation is in terms of the Mann-Whitney-Wilcoxon functional generalized to the case that ties between observations from different distributions may occur with positive probability. For details see Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition, p.155.

**Usage**

```
mwtie_fr(k, alpha, m, n, eps1_, eps2_, x, y)
```

**Arguments**

k	total number of grouped values which can be distinguished in the pooled sample
alpha	significance level
m	size of Sample 1
n	size of Sample 2
eps1_	absolute value of the left-hand limit of the hypothetical equivalence range for $\pi_+/(1 - \pi_0) - 1/2$
eps2_	right-hand limit of the hypothetical equivalence range for $\pi_+/(1 - \pi_0) - 1/2$
x	row vector with the $m$ observations making up Sample1 as components
y	row vector with the $n$ observations making up Sample2 as components

**Details**

Notation:  $\pi_+$  and  $\pi_0$  stands for the functional defined by  $\pi_+ = P[X > Y]$  and  $\pi_0 = P[X = Y]$ , respectively, with  $X \sim F \equiv$  cdf of Population 1 being independent of  $Y \sim G \equiv$  cdf of Population 2.

**Value**

alpha	significance level
m	size of Sample 1
n	size of Sample 2
eps1_	absolute value of the left-hand limit of the hypothetical equivalence range for $\pi_+/(1 - \pi_0) - 1/2$
eps2_	right-hand limit of the hypothetical equivalence range for $\pi_+/(1 - \pi_0) - 1/2$

WXY_TIE	observed value of the $U$ -statistics – based estimator of $\pi_+/(1 - \pi_0)$
SIGMAH	square root of the estimated asymptotic variance of $W_+/(1 - W_0)$
CRIT	upper critical bound to $ W_+/(1 - W_0) - 1/2 - (\varepsilon'_2 - \varepsilon'_1)/2 /\hat{\sigma}$
REJ	indicator of a positive [=1] vs negative [=0] rejection decision to be taken with the data under analysis

### Author(s)

Stefan Wellek <stefan.wellek@zi-mannheim.de>  
 Peter Ziegler <peter.ziegler@zi-mannheim.de>

### References

Wellek S, Hampel B: A distribution-free two-sample equivalence test allowing for tied observations. *Biometrical Journal* 41 (1999), 171-186.

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 6.4.

### Examples

```
x <- c(1,1,3,2,2,3,1,1,1,2,1,2,2,2,1,2,1,3,2,1,2,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,2,1,3,1,3,2,1,1,
  2,1,2,1,1,2,2,1,2,1,1,1,1,1,2,2,1,2,2,1,3,1,2,1,1,2,2,1,2,2,1,1,1,3,2,1,1,1,2,1,
  3,3,3,1,2,1,2,2,1,1,1,2,2,1,1,2,1,1,2,3,1,3,2,1,1,1,1,2,2,2,1,1,2,2,3,2,1,2,1,1,
  2,2,1,2,2,2,1,1,2,3,2,1,3,2,1,1,1,2,2,2,1,2,2,1,1,1,1,2,1,1,1,2,1,2,1,2,2,1,2,2,
  2,1,1,2,1,2,2,1,1,1,1,3,1,1,2,2,1,1,1,2,2,2,1,2,3,2,2,1,2,1,2,1,1,2,1,2,2,1,1,1,
  2,2,2,2)
y <- c(2,1,2,2,1,1,2,2,2,1,1,2,1,3,3,1,1,1,1,1,2,2,3,1,1,1,3,1,1,1,1,1,1,1,1,2,2,3,2,1,
  2,2,2,1,2,1,1,2,2,1,2,1,1,1,1,2,1,2,1,1,3,1,1,1,2,2,2,1,1,1,1,2,1,2,1,1,2,2,2,2,
  2,1,1,1,3,2,2,2,1,2,3,1,2,1,1,1,2,1,3,3,1,2,2,2,2,2,1,2,1,1,1,1,2,2,1,1,1,1,2,
  1,3,1,1,2,1,2,1,2,2,2,1,2,2,2,1,1,1,2,1,2,1,2,1,1,1,2,1,2,2,1,1,1,1,2,2,3,1,3,1,
  1,2,2,2,1,1,1,1,2,1,1,3,2,2,3,1,2,2,1,1,2,1,1,2,1,2,2,1,2,1,2,2,2,1,1,1,1,1,1,1,
  1,1,1,2,1,3,2,2,1,1,1,2,2,1,1,2,1,2,1,2,2,2,1,2,3,1,1,2,1,2,2,1,1,1,1,2,2,2,1,1,
  3,2,1,2,2,2,1,1,1,2,1,2,2,1,2,1,1,2)
```

mwtie\_fr(3,0.05,204,258,0.10,0.10,x,y)

---

mwtie\_xy

*Distribution-free two-sample equivalence test for tied data: test statistic and critical upper bound*

---

### Description

Implementation of the asymptotically distribution-free test for equivalence of discrete distributions in terms of the Mann-Whitney-Wilcoxon functional generalized to the case that ties between observations from different distributions may occur with positive probability. For details see Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition, § 6.4.

