

Package 'ratesci'

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Type Package

Title Confidence Intervals for Comparisons of Binomial or Poisson Rates

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Description Computes confidence intervals for the rate (or risk) difference ('RD') or rate ratio (or relative risk, 'RR') for binomial proportions or Poisson rates, or for odds ratio ('OR', binomial only). Also confidence intervals for a single binomial or Poisson rate, and intervals for matched pairs. Includes skewness-corrected asymptotic score ('SCAS') methods, which have been developed in Laud (2017) <[doi:10.1002/pst.1813](https://doi.org/10.1002/pst.1813)> from Miettinen & Nurminen (1985) <[doi:10.1002/sim.4780040211](https://doi.org/10.1002/sim.4780040211)> and Gart & Nam (1988) <[doi:10.2307/2531848](https://doi.org/10.2307/2531848)>. The same score produces hypothesis tests analogous to the test for binomial RD and RR by Farrington & Manning (1990) <[doi:10.1002/sim.4780091208](https://doi.org/10.1002/sim.4780091208)>, or the McNemar test for paired data. The package also includes MOVER methods (Method Of Variance Estimates Recovery) for all contrasts, derived from the Newcombe method but with options to use equal-tailed intervals in place of the Wilson score method, and generalised for Bayesian applications incorporating prior information. So-called 'exact' methods for strictly conservative coverage are approximated using continuity corrections, and the amount of correction can be selected to avoid over-conservative coverage. Also includes methods for stratified calculations (e.g. meta-analysis), either assuming fixed effects (matching the CMH test) or incorporating stratum heterogeneity.

Depends R (>= 3.6.0)

License GPL-3

Encoding UTF-8

RoxygenNote 7.3.2

Imports polynom

Suggests testthat

URL <https://github.com/petelaud/ratesci>

BugReports <https://github.com/petelaud/ratesci/issues>

NeedsCompilation no

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jeffreysci	<i>Jeffreys and other approximate Bayesian confidence intervals for a single binomial or Poisson rate.</i>
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Description

Generalised approximate Bayesian confidence intervals based on a Beta (for binomial rates) or Gamma (for Poisson rates) conjugate priors. Encompassing the Jeffreys method (with Beta(0.5, 0.5) or Gamma(0.5) respectively), as well as any user-specified prior distribution. Clopper-Pearson method (as quantiles of a Beta distribution as described in Brown et al. 2001) also included by way of a "continuity correction" parameter.

Usage

```
jeffreysci(
  x,
  n,
  ai = 0.5,
  bi = 0.5,
  cc = 0,
  level = 0.95,
```

```
distrib = "bin",
adj = TRUE,
...
)
```

Arguments

x	Numeric vector of number of events.
n	Numeric vector of sample sizes (for binomial rates) or exposure times (for Poisson rates).
ai, bi	Numbers defining the Beta prior distribution (default ai = bi = 0.5 for Jeffreys interval). Gamma prior for Poisson rates requires only ai.
cc	Number or logical specifying (amount of) "continuity correction". cc = 0 (default) gives Jeffreys interval, cc = 0.5 gives the Clopper-Pearson interval (or Garwood for Poisson). A value between 0 and 0.5 allows a compromise between proximate and conservative coverage.
level	Number specifying confidence level (between 0 and 1, default 0.95).
distrib	Character string indicating distribution assumed for the input data: "bin" = binomial (default), "poi" = Poisson.
adj	Logical (default TRUE) indicating whether to apply the boundary adjustment recommended on p108 of Brown et al. (set to FALSE if informative priors are used)
...	Other arguments.

Author(s)

Pete Laud, <p.j.laud@sheffield.ac.uk>

References

Laud PJ. Equal-tailed confidence intervals for comparison of rates. *Pharmaceutical Statistics* 2017; 16:334-348.

Brown LD, Cai TT, DasGupta A. Interval estimation for a binomial proportion. *Statistical Science* 2001; 16(2):101-133

Examples

```
# Jeffreys method:
jeffreysci(x = 5, n = 56)
```

moverbci

Approximate Bayesian ("MOVER-B") confidence intervals for comparisons of independent binomial or Poisson rates.

Description

Wrapper function for the MOVER-B methods. Approximate Bayesian confidence intervals for the rate (or risk) difference ("RD") or ratio ("RR") for independent binomial or Poisson rates, or for odds ratio ("OR", binomial only). (developed from Newcombe, Donner & Zou, Li et al, and Fagerland & Newcombe, and generalised as "MOVER-B" in forthcoming publication) including special case "MOVER-J" using non-informative priors with optional continuity correction. This function is vectorised in x1, x2, n1, and n2.

Usage

```
moverbci(
  x1,
  n1,
  x2,
  n2,
  a1 = 0.5,
  b1 = 0.5,
  a2 = 0.5,
  b2 = 0.5,
  distrib = "bin",
  contrast = "RD",
  level = 0.95,
  cc = 0,
  ...
)
```

Arguments

x1, x2	Numeric vectors of numbers of events in group 1 & group 2 respectively.
n1, n2	Numeric vectors of sample sizes (for binomial rates) or exposure times (for Poisson rates) in each group.
a1, b1, a2, b2	Numbers defining the Beta(ai,bi) prior distributions for each group (default ai = bi = 0.5 for Jeffreys uninformative priors). Gamma priors for Poisson rates require only a1, a2.
distrib	Character string indicating distribution assumed for the input data: "bin" = binomial (default), "poi" = Poisson.
contrast	Character string indicating the contrast of interest: "RD" = rate difference (default), "RR" = rate ratio, "OR" = odds ratio. contrast="p" gives an interval for the single proportion x1/n1.
level	Number specifying confidence level (between 0 and 1, default 0.95).

cc Number or logical specifying (amount of) continuity correction (default FALSE).
 Numeric value is taken as the gamma parameter in Laud 2017, Appendix S2 (de-
 fault 0.5 if cc = TRUE). Forced equal to 0.5 if type = "exact".