**Usage**

```
mwtie_xy(alpha,m,n,eps1_,eps2_,x,y)
```

**Arguments**

alpha	significance level
m	size of Sample 1
n	size of Sample 2
eps1_	absolute value of the left-hand limit of the hypothetical equivalence range for $\pi_+/(1 - \pi_0) - 1/2$
eps2_	right-hand limit of the hypothetical equivalence range for $\pi_+/(1 - \pi_0) - 1/2$
x	row vector with the $m$ observations making up Sample1 as components
y	row vector with the $n$ observations making up Sample2 as components

**Details**

Notation:  $\pi_+$  and  $\pi_0$  stands for the functional defined by  $\pi_+ = P[X > Y]$  and  $\pi_0 = P[X = Y]$ , respectively, with  $X \sim F \equiv$  cdf of Population 1 being independent of  $Y \sim G \equiv$  cdf of Population 2.

**Value**

alpha	significance level
m	size of Sample 1
n	size of Sample 2
eps1_	absolute value of the left-hand limit of the hypothetical equivalence range for $\pi_+/(1 - \pi_0) - 1/2$
eps2_	right-hand limit of the hypothetical equivalence range for $\pi_+/(1 - \pi_0) - 1/2$
WXY_TIE	observed value of the $U$ -statistics – based estimator of $\pi_+/(1 - \pi_0)$
SIGMAH	square root of the estimated asymptotic variance of $W_+/(1 - W_0)$
CRIT	upper critical bound to $ W_+/(1 - W_0) - 1/2 - (\varepsilon'_2 - \varepsilon'_1)/2 /\hat{\sigma}$
REJ	indicator of a positive [=1] vs negative [=0] rejection decision to be taken with the data under analysis

**Author(s)**

Stefan Wellek <stefan.wellek@zi-mannheim.de>  
 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

- Wellek S, Hampel B: A distribution-free two-sample equivalence test allowing for tied observations. *Biometrical Journal* 41 (1999), 171-186.
- Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 6.4.

**Examples**

```
x <- c(1,1,3,2,2,3,1,1,1,2)
y <- c(2,1,2,2,1,1,2,2,2,1,1,2)
mwte_xy(0.05,10,12,0.10,0.10,x,y)
```

---

 postmys

*Bayesian posterior probability of the alternative hypothesis in the setting of the one-sample t-test for equivalence*

---

**Description**

Evaluation of the integral appearing on the right-hand side of equation (3.6) on p. 38 of Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition

**Usage**

```
postmys(n,dq,sd,eps1,eps2,tol)
```

**Arguments**

n	sample size
dq	mean within-pair difference observed in the sample under analysis
sd	square root of the sample variance of the within-pair differences
eps1	absolute value of the left-hand limit of the hypothetical equivalence range for $\delta/\sigma_D$
eps2	right-hand limit of the hypothetical equivalence range for $\delta/\sigma_D$
tol	tolerance for the error induced through truncating the range of integration on the right

**Details**

The program uses 96-point Gauss-Legendre quadrature.

**Value**

n	sample size
dq	mean within-pair difference observed in the sample under analysis
sd	square root of the sample variance of the within-pair differences
eps1	absolute value of the left-hand limit of the hypothetical equivalence range for $\delta/\sigma_D$
eps2	right-hand limit of the hypothetical equivalence range for $\delta/\sigma_D$
tol	tolerance for the error induced through truncating the range of integration on the right
PPOST	posterior probability of the set of all $(\delta, \sigma_D)$ such that $-\varepsilon_1 < \delta/\sigma_D < \varepsilon_2$

**Author(s)**

Stefan Wellek <stefan.wellek@zi-mannheim.de>  
 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 3.2.

**Examples**

```
postmys(23, 0.16, 3.99, 0.5, 0.5, 1e-6)
```

---

powsign	<i>Nonconditional power of the UMPU sign test for equivalence and its nonrandomized counterpart</i>
---------	---

---

**Description**

The program computes for each possible value of the number  $n_0$  of zero observations the power conditional on  $N_0 = n_0$  and averages these conditional power values with respect to the distribution of  $N_0$ . Equivalence is defined in terms of the logarithm of the ratio  $p_+/p_-$ , where  $p_+$  and  $p_-$  denotes the probability of obtaining a positive and negative sign, respectively.

**Usage**

```
powsign(alpha, n, eps1, eps2, poa)
```

**Arguments**

alpha	significance level
n	sample size
eps1	absolute value of the lower limit of the hypothetical equivalence range for $\log(p_+/p_-)$ .
eps2	upper limit of the hypothetical equivalence range for $\log(p_+/p_-)$ .
poa	probability of a tie under the alternative of interest

**Value**

alpha	significance level
n	sample size
eps1	absolute value of the lower limit of the hypothetical equivalence range for $\log(p_+/p_-)$ .
eps2	upper limit of the hypothetical equivalence range for $\log(p_+/p_-)$ .
poa	probability of a tie under the alternative of interest
POWNONRD	power of the nonrandomized version of the test against the alternative $p_+ = p_- = (1 - p_o)/2$
POW	power of the randomized UMPU test against the alternative $p_+ = p_- = (1 - p_o)/2$

**Note**

A special case of the test whose power is computed by this program, is the exact conditional equivalence test for the McNemar setting (cf. Wellek 2010, pp. 76-77).

**Author(s)**

Stefan Wellek <stefan.wellek@zi-mannheim.de>

Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 5.1.

**Examples**

```
powsign(0.06580, 50, 0.847298, 0.847298, 0.26)
```

---

pow_abe	<i>Confidence interval inclusion test for average bioequivalence: exact power against an arbitrary specific alternative</i>
---------	---

---

**Description**

Evaluation of the integral on the right-hand side of equation (10.11) of p. 317 of Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition

**Usage**

```
pow_abe(m,n,alpha,delta_0,delta,sig)
```

**Arguments**

m	sample size in sequence group T(est)/R(eference)
n	sample size in sequence group R(eference)/T(est)
alpha	significance level
delta_0	equivalence margin to the absolute value of the log-ratio $\mu_T^*$ and $\mu_R^*$ of the formulation effects
delta	assumed true value of $ \log(\mu_T^*/\mu_R^*) $ , with $0 \leq \delta < \delta_0$
sig	theoretical standard deviation of the log within-subject bioavailability ratios in each sequence group

**Details**

The program uses 96-point Gauss-Legendre quadrature.

**Value**

m	sample size in sequence group T(est)/R(eference)
n	sample size in sequence group R(eference)/T(est)
alpha	significance level
del_0	equivalence margin to the absolute value of the log-ratio $\mu_T^*$ and $\mu_R^*$ of the formulation effects
del	assumed true value of $ \log(\mu_T^*/\mu_R^*) $ , with $0 \leq \delta < \delta_0$
POW_ABE	power of the interval inclusion test for average bioequivalence against the specific alternative given by $(\delta, \sigma)$

**Author(s)**

Stefan Wellek <stefan.wellek@zi-mannheim.de>  
 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 10.2.1.

**Examples**

```
pow_abe(12, 13, 0.05, log(1.25), log(1.25)/2, 0.175624)
```

---

po_pbibe	<i>Bayesian posterior probability of the alternative hypothesis of probability-based individual bioequivalence (PBIBE)</i>
----------	--

---

**Description**

Implementation of the algorithm presented in § 10.3.3 of Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition.

**Usage**

```
po_pbibe(n, eps, pio, zq, s, tol, sw, ihmax)
```

**Arguments**

n	sample size
eps	equivalence margin to an individual log-bioavailability ratio
pio	prespecified lower bound to the probability of obtaining an individual log-bioavailability ratio falling in the equivalence range $(-\varepsilon, \varepsilon)$
zq	mean log-bioavailability ratio observed in the sample under analysis
s	square root of the sample variance of the log-bioavailability ratios

tol	maximum numerical error allowed for transforming the hypothesis of PBIBE into a region in the parameter space of the log-normal distribution assumed to underlie the given sample of individual bioavailability ratios
sw	step width used in the numerical procedure yielding results at a level of accuracy specified by the value chosen for tol
ihmax	maximum number of interval halving steps to be carried out in finding the region specified in the parameter space according to the criterion of PBIBE

### Details

The program uses 96-point Gauss-Legendre quadrature.