... Additional arguments.

Author(s)

Pete Laud, <p.j.laud@sheffield.ac.uk>

moverci *MOVER confidence intervals for comparisons of independent bino-
 mial or Poisson rates.*

Description

Confidence intervals applying the MOVER method ("Method of Variance Estimates Recovery", developed from the Newcombe method for binomial RD) across different contrasts (RD, RR, OR) and distributions (binomial, Poisson) using equal-tailed Jeffreys intervals instead of the Wilson score method for the event rates. Also allows more general Beta and Gamma priors for an approximate Bayesian confidence interval incorporating prior beliefs about the group event rates. This function is vectorised in x1, x2, n1, and n2.

Usage

```
moverci(
  x1,
  n1,
  x2 = NULL,
  n2 = NULL,
  a1 = 0.5,
  b1 = 0.5,
  a2 = 0.5,
  b2 = 0.5,
  cc = FALSE,
  level = 0.95,
  distrib = "bin",
  contrast = "RD",
  type = "jeff",
  adj = FALSE,
  ...
)
```

Arguments

x1, x2 Numeric vectors of numbers of events in group 1 & group 2 respectively.

n1, n2 Numeric vectors of sample sizes (for binomial rates) or exposure times (for Poisson rates) in each group.

a1, b1, a2, b2	Numbers defining the Beta(ai,bi) prior distributions for each group (default ai = bi = 0.5 for Jeffreys method). Gamma priors for Poisson rates require only a1, a2.
cc	Number or logical specifying (amount of) continuity correction (default FALSE). Numeric value is taken as the gamma parameter in Laud 2017, Appendix S2 (default 0.5 if cc = TRUE). Forced equal to 0.5 if type = "exact".
level	Number specifying confidence level (between 0 and 1, default 0.95).
distrib	Character string indicating distribution assumed for the input data: "bin" = binomial (default), "poi" = Poisson.
contrast	Character string indicating the contrast of interest: "RD" = rate difference (default), "RR" = rate ratio, "OR" = odds ratio. contrast="p" gives an interval for the single proportion $x1/n1$.
type	Character string indicating the method used for the intervals for the individual group rates. "jeff" = Jeffreys equal-tailed intervals (default); "exact" = Clopper-Pearson/Garwood exact intervals (note this does NOT result in a strictly conservative interval for the contrast, except for contrast = "p". The scoreci function with cc = TRUE is recommended as a superior approximation of 'exact' methods); "midp" = mid-p intervals; "SCAS" = SCAS non-iterative intervals; "wilson" = Wilson score intervals (as per Newcombe 1998). (Rao score is used for distrib = "poi") NB: "wilson" option is included only for legacy validation against previous published method by Newcombe. It is not recommended, as type = "jeff" or other equal-tailed options achieve much better coverage properties.
adj	Logical (default FALSE) indicating whether to apply the boundary adjustment for Jeffreys intervals recommended on p108 of Brown et al. (type = "jeff" only: set to FALSE if using informative priors)
...	Additional arguments.

Value

A matrix containing the confidence interval for the requested contrast

Author(s)

Pete Laud, <p.j.laud@sheffield.ac.uk>

References

- Laud PJ. Equal-tailed confidence intervals for comparison of rates. *Pharmaceutical Statistics* 2017; 16:334-348.
- Newcombe RG. Interval estimation for the difference between independent proportions: comparison of eleven methods. *Statistics in Medicine* 1998;
- Donner A, Zou G. Closed-form confidence intervals for functions of the normal mean and standard deviation. *Statistical Methods in Medical Research*
- Fagerland MW, Newcombe RG. Confidence intervals for odds ratio and relative risk based on the inverse hyperbolic sine transformation. *Statistics in Medicine* 2013; 32(16):2823-2836.

Li HQ, Tang ML, Wong WK. Confidence intervals for ratio of two Poisson rates using the method of variance estimates recovery. *Computational Statistics* 2014; 29(3-4):869-889.

Examples

```
# Binomial RD, MOVER-J method:
moverci(x1 = 5, n1 = 56, x2 = 0, n2 = 29)

# Binomial RD, Newcombe method:
moverci(x1 = 5, n1 = 56, x2 = 0, n2 = 29, type = "wilson")
```

pairbinci

Confidence intervals for comparisons of paired binomial rates.

Description

Confidence intervals for the rate (or risk) difference ('RD'), rate ratio ('RR') or odds ratio ('OR'), for paired binomial data. (For paired Poisson rates, suggest use the `tdasci` function with `distrib = "poi"`, and `weighting = "MH"`, with `pairs` as strata.) This function applies the score-based Tango and Tang methods for RD and RR respectively, with iterative and closed-form versions, as well as an experimental method using the stratified TDAS method with `pairs` as strata. Also includes MOVER options using the Method of Variance Estimates Recovery for paired RD and RR. For OR, intervals are produced based on transforming various intervals for the single proportion, including SCAS, mid-p and Jeffreys. All methods have options for continuity correction, and the magnitude of correction can be customised.

Usage

```
pairbinci(
  x,
  contrast = "RD",
  level = 0.95,
  cc = FALSE,
  cctype = "constant",
  method_RD = "Score_closed",
  method_RR = "Score_closed",
  method_OR = "SCAS",
  moverbase = "SCAS",
  theta0 = NULL,
  precis = 6
)
```

Arguments

x A numeric vector object specified as $c(a, b, c, d)$ where: a is the number of pairs with the event (e.g. success) under both conditions (e.g. treated/untreated, or case/control) b is the count of the number with the event on condition 1 only (= $n1$) c is the count of the number with the event on condition 2 only (= $n2$) d

	is the number of pairs with no event under both conditions (Note the order of a and d is only important for contrast="RR".)
contrast	Character string indicating the contrast of interest: "RD" = rate difference (default), "RR" = rate ratio, "OR" = odds ratio.
level	Number specifying confidence level (between 0 and 1, default 0.95).
cc	Number or logical (default FALSE) specifying (amount of) continuity correction. When a score-based method is used, cc = 0.5 corresponds to the continuity-corrected McNemar test.
cctype	Character string indicating the type of continuity correction ("constant" or "del-rocco") to be applied for contrast = "RR". (Note: both options produce non-equivariant intervals, an improved correction is currently under evaluation - watch this space.)
method_RD	Character string indicating the confidence interval method to be used for contrast = "RD". "Score" = iterative Tango asymptotic score, "Score_closed" = closed form solution for Tango interval (default), "MOVER" = hybrid MOVER method for paired RD (as per "method 8" in Newcombe, but with a choice of input methods - see moverbase), "MOVER_newc" = hybrid MOVER method with "correction" to correlation estimate (Newcombe's "method 10"), "TDAS" = t-distribution asymptotic score (experimental method, seems to struggle with low numbers).
method_RR	Character string indicating the confidence interval method to be used for contrast = "RR". "Score" = iterative Tang asymptotic score, "Score_closed" = closed form solution for Tang interval (default), "MOVER" = hybrid MOVER method for paired RR, "MOVER_newc" = hybrid MOVER method with "correction" to correlation estimate from Newcombe's RD method, "TDAS" = t-distribution asymptotic score (experimental method, seems to struggle with low numbers).
method_OR	Character string indicating the confidence interval method to be used for contrast = "OR", all of which are based on transformation of an interval for a single proportion $b/(b+c)$: "SCAS" = transformed skewness-corrected score (default), "jeff" = transformed Jeffreys, "midp" = transformed mid-p, "wilson" = transformed Wilson score - included for reference only, not recommended.
moverbase	Character string indicating the base method used as input for the MOVER methods (when method_RR or method_RD = "MOVER"): "wilson" = Wilson score (not recommended, known to be skewed), "jeff" = Jeffreys equal-tailed interval, "midp" = mid-p, "SCAS" = skewness-corrected score (default)
theta0	Number to be used in a one-sided significance test (e.g. non-inferiority margin). 1-sided p-value will be < 0.025 iff 2-sided 95% excludes theta0. NB: can also be used for a superiority test by setting theta0 = 0.
precis	Number (default 6) specifying precision (i.e. number of decimal places) to be used in optimisation subroutine for the confidence interval.

Value

A list containing the following components:

data the input data in 2x2 matrix form

estimates the requested contrast, with its confidence interval and the specified confidence level

pval the corresponding 2-sided significance test against the null hypothesis that $p_1 = p_2$ (McNemar's test), and one-sided significance tests against the null hypothesis that $\theta \geq$ or \leq θ_0 as specified

Author(s)

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References

Tango T. Equivalence test and confidence interval for the difference in proportions for the paired-sample design. *Statistics in Medicine* 1998; 17:891-908

Newcombe RG. Improved confidence intervals for the difference between binomial proportions based on paired data. *Statistics in Medicine* 1998; 17:2635-2650

Tango T. Improved confidence intervals for the difference between binomial proportions based on paired data by Robert G. Newcombe, *Statistics in Medicine*, 17, 2635-2650 (1998). *Statistics in Medicine* 1999; 18(24):3511-3513

Nam J-M, Blackwelder WC. Analysis of the ratio of marginal probabilities in a matched-pair setting. *Stat Med* 2002; 21(5):689-699

Tang N-S, Tang M-L, Chan ISF. On tests of equivalence via non-unity relative risk for matched-pair design. *Statistics in Medicine* 2003; 22:1217-1233

Agresti A, Min Y. Simple improved confidence intervals for comparing matched proportions. *Statistics in Medicine* 2005; 24:729-740

Tang M-L, Li H-Q, Tang N-S. Confidence interval construction for proportion ratio in paired studies based on hybrid method. *Statistical Methods in Medical Research* 2010; 21(4):361-378

Tang N-S et al. Asymptotic confidence interval construction for proportion difference in medical studies with bilateral data. *Statistical Methods in Medical Research*. 2011; 20(3):233-259

Yang Z, Sun X and Hardin JW. A non-iterative implementation of Tango's score confidence interval for a paired difference of proportions. *Statistics in Medicine* 2013; 32:1336-1342

Fagerland MW, Lydersen S, Laake P. Recommended tests and confidence intervals for paired binomial proportions. *Statistics in Medicine* 2014; 33(16):2850-2875

Laud PJ. Equal-tailed confidence intervals for comparison of rates. *Pharmaceutical Statistics* 2017; 16:334-348.