### Value

n	sample size
eps	equivalence margin to an individual log-bioavailability ratio
pio	prespecified lower bound to the probability of obtaining an individual log-bioavailability ratio falling in the equivalence range $(-\varepsilon, \varepsilon)$
zq	mean log-bioavailability ratio observed in the sample under analysis
s	square root of the sample variance of the log-bioavailability ratios
tol	maximum numerical error allowed for transforming the hypothesis of PBIBE into a region in the parameter space of the log-normal distribution assumed to underlie the given sample of individual bioavailability ratios
sw	step width used in the numerical procedure yielding results at a level of accuracy specified by the value chosen for tol
ihmax	maximum number of interval halving steps to be carried out in finding the region specified in the parameter space according to the criterion of PBIBE
PO_PBIBE	posterior probability of the alternative hypothesis of PBIBE

### Author(s)

Stefan Wellek <stefan.wellek@zi-mannheim.de>  
Peter Ziegler <peter.ziegler@zi-mannheim.de>

### References

- Wellek S: Bayesian construction of an improved parametric test for probability-based individual bioequivalence. *Biometrical Journal* 42 (2000), 1039-52.
- Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 10.3.3.

### Examples

```
po_pbibe(20,0.25,0.75,0.17451,0.04169, 10e-10,0.01,100)
```



---

sgnrk	<i>Signed rank test for equivalence of an arbitrary continuous distribution of the intraindividual differences in terms of the probability of a positive sign of a Walsh average: test statistic and critical upper bound</i>
-------	---

---

## Description

Implementation of the paired-data analogue of the Mann-Whitney-Wilcoxon test for equivalence of continuous distributions. The continuity assumption relates to the intraindividual differences  $D_i$ . For details see Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition, § 5.4.

## Usage

```
sgnrk(alpha, n, qp1, qp2, d)
```

## Arguments

alpha	significance level
n	sample size
qp1	lower equivalence limit $q'_+$ to the target functional $q_+$
qp2	upper equivalence limit $q''_+$ to the target functional $q_+$
d	row vector with the intraindividual differences for all $n$ pairs as components

## Details

$q_+$  is the probability of getting a positive sign of the so-called Walsh-average of a pair of within-subject differences and can be viewed as a natural paired-observations analogue of the Mann-Whitney functional  $\pi_+ = P[X > Y]$ .

## Value

alpha	significance level
n	sample size
qp1	lower equivalence limit $q'_+$ to the target functional $q_+$
qp2	upper equivalence limit $q''_+$ to the target functional $q_+$
U_p1	observed value of the $U$ -statistics estimator of $q_+$
SIGMAH	square root of the estimated asymptotic variance of $U_+$
CRIT	upper critical bound to $ U_+ - (q'_+ + q''_+)/2 /\hat{\sigma}$
REJ	indicator of a positive [=1] vs negative [=0] rejection decision to be taken with the data under analysis

**Author(s)**

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**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 5.4.

**Examples**

```
d <- c(-0.5,0.333,0.667,1.333,1.5,-2.0,-1.0,-0.167,1.667,0.833,-2.167,-1.833,
      4.5,-7.5,2.667,3.333,-4.167,5.667,2.333,-2.5)
sgnrk(0.05,20,0.2398,0.7602,d)
```

---

 srktie\_d

*Generalized signed rank test for equivalence for tied data: test statistic and critical upper bound*

---

**Description**

Implementation of a generalized version of the signed-rank test for equivalence allowing for arbitrary patterns of ties between the within-subject differences. For details see Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition, § 5.5.

**Usage**

```
srktie_d(n,alpha,eps1,eps2,d)
```

**Arguments**

n	sample size
alpha	significance level
eps1	absolute value of the left-hand limit of the hypothetical equivalence range for $q_+/(1 - q_0) - 1/2$
eps2	right-hand limit of the hypothetical equivalence range for $q_+/(1 - q_0) - 1/2$
d	row vector with the intraindividual differences for all $n$ pairs as components

**Details**

Notation:  $q_+$  and  $q_0$  stands for the functional defined by  $q_+ = P[D_i + D_j > 0]$  and  $q_0 = P[D_i + D_j = 0]$ , respectively, with  $D_i$  and  $D_j$  as the intraindividual differences observed in two individuals independently selected from the underlying bivariate population.