DelRocco N et al. New Confidence Intervals for Relative Risk of Two Correlated Proportions. *Statistics in Biosciences* 2023; 15:1-30

Chang P et al. Continuity corrected score confidence interval for the difference in proportions in paired data. *Journal of Applied Statistics* 2024; 51-1:139-152

Examples

```
# Data example from Agresti-Min 2005
pairbinci(x = c(53, 16, 8, 9), contrast = "RD", method_RD = "Score")
pairbinci(x = c(53, 16, 8, 9), contrast = "RD", method_RD = "TDAS")
pairbinci(x = c(53, 16, 8, 9), contrast = "RR", method_RR = "Score")
```

```

pairbinci(x = c(53, 16, 8, 9), contrast = "RR", method_RR = "TDAS")
pairbinci(x = c(53, 16, 8, 9), contrast = "OR", method_OR = "SCAS")
# Example from Fagerland et al 2014
pairbinci(x = c(1, 1, 7, 12), contrast = "RD", method_RD = "Score_closed")
pairbinci(x = c(1, 1, 7, 12), contrast = "RD", method_RD = "MOVER_newc", moverbase = "wilson")
pairbinci(x = c(1, 1, 7, 12), contrast = "RD", method_RD = "MOVER_newc", moverbase = "SCAS")
pairbinci(x = c(1, 1, 7, 12), contrast = "RR", method_RR = "Score_closed")
pairbinci(x = c(1, 1, 7, 12), contrast = "RR", method_RR = "MOVER_newc", moverbase = "wilson")
pairbinci(x = c(1, 1, 7, 12), contrast = "RR", method_RR = "MOVER_newc", moverbase = "SCAS")
pairbinci(x = c(1, 1, 7, 12), contrast = "OR", method_OR = "wilson")
pairbinci(x = c(1, 1, 7, 12), contrast = "OR", method_OR = "midp")
pairbinci(x = c(1, 1, 7, 12), contrast = "OR", method_OR = "SCAS")

```

rateci

Selected confidence intervals for the single binomial or Poisson rate.

Description

Confidence intervals for the single binomial or Poisson rate. Including SCAS or Jeffreys intervals, with or without continuity correction, and 'exact' Clopper-Pearson/Garwood or mid-p intervals. This function is vectorised in x, n.

Usage

```
rateci(x, n, distrib = "bin", level = 0.95, cc = FALSE, precis = 6)
```

Arguments

x	Numeric vector of number of events.
n	Numeric vector of sample size (for binomial rate) or exposure times (for Poisson rate).
distrib	Character string indicating distribution assumed for the input data: "bin" = binomial (default), "poi" = Poisson.
level	Number specifying confidence level (between 0 and 1, default 0.95).
cc	Number or logical (default FALSE) specifying continuity correction.
precis	Number (default 6) specifying precision (i.e. number of decimal places) to be used in optimisation subroutine for the SCAS and exact methods.

Value

A list containing, for each method, a matrix containing lower and upper confidence limits for each value of x and n. Methods shown depend on the cc parameter, which specifies whether the continuity correction is applied to the SCAS and Jeffreys methods. The corresponding 'exact' method is Clopper-Pearson/Garwood if cc == TRUE and mid-p if cc == FALSE.

Author(s)

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scasci	<i>Skewness-corrected asymptotic score ("SCAS") confidence intervals for comparisons of independent binomial or Poisson rates.</i>
--------	--

Description

Wrapper function for the SCAS method. Score-based confidence intervals for the rate (or risk) difference ("RD") or ratio ("RR") for independent binomial or Poisson rates, or for odds ratio ("OR", binomial only), or the single rate ("p"). (This is the "GNbc" method from Laud & Dane, developed from Gart & Nam, and generalised as "SCAS" in Laud 2017) including optional continuity correction. This function is vectorised in x1, x2, n1, and n2. Vector inputs may also be combined into a single stratified analysis (e.g. meta-analysis). This method assumes the contrast is constant across strata (fixed effects). For a 'random-effects' method use tdasci (or scoreci with random = TRUE).

Usage

```
scasci(
  x1,
  n1,
  x2 = NULL,
  n2 = NULL,
  distrib = "bin",
  contrast = "RD",
  level = 0.95,
  cc = FALSE,
  theta0 = NULL,
  precis = 6,
  plot = FALSE,
  hetplot = FALSE,
  xlim = NULL,
  ylim = NULL,
  plotmax = 100,
  stratified = FALSE,
  weighting = NULL,
  MNTol = 1e-08,
  wt = NULL,
  warn = TRUE,
  ...
)
```

Arguments

x1, x2	Numeric vectors of numbers of events in group 1 & group 2 respectively.
n1, n2	Numeric vectors of sample sizes (for binomial rates) or exposure times (for Poisson rates) in each group.
distrib	Character string indicating distribution assumed for the input data: "bin" = binomial (default), "poi" = Poisson.

contrast	Character string indicating the contrast of interest: "RD" = rate difference (default), "RR" = rate ratio, "OR" = odds ratio. contrast="p" gives an interval for the single proportion or rate $x1/n1$.
level	Number specifying confidence level (between 0 and 1, default 0.95).
cc	Number or logical (default FALSE) specifying (amount of) continuity correction. Numeric value is taken as the gamma parameter in Laud 2017, Appendix S2 (default 0.5 for 'conventional' correction if cc = TRUE). IMPORTANT NOTES: <ol style="list-style-type: none"> 1. This is a 'continuity correction' aimed at approximating strictly conservative coverage, NOT for dealing with zero cell counts. Such 'sparse data adjustments' are not needed in the score method, except to deal with double-zero cells for RD (& double-100% cells for binomial RD & RR) with IVS/INV weights. 2. The continuity corrections provided here have not been fully tested for stratified methods, but are found to match the Mantel-Haenszel corrected test, when cc = 0.5 for any of the binomial contrasts. Flexibility is included for a less conservative correction, such as cc = 0.25 suggested in Laud 2017 (see Appendix S3.4), or cc = 3/16 = 0.1875 in Mehrotra & Railkar (2000)
theta0	Number to be used in a one-sided significance test (e.g. non-inferiority margin). 1-sided p-value will be <0.025 iff 2-sided 95\ excludes theta0. By default, a two-sided test against theta0 = 0 (for RD) or 1 (for RR/OR) is also output.
precis	Number (default 6) specifying precision (i.e. number of decimal places) to be used in optimisation subroutine for the confidence interval.
plot	Logical (default FALSE) indicating whether to output plot of the score function
hetplot	Logical (default FALSE) indicating whether to output plots for evaluating heterogeneity of stratified datasets.
xlim	pair of values indicating range of values to be plotted.
ylim	pair of values indicating range of values to be plotted.
plotmax	Numeric value indicating maximum value to be displayed on x-axis of plots (useful for ratio contrasts which can be infinite).
stratified	Logical (default FALSE) indicating whether to combine vector inputs into a single stratified analysis. IMPORTANT NOTE: The mechanism for stratified calculations is enabled for contrast = "p", but the performance of the resulting intervals has not been fully evaluated.
weighting	String indicating which weighting method to use if stratified = "TRUE": "IVS" = Inverse Variance of Score (see Laud 2017 for details), "INV" = Inverse Variance (bcf omitted, default for contrast = "OR"), "MH" = Mantel-Haenszel (default for contrast = "RD" or "RR"), "MN" = Miettinen-Nurminen weights. (similar to MH for contrast = "RD" or "RR", similar to INV for contrast = "OR") For CI consistent with a CMH test, select skew = FALSE, random = FALSE, and use default MH weighting for RD/RR and INV for OR. Weighting = 'MN' also matches the CMH test.
MNtol	Numeric value indicating convergence tolerance to be used in iteration with weighting = "MN".
wt	Numeric vector containing (optional) user-specified weights.
warn	Logical (default TRUE) giving the option to suppress warnings.
...	Other arguments.

Value

A list containing the following components:

estimates a matrix containing estimates of the rates in each group and of the requested contrast, with its confidence interval

pval a matrix containing details of the corresponding 2-sided significance test against the null hypothesis that $p_1 = p_2$, and one-sided significance tests against the null hypothesis that $\theta \geq$ or \leq θ_0

call details of the function call

If stratified = TRUE, the following outputs are added:

Qtest a vector of values describing and testing heterogeneity

weighting a string indicating the selected weighting method

stratdata a matrix containing stratum estimates and weights

Author(s)

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References

Laud PJ. Equal-tailed confidence intervals for comparison of rates. *Pharmaceutical Statistics* 2017; 16:334-348.

Laud PJ. Corrigendum: Equal-tailed confidence intervals for comparison of rates. *Pharmaceutical Statistics* 2018; 17:290-293.

scaspci	<i>Skewness-corrected asymptotic score ("SCAS") confidence intervals for single binomial or Poisson rate using closed-form calculations. This function is vectorised in x, n.</i>
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Description

Skewness-corrected asymptotic score ("SCAS") confidence intervals for single binomial or Poisson rate using closed-form calculations. This function is vectorised in x, n.

Usage

```
scaspci(x, n, distrib = "bin", level = 0.95, cc = FALSE, ...)
```

Arguments

x	Numeric vector of number of events.
n	Numeric vector of sample sizes (for binomial rates) or exposure times (for Poisson rates).
distrib	Character string indicating distribution assumed for the input data: "bin" = binomial (default), "poi" = Poisson.
level	Number specifying confidence level (between 0 and 1, default 0.95).
cc	Number or logical (default FALSE) specifying (amount of) continuity correction. Numeric value is taken as the gamma parameter in Laud 2017, Appendix S2 (default 0.5 for 'conventional' correction if cc = TRUE).
...	Other arguments.

Author(s)

Pete Laud, <p.j.laud@sheffield.ac.uk>

scoreci	<i>Score confidence intervals for comparisons of independent binomial or Poisson rates.</i>
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Description

Score-based confidence intervals for the rate (or risk) difference ("RD") or ratio ("RR") for independent binomial or Poisson rates, or for odds ratio ("OR", binomial only). Including options for bias correction (from Miettinen & Nurminen), skewness correction ("GNbc" method from Laud & Dane, developed from Gart & Nam, and generalised as "SCAS" in Laud 2017) and continuity correction (for strictly conservative coverage). Also includes score intervals for a single binomial proportion or Poisson rate. Based on the Wilson score interval, when corrected for skewness, coverage is almost identical to the mid-p method, or Clopper-Pearson when also continuity-corrected. Hypothesis tests for superiority or non-inferiority are provided using the same score, to ensure consistency between test and CI. This function is vectorised in x1, x2, n1, and n2. Vector inputs may also be combined into a single stratified analysis (e.g. meta-analysis), either using fixed effects, or the more general random effects "TDAS" method, which incorporates stratum variability using a t-distribution score (inspired by Hartung-Knapp-Sidik-Jonkman). For fixed-effects analysis of stratified datasets, with weighting = "MH" for RD or RR, or weighting = "INV" for OR, omitting the skewness correction produces the CMH test, together with a coherent confidence interval for the required contrast.