**Value**

n	sample size
alpha	significance level
eps1	absolute value of the left-hand limit of the hypothetical equivalence range for $q_+/(1 - q_0) - 1/2$
eps2	right-hand limit of the hypothetical equivalence range for $q_+/(1 - q_0) - 1/2$
U_p1	observed value of the $U$ -statistics estimator of $q_+$
U_0	observed value of the $U$ -statistics estimator of $q_0$
UAS_PL	observed value of $U_+/(1 - U_0)$
TAUHAS	square root of the estimated asymptotic variance of $\sqrt{n}U_+/(1 - U_0)$
CRIT	upper critical bound to $\sqrt{n} U_+/(1 - U_0) - 1/2 - (\varepsilon_2 - \varepsilon_1)/2 /\hat{\tau}$
REJ	indicator of a positive [=1] vs negative [=0] rejection decision to be taken with the data under analysis

**Note**

The function srktie\_d can be viewed as the paired-data analogue of mwtie\_xy

**Author(s)**

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 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 5.5.

**Examples**

```
d <- c(0.8,0.2,0.0,-0.1,-0.3,0.3,-0.1,0.4,0.6,0.2,0.0,-0.2,-0.3,0.0,0.1,0.3,-0.3,
      0.1,-0.2,-0.5,0.2,-0.1,0.2,-0.1)
srktie_d(24,0.05,0.2602,0.2602,d)
```

---

 srktie\_m

*Analogue of srktie\_d for settings where the distribution of intraindividual differences is concentrated on a finite lattice*

---

**Description**

Analogue of the function srktie\_d tailored for settings where the distribution of the within-subject differences is concentrated on a finite lattice. For details see Wellek S (2010) Testing statistical hypotheses of equivalence and noninferiority. Second edition, pp.112-3.

**Usage**

```
srktie_m(n,alpha,eps1,eps2,w,d)
```

**Arguments**

n	sample size
alpha	significance level
eps1	absolute value of the left-hand limit of the hypothetical equivalence range for $q_+/(1 - q_0) - 1/2$
eps2	right-hand limit of the hypothetical equivalence range for $q_+/(1 - q_0) - 1/2$
w	span of the lattice in which the intraindividual differences take their values
d	row vector with the intraindividual differences for all $n$ pairs as components

**Details**

Notation:  $q_+$  and  $q_0$  stands for the functional defined by  $q_+ = P[D_i + D_j > 0]$  and  $q_0 = P[D_i + D_j = 0]$ , respectively, with  $D_i$  and  $D_j$  as the intraindividual differences observed in two individuals independently selected from the underlying bivariate population.

**Value**

n	sample size
alpha	significance level
eps1	absolute value of the left-hand limit of the hypothetical equivalence range for $q_+/(1 - q_0) - 1/2$
eps2	right-hand limit of the hypothetical equivalence range for $q_+/(1 - q_0) - 1/2$
w	span of the lattice in which the intraindividual differences take their values
U_p1	observed value of the $U$ -statistics estimator of $q_+$
U_0	observed value of the $U$ -statistics estimator of $q_0$
UAS_PL	observed value of $U_+/(1 - U_0)$
TAUHAS	square root of the estimated asymptotic variance of $\sqrt{n}U_+/(1 - U_0)$
CRIT	upper critical bound to $\sqrt{n} U_+/(1 - U_0) - 1/2 - (\varepsilon_2 - \varepsilon_1)/2 /\hat{\tau}$
REJ	indicator of a positive [=1] vs negative [=0] rejection decision to be taken with the data under analysis

**Author(s)**

Stefan Wellek <stefan.wellek@zi-mannheim.de>  
 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, pp. 112-114.

**Examples**

```
d <- c(0.8,0.2,0.0,-0.1,-0.3,0.3,-0.1,0.4,0.6,0.2,0.0,-0.2,-0.3,0.0,0.1,0.3,-0.3,
       0.1,-0.2,-0.5,0.2,-0.1,0.2,-0.1)
srktie_m(24,0.05,0.2602,0.2602,0.1,d)
```

---

tt1st	<i>Critical constants and power against the null alternative of the one-sample t-test for equivalence with an arbitrary, maybe nonsymmetric choice of the limits of the equivalence range</i>
-------	---

---

**Description**

The function computes the critical constants defining the uniformly most powerful invariant test for the problem  $\delta/\sigma_D \leq \theta_1$  or  $\delta/\sigma_D \geq \theta_2$  versus  $\theta_1 < \delta/\sigma_D < \theta_2$ , with  $(\theta_1, \theta_2)$  as a fixed nondegenerate interval on the real line. In addition, tt1st outputs the power against the null alternative  $\delta = 0$ .