Usage

```
scoreci(
  x1,
  n1,
  x2 = NULL,
  n2 = NULL,
  distrib = "bin",
```

```

contrast = "RD",
level = 0.95,
skew = TRUE,
simpleskew = FALSE,
ORbias = TRUE,
RRtang = NULL,
bcf = TRUE,
cc = FALSE,
theta0 = NULL,
precis = 6,
plot = FALSE,
plotmax = 100,
hetplot = FALSE,
xlim = NULL,
ylim = NULL,
stratified = FALSE,
weighting = NULL,
MNtol = 1e-08,
wt = NULL,
sda = NULL,
fda = NULL,
dropzeros = FALSE,
tdas = NULL,
random = FALSE,
prediction = FALSE,
warn = TRUE,
...
)

```

Arguments

x1, x2	Numeric vectors of numbers of events in group 1 & group 2 respectively.
n1, n2	Numeric vectors of sample sizes (for binomial rates) or exposure times (for Poisson rates) in each group.
distrib	Character string indicating distribution assumed for the input data: "bin" = binomial (default), "poi" = Poisson.
contrast	Character string indicating the contrast of interest: "RD" = rate difference (default), "RR" = rate ratio, "OR" = odds ratio. contrast="p" gives an interval for the single proportion or rate $x1/n1$.
level	Number specifying confidence level (between 0 and 1, default 0.95).
skew	Logical (default TRUE) indicating whether to apply skewness correction (for the SCAS method recommended in Laud 2017) or not (for the Miettinen-Nurminen method).
simpleskew	Logical (default FALSE) indicating whether to use the "simplified" skewness correction instead of the quadratic solution. See Laud 2021 for details. NOTE: this version of the score is only suitable for obtaining confidence limits, not p-values.

ORbias	Logical (default is TRUE for contrast="OR", otherwise NULL) indicating whether to apply additional bias correction for OR derived from Gart 1985. (Corrigendum to Laud 2017, published May 2018). Only applies if contrast is "OR".
RRtang	Logical indicating whether to use Tang's score for RR: $S_{\theta} = (\hat{p}_1 - \hat{p}_2 * \theta) / \hat{p}_2 d$ (see Tang 2020). Default TRUE for stratified = TRUE, with weighting = "IVS" or "INV". Forced to FALSE for stratified = TRUE, with other weightings. Experimental for distrib = "poi".
bcf	Logical (default TRUE) indicating whether to apply bias correction in the score denominator. Applicable to distrib = "bin" only. (NB: bcf = FALSE option is really only included for legacy validation against previous published methods (i.e. Gart & Nam, Mee, or standard Chi-squared test). Ignored for contrast = "p".
cc	Number or logical (default FALSE) specifying (amount of) continuity correction. Numeric value is taken as the gamma parameter in Laud 2017, Appendix S2 (default 0.5 for 'conventional' correction if cc = TRUE). IMPORTANT NOTES: <ol style="list-style-type: none"> 1. This is a 'continuity correction' aimed at approximating strictly conservative coverage, NOT for dealing with zero cell counts. Such 'sparse data adjustments' are not needed in the score method, except to deal with double-zero cells for RD (& double-100% cells for binomial RD & RR) with IVS/INV weights. 2. The continuity corrections provided here have not been fully tested for stratified methods, but are found to match the Mantel-Haenszel corrected test, when cc = 0.5 for any of the binomial contrasts. Flexibility is included for a less conservative correction, such as cc = 0.25 suggested in Laud 2017 (see Appendix S3.4), or cc = 3/16 = 0.1875 in Mehrotra & Railkar (2000)
theta0	Number to be used in a one-sided significance test (e.g. non-inferiority margin). 1-sided p-value will be <0.025 iff 2-sided 95\ excludes theta0. (If bcf = FALSE and skew = FALSE this gives a Farrington-Manning test.) By default, a two-sided test against theta0 = 0 (for RD) or 1 (for RR/OR) is also output: <ul style="list-style-type: none"> • If bcf = FALSE and skew = FALSE this is the same as K. Pearson's Chi-squared test in the single stratum case. • bcf = TRUE gives E. Pearson's 'N-1' Chi-squared test for a single stratum, (Recommended by Campbell 2007: https://doi.org/10.1002/sim.2832) and (with default weighting and random = FALSE) the CMH test for stratified tables. • Default bcf = TRUE and skew = TRUE produces a skewness-corrected version of the 'N-1' Chi-squared test or CMH.
precis	Number (default 6) specifying precision (i.e. number of decimal places) to be used in optimisation subroutine for the confidence interval.
plot	Logical (default FALSE) indicating whether to output plot of the score function
plotmax	Numeric value indicating maximum value to be displayed on x-axis of plots (useful for ratio contrasts which can be infinite).
hetplot	Logical (default FALSE) indicating whether to output plots for evaluating heterogeneity of stratified datasets.
xlim	pair of values indicating range of values to be plotted.

<code>ylim</code>	pair of values indicating range of values to be plotted.
<code>stratified</code>	Logical (default FALSE) indicating whether to combine vector inputs into a single stratified analysis. IMPORTANT NOTE: The mechanism for stratified calculations is enabled for contrast = "p", but the performance of the resulting intervals has not been fully evaluated.
<code>weighting</code>	String indicating which weighting method to use if stratified = "TRUE": "IVS" = Inverse Variance of Score (see Laud 2017 for details), "INV" = Inverse Variance (bcf omitted, default for contrast = "OR"), "MH" = Mantel-Haenszel (default for contrast = "RD" or "RR"), "MN" = Miettinen-Nurminen weights. (similar to MH for contrast = "RD" or "RR", similar to INV for contrast = "OR") For CI consistent with a CMH test, select skew = FALSE, random = FALSE, and use default MH weighting for RD/RR and INV for OR. Weighting = 'MN' also matches the CMH test.
<code>MNtol</code>	Numeric value indicating convergence tolerance to be used in iteration with weighting = "MN".
<code>wt</code>	Numeric vector containing (optional) user-specified weights.
<code>sda</code>	Sparse data adjustment to avoid zero variance when $x_1 + x_2 = 0$: Only applied when stratified = TRUE. Default 0.5 for RD with IVS/INV weights. Not required for RR/OR, default is to remove double-zero strata instead.
<code>fda</code>	Full data adjustment to avoid zero variance when $x_1 + x_2 = n_1 + n_2$: Only applied when stratified = TRUE. Default 0.5 for RD & RR with IVS/INV weights. Not required for OR, default is to remove affected strata.
<code>dropzeros</code>	Logical (default FALSE) indicating whether to drop uninformative strata for RR/OR (i.e. strata with $x_1 = 0$ and $x_2 = 0$), even when the choice of weights would allow them to be retained for a fixed effects analysis. Has no effect on estimates, just the heterogeneity test.
<code>tdas</code>	(deprecated: parameter renamed to random)
<code>random</code>	Logical (default FALSE) indicating whether to perform random effects meta-analysis for stratified data, using the t-distribution (TDAS) method for stratified data (defined in Laud 2017). NOTE: If random = TRUE, then skew = TRUE only affects the per-stratum estimates.
<code>prediction</code>	Logical (default FALSE) indicating whether to produce a prediction interval (work in progress).
<code>warn</code>	Logical (default TRUE) giving the option to suppress warnings.
<code>...</code>	Other arguments.

Value

A list containing the following components:

estimates a matrix containing estimates of the rates in each group and of the requested contrast, with its confidence interval

pval a matrix containing details of the corresponding 2-sided significance test against the null hypothesis that $p_1 = p_2$, and one-sided significance tests against the null hypothesis that $\theta \geq$ or \leq θ_0

call details of the function call

If stratified = TRUE, the following outputs are added:

Qtest a vector of values describing and testing heterogeneity

weighting a string indicating the selected weighting method

stratdata a matrix containing stratum estimates and weights

Author(s)

Pete Laud, <p.j.laud@sheffield.ac.uk>

References

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Gart JJ. Analysis of the common odds ratio: corrections for bias and skewness. *Bulletin of the International Statistical Institute* 1985, 45th session, book 1, 175-176.

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Gart JJ, Nam Jm. Approximate interval estimation of the difference in binomial parameters: correction for skewness and extension to multiple tables. *Biometrics* 1990; 46(3):637-643.

Tang Y. Score confidence intervals and sample sizes for stratified comparisons of binomial proportions. *Statistics in Medicine* 2020; 39:3427-3457.

Examples

```
# Binomial RD, SCAS method:
scoreci(
  x1 = c(12, 19, 5), n1 = c(16, 29, 56),
  x2 = c(1, 22, 0), n2 = c(16, 30, 29)
)

# Binomial RD, MN method:
scoreci(
  x1 = c(12, 19, 5), n1 = c(16, 29, 56),
  x2 = c(1, 22, 0), n2 = c(16, 30, 29), skew = FALSE
)
```

```

# Poisson RR, SCAS method:
scoreci(x1 = 5, n1 = 56, x2 = 0, n2 = 29, distrib = "poi", contrast = "RR")

# Poisson RR, MN method:
scoreci(
  x1 = 5, n1 = 56, x2 = 0, n2 = 29, distrib = "poi",
  contrast = "RR", skew = FALSE
)

# Binomial rate, SCAS method:
scoreci(x1 = c(5, 0), n1 = c(56, 29), contrast = "p")

# Binomial rate, Wilson score method:
scoreci(x1 = c(5, 0), n1 = c(56, 29), contrast = "p", skew = FALSE)

# Poisson rate, SCAS method:
scoreci(x1 = c(5, 0), n1 = c(56, 29), distrib = "poi", contrast = "p")

# Stratified example, using data from Hartung & Knapp:
scoreci(
  x1 = c(15, 12, 29, 42, 14, 44, 14, 29, 10, 17, 38, 19, 21),
  x2 = c(9, 1, 18, 31, 6, 17, 7, 23, 3, 6, 12, 22, 19),
  n1 = c(16, 16, 34, 56, 22, 54, 17, 58, 14, 26, 44, 29, 38),
  n2 = c(16, 16, 34, 56, 22, 55, 15, 58, 15, 27, 45, 30, 38),
  stratified = TRUE
)

# TDAS example, using data from Hartung & Knapp:
scoreci(
  x1 = c(15, 12, 29, 42, 14, 44, 14, 29, 10, 17, 38, 19, 21),
  x2 = c(9, 1, 18, 31, 6, 17, 7, 23, 3, 6, 12, 22, 19),
  n1 = c(16, 16, 34, 56, 22, 54, 17, 58, 14, 26, 44, 29, 38),
  n2 = c(16, 16, 34, 56, 22, 55, 15, 58, 15, 27, 45, 30, 38),
  stratified = TRUE, random = TRUE
)

# Stratified example, with extremely rare instance of non-calculable skewness
# correction seen on plot of score function:
scoreci(
  x1 = c(1, 16), n1 = c(20, 40), x2 = c(0, 139), n2 = c(80, 160),
  contrast = "RD", skew = TRUE, simpleskew = FALSE,
  distrib = "bin", stratified = TRUE, plot = TRUE, weighting = "IVS"
)

```

Description

Wrapper function for the TDAS method. Score-based stratified confidence intervals for the rate (or risk) difference ("RD") or ratio ("RR") for independent binomial or Poisson rates, or for odds ratio ("OR", binomial only), or for prevalence or incidence rate ("p"). This function combines vector inputs into a single stratified random effects analysis (e.g. meta-analysis), incorporating any stratum variability into the confidence interval.