**Usage**

```
tt1st(n,alpha,theta1,theta2,tol,itmax)
```

**Arguments**

n	sample size
alpha	significance level
theta1	lower equivalence limit to $\delta/\sigma_D$
theta2	upper equivalence limit to $\delta/\sigma_D$
tol	tolerable deviation from $\alpha$ of the rejection probability at either boundary of the hypothetical equivalence interval
itmax	maximum number of iteration steps

**Value**

n	sample size
alpha	significance level
theta1	lower equivalence limit to $\delta/\sigma_D$
theta2	upper equivalence limit to $\delta/\sigma_D$
IT	number of iteration steps performed until reaching the stopping criterion corresponding to TOL
C1	left-hand limit of the critical interval for the one-sample $t$ -statistic
C2	right-hand limit of the critical interval for the one-sample $t$ -statistic
ERR1	deviation of the rejection probability from $\alpha$ under $\delta/\sigma_D = \theta_1$
ERR2	deviation of the rejection probability from $\alpha$ under $\delta/\sigma_D = \theta_2$
POW0	power of the UMPI test against the alternative $\delta = 0$

**Note**

If the output value of ERR2 is NA, the deviation of the rejection probability at the right-hand boundary of the hypothetical equivalence interval from  $\alpha$  is smaller than the smallest real number representable in R.

**Author(s)**

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**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 5.3.

**Examples**

```
tt1st(36,0.05, -0.4716,0.3853,1e-10,50)
```

---

tt2st	<i>Critical constants and power against the null alternative of the two-sample t-test for equivalence with an arbitrary, maybe nonsymmetric choice of the limits of the equivalence range</i>
-------	---

---

**Description**

The function computes the critical constants defining the uniformly most powerful invariant test for the problem  $(\xi - \eta)/\sigma \leq -\varepsilon_1$  or  $(\xi - \eta)/\sigma \geq \varepsilon_2$  versus  $-\varepsilon_1 < (\xi - \eta)/\sigma < \varepsilon_2$ , with  $\xi$  and  $\eta$  denoting the expected values of two normal distributions with common variance  $\sigma^2$  from which independent samples are taken. In addition, tt2st outputs the power against the null alternative  $\xi = \eta$ .

**Usage**

```
tt2st(m,n,alpha,eps1,eps2,tol,itmax)
```

**Arguments**

m	size of the sample from $\mathcal{N}(\xi, \sigma^2)$
n	size of the sample from $\mathcal{N}(\eta, \sigma^2)$
alpha	significance level
eps1	absolute value of the lower equivalence limit to $(\xi - \eta)/\sigma$
eps2	upper equivalence limit to $(\xi - \eta)/\sigma$
tol	tolerable deviation from $\alpha$ of the rejection probability at either boundary of the hypothetical equivalence interval
itmax	maximum number of iteration steps

**Value**

m	size of the sample from $\mathcal{N}(\xi, \sigma^2)$
n	size of the sample from $\mathcal{N}(\eta, \sigma^2)$
alpha	significance level
eps1	absolute value of the lower equivalence limit to $(\xi - \eta)/\sigma$
eps2	upper equivalence limit to $(\xi - \eta)/\sigma$
IT	number of iteration steps performed until reaching the stopping criterion corresponding to TOL
C1	left-hand limit of the critical interval for the two-sample $t$ -statistic
C2	right-hand limit of the critical interval for the two-sample $t$ -statistic
ERR1	deviation of the rejection probability from $\alpha$ under $(\xi - \eta)/\sigma = -\varepsilon_1$
ERR2	deviation of the rejection probability from $\alpha$ under $(\xi - \eta)/\sigma = \varepsilon_2$
POW0	power of the UMPI test against the alternative $\xi = \eta$

**Note**

If the output value of ERR2 is NA, the deviation of the rejection probability at the right-hand boundary of the hypothetical equivalence interval from  $\alpha$  is smaller than the smallest real number representable in R.

**Author(s)**

Stefan Wellek <stefan.wellek@zi-mannheim.de>  
 Peter Ziegler <peter.ziegler@zi-mannheim.de>

**References**

Wellek S: Testing statistical hypotheses of equivalence and noninferiority. Second edition. Boca Raton: Chapman & Hall/CRC Press, 2010, § 6.1.

**Examples**

```
tt2st(12, 12, 0.05, 0.50, 1.00, 1e-10, 50)
```

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