Usage

```
tdasci(
  x1,
  n1,
  x2 = NULL,
  n2 = NULL,
  distrib = "bin",
  contrast = "RD",
  level = 0.95,
  cc = FALSE,
  theta0 = NULL,
  precis = 6,
  plot = FALSE,
  hetplot = FALSE,
  plotmax = 100,
  xlim = NULL,
  ylim = NULL,
  weighting = NULL,
  MNtol = 1e-08,
  wt = NULL,
  skew = TRUE,
  prediction = FALSE,
  warn = TRUE,
  ...
)
```

Arguments

x1, x2	Numeric vectors of numbers of events in group 1 & group 2 respectively.
n1, n2	Numeric vectors of sample sizes (for binomial rates) or exposure times (for Poisson rates) in each group.
distrib	Character string indicating distribution assumed for the input data: "bin" = binomial (default), "poi" = Poisson.
contrast	Character string indicating the contrast of interest: "RD" = rate difference (default), "RR" = rate ratio, "OR" = odds ratio. contrast="p" gives an interval for the single proportion or rate $x1/n1$.
level	Number specifying confidence level (between 0 and 1, default 0.95).
cc	Number or logical (default FALSE) specifying (amount of) continuity correction. Numeric value is taken as the gamma parameter in Laud 2017, Appendix S2 (default 0.5 for 'conventional' correction if cc = TRUE). IMPORTANT NOTES:

1. This is a 'continuity correction' aimed at approximating strictly conservative coverage, NOT for dealing with zero cell counts. Such 'sparse data adjustments' are not needed in the score method, except to deal with double-zero cells for RD (& double-100% cells for binomial RD & RR) with IVS/INV weights.
2. The continuity corrections provided here have not been fully tested for stratified methods, but are found to match the Mantel-Haenszel corrected test, when $cc = 0.5$ for any of the binomial contrasts. Flexibility is included for a less conservative correction, such as $cc = 0.25$ suggested in Laud 2017 (see Appendix S3.4), or $cc = 3/16 = 0.1875$ in Mehrotra & Railkar (2000)

theta0	Number to be used in a one-sided significance test (e.g. non-inferiority margin). 1-sided p-value will be <0.025 iff 2-sided 95\ excludes theta0. By default, a two-sided test against $\theta_0 = 0$ (for RD) or 1 (for RR/OR) is also output.
precis	Number (default 6) specifying precision (i.e. number of decimal places) to be used in optimisation subroutine for the confidence interval.
plot	Logical (default FALSE) indicating whether to output plot of the score function
hetplot	Logical (default FALSE) indicating whether to output plots for evaluating heterogeneity of stratified datasets.
plotmax	Numeric value indicating maximum value to be displayed on x-axis of plots (useful for ratio contrasts which can be infinite).
xlim	pair of values indicating range of values to be plotted.
ylim	pair of values indicating range of values to be plotted.
weighting	String indicating which weighting method to use if stratified = "TRUE": "IVS" = Inverse Variance of Score (see Laud 2017 for details), "INV" = Inverse Variance (bcf omitted, default for contrast = "OR"), "MH" = Mantel-Haenszel (default for contrast = "RD" or "RR"), "MN" = Miettinen-Nurminen weights. (similar to MH for contrast = "RD" or "RR", similar to INV for contrast = "OR") For CI consistent with a CMH test, select skew = FALSE, random = FALSE, and use default MH weighting for RD/RR and INV for OR. Weighting = 'MN' also matches the CMH test.
MNtol	Numeric value indicating convergence tolerance to be used in iteration with weighting = "MN".
wt	Numeric vector containing (optional) user-specified weights.
skew	Logical (default TRUE) indicating whether to apply skewness correction (for the SCAS method recommended in Laud 2017) or not (for the Miettinen-Nurminen method) to the per-stratum estimates provided in the output. Has no effect on the TDAS interval itself.
prediction	Logical (default FALSE) indicating whether to produce a prediction interval (work in progress).
warn	Logical (default TRUE) giving the option to suppress warnings.
...	Other arguments.

Value

A list containing the following components:

estimates a matrix containing estimates of the rates in each group and of the requested contrast, with its confidence interval

pval a matrix containing details of the corresponding 2-sided significance test against the null hypothesis that $p_1 = p_2$, and one-sided significance tests against the null hypothesis that $\theta \geq$ or $\leq \theta_0$

Qtest a vector of values describing and testing heterogeneity

weighting a string indicating the selected weighting method

stratdata a matrix containing stratum estimates and weights

call details of the function call

Author(s)

Pete Laud, <p.j.laud@sheffield.ac.uk>

References

Laud PJ. Equal-tailed confidence intervals for comparison of rates. *Pharmaceutical Statistics* 2017; 16:334-348.

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